(19)中華民國智慧財產局
(12)發明說明書公開本 (11)公開編號：TW 201141507 A1
(43)公開日： 中華民國 100 (2011) 年 12 月 01 日

(21)申請案號：100105575 (22)申請日： 中華民國 100 (2011) 年 02 月 18 日
(51)Int. Cl.： *A61K38/16 (2006.01)* *A61K39/44 (2006.01)*
A61P25/28 (2006.01) *A61P37/00 (2006.01)*
A61P9/00 (2006.01) *A61P17/06 (2006.01)*
(30)優先權：2010/02/18 美國 61/305,706
2010/04/23 世界智慧財產權組織 PCT/US2010/032270
2010/10/19 世界智慧財產權組織 PCT/US2010/053157
(71)申請人：創世泰克藥業股份有限公司 (美國) TRANSTECH PHARMA, INC. (US)
美國
(72)發明人：羅瑟琳 羅伯特 ROTHLEIN, ROBERT (US)；偉伯斯特 傑佛瑞C WEBSTER, JEFFREY C. (US)；布萊克 葛萊高瑞T BLECK, GREGORY T. (US)；凱崔葛達 瑪登 KATRAGADDA, MADAN (IN)；瑞杰德海雅凱薩 曼納傑 RAJADHYAKSHA, MANOJ (US)；維蘭德 柏納德N VIOLAND, BERNARD N. (US)；溫特蘭 喬 安 WENTLAND, JO-ANN (US)
(74)代理人：陳長文
申請實體審查：無 申請專利範圍項數：29 項 圖式數：12 共 677 頁

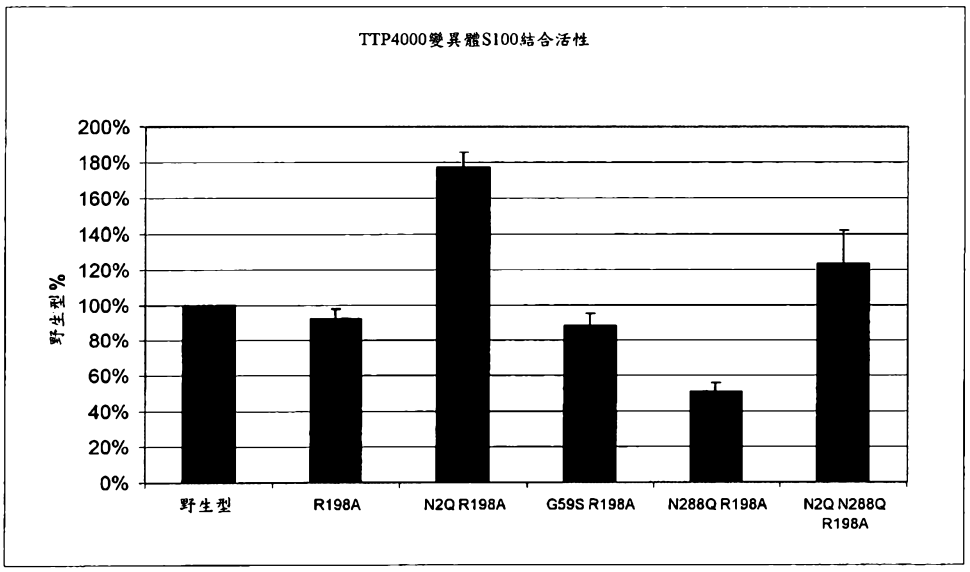
(54)名稱

ＲＡＧＥ融合蛋白組合物及使用方法

RAGE FUSION PROTEIN COMPOSITIONS AND METHODS OF USE

(57)摘要

本發明揭示包含 RAGE 多肽之融合蛋白，其中該 RAGE 多肽包含哺乳動物野生型 RAGE 肽之片段及相對於該野生型 RAGE 肽在該融合蛋白之該 RAGE 多肽部分中的至少一個點突變。該點突變可移除及/或改變糖基化位點或酶裂解位點。亦揭示編碼此等蛋白質之核酸以及使用此等蛋白質治療 RAGE 介導之病變之方法。



(19)中華民國智慧財產局
(12)發明說明書公開本 (11)公開編號：TW 201141507 A1
(43)公開日： 中華民國 100 (2011) 年 12 月 01 日

(21)申請案號：100105575 (22)申請日： 中華民國 100 (2011) 年 02 月 18 日
(51)Int. Cl.： *A61K38/16 (2006.01)* *A61K39/44 (2006.01)*
A61P25/28 (2006.01) *A61P37/00 (2006.01)*
A61P9/00 (2006.01) *A61P17/06 (2006.01)*
(30)優先權：2010/02/18 美國 61/305,706
2010/04/23 世界智慧財產權組織 PCT/US2010/032270
2010/10/19 世界智慧財產權組織 PCT/US2010/053157
(71)申請人：創世泰克藥業股份有限公司 (美國) TRANSTECH PHARMA, INC. (US)
美國
(72)發明人：羅瑟琳 羅伯特 ROTHLEIN, ROBERT (US)；偉伯斯特 傑佛瑞C WEBSTER, JEFFREY C. (US)；布萊克 葛萊高瑞T BLECK, GREGORY T. (US)；凱崔葛達 瑪登 KATRAGADDA, MADAN (IN)；瑞杰德海雅凱薩 曼納傑 RAJADHYAKSHA, MANOJ (US)；維蘭德 柏納德N VIOLAND, BERNARD N. (US)；溫特蘭 喬 安 WENTLAND, JO-ANN (US)
(74)代理人：陳長文
申請實體審查：無 申請專利範圍項數：29 項 圖式數：12 共 677 頁

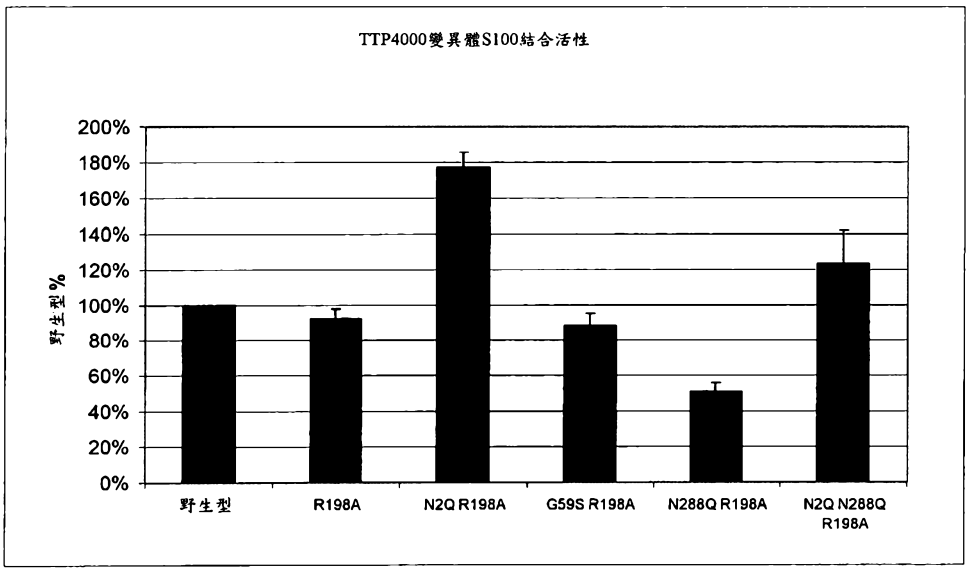
(54)名稱

ＲＡＧＥ融合蛋白組合物及使用方法

RAGE FUSION PROTEIN COMPOSITIONS AND METHODS OF USE

(57)摘要

本發明揭示包含 RAGE 多肽之融合蛋白，其中該 RAGE 多肽包含哺乳動物野生型 RAGE 肽之片段及相對於該野生型 RAGE 肽在該融合蛋白之該 RAGE 多肽部分中的至少一個點突變。該點突變可移除及/或改變糖基化位點或酶裂解位點。亦揭示編碼此等蛋白質之核酸以及使用此等蛋白質治療 RAGE 介導之病變之方法。



六、發明說明：

【發明所屬之技術領域】

本發明係關於包含晚期糖基化終產物受體(「RAGE」)之融合蛋白、編碼RAGE融合蛋白之核酸及使用此等蛋白質之方法。

相關申請案之交叉參考

本申請案根據35 U.S.C. § 119(e)主張2010年2月18日申請之美國臨時專利申請案第61/305,706號的優先權且根據35 U.S.C. 365(c)主張2010年4月23日申請之國際申請案第PCT/US2010/032270號及2010年10月19日申請之國際申請案第PCT/US2010/053157號的優先權。2010年4月23日申請之國際申請案第PCT/US2010/032270號及國際申請案第PCT/US2010/053157號各根據35 U.S.C. § 119(e)主張2010年2月18日申請之美國臨時專利申請案第61/305,706號的優先權。美國臨時專利申請案第61/305,706號及國際申請案第PCT/US2010/032270號及第PCT/US2010/053157號之揭示內容皆以全文引用的方式併入本文中。

【先前技術】

蛋白質或脂質與醛醣一起培育引起蛋白質上之胺基發生非酶促糖基化及氧化而形成安瑪多立加合物(Amadori adduct)。該等加合物再隨時間經歷重排、脫水及與其他蛋白質交聯而形成稱為晚期糖基化終產物(「AGE」)之複合物。促進AGE形成之因素包括延遲之蛋白質轉換(例如在澱粉樣變性病(amyloidoses)中)、具有高離胺酸含量之巨分

子之累積及高血糖含量(例如在糖尿病中)(Hori等人，*J. Biol. Chem.* **270**: 25752-761, (1995))。AGE已牽涉於包括與糖尿病及正常衰老相關之併發症的多種病症中。

AGE展現與單核細胞、巨噬細胞、微血管結構(microvasculature)之內皮細胞、平滑肌細胞、系膜細胞(mesengial cell)及神經元上的細胞表面受體特異性及可飽和地結合。晚期糖基化終產物受體(「RAGE」)為免疫球蛋白超基因分子家族之一員。RAGE之細胞外(N端)域包括3個免疫球蛋白型區域：1個V(可變)型域，繼之以2個C型(恆定)域(Neeper等人，*J. Biol. Chem.*, **267**:14998-15004 (1992)；Schmidt等人，*Circ.* (*增刊*) **96**#194 (1997))。單一跨膜域及高度帶電之較短胞漿尾部(cytosolic tail)緊跟在細胞外域之後。N端細胞外域可藉由蛋白質水解RAGE或藉由用以產生包含V域及C域之可溶性RAGE(sRAGE)之分子生物學方法來分離。

RAGE表現於多種細胞類型上，包括白血球、神經元、小膠質細胞(microglial cell)及血管內皮(例如Hori等人，*J. Biol. Chem.*, **270**:25752-761 (1995))。亦在衰老組織(Schleicher等人，*J. Clin. Invest.*, **99 (3)**: 457-468 (1997))以及糖尿病性視網膜、血管結構及腎臟(Schmidt等人，*Nature Med.*, **1**:1002-1004 (1995))中發現RAGE含量增加。

除AGE之外，其他化合物亦可結合於及調節RAGE。RAGE可結合於多種在功能上及在結構上不同之配位體，包括澱粉樣蛋白β(Aβ)、血清澱粉樣蛋白A(SAA)、晚期糖

基化終產物(AGE)、S100(鈣粒蛋白(Calgranulin)家族之促炎成員)、羧甲基離胺酸(CML)、兩性蛋白(amphoterin)及CD11b/CD18(Bucciarelli等人，*Cell Mol. Life Sci.*, **59**: 1117-128 (2002)；Chavakis等人，*Microbes Infect.*, **6**:1219-1225 (2004)；Kokkola等人，*Scand. J. Immunol.*, **61**:1-9 (2005)；Schmidt等人，*J. Clin. Invest.*, **108**:949-955 (2001)；Rocken等人，*Am. J. Pathol.*, **162**:1213-1220 (2003))。

諸如AGE、S100/鈣粒蛋白、β-澱粉樣蛋白、CML(N^{ε}-羧甲基離胺酸)及兩性蛋白之配位體與RAGE結合已顯示可調節多種基因之表現。此等相互作用可接著起始信號轉導機制，包括p38活化、p21ras、MAP激酶、Erk1-2磷酸化、及發炎性信號傳導之轉錄介體NF-κB之活化(Yeh等人，*Diabetes*, **50**:1495-1504 (2001))。舉例而言，在許多細胞類型中，RAGE與其配位體之間的相互作用會產生氧化壓力(oxidative stress)，其進而引起自由基敏感轉錄因子NF-κB之活化及NF-κB調控基因(諸如細胞激素IL-1β及TNF-α)之活化。此外，RAGE表現經由NF-κB上調且顯示在發炎或氧化壓力部位表現增加(Tanaka等人，*J. Biol. Chem.*, **275**:25781-25790 (2000))。因此，上升且通常有害之螺旋(spiral)會由因配位體結合起始之正反饋迴路(positive feedback loop)推動。

不同組織及器官中之RAGE之活化會導致許多病理生理學結果。RAGE已牽涉於包括以下之多種病狀中：急性及

慢性發炎(Hofmann等人，*Cell* **97**:889-901 (1999))、諸如血管通透性增加之糖尿病晚期併發症之顯現(Wautier等人，*J. Clin. Invest.*, **97**:238-243 (1995))、腎病(Teillet等人，*J. Am. Soc. Nephrol.*, **11**:1488-1497 (2000))、動脈硬化(Vlassara等人，*The Finnish Medical Society DUODECIM, Ann. Med.*, **28**:419-426 (1996))、及視網膜病(Hammes等人，*Diabetologia*, **42**:603-607 (1999))。RAGE亦已牽涉於阿茲海默氏病(Alzheimer's disease)(Yan等人，*Nature*, **382**:685-691 (1996))中及腫瘤侵襲及轉移中(Taguchi等人，*Nature*, **405**:354-357 (2000))。

儘管RAGE在多種不同疾病模型中有廣泛表現且且其具有明顯的多效性作用，但RAGE似乎並不為正常發育所必需。舉例而言，RAGE基因剔除小鼠無明顯異常表型，此表明儘管RAGE在長期受刺激下會在疾病病理學中起作用，但抑制RAGE似乎不會促成任何不合需要之急性表型(Liliensiek等人，*J. Clin. Invest.* **113**:1641-50 (2004))。

拮抗生理配位體與RAGE之結合可下調由過高濃度之AGE及其他RAGE配位體所引起之病理生理學變化。藉由減少內源性配位體與RAGE之結合，可減輕與RAGE介導之病症相關之症狀。可溶性RAGE(sRAGE)能夠有效地拮抗RAGE配位體與RAGE結合。然而，sRAGE在活體內投與時會具有過短以至於不適用於治療一或多種病症的半衰期。

包含RAGE配位體域與第二多肽連接之融合蛋白可提供拮抗天然RAGE配位體之能力，同時具有足夠長以至於在

治療上適用的半衰期。另外，在某些實施例中，此等融合蛋白可在於大規模生物反應器中表現蛋白質期間藉由蛋白質加工(例如糖基化及/或酶介導之裂解)而修飾。相較於未以任何方式修飾之分子，此加工可減小融合蛋白之半衰期。因此，本發明之化合物及方法解決開發能拮抗AGE及其他生理配位體與RAGE受體結合且具有所需之藥物動力學概況之化合物的需要。

【發明內容】

本發明之實施例係關於包含晚期糖基化終產物受體(「RAGE」)之融合蛋白。在某些實施例中，RAGE融合蛋白包含相對於野生型RAGE具有至少一個點突變之RAGE蛋白，及編碼其之核酸序列。本發明之其他實施例包含經最佳化而用於產生本發明之融合蛋白的核酸序列及構築體以及使用此等RAGE融合蛋白用於治療病症之組合物及方法。

在某些實施例中，本發明包含含有晚期糖基化終產物受體(RAGE)多肽與免疫球蛋白多肽連接之融合蛋白，其中該RAGE多肽包含具有配位體結合域之哺乳動物RAGE的片段，且其中該融合蛋白相對於野生型序列在該RAGE多肽或該免疫球蛋白多肽之至少一者中具有至少一個突變，其中該突變移除及/或改變糖基化位點或酶裂解位點中的至少一者。在一些實施例中，酶裂解位點為弗林蛋白酶(furin)裂解位點。在某些實施例中，免疫球蛋白多肽包含C_H2域或C_H2域之片段。此外，在某些實施例中，至少一部

分鉸鏈區不包括在C_H2域片段中。此外，在某些實施例中，C_H2域經由其C端與免疫球蛋白多肽之C_H3域之N端連接。

舉例而言，在一些實施例中，本發明提供一種包含RAGE多肽及免疫球蛋白多肽之融合蛋白，其中：a)該RAGE多肽包含含有RAGE配位體結合域之哺乳動物野生型RAGE肽之片段，且其中該RAGE多肽相對於野生型RAGE肽在一或多個殘基處包含一或多個點突變以移除及/或改變至少一個糖基化位點；且b)該免疫球蛋白多肽包含C_H2域之至少一個片段。在一實施例中，至少一部分鉸鏈區不作為C_H2域之片段之一部分被包括。在一實施例中，藉由突變移除及/或改變之糖基化位點位於RAGE多肽之配位體結合域中。

在其他實施例中，本發明提供一種包含RAGE多肽及免疫球蛋白多肽之融合蛋白，其中：a)該RAGE多肽包含含有RAGE配位體結合域之哺乳動物野生型RAGE肽之片段，且其中該RAGE多肽相對於野生型RAGE肽在一或多個殘基處包含一或多個點突變以移除及/或改變酶裂解位點；且b)該免疫球蛋白多肽包含免疫球蛋白之C_H2域及C_H3域之至少一個片段。在一實施例中，C_H2域之片段不包括至少一部分鉸鏈區。在某些實施例中，酶裂解位點為弗林蛋白酶裂解位點。

在其他實施例中，本發明提供一種包含RAGE多肽及免疫球蛋白多肽之融合蛋白，其中：a)該RAGE多肽包含含

有RAGE配位體結合域之哺乳動物野生型RAGE肽之片段，且其中該RAGE多肽i)相對於野生型RAGE肽在一或多個殘基處包含一或多個點突變以移除及/或改變至少一個糖基化位點，及ii)相對於野生型RAGE肽在一或多個殘基處包含一或多個點突變以移除及/或改變弗林蛋白酶裂解位點；且b)該免疫球蛋白多肽包含免疫球蛋白之C_H2域及C_H3域之至少一個片段。在一實施例中，C_H2域之片段不包括至少一部分鉸鏈區。

在另一實施例中，本發明包含編碼如本文所述之RAGE融合蛋白之核酸。亦提供包含此等核酸之表現載體以及經此等載體轉染之宿主細胞。

在其他實施例中，本發明包含用於治療個體之RAGE介導之病症的方法及組合物。該方法可包含向該個體投與本發明之RAGE融合蛋白。該組合物可包含本發明之RAGE融合蛋白及醫藥學上可接受之載劑。

各種優點可與本發明融合蛋白之特定實施例相關。在一實施例中，本發明之RAGE融合蛋白相對於野生型RAGE融合蛋白(亦即不具有會移除及/或改變糖基化位點或酶裂解位點之一或多個點突變的RAGE融合蛋白)可具有增高之代謝穩定性。此外，本發明之RAGE融合蛋白可對RAGE配位體展現高親和力(亦即生理上相關的)結合。在某些實施例中，本發明之RAGE融合蛋白可以在高奈莫耳至低微莫耳範圍內之親和力且以高於類似野生型RAGE融合蛋白之親和力結合於RAGE配位體(例如S100b、澱粉樣蛋白-β、羧

甲基-離胺酸)。藉由以高親和力與生理RAGE配位體結合，本發明之RAGE融合蛋白可用於抑制內源性配位體與RAGE結合，藉此提供一種改善RAGE介導之疾病的手段。

存在有本發明之其他特徵，將在下文中對其作出描述。應瞭解本發明之應用不限於以下申請專利範圍、說明書及圖式中所述之詳情。本發明可包含其他實施例且能夠以各種方式來實施或實現。

【實施方式】

參考附圖，本發明之各種特徵、態樣及優點將變得更加明顯。

除非有相反指示，否則以下說明書中所闡述之數值參數為可視由本發明設法獲得之所要性質而變化的近似值。在最低限度上且不試圖使等同原則之應用限於申請專利範圍範疇，各數值參數應至少根據所報導之有效數位的數字且藉由應用一般捨位技術來解釋。

更應注意，除非明確且肯定地限於一個指示物，否則如本說明書中所用之單數形式「一」及「該」包括複數個指示物。除非上下文另外明確指出，否則術語「或」可與術語「及/或」互換使用。

此外，術語「部分」及「片段」可互換地用於指多肽、核酸或其他分子構築體之部分。

「多肽」及「蛋白質」在本文中可互換地用於描述可包含部分或全長蛋白質之蛋白質分子。

如此項技術中所知，「蛋白質」、「肽」、「多肽」及「寡

肽」為α碳經由肽鍵連接之胺基酸(通常為L-胺基酸)的鏈，該等肽鍵係由一個胺基酸之α碳之羧基與另一胺基酸之α碳之胺基之間的縮合反應形成。通常，構成蛋白質之胺基酸按順序編號，在胺基端殘基處開始且在朝著蛋白質之羧基端殘基之方向上逐漸增加。

本文揭示之肽、多肽及蛋白質序列使用胺基酸之常用1字母代碼或常用3字母代碼。舉例而言，如本文所用，胺基酸包括以下非限制性列項：甘胺酸被表示為Gly或G；丙胺酸被表示為Ala或A；異白胺酸被表示為Ile或I；天冬醯胺被表示為Asn或N；麩醯胺酸被表示為Gln或Q；絲胺酸被表示為Ser或S；蘇胺酸被表示為Thr或T；蛋白質被表示為Pro或P；精胺酸被表示為Arg或R；麩胺酸被表示為Glu或E；離胺酸被表示為Lys或K；組胺酸被表示為His或H；白胺酸被表示為Leu或L；且焦麩胺酸被表示為pE。

如本文所用，術語「上游」在分子為蛋白質時係指某一殘基在第二殘基之N端，或在分子為核酸時係指某一殘基在第二殘基之5'處。亦如本文所用，術語「下游」在分子為蛋白質時係指某一殘基在第二殘基之C端，或在分子為核酸時係指某一殘基在第二殘基之3'處。

除非另外定義，否則本文中所用之所有技術及科學術語皆具有與一般技術者之通常理解相同之含義。專業人員尤其可參閱Current Protocols in Molecular Biology(參見例如Ausubel, F.M.等人，*Short Protocols in Molecular Biology*，第4版，第2章，John Wiley & Sons, N.Y.)以瞭解

此項技術之定義及術語。胺基酸殘基之縮寫為此項技術中用於指代20種常見L-胺基酸之一的標準3字母及/或1字母代碼。

「核酸」為諸如去氧核糖核酸(DNA)或核糖核酸(RNA)之聚核苷酸。該術語可用於包括單股核酸、雙股核酸以及由核苷酸或核苷類似物製備之RNA及DNA。

術語「載體」係指可用於將第二核酸分子轉運入細胞中之核酸分子。在一實施例中，載體允許插入該載體中之DNA序列的複製。載體可包含增強核酸分子在至少一些宿主細胞中之表現的啟動子。載體可自主(染色體外)複製或可整合於宿主細胞染色體中。在一實施例中，載體可包含能夠產生源於插入載體中之核酸序列之至少一部分的蛋白質之表現載體。

如此項技術中所知，使核酸序列彼此雜交之條件可被描述為在低嚴格度至高嚴格度範圍內。一般而言，高度嚴格的雜交條件係指在高溫下於低鹽緩衝液中洗滌雜交體。雜交可如下進行：在65℃下使用此項技術中之標準雜交溶液(諸如0.5 M $NaHPO_4$、7%十二烷基硫酸鈉(SDS))過濾所結合之DNA，且在0.25 M $NaHPO_4$、3.5% SDS中洗滌，隨後視探針長度而定在室溫至68℃之範圍內的溫度下在0.1×SSC/0.1% SDS中洗滌。舉例而言，高嚴格度的洗滌包含對於14個鹼基之寡核苷酸探針在37℃下，或對於17個鹼基之寡核苷酸探針在48℃下，或對於20個鹼基之寡核苷酸探針在55℃下，或對於25個鹼基之寡核苷酸探針在60℃

下，或對於長度為約250個核苷酸之核苷酸探針在65℃下在6×SSC/0.05%焦磷酸鈉中洗滌。核酸探針可藉由用例如[γ-^{32}P]ATP作末端標記，或藉由隨機引子標記來合併經放射性標記之核苷酸(諸如[α-^{32}P]dCTP)而經放射性核苷酸標記。或者，探針可藉由合併經生物素標記或經螢光素標記之核苷酸而被標記，且使用抗生蛋白鏈菌素(Streptavidin)或抗螢光素抗體來偵測探針。

如本文所用，「小有機分子」為含有至少一個碳原子之分子量小於2,000道爾頓(Dalton)的分子。

術語「融合蛋白」係指具有源於兩種或兩種以上蛋白質之胺基酸序列的蛋白質或多肽。融合蛋白亦可包括源於各別蛋白質之胺基酸部分之間的胺基酸連接區域。

如本文所用，「免疫球蛋白肽」可包含免疫球蛋白重鏈或其一部分。在一實施例中，重鏈之部分可為Fc片段或其一部分。如本文所用，Fc片段包含免疫球蛋白的重鏈鉸鏈多肽及重鏈之C_H2及C_H3域，呈單體或二聚形式。或者，C_H1及Fc片段可用作免疫球蛋白多肽。重鏈(或其部分)或免疫球蛋白多肽可源於以下任一已知重鏈同型或為以下任一已知重鏈同型之片段：例如IgG(γ)、IgM(μ)、IgD(δ)、IgE(ε)或IgA(α)。此外，重鏈(或其部分)或免疫球蛋白多肽可源於以下任一已知重鏈亞型或為以下任一已知重鏈亞型之片段：例如IgG1(γ1)、IgG2(γ2)、IgG3(γ3)、IgG4(γ4)、IgA1(α1)、IgA2(α2)，或此等同型或亞型之改變生物活性的突變體。可改變之生物活性之一實例包括例如藉由修飾

鉸鏈區使同型與一些Fc受體結合之能力降低。

術語「一致性」或「一致性百分比」係指兩個胺基酸序列之間或兩個核酸序列之間的序列一致性。一致性百分比可藉由比對兩個序列來測定且係指由所比較序列共有之位置處之相同殘基(亦即胺基酸或核苷酸)的數值。序列比對及比較可使用此項技術中之標準演算法(例如Smith及Waterman, 1981, *Adv. Appl. Math.* 2:482；Needleman及Wunsch, 1970, *J. Mol. Biol.* 48:443；Pearson及Lipman, 1988, *Proc. Natl. Acad. Sci., USA*, 85:2444)或利用可公開獲得之此等演算法之電腦化版本(Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive, Madison, WI)(如BLAST及FASTA)來進行。此外，可經由馬里蘭州貝什斯達之國家衛生研究所(National Institutes of Health, Bethesda MD)獲得之ENTREZ可用於序列比較。在一實施例中，兩個序列之一致性百分比可使用空位權重為1以至於各胺基酸空位就如同其為兩個序列之間的單一胺基酸錯配般被加權的GCG來測定。

如本文所用，術語「保守殘基」係指在具有相同結構及/或功能之複數種蛋白質之間相同的胺基酸。具有保守殘基之區域對於蛋白質結構或功能可為重要的。因此，如三維蛋白質中所鑑別之鄰接保守殘基對於蛋白質結構或功能可為重要的。為了發現3-D結構之保守殘基或保守區域，可對來自不同物種或同一物種之個體之相同或類似蛋

白質的序列作比較。

如本文所用，術語「同系物」意謂與野生型胺基酸序列具有一定程度之同源性或一致性的多肽。同源性比較可藉由眼睛或更通常藉助於可易於獲得之序列比較程式來進行。此等可購得之電腦程式可計算兩個或兩個以上序列之間的同源性百分比(例如Wilbur, W. J.及Lipman, D. J., 1983, *Proc. Natl. Acad. Sci. USA*, 80:726-730)。舉例而言，同源序列可理解為包括在替代性實施例中彼此至少70%一致、75%一致、85%一致、90%一致、95%一致、96%一致、97%一致、98%一致或99%一致的胺基酸序列。

如本文所用，術語與其至少90%一致包括與指定序列之一致性在90%至99.99%範圍內之序列且包括其間之所有範圍。因此，術語與其至少90%一致包括與指定序列91%、91.5%、92%、92.5%、93%、93.5%、94%、94.5%、95%、95.5%、96%、96.5%、97%、97.5%、98%、98.5%、99%、99.5%一致之序列。類似地，術語至少70%一致包括一致性在70%至99.99%範圍內之序列且包括其間之所有範圍。一致性百分比之測定可使用諸如(但不限於)本文所述之演算法的演算法測定。

如本文所用，多肽或蛋白質「域」包含多肽或蛋白質之包含獨立單元的區域。域可根據結構、序列及/或生物活性加以定義。在一實施例中，多肽域可包含蛋白質之以實質上獨立於蛋白質其餘部分之方式摺疊的區域。可使用諸如(但不限於)PFAM、PRODOM、PROSITE、BLOCKS、

PRINTS、SBASE、ISREC PROFILES、SAMRT及PROCLASS之域資料庫來鑑別域。

如本文所用，「免疫球蛋白域」為在結構上與免疫球蛋白之一個域同源或一致之胺基酸序列。免疫球蛋白域之胺基酸序列之長度可為任何長度。在一實施例中，免疫球蛋白域可少於250個胺基酸。在一個例示性實施例中，免疫球蛋白域之長度可為約80-150個胺基酸。舉例而言，IgG之可變區以及C_H1、C_H2及C_H3區為各免疫球蛋白域。在另一實例中，IgM之可變區、C_H1、C_H2、C_H3及C_H4區為各免疫球蛋白域。

如本文所用，「RAGE免疫球蛋白域」為來自RAGE蛋白的在結構上與免疫球蛋白之一個域同源或一致之胺基酸序列。舉例而言，RAGE免疫球蛋白域可包含RAGE V域、RAGE Ig樣C1型1域(「C1域」)或RAGE Ig樣C2型2域(「C2域」)。

如本文所用，「域間連接子」包含將兩個域連接在一起之多肽。鉸鏈區為IgG中的域間連接子之實例。

如本文所用，「直接連接」標識介於兩個不同基團(例如核酸序列、多肽、多肽域)之間且在所連接之兩個基團之間不具有任何介入原子的共價鍵聯。

如本文所用，「配位體結合域」或「配位體結合位點」包含蛋白質中直接與配位體相互作用之殘基或與極接近於直接與配位體相互作用之彼等殘基定位配位體有關的殘基。配位體結合域中之殘基之相互作用可用模型或結構中

殘基與配位體之空間接近性(spatial proximity)定義。術語配位體結合域包括配位體結合域或其部分之同系物。就此而言，可基於殘基之極性、電荷、溶解性、疏水性或親水性之類似性在配位體結合域中進行有意的胺基酸取代，只要保留配位體結合域之結合特異性即可。配位體結合域可存在於蛋白質或多肽之一或多個配位體結合域中。

如本文所用，術語「相互作用」係指配位體或化合物或其部分或片段與一部分第二相關分子之間的接近性狀況。相互作用可為非共價相互作用，例如由氫鍵結合、凡得瓦爾力(van der Waals)相互作用或者靜電或疏水性相互作用所致，或其可為共價相互作用。

如本文所用，「配位體」係指與配位體結合域相互作用之分子或化合物或實體，包括受質或其類似物或部分。如本文所述，術語「配位體」可指結合於相關蛋白質之化合物。配位體可為促效劑、拮抗劑或調節劑。或者，配位體可能不具有生物效應。或者，配位體可阻斷其他配位體之結合，藉此抑制生物效應。配位體可包括(但不限於)小分子抑制劑。此等小分子可包括肽、肽模擬物、有機化合物及其類似物。配位體亦可包括多肽及/或蛋白質。

如本文所用，「調節劑化合物」係指可改變相關分子之生物活性的分子。調節劑化合物可增加或減小相關分子之活性，或改變相關分子之物理或化學特徵或功能或免疫性質。對於RAGE，調節劑化合物可增加或減小RAGE或其一部分之活性，或改變RAGE或其一部分之特徵或功能或免

疫性質。調節劑化合物可包括天然及/或化學合成或人造之肽、經修飾之肽(例如磷酸肽)、抗體、碳水化合物、單醣、寡醣、多醣、醣脂、雜環化合物、核苷或核苷酸或其部分以及小有機或無機分子。調節劑化合物可為內源性生理化合物或其可為天然或合成化合物。或者，調節劑化合物可為小有機分子。術語「調節劑化合物」亦包括經化學修飾之配位體或化合物，且包括異構體及外消旋形式。

「促效劑」包含可結合於受體而形成能引發對所涉及受體具有特異性之藥理學反應之複合物的化合物。

「拮抗劑」包含可結合於生物分子而形成不會引起實質性藥理學反應且可抑制由促效劑誘導之生物反應之複合物的化合物。在一些情況下，生物分子可為受體(例如RAGE)。此外，在一些情況下，生物分子可為促效劑，以至於拮抗劑可結合於促效劑且阻止促效劑與其目標相互作用。

RAGE促效劑因此可結合於RAGE且刺激RAGE介導之細胞過程，且RAGE拮抗劑可抑制RAGE介導之過程受RAGE促效劑刺激。舉例而言，在一實施例中，由RAGE促效劑刺激之細胞過程包含TNF-α基因轉錄之活化。

術語「肽模擬物」係指在分子之間的相互作用中充當肽替代物之結構(Morgan等人，1989, *Ann. Reports Med. Chem.*, 24:243-252)。肽模擬物可包括可能含有或可能不含有胺基酸及/或肽鍵但保留肽或促效劑或拮抗劑之結構及功能特徵的合成結構。肽模擬物亦包括類肽(peptoid)、寡

類肽(oligopeptoid)(Simon等人，1972, *Proc. Natl. Acad, Sci., USA*, 89:9367)；及含有代表對應於本發明之肽或促效劑或拮抗劑之所有可能的胺基酸序列的指定長度之肽的肽文庫。

術語「治療」係指改良疾病或病症之症狀或改良個體之病狀。如本文所用之術語「治療」係指全面治療個體所罹患之既定病症，包括減輕由彼病症引起之一種症狀或大多數症狀。

術語「治癒」係指恢復個體健康及/或減輕個體之疾病或病症之所有或實質上所有的症狀。

術語「預防病症發作」係指阻止某一個體患上該病症，不然該個體將會患上該病症。

如本文所用，術語「EC50」被定義為產生50%所測定之生物效應之藥劑濃度。舉例而言，具有可量測之生物效應的治療劑之EC50可包含藥劑展現50%生物效應時之值。

如本文所用，術語「IC50」被定義為對所測定之效應有50%抑制之藥劑濃度。舉例而言，RAGE結合之拮抗劑之IC50可包含拮抗劑使配位體與RAGE之配位體結合域之結合減少50%時的值。

如本文所用，片語「治療有效量」應意謂將引發所尋求之個體治療反應之藥物或醫藥劑的量。

在此等方法中，會影響構成治療有效量之量的因素包括(但不限於)個體之尺寸及重量、治療劑之生物降解性、治療劑之活性、受影響區域之大小以及其生物可用性。該片

語包括相較於尚未接受此量之相應個體，可改良治療、痊癒或改善副作用或者減慢疾病或病症之進展速率的量。

如本文所用之術語「醫藥學上可接受之載劑」可指適於在人類或動物個體中使用，例如適於作為治療組合物來投與而用以治療RAGE介導之病症或疾病的化合物及組合物。

術語「醫藥組合物」在本文中用於表示可例如經口、非經腸、局部、藉由吸入噴霧劑、腦室內、鞘內、鼻內、經直腸或以如本文所述之任何其他形式之投藥途徑，以含有習知無毒載劑、稀釋劑、佐劑、媒劑及其類似物之單位劑量調配物形式向哺乳動物宿主投與的組合物。

如本文所用之術語「非經腸」包括皮下注射、靜脈內、肌肉內、腦池內注射或輸注技術。

如本文所用，「排斥」係指組織上之導致細胞、組織或器官破壞或導致細胞、組織或器官損傷的免疫或發炎反應。所排斥之細胞、組織或器官可源於發動排斥反應之相同個體，或可自不同個體移植於正展現排斥現象之個體中。

如本文所用，術語「細胞」係指哺乳動物生命系統之各包含獨立生命系統之結構及功能單元。如此項技術中所知，細胞包括細胞核、細胞質、胞內細胞器及封閉該細胞且使該細胞獨立於其他細胞之細胞壁。

如本文所用，術語「組織」係指具有類似結構及功能或一起起作用而執行特定功能之細胞的聚集體。組織可包括

類似細胞及圍繞該等細胞之細胞間物質的集合。組織包括(但不限於)肌肉組織、神經組織及骨。

如本文所用，「器官」係指動物中專用於達成某一特定功能之完全分化的結構及功能單元。器官可包含一組執行某一特定功能或一組功能的組織。器官包括(但不限於)心臟、肺臟、腦、眼睛、胃、脾臟、胰臟、腎臟、肝臟、腸、皮膚、子宮、膀胱及骨。

「穩定」調配物為所含之RAGE融合蛋白在儲存之後基本上保留其物理及化學穩定性及生物活性的調配物。量測蛋白質穩定性之各種分析技術可用於此項技術中且綜述於Peptide and Protein Drug Delivery, 247-301, Vincent Lee編，Marcel Dekker, Inc., New York, N.Y., Pubs. (1991)及Jones, A. Adv. Drug Delivery Rev. 10: 29-90 (1993)中。可在選定溫度下在選定時期內量測穩定性。在快速篩檢中，調配物可保持在40℃下1週至1個月，在此時量測穩定性。舉例而言，凍乾及儲存之後的聚集程度可用作RAGE融合蛋白穩定性之指標。舉例而言，「穩定」調配物可為少於約10%且較佳少於約5%之RAGE融合蛋白以聚集體形式存在於調配物中的調配物。在其他實施例中，可測定在凍乾調配物之凍乾及儲存之後聚集體形成之增加。舉例而言，「穩定」凍乾調配物可為當將凍乾調配物在40℃下保溫至少1週時，凍乾調配物中之聚集體增加不到約5%或不到約3%的調配物。在其他實施例中，RAGE融合蛋白調配物之穩定性可使用生物活性檢測(諸如如本文所述之結合檢測)

來量測。

「復原」調配物為已藉由於稀釋劑中溶解凍乾RAGE融合蛋白調配物以至於使RAGE融合蛋白分散及/或溶解於復原調配物中而製備的調配物。復原調配物可適於向欲用該融合蛋白治療之患者投與(例如非經腸投與)，且在本發明之某些實施例中，可為適於皮下投與之調配物。

「等張」意謂相關調配物具有約240至約340 mOsm/kg之滲透壓。在一實施例中，等張調配物為具有基本上與人類血液(285-310 mOsm/kg)相同之滲透壓的調配物。等張性可使用蒸氣壓或冰點下降型滲壓計來量測。

「凍乾保護劑」為在與RAGE融合蛋白組合時顯著防止或降低蛋白質在凍乾及後續儲存後之化學及/或物理不穩定性的分子。例示性凍乾保護劑包括糖類，諸如蔗糖或海藻糖(trehalose)；多元醇，諸如糖醇，例如赤藻糖醇(erythritol)、阿拉伯糖醇(arabitol)、木糖醇、山梨糖醇及甘露糖醇；或其組合。在一實施例中，凍乾保護劑可包含糖。在另一實施例中，凍乾保護劑可包含非還原糖。在另一實施例中，凍乾保護劑可包含非還原糖，諸如蔗糖。凍乾保護劑可以「凍乾保護量」添加至預凍乾之調配物中，其意謂在該凍乾保護量之凍乾保護劑存在下在凍乾蛋白質之後，RAGE融合蛋白在凍乾及儲存之後基本上保留其物理及化學穩定性及生物活性。

用於本文中之凍乾調配物的「稀釋劑」為醫藥學上可接受的(對於投與人類安全且無毒)且適用於製備復原調配物

之稀釋劑。例示性稀釋劑包括無菌水、注射用抑菌水(BWFI)、pH值緩衝溶液(例如磷酸鹽緩衝鹽水)、無菌鹽水溶液、林格氏溶液(Ringer's solution)或右旋糖溶液。在一實施例中，稀釋劑提供適於注射之復原調配物。在另一實施例中，當稀釋劑提供適於注射之復原調配物時，稀釋劑可包含注射用水(WFI)。

用於復原調配物之「防腐劑」為可添加至稀釋劑或復原調配物中以基本上降低復原調配物中之細菌作用的化合物。在一實施例中，一定量之防腐劑可以適用於便於產生多用途復原調配物之量添加。潛在防腐劑之實例包括十八烷基二甲基苄基氯化銨、氯化六烴季銨、氯化苯甲烴銨(烷基苄基二甲基氯化銨之混合物，其中烷基為長鏈化合物)及苄索氯銨(benzethonium chloride)。其他類型之防腐劑包括芳族醇(諸如苯酚)、丁醇及苄醇、對羥基苯甲酸烯丙酯(諸如對羥基苯甲酸甲酯或對羥基苯甲酸丙酯)、兒茶酚、間苯二酚、環己醇、3-戊醇及間甲酚、

用於凍乾調配物之「增積劑」為增加凍乾混合物之質量且促成凍乾塊之物理結構(例如便於產生維持開孔結構之基本上均一之凍乾塊)的化合物。例示性增積劑包括(但不限於)甘露糖醇、甘胺酸及山梨糖醇。

RAGE融合蛋白

本發明之實施例包含融合蛋白、編碼此等融合蛋白之核酸、製備此等融合蛋白之方法及使用此等融合蛋白之方法。

舉例而言，在某些實施例中，本發明之融合蛋白包含晚期終產物受體(RAGE)多肽，其中該RAGE多肽包含哺乳動物野生型RAGE肽之片段，且其中相對於野生型RAGE肽，在該融合蛋白之該RAGE多肽部分中存在有至少一個點突變。在一實施例中，融合蛋白可包含RAGE多肽及免疫球蛋白多肽，其中該RAGE多肽包含哺乳動物野生型RAGE肽之片段，且其中相對於野生型RAGE肽在該融合蛋白之該RAGE多肽部分中及/或在該RAGE融合蛋白之該免疫球蛋白部分中存在有至少一個點突變。

舉例而言，在某些實施例中，本發明包含含有RAGE多肽與免疫球蛋白多肽連接之融合蛋白，其中該RAGE多肽包含具有配位體結合域之哺乳動物RAGE的片段，且其中相對於野生型序列在該融合蛋白之該RAGE多肽或該免疫球蛋白多肽之至少一者中存在有至少一個突變，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。

RAGE多肽可來自任何哺乳動物。在某些實施例中，RAGE多肽為人類RAGE多肽。此外，免疫球蛋白多肽可來自任何哺乳動物。在某些實施例中，免疫球蛋白多肽為人類免疫球蛋白多肽。

點突變可經選擇以在RAGE融合蛋白之性質方面提供有益效應。如本文中更詳細描述，對於RAGE融合蛋白及/或使用或製備此等蛋白質之方法之各種實施例中的各者，RAGE融合蛋白可經修飾以改良分子性質。舉例而言，相

較於相對於野生型序列在RAGE多肽或免疫球蛋白多肽之至少一者中不具有至少一個突變的RAGE融合蛋白，本發明之RAGE融合蛋白可具有改良之配位體結合，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。或者或另外，相較於相對於野生型序列在RAGE多肽或免疫球蛋白多肽之至少一者中不具有至少一個突變的RAGE融合蛋白，本發明之RAGE融合蛋白可具有改良之穩定性，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。或者或另外，相較於相對於野生型序列在RAGE多肽或免疫球蛋白多肽之至少一者中不具有至少一個突變的RAGE融合蛋白，本發明之RAGE融合蛋白可具有改良之藥物動力學概況，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。

舉例而言，在某些實施例中，點突變改變野生型RAGE多肽中存在於糖基化位點處之序列。以此方式，糖基化之類型及/或程度可被改變。

糖基化位點可為見於蛋白質中之各種類型之糖基化位點之一。舉例而言，在某些實施例中，糖基化識別位點為NXS或NXT。在某些實施例中，X不為脯胺酸。因此，在某些實施例中，點突變使野生型RAGE多肽之序列自NIT改變成QIT，及/或自NGS改變成QGS，及/或自NGS改變成NSS，及/或自NST改變成QST，以移除及/或改變至少一個糖基化位點。在一些實施例中，糖基化位點位於RAGE融合蛋白之RAGE部分中。舉例而言，在某些實施例中，糖

基化位點可位於配位體結合位點或配位體結合域內。或者及/或另外，糖基化位點位於RAGE融合蛋白之免疫球蛋白部分中。或者，可靶向可存在於RAGE融合蛋白中之其他糖基化位點。

在某些實施例中，酶裂解位點為弗林蛋白酶裂解位點，以至於點突變改變野生型RAGE多肽中存在於弗林蛋白酶裂解RAGE多肽之識別位點處的序列。舉例而言，在替代性實施例中，點突變使野生型RAGE多肽之序列發生以下之一種改變：(i)PRHRALR變成PRHAALR；(ii)PRHRALR變成PRHKALR；(iii)PRHRALR變成PRHRALA；(iv)PRHRALR變成PRHRALK；(v)PRHRALR變成PRHRALH；(vi)PRHRALR變成PRHRALT；(vii)PRHRALR變成PRHHALR；或(viii)PRHRALR變成PRHTALR，以改變及/或移除弗林蛋白酶裂解位點。

在某些實施例中，融合蛋白之RAGE多肽部分不包括N端前導肽。舉例而言，在某些實施例中，融合蛋白之RAGE多肽部分不包括由野生型RAGE之胺基酸1-23組成之N端前導肽。或者，在某些實施例中，融合蛋白之RAGE多肽部分不包括由野生型RAGE多肽之胺基酸1-22組成之N端前導肽。或者，在其他實施例中，融合蛋白之RAGE多肽部分不包括由野生型RAGE多肽之胺基酸1-24組成之N端前導肽。

在某些實施例中，至少一個突變包含經加工以至於融合蛋白之RAGE多肽部分不包括由野生型RAGE多肽之胺基酸

1-23組成之N端前導肽的人類RAGE多肽之以下至少一者：(i) N2Q；(ii) N58Q；(iii) G59S；(iv) N2Q及N58Q；或(v) N2Q及G59S。舉例而言，在此編號系統中，RAGE融合蛋白對應於SEQ ID NO: 34之RAGE融合蛋白(一種具有兩個如下文中更詳細描述之RAGE免疫球蛋白樣域之RAGE融合蛋白)的胺基酸序列，其中不包括胺基酸1-23之信號序列且RAGE融合蛋白包含移除及/或改變糖基化位點及/或弗林蛋白酶裂解位點之一或多個點突變，其係基於相對於全長野生型RAGE序列(SEQ ID NO: 1)自胺基酸24開始之編號。此外，在此編號系統中，RAGE融合蛋白對應於SEQ ID NO: 37之RAGE融合蛋白(一種具有一個如下文中更詳細描述之RAGE免疫球蛋白樣域之RAGE融合蛋白)的胺基酸序列，其中不包括胺基酸1-23之信號序列且RAGE融合蛋白包含移除及/或改變糖基化位點及/或弗林蛋白酶裂解位點之一或多個點突變，其係基於相對於全長野生型RAGE序列(SEQ ID NO: 1)自胺基酸24開始之編號。舉例而言，SEQ ID NO: 62提供具有兩個RAGE域之RAGE融合蛋白之胺基酸序列，其中第一RAGE域包括將對應於SEQ ID NO: 1之全長RAGE野生型序列中之N25Q的N2Q點突變。類似地，SEQ ID NO: 63提供具有兩個RAGE域之RAGE融合蛋白之胺基酸序列，且具有將對應於全長野生型序列中之N81Q的N58Q點突變。類似序列可用具有單一RAGE域(例如SEQ ID NO: 57、37、36及35)或三個域之RAGE融合蛋白產生。舉例而言，如本文中更詳細描述，SEQ ID NO: 225為

一種具有對應於RAGE之胺基酸24至136之單一RAGE免疫球蛋白樣域的融合蛋白，其中在該融合蛋白之位置2(亦即對應於全長RAGE蛋白之胺基酸25)、58及173處具有突變。

如本文中詳述，RAGE多肽可為全長RAGE之片段。SEQ ID NO: 1提供全長RAGE之胺基酸序列。

在某些實施例中，人類RAGE多肽經加工以至於融合蛋白之RAGE多肽部分不包括由野生型RAGE多肽之胺基酸1-23組成之N端前導肽。在此實施例中，在糖基化位點處包含至少一個突變之RAGE多肽可包含如以下至少一者所示之序列：(i) SEQ ID NO: 8、SEQ ID NO: 16或SEQ ID NO: 20；或(ii) N端麩醯胺酸已環化而形成焦麩胺酸之SEQ ID NO: 8、SEQ ID NO: 16或SEQ ID NO: 20。

類似地，在某些實施例中，移除弗林蛋白酶裂解位點之突變包含不包括由野生型RAGE多肽之胺基酸1-23組成之N端前導肽的人類RAGE多肽之R195A、R195K、R195T、R195H、R198A、R198K、R198H、R198T中之至少一者。在此實施例中，在弗林蛋白酶裂解位點處包含至少一個突變之RAGE多肽可包含如SEQ ID NO: 20或N端麩醯胺酸已環化而形成焦麩胺酸之SEQ ID NO: 20所示之序列。此位點不存在於SEQ ID NO: 57、37、36及35之較短RAGE融合蛋白中。

如本文中更詳細描述，在某些實施例中，RAGE融合蛋白之免疫球蛋白部分經修飾以改良分子性質。舉例而言，

在某些實施例中，RAGE融合蛋白在具有兩個RAGE免疫球蛋白樣域之人類RAGE融合蛋白(例如SEQ ID NO: 34)之位置288處的糖基化位點處包含突變，其中該融合蛋白之RAGE多肽部分不包括由野生型RAGE多肽之胺基酸1-23組成之N端前導肽。在某些實施例中，突變使具有胺基酸序列NST之糖基化位點改變成QST。在一實施例中，相對於如SEQ ID NO: 34呈現之RAGE融合序列，突變包含N288Q。類似蛋白質可以僅具有1個RAGE域之RAGE融合蛋白(TTP3000)(例如SEQ ID NO: 37)形式製得。在此情況下，可在位置173處發現免疫球蛋白突變。具有單一RAGE域且在位置2、58及173處具有突變之RAGE融合蛋白的實例如SEQ ID NO: 225所提供(圖6FF)。此項技術之相關人士應瞭解關於具有兩個RAGE域之融合蛋白所述之突變可在僅具有1個RAGE域之RAGE融合蛋白或具有3個RAGE域之蛋白質中的類似位置處產生。弗林蛋白酶裂解位點不存在於如SEQ ID NO: 57、37、36及35中所說明之僅具有1個域之較短RAGE融合蛋白中，而是將存在於具有3個RAGE免疫球蛋白樣域之野生型RAGE融合蛋白中。

此外，如本文所述，對於本發明之RAGE融合蛋白、核酸構築體及/或其他組合物、方法及系統之實施例中的各者，免疫球蛋白多肽可包含C_H2域或C_H2域之片段。在一實施例中，C_H2域或C_H2域之片段不包括至少一部分鉸鏈區。在某些實施例中，C_H2域或C_H2域之片段經由其C端與免疫球蛋白多肽之C_H3域或C_H3域之片段的N端連接。

免疫球蛋白域可源於如此項技術中所知之各種免疫球蛋白。在某些實施例中，免疫球蛋白包含人類IgG。因此，在某些實施例中，免疫球蛋白之C_H2及C_H3域包含SEQ ID NO: 38、或無C端離胺酸之SEQ ID NO: 38(亦即SEQ ID NO: 86)、或無N端脯胺酸之SEQ ID NO: 38、或無N端脯胺酸及末端離胺酸之SEQ ID NO: 38(SEQ ID NO: 88)。在一實施例中，C_H2域包含SEQ ID NO: 90或91。在一實施例中，不包括在C_H2域(或其片段)中之鉸鏈區之部分具有如SEQ ID NO: 223或SEQ ID NO: 224中所示之序列。SEQ ID NO: 89提供在對應於SEQ ID NO: 34之位置288之位置處突變的人類IgG免疫球蛋白之C_H2及C_H3域的說明性實例。

因此，在某些實施例中，本發明可包含RAGE融合蛋白，其包含含有如SEQ ID NO: 62至81、SEQ ID NO: 92至190、或SEQ ID NO: 58-61、82、200或201中之任一者所示之胺基酸序列的RAGE多肽。此外，在某些實施例中，本發明可包含RAGE融合蛋白，其包含具有如SEQ ID NO: 62至81、SEQ ID NO: 92至190、或SEQ ID NO: 58-61、82、200或201中之任一者所示之胺基酸序列的RAGE多肽。

本發明之RAGE融合蛋白彼此可形成非共價締合。因此，在某些實施例中，本發明之融合蛋白係呈單體、二聚體、三聚體、四聚體或其混合物形式。

舉例而言，在一些實施例中，本發明提供一種包含RAGE多肽及免疫球蛋白多肽之融合蛋白，其中：(a)該

RAGE多肽包含含有RAGE配位體結合域之哺乳動物野生型RAGE多肽之片段，且其中該RAGE多肽相對於野生型RAGE多肽在一或多個殘基處包含一或多個點突變以移除及/或改變糖基化位點；且(b)該免疫球蛋白多肽包含免疫球蛋白之C_H2域及C_H3域之至少一個片段。在一實施例中，C_H2域或其片段可操作地與C_H3域連接。在其他實施例中，本發明提供一種包含RAGE多肽及免疫球蛋白多肽之融合蛋白，其中：(a)該RAGE多肽包含含有RAGE配位體結合域之哺乳動物野生型RAGE多肽之片段，且其中該RAGE多肽相對於野生型RAGE多肽在一或多個殘基處包含一或多個點突變以移除及/或改變弗林蛋白酶裂解位點；且(b)該免疫球蛋白多肽包含免疫球蛋白之C_H2域及C_H3域之至少一個片段。在一實施例中，C_H2域或其片段可操作地與C_H3域連接。

在其他實施例中，本發明提供一種包含RAGE多肽及免疫球蛋白多肽之融合蛋白，其中：(a)該RAGE多肽包含含有RAGE配位體結合域之哺乳動物野生型RAGE多肽之片段，且其中該RAGE融合蛋白(i)相對於野生型RAGE多肽及/或免疫球蛋白在一或多個殘基處包含一或多個點突變以移除及/或改變糖基化位點，及/或(ii)相對於野生型RAGE肽在一或多個殘基處包含一或多個點突變以移除及/或改變弗林蛋白酶裂解位點；且(b)該免疫球蛋白多肽包含免疫球蛋白之C_H2域及C_H3域之至少一個片段。在一實施例中，C_H2域或其片段可操作地與C_H3域連接。如本文所述，

在某些實施例中，且如下文中更詳細描述，免疫球蛋白多肽包含C_H2域之不包括至少一部分鉸鏈區的片段。此外，在某些實施例中，不作為C_H2域之一部分被包括之鉸鏈區或其部分具有或包含如SEQ ID NO: 223或SEQ ID NO: 224所示之序列。

相對於野生型RAGE融合蛋白(亦即無一或多個移除糖基化位點或弗林蛋白酶裂解位點之點突變的RAGE融合蛋白)，本發明之融合蛋白中之野生型RAGE肽的突變可增加代謝穩定性、藥物動力學半衰期及/或結合親和力。在某些實施例中，本發明之RAGE融合蛋白可以高奈莫耳至低微莫耳範圍內之親和力結合於RAGE配位體(諸如S100b)。此外，在一些實施例中，本發明之RAGE融合蛋白對RAGE配位體可具有大於相應野生型RAGE融合蛋白的親和力。舉例而言，在某些實施例中，在RAGE多肽部分中具有至少一個移除N2及/或N58處之糖基化位點之點突變的本發明之融合蛋白對s100b可具有大於類似野生型RAGE融合蛋白之結合親和力且可具有至少兩倍的結合親和力。

圖1-8提供本發明之各種胺基酸及核酸構築體之實例。

舉例而言，圖1提供全長人類RAGE之胺基酸序列(SEQ ID NO: 1)、對應於胺基酸1-22之信號序列已經移除之全長人類RAGE的胺基酸序列(SEQ ID NO: 2)及對應於胺基酸1-23之信號序列已經移除之全長人類RAGE的胺基酸序列(SEQ ID NO: 3)(圖1A)。圖1中亦提供人類RAGE之可用於本發明之RAGE融合蛋白中的各種片段(SEQ ID NO: 4-24及

44)(圖1C-1F及圖1J)以及編碼此等RAGE多肽序列及RAGE多肽序列之片段的DNA序列(SEQ ID NO: 25-29)(圖1G-1H)。圖1(圖1I及圖1J)中亦展示包含C_H2及C_H3域之人類免疫球蛋白多肽之胺基酸序列，其中該C_H2不包括至少一部分鉸鏈區(SEQ ID NO: 38)；包含C_H2及C_H3域之人類免疫球蛋白多肽之胺基酸序列，其中該C_H2包括至少一部分鉸鏈區(SEQ ID NO: 40)；包含包括至少一部分鉸鏈之C_H2域之人類免疫球蛋白多肽的胺基酸序列(SEQ ID NO: 42)；包含C_H3域之人類免疫球蛋白多肽之胺基酸序列；以及編碼包含C_H2及C_H3域之人類免疫球蛋白多肽之DNA序列，其中該C_H2不包括至少一部分鉸鏈區(SEQ ID NO: 41)且其中該C_H2包括至少一部分鉸鏈區(SEQ ID NO: 39)。圖1中亦提供RAGE之片段之序列，其中N端麩醯胺酸(Q)已環化成焦麩胺酸(圖1K及1L)。圖1M提供SEQ ID NO: 52及53，其分別為編碼SEQ ID NO: 38及40之免疫球蛋白多肽的替代核酸序列。

如下文中更詳細描述，圖2及3提供編碼本發明之RAGE融合蛋白的各種核酸構築體之序列。圖4及5提供本發明之各種RAGE融合蛋白之胺基酸序列。

突變殘基之位置在本文中係關於對應於全長蛋白質之胺基酸1-23之N端序列已經移除的哺乳動物RAGE來加以描述。舉例而言，N2對應於無信號序列之RAGE多肽(SEQ ID NO: 3)之位置2處的麩醯胺酸殘基(N)；此將對應於全長RAGE(SEQ ID NO: 1)之位置25處之麩醯胺酸(參見圖1)。

因此，任何前述實施例之融合蛋白可包含含有SEQ ID NO: 3之人類RAGE肽之片段的RAGE多肽。因此，如上所述，在關於本文使用之特定點突變之描述中，RAGE及/或免疫球蛋白多肽突變之位置係基於SEQ ID NO: 3或具有兩個RAGE域且如SEQ ID NO: 34中所示之RAGE融合蛋白之胺基酸序列的殘基編號。SEQ ID NO: 3之胺基酸序列對應於無信號序列之人類RAGE之全長序列(亦即無殘基1-23之SEQ ID NO: 1)。SEQ ID NO: 34之胺基酸序列對應於無信號序列之具有兩個RAGE域之人類RAGE融合蛋白的序列(亦即無殘基1-23之SEQ ID NO: 1)。此項技術之相關人士應瞭解關於具有兩個RAGE域之融合蛋白(例如SEQ ID NO: 34)所述之突變可在僅具有1個RAGE域之RAGE融合蛋白或具有3個RAGE域之RAGE融合蛋白中的類似位置處產生。此弗林蛋白酶裂解位點不存在於如SEQ ID NO: 57、37、36及35中所說明之僅具有1個域的較短RAGE融合蛋白中。

在RAGE多肽包含移除糖基化位點之點突變的融合蛋白之某些實施例中，該點突變可位於RAGE配位體結合域中。在該種實施例中，移除糖基化位點之點突變或者可在不包括信號序列之融合蛋白之N端的前100、90、80、70、60、50、40或30個胺基酸內。

在另一實施例中，本發明提供任何前述實施例之融合蛋白，其中：(a) RAGE多肽包含人類野生型RAGE肽(SEQ ID NO: 3)中含有RAGE配位體結合域及SEQ ID NO: 3之至少前200個胺基酸的片段，且其中RAGE多肽(i)在殘基2或58

之一或兩者處包含一或多個點突變以移除及/或改變糖基化位點；及/或(ii)在殘基193至198中之一或多者處包含一點突變以移除及/或改變弗林蛋白酶裂解位點；且(b)免疫球蛋白多肽包含免疫球蛋白之C_H2域及C_H3域之至少一個片段。在一些實施例中，本發明提供任何前述實施例之融合蛋白，其中RAGE配位體結合域包含融合蛋白之大部分N端域。

在一些實施例中，RAGE多肽包含選自由以下組成之群的點突變：(a) N2Q；(b) N58Q；(c) N2Q及N58Q，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽包含SEQ ID NO: 13、14、15、16、46、48或49。在其他實施例中，RAGE多肽包含選自由以下組成之群的點突變：(a) N2Q；(b) N58Q；(c)N2Q及N58Q，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽為SEQ ID NO: 13、14、15、16、46、48或49。

在其他實施例中，點突變對應於選自由以下組成之群的點突變：(a) R195A；(b) R195K；(c) R198A；(d) R198K；(e) R198H；及(f) R198T，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽包含SEQ ID NO: 5、6、17、18、19、20、45、50或51。或者，點突變對應於選自由以下組成之群的點突變：(a) R195A；(b) R195K；(c) R198A；(d) R198K；(e) R198H；及(f) R198T，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽為SEQ ID NO: 5、6、17、18、19、20、45、50或51。

在其他實施例中，點突變對應於選自由以下組成之群的點突變：(a) N2Q；(b) N58Q；(c) N2Q及N58Q；(d) R195A；(e) R195K；(f) R198A；(g) R198K；(h) R198H；(i) R198T；(j) N2Q及R198A；(k) N58Q及R198A；及(l) N2Q、N58Q及R198A，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽包含SEQ ID NO: 5、6、17、18、19、20、45、50或51。在其他實施例中，點突變對應於選自由以下組成之群的點突變：(a) N2Q；(b) N58Q；(c) N2Q及N58Q；(d) R195A；(e) R195K；(f) R198A；(g) R198K；(h) R198H；(i) R198T；(j) N2Q及R198A；(k) N58Q及R198A；及(l) N2Q、N58Q及R198A，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽為SEQ ID NO: 5、6、17、18、19、20、45、50或51。

在其他實施例中，點突變對應於選自由以下組成之群的點突變：單獨或呈任何可能之組合形式的R195H、R195T及/或G59S，及/或上述突變與R195H、R195T及/或G59S中之至少一者的組合，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽包含SEQ ID NO: 5、6、17、18、19、20、45、50或51。在其他實施例中，點突變對應於選自由以下組成之群的點突變：單獨或呈任何可能之組合形式的R195H、R195T及/或G59S，及/或上述突變，其中突變位置係相對於SEQ ID NO: 3，且其中RAGE多肽為SEQ ID NO: 5、6、17、18、19、20、45、50或51。

以下表1提供本發明之例示性突變之非限制性彙編，其

中相對於具有如SEQ ID NO: 34所示之胺基酸序列之RAGE融合蛋白提供突變位置。表1之實際胺基酸序列(亦即SEQ ID NO: 62至81、SEQ ID NO: 92至190及SEQ ID NO: 58-61、82、200及201)展示於圖6A-6EE中。

表 1

突變	TTP4000之加工變異體(SEQ ID NO:)					
	(-)1-23 信號	(-)1-23 信號 (-) C端K	(-)1-23 信號 (+) pE	(-)1-24 信號	(-)1-24 信號 (-) C端K	(-)1-23信號 (-)C端K (+) pE
N2Q	62	92	112	132	152	172
N58Q	63	93	113	133	153	173
N2Q、N58Q	64	94	114	134	154	174
R195A	65	95	115	135	155	175
R195K	66	96	116	136	156	176
R198A	67	97	117	137	157	177
R198K	68	98	118	138	158	178
R198H	69	99	119	139	159	179
R198T	70	100	120	140	160	180
N2Q、R198A	71	101	121	141	161	181
N58Q、R198A	72	102	122	142	162	182
N2Q、N58Q、R198A	73	103	123	143	163	183
N288Q	74	104	124	144	164	184
N2Q、N288Q	75	105	125	145	165	185
N58Q、N288Q	76	106	126	146	166	186
N2Q、N58Q、N288Q	77	107	127	147	167	187
N2Q、R198A、N288Q	78	108	128	148	168	188
N58Q、R198A、N288Q	79	109	129	149	169	189
N2Q、N58Q、	80	110	130	150	170	190

R198A、N288Q						
G59S、R198A	81	111	131	151	171	200
N2Q、G59S、R198A	58	59	60	61	82	201

在其他實施例中，本發明之融合蛋白包含與上述序列之一至少70%、75%、80%、85%、90%、95%、96%、97%、98%或99%一致的胺基酸序列。在其他實施例中，本發明之融合蛋白包含與SEQ ID NO: 62至81、SEQ ID NO: 92至190、或SEQ ID NO: 58-61、82、200或201至少70%、75%、80%、85%、90%、95%、96%、97%、98%或99%一致的胺基酸序列，其中RAGE融合蛋白之RAGE多肽部分(i)在一或多個殘基處包含一或多個點突變以移除及/或改變糖基化位點；及/或(ii)在一或多個殘基處包含一點突變以移除及/或改變弗林蛋白酶裂解位點。

在另一實施例中，本發明之融合蛋白包含如SEQ ID NO: 62至81、SEQ ID NO: 92至190或SEQ ID NO: 58-61、82、200或201中之任一者所示的胺基酸序列。在另一實施例中，本發明之融合蛋白為SEQ ID NO: 62至81、SEQ ID NO: 92至190或SEQ ID NO: 58-61、82、200或201中之任一者的胺基酸序列。

本發明之融合蛋白之RAGE多肽可包含含有RAGE配位體結合域之哺乳動物野生型RAGE肽之片段。在一實施例中，RAGE肽之片段可包含來自野生型RAGE肽之至少一段不間斷的25、26、27、28、29、30、31、32、33、34、35、36、37、38、39、40、41、42、43、44、45、46、

47、48、49、50、55、60、65、70、75、80、85、90、95、100、105、110、115、120、125、130、135、140、145、150、155、160、165、170、175、180、185、190、195、200、205、210、215、220、225、230、235、240、245或250個胺基酸的序列。在一實施例中，RAGE多肽包含SEQ ID NO: 6(圖1C)之人類野生型RAGE肽之片段。

任何前述實施例之RAGE多肽之RAGE配位體結合域可包含RAGE V域，參見例如SEQ ID NO: 7、SEQ ID NO: 8、SEQ ID NO: 46(圖1D及1K)及SEQ ID NO: 191、SEQ ID NO: 192或SEQ ID NO: 193(圖8C)。或者，可使用與RAGE V域或其片段至少95%一致之序列。

在另一實施例中，任何前述實施例之RAGE配位體結合域可包含SEQ ID NO: 9或與其至少95%一致之序列、或SEQ ID NO: 10或與其至少95%一致之序列(圖1D)、或SEQ ID NO: 47或與其至少95%一致之序列(圖1K)、或SEQ ID NO: 194或與其至少95%一致之序列、或SEQ ID NO: 195或與其至少95%一致之序列(圖8C)。

在另一實施例中，配位體結合域可包含SEQ ID NO: 1(圖1)之胺基酸23-53。在另一實施例中，配位體結合域可包含SEQ ID NO: 1之胺基酸24-52。在另一實施例中，配位體結合域可包含SEQ ID NO: 1之胺基酸31-52。在另一實施例中，配位體結合域可包含SEQ ID NO: 1之胺基酸31-116。在另一實施例中，配位體結合域可包含SEQ ID NO: 1之胺基酸19-52。舉例而言，配位體結合域可包含

RAGE V域或其一部分，諸如RAGE配位體結合域(例如SEQ ID NO: 1之胺基酸1-118、23-118、24-118、31-118、1-116、23-116、24-116、31-116、1-54、23-54、24-54、31-54、1-53、23-53、24-53或31-53或其片段)。或可使用功能性結合RAGE配位體之多肽片段。或者，可使用與RAGE V域或其片段(例如如上所述)至少70%、75%、80%、85%、90%、95%、97%、98%或99%一致之序列。

另外，如此項技術中所知，在融合蛋白之N端為麩醯胺酸(例如在移除包含SEQ ID NO: 1之殘基1-23之信號序列之後)之實施例中，麩醯胺酸(例如對於包含胺基酸24-118之多肽或SEQ ID NO: 1而言為Q24)可環化而形成焦麩胺酸(pE)。如本文所述，在N端麩醯胺酸環化成pE之此等實施例之各者中，包含RAGE配位體結合域之序列可含有至少一個改變糖基化位點之點突變，或含有一個移除糖基化位點之點突變，或可含有兩個或兩個以上移除及/或改變兩個糖基化位點之點突變。此外，RAGE序列可包含改變及/或移除酶(例如弗林蛋白酶)裂解位點之突變。

如本文中更詳細描述，本發明之RAGE融合蛋白可表現於細胞中。圖7提供可用於編碼本發明之RAGE融合蛋白的核酸序列，其中SEQ ID NO: 221包含野生型核酸序列(亦即人類RAGE及人類免疫球蛋白之野生型)，及針對表現經最佳化之核酸序列(SEQ ID NO: 222)。此外，圖8A提供對應於人類RAGE之信號序列的野生型及經修飾核酸序列(SEQ ID NO: 84及85)。

因此，在某些實施例中，RAGE多肽可進一步包含信號序列殘基。舉例而言，融合蛋白之信號序列可包含天然人類RAGE信號序列(SEQ ID NO: 83)或已自天然序列經修飾而成之信號序列(例如SEQ ID NO: 84)、或前導序列具有甘胺酸而非甲硫胺酸作為首個殘基之信號序列(參見例如Neeper等人，1992)。

如此項技術中所公認，當表現於某些重組系統中時，本發明之RAGE融合蛋白的C_H3區可使C端胺基酸經由轉譯後修飾而裂解去除。(參見例如Li，等人，*BioProcessing J.*, **4**:23-30 (2005))。在一實施例中，裂解去除之C端胺基酸為離胺酸(K)。因此，在本發明之蛋白質及蛋白質組合物之各者的替代性實施例中，本發明之RAGE融合蛋白可包含具有無C端離胺酸(K)之胺基酸序列之多肽。此等融合蛋白之非限制性實例包括SEQ ID NO: 92-111、152-171、59及82。

如本文中所論述，融合蛋白亦可包含源於免疫球蛋白之多肽。在各種實施例中，且如本文所揭示之例示性實施例中所說明，RAGE融合蛋白在某一殘基處包含一點突變以移除RAGE融合蛋白之免疫球蛋白多肽內的糖基化位點。舉例而言，在一實施例中，RAGE融合蛋白可包含相對於如SEQ ID NO: 34所示之序列在位置288處之突變(例如N288Q)及/或相對於如SEQ ID NO: 37所示之序列在位置173處之突變(例如N173Q)。

在某些實施例中，免疫球蛋白多肽包含不包括至少一部

分鉸鏈區之C_H2域或C_H2域之片段。舉例而言，在替代性實施例中，不作為C_H2域之一部分被包括之鉸鏈區具有如SEQ ID NO: 223或224所示之序列。在某些實施例中，C_H2域或其片段經由其C端與免疫球蛋白多肽之C_H3域或其片段之N端連接。

因此，在某些實施例中，免疫球蛋白多肽包含免疫球蛋白之C_H2域之至少一個片段及C_H3域之至少一個片段。在一實施例中，免疫球蛋白多肽可包含免疫球蛋白重鏈或其一部分(亦即片段)。舉例而言，重鏈片段可包含源於免疫球蛋白之Fc片段之多肽，其中該Fc片段包含重鏈鉸鏈多肽及免疫球蛋白重鏈之呈單體形式的C_H2及C_H3域。重鏈(或其部分)可源於以下任一已知重鏈同型：IgG(γ)、IgM(μ)、IgD(δ)、IgE(ε)或IgA(α)。此外，重鏈(或其部分)可源於以下任一已知重鏈亞型：IgG1(γ1)、IgG2(γ2)、IgG3(γ3)、IgG4(γ4)、IgA1(α1)、IgA2(α2)，或此等同型或亞型之改變生物活性的突變體。免疫球蛋白可包含人類IgG1之C_H2及C_H3域或此等域中之任一者或兩者之部分。在一個例示性實施例中，包含人類IgG1之C_H2及C_H3域或其一部分之多肽可包含SEQ ID NO: 40(圖1)或其一部分。在一實施例中，包含人類IgG1之C_H2及C_H3域或其一部分之多肽可包含SEQ ID NO: 38或其片段。免疫球蛋白肽可由SEQ ID NO: 39或SEQ ID NO: 41(圖1)之核酸序列編碼。SEQ ID NO: 38或SEQ ID NO: 40中之免疫球蛋白序列亦可由SEQ ID NO: 52或SEQ ID NO: 53(圖1)編碼，其中在序列之C端

處沉默鹼基向編碼脯胺酸(CCG變成CCC)及甘胺酸(GGT變成GGG)之密碼子改變移除末端密碼子附近的隱蔽性RNA剪接位點(亦即SEQ ID NO: 39之核苷酸622-627經修飾而產生SEQ ID NO: 52或SEQ ID NO: 41之核苷酸652-657經修飾而產生SEQ ID NO: 53)。在另一實施例中，C_H2域或其片段包含SEQ ID NO: 42(圖1)。在另一實施例中，SEQ ID NO: 42之片段包含構成至少一部分Fc鉸鏈區之前10或11個胺基酸已經移除的SEQ ID NO: 42(參見例如SEQ ID NO: 90或91)。

免疫球蛋白鏈之Fc部分之鉸鏈區在活體內可具有促炎性。因此，在一實施例中，本發明之RAGE融合蛋白包含源於RAGE之域間連接子而非源於免疫球蛋白之域間鉸鏈多肽。

因此，在某些實施例中，RAGE融合蛋白可包含RAGE多肽直接與免疫球蛋白多肽連接，其中該免疫球蛋白多肽包含免疫球蛋白之C_H2域之至少一個片段及C_H3域之至少一個片段。在一實施例中，C_H2域或其片段包含SEQ ID NO: 42(圖1)。在一實施例中，SEQ ID NO: 42之片段包含構成至少一部分Fc鉸鏈區之前10或11個胺基酸已經移除的SEQ ID NO: 42(參見例如SEQ ID NO: 90或91)(圖8B)。舉例而言，如上所述，在某些實施例中，已自C_H2域移除之此11或10個胺基酸的鉸鏈區分別具有如SEQ ID NO: 223或224所示之序列(圖8C)。

如上所述，在某些實施例中，C_H2域經由其C端與免疫

球蛋白多肽之C_H3域之N端連接。舉例而言，在某些實施例中，融合蛋白之任一前述實施例之免疫球蛋白多肽可包含SEQ ID NO: 86、87、88或89中之任一者。如圖8B中所示，SEQ ID NO: 89包含對應於如SEQ ID NO: 34之RAGE融合蛋白中所示之N288Q的突變以便移除RAGE融合蛋白之免疫球蛋白部分中之糖基化位點。

本發明之RAGE融合蛋白中使用的RAGE多肽可包含一個RAGE免疫球蛋白域或多個RAGE免疫球蛋白域。或者或另外，RAGE之片段可包含域間連接子。舉例而言，RAGE多肽可包含RAGE免疫球蛋白域與上游(亦即較接近N端)或下游(亦即較接近C端)域間連接子連接。

在一些實施例中，RAGE多肽可包含兩個(或兩個以上)各由域間連接子連接於彼此的RAGE免疫球蛋白域。在此等實施例中，RAGE多肽可包含多個由一或多個域間連接子連接於彼此的RAGE免疫球蛋白域。RAGE多肽可進一步包含末端域間連接子與N端RAGE免疫球蛋白域及/或C端免疫球蛋白域連接。RAGE免疫球蛋白域與域間連接子之其他組合屬於本發明範疇內。

在一實施例中，RAGE多肽包含RAGE域間連接子與RAGE免疫球蛋白域連接，以至於RAGE免疫球蛋白域之C端胺基酸與RAGE域間連接子之N端胺基酸連接，且RAGE域間連接子之C端胺基酸直接與免疫球蛋白多肽之N端胺基酸連接。如上所述，包含免疫球蛋白之C_H2域之多肽可包含免疫球蛋白之C_H2域及C_H3域之至少一個片段，例如人

類IgG1之C_H2及C_H3域之至少一個片段。舉例而言，免疫球蛋白多肽可包含已至少部分移除鉸鏈區之C_H2域的片段。

在一實施例中，RAGE融合蛋白可包含2個源於RAGE蛋白之免疫球蛋白域及2個源於人類Fc多肽之免疫球蛋白域。RAGE融合蛋白可包含第一RAGE免疫球蛋白域及第一RAGE域間連接子與第二RAGE免疫球蛋白域及第二RAGE域間連接子連接，以至於第一域間連接子之N端胺基酸與第一RAGE免疫球蛋白域之C端胺基酸連接，第二RAGE免疫球蛋白域之N端胺基酸與第一域間連接子之C端胺基酸連接，第二域間連接子之N端胺基酸與第二RAGE免疫球蛋白域之C端胺基酸連接，且RAGE第二域間連接子之C端胺基酸與C_H2免疫球蛋白域之N端胺基酸連接。在另一實施例中，RAGE第二域間連接子之C端胺基酸直接與C_H2免疫球蛋白域之N端胺基酸連接。此等構築體之實例如SEQ ID NO: 32、33、34及56所提供(圖4)。

或者，三域RAGE融合蛋白可包含1個源於RAGE之免疫球蛋白域及2個源於人類Fc多肽之免疫球蛋白域。舉例而言，RAGE融合蛋白可包含單一RAGE免疫球蛋白域經由RAGE域間連接子與C_H2免疫球蛋白域或C_H2免疫球蛋白域之一部分的N端胺基酸連接。在另一實施例中，RAGE域間連接子之C端胺基酸直接與C_H2免疫球蛋白域或C_H2免疫球蛋白域之一部分的N端胺基酸連接。此等構築體之實例如SEQ ID NO: 35、36、37及57所提供(圖5)。

RAGE域間連接子片段可包含天然位於RAGE免疫球蛋白域之下游且因此與RAGE免疫球蛋白域連接的肽序列。舉例而言，對於RAGE V域，域間連接子可包含天然位於V域之下游的胺基酸序列(圖1F)。在一實施例中，連接子可包含SEQ ID NO: 21，對應於全長RAGE(SEQ ID NO: 1)之胺基酸117-123。或者，連接子可包含具有天然RAGE序列之其他部分的肽。舉例而言，可使用包含在SEQ ID NO: 21之上游及下游之若干個胺基酸(例如1-3、1-5、或1-10或1-15個胺基酸)的域間連接子。因此，在一實施例中，域間連接子包含含有全長RAGE(SEQ ID NO: 1)之胺基酸117-136的SEQ ID NO: 23。或者，可使用自連接子之任一端缺失例如1、2或3個胺基酸之SEQ ID NO: 21的片段。在替代性實施例中，連接子可包含與SEQ ID NO: 21或SEQ ID NO: 23至少70%、75%、80%、85%、90%、95%、96%、97%、98%或99%一致之肽。

對於RAGE C1域，連接子可包含天然位於C1域之下游的肽序列。在一實施例中，連接子可包含SEQ ID NO: 22，對應於全長RAGE(SEQ ID NO: 1)之胺基酸222-251。或者，連接子可包含具有天然RAGE序列之其他部分的肽。舉例而言，可使用包含在SEQ ID NO：22之上游及下游之若干個胺基酸(例如1-3、1-5、或1-10或1-15個胺基酸)的連接子。或者，可使用自連接子之任一端缺失例如1-3、1-5、或1-10、或1-15個胺基酸之SEQ ID NO: 22的片段。舉例而言，在一實施例中，RAGE域間連接子可包含SEQ ID

NO: 24，對應於全長RAGE(SEQ ID NO: 1)之胺基酸222-226。在替代性實施例中，連接子可包含與SEQ ID NO: 22或SEQ ID NO: 24至少70%、75%、80%、85%、90%、95%、96%、97%、98%或99%一致之肽。

本文提供可用於產生移除糖基化位點及/或酶裂解位點之各種點突變之胺基酸取代的實例。因此，如本文所述，可用麩醯胺酸(Q)取代天冬醯胺(N)。此外，可用離胺酸(K)或組胺酸(H)取代精胺酸(R)。或者，在替代性實施例中，可用例如丙胺酸(A)或蘇胺酸(T)之中性胺基酸取代精胺酸(R)。或者，可用中性胺基酸取代彼此，例如可用絲胺酸(S)取代甘胺酸(G)。

另外，熟習此項技術者將認識到改變、添加或缺失編碼序列中之單一胺基酸或較小百分比之胺基酸(通常小於約5%，更通常小於約1%)的個別取代、缺失或添加為保守修飾之變異，其中改變導致某個胺基酸經一個在化學上類似之胺基酸取代。此項技術中熟知提供功能上類似之胺基酸的保守性取代表。以下實例群組各含有可保守性取代彼此之胺基酸：

1)丙胺酸(A)、絲胺酸(S)、蘇胺酸(T)；

2)天冬胺酸(D)、麩胺酸(E)；

3)天冬醯胺(N)、麩醯胺酸(Q)；

4)精胺酸(R)、離胺酸(K)；

5)異白胺酸(I)、白胺酸(L)、甲硫胺酸(M)、纈胺酸(V)；及

6)苯丙胺酸(F)、酪胺酸(Y)、色胺酸(W)。

一般而言，保守性取代為取代性胺基酸(天然存在或經修飾)在結構上與所取代之胺基酸相關，亦即具有與所取代之胺基酸大致相同之尺寸及電子性質的取代。因此，取代性胺基酸將在側鏈中具有與原始胺基酸相同或類似之官能基。「保守性取代」亦可涉及利用除側鏈中之官能基經適合保護基保護以外與所取代之胺基酸相同的取代性胺基酸。

此外，如此項技術中所知，胺基酸可藉由酶促或非酶促反應機制自其天然結構而經化學修飾。舉例而言，在一實施例中，N端麩胺酸或麩醯胺酸可隨著水之失去而環化以形成焦麩胺酸(pyroE或pE)(Chelius等人，*Anal.Chem*, **78**: 2370-2376 (2006)及Burstein等人，*Proc. National Acad. Sci.*, **73**:2604-2608 (1976))。或者，具有N端焦麩胺酸之融合蛋白可潛在地經由編碼蛋白質中經由轉譯後加工變為N端(例如當SEQ ID NO：1之殘基24為麩胺酸而非麩醯胺酸時)之位置處之麩胺酸的核酸序列而獲得。本發明之融合蛋白包含其他化學修飾，其可在表現及/或純化期間藉由酶促或非酶促反應機制發生，或可經添加而有助於蛋白質功能之其他態樣。

本發明融合蛋白可活體內或活體外經由非共價相互作用締合而形成多聚體。因此，在融合蛋白之任何前述實施例中，融合蛋白可呈單體、二聚體、三聚體、四聚體或其混合物形式。

存在有可與本發明之特定實施例相關的各種優點。在某些實施例中，且如下文中更詳細論述，相對於含有未突變野生型RAGE肽之相應融合蛋白，本發明之RAGE融合蛋白在向個體投與時可具有代謝穩定性。

此外，如下文中更詳細論述，相對於含有未突變野生型RAGE肽之相應融合蛋白，本發明之RAGE融合蛋白可對RAGE配位體展現較高親和力結合。在某些實施例中，本發明之RAGE融合蛋白以高奈莫耳至低微莫耳範圍內之親和力結合於RAGE配位體。藉由以高親和力與生理RAGE配位體結合，本發明之RAGE融合蛋白可用於抑制內源性配位體與RAGE結合，藉此提供一種改善RAGE介導之疾病之手段。

產生RAGE融合蛋白之方法

本發明亦包含一種製備任一上述融合蛋白實施例之RAGE融合蛋白的方法。因此，在一實施例中，本發明包含表現編碼任一本文所述之融合蛋白實施例的核酸序列。

本發明之核酸構築體可編碼具有如本文所述之實施例中之各者的RAGE融合蛋白。舉例而言，在某些實施例中，本發明包含編碼包含RAGE多肽與免疫球蛋白多肽連接之融合蛋白的經分離核酸，其中該RAGE多肽包含具有配位體結合域之哺乳動物RAGE的片段，且其中該融合蛋白相對於野生型序列在該RAGE多肽或該免疫球蛋白多肽之至少一者中包含至少一個突變，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。在某些實施例

中，免疫球蛋白多肽包含C_H2域之至少一個片段。在某些實施例中，C_H2域或其片段不包括鉸鏈區。此外，在某些實施例中，酶裂解位點為弗林蛋白酶裂解位點。

RAGE融合蛋白可藉由重組DNA技術而經工程改造。舉例而言，在一實施例中，本發明可包含核酸序列，其包含以下序列、與以下序列互補或與以下序列具有顯著一致性：編碼任一上述融合蛋白實施例之聚核苷酸序列。舉例而言，所連接之RAGE多肽及免疫球蛋白多肽可由重組DNA構築體編碼。方法可進一步包含將DNA構築體併入表現載體中之步驟。此外，方法可包含將表現載體插入宿主細胞中之步驟。

以上關於本發明之各種RAGE融合蛋白所述之實施例中的各者皆包括在用於產生此等RAGE融合蛋白之核酸構築體、表現載體及宿主細胞中。

因此，本發明之實施例可包含編碼本發明之RAGE融合蛋白之核酸分子。在某些實施例中，本發明提供一種編碼胺基酸序列SEQ ID NO: 62至81、92至190、58至61、82或200、201之一的核酸分子。

在其他實施例中，核酸分子編碼包含與表1之RAGE融合蛋白(亦即SEQ ID NO: 62至81、92至190、58至61、82或201)之一至少70%、75%、80%、85%、90%、95%、96%、97%、98%或99%一致之胺基酸序列的RAGE融合蛋白，其中RAGE融合蛋白之RAGE多肽部分(i)在一或多個殘基處包含一或多個點突變以移除及/或改變糖基化位點；及/或(ii)

在一或多個殘基處包含一點突變以移除及/或改變弗林蛋白酶裂解位點。

在另一實施例中，核酸編碼包含免疫球蛋白多肽之融合蛋白，其中該免疫球蛋白多肽相對於天然免疫球蛋白胺基酸序列在該免疫球蛋白多肽中包含移除及/或改變糖基化位點的點突變。

點突變可經選擇以在RAGE融合蛋白之性質方面提供有益效應。舉例而言，在某些實施例中，點突變改變野生型RAGE多肽中存在於糖基化位點處之序列。以此方式，糖基化之類型及/或程度可被改變。

糖基化位點可為見於蛋白質中之各種類型之糖基化位點之一。舉例而言，在某些實施例中，糖基化識別位點為NXS或NXT。在某些實施例中，X不為脯胺酸。因此，在某些實施例中，點突變使野生型RAGE多肽之序列自NIT改變成QIT及/或自NGS改變成QGS、及/或自NGS改變成NSS及/或自NST改變成QST以移除及/或改變至少一個糖基化位點。在一些實施例中，糖基化位點位於RAGE融合蛋白之RAGE部分中。舉例而言，在某些實施例中，糖基化位點可位於配位體結合位點或配位體結合域內。或者及/或另外，糖基化位點位於RAGE融合蛋白之免疫球蛋白部分中。或者，可靶向可存在於RAGE融合蛋白中之其他糖基化位點。

在某些實施例中，酶裂解位點為弗林蛋白酶裂解位點，因此點突變改變野生型RAGE多肽中存在於弗林蛋白酶裂

解RAGE多肽之識別位點處的序列。舉例而言，在替代性實施例中，點突變使野生型RAGE多肽之序列發生以下之一種改變：(i)PRHRALR變成PRHAALR；(ii)PRHRALR變成PRHKALR；(iii)PRHRALR變成PRHRALA；(iv)PRHRALR變成PRHRALK；(v)PRHRALR變成PRHRALH；(vi)PRHRALR變成PRHRALT；(vii)PRHRALR變成PRHHALR；或(viii)PRHRALR變成PRHTALR，以移除及/或改變弗林蛋白酶裂解位點。

在其他實施例中，核酸包含與SEQ ID NO: 202、203、204、205、206、207、208、209、210、211、212、213、214、215、216、217、218、219或220至少70%、75%、80%、85%、90%、95%、96%、97%、98%或99%一致之的核酸序列，其中該核酸序列編碼一種融合蛋白，其中該融合蛋白之RAGE多肽部分(i)在一或多個殘基處包含一或多個點突變以移除及/或改變糖基化位點；及/或(ii)在一或多個殘基處包含一點突變以移除及/或改變弗林蛋白酶裂解位點。在另一實施例中，本發明提供一種核酸序列，其包含SEQ ID NO: 202、203、204、205、206、207、208、209、210、211、212、213、214、215、216、217、218、219或220。

如本文中更詳細描述，本發明之RAGE融合蛋白可表現於培養之細胞中以便產生經純化蛋白質製劑。圖7提供可用於編碼本發明之RAGE融合蛋白之核酸序列，其中SEQ ID NO: 221包含野生型核酸序列(亦即人類RAGE及人類免

疫球蛋白之野生型)，及針對細胞培養表現經最佳化之核酸序列(SEQ ID NO: 222)。此外，圖8A提供對應於人類RAGE之信號序列之野生型及經修飾核酸序列(SEQ ID NO: 84及85)。

因此，在某些實施例中，編碼本發明RAGE多肽之核酸分子另外編碼信號序列。如本文別處所述，RAGE多肽可包含天然信號序列(SEQ ID NO: 83)或已自天然序列修飾以達成在細胞培養中表現改良的信號序列。因此，編碼本發明RAGE多肽之核酸分子可進一步包含天然核酸信號序列(SEQ ID NO: 84)或已自天然核酸序列修飾之核酸信號序列(例如SEQ ID NO: 85)。

本發明之融合蛋白可包含免疫球蛋白之C_H2及C_H3域之至少一個片段。在一實施例中，免疫球蛋白之C_H2及C_H3域之片段包含SEQ ID NO: 38。免疫球蛋白肽可由SEQ ID NO: 39或SEQ ID NO: 41之核酸序列編碼。SEQ ID NO: 38或SEQ ID NO: 40中之免疫球蛋白序列亦可由SEQ ID NO: 52或SEQ ID NO: 53編碼，其中在序列之C端處沉默鹼基向編碼脯胺酸(CCG變成CCC)及甘胺酸(GGT變成GGG)之密碼子改變移除末端密碼子附近的隱蔽性RNA剪接位點(亦即SEQ ID NO: 39之核苷酸622-627經修飾而產生SEQ ID NO: 52或SEQ ID NO: 41之核苷酸652-657經修飾而產生SEQ ID NO: 53)。

如上所述，RAGE融合蛋白可由重組DNA構築體編碼且方法可包含將DNA構築體併入表現載體中之步驟。因此，

本發明之實施例亦包含編碼核酸之表現載體，其中該等核酸編碼本發明之RAGE融合蛋白。此外，方法可包含將表現載體轉染入宿主細胞中。本發明之表現載體及經轉染宿主細胞可編碼具有如本文所述之實施例中之各者的RAGE融合蛋白。

因此，在某些實施例中，本發明包含含有編碼包含RAGE多肽與免疫球蛋白多肽連接之融合蛋白之經分離核酸的表現載體，其中該RAGE多肽包含具有配位體結合域之哺乳動物RAGE的片段，且其中該融合蛋白相對於野生型序列在該RAGE多肽或該免疫球蛋白多肽之至少一者中包含至少一個突變，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。在某些實施例中，免疫球蛋白多肽包含C_H2域之至少一個片段。此外，在某些實施例中，C_H2域或其片段不包括鉸鏈區。此外，在某些實施例中，酶裂解位點為弗林蛋白酶裂解位點。

然而，本發明之其他實施例亦包含經編碼核酸序列之表現載體轉染之細胞，其中該等核酸序列編碼本發明之RAGE融合蛋白。因此，在某些實施例中，本發明包含經包含編碼融合蛋白之經分離核酸之表現載體轉染的宿主細胞，其中該融合蛋白包含RAGE多肽與免疫球蛋白多肽連接，其中該RAGE多肽包含具有配位體結合域之哺乳動物RAGE的片段，且其中該融合蛋白相對於野生型序列在RAGE多肽或免疫球蛋白多肽之至少一者中具有至少一個突變，其中該突變移除及/或改變糖基化位點或酶裂解位

點中之至少一者。在一些實施例中，免疫球蛋白多肽包含C_H2域之至少一個片段。此外，在某些實施例中，C_H2域或其片段不包括鉸鏈區。此外，在某些實施例中，酶裂解位點為弗林蛋白酶裂解位點。

關於包含將DNA構築體併入表現載體中之本發明方法，可藉由融合不同長度之人類RAGE之5'cDNA序列與人類免疫球蛋白多肽(例如IgG1 Fc(γ1))之3'cDNA序列來構築質體以表現RAGE-IgG融合蛋白。可使用標準重組技術將表現卡匣序列插入諸如pcDNA3.1表現載體(Invitrogen, CA)之表現載體中。或者，可使用其他載體。

關於包含將表現載體轉染入宿主細胞中之本發明方法，RAGE融合蛋白可表現於哺乳動物表現系統，包括使用病毒(諸如反轉錄病毒、腺病毒或桿狀病毒)將表現構築體引入哺乳動物細胞中的系統中。可用作用於表現之宿主之哺乳動物細胞株在此項技術中為熟知的且包括許多可獲自美國菌種保存中心(American Type Culture Collection，ATCC)之永生化細胞株。此等尤其包括中國倉鼠卵巢(CHO)細胞、人類胚腎(HEK)293、NS0、SP2細胞、海拉細胞(HeLa cell)、幼小倉鼠腎(BHK)細胞、猴腎細胞(COS)、人類肝細胞癌細胞(例如Hep G2)、A549細胞、及許多其他細胞株。在某些實施例中，使用CHO或HEK 293細胞。

可藉由測定哪些細胞株具有高RAGE融合蛋白表現量來選擇細胞株。其他可使用之細胞株為昆蟲細胞株，諸如Sf9或Sf21細胞。植物宿主細胞包括例如煙草屬

(Nicotiana)、芥菜屬(Arabidopsis)、浮萍屬(duckweed)、玉米、小麥、馬鈴薯等。細菌宿主細胞包括大腸桿菌(E. coli)及鏈黴菌(Streptomyces)物種。酵母宿主細胞包括粟酒裂殖酵母(Schizosaccharomyces pombe)、釀酒酵母(Saccharomyces cerevisiae)及甲醇酵母(Pichia pastoris)當將編碼RAGE融合蛋白基因之重組表現載體引入哺乳動物宿主細胞中時，藉由培養宿主細胞一段足以使RAGE融合蛋白表現於宿主細胞中或分泌RAGE融合蛋白於宿主細胞生長之培養基中之時期來產生RAGE融合蛋白。可使用標準蛋白質純化方法自培養基回收RAGE融合蛋白。

編碼RAGE融合蛋白之核酸分子及包含此等核酸分子之表現載體可用於轉染適合哺乳動物、植物、細菌或酵母宿主細胞。轉型可藉由任何已知用於將聚核苷酸引入宿主細胞中之方法達成。用於將異源聚核苷酸引入哺乳動物細胞中之方法在此項技術中為熟知的且包括葡聚糖介導之轉染、磷酸鈣沈澱、凝聚胺(polybrene)介導之轉染、原生質體融合、電穿孔、囊封聚核苷酸於脂質體中及直接顯微注射DNA於核中。另外，可使用市售轉染劑(例如Fugene 6，購自Roche Molecular Bichemicals及Invitrogen)。

此外，核酸分子可藉由病毒載體引入哺乳動物細胞中。轉型植物細胞之方法在此項技術中為熟知的，包括例如農桿菌屬(Agrobacterium)介導之轉型、基因槍轉型(biolistic transformation)、直接注射、電穿孔及病毒轉型。轉型細菌及酵母細胞之方法亦為此項技術中所熟知。

表現載體亦可使用DNA基因槍傳遞至表現系統，其中質體經沈澱於顯微粒子，較佳金上，且該等粒子經推進入目標細胞或表現系統中。DNA基因槍技術在此項技術中為熟知的且例如「基因槍」之用於將微粒傳遞至細胞中之裝置(例如Helios基因槍，Bio-Rad Labs., Hercules, CA)及傳遞至皮膚中之裝置(PMED Device, PowderMed Ltd., Oxford, UK)可購得。

可使用許多已知技術增強RAGE融合蛋白自產生細胞株之表現。舉例而言，麩胺醯胺合成酶基因表現系統(GS系統)及血漿編碼之新黴素抗性系統(plasma-encoded neomycin resistance system)為常見用於增強在某些條件下之表現的方法。

在某些實施例中，重組表現載體可轉染入中國倉鼠卵巢細胞(CHO)或HEK細胞中且經表現最佳化。在替代性實施例中，細胞可產生0.1至20公克/公升、或0.5至10公克/公升、或約1-2公克/公升蛋白質。

如此項技術中所知，此等核酸構築體可藉由突變，例如藉由用包含相關突變之引子進行核酸模板之PCR擴增而修飾。以此方式，可設計包含對RAGE配位體之不同親和力的多肽。在一實施例中，經突變之序列可與起始DNA 90%或90%以上一致。因而，變異體可包括在嚴格條件(亦即等效於在1莫耳鹽中，在DNA雙螺旋之熔融溫度(TM)以下約20-27℃)下雜交之核苷酸序列。

可藉由將表現載體轉染入適當宿主中來表現編碼序列。

舉例而言，重組載體可穩定轉染入中國倉鼠卵巢(CHO)細胞、及表現經選擇及選殖之RAGE融合蛋白之細胞中。在一實施例中，藉由施用抗生素G418，針對質體編碼之新黴素抗性選擇表現重組構築體之細胞。可選擇個別純系且如藉由細胞上清液之西方墨點分析所偵測，表現高含量之重組蛋白質之純系可經增殖，且使用蛋白A管柱藉由親和力層析純化基因產物。

本發明之RAGE融合蛋白可包含超越不包含本文所述之突變之RAGE多肽的改良活體內穩定性。RAGE融合蛋白可進一步經修飾以增加穩定性、功效、效能及生物可用性。因此，本發明之RAGE融合蛋白可藉由轉譯後加工或藉由化學修飾而修飾。舉例而言，RAGE融合蛋白可合成製備以包括L-胺基酸、D-胺基酸或非天然胺基酸、α雙取代胺基酸、或N-烷基胺基酸。另外，蛋白質可藉由乙醯化、醯化、ADP-核糖基化、醯胺化、連接脂質(諸如磷脂醯肌醇(phosphatidyinositol))、形成雙硫鍵及其類似修飾而修飾。此外，可添加聚乙二醇以增加RAGE融合蛋白之生物穩定性。

RAGE拮抗劑與RAGE融合蛋白之結合

本發明之RAGE融合蛋白可用於許多應用中。舉例而言，本發明之RAGE融合蛋白可在結合檢測中使用以鑑別RAGE配位體，諸如RAGE促效劑、拮抗劑或調節劑。

舉例而言，在一實施例中，本發明提供一種偵測RAGE調節劑之方法，其包含：(a)提供任一以上實施例之RAGE

融合蛋白；(b)混合相關化合物及對RAGE具有已知結合親和力之配位體與該RAGE融合蛋白；及(c)量測在該相關化合物存在下，該已知RAGE配位體與該RAGE融合蛋白之結合。

RAGE融合蛋白亦可用於偵測RAGE調節劑之套組中。舉例而言，在一實施例中，本發明套組可包含：(a)對RAGE具有已知結合親和力之化合物作為陽性對照；(b)任一以上實施例之RAGE融合蛋白；及(c)使用說明書。

舉例而言，RAGE融合蛋白可在基本上如描述於美國專利第6,908,741號中之用以鑑別潛在RAGE配位體的結合檢測中使用，該專利以全文引用的方式併入本文中。在該種結合檢測之一個例示性實施例中，已知RAGE配位體可以每孔約5微克之濃度塗鋪於固體基板(例如Maxisorb板)上，其中各孔含有約100微升(μL)之總體積。板可在4℃下培育隔夜以使配位體吸附或結合基板。或者，可使用較高溫度(例如室溫)下較短之培育期。在允許配位體結合基板之一段時期之後，可抽吸檢測孔且可添加阻斷緩衝液(例如1% BSA於50 mM咪唑緩衝液(pH 7.2)中)以阻斷非特異性結合。舉例而言，在室溫下，阻斷緩衝液可添加至板中，持續1小時。板可接著經抽吸及/或用洗滌緩衝液洗滌。在一實施例中，包含20 mM咪唑、150 mM NaCl、0.05%吐溫-20(Tween-20)、5 mM $CaCl_2$及5 mM $MgCl_2$之緩衝液(pH 7.2)可用作洗滌緩衝液。RAGE融合蛋白可接著以遞增稀釋度添加至檢測孔中。可接著使RAGE融合蛋白與檢測孔中

固定之配位體一起培育以使結合可達成平衡。在一實施例中，在37℃下使RAGE融合蛋白與固定之配位體一起培育約1小時。在替代性實施例中，可使用較低溫度下較長之培育期。在已培育RAGE融合蛋白及固定之配位體之後，板可經洗滌以移除任何未結合之RAGE融合蛋白。與固定之配位體結合之RAGE融合蛋白可以多種方式偵測。在一實施例中，偵測使用ELISA。因此，在一實施例中，含有單株小鼠抗人類IgG1、經生物素標記之山羊抗小鼠IgG及抗生蛋白(avidin)連接之鹼性磷酸酶的免疫偵測複合物可添加至檢測孔中固定的RAGE融合蛋白中。可使免疫偵測複合物與固定之RAGE融合蛋白結合以使RAGE融合蛋白與免疫偵測複合物之間的結合達成平衡。舉例而言，可在室溫下使複合物與RAGE融合蛋白結合1小時。在彼點時，可藉由用洗滌緩衝液洗滌檢測孔移除任何未結合之複合物。可藉由添加鹼性磷酸酶受質磷酸對硝苯酯(PNPP)且將PNPP向對硝苯酚(PNP)之轉化量測為405 nm下吸光度之增加來偵測結合之複合物。

本發明之結合檢測可用於定量配位體與RAGE之結合。在一實施例中，RAGE配位體以奈莫耳(nM)或微莫耳(μM)親和力與RAGE融合蛋白結合。在替代性實施例中，RAGE配位體可以在0.1至1000奈莫耳(nM)、或1至500 nM、或10至80 nM之範圍內或屬於此等範圍內之範圍的結合親和力與本發明之RAGE融合蛋白結合。

細胞效應之調節

本發明之RAGE融合蛋白之實施例可用於調節由RAGE介導之生物反應。舉例而言，RAGE融合蛋白可經設計以調節RAGE誘導之基因表現增加。因此，在一實施例中，本發明之RAGE融合蛋白可用於調節生物酶之功能。舉例而言，RAGE與其配位體之間的相互作用可產生NF-κB及NF-κB調控之基因(諸如細胞激素IL-1β、TNF-α及其類似物)之氧化壓力及活化。此外，若干其他調控路徑，諸如涉及p21ras、MAP激酶、ERK1及ERK2之調控路徑，已顯示因AGE及其他配位體與RAGE結合而活化。

RAGE融合蛋白之生理特徵

儘管sRAGE可在RAGE介導之疾病之調節方面具有治療益處，但人類sRAGE作為獨立(stand-alone)治療劑可能會具有基於sRAGE在血漿中之半衰期相對較短的限制。舉例而言，儘管齧齒動物sRAGE在正常及糖尿病大鼠中具有約20小時之半衰期，但當藉由sRAGE之免疫反應性保持加以評估時，人類sRAGE具有小於2小時之半衰期(Renard等人，*J. Pharmacol. Exp. Ther.*, **290**:1458-1466 (1999))。

1. 免疫球蛋白鉸鏈之修飾

為了產生具有與sRAGE類似之結合特徵但藥物動力學概況更穩定的RAGE治療劑，可使用包含RAGE配位體結合位點與一或多個免疫球蛋白域連接之RAGE融合蛋白。如此項技術中所知，免疫球蛋白域可包括免疫球蛋白重鏈之Fc部分。

免疫球蛋白Fc部分可賦予RAGE融合蛋白若干屬性。舉

5

例而言，Fc融合蛋白可使此等融合蛋白之血清半衰期增加通常數小時至數天。藥物動力學穩定性之增加通常係由Fc片段之C_H2與C_H3區之間的連接子與FcRn受體的相互作用所導致(Wines等人，*J. Immunol.*, **164**:5313-5318 (2000))。

儘管包含免疫球蛋白Fc多肽之融合蛋白可提供增加穩定性之優點，但此等融合蛋白在引入宿主中時可引發發炎反應。發炎反應可大部分歸因於融合蛋白之免疫球蛋白的Fc部分。若目標在需要消除之患病細胞類型(例如癌細胞及/或導致自體免疫疾病之淋巴細胞之群體)上表現，則促炎反應可為所需特徵。若目標為可溶性蛋白質，則促炎反應可為中性特徵，因為大多數可溶性蛋白質不活化免疫球蛋白。然而，若目標在其破壞將導致不良副作用之細胞類型上表現，則促炎反應可為負性特徵。此外，若發炎性級聯在融合蛋白與組織目標結合之位點處建立，則促炎反應可為負性特徵，因為許多發炎介體可對周圍組織不利及/或可導致全身性效應。

免疫球蛋白Fc片段上之主要促炎位點位於C_H1與C_H2之間的鉸鏈區上。此鉸鏈區與各種白血球上之FcR1-3相互作用且觸發此等細胞攻擊目標。(Wines等人，*J. Immunol.*, **164**:5313-5318 (2000))。

作為RAGE所介導疾病之治療劑之RAGE融合蛋白不可以產生發炎反應。因此，本發明之RAGE融合蛋白之實施例可包含含有RAGE多肽與免疫球蛋白域連接之RAGE融合蛋白，其中免疫球蛋白之Fc鉸鏈區經移除且經RAGE多肽置

換。以此方式，RAGE融合蛋白與發炎性細胞上之Fc受體之間的相互作用可降至最小。然而，必需維持適當堆疊及RAGE融合蛋白之各種免疫球蛋白域之間的其他三維結構相互作用。因此，本發明之RAGE融合蛋白之實施例可替換生物學上惰性但結構上類似之使RAGE之V域與C1域分開的RAGE域間連接子、或使RAGE之C1域與C2域分開之RAGE域間連接子，從而代替免疫球蛋白重鏈之正常鉸鏈區。因此，RAGE融合蛋白之RAGE多肽可包含天然見於RAGE免疫球蛋白域之下游之域間連接子序列，以形成RAGE免疫球蛋白域/連接子片段。以此方式，可維持免疫球蛋白域之間由RAGE或免疫球蛋白促成之三維相互作用。

在一實施例中，相較於sRAGE或相較於類似野生型RAGE融合蛋白，本發明之RAGE融合蛋白可包含實質性增加之藥物動力學穩定性。因此，在一實施例中，本發明之RAGE融合蛋白可作為治療RAGE介導之疾病而不產生不可接受之發炎程度的手段，用於拮抗生理配位體與RAGE之結合。相較於IgG，本發明之RAGE融合蛋白可實質性降低產生促炎反應。另外，相對於類似野生型RAGE融合蛋白，本發明之RAGE融合蛋白之血漿濃度可隨時間增加。

2. 移除糖基化及弗林蛋白酶裂解之突變

a. 藥物動力學

在某些實施例中，相對於野生型序列，本發明之RAGE融合蛋白在RAGE多肽或免疫球蛋白多肽之至少一者中具

有至少一個突變，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。舉例而言，一或多個突變可移除弗林蛋白酶裂解位點。或者及/或另外，一或多個突變可移除糖基化位點。

弗林蛋白酶裂解具有裂解包含兩個RAGE域之融合蛋白(例如具有如SEQ ID NO: 32、33、34及56中所示之胺基酸序列)之約位置193-198處的RAGE融合蛋白之潛力。因而，在某些實施例中，弗林蛋白酶裂解位點之突變可預期改良RAGE融合蛋白相較於野生型序列的藥物動力學概況。

此外，融合蛋白之RAGE及/或免疫球蛋白部分中之糖基化位點的突變可能能夠影響蛋白質之穩定性及/或藥物動力學概況。因而，在某些實施例中，糖基化位點之突變可改良RAGE融合蛋白相較於野生型序列的藥物動力學概況。

圖9-11說明相較於具有野生型序列之類似RAGE融合蛋白，本發明之RAGE融合蛋白之實施例可改良藥物動力學概況的程度。圖9-10中之資料展示在以10 mg/kg靜脈內投與本發明之RAGE融合蛋白之後，該RAGE融合蛋白在小鼠中之藥物動力學及穩定性。圖11中之資料展示RAGE融合蛋白在血漿中之活體外穩定性。所使用之RAGE融合蛋白如下：

批次1-來自CHO細胞之SEQ ID NO: 56(野生型)；

批次2-來自HEK細胞之SEQ ID NO: 56(野生型)；

批次3-來自HEK細胞之SEQ ID NO: 67(R198A)；

批次4-來自HEK細胞之SEQ ID NO: 71(R198A及N2Q)；及

批次5-來自HEK細胞之SEQ ID NO: 72(R198A及N58Q)。

如圖9中所示，相較於其他所測試之RAGE融合蛋白，具有R198A(批次3)以及R198A及N2Q突變(批次4)之RAGE融合蛋白可隨時間保持為較高血漿濃度(圖9A及圖9B)。此效應可在0-336小時(圖9A)及0-48小時(圖9B)之時期內觀測到。

圖10展示在向小鼠靜脈內投與(10 mg/kg)之後，所測試之批次1-5之RAGE融合蛋白的平均藥物動力學參數。可發現，用曲線下面積(AUC)評估得知，總體藥物暴露在具有R198A及N2Q突變(批次4)以及R198A及N58Q突變(批次5)之RAGE融合蛋白中可大於野生型RAGE融合蛋白(批次1及2)及僅具有R198A突變之RAGE融合蛋白(批次3)的總體藥物暴露。

此外，在某些實施例中，相較於野生型RAGE融合蛋白，具有突變之RAGE融合蛋白之總身體清除率(Clp)可能不同。因此，可發現，具有R198A及N2Q突變(批次4)以及R198A及N58Q突變(批次5)之RAGE融合蛋白具有比野生型RAGE融合蛋白(批次1及2)及僅具有R198A突變之RAGE融合蛋白(批次3)低的總身體清除率。此外，在某些實施例中，具有R198A及N2Q突變(批次4)以及R198A及N58Q突變(批次5)之RAGE融合蛋白的穩態分佈容積(Vss)可低於批次

1及2(野生型)及批次3(R198A)的穩態分佈容積。

較高活體內血漿濃度可歸因於多種因素。1個因素可為融合蛋白在血漿中之穩定性(亦即相較於RAGE融合蛋白之主動攝取及/或清除)。圖11展示所測試之上述批次1至5之RAGE融合蛋白的活體外穩定性資料。可發現，在某些實施例中，相較於野生型RAGE融合蛋白(批次1及2)或具有R198A突變及在較長時間點具有N58Q及R198A突變之RAGE融合蛋白(批次5)，具有R198A及N2Q突變之RAGE融合蛋白(批次4)具有增加之血漿中穩定性。

因此，在某些實施例中，相較於具有野生型序列之類似蛋白質，具有移除弗林蛋白酶裂解位點之突變(例如R198A)與移除及/或減少RAGE之配位體結合域及/或配位體結合位點中之糖基化之突變(例如N2Q及/或N58Q)兩者的RAGE融合蛋白可提供改良之藥物動力學概況。

b. 配位體結合

RAGE融合蛋白可藉由結合於可在活體內與RAGE相互作用之配位體以至於降低RAGE配位體在個體中之潛在有害效應而充當治療劑。舉例而言，如下文中更詳細論述，具有配位體結合域之RAGE融合蛋白可結合於澱粉樣蛋白-β以便減少且在一些實施例中逆轉阿茲海默氏病中之斑塊形成。

RAGE之糖基化具有降低配位體結合之潛力(參見例如Owasa等人，*Biochimica et Biophysica Acta*, **1770**: 1468-1474 (2007))。初始用在各種條件下培養之野生型RAGE融

合蛋白(例如SEQ ID NO: 32、33、34及56)之研究指示在使糖基化降低之條件下，例如在衣黴素(tunicamycin)(用以抑制在醣蛋白合成之第一步驟中將來自UDP-N-乙醯葡糖胺之N-乙醯葡糖胺-1-磷酸酯(P-GlcNAc)轉移至磷酸多萜醇(dolichol phosphate)的糖基轉移酶)存在下，及/或在2-去氧- D-葡萄糖(例如用以抑制己糖激酶及葡萄糖磷酸異構酶以便降低由此等酶介導之糖基化)中生長來培養RAGE融合蛋白可導致0-聚糖及1-聚糖佔有率增加且伴隨2-聚糖及3-聚糖佔有率降低的RAGE融合蛋白增加，如逆相高壓液相層析(RP-HPLC)及液相層析質譜(LC-MS)所量測。舉例而言，已發現對於自在衣黴素存在下培養之細胞表現之RAGE融合蛋白，存在糖基化自展現約67% 3-聚糖及22% 2-聚糖之RAGE融合蛋白之群體向展現約42% 3-聚糖、16% 2-聚糖及31% 0-聚糖之RAGE融合蛋白之群體的減小。當RAGE融合蛋白自對應於3-聚糖、2-聚糖或0-聚糖RAGE融合蛋白之RP-HPLC峰分離時，已發現相較於具有100%之相對結合之對照RAGE融合蛋白(亦即67% 3-聚糖與22% 2-聚糖RAGE融合蛋白之混合物)，0-聚糖RAGE融合蛋白展現結合增加529%(資料未展示)。關於0-聚糖RAGE融合蛋白所見之結合增加在相較於用3-聚糖溶離份所見之結合時甚至更大(亦即結合約增加10倍)(資料未展示)。

圖12提供展示各種RAGE融合蛋白突變體之相對結合的資料。可發現，如關於N2Q、R198A突變體與N2Q、N288Q、R198A突變體兩者所示，RAGE融合蛋白之N2Q突

變顯著改良配位體(S100b)與RAGE融合蛋白之結合。有趣的是，N2Q、R198A突變體為顯示血漿中之藥物動力學半衰期及穩定性顯著改良的構築體(圖9-11)。

用RAGE融合蛋白治療疾病

本發明亦包含治療人類個體之RAGE介導之病症的方法。在一實施例中，方法可包含向個體投與包含任一前述實施例之RAGE融合蛋白的RAGE融合蛋白。

RAGE融合蛋白可以醫藥調配物形式投與。醫藥調配物可包含RAGE融合蛋白、凍乾保護劑及緩衝劑。

已使用多種動物模型來驗證作為治療劑調節RAGE之化合物的用途。此等模型之實例如下：

a) sRAGE藉由抑制經由RAGE發生之內皮、平滑肌及巨噬細胞活化而在大鼠再狹窄模型中在糖尿病大鼠與正常大鼠兩者中抑制動脈損傷後之新生血管內膜形成(Zhou等人，*Circulation* **107**:2238-2243 (2003))；

b) 使用sRAGE或抗RAGE抗體抑制RAGE/配位體相互作用可在全身性澱粉樣變性病之小鼠模型中減少澱粉樣蛋白斑塊形成(Yan等人，*Nat. Med.*, **6**:643-651 (2000))。伴隨澱粉樣蛋白斑塊減少有所治療動物中發炎性細胞激素介白素-6(IL-6)及巨噬細胞群落刺激因子(M-CSF)之減少以及NF-kB之活化之減低；

c) RAGE轉殖基因小鼠(RAGE過度表現者及RAGE顯性負性表現者)在AD之小鼠模型中展現斑塊形成及認知不足(Arancio等人，*EMBO J.*, **23**:4096-4105 (2004))；

d) 用sRAGE治療糖尿病大鼠降低了血管通透性(Bonnardel-Phu等人，*Diabetes*, **48**:2052-2058 (1999))；

e) 用sRAGE治療減少了糖尿病性脂蛋白元E-缺失小鼠中之動脈粥樣硬化病變且防止在db/db小鼠中有糖尿病腎病變之功能及形態指數(Hudson等人，*Arch. Biochem. Biophys.*, **419**:80-88 (2003))；及

f) sRAGE減弱膠原蛋白誘發之關節炎之小鼠模型(Hofmann等人，*Genes Immunol.*, **3**:123-135 (2002))、實驗性過敏性腦脊隨炎之小鼠模型(Yan等人，*Nat. Med.* **9**:28-293 (2003))及發炎性腸病之小鼠模型(Hofmann等人，*Cell*, **97**:889-901 (1999))中之發炎的嚴重性。

因此，在一實施例中，本發明之RAGE融合蛋白可用於治療糖尿病及/或由RAGE介導之糖尿病引起之併發症的症狀。在替代性實施例中，糖尿病或糖尿病晚期併發症之症狀可包含糖尿病腎病變、糖尿病視網膜病變、糖尿病足部潰瘍、糖尿病之心血管併發症、或糖尿病神經病變。

最初鑑別為表現與糖尿病之病理學相關之分子的受體，RAGE自身對糖尿病併發症之病理生理學至關重要。在活體內，抑制RAGE與其配位體之相互作用已顯示在糖尿病併發症及發炎之多個模型中具有治療性(Hudson等人，*Arch. Biochem. Biophys.*, **419**:80-88 (2003))。舉例而言，用抗RAGE抗體治療兩個月使糖尿病性小鼠中腎功能正常化且使異常腎組織病變減輕(Flyvbjerg等人，*Diabetes* **53**:166-172 (2004))。此外，用結合RAGE配位體且抑制

RAGE/配位體相互作用之可溶形式的RAGE治療減輕糖尿病性脂蛋白元E缺失小鼠中之動脈粥樣硬化病變且減少db/db小鼠中之糖尿病腎病變的功能及形態病變(Bucciarelli等人，*Circulation* **106**:2827-2835 (2002))。

此外，已顯示在腎衰竭中，在高血糖症及與全身性或局部氧化壓力相關之其他病狀存在下，最終導致形成晚期糖基化終產物(AGE)之巨分子的非酶促糖氧化(glycoxidation)在發炎部位增強(Dyer等人，*J. Clin. Invest.*, **91**:2463-2469 (1993)；Reddy等人，*Biochem.*, **34**:10872-10878 (1995)；Dyer等人，*J. Biol. Chem.*, **266**:11654-11660 (1991)；Degenhardt等人，*Cell Mol. Biol.*, **44**:1139-1145 (1998))。AGE在血管結構中之累積可局部發生，如在由見於具有透析相關之澱粉樣變性病之患者中的AGE-β_2-微球蛋白構成之關節澱粉樣蛋白中(Miyata等人，*J. Clin. Invest.*, **92**:1243-1252 (1993)；Miyata等人，*J. Clin. Invest.*, **98**:1088-1094 (1996))，或一般而言，如由糖尿病患者之血管結構及組織例示(Schmidt等人，*Nature Med.*, **1**:1002-1004 (1995))。糖尿病患者中AGE隨時間之累進性累積表明內源性清除機制在AGE沈積部位不能有效發揮作用。此等累積之AGE具有藉由許多機制改變細胞性質之能力。儘管RAGE在正常組織及血管結構中以低含量表現，但在受體之配位體累積之環境中，已顯示RAGE變得經上調(Li等人，*J. Biol. Chem.*, **272**:16498-16506 (1997)；Li等人，*J. Biol. Chem.*, **273**:30870-30878 (1998)；Tanaka等人，*J.*

Biol. Chem., **275**:25781-25790 (2000))。在糖尿病性血管結構之內皮、平滑肌細胞及浸潤性單核吞噬細胞中，RAGE表現增加。此外，細胞培養中之研究已證明AGE-RAGE相互作用引起在血管內平衡(vascular homeostasis)中重要之細胞性質改變。

在其他實施例中，本發明之RAGE融合蛋白亦可用於治療或逆轉澱粉樣疾病及阿茲海默氏病。RAGE為澱粉樣蛋白β(Aβ)以及其他類澱粉蛋白生成蛋白質(包括SAA及支鏈澱粉)之受體(Yan等人，*Nature*, **382**:685-691 (1996)；Yan等人，*Proc. Natl. Acad. Sci., USA*, **94**:5296-5301 (1997)；Yan等人，*Nat. Med.*, **6**:643-651 (2000)；Sousa等人，*Lab Invest.*, **80**:1101-1110 (2000))。此外，包括AGE、S100b及Aβ蛋白質之RAGE配位體見於人類中老年斑周圍之組織中(Luth等人，*Cereb. Cortex* **15**:211-220 (2005)；Petzold等人，*Neurosci. Lett.*., **336**:167-170 (2003)；Sasaki等人，*Brain Res.*, **12**:256-262 (2001；Yan等人，*Restor. Neurol Neruosci.*, **12**:167-173 (1998))。已顯示RAGE結合無論次單元(澱粉樣蛋白-β肽、支鏈澱粉、血清澱粉樣蛋白A、朊病毒源性肽)之組成如何之β片原纖維材料(Yan等人，*Nature*, **382**:685-691 (1996)；Yan等人，*Nat. Med.*, **6**:643-651 (2000))。此外，澱粉樣蛋白之沈積已顯示導致RAGE之表現增強。舉例而言，在阿茲海默氏病(AD)患者之腦中，RAGE在神經元及神經膠質中之表現增加(Yan,等人，*Nature* **382**:685-691 (1996))。與RAGE配位體之表現並

行，RAGE在患有AD之個體之海馬區(hippocampus)中之星形膠質細胞(astrocyte)及微神經膠質細胞中上調，但不在不患有AD之個體中上調(Lue等人，*Exp. Neurol.*, **171**:29-45 (2001))。此等研究結果表明表現RAGE之細胞係經由老年斑附近之RAGE/RAGE配位體相互作用活化。此外，在活體外，微神經膠質細胞之Aβ介導活化可用針對RAGE之配位體結合域的抗體阻斷(Yan等人，*Proc. Natl. Acad. Sci., USA*, **94**:5296-5301 (1997))。亦已證明RAGE可充當原纖維裝配之焦點(focal point)(Deane等人，*Nat. Med.* **9**:907-913 (2003))。

此外，使用sRAGE或抗RAGE抗體活體內抑制RAGE/配位體相互作用可減少全身性澱粉樣變性病之小鼠模型中的澱粉樣蛋白斑塊形成(Yan等人，*Nat. Med.*, **6**:643-651 (2000))。在神經元中過度表現人類RAGE及具有瑞典及倫敦突變之人類澱粉樣前驅體蛋白(APP)(突變hAPP)之雙重轉殖基因小鼠顯現早於其單一突變hAPP轉殖基因對應物的學習缺陷及神經病理學異常。相反，歸因於在相同突變hAPP背景上表現顯性負性形式之RAGE之神經元而具有減弱之Aβ信號傳導能力的雙重轉殖基因小鼠相較於其單一APP轉殖基因對應物，展示神經病理學及學習異常之延遲發作(Arancio等人，*EMBO J.*, **23**:4096-4105 (2004))。

此外，抑制RAGE-澱粉樣蛋白相互作用已顯示降低細胞RAGE及細胞應激標記之表現(以及NF-κB活化)，且減少澱粉樣蛋白沈積(Yan等人，*Nat. Med.*, **6**:643-651 (2000))，表

明RAGE-澱粉樣蛋白相互作用在干擾富含澱粉樣蛋白之環境中之細胞性質中(甚至在早期)及在澱粉樣蛋白累積中均具有作用。

因此，本發明之RAGE融合蛋白亦可用於減輕澱粉樣變性病且減少澱粉樣蛋白斑塊及與阿茲海默氏病(AD)相關之認知功能障礙。如上所述，sRAGE已顯示在AD之動物模型中減少腦中澱粉樣蛋白斑塊形成與隨後發炎性標記之增加兩者。在使用阿茲海默氏病之小鼠模型之研究中，已顯示RAGE拮抗劑可逆轉斑塊形成及認知喪失。在美國專利公開案第US 2005/0026811號中，小分子RAGE拮抗劑可用於抑制阿茲海默氏病小鼠中Aβ沈積之進展及減小先前存在之斑塊的體積(US 2005/0026811，¶¶ 581-586處)。此外，用此等小分子RAGE拮抗劑治療可改良此等阿茲海默氏病小鼠模型中之認知能力(US 2005/0026811，¶¶ 587-590處)。因此，在阿茲海默氏病之小鼠模型中，相較於未用小分子RAGE拮抗劑治療之彼等阿茲海默氏病小鼠，已顯現Aβ斑塊及認知喪失且用小分子RAGE拮抗劑治療之彼等小鼠展現斑塊體積減小及認知能力改良，表明RAGE拮抗劑化合物可延遲或減緩認知能力之喪失，或可改良罹患阿茲海默氏型癡呆症之個體之認知能力。

此外，已在細胞檢測與動物研究兩者中顯示RAGE介導循環Aβ跨越血腦障壁(BBB)之轉胞吞作用(transcytosis)。所述之Aβ轉胞吞作用的增加導致神經元氧化壓力及腦血流量之持續減小。RAGE之效應可由RAGE調節劑(例如抗

RAGE抗體或sRAGE)抑制(參見例如Mackic等人，J. Clin. Invest., 102:734-743 (1998)；亦參見Kumar等人，Neurosci., Program，第141頁 (2000))。此等研究結果已由其他研究證實(參見例如美國專利第6,825,164號，第17欄，第48行至第18欄，第43行；Deane等人，Nature Medicine, 9:907-913 (2003))。減少腦灌注會促成可能與Aβ協同作用而使癡呆症惡化之缺血性病變。此外，腦血流量不足會改變越過血腦障壁之Aβ運輸，藉此減小Aβ清除率及促進Aβ在腦中之累積(參見Girouard及Iadecola, J. Appl. Physiol., 100, 328-335 (2006)，第332頁)。因此，由RAGE拮抗劑促進之腦血流量之增加可減輕阿茲海默氏病之症狀或延遲阿茲海默氏病之顯現之發作，或兩者。舉例而言，RAGE拮抗劑可延遲或減緩認知能力之喪失，或可改良罹患阿茲海默氏型癡呆症之個體之認知能力，或兩者。

阿茲海默氏病可利用NINCDS及DSM準則、簡易智能狀態測驗(Mini-Mental State Examination)及具有特定限制之臨床癡呆症評級系統(Clinical Dementia Rating)診斷。本發明之一態樣包括改良認知能力，其包含投與本發明之RAGE融合蛋白。認知能力可用阿茲海默氏病評估量表之認知分量表(ADAS-cog)評估，如此項技術中所知，其基於0至70之量表對認知功能計分，較高計分指示較大認知損傷。因此，計分減小表明認知改良。本發明之一態樣包括向個體投與本發明之RAGE融合蛋白以減小個體之ADAS-cog計分。個體可為罹患阿茲海默氏型癡呆症、輕度至中

度阿茲海默氏病或重度阿茲海默氏病之人類。

此外，阿茲海默氏病之進展亦可經由檢驗以下四方面之功能而在人類中進行評估：全身(General)、認知、行為及日常生活之活動。該種評估可使用基於臨床醫師詢問之印象變化(CIBIC或CIBIC增強版)來進行。本發明之一態樣包括改良個體功能，其包含投與本發明之RAGE融合蛋白。在一實施例中，個體功能為全身、認知、行為及日常生活之活動中之一或多者。

在另一實施例中，本發明之RAGE融合蛋白可用於治療與頭部損傷相關之癡呆症。在一實施例中，個體之認知能力得以改良。在另一實施例中，個體之認知能力得以維持。在另一實施例中，個體之認知能力之喪失速率得以減緩。

此外，本發明之RAGE融合蛋白可用於治療動脈粥樣硬化及其他心血管病症。因此，已顯示缺血性心臟病在糖尿病患者中尤其高發(Robertson, 等人，*Lab Invest.*, **18**:538-551 (1968)；Kannel等人，*J. Am. Med. Assoc.*, **241**:2035-2038 (1979)；Kannel等人，*Diab. Care*, **2**:120-126 (1979))。此外，研究已顯示動脈粥樣硬化在糖尿病患者中比在未罹患糖尿病之患者中更早發生及更廣泛(參見例如Waller等人，*Am. J. Med.*, **69**:498-506 (1980)；Crall等人，*Am. J. Med.* **64**:221-230 (1978)；Hamby等人，*Chest*, **2**:251-257 (1976)；及Pyorala等人，*Diab. Metab. Rev.*, **3**:463-524 (1978))。儘管在糖尿病背景中動脈粥樣硬化速

發之原因有許多，但已顯示AGE之降低可減少斑塊形成。

在另一實施例中，本發明之RAGE融合蛋白可用於治療癌症。在一實施例中，使用本發明之RAGE融合蛋白治療之癌症包含表現RAGE之癌細胞。舉例而言，可用本發明之RAGE融合蛋白治療之癌症包括某些肺癌、某些神經膠質瘤、某些乳頭狀瘤及其類似癌症。兩性蛋白為一種高遷移率的第I組非組蛋白染色體DNA結合蛋白(Rauvala等人，*J. Biol. Chem.*, **262**:16625-16635 (1987)；Parkikinen等人，*J. Biol. Chem.* **268**:19726-19738 (1993))，其已顯示與RAGE相互作用。已顯示兩性蛋白促進神經突生長，以及充當纖維蛋白溶解系統中蛋白酶複合物之裝配的表面(亦已知促進細胞運動性)。此外，阻斷RAGE之局部腫瘤生長抑制效應已在原發性腫瘤模型(C6神經膠質瘤)、路易斯肺轉移模型(Taguchi等人，*Nature* **405**:354-360 (2000))及表現v-Ha-*ras*轉殖基因之小鼠中之自發出現的乳頭狀瘤(Leder等人，*Proc. Natl. Acad. Sci.*, **87**:9178-9182 (1990))中觀測到。

在另一實施例中，本發明之RAGE融合蛋白可用於治療發炎。在替代性實施例中，本發明之RAGE融合蛋白可用於治療與發炎性腸病相關之發炎、與類風濕性關節炎相關之發炎、與牛皮癬相關之發炎、與多發性硬化症相關之發炎、與低氧症相關之發炎、與中風相關之發炎、與心臟病發作相關之發炎、與出血性休克相關之發炎、與敗血症相關之發炎、與器官移植相關之發炎、與創傷癒合不良相關

之發炎、或與自身(例如自體免疫)或非自身(例如經移植之)細胞、組織或器官之排斥反應相關的發炎。

舉例而言，在用溶血栓藥治療之後，諸如粒細胞之發炎性細胞浸潤缺血組織且產生氧自由基，其會破壞比因低氧症殺死之細胞要多的細胞。用抗體或其他蛋白質拮抗劑抑制嗜中性球上使得嗜中性球能夠浸潤組織之受體已顯示可改善反應。因為RAGE為此嗜中性球受體之配位體，所以含有RAGE之片段之RAGE融合蛋白可充當誘餌(decoy)且防止嗜中性球運輸至再灌注之部位且因此防止進一步的組織破壞。RAGE在防止發炎方面之作用可由顯示sRAGE可能藉由抑制經由RAGE發生之內皮、平滑肌細胞增殖及巨噬細胞活化而在大鼠再狹窄模型中在糖尿病大鼠與正常大鼠兩者中抑制動脈損傷後之新生血管內膜擴張的研究表明(Zhou等人，*Circulation*, **107**:2238-2243 (2003))。此外，sRAGE抑制包括延遲型過敏、實驗性自體免疫性腦炎及發炎性腸病之發炎的模型(Hofman等人，*Cell*, **97**:889-901 (1999))。

在一實施例中，本發明之RAGE融合蛋白可用於治療基於自體免疫之病症。舉例而言，在一實施例中，本發明之RAGE融合蛋白可用於治療腎衰竭。因此，本發明之RAGE融合蛋白可用於治療全身性狼瘡腎炎或發炎性狼瘡腎炎。舉例而言，已證實S100/鈣粒蛋白構成特徵在於兩個由連接肽連接之EF手區域的密切相關之鈣結合多肽的家族(Schafer等人，*TIBS*, **21**:134-140 (1996)；Zimmer等人，

Brain Res. Bull., **37**:417-429 (1995)；Rammes等人，*J. Biol. Chem.*, **272**:9496-9502 (1997)；Lugering等人，*Eur. J. Clin. Invest.*, **25**:659-664 (1995))。儘管其缺乏信號肽，但長久以來已知S100/鈣粒蛋白可進入細胞外空間，尤其在如囊腫性纖維化及類風濕性關節炎中之慢性免疫/發炎性反應的部位處。RAGE為S100/鈣粒蛋白家族之許多成員之受體，其介導該等成員對諸如淋巴細胞及單核吞噬細胞之細胞的促炎效應。此外，關於延遲型過敏反應、IL-10缺失小鼠中之結腸炎、膠原蛋白誘發之關節炎及實驗性自體免疫性腦炎模型之研究表明RAGE-配位體相互作用(推測與S-100/鈣粒蛋白之相互作用)在炎症級聯中具有近端作用(proximal role)。

在一實施例中，本發明之RAGE融合蛋白可用於治療再狹窄。在一實施例中，個體罹患糖尿病。

第I型糖尿病為一種可藉由用本發明之RAGE融合蛋白治療而得以預防或改善的自體免疫病症。舉例而言，已顯示sRAGE可允許脾細胞自非肥胖糖尿病(NOD)小鼠轉移至患有重度複合免疫缺乏症之NOD小鼠(NOD重度複合免疫缺陷小鼠(NOD-scid mice))。NOD-scid小鼠並未自發地展現糖尿病，而是需要存在有能夠破壞胰島細胞之免疫細胞以至於糖尿病因而被誘發。已發現相較於未用sRAGE治療之NOD-scid接受者，用sRAGE治療之NOD-scid接受者展現由自糖尿病(NOD)小鼠轉移之脾細胞誘發之糖尿病的發作降低(美國專利公開案2002/0122799)。如US 2002/0122799中

所述，此模型中使用sRAGE得到之實驗結果與人類疾病有關，諸如未來免疫療法及胰島移植可能出現之臨床背景。

因此，在一實施例中，本發明之RAGE融合蛋白可用於治療與器官、組織或複數個細胞中之至少一者自第一部位移植至第二部位相關的發炎。第一及第二部位可位於不同個體中或位於同一個體中。在替代性實施例中，所移植之細胞、組織或器官包含以下之細胞：胰臟、皮膚、肝、腎、心臟、肺、骨髓、血液、骨、肌肉、內皮細胞、動脈、靜脈、軟骨、甲狀腺、神經系統或幹細胞。舉例而言，投與本發明之RAGE融合蛋白可用於有助於胰島細胞自第一非糖尿病性個體移植至第二糖尿病性個體。

在另一實施例中，本發明可提供一種藉由向個體投與一定量之本發明之RAGE融合蛋白來治療骨質疏鬆症的方法。(Zhou等人，*J. Exp. Med.*, **203**:1067-1080 (2006))。在一實施例中，治療骨質疏鬆症之方法可進一步包含增加個體之骨密度或降低個體之骨密度減小速率的步驟。

因此，在各種所選實施例中，本發明可提供一種抑制個體中AGE與RAGE之相互作用的方法，其係藉由向該個體投與足以抑制此相互作用之一定量的本發明之RAGE融合蛋白來達成。使用本發明之RAGE融合蛋白治療之個體可為動物。在一實施例中，該個體為人類。該個體可罹患AGE相關性疾病，諸如糖尿病、糖尿病併發症，諸如腎病、神經病、視網膜病、足部潰瘍、澱粉樣變性病或腎衰竭及發炎。或者，個體可為患有阿茲海默氏病之個體。在

一個替代性實施例中，個體可為患有癌症之個體。在其他實施例中，個體可罹患全身性紅斑狼瘡(systemic lupus erythmetosis)或發炎性狼瘡腎炎。其他疾病可由RAGE介導且因此可使用本發明之RAGE融合蛋白來治療。因此，在本發明之其他替代性實施例中，RAGE融合蛋白可用於治療人類或動物個體之克羅恩氏病(Crohn's disease)、關節炎、血管炎(vasculitis)、腎病、視網膜病及神經病。在其他實施例中，涉及自體免疫反應(例如自身排斥)與非自體免疫反應(例如非自身排斥)兩者之發炎可由RAGE介導且因此可使用本發明之RAGE融合蛋白來治療。

如上所述，本發明係關於任何前述實施例之用於抑制個體中AGE與RAGE之相互作用的RAGE融合蛋白，該抑制係藉由向該個體投與足以抑制此相互作用之一定量的本發明之RAGE融合蛋白來達成。在一實施例中，RAGE融合蛋白可用於治療RAGE介導之病症或疾病之醫藥中。

因此，本發明之實施例亦係關於RAGE融合蛋白用於治療任一種或數種以下病狀之用途：糖尿病或糖尿病晚期併發症、骨質疏鬆症、澱粉樣變性病、阿茲海默氏病、癌症、腎衰竭、或與自體免疫性、發炎性腸病、類風濕性關節炎、牛皮癬、多發性硬化症、低氧症、中風、心臟病發作、出血性休克、敗血症、器官移植或創傷癒合不良相關之發炎。

本發明亦係關於RAGE融合蛋白用於製造用以治療任一種或數種以下疾病之藥劑的用途：糖尿病或糖尿病晚期併

發症、骨質疏鬆症、澱粉樣變性病、阿茲海默氏病、癌症、腎衰竭、或與自體免疫性、發炎性腸病、類風濕性關節炎、牛皮癬、多發性硬化症、低氧症、中風、心臟病發作、出血性休克、敗血症、器官移植或創傷癒合不良相關之發炎。

治療有效量可包含能夠抑制及/或預防個體中RAGE與AGE或其他類型之內源性RAGE配位體之相互作用的量。因此，該量將隨所治療之個體而變化。化合物之投與可每小時、每日、每週、每月、每年或以單一事件進行。在各種替代性實施例中，RAGE融合蛋白之治療有效量可在每kg體重約1 ng至每kg體重約100 mg、或每kg體重約10 μg至每kg體重約50 mg、或每kg體重約100 μg至每kg體重約20 mg之範圍內。實際有效量可使用此項技術中之標準方法，藉由劑量/反應檢測來確立(Johnson等人，*Diabetes*. **42**: 1179, (1993))。因此，如此項技術中之相關人士所知，有效量可視化合物之生物可用性、生物活性及生物可降解性而定。

組合物

本發明可包括含有任一前述實施例之RAGE融合蛋白及醫藥學上可接受之載劑的組合物。

醫藥學上可接受之載劑可包含此項技術中已知之任何標準的醫藥學上已被接受之載劑。在一實施例中，醫藥載劑可為液體且RAGE融合蛋白或核酸構築體調配物可呈溶液形式。在另一實施例中，醫藥學上可接受之載劑可為呈粉

末、凍乾粉末或錠劑形式之固體。或者，醫藥載劑可為凝膠、栓劑或乳膏。在替代性實施例中，載劑可包含脂質體、微膠囊、聚合物囊封細胞或病毒。因此，術語醫藥學上可接受之載劑涵蓋(但不限於)任何標準的醫藥學上已被接受之載劑，諸如水、醇類、磷酸鹽緩衝生理食鹽水溶液、糖類(例如蔗糖或甘露糖醇)、油或乳液(諸如油/水乳液或三酸甘油酯乳液)、各種類型之濕潤劑、錠劑、包衣錠劑及膠囊劑。

在某些實施例中，RAGE融合蛋白可以中性形式(包括兩性離子形式)或以帶正電或負電之物質形式存在。在一些實施例中，RAGE融合蛋白可與相對離子錯合而形成醫藥學上可接受之鹽。

術語「醫藥學上可接受之鹽」係指包含一或多種RAGE融合蛋白及一或多種相對離子之錯合物，其中該等相對離子源於醫藥學上可接受之無機及有機酸及鹼。

醫藥學上可接受之無機鹼包括金屬離子。更佳之金屬離子包括(但不限於)適當鹼金屬鹽離子、鹼土金屬鹽離子及其他生理學上可接受之金屬離子。源於無機鹼之鹽包括鋁鹽、銨鹽、鈣鹽、鈷鹽、鎳鹽、鉬鹽、釩鹽、錳鹽、鉻鹽、硒鹽、錫鹽、銅鹽、鐵鹽、亞鐵鹽、鋰鹽、鎂鹽、錳鹽、亞錳鹽、鉀鹽、鈷鹽、鈉鹽及鋅鹽，且呈其常見原子價形式。

本發明之RAGE融合蛋白的醫藥學上可接受之酸加成鹽可由包括(但不限於)以下之酸製備：甲酸、乙酸、乙醯胺

基苯甲酸、己二酸、抗壞血酸、硼酸、丙酸、苯甲酸、樟腦酸(camphoric acid)、碳酸、環己胺磺酸、去氫膽酸(dehydrocholic acid)、丙二酸、依地酸(edetic acid)、乙基硫酸、芬地柞酸(fendizoic acid)、偏磷酸、丁二酸、乙醇酸、葡糖酸、乳酸、蘋果酸、酒石酸、鞣酸(tannic acid)、檸檬酸、硝酸、抗壞血酸、葡糖醛酸、順丁烯二酸、葉酸、反丁烯二酸、丙酸、丙酮酸、天冬胺酸、麩胺酸、苯甲酸、鹽酸、氫溴酸、氫碘酸、離胺酸、異檸檬酸、三氟乙酸、雙羥酸(pamoic acid)、丙酸、鄰胺基苯甲酸、甲磺酸、乳清酸(orotic acid)、草酸、酮基丁二酸(oxalacetic acid)、油酸、硬脂酸、水楊酸、胺基水楊酸、矽酸鹽(silicate)、對羥苯甲酸、菸鹼酸、苯乙酸、杏仁酸(mandelic acid)、恩波酸(embonic acid)、磺酸、甲烷磺酸、磷酸、膦酸、乙烷磺酸、乙烷二磺酸、鉀、苯磺酸、泛酸(pantothenic acid)、萘磺酸、甲苯磺酸、2-羥基乙烷磺酸、對胺基苯磺酸、硫酸、硝酸、亞硝酸、硫酸單甲酯、環己基胺磺酸、β-羥基丁酸、甘胺酸、甘胺醯基甘胺酸、麩胺酸、二甲胂酸鹽(cacodylate)、二胺基己酸、樟腦磺酸(camphorsulfonic acid)、葡糖酸、硫氰酸、酮戊二酸(oxoglutaric acid)、5-磷酸吡哆醛、氯苯氧乙酸(chlorophenoxyacetic acid)、十一酸(undecanoic acid)、N-乙醯基-L-天冬胺酸、半乳糖二酸及半乳糖醛酸。

醫藥學上可接受之有機鹼包括三甲胺、二乙胺、N,N'-二苯甲基乙二胺、氯普魯卡因(chloroprocaine)、膽鹼、二

苯甲基胺、二乙醇胺、乙二胺、葡甲胺(N-甲基葡糖胺)、普魯卡因(procaine)、環胺、四級銨陽離子、精胺酸、甜菜鹼、咖啡鹼(caffeine)、克立咪唑(clemizole)、2-乙胺基乙醇、2-二乙胺基乙醇、2-二甲胺基乙醇、乙二胺、丁胺、乙醇胺、乙二胺、N-乙基嗎啉、N-乙基哌啶、乙基葡糖胺、還原葡糖胺(glucamine)、葡糖胺(glucosamine)、組胺酸、海卓胺(hydrabamine)、咪唑、異丙胺、甲基葡糖胺、嗎啉、哌嗪、吡啶、吡哆醇(pyridoxine)、釹(neodymium)、哌啶、聚胺樹脂、普魯卡因、嘌呤、可可豆鹼(theobromine)、三乙胺、三丙胺、三乙醇胺、緩血酸胺(tromethamine)、甲胺、牛磺酸(taurine)、膽酸鹽、6-胺基-2-甲基-2-庚醇、2-胺基-2-甲基-1,3-丙二醇、2-胺基-2-甲基-1-丙醇、脂族單羧酸及二羧酸、經苯基取代之烷酸、羥基烷酸、芳族酸、脂族及芳族磺酸、鍶(strontium)、三(羥甲基)甲基甘胺酸(tricine)、肼、苯基環己基胺、2-(N-嗎啉基)乙烷磺酸、雙(2-羥乙基)胺基-參(羥甲基)甲烷、N-(2-乙醯胺基)-2-胺基乙烷磺酸、1,4-哌嗪二乙烷磺酸、3-(N-嗎啉基)-2-羥基丙烷磺酸、1,3-雙[參(羥甲基)甲基胺基]丙烷、4-嗎啉丙烷磺酸、4-(2-羥乙基)哌嗪-1-乙烷磺酸、2-[(2-羥基-1,1-雙(羥甲基)乙基)胺基]乙烷磺酸、N,N-雙(2-羥乙基)-2-胺基乙烷磺酸、4-(N-嗎啉基)丁烷磺酸、3-(N,N-雙[2-羥乙基]胺基)-2-羥基丙烷磺酸、2-羥基-3-[參(羥甲基)甲胺基]-1-丙烷磺酸、4-(2-羥乙基)哌嗪-1-(2-羥基丙烷磺酸)、哌嗪-1,4-雙(2-羥基丙烷磺酸)二水合物、4-

(2-羥乙基)-1-哌嗪丙烷磺酸、N,N-雙(2-羥乙基)甘胺酸、N-(2-羥乙基)哌嗪-N'-(4-丁烷磺酸)、N-[參(羥甲基)甲基]-3-胺基丙烷磺酸、N-參(羥甲基)甲基-4-胺基丁烷磺酸、N-(1,1-二甲基-2-羥乙基)-3-胺基-2-羥基丙烷磺酸、2-(環己基胺基)乙烷磺酸、3-(環己基胺基)-2-羥基-1-丙烷磺酸、3-(環己基胺基)-1-丙烷磺酸、N-(2-乙醯胺基)亞胺基二乙酸、4-(環己基胺基)-1-丁烷磺酸、N-[參(羥甲基)甲基]甘胺酸、2-胺基-2-(羥甲基)-1,3-丙二醇及胺丁三醇(trometamol)。

在本發明之另一態樣中，本發明之RAGE融合蛋白可與其他已知治療劑一起用於輔助治療性或組合治療性治療中。以下為可與本發明之RAGE融合蛋白調節劑組合利用之佐劑及其他治療劑的非窮舉的列項：

抗癌劑之藥理學分類：

1. 烷基化劑：環磷醯胺(Cyclophosphamide)、亞硝基脲(nitrosourea)、卡鉑(carboplatin)、順鉑(cisplatin)、丙卡巴肼(procarbazine)
2. 抗生素：博萊黴素(Bleomycin)、道諾黴素(Daunorubicin)、小紅莓(Doxorubicin)
3. 抗代謝物：甲胺喋呤(Methotrexate)、阿糖胞苷(Cytarabine)、氟尿嘧啶(Fluorouracil)、硫唑嘌呤(Azathioprine)、6-巯基嘌呤及細胞毒性癌症化學治療劑
4. 植物生物鹼：長春鹼(Vinblastine)、長春新鹼

(Vincristine)、依託泊苷(Etoposide)、太平洋紫杉醇(Paclitaxel)，

5. 激素：他莫昔芬(Tamoxifen)、乙酸奥曲肽(Octreotide acetate)、非那雄安(Finasteride)、氟他胺(Flutamide)

6. 生物反應調節劑：干擾素(Interferon)、介白素(Interleukin)

用於類風濕性關節炎之治療劑之藥理學分類

1. 止痛劑：阿司匹靈(Aspirin)

2. NSAID(非類固醇消炎藥)：布洛芬(Ibuprofen)、萘普生(Naproxen)、雙氯芬酸(Diclofenac)

3. DMARD(疾病改善抗風濕藥)：甲胺喋呤(Methotrexate)、金製劑(gold preparation)、羥氯喹(hydroxychloroquine)、柳氮磺胺吡啶(sulfasalazine)

4. 生物反應調節劑-DMARD：依那西普(Etanercept)、英利昔單抗、糖皮質激素(Glucocorticoids)，諸如倍氯米松(beclomethasone)、甲潑尼龍(methylprednisolone)、倍他米松(betamethasone)、潑尼松(prednisone)、地塞米松(dexamethasone)及氫皮質酮(hydrocortisone)

用於糖尿病之治療劑之藥理學分類

1. 磺醯脲(Sulfonylureas)：甲苯磺丁脲(Tolbutamide)、妥拉磺脲(Tolazamide)、格列本脲(Glyburide)、格列吡嗪(Glipizide)

2. 雙胍(Biguanide)：二甲雙胍(Metformin)

3. 其他口服藥劑：醣祿(Acarbose)、曲格列酮

(Troglitazone)

4.胰島素

用於阿茲海默氏病之治療劑之藥理學分類

1.膽鹼酯酶抑制劑(Cholinesterase Inhibitor)：塔克林(Tacrine)、冬尼培唑(Donepezil)

2.抗精神病藥：氟哌啶醇(Haloperidol)、硫利達嗪(Thioridazine)

3.抗抑鬱藥：地昔帕明(Desipramine)、氟西汀(Fluoxetine)、曲唑酮(Trazodone)、帕羅西汀(Paroxetine)

4.抗驚厥藥：卡馬西平(Carbamazepine)、丙戊酸(Valproic acid)

在一實施例中，本發明組合物可包含一定量之RAGE融合蛋白與單一或多種其他治療劑組合。除上文所述之藥劑之外，以下治療劑亦可與本發明之RAGE融合蛋白組合使用：免疫抑制劑，諸如環孢素(cyclosporin)、他克莫司(tacrolimus)、雷帕黴素(rapamycin)及其他FK-506型免疫抑制劑。

在一實施例中，本發明因此可提供一種治療RAGE介導之疾病之方法，該方法包含向個體投與一定量之本發明融合蛋白與選自由以下組成之群之治療劑的組合：烷基化劑、抗代謝物、植物生物鹼、抗生素、激素、生物反應調節劑、止痛劑、NSAID、DMARD、生物反應調節劑(例如糖皮質激素)、磺醯脲、雙胍、胰島素、膽鹼酯酶抑制

劑、抗精神病藥、抗抑鬱藥、抗驚厥藥及免疫抑制劑(諸如環孢素、他克莫司、雷帕黴素及其他FK-506型免疫抑制劑)。在另一實施例中，本發明提供如上所述之本發明醫藥組合物，其進一步包含一或多種選自由以下組成之群之治療劑：烷基化劑、抗代謝物、植物生物鹼、抗生素、激素、生物反應調節劑、止痛劑、NSAID、DMARD、生物反應調節劑(例如糖皮質激素)、磺醯脲、雙胍、胰島素、膽鹼酯酶抑制劑、抗精神病藥、抗抑鬱藥、抗驚厥藥及免疫抑制劑(諸如環孢素、他克莫司、雷帕黴素及其他FK-506型免疫抑制劑)。

當本發明係關於一種治療RAGE介導之疾病的方法且該方法包含向個體投與一定量之RAGE融合蛋白與另一治療劑之組合時，投與RAGE融合蛋白及另一活性劑之順序可為同時、連續或依序投與。

凍乾調配物

在其他實施例中，本發明亦提供包含RAGE融合蛋白之調配物。調配物之實施例可包含凍乾保護劑、RAGE融合蛋白及緩衝劑之固體混合物。固體可藉由凍乾包含凍乾保護劑、RAGE融合蛋白及緩衝劑之水溶液而製備。

RAGE融合蛋白調配物可包含經調配以供診所使用或作為處方藥品使用的穩定治療劑。舉例而言，在某些實施例中，RAGE融合蛋白調配物在攝氏40度下1週之後可展現不到10%、或不到5%、或不到3%之分解。

此外，RAGE融合蛋白調配物可在於稀釋劑中復原之後

為穩定的。在某些實施例中，不到約10%、或約5%、或約4%、或約3%、或約2%、或約1%之RAGE融合蛋白以聚集體形式存在於RAGE融合蛋白調配物中。

投與本發明之基於核酸或基於蛋白質之組合物、尤其如本文所述之RAGE融合蛋白或表現構築體之方法可為許多此項技術中熟知之方法中之任一者。此等方法包括局部或全身投與且可經腦室內、鞘內、皮內、肌肉內、腹膜內、靜脈內、動脈內、皮下、經直腸、經口、經頰、舌下、鼻內，或以氣霧劑形式投與。此外，可能需要藉由任何適合途徑，包括經由注射或經由輸注使用泵經心室內、鞘內、腦室內及硬膜外投與來將本發明之基於核酸或基於蛋白質之組合物引入中樞神經系統中。舉例而言，心室內注射可藉由使用與儲集囊(reservoir)(諸如奧瑪耶儲集囊(Ommaya reservoir))連接之心室內導管而變得容易。使用泵之輸注可例如藉由使用與導管連接之可植入泵而變得容易。在另一實施例中，腦室內注射可藉由使用與導管連接之可植入泵而變得容易。

此等及其他植入物及人造器官(prosthetics)可用本發明之融合蛋白或用含有表現本發明之融合蛋白之核酸的表現構築體處理。以此方式，本發明之融合蛋白可直接投與受影響之特定組織。

引入方法亦可利用可再裝填或生物可降解的裝置來提供。此外，預期投藥可藉由對裝置、植入物、支架或人造器官塗佈而發生。

如本文中更詳細描述，RAGE已牽涉於多種疾病狀況之發病機制中。因此，本發明之RAGE融合蛋白調配物可用於治療多種RAGE介導之病症。

在某些實施例中，本發明之RAGE融合蛋白調配物可用於治療糖尿病之症狀或糖尿病晚期併發症之症狀。舉例而言，糖尿病或糖尿病晚期併發症之症狀包含糖尿病腎病變、糖尿病視網膜病變、糖尿病足部潰瘍、心血管併發症或糖尿病神經病變中之至少一者。

在其他實施例中，本發明之RAGE融合蛋白調配物可用於治療以下至少一者：澱粉樣變性病、阿茲海默氏病、癌症、腎衰竭、或與自體免疫性、發炎性腸病、類風濕性關節炎、牛皮癬、多發性硬化症、低氧症、中風、心臟病發作、出血性休克、敗血症、器官移植或創傷癒合不良相關之發炎。

或者，RAGE融合蛋白調配物可用於治療骨質疏鬆症。舉例而言，在某些實施例中，投與本發明之RAGE融合蛋白使個體之骨密度增加或使個體之骨密度減小速率降低。

在一些實施例中，使用本發明之RAGE融合蛋白調配物治療之自體免疫性可包含以下至少一者之排斥反應：皮膚細胞、胰臟細胞、神經細胞、肌細胞、內皮細胞、心臟細胞、肝細胞、腎細胞、心臟、骨髓細胞、骨、血球、動脈細胞、靜脈細胞、軟骨細胞、甲狀腺、細胞或幹細胞。或者，RAGE融合蛋白調配物可用於治療腎衰竭。

在某些實施例中，RAGE融合蛋白調配物可用於治療與

器官、組織或複數個細胞中之至少一者自第一部位移植至第二部位相關的發炎及/或排斥反應。第一及第二部位可位於不同個體中或位於同一個體中。可使用本發明之RAGE融合蛋白調配物改良多種不同細胞類型之移植。舉例而言，所移植之細胞、組織或器官可包含胰臟、皮膚、肝、腎、心臟、骨髓、血液、骨、肌肉、動脈、靜脈、軟骨、甲狀腺、神經系統或幹細胞之細胞、組織或器官。

多種凍乾保護劑可用於本發明之凍乾RAGE融合蛋白調配物中。在一些實施例中，凍乾保護劑可包含非還原糖。舉例而言，非還原糖可包含蔗糖、甘露糖醇或海藻糖。此外，多種緩衝劑可用於凍乾RAGE融合蛋白調配物中。在某些實施例中，緩衝劑可包含組胺酸。

固體凍乾RAGE融合蛋白調配物可包含其他組分。在某些實施例中，RAGE融合蛋白調配物可進一步包含界面活性劑、螯合劑或增積劑中之至少一者。

在一實施例中，本發明包含含有凍乾RAGE融合蛋白於稀釋劑中復原的復原調配物，其中復原調配物中之RAGE融合蛋白濃度在約1 mg/mL至約400 mg/mL之範圍內。或者，可如本文所述使用RAGE融合蛋白之其他濃度。

在其他實施例中，本發明亦可包含製備RAGE融合蛋白之穩定復原調配物之方法。復原調配物可包含適於直接使用(例如直接向個體投與)或可經進一步稀釋及/或與傳遞劑混合之濃度。

在某些實施例中，方法可包含於稀釋劑中復原RAGE融

合蛋白與凍乾保護劑之凍乾混合物以便使復原調配物中之RAGE融合蛋白濃度在約1 mg/mL至約400 mg/mL之範圍內。或者，可如本文所述使用如本文所述之其他濃度。

多種凍乾保護劑可用於本發明之復原RAGE融合蛋白調配物中。在一些實施例中，凍乾保護劑可包含非還原糖。舉例而言，非還原糖可包含蔗糖、甘露糖醇或海藻糖。此外，多種緩衝劑可用於凍乾RAGE融合蛋白調配物中。在某些實施例中，緩衝劑可包含組胺酸。

復原RAGE融合蛋白調配物可包含其他組分。在某些實施例中，RAGE融合蛋白調配物可進一步包含界面活性劑、螯合劑或增積劑中之至少一者。

適用於醫藥之多種稀釋劑可用於復原凍乾RAGE融合蛋白。在一實施例中，凍乾RAGE融合蛋白為無菌的。此外，在一實施例中，稀釋劑為無菌的。在一實施例中，稀釋劑可包含注射用水(WFI)。此外，在某些實施例中，稀釋劑之添加量係基於RAGE融合蛋白之治療劑量及藥物動力學概況以及所投與之調配物與載劑之生物相容性。在一實施例中，復原調配物為等張的。

復原RAGE融合蛋白調配物可適於藉由多種途徑且按治療相關RAGE介導之病症所需進行投與。在某些實施例中，復原RAGE融合蛋白調配物適於以以下至少一種途徑向個體投與調配物：靜脈內、腹膜內、皮下、心室內、鞘內、腦室內或硬膜外。

在其他實施例中，本發明可包含包括RAGE融合蛋白之

製品。舉例而言，在某些實施例中，製品可包含容納凍乾RAGE融合蛋白之容器及關於用稀釋劑復原凍乾調配物之說明書。在某些實施例中，製品可包含容納包含凍乾保護劑、RAGE融合蛋白及緩衝劑之凍乾混合物之調配物的容器。製品亦可包含關於用稀釋劑復原凍乾調配物之說明書。

多種凍乾保護劑可用於本發明之製品中。在一些實施例中，凍乾保護劑可包含非還原糖。舉例而言，非還原糖可包含蔗糖、甘露糖醇或海藻糖。此外，多種緩衝劑可用於凍乾RAGE融合蛋白調配物中。在某些實施例中，緩衝劑可包含組胺酸。

本發明之製品之RAGE融合蛋白調配物可包含其他組分。在某些實施例中，凍乾RAGE融合蛋白調配物可進一步包含界面活性劑、螯合劑或增積劑中之至少一者。

可提供適用於醫藥之多種稀釋劑用以復原凍乾RAGE融合蛋白。在一實施例中，凍乾調配物為無菌的。另外或或者，稀釋劑可為無菌的。在一實施例中，稀釋劑可包含注射用水(WFI)。因此，製品可進一步包含容納用於復原凍乾調配物之稀釋劑之第二容器，其中該稀釋劑為注射用水(WFI)。在一實施例中，復原調配物為等張的。

此外，在某些實施例中，稀釋劑之添加量係基於RAGE融合蛋白之治療劑量及藥物動力學概況以及所投與之調配物與載劑之生物相容性。在替代性實施例中，說明書係關於復原凍乾調配物以便獲得如本文所述之濃度。舉例而

言，在某些實施例中，說明書係關於復原凍乾調配物以便使復原調配物中之RAGE融合蛋白濃度在約40 mg/mL至約100 mg/mL之範圍內。

此外，在某些實施例中，當根據所提供之說明書復原時，復原RAGE融合蛋白調配物可適於藉由多種途徑且按治療相關RAGE介導之病症所需進行投與。在某些實施例中，復原RAGE融合蛋白調配物適於以以下至少一種途徑向個體投與調配物：靜脈內、腹膜內、皮下、心室內、鞘內、腦室內或硬膜外。

在調配物、製品、製備包含RAGE融合蛋白之調配物之方法的某些實施例中，復原調配物中之RAGE融合蛋白濃度可為至少10 mg/mL、或至少20 mg/mL、或至少50 mg/mL。在替代性實施例中，復原調配物中之RAGE融合蛋白濃度可為至少100 mg/mL、或200 mg/mL、或400 mg/mL。舉例而言，在替代性實施例中，復原調配物中之RAGE融合蛋白濃度為至少約0.5至400 mg/mL、或約1至200 mg/mL、40至400 mg/mL、50至400 mg/mL、40至100 mg/mL、50至100 mg/mL、或約40-50 mg/mL。

任何本文所述之實施例皆可用作本發明調配物中之RAGE融合蛋白。因此，如本文所述之RAGE融合蛋白之實施例可供凍乾調配物、復原凍乾調配物、或製備凍乾調配物或復原凍乾調配物之方法、或包含本發明之凍乾調配物或復原凍乾調配物之製品中的各者使用。

凍乾調配物之製備

在另一實施例中，本發明提供預凍乾調配物、凍乾調配物、復原調配物及其製備方法。

在製備如上所述之相關RAGE融合蛋白之後，可產生「預凍乾調配物」。存在於預凍乾調配物中之RAGE融合蛋白之量可考慮所要劑量體積、投藥模式等加以確定。在一實施例中，預凍乾調配物中之融合蛋白之量可大於1 mg/mL。此外，在某些實施例中，預凍乾調配物中之融合蛋白之量可小於約5 mg/mL、10 mg/mL、50 mg/mL、100 mg/mL或200 mg/mL。

在另一實施例中，預凍乾調配物可為pH值約為4-8之pH緩衝溶液。在另一實施例中，預凍乾調配物可為pH值約為5-7之pH緩衝溶液。例示性緩衝劑包括組胺酸、磷酸鹽、Tris、檸檬酸鹽、丁二酸鹽及如本文所述之其他有機酸。緩衝劑濃度可視例如緩衝劑及調配物之所要等張性(例如復原調配物之所要等張性)而定為約1 mM至約100 mM、或小於約50 mM、或約2 mM至約50 mM、或小於約15 mM、或約3 mM至約15 mM。在一實施例中，緩衝劑為組胺酸。

凍乾保護劑可添加至預凍乾調配物中。在一實施例中，凍乾保護劑包含糖。在另一實施例中，凍乾保護劑包含非還原糖。在另一實施例中，凍乾保護劑包含非還原糖蔗糖。或者，非還原糖可包含甘露糖醇。或者，非還原糖可包含海藻糖。預凍乾調配物中之凍乾保護劑之量通常使得在復原之後所得調配物將為等張的。然而，高張性復原調配物亦可為適合的，例如在用於周邊非經腸投與之調配物

中。此外，凍乾保護劑之量不應低得以致於蛋白質在凍乾之後有不可接受之量的降解及/或聚集現象。在替代性實施例中，不可接受之量的聚集可為有20%、或10%、或5%或5%以上之RAGE融合蛋白以聚集體形式存在於調配物中時的情況。預凍乾調配物中之凍乾保護劑濃度之例示性範圍可為小於約400 mM。在另一實施例中，預凍乾調配物中之凍乾保護劑濃度之範圍為小於約100 mM。在替代性實施例中，預凍乾調配物中之凍乾保護劑濃度之範圍可因此在約0.5 mM至400 mM、或約2 mM至200 mM、或約30 mM至約150 mM、或約60-65 mM之範圍內。或者，可使用屬於此等範圍內之範圍。此外，在一些實施例中，以能使得復原調配物等張之量添加凍乾保護劑。

預凍乾調配物中之RAGE融合蛋白與凍乾保護劑的比率係針對各RAGE融合蛋白與凍乾保護劑之組合加以選擇。在具有高RAGE融合蛋白濃度(例如大於或等於約50 mg/mL)之等張復原調配物之一實施例中，凍乾保護劑與RAGE融合蛋白之莫耳比可為約50至約1500莫耳凍乾保護劑：1莫耳RAGE融合蛋白。在另一實施例中，凍乾保護劑與RAGE融合蛋白之莫耳比可為約150至約1000莫耳凍乾保護劑：1莫耳融合蛋白。在另一實施例中，凍乾保護劑與RAGE融合蛋白之莫耳比可為約150至約300莫耳凍乾保護劑：1莫耳RAGE融合蛋白。或者，可使用屬於此等範圍內之範圍。舉例而言，當凍乾保護劑為非還原糖(諸如蔗糖、海藻糖或甘露糖醇)時，此等範圍可為適合的。

在本發明之另一實施例中，界面活性劑可添加至預凍乾調配物中。或者，或此外，界面活性劑可添加至凍乾調配物及/或復原調配物中。例示性界面活性劑包括非離子界面活性劑，諸如聚山梨醇酯(例如聚山梨醇酯20或80)(吐溫20™或吐溫80™)；泊洛沙姆(poloxamer)(例如泊洛沙姆188)。界面活性劑之添加量使得復原蛋白質之聚集減少且使復原後之微粒形成減至最少。舉例而言，界面活性劑可以約0.001%至0.5%之量存在於預凍乾調配物中。舉例而言，在界面活性劑包含聚山梨醇酯80之一實施例中，界面活性劑可以約0.005%至0.05%、或約0.008%至0.012%、或約0.01%之量存在於預凍乾調配物中。或者，界面活性劑可存在於調配物中以至於最終濃度在0.001 mg/mL至約100 mg/mL、或約0.01 mg/mL至約10 mg/mL之範圍內。或者，可使用屬於此等範圍內之範圍。

在本發明之某些實施例中，凍乾保護劑(諸如蔗糖或組胺酸)與增積劑(例如甘露糖醇或甘胺酸)之混合物可用於製備預凍乾調配物。增積劑可允許產生均一的凍乾塊而其中無過多凹穴(pocket)等。

其他醫藥學上可接受之載劑、賦形劑或穩定劑(諸如Remington's Pharmaceutical Sciences 第16版，Osol, A.編(1980)中所述之載劑、賦形劑或穩定劑)可包括在預凍乾調配物(及/或凍乾調配物及/或復原調配物)中，其限制條件為其不會不利地影響調配物之所要特徵。可接受之載劑、賦形劑或穩定劑在所採用之劑量及濃度下對接受者無毒性

且包括其他緩衝劑；防腐劑；共溶劑；抗氧化劑，包括抗壞血酸及甲硫胺酸；螯合劑，諸如EDTA；金屬錯合物(例如Zn-蛋白質錯合物)；生物可降解聚合物(諸如聚酯)；及/或成鹽相對離子(諸如鈉)。

本發明之RAGE融合蛋白調配物亦可含有為所治療之特定適應症所必需之其他蛋白質。可選擇其他蛋白質以使該等蛋白質各自具有不會不利地影響彼此或RAGE融合蛋白之互補活性。此等蛋白質適合以可有效地達成預定目的之量以組合形式存在。

對於活體內投藥，本發明之RAGE融合蛋白調配物可為無菌的。此可藉由在凍乾及復原之前或之後經無菌過濾膜過濾來達成。

在將RAGE融合蛋白、凍乾保護劑及其他視情況選用之組分混合在一起之後，可凍乾調配物。許多不同的冷凍乾燥器可用於此目的，諸如Hull50™(Hull, USA)或GT20™(Leybold-Heraeus, Germany)冷凍乾燥器。冷凍乾燥係藉由冷凍調配物且隨後在適於一次乾燥(primary drying)之溫度下使冰自冷凍內含物昇華而達成。在此條件下，產物溫度低於調配物之共熔點或塌陷溫度(collapse temperature)。通常，一次乾燥之架層溫度(shelf temperature)將在適合壓力(範圍通常為約50至250毫托(mTorr))下在約-50至25℃之範圍內(限制條件為產物在一次乾燥期間保持冷凍狀態)。在一實施例中，壓力為約100毫托且樣品可在約-30與25℃之間凍乾。調配物、容納樣品之容器(例如玻璃小瓶)之尺

寸及類型以及液體體積可決定乾燥所需之時間，其可在數小時至數天之範圍內(例如40-60小時)。冷凍乾燥條件可視調配物及小瓶尺寸而變化。

在一些情況下，可能需要在欲進行蛋白質之復原之容器中凍乾蛋白質調配物以避免轉移步驟。在此情況下，容器可例如為2、3、5、10、20、50、100或250立方公分(cc)小瓶。在一實施例中，容器為適於製備具有小於或等於100 mL之體積之復原調配物的任何容器。

作為一般陳述，凍乾將產生水分含量小於約5%之凍乾調配物。在一實施例中，凍乾調配物之水分含量小於約3%。在另一實施例中，凍乾調配物之水分含量小於約1%。

凍乾調配物之復原

在所要階段，通常當向患者或個體投與RAGE融合蛋白時，可用稀釋劑復原凍乾調配物以至於復原調配物中之RAGE融合蛋白濃度為約大於10 mg/mL，或大於20 mg/mL，或大於50 mg/mL，或為約30-50 mg/mL，或為約50 mg/mL。在替代性實施例中，復原調配物中之RAGE融合蛋白濃度可為至少100 mg/mL、或200 mg/mL、或400 mg/mL。舉例而言，在替代性實施例中，復原調配物中之RAGE融合蛋白濃度可在約1 mg/mL至約600 mg/mL、或約1 mg/mL至約500 mg/mL、或約1 mg/mL至約400 mg/mL、或約1 mg/mL至約200 mg/mL、或約10 mg/mL至約400 mg/mL、或約10 mg/mL至約200 mg/mL、或約40 mg/mL至

約400 mg/mL、或約40 mg/mL至約200 mg/mL、或約50 mg/mL至約400 mg/mL、或約50 mg/mL至約200 mg/mL之範圍內。在其他實施例中，復原調配物中之RAGE融合蛋白濃度為約40 mg/mL至約100 mg/mL、或約50 mg/mL至約100 mg/mL、或約40 mg/mL至約50 mg/mL。復原調配物中之此等RAGE融合蛋白濃度被認為在意欲皮下傳遞復原調配物時尤其適用。然而，對於其他投藥途徑(諸如靜脈內投藥)，復原調配物中之蛋白質濃度較低可為所要的(例如有約5-50 mg/mL、或約10-40 mg/mL RAGE融合蛋白存在於復原調配物中)。因此，在一些實施例中，復原調配物中之融合蛋白之濃度可與預凍乾調配物中之融合蛋白之濃度相同或不到後者的2倍。

在某些實施例中，復原調配物中之融合蛋白濃度顯著高於預凍乾調配物中之融合蛋白濃度。舉例而言，在某些實施例中，復原調配物中之融合蛋白濃度可為預凍乾調配物之融合蛋白濃度的約2-40倍、或2-10倍、或3-8倍。在一實施例中，復原調配物中之RAGE融合蛋白濃度可為預凍乾調配物之RAGE融合蛋白濃度的約3-6倍。在預凍乾調配物中之RAGE融合蛋白之濃度為約15 mg/mL的另一實施例中，復原調配物中之RAGE融合蛋白之濃度大於或等於約50 mg/mL(例如大至少3倍或至少4倍)。

由於體積限制(小於或等於1.5 mL)及劑量需要(大於或等於100 mg)，高蛋白質濃度之傳遞通常對皮下投藥有利或為皮下投藥所需。然而，該等蛋白質濃度(大於或等於50

mg/mL)在製造過程中可能難以達成，此係因為在高濃度下，蛋白質可能在加工期間具有聚集傾向且變得難以操作(例如泵送)及無菌過濾。或者，凍乾過程可提供一種允許蛋白質濃縮之方法。舉例而言，RAGE融合蛋白可以一定體積(Vf)填充入小瓶中且接著進行凍乾。凍乾RAGE融合蛋白接著用小於原始體積之體積(Vr)(例如Vr=0.25 Vf)之水或防腐劑(例如BWFI)復原，從而使復原溶液中之RAGE融合蛋白濃度較高。此過程亦使緩衝劑及賦形劑濃縮。對於皮下投藥，需要溶液等張。

復原通常在約25℃之溫度下進行以確保完全水合，但必要時亦可採用其他溫度。復原所需之時間可視例如稀釋劑類型、賦形劑及蛋白質之量而定。例示性稀釋劑包括無菌水、注射用抑菌水(BWFI)、pH緩衝溶液(例如磷酸鹽緩衝鹽水)、無菌鹽水溶液、林格氏溶液或右旋糖溶液。在一實施例中，稀釋劑提供適於注射之復原調配物。在另一實施例中，當稀釋劑提供適於注射之復原調配物時，稀釋劑包含注射用水(WFI)。稀釋劑視情況含有防腐劑。防腐劑之用量可藉由用蛋白質及防腐劑功效測試評估不同防腐劑濃度之相容性來確定。

復原調配物之投與

復原調配物可根據已知方法投與哺乳動物(諸如人類)，該等方法諸如有經靜脈內投藥(以快速推注形式或藉由在一段時間內連續輸注)、藉由肌肉內、腹膜內、腦脊髓內(intracerobrospinal)、皮下、關節內、滑膜內、鞘內、心

室內、腦室內、硬膜外、經口、局部、吸入途徑。

在實施例中，復原調配物可藉由皮下(亦即皮膚以下)投藥向哺乳動物投與。出於此等目的，復原調配物可使用注射器加以注射。然而，可利用用於投與復原調配物之其他裝置，諸如注射裝置(例如Inject-ease™及Genject™裝置)、注射筆(諸如GenPen™)、無針裝置(例如MediJector™及BioJector™)及皮下貼片傳遞系統。

RAGE融合蛋白之適當劑量或治療有效量將例如視欲治療之病狀、病狀之嚴重性及進程、是否為了預防或治療目的而投與RAGE融合蛋白、先前療法、患者臨床病史及對RAGE融合蛋白之反應以及主治醫師之判斷而定。RAGE融合蛋白可一次性地或經一系列療程投與個體。RAGE融合蛋白可以單一治療形式或與其他藥物或療法結合藉由同時、依序或連續投與之方式來投與。在一實施例中，無論是例如藉由一次抑或多次各別投藥，約0.1-20 mg/kg之劑量均為用於向個體投與之初始候選劑量。如上所述，其他給藥方案可能適用。

製品

在本發明之另一實施例中，提供一種含有本發明調配物之製品且其可提供關於該調配物之復原及/或使用的說明書。該製品可包含容器。適合容器包括例如瓶、小瓶(例如雙腔小瓶)、注射器(諸如雙腔注射器)及試管。容器可由多種材料(諸如玻璃或塑膠)形成。容器可容納凍乾調配物。在某些實施例中，可能存在有標籤貼於容器上，或由

容器所附帶。該標籤可指示關於復原及/或使用之說明。舉例而言，在某些實施例中，標籤可指示使凍乾調配物復原為如上所述之蛋白質濃度。標籤可進一步指示調配物適用於或意欲用於皮下投藥。

容納調配物之容器可允許反覆投與(例如2-6、或2-10、或2-50次投藥)調配物。製品可進一步包括自商業及使用者觀點來看合乎需要的其他材料，包括其他緩衝劑、稀釋劑、過濾器、針、注射器及具有使用說明之包裝插頁。

實例

在以下實例中進一步說明由本發明所涵蓋之發明概念的特徵及優點。

實例1A：產生RAGE融合蛋白

構築兩個質體以表現RAGE-IgG融合蛋白。兩個質體係藉由使來自人類RAGE之不同長度之5' cDNA序列與來自人類IgG Fc(γ1)之相同3' cDNA序列連接而構築。此等表現序列(亦即連接產物)接著插入pcDNA3.1表現載體(Invitrogen, CA)中。編碼兩種野生型RAGE融合蛋白之核酸序列展示於圖2及圖3中。對於TTP-4000 RAGE融合蛋白，1至753之核酸序列(以粗體突出)編碼RAGE N端蛋白質序列，而754至1386之核酸序列編碼IgG蛋白質序列(圖2)。對於TTP-3000，1至408之核酸序列(以粗體突出)編碼RAGE N端蛋白質序列，而409至1041之核酸序列編碼IgG蛋白質序列(圖3)。

為了產生RAGE融合蛋白，將包含SEQ ID NO: 30或SEQ

ID NO: 31之核酸序列之表現載體穩定轉染於CHO細胞中。選擇具有由質體賦予之新黴素(neomycin)抗性的陽性轉型體且進行選殖。擴增藉由上清液之西方墨點分析而偵測之高產純系且使用蛋白A管柱藉由親和力層析來純化基因產物。表現可經最佳化以使細胞可以每公升約1.3公克之量產生重組TTP-4000。

實例1B：替代性產生四域RAGE融合蛋白

構築質體以表現RAGE-IgG融合蛋白。該質體係藉由使來自人類RAGE之5' cDNA序列與來自人類IgG Fc(γ1)之3' cDNA序列連接而構築。使用PCR來擴增cDNA。此外，在5'端上，PCR引子添加用於選殖之Eco RI限制酶位點及Kozak共同轉譯起始序列。在3'端上，PCR引子添加Xho I限制，其恰好越過未端密碼子。在3'端上，PCR引子亦包括兩個沉默鹼基變化，其移除免疫球蛋白部分中在未端密碼子附近之隱蔽性RNA剪接位點。編碼脯胺酸(殘基459，基於SEQ ID NO: 32中之蛋白質序列中之編號)之密碼子自CCG變化成CCC，且編碼甘胺酸(殘基460，基於SEQ ID NO: 32中之蛋白質序列中之編號)之密碼子自GGT變化成GGG。PCR片段用Eco RI及Xho I消化且接著插入已用Mfe I消化(以形成與Eco RI相容之端)且用Xho I消化的反轉錄病毒載體質體(retrovector plasmid)(pCNS-newMCS-WPRE (new起點)，購自Gala, Inc.)中。對所選殖質體之插入部分及選殖接合點(cloning junction)進行定序以確保在選殖期間無突變發生。

為了產生RAGE-IgG融合蛋白，將包含核酸序列SEQ ID NO: 54之表現載體穩定轉染於CHO細胞中。

由經轉染細胞表現之RAGE融合蛋白TTP-4000之序列藉由多種表徵研究確認為SEQ ID NO: 34或SEQ ID NO: 56、或SEQ ID NO: 34與SEQ ID NO: 56兩者。因而，裂解由SEQ ID NO: 32之前23個胺基酸編碼之信號序列，且N端殘基為麩醯胺酸(Q)或焦麩胺酸(pE)或其混合物。表徵研究亦顯示在N2及N288(基於SEQ ID NO: 34或SEQ ID NO: 56之編號)處之糖基化位點且顯示RAGE融合蛋白之C_H3區可在表現於此重組系統中時經由轉譯後修飾使其C端殘基裂解去除。

實例1C：替代性產生三域RAGE融合蛋白

可以上文關於TTP-4000所述之方式構築質體以表現三域RAGE-IgG融合蛋白(例如1個RAGE域及2個IgG域)，諸如TTP-3000。質體係藉由將來自人類RAGE之編碼人類RAGE之胺基酸1-136的5' cDNA序列與來自人類IgG Fc(γ1)之3' cDNA序列連接而構築。可使用PCR來擴增cDNA。在5'端上，PCR引子可添加用於選殖之限制性位點(例如如用於TTP-4000之Eco RI限制酶位點)及Kozak共同轉譯起始序列。在3'端上，PCR引子亦可添加限制性位點(例如Xho I限制性位點)，其恰好越過未端密碼子。PCR引子亦可包括沉默鹼基變化，其可被需要以移除任何隱蔽性RNA剪接位點，諸如如實例1B中所述位於免疫球蛋白C_H2域之3'端處之隱蔽性RNA剪接位點。為了移除此等隱蔽性剪接位點，

編碼SEQ ID NO: 35之脯胺酸344之密碼子(亦即殘基1030-1032，基於SEQ ID NO: 31中之DNA序列中之編號)可自CCG變化成CCC，且編碼SEQ ID NO: 35之甘胺酸345之密碼子(亦即殘基1033-1035，基於SEQ ID NO: 31中之DNA序列中之編號)可自GGT變化成GGG。PCR片段可接著用適當限制酶(例如Eco RI及Xho I)消化，且插入反轉錄病毒載體質體pCNS-newMCS-WPRE(new起點；購自Gala, Inc, Inc.)中。載體可用Mfe I消化而形成與Eco RI相容之端，且用Xho I消化。可對所選殖質體之插入部分及選殖接合點進行定序以確保在選殖期間無突變發生。

為了產生RAGE-IgG融合蛋白，如實例1A及1B中所述，包含核酸序列SEQ ID NO: 55(亦即包含移除隱蔽性剪接位點之DNA序列之變化)之表現載體可穩定轉染於CHO細胞中。

由經轉染細胞表現之RAGE融合蛋白TTP-3000之序列可為SEQ ID NO: 36、SEQ ID NO: 37或SEQ ID NO: 57、或SEQ ID NO: 36、SEQ ID NO: 37及/或SEQ ID NO: 57之組合。因而，可裂解由SEQ ID NO: 35之前22及/或23個胺基酸編碼之信號序列且N端殘基可為麩醯胺酸(Q)或焦麩胺酸(pE)或其混合物。糖基化可存在於N2及N174(基於SEQ ID NO: 37或SEQ ID NO: 57之編號)之位點處及/或可存在之其他糖基化位點處。RAGE融合蛋白之C_H3區可在表現於此重組系統中時經由轉譯後修飾使其C端殘基裂解去除。

實例2 產生RAGE融合蛋白突變體

野生型TTP-4000 RAGE質體DNA可作為模板使用以下策略來用於定點突變誘發及製備正向及反向引子。

為了在殘基288處插入突變，可使用相對於野生型TTP-4000 RAGE質體含有突變位點且長度為32-34個核苷酸的正向引子。一般而言，該引子在該突變位點下游包括約10個核苷酸。舉例而言，編碼N288Q突變之正向引子序列為5'-GCCTCGGGAGGAACAGTA**cAg**TCCACCTACC(SEQ ID NO: 196)，其中粗體小寫字母表示相對於野生型TTP-4000 RAGE質體突變之核苷酸。使用此引子與反向引子組合來藉由PCR擴增融合蛋白DNA，所編碼之胺基酸可自野生型天冬醯胺(aAc)變化成麩醯胺酸(cAg)。使用在15-20個核苷酸之5'端處含有與正向引子重疊之區域的反向引子。因此，反向引子序列可為5'-**TACTGTTCCTCCCGAGGC**TTGGTCTTGG(SEQ ID NO: 197)，其中加下劃線之字母為與SEQ ID NO: 196之正向引子重疊之區域。

為了在殘基198處插入突變R198A，使用具有序列5'-GCCTCGGCACCGGGCCCTG**gcG**ACCGCCCCTAT(SEQ ID NO: 198)之正向引子及具有序列5'-**CAGGGCCCGGTGCCGAGGC**AGGCCAGGGGA(SEQ ID NO: 199)之反向引子。使用此等引子來擴增插入DNA使得野生型精胺酸(cgG)變化成丙胺酸(gcG)。

可使用突變正向及反向引子對，以甲基化野生型或突變質體DNA作為模板，使用基於預期引子退火溫度之標準擴增條件，藉由PCR來產生突變體。PCR產物可轉型至

DH5α-Ti化學感受態細胞中，在含有100 μg/ml安比西林(ampicillin)且經預熱之LB瓊脂板上展佈，在37℃下培育隔夜。接著藉由群落PCR分析群落以確認轉型體含有具有預期尺寸之插入物。藉由DNA定序確認突變DNA序列之序列。

使用類似技術，可製備SEQ ID NO: 202至220之各者。

實例3：用表現突變RAGE融合蛋白之純系轉染HEK及CHO細胞

基本上如製造商所指示，使用Fegene 6(Roche)，在6孔板中，用TTP-4000野生型或突變體之經純化質體DNA轉染HEK 293F細胞或CHO細胞。在24小時之轉染時期之後，將細胞轉移至150-mm器皿中，且在含有用於選擇之1 mg/mL G418的培養基中生長。在15-20天之後，使用含有0.25%胰蛋白酶-EDTA之3 mm選殖圓盤分離抗生素抗性個別群落。在24孔板中擴增所收集之細胞且使用DMEM-10% FBS、1 mg/mL G418，在37℃、含5% CO_2之濕潤培育箱中培養。

可使用抗RAGE mAb及抗人類IgG Fc抗體，藉由間接ELISA測試各個別純系之上清液中的RAGE融合蛋白之表現。此外，亦可使用S100b及抗人類IgG Fc-AP抗體，藉由間接ELISA檢測所表現之RAGE融合蛋白的受體-配位體結合活性。舉例而言，為了檢測RAGE融合蛋白，用抗RAGE mAb、抗人類IgG Fc多株抗體或S100b塗鋪96孔ELISA板之各孔。接著用1% BSA-TBS阻斷板，添加培養上清液，且

接著添加鹼性磷酸酶結合之山羊抗人類IgG Fc以偵測RAGE融合蛋白之結合(亦即，RAGE融合蛋白可結合於塗鋪於板上之RAGE配位體、抗RAGE mAb或抗人類IgG抗體)。各培育皆繼之以用含有0.05%吐溫20之TBS將板洗滌4次。添加pNPP受質且用微板讀取器偵測405 nm下之吸光度值。

陽性純系進一步藉由限制稀釋法來純化且不同RAGE融合蛋白突變體之最終純系可接著用於蛋白質表現。

實例4：TTP-4000之表現及純化

使用DMEM-10% FBS、0.5 mg/mL G418於T225燒瓶中，使表現TTP-4000野生型RAGE融合蛋白或其變異體(亦即突變體)之穩定細胞在37℃、含5% CO_2之濕潤培育箱中生長1週且接著轉移至5 L波生物反應器(wave bioreactor)或滾瓶(roller bottle)中。每週藉由間接ELISA，測試上清液中的S100b結合活性及蛋白質表現量。

在培養10-25天之後，收集培養基且在4℃下在10,000× g下離心30分鐘。接著依序用0.4 μm過濾器及0.2 μm過濾器過濾上清液。添加1/20體積之1 M Tris-HCl(pH 8.0)至經過濾之培養基(亦即上清液)中且裝載在蛋白A管柱上。管柱用約20倍體積之含有1 M NaCl的PBS洗滌直至UV偵測器上之OD 280 nm<0.05。蛋白質接著用25 mM乙酸鹽(pH 3.5)溶離且用溶離份收集器收集。用1.5 M Tris鹼溶液使溶離液之pH值調整至6.5並用Amicon超離心過濾裝置濃縮且在4℃下用磷酸鹽緩衝鹽水(PBS)透析隔夜。

藉由間接ELISA測試經純化蛋白質之S100b結合活性。利用ELISA與280 nm下之UV吸光度兩者來測定蛋白質濃度。亦使用SDS-PAGE及基於微流體晶片之自動電泳系統，藉由電泳分析經純化蛋白質之樣品的純度、分子量及蛋白質濃度。

實例5：RAGE融合蛋白在小鼠中之藥物動力學

此實驗檢驗在以10 mg/kg IV投與本發明之RAGE融合蛋白之後，該RAGE融合蛋白在CD-1小鼠中之藥物動力學及活體外穩定性。使用經設計用以藉由偵測融合蛋白之RAGE及免疫球蛋白部分來量測融合蛋白的酶聯結免疫吸附檢測(ELISA)測定RAGE融合蛋白(例如TTP4000及其如下文描述之變異體)在小鼠血漿中的濃度。在此檢測中，96孔微量滴定板經每孔100 μL之1 μg/mL之於碳酸鹽緩衝液(pH 9.6)中的RAGE單株抗體(R & D Systems, #MAB1145)塗鋪。在4℃下培育隔夜之後，各板用洗滌緩衝液(0.05%吐溫-20+磷酸鹽緩衝鹽水(PBS))洗滌且在室溫下用阻斷緩衝液(3%牛血清白蛋白(BSA)、0.05%吐溫-20、PBS)處理約2小時。檢測板接著用0.05%吐溫-20、PBS洗滌緩衝液洗滌且將每孔100 μL之以下任一者裝載於板上：(1) TTP4000血漿校正標準物(亦即添加有已知濃度之TTP4000且接著經連續稀釋之樣品)；(2)品質對照物(亦即添加有已知濃度之TTP4000、界定檢測之定量範圍且用於監測檢測能力的樣品)；及(3)已於樣品稀釋劑(亦即3% BSA、0.05%吐溫-20、PBS)中稀釋之小鼠血漿樣品。該等板接著在室溫下

在板振盪器上培育1小時。該等板接著用0.05%吐溫-20、PBS洗滌且添加每孔100 μL偵測抗體(購自Jackson Immuno Research之經生物素標記之小鼠抗人類IgG，具有Fc特異性，按1:1000稀釋)，隨後在室溫下在振盪下培育1小時。該等板再次用0.05%吐溫-20、PBS洗滌緩衝液洗滌且每孔添加100 μL新鮮製備之抗生蛋白鏈菌素/HRP的稀釋液(1:100,000)，且該等板在室溫下在振盪下培育30分鐘。在培育30分鐘之後，洗滌各板且添加每孔100 μL 3,3',5'5'-四甲基聯苯胺(TMB)受質，且使其在室溫下，在無振盪下培育約10分鐘。藉由每孔添加100 μL 2 M H_2SO_4來終止反應。使用Molecular Devices分光光度計(Lm1-Lm2：Lm1=450 nm，Lm2=650 nm)測定吸光度。使用SoftMax Pro軟體、4參數擬合確定各種RAGE融合蛋白之血漿濃度。

用於此實驗中之RAGE融合蛋白如下：

批次1-來自CHO細胞之SEQ ID NO: 56(野生型)；

批次2-來自HEK細胞之SEQ ID NO: 56(野生型)；

批次3-來自HEK細胞之SEQ ID NO: 67(相對於野生型，R198A突變)；

批次4-來自HEK細胞之SEQ ID NO: 71(相對於野生型，R198A及N2Q突變)；

批次5-來自HEK細胞之SEQ ID NO: 72(相對於野生型，R198A及N58Q突變)。

如圖9中所示，相較於其他所測試之RAGE融合蛋白，批

次3(R198A)及批次4(R198A及N2Q)之RAGE融合蛋白隨時間保持為較高血漿濃度(圖9A及圖9B)。在0-336小時(圖9A)及0-48小時(圖9B)之時期內觀測到此效應。

圖10展示在以10 mg/kg向小鼠靜脈內投藥之後，所測試之批次1-5之RAGE融合蛋白的平均藥物動力學參數。用曲線下面積(AUC)評估得知，總體藥物暴露在批次4(R198A及N2Q)及批次5(R198A及N58Q)之RAGE融合蛋白中大於批次1及2(野生型)及批次3(R198A)的總體藥物暴露。批次4(R198A及N2Q)及批次5(R198A及N58Q)之RAGE融合蛋白的總身體清除率(Clp)低於批次1及2(野生型)及批次3(R198A)之總身體清除率。批次4(R198A及N2Q)及批次5(R198A及N58Q)之RAGE融合蛋白的穩態分佈容積(Vss)低於批次1及2(野生型)及批次3(R198A)之穩態分佈容積。

圖11展示上述所測試之批次1至5之RAGE融合蛋白的活體外穩定性資料。圖11A以表格形式提供此資料，而圖11B以圖解形式提供此資料。在37℃下培育新鮮小鼠血漿(藥物濃度1.0 μg/mL)，且樣品係得自0-48小時期間。

實例6：量測突變RAGE融合蛋白之配位體結合

使用來自個別純系之上清液來量測突變TTP-4000蛋白質之表現及所表現之蛋白質與RAGE配位體S100b結合之能力。

結合檢測為間接ELISA，使用S100b作為RAGE配位體，且使用經鹼性磷酸酶(AP)標記之抗人類IgG Fc抗體來偵測RAGE與S100b之結合。在4℃下，使用100 nM碳酸氫鹽/碳

酸鹽塗鋪緩衝液(pH 9.6)，用每孔100 μl之5 μg/ml S100b塗鋪96孔ELISA板之各孔隔夜。該板接著在室溫下用每孔300 μl之1% BSA-TBST阻斷2小時。接著，添加每孔100 μl培養上清液或經純化突變RAGE融合蛋白，且接著添加每孔100 μl已用1% BSA-TBST按1:2500稀釋的鹼性磷酸酶結合之山羊抗人類IgG Fc。各培育皆繼之以用含有0.05%吐溫20之TBS(TBST)單獨洗滌4次。添加鹼性磷酸酶受質磷酸對硝基苯酯(pNPP)，且用微板讀取器偵測405 nm下之吸光度值並相對於重量百分比(wt %)加以校正。結果顯示於圖12中。

所有公開案及專利申請案皆以引用的方式併入本文中，其引用程度就如同特定及個別地指示將各個別公開案或專利申請案以引用的方式併入一般。

儘管已出於理解清晰性之目的藉由說明及舉例方式較詳細地描述了上述發明，但很顯然，可在隨附實施例之範疇內實施某些變化及修改。

【圖式簡單說明】

圖1展示根據本發明之替代性實施例的各種RAGE序列及免疫球蛋白序列：**圖A**，SEQ ID NO: 1，人類RAGE之胺基酸序列；及SEQ ID NO: 2，人類RAGE之無胺基酸1-22之信號序列的胺基酸序列；**圖B**，SEQ ID NO: 3，人類RAGE之無胺基酸1-23之信號序列的胺基酸序列；**圖C**，SEQ ID NO: 4，人類sRAGE之胺基酸序列；SEQ ID NO: 5，人類sRAGE之無胺基酸1-22之信號序列的胺基酸序列，及SEQ

ID NO: 6，人類sRAGE之無胺基酸1-23之信號序列的胺基酸序列；**圖D**，SEQ ID NO: 7，包含人類RAGE之V域之胺基酸序列；SEQ ID NO: 8，包含人類RAGE之V域之替代性胺基酸序列；SEQ ID NO: 9，人類RAGE之V域之N端片段；SEQ ID NO: 10，人類RAGE之V域之替代性N端片段；SEQ ID NO: 11，人類RAGE之胺基酸124-221之胺基酸序列；SEQ ID NO: 12，人類RAGE之胺基酸227-317之胺基酸序列；SEQ ID NO: 13，人類RAGE之胺基酸23-123之胺基酸序列；**圖E**，SEQ ID NO: 14，人類RAGE之胺基酸24-123之胺基酸序列；SEQ ID NO: 15，人類RAGE之胺基酸23-136之胺基酸序列；SEQ ID NO: 16，人類RAGE之胺基酸24-136之胺基酸序列；SEQ ID NO: 17，人類RAGE之胺基酸23-226之胺基酸序列；SEQ ID NO: 18，人類RAGE之胺基酸24-226之胺基酸序列；**圖F**，SEQ ID NO: 19，人類RAGE之胺基酸23-251之胺基酸序列；SEQ ID NO: 20，人類RAGE之胺基酸24-251之胺基酸序列；SEQ ID NO: 21，RAGE域間連接子；SEQ ID NO: 22，第二RAGE域間連接子；SEQ ID NO: 23，第三RAGE域間連接子；SEQ ID NO: 24，第四RAGE域間連接子；**圖G**，SEQ ID NO: 25，編碼人類RAGE胺基酸1-118之DNA；SEQ ID NO: 26，編碼人類RAGE胺基酸1-123之DNA；及SEQ ID NO: 27，編碼人類RAGE胺基酸1-136之DNA；**圖H**，SEQ ID NO: 28，編碼人類RAGE胺基酸1-230之DNA；及SEQ ID NO: 29，編碼人類RAGE胺基酸1-251之DNA；**圖I**，

SEQ ID NO: 38，人類IgG之C_H2及C_H3域之部分胺基酸序列；SEQ ID NO: 39，編碼人類IgG之人類C_H2及C_H3域之一部分的DNA；SEQ ID NO: 40，人類IgG之C_H2及C_H3域之胺基酸序列；**圖J**，SEQ ID NO: 41，編碼人類IgG之人類C_H2及C_H3域之DNA；SEQ ID NO: 42，人類IgG之C_H2域之胺基酸序列；SEQ ID NO: 43，人類IgG之C_H3域之胺基酸序列；及SEQ ID NO: 44，第五RAGE域間連接子；**圖K**，SEQ ID NO: 45，人類sRAGE之無胺基酸1-23之信號序列的胺基酸序列，其中N端處之麩醯胺酸殘基已環化而形成焦麩胺酸，SEQ ID NO: 46，包含人類sRAGE之V域之替代性胺基酸序列，其中N端處之麩醯胺酸殘基已環化而形成焦麩胺酸，SEQ ID NO: 47，人類RAGE之V域之替代性N端片段，其中N端處之麩醯胺酸殘基已環化而形成焦麩胺酸，SEQ ID NO: 48，人類RAGE之胺基酸24-123之胺基酸序列，其中N端處之麩醯胺酸殘基已環化而形成焦麩胺酸；**圖L**，SEQ ID NO: 49，人類RAGE之胺基酸24-136之胺基酸序列，其中N端處之麩醯胺酸殘基已環化而形成焦麩胺酸，SEQ ID NO: 50，人類RAGE之胺基酸24-226之胺基酸序列，其中N端處之麩醯胺酸殘基已環化而形成焦麩胺酸，SEQ ID NO: 51，人類RAGE之胺基酸24-251之胺基酸序列，其中N端處之麩醯胺酸殘基已環化而形成焦麩胺酸；**圖M**，SEQ ID NO: 52，編碼SEQ ID NO: 38中之人類IgG之人類C_H2及C_H3域的一部分之替代性DNA序列，及SEQ ID NO: 53，編碼SEQ ID NO: 40中之人類IgG之人類

5

C_H2及C_H3域的替代性DNA序列；

圖2展示編碼根據本發明之一實施例之第一RAGE融合蛋白(TTP-4000)編碼區的替代性DNA序列SEQ ID NO: 30(圖A)及SEQ ID NO: 54(圖B)。以粗體突出之編碼序列1-753編碼RAGE N端蛋白質序列，而序列754-1386編碼無鉸鏈區之人類IgG Fc(γ1)蛋白質序列；

圖3展示編碼根據本發明之一實施例之第二RAGE融合蛋白(TTP-3000)編碼區的替代性DNA序列SEQ ID NO: 31(圖A)及SEQ ID NO: 55(圖B)。以粗體突出之編碼序列1-408編碼RAGE N端蛋白質序列，而序列409-1041編碼無鉸鏈區之人類IgG Fc(γ1)蛋白質序列；

圖4展示各自編碼根據本發明之替代性實施例之四域RAGE融合蛋白的胺基酸序列SEQ ID NO: 32、SEQ ID NO: 33、SEQ ID NO: 34及SEQ ID NO: 56。RAGE序列以粗體字突出；

圖5展示各自編碼根據本發明之替代性實施例之三域RAGE融合蛋白的胺基酸序列SEQ ID NO: 35、SEQ ID NO: 36、SEQ ID NO: 37及SEQ ID NO: 57。RAGE序列以粗體字突出；

圖6展示根據本發明之替代性實施例的包含RAGE多肽序列及免疫球蛋白多肽序列之各種RAGE融合蛋白。該等RAGE融合蛋白對應於SEQ ID NO: 34之RAGE融合蛋白(TTP4000)之胺基酸序列，其中胺基酸1-23之信號序列已經移除且RAGE融合蛋白包含移除糖基化位點及/或弗林蛋

白酶裂解位點之一或多個點突變，其係基於相對於全長野生型RAGE序列(SEQ ID NO: 1)自胺基酸24開始之編號。各序列如下提供：**圖A**，SEQ ID NO: 62，具有N2Q(亦即對應於全長野生型序列中之N25Q)點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 63，具有N58Q點突變(亦即對應於全長野生型序列中之N81Q)之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 64，具有N2Q及N58Q點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 65，具有R195A點突變之TTP4000 RAGE融合蛋白之胺基酸序列；**圖B**，SEQ ID NO: 66，具有R195K點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 67，具有R198A點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 68，具有R198K點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 69，具有R198H點突變之TTP4000 RAGE融合蛋白之胺基酸序列；**圖C**，SEQ ID NO: 70，具有R198T點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 71，具有N2Q及R198A點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 72，具有N58Q及R198A點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 73，具有N2Q、N58Q及R198A點突變之TTP4000 RAGE融合蛋白之胺基酸序列；**圖D**，SEQ ID NO: 74，具有N288Q點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 75，具有N2Q及N288Q點突變之TTP4000 RAGE融合蛋白

之胺基酸序列；SEQ ID NO: 76，具有N58Q及N288Q點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 77，具有N2Q、N58Q及N288Q點突變之TTP4000 RAGE融合蛋白之胺基酸序列；**圖E**，SEQ ID NO: 78，具有N2Q、R198A及N288Q點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 79，具有N58Q、R198A及N288Q點突變之TTP4000 RAGE融合蛋白之胺基酸序列；SEQ ID NO: 80，具有N2Q、N58Q、R198A及N288Q點突變之TTP4000 RAGE融合蛋白之胺基酸序列；及SEQ ID NO: 81，具有G59S及R198A點突變之TTP4000 RAGE融合蛋白之胺基酸序列；**圖F至圖J**展示SEQ ID NO: 92至111，其分別對應於SEQ ID NO: 62至81，例外之處為C端離胺酸已經移除；**圖K至圖O**展示SEQ ID NO: 112至131，其分別對應於SEQ ID NO: 62至81，例外之處為存在有N端焦麩胺酸殘基替代N端麩醯胺酸殘基；**圖P至圖T**展示SEQ ID NO: 132至151，其分別對應於SEQ ID NO: 62至81，例外之處為N端麩醯胺酸已經移除；**圖U至圖Y**展示SEQ ID NO: 152至171，其分別對應於SEQ ID NO: 132至151，例外之處為C端離胺酸已經移除；**圖Z至圖DD**展示SEQ ID NO: 172至190以及SEQ ID NO: 200，其分別對應於SEQ ID NO: 62至81，例外之處為存在有N端焦麩胺酸殘基替代N端麩醯胺酸殘基且C端離胺酸已經移除；**圖EE-FF**展示SEQ ID NO: 58、59、60、61、82及201，其對應於具有N2Q、G59S及R198A點突變之TTP4000 RAGE融合蛋白(亦即SEQ ID NO:

34)之胺基酸序列(SEQ ID NO: 58)以及C端離胺酸已經移除之SEQ ID NO: 58(SEQ ID NO: 59)、例外之處為存在有N端焦麩胺酸殘基替代N端麩醯胺酸殘基之SEQ ID NO: 58(SEQ ID NO: 60)、例外之處為N端麩醯胺酸已經移除之SEQ ID NO: 58(SEQ ID NO: 61)、C端離胺酸已經移除之SEQ ID NO: 61(SEQ ID NO: 82)、例外之處為存在有N端焦麩胺酸殘基替代N端麩醯胺酸殘基且C端離胺酸已經移除之SEQ ID NO: 58(SEQ ID NO: 201)；及對應於具有1個RAGE免疫球蛋白域及在3個糖基化位點處之突變之RAGE融合蛋白的SEQ ID NO: 225；

圖7展示編碼SEQ ID NO: 34(TTP4000)之TTP4000 RAGE融合蛋白之DNA序列的替代性實施例，其中該RAGE融合蛋白包含移除糖基化位點及/或弗林蛋白酶裂解位點之一或多個點突變：**圖A**，SEQ ID NO: 221，編碼TTP4000 RAGE融合蛋白之核苷酸序列；**圖B**，SEQ ID NO: 222，編碼TTP4000 RAGE融合蛋白之替代性核苷酸序列；

圖8A展示人類RAGE之天然胺基酸信號序列(SEQ ID NO: 83)，以及編碼人類RAGE之天然胺基酸信號序列之DNA序列的替代性實施例(天然DNA信號序列為SEQ ID NO: 84，經修飾DNA信號序列為SEQ ID NO: 85)；

圖8B展示融合蛋白之免疫球蛋白部分之各種胺基酸序列；SEQ ID NO: 86對應於SEQ ID NO: 38，例外之處為C端離胺酸已經移除；SEQ ID NO: 87對應於SEQ ID NO: 40，例外之處為C端離胺酸已經移除；SEQ ID NO: 88對應

於SEQ ID NO: 40，例外之處為前11個N端胺基酸及1個C端離胺酸已經移除；SEQ ID NO: 89對應於SEQ ID NO: 40，例外之處為前11個N端胺基酸已經移除且存在有自N變成Q之點突變(以粗體字顯示)；SEQ ID NO: 90對應於SEQ ID NO: 42，例外之處為前10個N端胺基酸已經移除；SEQ ID NO: 91對應於SEQ ID NO: 42，例外之處為前11個N端胺基酸已經移除；

圖8C-SEQ ID NO: 191對應於SEQ ID NO: 46，例外之處為具有N2Q點突變；SEQ ID NO: 192對應於SEQ ID NO: 46，例外之處為具有N2Q及N58Q點突變；SEQ ID NO: 193對應於SEQ ID NO: 46，例外之處為具有N58Q點突變；SEQ ID NO: 194對應於SEQ ID NO: 47，例外之處為具有N2Q點突變；SEQ ID NO: 195對應於SEQ ID NO: 47，例外之處為具有N2Q點突變及N端焦麩胺酸殘基；SEQ ID NO: 196，編碼移除免疫球蛋白多肽中之糖基化位點之突變的正向引子序列；SEQ ID NO: 197，具有與SEQ ID NO: 196之重疊區的反向引子序列；SEQ ID NO: 198，編碼移除RAGE多肽中之弗林蛋白酶裂解位點之突變的正向引子序列；SEQ ID NO: 199，具有與SEQ ID NO: 198之重疊區的反向引子序列；SEQ ID NO: 223，對應於包含IgG1之鉸鏈區之含有11個胺基酸的肽；及SEQ ID NO: 224，對應於包含IgG1之鉸鏈區之含有10個胺基酸的肽；

圖8D展示可編碼SEQ ID NO: 62、92、112、132、152及172之融合蛋白的核酸序列SEQ ID NO: 202；

圖8E展示可編碼SEQ ID NO: 63、93、113、133、153及173之融合蛋白的核酸序列SEQ ID NO: 203；

圖8F展示可編碼SEQ ID NO: 64、94、114、134、154及174之融合蛋白的核酸序列SEQ ID NO: 204；

圖8G展示可編碼SEQ ID NO: 65、95、115、135、155及175之融合蛋白的核酸序列SEQ ID NO: 205；

圖8H展示可編碼SEQ ID NO: 66、96、116、136、156及176之融合蛋白的核酸序列SEQ ID NO: 206；

圖8I展示可編碼SEQ ID NO: 67、97、117、137、157及177之融合蛋白的核酸序列SEQ ID NO: 207；

圖8J展示可編碼SEQ ID NO: 68、98、118、138、158及178之融合蛋白的核酸序列SEQ ID NO: 208；

圖8K展示可編碼SEQ ID NO: 69、99、119、139、159及179之融合蛋白的核酸序列SEQ ID NO: 209；

圖8L展示可編碼SEQ ID NO: 70、100、120、140、160及180之融合蛋白的核酸序列SEQ ID NO: 210；

圖8M展示可編碼SEQ ID NO: 71、101、121、141、161及181之融合蛋白的核酸序列SEQ ID NO: 211；

圖8N展示可編碼SEQ ID NO: 72、102、122、142、162及182之融合蛋白的核酸序列SEQ ID NO: 212；

圖8O展示可編碼SEQ ID NO: 73、103、123、143、163及183之融合蛋白的核酸序列SEQ ID NO: 213；

圖8P展示可編碼SEQ ID NO: 74、104、124、144、164及184之融合蛋白的核酸序列SEQ ID NO: 214；

圖8Q展示可編碼SEQ ID NO: 75、105、125、145、165及185之融合蛋白的核酸序列SEQ ID NO: 215；

圖8R展示可編碼SEQ ID NO: 76、106、126、146、166及186之融合蛋白的核酸序列SEQ ID NO: 216；

圖8S展示可編碼SEQ ID NO: 77、107、127、147、167及187之融合蛋白的核酸序列SEQ ID NO: 217；

圖8T展示可編碼SEQ ID NO: 78、108、128、148、168及188之融合蛋白的核酸序列SEQ ID NO: 219；

圖8U展示可編碼SEQ ID NO: 79、109、129、149、169及189之融合蛋白的核酸序列SEQ ID NO: 219；

圖8V展示可編碼SEQ ID NO: 80、110、130、150、170及190之融合蛋白的核酸序列SEQ ID NO: 220；

圖9展示本文所述之批次1-5之RAGE融合蛋白的藥物動力學概況之差異。在0-336小時(**圖9A**)及0-48小時(**圖9B**)之時段內量測血漿濃度；

圖10展示在以10 mg/kg向小鼠靜脈內投藥之後，本文所述之批次1-5之RAGE融合蛋白的平均藥物動力學參數；

圖11展示以下所述之批次1至5之RAGE融合蛋白的活體外穩定性資料。**圖11A**以表格形式提供此資料，而**圖11B**以圖解形式提供此資料；及

圖12展示各種突變RAGE融合蛋白之相對結合親和力。

序列表

<110> 美商創世泰克藥業股份有限公司

<120> RAGE融合蛋白組合物及使用方法

<130> 61568-396928

<140> 100105575
<141> 2011-02-18

<150> 61/305,706
<151> 2010-02-18

<150> PCT/US2010/032270
<151> 2010-04-23

<150> PCT/US2010/053157
<151> 2010-10-19

<160> 225

<170> PatentIn version 3.5

<210> 1
<211> 404
<212> PRT
<213> 智人

<400> 1

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

Trp Gly Ala Val Val Gly Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu
20 25 30

Pro Leu Val Leu Lys Cys Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg
35 40 45

Leu Glu Trp Lys Leu Asn Thr Gly Arg Thr Glu Ala Trp Lys Val Leu
50 55 60

Ser Pro Gln Gly Gly Gly Pro Trp Asp Ser Val Ala Arg Val Leu Pro
65 70 75 80

Asn Gly Ser Leu Phe Leu Pro Ala Val Gly Ile Gln Asp Glu Gly Ile
85 90 95

Phe Arg Cys Gln Ala Met Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn
100 105 110

Tyr Arg Val Arg Val Tyr Gln Ile Pro Gly Lys Pro Glu Ile Val Asp
115 120 125

Ser Ala Ser Glu Leu Thr Ala Gly Val Pro Asn Lys Val Gly Thr Cys
130 135 140

Val Ser Glu Gly Ser Tyr Pro Ala Gly Thr Leu Ser Trp His Leu Asp
145 150 155 160

Gly Lys Pro Leu Val Pro Asn Glu Lys Gly Val Ser Val Lys Glu Gln
165 170 175

Thr Arg Arg His Pro Glu Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu
180 185 190

Met Val Thr Pro Ala Arg Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys
195 200 205

Ser Phe Ser Pro Gly Leu Pro Arg His Arg Ala Leu Arg Thr Ala Pro
210 215 220

Ile Gln Pro Arg Val Trp Glu Pro Val Pro Leu Glu Glu Val Gln Leu
225 230 235 240

Val Val Glu Pro Glu Gly Gly Ala Val Ala Pro Gly Gly Thr Val Thr
245 250 255

Leu Thr Cys Glu Val Pro Ala Gln Pro Ser Pro Gln Ile His Trp Met
260 265 270

Lys Asp Gly Val Pro Leu Pro Leu Pro Pro Ser Pro Val Leu Ile Leu
275 280 285

Pro Glu Ile Gly Pro Gln Asp Gln Gly Thr Tyr Ser Cys Val Ala Thr
290 295 300

His Ser Ser His Gly Pro Gln Glu Ser Arg Ala Val Ser Ile Ser Ile
305 310 315 320

Ile Glu Pro Gly Glu Glu Gly Pro Thr Ala Gly Ser Val Gly Gly Ser
325 330 335

Gly Leu Gly Thr Leu Ala Leu Ala Leu Gly Ile Leu Gly Gly Leu Gly
340 345 350

Thr Ala Ala Leu Leu Ile Gly Val Ile Leu Trp Gln Arg Arg Gln Arg
355 360 365

Arg Gly Glu Glu Arg Lys Ala Pro Glu Asn Gln Glu Glu Glu Glu Glu
370 375 380

Arg Ala Glu Leu Asn Gln Ser Glu Glu Pro Glu Ala Gly Glu Ser Ser
385 390 395 400

Thr Gly Gly Pro

<210> 2
<211> 382
<212> PRT
<213> 智人

<400> 2

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu Leu Thr
100 105 110

Ala Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr
115 120 125

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

Asn Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu

145 150 155 160

Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg
165 170 175

Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu
180 185 190

Pro Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp
195 200 205

Glu Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly
210 215 220

Gly Ala Val Ala Pro Gly Gly Thr Val Thr Leu Thr Cys Glu Val Pro
225 230 235 240

Ala Gln Pro Ser Pro Gln Ile His Trp Met Lys Asp Gly Val Pro Leu
245 250 255

Pro Leu Pro Pro Ser Pro Val Leu Ile Leu Pro Glu Ile Gly Pro Gln
260 265 270

Asp Gln Gly Thr Tyr Ser Cys Val Ala Thr His Ser Ser His Gly Pro
275 280 285

Gln Glu Ser Arg Ala Val Ser Ile Ser Ile Ile Glu Pro Gly Glu Glu
290 295 300

Gly Pro Thr Ala Gly Ser Val Gly Gly Ser Gly Leu Gly Thr Leu Ala
305 310 315 320

Leu Ala Leu Gly Ile Leu Gly Gly Leu Gly Thr Ala Ala Leu Leu Ile

325 330 335

Gly Val Ile Leu Trp Gln Arg Arg Gln Arg Arg Gly Glu Glu Arg Lys
340 345 350

Ala Pro Glu Asn Gln Glu Glu Glu Glu Glu Arg Ala Glu Leu Asn Gln
355 360 365

Ser Glu Glu Pro Glu Ala Gly Glu Ser Ser Thr Gly Gly Pro
370 375 380

<210> 3
<211> 381
<212> PRT
<213> 智人

<400> 3

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Gly Gly Thr Val Thr Leu Thr Cys Glu Val Pro Ala
225 230 235 240

Gln Pro Ser Pro Gln Ile His Trp Met Lys Asp Gly Val Pro Leu Pro
245 250 255

Leu Pro Pro Ser Pro Val Leu Ile Leu Pro Glu Ile Gly Pro Gln Asp
260 265 270

Gln Gly Thr Tyr Ser Cys Val Ala Thr His Ser Ser His Gly Pro Gln
275 280 285

Glu Ser Arg Ala Val Ser Ile Ser Ile Ile Glu Pro Gly Glu Glu Gly
290 295 300

Pro Thr Ala Gly Ser Val Gly Gly Ser Gly Leu Gly Thr Leu Ala Leu
305 310 315 320

Ala Leu Gly Ile Leu Gly Gly Leu Gly Thr Ala Ala Leu Leu Ile Gly
325 330 335

Val Ile Leu Trp Gln Arg Arg Gln Arg Arg Gly Glu Glu Arg Lys Ala
340 345 350

Pro Glu Asn Gln Glu Glu Glu Glu Glu Arg Ala Glu Leu Asn Gln Ser
355 360 365

Glu Glu Pro Glu Ala Gly Glu Ser Ser Thr Gly Gly Pro
370 375 380

<210> 4
<211> 339
<212> PRT
<213> 智人

<400> 4

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

Trp Gly Ala Val Val Gly Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu
20 25 30

Pro Leu Val Leu Lys Cys Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg
35 40 45

Leu Glu Trp Lys Leu Asn Thr Gly Arg Thr Glu Ala Trp Lys Val Leu
50 55 60

Ser Pro Gln Gly Gly Gly Pro Trp Asp Ser Val Ala Arg Val Leu Pro
65 70 75 80

Asn Gly Ser Leu Phe Leu Pro Ala Val Gly Ile Gln Asp Glu Gly Ile
85 90 95

Phe Arg Cys Gln Ala Met Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn
100 105 110

Tyr Arg Val Arg Val Tyr Gln Ile Pro Gly Lys Pro Glu Ile Val Asp
115 120 125

Ser Ala Ser Glu Leu Thr Ala Gly Val Pro Asn Lys Val Gly Thr Cys
130 135 140

Val Ser Glu Gly Ser Tyr Pro Ala Gly Thr Leu Ser Trp His Leu Asp
145 150 155 160

Gly Lys Pro Leu Val Pro Asn Glu Lys Gly Val Ser Val Lys Glu Gln
165 170 175

Thr Arg Arg His Pro Glu Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu
180 185 190

Met Val Thr Pro Ala Arg Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys
195 200 205

Ser Phe Ser Pro Gly Leu Pro Arg His Arg Ala Leu Arg Thr Ala Pro
210 215 220

Ile Gln Pro Arg Val Trp Glu Pro Val Pro Leu Glu Glu Val Gln Leu
225 230 235 240

Val Val Glu Pro Glu Gly Gly Ala Val Ala Pro Gly Gly Thr Val Thr
245 250 255

Leu Thr Cys Glu Val Pro Ala Gln Pro Ser Pro Gln Ile His Trp Met
260 265 270

Lys Asp Gly Val Pro Leu Pro Leu Pro Pro Ser Pro Val Leu Ile Leu
275 280 285

Pro Glu Ile Gly Pro Gln Asp Gln Gly Thr Tyr Ser Cys Val Ala Thr
290 295 300

His Ser Ser His Gly Pro Gln Glu Ser Arg Ala Val Ser Ile Ser Ile
305 310 315 320

Ile Glu Pro Gly Glu Glu Gly Pro Thr Ala Gly Ser Val Gly Gly Ser
325 330 335

Gly Leu Gly

<210> 5
<211> 317
<212> PRT
<213> 智人

<400> 5

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu Leu Thr
100 105 110

Ala Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr
115 120 125

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

Asn Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu
145 150 155 160

Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg
165 170 175

Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu
180 185 190

Pro Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp
195 200 205

Glu Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly
210 215 220

Gly Ala Val Ala Pro Gly Gly Thr Val Thr Leu Thr Cys Glu Val Pro
225 230 235 240

Ala Gln Pro Ser Pro Gln Ile His Trp Met Lys Asp Gly Val Pro Leu
245 250 255

Pro Leu Pro Pro Ser Pro Val Leu Ile Leu Pro Glu Ile Gly Pro Gln
260 265 270

Asp Gln Gly Thr Tyr Ser Cys Val Ala Thr His Ser Ser His Gly Pro
275 280 285

Gln Glu Ser Arg Ala Val Ser Ile Ser Ile Ile Glu Pro Gly Glu Glu
290 295 300

Gly Pro Thr Ala Gly Ser Val Gly Gly Ser Gly Leu Gly
305 310 315

<210> 6
<211> 316
<212> PRT
<213> 智人

<400> 6

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys

1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

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

180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Gly Gly Thr Val Thr Leu Thr Cys Glu Val Pro Ala
225 230 235 240

Gln Pro Ser Pro Gln Ile His Trp Met Lys Asp Gly Val Pro Leu Pro
245 250 255

Leu Pro Pro Ser Pro Val Leu Ile Leu Pro Glu Ile Gly Pro Gln Asp
260 265 270

Gln Gly Thr Tyr Ser Cys Val Ala Thr His Ser Ser His Gly Pro Gln
275 280 285

Glu Ser Arg Ala Val Ser Ile Ser Ile Ile Glu Pro Gly Glu Glu Gly
290 295 300

Pro Thr Ala Gly Ser Val Gly Gly Ser Gly Leu Gly
305 310 315

<210> 7
<211> 94
<212> PRT
<213> 智人

<400> 7

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg
85 90

<210> 8
<211> 93
<212> PRT
<213> 智人

<400> 8

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg
85 90

<210> 9
<211> 30
<212> PRT
<213> 智人

<400> 9

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys
20 25 30

<210> 10
<211> 29
<212> PRT
<213> 智人

<400> 10

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys
20 25

<210> 11
<211> 98
<212> PRT
<213> 智人

<400> 11

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

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

Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu Lys Gly Val
35 40 45

Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly Leu Phe Thr
50 55 60

Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly Asp Pro Arg
65 70 75 80

Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg His Arg Ala
85 90 95

Leu Arg

<210> 12
<211> 91
<212> PRT
<213> 智人

<400> 12

Pro Arg Val Trp Glu Pro Val Pro Leu Glu Glu Val Gln Leu Val Val
1 5 10 15

Glu Pro Glu Gly Gly Ala Val Ala Pro Gly Gly Thr Val Thr Leu Thr
20 25 30

Cys Glu Val Pro Ala Gln Pro Ser Pro Gln Ile His Trp Met Lys Asp
35 40 45

Gly Val Pro Leu Pro Leu Pro Pro Ser Pro Val Leu Ile Leu Pro Glu
50 55 60

Ile Gly Pro Gln Asp Gln Gly Thr Tyr Ser Cys Val Ala Thr His Ser
65 70 75 80

Ser His Gly Pro Gln Glu Ser Arg Ala Val Ser
85 90

<210> 13
<211> 101
<212> PRT
<213> 智人

<400> 13

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys
100

<210> 14
<211> 100
<212> PRT
<213> 智人

<400> 14

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

Ile Pro Gly Lys
100

<210> 15

<211> 114
<212> PRT
<213> 智人

<400> 15

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu Leu Thr
100 105 110

Ala Gly

<210> 16
<211> 113
<212> PRT
<213> 智人

<400> 16

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly

<210> 17
<211> 204
<212> PRT
<213> 智人

<400> 17

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu Leu Thr
100 105 110

Ala Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr
115 120 125

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

Asn Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu
145 150 155 160

Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg
165 170 175

Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu
180 185 190

Pro Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln
195 200

<210> 18
<211> 203
<212> PRT
<213> 智人

<400> 18

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

Ala Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn

130 135 140

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln
195 200

<210> 19
<211> 229
<212> PRT
<213> 智人

<400> 19

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu Leu Thr
100 105 110

Ala Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr
115 120 125

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

Asn Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu
145 150 155 160

Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg
165 170 175

Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu
180 185 190

Pro Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp
195 200 205

Glu Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly
210 215 220

Gly Ala Val Ala Pro
225

<210> 20
<211> 228

<212> PRT
<213> 智人

<400> 20

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro
225

<210> 21
<211> 7
<212> PRT
<213> 智人

<400> 21

Val Tyr Gln Ile Pro Gly Lys
1 5

<210> 22
<211> 30
<212> PRT
<213> 智人

<400> 22

Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro Val Pro Leu Glu Glu
1 5 10 15

Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala Val Ala Pro

20 25 30

<210> 23
<211> 20
<212> PRT
<213> 智人

<400> 23

Val Tyr Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu
1 5 10 15

Leu Thr Ala Gly
20

<210> 24
<211> 5
<212> PRT
<213> 智人

<400> 24

Thr Ala Pro Ile Gln
1 5

<210> 25
<211> 354
<212> DNA
<213> 智人

<400> 25
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctac 354

<210> 26
<211> 369
<212> DNA
<213> 智人

<400> 26
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaag 369

<210> 27
<211> 408
<212> DNA
<213> 智人

<400> 27
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaagc cagaaattgt agattctgcc tctgaactca cggctggt 408

<210> 28
<211> 690
<212> DNA
<213> 智人

<400> 28
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaagc cagaaattgt agattctgcc tctgaactca cggctggtgt tcccaataag 420

gtggggacat gtgtgtcaga ggggagctac cctgcaggga ctcttagctg gcacttggat 480

gggaagcccc tggtgcctaa tgagaaggga gtatctgtga aggaacagac caggagacac 540

cctgagacag ggctcttcac actgcagtcg gagctaatgg tgaccccagc ccggggagga 600

gatccccgtc ccaccttctc ctgtagcttc agcccaggcc ttccccgaca ccgggccttg 660

cgcacagccc ccatccagcc ccgtgtctgg 690

<210> 29
<211> 753
<212> DNA
<213> 智人

<400> 29
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaagc cagaaattgt agattctgcc tctgaactca cggctggtgt tcccaataag 420

gtggggacat gtgtgtcaga ggggagctac cctgcaggga ctcttagctg gcacttggat 480

gggaagcccc tggtgcctaa tgagaaggga gtatctgtga aggaacagac caggagacac 540

cctgagacag ggctcttcac actgcagtcg gagctaatgg tgaccccagc ccggggagga 600

gatccccgtc ccaccttctc ctgtagcttc agcccaggcc ttccccgaca ccgggccttg 660

cgcacagccc ccatccagcc ccgtgtctgg gagcctgtgc ctctggagga ggtccaattg 720

gtggtggagc cagaaggtgg agcagtagct cct 753

<210> 30
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 30
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaagc cagaaattgt agattctgcc tctgaactca cggctggtgt tcccaataag 420

gtggggacat gtgtgtcaga ggggagctac cctgcaggga ctcttagctg gcacttggat 480

gggaagcccc tggtgcctaa tgagaaggga gtatctgtga aggaacagac caggagacac 540

cctgagacag ggctcttcac actgcagtcg gagctaatgg tgaccccagc ccggggagga 600

gatccccgtc ccaccttctc ctgtagcttc agcccaggcc ttccccgaca ccgggccttg 660

cgcacagccc ccatccagcc ccgtgtctgg gagcctgtgc ctctggagga ggtccaattg 720

gtggtggagc cagaaggtgg agcagtagct cctccgtcag tcttcctctt ccccccaaaa 780

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg 840

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat 900

gccaagacaa agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtcctc 960

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 1020

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 1080

caggtgtaca ccctgccccc atcccgggat gagctgacca agaaccaggt cagcctgacc 1140

tgcctggtca aaggcttcta tcccagcgac atcgccgtgg agtgggagag caatgggcag 1200

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc 1260

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc 1320

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt 1380

aaatga 1386

〈210〉 31
〈211〉 1041
〈212〉 DNA
〈213〉 人工序列

〈220〉
〈223〉 人工=合成構築體

<400> 31

atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaagc cagaaattgt agattctgcc tctgaactca cggctggtcc gtcagtcttc 420

ctcttccccc caaaacccaa ggacaccctc atgatctccc ggacccctga ggtcacatgc 480

gtggtggtgg acgtgagcca cgaagaccct gaggtcaagt tcaactggta cgtggacggc 540

gtggaggtgc ataatgccaa gacaaagccg cgggaggagc agtacaacag cacgtaccgt 600

gtggtcagcg tcctcaccgt cctgcaccag gactggctga atggcaagga gtacaagtgc 660

aaggtctcca acaaagccct cccagccccc atcgagaaaa ccatctccaa agccaaaggg 720

cagccccgag aaccacaggt gtacaccctg cccccatccc gggatgagct gaccaagaac 780

caggtcagcc tgacctgcct ggtcaaaggc ttctatccca gcgacatcgc cgtggagtgg 840

gagagcaatg ggcagccgga gaacaactac aagaccacgc ctcccgtgct ggactccgac 900

ggctccttct tcctctacag caagctcacc gtggacaaga gcaggtggca gcaggggaac 960

gtcttctcat gctccgtgat gcatgaggct ctgcacaacc actacacgca gaagagcctc 1020

tccctgtctc cgggtaaatg a 1041

<210> 32
<211> 461
<212> PRT
<213> 人工序列

<220>

<223> 人工=合成構築體

<400> 32

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

Trp Gly Ala Val Val Gly Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu
20 25 30

Pro Leu Val Leu Lys Cys Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg
35 40 45

Leu Glu Trp Lys Leu Asn Thr Gly Arg Thr Glu Ala Trp Lys Val Leu
50 55 60

Ser Pro Gln Gly Gly Gly Pro Trp Asp Ser Val Ala Arg Val Leu Pro
65 70 75 80

Asn Gly Ser Leu Phe Leu Pro Ala Val Gly Ile Gln Asp Glu Gly Ile
85 90 95

Phe Arg Cys Gln Ala Met Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn
100 105 110

Tyr Arg Val Arg Val Tyr Gln Ile Pro Gly Lys Pro Glu Ile Val Asp
115 120 125

Ser Ala Ser Glu Leu Thr Ala Gly Val Pro Asn Lys Val Gly Thr Cys
130 135 140

Val Ser Glu Gly Ser Tyr Pro Ala Gly Thr Leu Ser Trp His Leu Asp
145 150 155 160

Gly Lys Pro Leu Val Pro Asn Glu Lys Gly Val Ser Val Lys Glu Gln
165 170 175

Thr Arg Arg His Pro Glu Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu
180 185 190

Met Val Thr Pro Ala Arg Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys
195 200 205

Ser Phe Ser Pro Gly Leu Pro Arg His Arg Ala Leu Arg Thr Ala Pro
210 215 220

Ile Gln Pro Arg Val Trp Glu Pro Val Pro Leu Glu Glu Val Gln Leu
225 230 235 240

Val Val Glu Pro Glu Gly Gly Ala Val Ala Pro 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 Ala Leu Pro Ala Pro 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 Asp Glu Leu 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

Gln 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 Gly Lys
450 455 460

<210> 33
<211> 439
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 33

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu Leu Thr
100 105 110

Ala Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr
115 120 125

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

Asn Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu
145 150 155 160

Thr Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg
165 170 175

Gly Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu
180 185 190

Pro Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp
195 200 205

Glu Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly
210 215 220

Gly Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
225 230 235 240

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

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
260 265 270

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
275 280 285

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
290 295 300

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
305 310 315 320

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
325 330 335

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
340 345 350

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
355 360 365

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
370 375 380

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
385 390 395 400

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
405 410 415

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
420 425 430

Leu Ser Leu Ser Pro Gly Lys
435

<210> 34
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 34

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 35
<211> 346
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 35

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

Trp Gly Ala Val Val Gly Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu
20 25 30

Pro Leu Val Leu Lys Cys Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg
35 40 45

Leu Glu Trp Lys Leu Asn Thr Gly Arg Thr Glu Ala Trp Lys Val Leu
50 55 60

Ser Pro Gln Gly Gly Gly Pro Trp Asp Ser Val Ala Arg Val Leu Pro
65 70 75 80

Asn Gly Ser Leu Phe Leu Pro Ala Val Gly Ile Gln Asp Glu Gly Ile
85 90 95

Phe Arg Cys Gln Ala Met Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn
100 105 110

Tyr Arg Val Arg Val Tyr Gln Ile Pro Gly Lys Pro Glu Ile Val Asp
115 120 125

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

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
145 150 155 160

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
165 170 175

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
180 185 190

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
195 200 205

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
210 215 220

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
225 230 235 240

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
245 250 255

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
260 265 270

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
275 280 285

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
290 295 300

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

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
325 330 335

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
340 345

<210> 36
<211> 324
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 36

Ala Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys
1 5 10 15

Lys Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn
20 25 30

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

Pro Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu
50 55 60

Pro Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met
65 70 75 80

Asn Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr
85 90 95

Gln Ile Pro Gly Lys Pro Glu Ile Val Asp Ser Ala Ser Glu Leu Thr
100 105 110

Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
115 120 125

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

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
145 150 155 160

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
165 170 175

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

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
195 200 205

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

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

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
245 250 255

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
260 265 270

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

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
290 295 300

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

Ser Pro Gly Lys

<210> 37
<211> 323
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 37

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
115 120 125

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

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
145 150 155 160

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
165 170 175

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

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
195 200 205

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

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

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
260 265 270

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

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
290 295 300

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

Pro Gly Lys

<210> 38
<211> 210
<212> PRT
<213> 智人

<400> 38

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
1 5 10 15

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
20 25 30

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
35 40 45

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
50 55 60

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
65 70 75 80

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
85 90 95

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
100 105 110

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
115 120 125

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
130 135 140

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
145 150 155 160

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
165 170 175

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
180 185 190

5

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
195 200 205

Gly Lys
210

<210> 39
<211> 633
<212> DNA
<213> 智人

<400> 39
ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 60

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 120

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 180

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 240

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 300

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 360

ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 420

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 480

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 540

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 600

cagaagagcc tctccctgtc tccgggtaaa tga 633

<210> 40
<211> 220
<212> PRT
<213> 智人

<400> 40

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

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
20 25 30

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
35 40 45

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
50 55 60

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
65 70 75 80

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
85 90 95

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
100 105 110

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
115 120 125

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
130 135 140

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

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

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
180 185 190

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
210 215 220

<210> 41
<211> 663
<212> DNA
<213> 智人

<400> 41
ccgtgcccag cacctgaact cctgggggga ccgtcagtct tcctcttccc cccaaaaccc 60

aaggacaccc tcatgatctc ccggacccct gaggtcacat gcgtggtggt ggacgtgagc 120

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 180

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 240

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 300

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 360

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 420

ctggtcaaag gcttctatcc cagcgacatc gccgtggagt gggagagcaa tgggcagccg 480

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 540

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 600

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 660

tga 663

<210> 42
<211> 113
<212> PRT
<213> 智人

<400> 42

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

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
20 25 30

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
35 40 45

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
50 55 60

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
65 70 75 80

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
85 90 95

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
100 105 110

Lys

<210> 43
<211> 107
<212> PRT
<213> 智人

<400> 43

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

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
50 55 60

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
65 70 75 80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
100 105

<210> 44
<211> 25
<212> PRT
<213> 智人

<400> 44

Ile Ser Ile Ile Glu Pro Gly Glu Glu Gly Pro Thr Ala Gly Ser Val
1 5 10 15

Gly Gly Ser Gly Leu Gly Thr Leu Ala
20 25

<210> 45
<211> 316
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 45

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Gly Gly Thr Val Thr Leu Thr Cys Glu Val Pro Ala
225 230 235 240

Gln Pro Ser Pro Gln Ile His Trp Met Lys Asp Gly Val Pro Leu Pro
245 250 255

Leu Pro Pro Ser Pro Val Leu Ile Leu Pro Glu Ile Gly Pro Gln Asp
260 265 270

Gln Gly Thr Tyr Ser Cys Val Ala Thr His Ser Ser His Gly Pro Gln
275 280 285

Glu Ser Arg Ala Val Ser Ile Ser Ile Ile Glu Pro Gly Glu Glu Gly
290 295 300

Pro Thr Ala Gly Ser Val Gly Gly Ser Gly Leu Gly
305 310 315

<210> 46
<211> 93
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa＝焦麩胺酸

<400> 46

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg
85 90

<210> 47

<211> 29
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 47

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys
20 25

<210> 48
<211> 100
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 48

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

Ile Pro Gly Lys
100

<210> 49
<211> 113
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa＝焦麩胺酸

<400> 49

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly

<210> 50
<211> 203
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 50

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro

50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln
195 200

<210> 51
<211> 228
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa＝焦麩胺酸

<400> 51

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro
225

<210> 52
<211> 633
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 52
ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 60

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 120

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 180

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 240

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 300

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 360

ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 420

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 480

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 540

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 600

cagaagagcc tctccctgtc tcccgggaaa tga 633

〈210〉 53
〈211〉 663
〈212〉 DNA
〈213〉 人工序列

〈220〉
〈223〉 人工=合成構築體

〈400〉 53
ccgtgcccag cacctgaact cctgggggga ccgtcagtct tcctcttccc cccaaaaccc 60

aaggacaccc tcatgatctc ccggacccct gaggtcacat gcgtggtggt ggacgtgagc 120

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 180

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 240

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 300

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 360

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 420

ctggtcaaag gcttctatcc cagcgacatc gccgtggagt gggagagcaa tgggcagccg 480

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 540

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 600

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tcccgggaaa 660

tga 663

<210> 54
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 54
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaagc cagaaattgt agattctgcc tctgaactca cggctggtgt tcccaataag 420

gtggggacat gtgtgtcaga ggggagctac cctgcaggga ctcttagctg gcacttggat 480

gggaagcccc tggtgcctaa tgagaaggga gtatctgtga aggaacagac caggagacac 540

cctgagacag ggctcttcac actgcagtcg gagctaatgg tgaccccagc ccggggagga 600

gatccccgtc ccaccttctc ctgtagcttc agcccaggcc ttccccgaca ccgggccttg 660

cgcacagccc ccatccagcc ccgtgtctgg gagcctgtgc ctctggagga ggtccaattg 720

gtggtggagc cagaaggtgg agcagtagct cctccgtcag tcttcctctt ccccccaaaa 780

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg 840

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat 900

gccaagacaa agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtcctc 960

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 1020

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 1080

caggtgtaca ccctgccccc atcccgggat gagctgacca agaaccaggt cagcctgacc 1140

tgcctggtca aaggcttcta tcccagcgac atcgccgtgg agtgggagag caatgggcag 1200

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc 1260

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc 1320

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctcccggg 1380

aaatga 1386

<210> 55
<211> 1041
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 55
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgctc aaaacatcac agcccggatt ggcgagccac tggtgctgaa gtgtaagggg 120

gcccccaaga aaccacccca gcggctggaa tggaaactga acacaggccg gacagaagct 180

tggaaggtcc tgtctcccca gggaggaggc ccctgggaca gtgtggctcg tgtccttccc 240

aacggctccc tcttccttcc ggctgtcggg atccaggatg aggggatttt ccggtgccag 300

gcaatgaaca ggaatggaaa ggagaccaag tccaactacc gagtccgtgt ctaccagatt 360

cctgggaagc cagaaattgt agattctgcc tctgaactca cggctggtcc gtcagtcttc 420

ctcttccccc caaaacccaa ggacaccctc atgatctccc ggacccctga ggtcacatgc 480

gtggtggtgg acgtgagcca cgaagaccct gaggtcaagt tcaactggta cgtggacggc 540

gtggaggtgc ataatgccaa gacaaagccg cgggaggagc agtacaacag cacgtaccgt 600

gtggtcagcg tcctcaccgt cctgcaccag gactggctga atggcaagga gtacaagtgc 660

aaggtctcca acaaagccct cccagccccc atcgagaaaa ccatctccaa agccaaaggg 720

cagccccgag aaccacaggt gtacaccctg cccccatccc gggatgagct gaccaagaac 780

caggtcagcc tgacctgcct ggtcaaaggc ttctatccca gcgacatcgc cgtggagtgg 840

gagagcaatg ggcagccgga gaacaactac aagaccacgc ctcccgtgct ggactccgac 900

ggctccttct tcctctacag caagctcacc gtggacaaga gcaggtggca gcaggggaac 960

gtcttctcat gctccgtgat gcatgaggct ctgcacaacc actacacgca gaagagcctc 1020

tccctgtctc ccgggaaatg a 1041

<210> 56
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 56

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 57
<211> 323
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 57

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
115 120 125

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

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
145 150 155 160

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
165 170 175

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

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
195 200 205

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

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

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
260 265 270

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

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
290 295 300

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

Pro Gly Lys

<210> 58
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 58

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 59
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 59

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 60
<211> 438
<212> PRT
<213> 智人

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 60

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

100 105 110

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn

275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 61

<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 61

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 62
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 62

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys

1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

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

180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

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

355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 63
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 63

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 64
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 64

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln

85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

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

260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys

435

<210> 65
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 65

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Ala Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 66
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 66

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly

165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Lys Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn

340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 67
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 67

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 68
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 68

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn

65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Lys Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp

245 250 255

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

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

420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 69
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 69

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu His Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 70
<211> 438
<212> PRT

<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 70

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr

145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Thr Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu

325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 71
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 71

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 72
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 72

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro

50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

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

225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

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

5

405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 73
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 73

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 74
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 74

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

Ala Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn

130 135 140

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

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

305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 75
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 75

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 76
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 76

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

35 40 45

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly

210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

385 390 395 400

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 77
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 77

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 78
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 78

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

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

115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp

290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 79
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 79

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 80
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 80

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr

20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu

195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

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

370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 81
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 81

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 82
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 82

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

100 105 110

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser

275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 83

<211> 23
<212> PRT
<213> 智人

<400> 83

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

Trp Gly Ala Val Val Gly Ala
20

<210> 84
<211> 69
<212> DNA
<213> 智人

<400> 84
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggggcagta 60

gtaggtgct 69

<210> 85
<211> 69
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 85
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgcc 69

<210> 86
<211> 209
<212> PRT
<213> 智人

<400> 86

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
1 5 10 15

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
20 25 30

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
35 40 45

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
50 55 60

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
65 70 75 80

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
85 90 95

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
100 105 110

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
115 120 125

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
130 135 140

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
145 150 155 160

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
165 170 175

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
180 185 190

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
195 200 205

Gly

<210> 87
<211> 219
<212> PRT
<213> 智人

<400> 87

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

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
20 25 30

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
35 40 45

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
50 55 60

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
65 70 75 80

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
85 90 95

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
100 105 110

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
115 120 125

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
130 135 140

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

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

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
180 185 190

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
210 215

<210> 88
<211> 208
<212> PRT
<213> 智人

<400> 88

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
1 5 10 15

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
20 25 30

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
35 40 45

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
50 55 60

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
65 70 75 80

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
85 90 95

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
100 105 110

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
115 120 125

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
130 135 140

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
145 150 155 160

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
165 170 175

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
180 185 190

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
195 200 205

<210> 89
<211> 208
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 89

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
1 5 10 15

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
20 25 30

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
35 40 45

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser Thr Tyr Arg Val
50 55 60

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
65 70 75 80

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
85 90 95

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
100 105 110

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
115 120 125

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
130 135 140

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
145 150 155 160

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
165 170 175

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
180 185 190

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
195 200 205

<210> 90
<211> 103
<212> PRT
<213> 智人

<400> 90

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
1 5 10 15

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
20 25 30

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
35 40 45

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
50 55 60

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
65 70 75 80

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
85 90 95

Lys Thr Ile Ser Lys Ala Lys
100

<210> 91
<211> 102
<212> PRT
<213> 智人

<400> 91

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
1 5 10 15

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
20 25 30

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
35 40 45

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
50 55 60

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
65 70 75 80

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
85 90 95

Thr Ile Ser Lys Ala Lys
100

<210> 92
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 92

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 93
<211> 437
<212> PRT
<213> 人工序列

<220>

<223> 人工=合成構築體

<400> 93

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 94
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 94

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 95
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 95

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Ala Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 96
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 96

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Lys Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 97
<211> 437

<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 97

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 98
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 98

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Lys Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 99
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 99

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu His Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 100
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 100

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Thr Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 101
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 101

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 102
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 102

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 103
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 103

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 104
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 104

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 105
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 105

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 106
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 106

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 107
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 107

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 108
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 108

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 109
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 109

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 110
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 110

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 111
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 111

Gln Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 112
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 112

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 113
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 113

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 114
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 114

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 115
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 115

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Ala Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 116
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 116

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Lys Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 117
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 117

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 118
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 118

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Lys Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 119
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 119

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu His Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 120
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa＝焦麩胺酸

<400> 120

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Thr Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 121
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)

<223> Xaa=焦麩胺酸

<400> 121

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 122
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 122

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 123
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 123

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 124
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 124

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 125
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 125

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 126
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 126

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 127
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 127

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 128
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 128

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 129
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 129

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 130
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 130

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 131
<211> 438
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa＝焦麩胺酸

<400> 131

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly Lys
435

<210> 132
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 132

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 133
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 133

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 134
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 134

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 135
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 135

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Ala Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 136
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 136

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Lys Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 137
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 137

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 138
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 138

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Lys Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 139
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 139

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu His Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 140
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 140

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Thr Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 141
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 141

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 142
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 142

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 143
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 143

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

5

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 144
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 144

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 145
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 145

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 146
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 146

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 147
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 147

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 148
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 148

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 149
<211> 437
<212> PRT
<213> 人工序列

<220>

<223> 人工=合成構築體

<400> 149

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 150
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 150

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 151
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 151

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 152
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 152

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 153
<211> 436

<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 153

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 154
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 154

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 155
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 155

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Ala Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 156
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 156

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Lys Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 157
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 157

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 158
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 158

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Lys Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 159
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 159

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu His Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 160
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 160

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Thr Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 161
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 161

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 162
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 162

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 163
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 163

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 164
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 164

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 165
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 165

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 166
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 166

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly Lys
435

<210> 167
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 167

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 168
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 168

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 169
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 169

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 170
<211> 436
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 170

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 171
<211> 436
<212> PRT
<213> 人工序列

<220>

<223> 人工=合成構築體

<400> 171

Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr Gly
20 25 30

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

Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro Ala
50 55 60

Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn Arg
65 70 75 80

Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln Ile
85 90 95

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

Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro Ala
115 120 125

Gly Thr Leu Ser Trp His Leu Asp Gly Lys Pro Leu Val Pro Asn Glu
130 135 140

Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr Gly
145 150 155 160

Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly Gly
165 170 175

Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro Arg
180 185 190

His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu Pro
195 200 205

Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly Ala
210 215 220

Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
225 230 235 240

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

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
260 265 270

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
275 280 285

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
290 295 300

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
305 310 315 320

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
325 330 335

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
340 345 350

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

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
370 375 380

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
385 390 395 400

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
405 410 415

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
420 425 430

Leu Ser Pro Gly
435

<210> 172
<211> 437
<212> PRT
<213> 人工

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 172

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 173
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 173

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 174
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 174

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 175
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 175

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Ala Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 176
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 176

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Lys Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 177
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 177

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 178
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 178

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Lys Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 179
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 179

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu His Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 180
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 180

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Thr Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 181
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa＝焦麩胺酸

<400> 181

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 182
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)

<223> Xaa=焦麩胺酸

<400> 182

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 183
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 183

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 184
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 184

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 185
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 185

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 186
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa =焦麩胺酸

<400> 186

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 187
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 187

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Arg Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 188
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 188

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 189
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 189

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 190
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 190

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 191
<211> 93
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 191

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg
85 90

<210> 192
<211> 93
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 192

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg
85 90

<210> 193
<211> 93
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)

<223> Xaa=焦麩胺酸

<400> 193

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg
85 90

<210> 194
<211> 29
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 194

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys
20 25

<210> 195
<211> 28
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 195

Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys Gly
1 5 10 15

Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys
20 25

<210> 196
<211> 31
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 196
gcctcgggag gaacagtaca gtccacctac c 31

<210> 197
<211> 28
<212> DNA
<213> 人工序列

<220>

<223> 人工=合成構築體

<400> 197
tactgttcct cccgaggctt ggtcttgg 28

<210> 198
<211> 33
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 198
gcctcggcac cgggccctgg cgaccgcccc tat 33

<210> 199
<211> 30
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 199
cagggcccgg tgccgaggca ggccagggga 30

<210> 200
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 200

Xaa Asn Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 201
<211> 437
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa=焦麩胺酸

<400> 201

Xaa Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Asn Ser Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Val Pro Asn Lys Val Gly Thr Cys Val Ser Glu Gly Ser Tyr Pro
115 120 125

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

Glu Lys Gly Val Ser Val Lys Glu Gln Thr Arg Arg His Pro Glu Thr
145 150 155 160

Gly Leu Phe Thr Leu Gln Ser Glu Leu Met Val Thr Pro Ala Arg Gly
165 170 175

Gly Asp Pro Arg Pro Thr Phe Ser Cys Ser Phe Ser Pro Gly Leu Pro
180 185 190

Arg His Arg Ala Leu Ala Thr Ala Pro Ile Gln Pro Arg Val Trp Glu
195 200 205

Pro Val Pro Leu Glu Glu Val Gln Leu Val Val Glu Pro Glu Gly Gly
210 215 220

Ala Val Ala Pro Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
225 230 235 240

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

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
260 265 270

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
275 280 285

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
290 295 300

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
305 310 315 320

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
325 330 335

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
340 345 350

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
355 360 365

5

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
370 375 380

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

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
405 410 415

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
420 425 430

Ser Leu Ser Pro Gly
435

<210> 202
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 202
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 203
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 203

atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 204
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 204
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 205
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 205
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca cgcggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 206
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 206
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca caaggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 207
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 207
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

gcgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 208
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 208
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

aagaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 209
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 209
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cataccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 210
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 210
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

acgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 211
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 211
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

gcgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 212
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 212
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

gcgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 213
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 213
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

gcgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac aactccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 214
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 214
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac cagtccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 215
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 215
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac cagtccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

〈210〉 216
〈211〉 1386

<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 216
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac cagtccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 217
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 217
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

cggaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac cagtccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 218
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 218
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

aacggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

gcgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac cagtccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 219
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 219
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agaacatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

gcgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac cagtccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 220
<211> 1386
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 220
atggcagccg gaacagcagt tggagcctgg gtgctggtcc tcagtctgtg gggcgctgtg 60

gtgggcgccc agcagatcac cgcccggatc ggcgagcctc tggtgctgaa gtgcaagggc 120

gctcctaaga agcctcctca gcggctcgag tggaagctga acaccggccg gaccgaggcc 180

tggaaggtgc tgtctcctca gggcggagga ccttgggact ccgtggcccg ggtgctgcct 240

cagggctccc tgttcctgcc tgccgtgggc atccaggacg agggcatctt caggtgccag 300

gccatgaacc ggaacggcaa agaaaccaag tccaactaca gagtgcgggt gtaccagatc 360

cctggcaagc ctgagatcgt ggactccgcc tccgagctga ccgctggcgt gcctaacaag 420

gtcggcacct gcgtgtccga gggctcctac cctgccggca ccctgtcctg gcatctggac 480

ggcaagcccc tggtgcctaa cgagaagggc gtgtccgtga aggaacagac caggcggcac 540

cctgagaccg gcctgttcac cctgcagtcc gagctgatgg tgacccctgc cagaggcggc 600

gaccctcggc ctaccttctc ctgctccttc tcccctggcc tgcctcggca ccgggccctg 660

gcgaccgccc ctatccagcc tagagtgtgg gagcctgtgc ctctcgagga agtgcagctg 720

gtcgtggagc ctgagggcgg agccgtggcc cctccttccg tgttcctgtt ccctcctaag 780

cctaaggaca ccctgatgat ctcccggacc cctgaggtga cctgcgtggt ggtggacgtg 840

tcccacgagg atcctgaggt gaagttcaac tggtacgtgg acggcgtgga ggtgcacaac 900

gccaagacca agcctcggga ggaacagtac cagtccacct accgggtggt gtccgtgctg 960

accgtgctgc accaggactg gctgaatggc aaagaataca agtgcaaggt ctccaacaag 1020

gccctgcctg cccctatcga gaaaaccatc tccaaggcca agggccagcc cagagagcct 1080

caggtctaca ccctgcctcc ctcccgggac gagctgacca agaaccaggt gtccctgacc 1140

tgcctggtga agggcttcta cccttccgac atcgccgtgg agtgggagtc caacggccag 1200

cctgagaaca actacaagac cacccctcct gtgctggact ccgacggctc cttcttcctg 1260

tactccaagc tgaccgtgga caagtcccgg tggcagcagg gcaacgtgtt ctcctgcagc 1320

gtgatgcacg aggccctgca caaccactac acccagaagt ccctgtccct gagccctggc 1380

aagtga 1386

<210> 221
<211> 1314
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 221
caaaacatca cagcccggat tggcgagcca ctggtgctga agtgtaaggg ggcccccaag 60

aaaccacccc agcggctgga atggaaactg aacacaggcc ggacagaggc ttggaaggtc 120

ctgtctcccc agggaggagg cccctgggac agtgtggctc gtgtccttcc caacggctcc 180

ctcttccttc cggctgtcgg gatccaggat gaggggattt tccggtgcca ggcaatgaac 240

aggaatggaa aggagaccaa gtccaactac cgagtccgtg tctaccagat tcctgggaag 300

ccagaaattg tagattctgc ctctgaactc acggctggtg ttcccaataa ggtggggaca 360

tgtgtgtcag aggggagcta ccctgcaggg actcttagct ggcacttgga tgggaagccc 420

ctggtgccta atgagaaggg agtatctgtg aaggaacaga ccaggagaca ccctgagaca 480

gggctcttca cactgcagtc ggagctaatg gtgaccccag cccggggagg agatccccgt 540

cccaccttct cctgtagctt cagcccaggc cttccccgac accgggcctt gcgcacagcc 600

cccatccagc cccgtgtctg ggagcctgtg cctctggagg aggtccaatt ggtggtggag 660

ccagaaggtg gagcagtagc tcctccgtca gtcttcctct tccccccaaa acccaaggac 720

accctcatga tctcccggac ccctgaggtc acatgcgtgg tggtggacgt gagccacgaa 780

gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca 840

aagccgcggg aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg 900

caccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca 960

gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 1020

accctgcccc catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctggtc 1080

aaaggcttct atcccagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 1140

aactacaaga ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag 1200

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat 1260

gaggctctgc acaaccacta cacgcagaag agcctctccc tgtctcccgg gaaa 1314

<210> 222
<211> 1314
<212> DNA
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 222
cagaacatca ccgcccggat cggcgagcct ctggtgctga agtgcaaggg cgctcctaag 60

aagcctcctc agcggctcga gtggaagctg aacaccggcc ggaccgaggc ctggaaggtg 120

ctgtctcctc agggcggagg accttgggac tccgtggccc gggtgctgcc taacggctcc 180

ctgttcctgc ctgccgtggg catccaggac gagggcatct tcaggtgcca ggccatgaac 240

cggaacggca aagaaaccaa gtccaactac agagtgcggg tgtaccagat ccctggcaag 300

cctgagatcg tggactccgc ctccgagctg accgctggcg tgcctaacaa ggtcggcacc 360

tgcgtgtccg agggctccta ccctgccggc accctgtcct ggcatctgga cggcaagccc 420

ctggtgccta acgagaaggg cgtgtccgtg aaggaacaga ccaggcggca ccctgagacc 480

ggcctgttca ccctgcagtc cgagctgatg gtgacccctg ccagaggcgg cgaccctcgg 540

cctaccttct cctgctcctt ctcccctggc ctgcctcggc accgggccct gcggaccgcc 600

cctatccagc ctagagtgtg ggagcctgtg cctctcgagg aagtgcagct ggtcgtggag 660

cctgagggcg gagccgtggc ccctccttcc gtgttcctgt tccctcctaa gcctaaggac 720

accctgatga tctcccggac ccctgaggtg acctgcgtgg tggtggacgt gtcccacgag 780

gatcctgagg tgaagttcaa ctggtacgtg gacggcgtgg aggtgcacaa cgccaagacc 840

aagcctcggg aggaacagta caactccacc taccgggtgg tgtccgtgct gaccgtgctg 900

caccaggact ggctgaatgg caaagaatac aagtgcaagg tctccaacaa ggccctgcct 960

gcccctatcg agaaaaccat ctccaaggcc aagggccagc ccagagagcc tcaggtctac 1020

accctgcctc cctcccggga cgagctgacc aagaaccagg tgtccctgac ctgcctggtg 1080

aagggcttct acccttccga catcgccgtg gagtgggagt ccaacggcca gcctgagaac 1140

aactacaaga ccacccctcc tgtgctggac tccgacggct ccttcttcct gtactccaag 1200

ctgaccgtgg acaagtcccg gtggcagcag ggcaacgtgt tctcctgcag cgtgatgcac 1260

gaggccctgc acaaccacta cacccagaag tccctgtccc tgagccctgg caag 1314

<210> 223
<211> 11
<212> PRT
<213> 智人

<400> 223

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
1 5 10

<210> 224
<211> 10
<212> PRT
<213> 智人

<400> 224

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
1 5 10

<210> 225
<211> 323
<212> PRT
<213> 人工序列

<220>
<223> 人工=合成構築體

<400> 225

Gln Gln Ile Thr Ala Arg Ile Gly Glu Pro Leu Val Leu Lys Cys Lys
1 5 10 15

Gly Ala Pro Lys Lys Pro Pro Gln Arg Leu Glu Trp Lys Leu Asn Thr
20 25 30

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

Trp Asp Ser Val Ala Arg Val Leu Pro Gln Gly Ser Leu Phe Leu Pro
50 55 60

Ala Val Gly Ile Gln Asp Glu Gly Ile Phe Arg Cys Gln Ala Met Asn
65 70 75 80

Arg Asn Gly Lys Glu Thr Lys Ser Asn Tyr Arg Val Arg Val Tyr Gln
85 90 95

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

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
115 120 125

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

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
145 150 155 160

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser Thr Tyr
165 170 175

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

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
195 200 205

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

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

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
260 265 270

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

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
290 295 300

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

Pro Gly Lys

201141507

發明專利說明書

（本說明書格式、順序及粗體字，請勿任意更動，※記號部分請勿填寫）

※ 申請案號：100105575

※ 申請日：100.2.18

※IPC 分類：C07K; A61K; A61P

A61K 38/16
A61K 39/44
A61P 25/28 (2006.01)
A61P 37/00 (2006.01)
A61P 9/00 (2006.01)
A61P 17/06 (2006.01)

一、發明名稱：（中文/英文）

RAGE融合蛋白組合物及使用方法

RAGE FUSION PROTEIN COMPOSITIONS AND METHODS OF USE

二、中文發明摘要：

本發明揭示包含RAGE多肽之融合蛋白，其中該RAGE多肽包含哺乳動物野生型RAGE肽之片段及相對於該野生型RAGE肽在該融合蛋白之該RAGE多肽部分中的至少一個點突變。該點突變可移除及/或改變糖基化位點或酶裂解位點。亦揭示編碼此等蛋白質之核酸以及使用此等蛋白質治療RAGE介導之病變之方法。

三、英文發明摘要：

Disclosed are fusion proteins comprising a RAGE polypeptide, wherein the RAGE polypeptide comprises a fragment of a mammalian wild type RAGE peptide and at least one point mutation in the RAGE polypeptide portion of the fusion protein relative to the wild type RAGE peptide. The point mutation may remove and/or alter a glycosylation site or an enzyme cleavage site. Also disclosed are nucleic acids encoding such proteins as well as methods of using such proteins for treating RAGE-mediated pathologies.

七、申請專利範圍：

1. 一種融合蛋白，其包含晚期糖基化終產物受體(RAGE)多肽與免疫球蛋白多肽連接，其中該RAGE多肽包含具有配位體結合域之哺乳動物RAGE之片段，且其中該RAGE融合蛋白相對於野生型序列，在該RAGE多肽或該免疫球蛋白多肽之至少一者中包含至少一個突變，其中該突變移除及/或改變糖基化位點或酶裂解位點中之至少一者。
2. 如請求項1之融合蛋白，其中該RAGE多肽為人類RAGE多肽。
3. 如請求項1或2之融合蛋白，其中該點突變改變野生型RAGE多肽中存在於糖基化位點處之序列。
4. 如前述請求項中任一項之融合蛋白，其中該糖基化位點具有胺基酸序列NXS或NXT，其中X為任何胺基酸。
5. 如前述請求項中任一項之融合蛋白，其中該點突變使野生型RAGE多肽之序列發生以下之至少一種改變：NIT變成QIT、或NGS變成QGS、或NGS變成NSS、或NST變成QST，以移除至少一個糖基化位點。
6. 如前述請求項中任一項之融合蛋白，其中該糖基化位點在該RAGE多肽之配位體結合位點或配位體結合域內。
7. 如請求項1之融合蛋白，其中該酶裂解位點為弗林蛋白酶裂解位點，以至於該點突變改變野生型RAGE多肽中存在於弗林蛋白酶裂解該RAGE多肽之識別位點處的序列。

8. 如請求項1及7之融合蛋白，其中該點突變使野生型RAGE多肽之胺基酸序列發生以下之一種改變：(i)PRHRALR變成PHRAALR；(ii)PRHRALR變成PRHKALR；(iii)PRHRALR變成PRHRALA；(iv)PRHRALR變成PRHRALK；(v)PRHRALR變成PRHRALH；或(vi)PRHRALR變成PRHRALT，以移除弗林蛋白酶裂解位點。

9. 如前述請求項中任一項之融合蛋白，其中該RAGE多肽不包括由野生型RAGE多肽之胺基酸1-23組成之N端前導肽(leader peptide)。

10. 如請求項1之融合蛋白，其中至少一個突變包含以下至少一者：(i) N2Q；(ii) N58Q；(iii) G59S；(iv) N2Q及N58Q；或(v) N2Q及G59S，其中不包括由野生型RAGE多肽之胺基酸1-23組成之N端前導肽的人類RAGE多肽。

11. 如請求項10之融合蛋白，其中不包括由野生型RAGE多肽之胺基酸1-23組成之N端前導肽的該人類RAGE多肽包含如以下至少一者所示之序列：(i) SEQ ID NO: 8、SEQ ID NO: 16或SEQ ID NO: 20；或(ii) N端麩醯胺酸已環化而形成焦麩胺酸之SEQ ID NO: 8、SEQ ID NO: 16或SEQ ID NO: 20。

12. 如請求項1之融合蛋白，其中移除該弗林蛋白酶裂解位點之該突變包含以下至少一者：R195A、R195K、R195T、R195H、R198A、R198K、R198H、R198T，其中不包括由野生型RAGE多肽之胺基酸1-23組成之N端前

導肽的人類RAGE多肽。

13. 如請求項12之融合蛋白，其中不包括由野生型RAGE多肽之胺基酸1-23組成之N端前導肽的該人類RAGE多肽包含如SEQ ID NO: 20或N端麩醯胺酸已環化而形成焦麩胺酸之SEQ ID NO: 20所示之序列。

14. 如前述請求項中任一項之融合蛋白，其中該免疫球蛋白多肽包含不包括至少一部分鉸鏈區之C_H2域的片段。

15. 如請求項14之融合蛋白，其中不包括在該C_H2域之該片段中的該鉸鏈區具有如SEQ ID NO: 223或SEQ ID NO: 224所示之序列。

16. 如請求項14及15之融合蛋白，其中該C_H2域經由其C端與免疫球蛋白多肽之C_H3域之N端連接。

17. 如請求項1之融合蛋白，其中該免疫球蛋白包含人類IgG。

18. 如請求項1之融合蛋白，其中該免疫球蛋白之C_H2域包含SEQ ID NO: 38或無C端離胺酸之SEQ ID NO: 38。

19. 一種融合蛋白，其包含含有如SEQ ID NO: 58-82、SEQ ID NO: 92-190或SEQ ID NO: 200或201中之任一者所示之胺基酸序列的RAGE多肽。

20. 一種包含RAGE多肽之融合蛋白，其中該RAGE多肽序列如SEQ ID NO: 58-82、SEQ ID NO: 92-190或SEQ ID NO: 200或201中之任一者所示。

21. 如前述請求項中任一項之融合蛋白，其呈單體、二聚體、三聚體、四聚體或其混合物形式。

5

22. 一種組合物，其包含如前述請求項中任一項之融合蛋白及醫藥學上可接受之載劑。

23. 一種經分離核酸，其編碼如請求項1至21中任一項之融合蛋白。

24. 一種表現載體，其包含編碼如請求項1至21中任一項之融合蛋白的核酸。

25. 一種宿主細胞，其經包含編碼如請求項1至21中任一項之融合蛋白之核酸的表現載體轉染。

26. 一種治療個體之RAGE介導之病症的方法，其包含向個體投與如請求項1至21中任一項之融合蛋白或如請求項22之組合物。

27. 如請求項26之方法，其中該RAGE介導之病症包含糖尿病或糖尿病晚期併發症之症狀。

28. 如請求項27之方法，其中糖尿病或糖尿病晚期併發症之該症狀包含糖尿病腎病變、糖尿病視網膜病變、糖尿病足部潰瘍、心血管併發症或糖尿病神經病變中之至少一者。

29. 如請求項26之方法，其中該RAGE介導之病症包含以下至少一者：澱粉樣變性病、阿茲海默氏病(Alzheimer's disease)、癌症、腎衰竭、與自體免疫性、發炎性腸病、類風濕性關節炎、牛皮癬、多發性硬化症、低氧症、中風、心臟病發作、出血性休克、敗血症、器官移植或創傷癒合不良相關之發炎。

八、圖式：

SEQ ID NO: 1

```
MAAGTAVGAW VLVLSLWGAV VGAQNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVSISI IEPGEEGPTA GSVGGSGLGT LALALGILGG
LGTAALLIGV ILWQRRQRRG EERKAPENQE EEEERAELNQ SEEPEAGESS
TGGP
```

SEQ ID NO: 2

```
                          AQNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVSISI IEPGEEGPTA GSVGGSGLGT LALALGILGG
LGTAALLIGV ILWQRRQRRG EERKAPENQE EEEERAELNQ SEEPEAGESS
TGGP
```

圖1A

SEQ ID NO: 3

```
                          QNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVSISI IEPGEEGPTA GSVGGSGLGT LALALGILGG
LGTAALLIGV ILWQRRQRRG EERKAPENQE EEEERAELNQ SEEPEAGESS
TGGP
```

圖1B

SEQ ID NO: 4

```
MAAGTAVGAW VLVLSLWGAV VGAQNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVSISI IEPGEEGPTA GSVGGSGLG
```

SEQ ID NO: 5

```
                          AQNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVSISI IEPGEEGPTA GSVGGSGLG
```

SEQ ID NO: 6

```
                           QNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVSISI IEPGEEGPTA GSVGGSGLG
```

圖1C

SEQ ID NO: 7

AQNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVR

SEQ ID NO: 8

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVR

SEQ ID NO: 9

AQNITARI GEPLVLKCKG APKKPPQRLE WK

SEQ ID NO: 10

QNITARI GEPLVLKCKG APKKPPQRLE WK

SEQ ID NO: 11

PEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL R

SEQ ID NO: 12

PRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVS

SEQ ID NO: 13

AQNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGK

圖1D

5

SEQ ID NO: 14

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGK

SEQ ID NO: 15

AQNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAG

SEQ ID NO: 16

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAG

SEQ ID NO: 17

AQNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQ

SEQ ID NO: 18

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQ

圖1E

SEQ ID NO: 19

AQNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA P

SEQ ID NO: 20

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA P

SEQ ID NO: 21

VYQIPGK

SEQ ID NO: 22

TAPIQPRVWE PVPLEEVQLV VEPEGGAVAP

SEQ ID NO: 23

VYQIPGKPEI VDSASELTAG

SEQ ID NO: 24

TAPIQ

圖1F

SEQ ID NO: 25

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTAC

SEQ ID NO: 26

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAG

SEQ ID NO: 27

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGT

圖1G

SEQ ID NO:28

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGTGT TCCCAATAAG GTGGGGACAT GTGTGTCAGA GGGGAGCTAC
CCTGCAGGGA CTCTTAGCTG GCACTTGGAT GGGAAGCCCC TGGTGCCTAA
TGAGAAGGGA GTATCTGTGA AGGAACAGAC CAGGAGACAC CCTGAGACAG
GGCTCTTCAC ACTGCAGTCG GAGCTAATGG TGACCCCAGC CCGGGGAGGA
GATCCCCGTC CCACCTTCTC CTGTAGCTTC AGCCCAGGCC TTCCCCGACA
CCGGGCCTTG CGCACAGCCC CCATCCAGCC CCGTGTCTGG

SEQ ID NO:29

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGTGT TCCCAATAAG GTGGGGACAT GTGTGTCAGA GGGGAGCTAC
CCTGCAGGGA CTCTTAGCTG GCACTTGGAT GGGAAGCCCC TGGTGCCTAA
TGAGAAGGGA GTATCTGTGA AGGAACAGAC CAGGAGACAC CCTGAGACAG
GGCTCTTCAC ACTGCAGTCG GAGCTAATGG TGACCCCAGC CCGGGGAGGA
GATCCCCGTC CCACCTTCTC CTGTAGCTTC AGCCCAGGCC TTCCCCGACA
CCGGGCCTTG CGCACAGCCC CCATCCAGCC CCGTGTCTGG GAGCCTGTGC
CTCTGGAGGA GGTCCAATTG GTGGTGGAGC CAGAAGGTGG AGCAGTAGCT
CCT

圖1H

SEQ ID NO: 38

PSVF LFPPKPKDTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG
VEVHNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP
IEKTISKAKG QPREPQVYTL PPSRDELTKN QVSLTCLVKG FYPSDIAVEW
ESNGQPENNY KTTPPVLDSD GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA
LHNHYTQKSL SLSPGK

SEQ ID NO: 39

CCGTCAG TCTTCCTCTT CCCCCCAAAA CCCAAGGACA CCCTCATGAT
CTCCCGGACC CCTGAGGTCA CATGCGTGGT GGTGGACGTG AGCCACGAAG
ACCCTGAGGT CAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCATAAT
GCCAAGACAA AGCCGCGGGA GGAGCAGTAC AACAGCACGT ACCGTGTGGT
CAGCGTCCTC ACCGTCCTGC ACCAGGACTG GCTGAATGGC AAGGAGTACA
AGTGCAAGGT CTCCAACAAA GCCCTCCCAG CCCCCATCGA GAAAACCATC
TCCAAAGCCA AAGGGCAGCC CCGAGAACCA CAGGTGTACA CCCTGCCCCC
ATCCCGGGAT GAGCTGACCA AGAACCAGGT CAGCCTGACC TGCCTGGTCA
AAGGCTTCTA TCCCAGCGAC ATCGCCGTGG AGTGGGAGAG CAATGGGCAG
CCGGAGAACA ACTACAAGAC CACGCCTCCC GTGCTGGACT CCGACGGCTC
CTTCTTCCTC TACAGCAAGC TCACCGTGGA CAAGAGCAGG TGGCAGCAGG
GGAACGTCTT CTCATGCTCC GTGATGCATG AGGCTCTGCA CAACCACTAC
ACGCAGAAGA GCCTCTCCCT GTCTCCGGGT AAATGA

SEQ ID NO: 40

PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI
AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV
MHEALHNHYT QKSLSLSPGK

圖11

SEQ ID NO: 41

CCGTGCCCAG CACCTGAACT CCTGGGGGGA CCGTCAGTCT TCCTCTTCCC
CCCAAAACCC AAGGACACCC TCATGATCTC CCGGACCCCT GAGGTCACAT
GCGTGGTGGT GGACGTGAGC CACGAAGACC CTGAGGTCAA GTTCAACTGG
TACGTGGACG GCGTGGAGGT GCATAATGCC AAGACAAAGC CGCGGGAGGA
GCAGTACAAC AGCACGTACC GTGTGGTCAG CGTCCTCACC GTCCTGCACC
AGGACTGGCT GAATGGCAAG GAGTACAAGT GCAAGGTCTC CAACAAAGCC
CTCCCAGCCC CCATCGAGAA AACCATCTCC AAAGCCAAAG GGCAGCCCCG
AGAACCACAG GTGTACACCC TGCCCCCATC CCGGGATGAG CTGACCAAGA
ACCAGGTCAG CCTGACCTGC CTGGTCAAAG GCTTCTATCC CAGCGACATC
GCCGTGGAGT GGGAGAGCAA TGGGCAGCCG GAGAACAACT ACAAGACCAC
GCCTCCCGTG CTGGACTCCG ACGGCTCCTT CTTCCTCTAC AGCAAGCTCA
CCGTGGACAA GAGCAGGTGG CAGCAGGGGA ACGTCTTCTC ATGCTCCGTG
ATGCATGAGG CTCTGCACAA CCACTACACG CAGAAGAGCC TCTCCCTGTC
TCCGGGTAAA TGA

SEQ ID NO: 42

PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAK

SEQ ID NO: 43

GQPREPQ VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI
AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV
MHEALHNHYT QKSLSLSPGK

SEQ ID NO: 44

ISI IEPGEEGPTA GSVGGSGLGT LA

圖1J

SEQ ID NO: 45

```
                          pENITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PGGTVTLTCE VPAQPSPQIH WMKDGVPLPL PPSPVLILPE IGPQDQGTYS
CVATHSSHGP QESRAVSISI IEPGEEGPTA GSVGGSGLG
```

SEQ ID NO: 46

```
  pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVR
```

SEQ ID NO: 47

```
  pENITARI GEPLVLKCKG APKKPPQRLE WK
```

SEQ ID NO: 48

```
  pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGK
```

圖1K

SEQ ID NO: 49

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAG

SEQ ID NO: 50

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQ

SEQ ID NO: 51

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA P

圖1L

SEQ ID NO: 52

CCGTCAG TCTTCCTCTT CCCCCCAAAA CCCAAGGACA CCCTCATGAT
CTCCCGGACC CCTGAGGTCA CATGCGTGGT GGTGGACGTG AGCCACGAAG
ACCCTGAGGT CAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCATAAT
GCCAAGACAA AGCCGCGGGA GGAGCAGTAC AACAGCACGT ACCGTGTGGT
CAGCGTCCTC ACCGTCCTGC ACCAGGACTG GCTGAATGGC AAGGAGTACA
AGTGCAAGGT CTCCAACAAA GCCCTCCCAG CCCCCATCGA GAAAACCATC
TCCAAAGCCA AAGGGCAGCC CCGAGAACCA CAGGTGTACA CCCTGCCCCC
ATCCCGGGAT GAGCTGACCA AGAACCAGGT CAGCCTGACC TGCCTGGTCA
AAGGCTTCTA TCCCAGCGAC ATCGCCGTGG AGTGGGAGAG CAATGGGCAG
CCGGAGAACA ACTACAAGAC CACGCCTCCC GTGCTGGACT CCGACGGCTC
CTTCTTCCTC TACAGCAAGC TCACCGTGGA CAAGAGCAGG TGGCAGCAGG
GGAACGTCTT CTCATGCTCC GTGATGCATG AGGCTCTGCA CAACCACTAC
ACGCAGAAGA GCCTCTCCCT GTCTCCCGGG AAATGA

SEQ ID NO: 53

CCGTGCCCAG CACCTGAACT CCTGGGGGGA CCGTCAGTCT TCCTCTTCCC
CCCAAAACCC AAGGACACCC TCATGATCTC CCGGACCCCT GAGGTCACAT
GCGTGGTGGT GGACGTGAGC CACGAAGACC CTGAGGTCAA GTTCAACTGG
TACGTGGACG GCGTGGAGGT GCATAATGCC AAGACAAAGC CGCGGGAGGA
GCAGTACAAC AGCACGTACC GTGTGGTCAG CGTCCTCACC GTCCTGCACC
AGGACTGGCT GAATGGCAAG GAGTACAAGT GCAAGGTCTC CAACAAAGCC
CTCCCAGCCC CCATCGAGAA AACCATCTCC AAAGCCAAAG GGCAGCCCCG
AGAACCACAG GTGTACACCC TGCCCCCATC CCGGGATGAG CTGACCAAGA
ACCAGGTCAG CCTGACCTGC CTGGTCAAAG GCTTCTATCC CAGCGACATC
GCCGTGGAGT GGGAGAGCAA TGGGCAGCCG GAGAACAACT ACAAGACCAC
GCCTCCCGTG CTGGACTCCG ACGGCTCCTT CTTCCTCTAC AGCAAGCTCA
CCGTGGACAA GAGCAGGTGG CAGCAGGGGA ACGTCTTCTC ATGCTCCGTG
ATGCATGAGG CTCTGCACAA CCACTACACG CAGAAGAGCC TCTCCCTGTC
TCCCGGGAAA TGA

圖1M

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGTGT TCCCAATAAG GTGGGGACAT GTGTGTCAGA GGGGAGCTAC
CCTGCAGGGA CTCTTAGCTG GCACTTGGAT GGGAAGCCCC TGGTGCCTAA
TGAGAAGGGA GTATCTGTGA AGGAACAGAC CAGGAGACAC CCTGAGACAG
GGCTCTTCAC ACTGCAGTCG GAGCTAATGG TGACCCCAGC CCGGGGAGGA
GATCCCCGTC CCACCTTCTC CTGTAGCTTC AGCCCAGGCC TTCCCCGACA
CCGGGCCTTG CGCACAGCCC CCATCCAGCC CCGTGTCTGG GAGCCTGTGC
CTCTGGAGGA GGTCCAATTG GTGGTGGAGC CAGAAGGTGG AGCAGTAGCT
CCTCCGTCAG TCTTCCTCTT CCCCCCAAAA CCCAAGGACA CCCTCATGAT
CTCCCGGACC CCTGAGGTCA CATGCGTGGT GGTGGACGTG AGCCACGAAG
ACCCTGAGGT CAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCATAAT
GCCAAGACAA AGCCGCGGGA GGAGCAGTAC AACAGCACGT ACCGTGTGGT
CAGCGTCCTC ACCGTCCTGC ACCAGGACTG GCTGAATGGC AAGGAGTACA
AGTGCAAGGT CTCCAACAAA GCCCTCCCAG CCCCCATCGA GAAAACCATC
TCCAAAGCCA AAGGGCAGCC CCGAGAACCA CAGGTGTACA CCCTGCCCCC
ATCCCGGGAT GAGCTGACCA AGAACCAGGT CAGCCTGACC TGCCTGGTCA
AAGGCTTCTA TCCCAGCGAC ATCGCCGTGG AGTGGGAGAG CAATGGGCAG
CCGGAGAACA ACTACAAGAC CACGCCTCCC GTGCTGGACT CCGACGGCTC
CTTCTTCCTC TACAGCAAGC TCACCGTGGA CAAGAGCAGG TGGCAGCAGG
GGAACGTCTT CTCATGCTCC GTGATGCATG AGGCTCTGCA CAACCACTAC
ACGCAGAAGA GCCTCTCCCT GTCTCCGGGT AAATGA

(SEQ ID NO: 30)

圖2A

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGTGT TCCCAATAAG GTGGGGACAT GTGTGTCAGA GGGGAGCTAC
CCTGCAGGGA CTCTTAGCTG GCACTTGGAT GGGAAGCCCC TGGTGCCTAA
TGAGAAGGGA GTATCTGTGA AGGAACAGAC CAGGAGACAC CCTGAGACAG
GGCTCTTCAC ACTGCAGTCG GAGCTAATGG TGACCCCAGC CCGGGGAGGA
GATCCCCGTC CCACCTTCTC CTGTAGCTTC AGCCCAGGCC TTCCCCGACA
CCGGGCCTTG CGCACAGCCC CCATCCAGCC CCGTGTCTGG GAGCCTGTGC
CTCTGGAGGA GGTCCAATTG GTGGTGGAGC CAGAAGGTGG AGCAGTAGCT
CCTCCGTCAG TCTTCCTCTT CCCCCCAAAA CCCAAGGACA CCCTCATGAT
CTCCCGGACC CCTGAGGTCA CATGCGTGGT GGTGGACGTG AGCCACGAAG
ACCCTGAGGT CAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCATAAT
GCCAAGACAA AGCCGCGGGA GGAGCAGTAC AACAGCACGT ACCGTGTGGT
CAGCGTCCTC ACCGTCCTGC ACCAGGACTG GCTGAATGGC AAGGAGTACA
AGTGCAAGGT CTCCAACAAA GCCCTCCCAG CCCCCATCGA GAAAACCATC
TCCAAAGCCA AAGGGCAGCC CCGAGAACCA CAGGTGTACA CCCTGCCCCC
ATCCCGGGAT GAGCTGACCA AGAACCAGGT CAGCCTGACC TGCCTGGTCA
AAGGCTTCTA TCCCAGCGAC ATCGCCGTGG AGTGGGAGAG CAATGGGCAG
CCGGAGAACA ACTACAAGAC CACGCCTCCC GTGCTGGACT CCGACGGCTC
CTTCTTCCTC TACAGCAAGC TCACCGTGGA CAAGAGCAGG TGGCAGCAGG
GGAACGTCTT CTCATGCTCC GTGATGCATG AGGCTCTGCA CAACCACTAC
ACGCAGAAGA GCCTCTCCCT GTCTCCCGGG AAATGA

(SEQ ID NO: 54)

圖2B

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGTCC GTCAGTCTTC CTCTTCCCCC CAAAACCCAA GGACACCCTC
ATGATCTCCC GGACCCCTGA GGTCACATGC GTGGTGGTGG ACGTGAGCCA
CGAAGACCCT GAGGTCAAGT TCAACTGGTA CGTGGACGGC GTGGAGGTGC
ATAATGCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCGT
GTGGTCAGCG TCCTCACCGT CCTGCACCAG GACTGGCTGA ATGGCAAGGA
GTACAAGTGC AAGGTCTCCA ACAAAGCCCT CCCAGCCCCC ATCGAGAAAA
CCATCTCCAA AGCCAAAGGG CAGCCCCGAG AACCACAGGT GTACACCCTG
CCCCCATCCC GGGATGAGCT GACCAAGAAC CAGGTCAGCC TGACCTGCCT
GGTCAAAGGC TTCTATCCCA GCGACATCGC CGTGGAGTGG GAGAGCAATG
GGCAGCCGGA GAACAACTAC AAGACCACGC CTCCCGTGCT GGACTCCGAC
GGCTCCTTCT TCCTCTACAG CAAGCTCACC GTGGACAAGA GCAGGTGGCA
GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGCT CTGCACAACC
ACTACACGCA GAAGAGCCTC TCCCTGTCTC CGGGTAAATG A

(SEQ ID NO: 31)

圖3A

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGGGCAGTA GTAGGTGCTC AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAAGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGTCC GTCAGTCTTC CTCTTCCCCC CAAAACCCAA GGACACCCTC
ATGATCTCCC GGACCCCTGA GGTCACATGC GTGGTGGTGG ACGTGAGCCA
CGAAGACCCT GAGGTCAAGT TCAACTGGTA CGTGGACGGC GTGGAGGTGC
ATAATGCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCGT
GTGGTCAGCG TCCTCACCGT CCTGCACCAG GACTGGCTGA ATGGCAAGGA
GTACAAGTGC AAGGTCTCCA ACAAAGCCCT CCCAGCCCCC ATCGAGAAAA
CCATCTCCAA AGCCAAAGGG CAGCCCCGAG AACCACAGGT GTACACCCTG
CCCCCATCCC GGGATGAGCT GACCAAGAAC CAGGTCAGCC TGACCTGCCT
GGTCAAAGGC TTCTATCCCA GCGACATCGC CGTGGAGTGG GAGAGCAATG
GGCAGCCGGA GAACAACTAC AAGACCACGC CTCCCGTGCT GGACTCCGAC
GGCTCCTTCT TCCTCTACAG CAAGCTCACC GTGGACAAGA GCAGGTGGCA
GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGCT CTGCACAACC
ACTACACGCA GAAGAGCCTC TCCCTGTCTC CCGGGAAATG A

(SEQ ID NO: 55).

圖3B

SEQ ID NO: 32

MAAGTAVGAW VLVLSLWGAV VGAQNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGVPNK VGTCVSEGSY
PAGTLSWHLD GKPLVPNEKG VSVKEQTRRH PETGLFTLQS ELMVTPARGG
DPRPTFSCSF SPGLPRHRAL RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA
PPSVFLFPPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN
AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI
SKAKGQPREP QVYTLPPSRD ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ
PENNYKTTPP VLDSDGSFFL YSKLTVDKSR WQQGNVFSCS VMHEALHNHY
TQKSLSLSPG K

SEQ ID NO: 33

AQNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 34

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 56

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖4

SEQ ID NO: 35

MAAGTAVGAW VLVLSLWGAV VGAQNITARI GEPLVLKCKG APKKPPQRLE
WKLNTGRTEA WKVLSPQGGG PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ
AMNRNGKETK SNYRVRVYQI PGKPEIVDSA SELTAGPSVF LFPPKPKDTL
MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP REEQYNSTYR
VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL
PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTTPPVLDSD
GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGK

SEQ ID NO: 36

AQNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGPSVF LFPPKPKDTL MISRTPEVTC VVVDVSHEDP
EVKFNWYVDG VEVHNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC
KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSRDELTKN QVSLTCLVKG
FYPSDIAVEW ESNGQPENNY KTTPPVLDSD GSFFLYSKLT VDKSRWQQGN
VFSCSVMHEA LHNHYTQKSL SLSPGK

SEQ ID NO: 37

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGPSVF LFPPKPKDTL MISRTPEVTC VVVDVSHEDP
EVKFNWYVDG VEVHNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC
KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSRDELTKN QVSLTCLVKG
FYPSDIAVEW ESNGQPENNY KTTPPVLDSD GSFFLYSKLT VDKSRWQQGN
VFSCSVMHEA LHNHYTQKSL SLSPGK

SEQ ID NO: 57

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGPSVF LFPPKPKDTL MISRTPEVTC VVVDVSHEDP
EVKFNWYVDG VEVHNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC
KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSRDELTKN QVSLTCLVKG
FYPSDIAVEW ESNGQPENNY KTTPPVLDSD GSFFLYSKLT VDKSRWQQGN
VFSCSVMHEA LHNHYTQKSL SLSPGK

圖5

SEQ ID NO: 62 (TTP4000 N2Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 63 (TTP4000 N58Q)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 64 (TTP4000 N2Q, N58Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 65 (TTP4000 R195A)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHAAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6A

SEQ ID NO: 66 (TTP4000 R195K)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHKAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 67 (TTP4000 R198A)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 68 (TTP4000 R198K)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
KTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 69 (TTP4000 R198H)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
HTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6B

SEQ ID NO: 70 (TTP4000 R198T)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
TTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 71 (TTP4000 N2Q, R198A)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 72 (TTP4000 N58Q, R198A)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 73 (TTP4000 N2Q, N58Q, R198A)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6C

SEQ ID NO: 74 (TTP4000 N288Q)

```
   QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 75 (TTP4000 N2Q, N288Q)

```
   QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 76 (TTP4000 N58Q, N288Q)

```
   QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 77 (TTP4000 N2Q, N58Q, N288Q)

```
   QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

圖6D

SEQ ID NO: 78 (TTP4000 N2Q, R198A, N288Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 79 (TTP4000 N58Q, R198A, N288Q)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 80 (TTP4000 N2Q, N58Q, R198A, N288Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 81 (TTP4000 G59S, R198A)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6E

5

SEQ ID NO: 92 (TTP4000 N2Q)

```
   QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 93 (TTP4000 N58Q)

```
   QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 94 (TTP4000 N2Q, N58Q)

```
   QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 95 (TTP4000 R195A)

```
   QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHAAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

圖6F

SEQ ID NO: 96 (TTP4000 R195K)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHKAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 97 (TTP4000 R198A)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 98 (TTP4000 R198K)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
KTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 99 (TTP4000 R198H)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
HTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6G

SEQ ID NO: 100 (TTP4000 R198T)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
TTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 101 (TTP4000 N2Q, R198A)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 102 (TTP4000 N58Q, R198A)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP **Q**GSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 103 (TTP4000 N2Q, N58Q, R198A)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP **Q**GSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6H

SEQ ID NO: 104 (TTP4000 N288Q)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 105 (TTP4000 N2Q, N288Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 106 (TTP4000 N58Q, N288Q)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 107 (TTP4000 N2Q, N58Q, N288Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6I

5

SEQ ID NO: 108 (TTP4000 N2Q, R198A, N288Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 109 (TTP4000 N58Q, R198A, N288Q)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 110 (TTP4000 N2Q, N58Q, R198A, N288Q)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 111 (TTP4000 G59S, R198A)

QNITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6J

SEQ ID NO: 112 (TTP4000 N2Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 113 (TTP4000 N58Q)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 114 (TTP4000 N2Q, N58Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 115 (TTP4000 R195A)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHAAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6K

SEQ ID NO: 116 (TTP4000 R195K)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHKAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 117 (TTP4000 R198A)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 118 (TTP4000 R198K)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
KTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 119 (TTP4000 R198H)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
HTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6L

SEQ ID NO: 120 (TTP4000 R198T)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
TTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 121 (TTP4000 N2Q, R198A)

pE**Q**ITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 122 (TTP4000 N58Q, R198A)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP **Q**GSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 123 (TTP4000 N2Q, N58Q, R198A)

pE**Q**ITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP **Q**GSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6M

SEQ ID NO: 124 (TTP4000 N288Q)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 125 (TTP4000 N2Q, N288Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 126 (TTP4000 N58Q, N288Q)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 127 (TTP4000 N2Q, N58Q, N288Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6N

SEQ ID NO: 128 (TTP4000 N2Q, R198A, N288Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 129 (TTP4000 N58Q, R198A, N288Q)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 130 (TTP4000 N2Q, N58Q, R198A, N288Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 131 (TTP4000 G59S, R198A)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6O

SEQ ID NO: 132 (TTP4000 N2Q)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 133 (TTP4000 N58Q)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 134 (TTP4000 N2Q, N58Q)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 135 (TTP4000 R195A)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHAAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6P

SEQ ID NO: 136 (TTP4000 R195K)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHKAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 137 (TTP4000 R198A)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 138 (TTP4000 R198K)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
KTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 139 (TTP4000 R198H)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
HTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6Q

SEQ ID NO: 140 (TTP4000 R198T)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
TTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 141 (TTP4000 N2Q, R198A)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 142 (TTP4000 N58Q, R198A)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 143 (TTP4000 N2Q, N58Q, R198A)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

圖6R

SEQ ID NO: 144 (TTP4000 N288Q)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 145 (TTP4000 N2Q, N288Q)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 146 (TTP4000 N58Q, N288Q)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 147 (TTP4000 N2Q, N58Q, N288Q)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

圖6S

SEQ ID NO: 148 (TTP4000 N2Q, R198A, N288Q)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 149 (TTP4000 N58Q, R198A, N288Q)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 150 (TTP4000 N2Q, N58Q, R198A, N288Q)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 151 (TTP4000 G59S, R198A)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6T

SEQ ID NO: 152 (TTP4000 N2Q)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 153 (TTP4000 N58Q)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 154 (TTP4000 N2Q, N58Q)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 155 (TTP4000 R195A)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHAAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

圖6U

5

SEQ ID NO: 156 (TTP4000 R195K)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHKAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 157 (TTP4000 R198A)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 158 (TTP4000 R198K)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
KTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 159 (TTP4000 R198H)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
HTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

圖6V

SEQ ID NO: 160 (TTP4000 R198T)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
TTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 161 (TTP4000 N2Q, R198A)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 162 (TTP4000 N58Q, R198A)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP **Q**GSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 163 (TTP4000 N2Q, N58Q, R198A)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP **Q**GSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6W

5

SEQ ID NO: 164 (TTP4000 N288Q)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 165 (TTP4000 N2Q, N288Q)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 166 (TTP4000 N58Q, N288Q)

```
    NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K
```

SEQ ID NO: 167 (TTP4000 N2Q, N58Q, N288Q)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

圖6X

SEQ ID NO: 168 (TTP4000 N2Q, R198A, N288Q)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 169 (TTP4000 N58Q, R198A, N288Q)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 170 (TTP4000 N2Q, N58Q, R198A, N288Q)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 171 (TTP4000 G59S, R198A)

NITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6Y

5

SEQ ID NO: 172 (TTP4000 N2Q)

```
 pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 173 (TTP4000 N58Q)

```
 pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 174 (TTP4000 N2Q, N58Q)

```
 pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 175 (TTP4000 R195A)

```
 pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHAAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

圖6Z

SEQ ID NO: 176 (TTP4000 R195K)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHKAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 177 (TTP4000 R198A)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 178 (TTP4000 R198K)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
KTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 179 (TTP4000 R198H)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
HTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6AA

SEQ ID NO: 180 (TTP4000 R198T)

```
 pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
TTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 181 (TTP4000 N2Q, R198A)

```
 pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 182 (TTP4000 N58Q, R198A)

```
 pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 183 (TTP4000 N2Q, N58Q, R198A)

```
 pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

圖6BB

SEQ ID NO: 184 (TTP4000 N288Q)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 185 (TTP4000 N2Q, N288Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 186 (TTP4000 N58Q, N288Q)

pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 187 (TTP4000 N2Q, N58Q, N288Q)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
RTAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

圖6CC

SEQ ID NO: 188 (TTP4000 N2Q, R198A, N288Q)

```
 pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 189 (TTP4000 N58Q, R198A, N288Q)

```
 pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 190 (TTP4000 N2Q, N58Q, R198A, N288Q)

```
 pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY QSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 200 (TTP4000 G59S, R198A)

```
 pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

圖6DD

SEQ ID NO: 58 (TTP4000 N2Q, G59S, R198A)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 59 (TTP4000 N2Q, G59S, R198A)

QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG

SEQ ID NO: 60 (TTP4000 N2Q, G59S, R198A)

pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

SEQ ID NO: 61 (TTP4000 N2Q, G59S, R198A)

QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

圖6EE

SEQ ID NO: 82 (TTP4000 N2Q, G59S, R198A)

```
    QITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 201 (TTP4000 N2Q, G59S, R198A)

```
  pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NSSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGVPNK VGTCVSEGSY PAGTLSWHLD GKPLVPNEKG
VSVKEQTRRH PETGLFTLQS ELMVTPARGG DPRPTFSCSF SPGLPRHRAL
ATAPIQPRVW EPVPLEEVQL VVEPEGGAVA PPSVFLFPPK PKDTLMISRT
PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY NSTYRVVSVL
TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL
YSKLTVDKSR WQQGNVFSCS VMHEALHNHY TQKSLSLSPG
```

SEQ ID NO: 225 (TTP 3000 N2Q, N58Q, N173Q)

```
   QQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVRVYQI
PGKPEIVDSA SELTAGPSVF LFPPKPKDTL MISRTPEVTC VVVDVSHEDP
EVKFNWYVDG VEVHNAKTKP REEQYQSTYR VVSVLTVLHQ DWLNGKEYKC
KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSRDELTKN QVSLTCLVKG
FYPSDIAVEW ESNGQPENNY KTTPPVLDSD GSFFLYSKLT VDKSRWQQGN
VFSCSVMHEA LHNHYTQKSL SLSPGK
```

圖6FF

SEQ ID NO: 221 (TTP4000 DNA 序列)

```
                    C AAAACATCAC AGCCCGGATT GGCGAGCCAC
TGGTGCTGAA GTGTAAGGGG GCCCCCAAGA AACCACCCCA GCGGCTGGAA
TGGAAACTGA ACACAGGCCG GACAGAGGCT TGGAAGGTCC TGTCTCCCCA
GGGAGGAGGC CCCTGGGACA GTGTGGCTCG TGTCCTTCCC AACGGCTCCC
TCTTCCTTCC GGCTGTCGGG ATCCAGGATG AGGGGATTTT CCGGTGCCAG
GCAATGAACA GGAATGGAAA GGAGACCAAG TCCAACTACC GAGTCCGTGT
CTACCAGATT CCTGGGAAGC CAGAAATTGT AGATTCTGCC TCTGAACTCA
CGGCTGGTGT TCCCAATAAG GTGGGGACAT GTGTGTCAGA GGGGAGCTAC
CCTGCAGGGA CTCTTAGCTG GCACTTGGAT GGGAAGCCCC TGGTGCCTAA
TGAGAAGGGA GTATCTGTGA AGGAACAGAC CAGGAGACAC CCTGAGACAG
GGCTCTTCAC ACTGCAGTCG GAGCTAATGG TGACCCCAGC CCGGGGAGGA
GATCCCCGTC CCACCTTCTC CTGTAGCTTC AGCCCAGGCC TTCCCCGACA
CCGGGCCTTG CGCACAGCCC CCATCCAGCC CCGTGTCTGG GAGCCTGTGC
CTCTGGAGGA GGTCCAATTG GTGGTGGAGC CAGAAGGTGG AGCAGTAGCT
CCTCCGTCAG TCTTCCTCTT CCCCCCAAAA CCCAAGGACA CCCTCATGAT
CTCCCGGACC CCTGAGGTCA CATGCGTGGT GGTGGACGTG AGCCACGAAG
ACCCTGAGGT CAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCATAAT
GCCAAGACAA AGCCGCGGGA GGAGCAGTAC AACAGCACGT ACCGTGTGGT
CAGCGTCCTC ACCGTCCTGC ACCAGGACTG GCTGAATGGC AAGGAGTACA
AGTGCAAGGT CTCCAACAAA GCCCTCCCAG CCCCCATCGA GAAAACCATC
TCCAAAGCCA AAGGGCAGCC CCGAGAACCA CAGGTGTACA CCCTGCCCCC
ATCCCGGGAT GAGCTGACCA AGAACCAGGT CAGCCTGACC TGCCTGGTCA
AAGGCTTCTA TCCCAGCGAC ATCGCCGTGG AGTGGGAGAG CAATGGGCAG
CCGGAGAACA ACTACAAGAC CACGCCTCCC GTGCTGGACT CCGACGGCTC
CTTCTTCCTC TACAGCAAGC TCACCGTGGA CAAGAGCAGG TGGCAGCAGG
GGAACGTCTT CTCATGCTCC GTGATGCATG AGGCTCTGCA CAACCACTAC
ACGCAGAAGA GCCTCTCCCT GTCTCCCGGG AAA
```

圖7A

SEQ ID NO: 222 (TTP4000 DNA序列)

```
                    C AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAG
```

圖7B

SEQ ID NO: 83 (TTP4000 天然胺基酸信號序列)
MAAGTAVGAW VLVLSLWGAV VGA

SEQ ID NO: 84 (TTP4000 天然DNA信號序列)
ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG GGGGGCAGTA GTAGGTGCT

SEQ ID NO: 85 (TTP4000 經修飾DNA信號序列)
ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG GGGCGCTGTG GTGGGCGCC

圖8A

SEQ ID NO: 86

```
            PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI
AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV
MHEALHNHYT QKSLSLSPG
```

SEQ ID NO: 87

```
PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI
AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV
MHEALHNHYT QKSLSLSPG
```

SEQ ID NO: 88

```
             SVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI
AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV
MHEALHNHYT QKSLSLSPG
```

SEQ ID NO: 89

```
             SVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYQ STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI
AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV
MHEALHNHYT QKSLSLSPG
```

SEQ ID NO: 90

```
            PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAK
```

SEQ ID NO: 91

```
             SVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW
YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA
LPAPIEKTIS KAK
```

圖8B

SEQ ID NO: 191
pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP NGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVR

SEQ ID NO: 192
pEQITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVR

SEQ ID NO: 193
pENITARI GEPLVLKCKG APKKPPQRLE WKLNTGRTEA WKVLSPQGGG
PWDSVARVLP QGSLFLPAVG IQDEGIFRCQ AMNRNGKETK SNYRVR

SEQ ID NO: 194
pEQITARI GEPLVLKCKG APKKPPQRLE WK

SEQ ID NO: 195
QITARI GEPLVLKCKG APKKPPQRLE WK

SEQ ID NO: 196
5'-GCCTCGGGAGGAACAGTA**cAg**TCCACCTACC

SEQ ID NO: 197
5'-TACTGTTCCTCCCGAGGCTTGGTCTTGG

SEQ ID NO: 198
5'-GCCTCGGCACCGGGCCCTG**gcG**ACCGCCCCTAT

SEQ ID NO: 199
5'-CAGGGCCCGGTGCCGAGGCAGGCCAGGGGA

SEQ ID NO: 223
PCPAPELLGG P

SEQ ID NO: 224
PCPAPELLGG

圖8C

SEQ ID NO: 202 (TTP4000 N2Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGCAGATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8D

SEQ ID NO: 203 (TTP4000 N58Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT CAGGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8E

SEQ ID NO: 204 (TTP4000 N2Q, N58Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGCAGATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT CAGGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8F

SEQ ID NO: 205 (TTP4000 R195A)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CGCGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8G

5

SEQ ID NO: 206 (TTP4000 R195K)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
C**AAG**GCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8H

SEQ ID NO: 207 (TTP4000 R198A)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **GCG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8I

SEQ ID NO: 208 (TTP4000 R198K)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **AAG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8J

SEQ ID NO: 209 (TTP4000 R198H)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **CAT**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8K

SEQ ID NO: 210 (TTP4000 R198T)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **ACG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8L

SEQ ID NO: 211 (TTP4000 N2Q, R198A)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AG**CAG**ATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **GCG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8M

SEQ ID NO: 212 (TTP4000 N58Q, R198A)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT **CAG**GGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **GCG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8N

SEQ ID NO: 213 (TTP4000 N2Q, N58Q, R198A)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AG**CAG**ATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT **CAG**GGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **GCG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC AACTCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8O

SEQ ID NO: 214 (TTP4000 N288Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC **CAG**TCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8P

SEQ ID NO: 215 (TTP4000 N2Q, N288Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AG**CAG**ATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC **CAG**TCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8Q

SEQ ID NO: 216 (TTP4000 N58Q, N288Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT **CAG**GGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC **CAG**TCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8R

SEQ ID NO: 217 (TTP4000 N2Q, N58Q, N288Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AG**CAG**ATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT **CAG**GGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG CGGACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC **CAG**TCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8S

SEQ ID NO: 218 (TTP4000 N2Q, R198A, N288Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AG**CAG**ATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT AACGGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **GCG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC **CAG**TCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8T

SEQ ID NO: 219 (TTP4000 N58Q, R198A, N288Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AGAACATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT **CAG**GGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **GCG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC **CAG**TCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8U

SEQ ID NO: 220 (TTP4000 N2Q, N58Q, R198A, N288Q)

ATGGCAGCCG GAACAGCAGT TGGAGCCTGG GTGCTGGTCC TCAGTCTGTG
GGGCGCTGTG GTGGGCGCCC AG**CAG**ATCAC CGCCCGGATC GGCGAGCCTC
TGGTGCTGAA GTGCAAGGGC GCTCCTAAGA AGCCTCCTCA GCGGCTCGAG
TGGAAGCTGA ACACCGGCCG GACCGAGGCC TGGAAGGTGC TGTCTCCTCA
GGGCGGAGGA CCTTGGGACT CCGTGGCCCG GGTGCTGCCT **CAG**GGCTCCC
TGTTCCTGCC TGCCGTGGGC ATCCAGGACG AGGGCATCTT CAGGTGCCAG
GCCATGAACC GGAACGGCAA AGAAACCAAG TCCAACTACA GAGTGCGGGT
GTACCAGATC CCTGGCAAGC CTGAGATCGT GGACTCCGCC TCCGAGCTGA
CCGCTGGCGT GCCTAACAAG GTCGGCACCT GCGTGTCCGA GGGCTCCTAC
CCTGCCGGCA CCCTGTCCTG GCATCTGGAC GGCAAGCCCC TGGTGCCTAA
CGAGAAGGGC GTGTCCGTGA AGGAACAGAC CAGGCGGCAC CCTGAGACCG
GCCTGTTCAC CCTGCAGTCC GAGCTGATGG TGACCCCTGC CAGAGGCGGC
GACCCTCGGC CTACCTTCTC CTGCTCCTTC TCCCCTGGCC TGCCTCGGCA
CCGGGCCCTG **GCG**ACCGCCC CTATCCAGCC TAGAGTGTGG GAGCCTGTGC
CTCTCGAGGA AGTGCAGCTG GTCGTGGAGC CTGAGGGCGG AGCCGTGGCC
CCTCCTTCCG TGTTCCTGTT CCCTCCTAAG CCTAAGGACA CCCTGATGAT
CTCCCGGACC CCTGAGGTGA CCTGCGTGGT GGTGGACGTG TCCCACGAGG
ATCCTGAGGT GAAGTTCAAC TGGTACGTGG ACGGCGTGGA GGTGCACAAC
GCCAAGACCA AGCCTCGGGA GGAACAGTAC **CAG**TCCACCT ACCGGGTGGT
GTCCGTGCTG ACCGTGCTGC ACCAGGACTG GCTGAATGGC AAAGAATACA
AGTGCAAGGT CTCCAACAAG GCCCTGCCTG CCCCTATCGA GAAAACCATC
TCCAAGGCCA AGGGCCAGCC CAGAGAGCCT CAGGTCTACA CCCTGCCTCC
CTCCCGGGAC GAGCTGACCA AGAACCAGGT GTCCCTGACC TGCCTGGTGA
AGGGCTTCTA CCCTTCCGAC ATCGCCGTGG AGTGGGAGTC CAACGGCCAG
CCTGAGAACA ACTACAAGAC CACCCCTCCT GTGCTGGACT CCGACGGCTC
CTTCTTCCTG TACTCCAAGC TGACCGTGGA CAAGTCCCGG TGGCAGCAGG
GCAACGTGTT CTCCTGCAGC GTGATGCACG AGGCCCTGCA CAACCACTAC
ACCCAGAAGT CCCTGTCCCT GAGCCCTGGC AAGTGA

圖8V

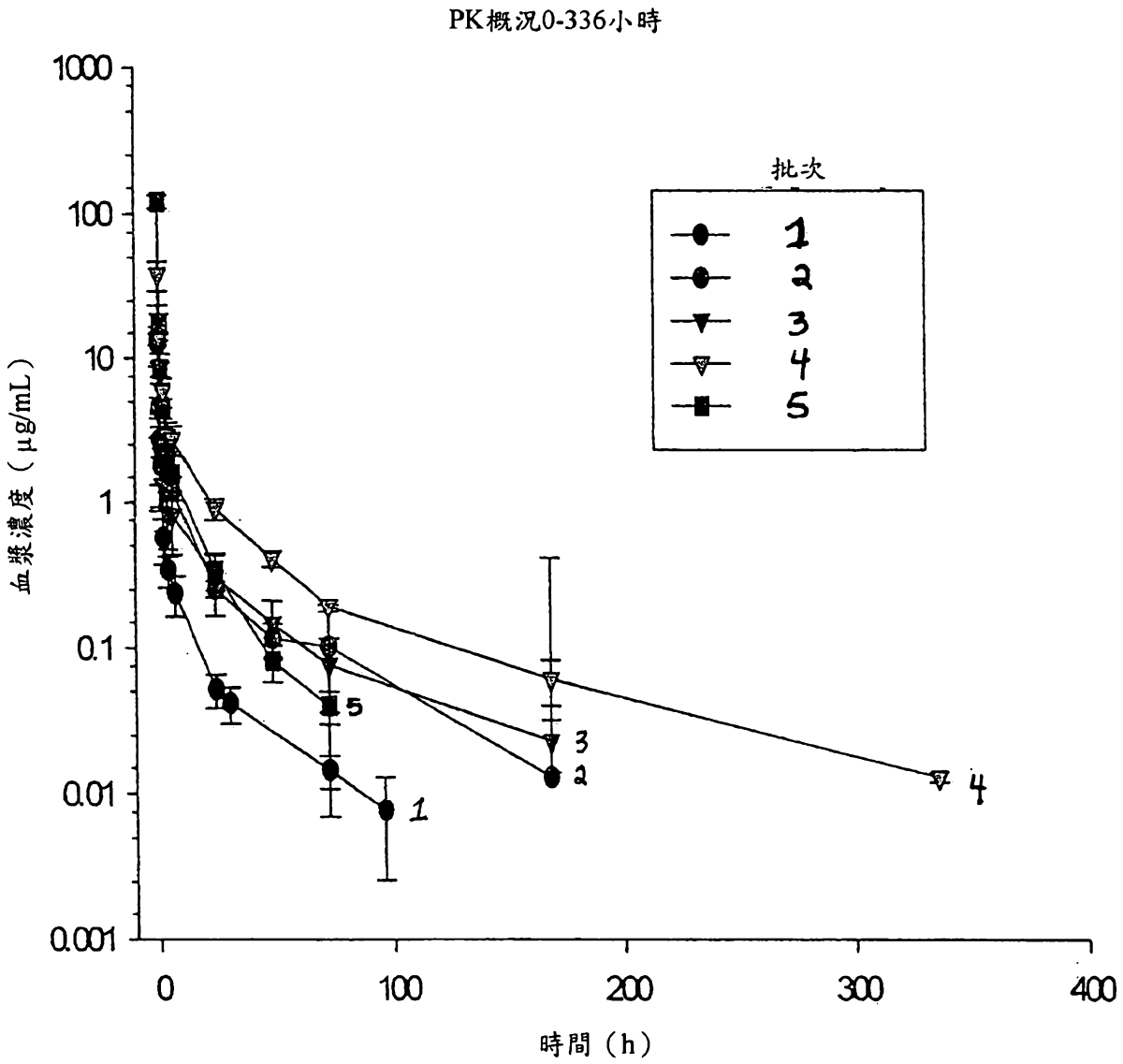

PK概況0-336小時
1000
100
10
1
0.1
0.01
0.001
血漿濃度（μg/mL）
0
100
200
300
400
時間（h）
批次
1
2
3
4
5
1
2
3
4
5

圖9A

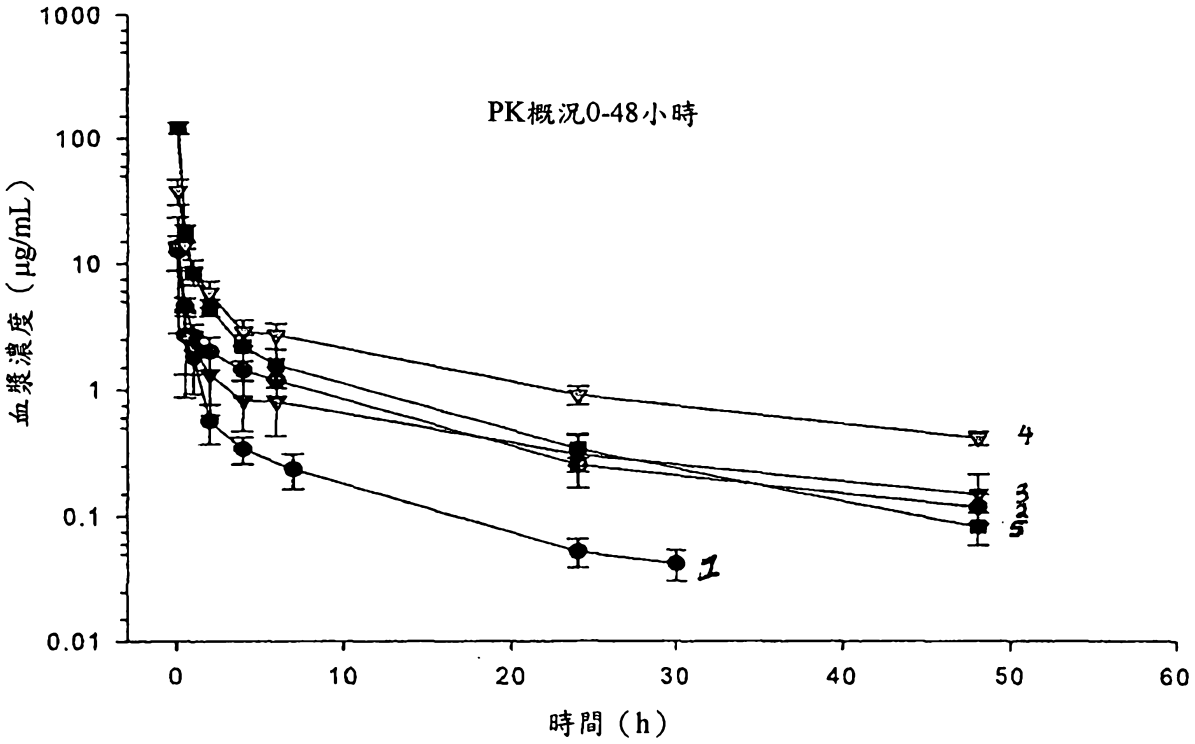

PK概況0-48小時
血漿濃度（μg/mL）
1000
100
10
1
0.1
0.01
0
10
20
30
40
50
60
時間（h）
4
3
2
5
1

圖9B

批次	AUC (0-24 h) (μg·h/mL)	AUC (0-inf) (μg·h/mL)	t 1/2 (h) (終末)	Cmax (μg/mL)	Clp (mL/d/kg)	Vss (L/kg)	% AUC (0-24 h) / AUC (0-inf)
1.	9.30	10.7	22.1	10.2	27500	12.9	87
2.	28.3	39.9	24.4	13.6	6090	4.95	71
3.	21.2	34.7	37.2	13.2	8840	11.1	61
4.	74.4	116	56.2	38.1	2120	2.91	64
5.	81.5	89	17.1	120	2740	0.652	92

圖10

時間(h)	1 濃度(μg/mL) 平均值	標準偏差	2 濃度(μg/mL) 平均值	標準偏差	3 濃度(μg/mL) 平均值	標準偏差	4 濃度(μg/mL) 平均值	標準偏差	5 濃度(μg/mL) 平均值	標準偏差
0	1.190	0.106	1.121	0.054	1.073	0.214	1.078	0.104	1.292	0.313
1	0.987	0.282	1.084	0.018	1.174	0.085	1.196	0.112	1.048	0.057
2	1.106	0.276	1.111	0.023	1.275	0.012	1.205	0.153	1.07	0.118
4	1.047	0.275	1.153	0.164	1.386	0.033	1.185	0.043	0.979	0.056
6	0.689	0.016	1.092	0.023	1.201	0.039	1.152	0.149	0.943	0.134
24	0.721	0.175	1.236	0.062	1.223	0.035	1.107	0.079	0.911	0.158
48	0.832	0.042	1.303	0.084	1.457	0.006	1.192	0.199	0.355	0.071

圖11A

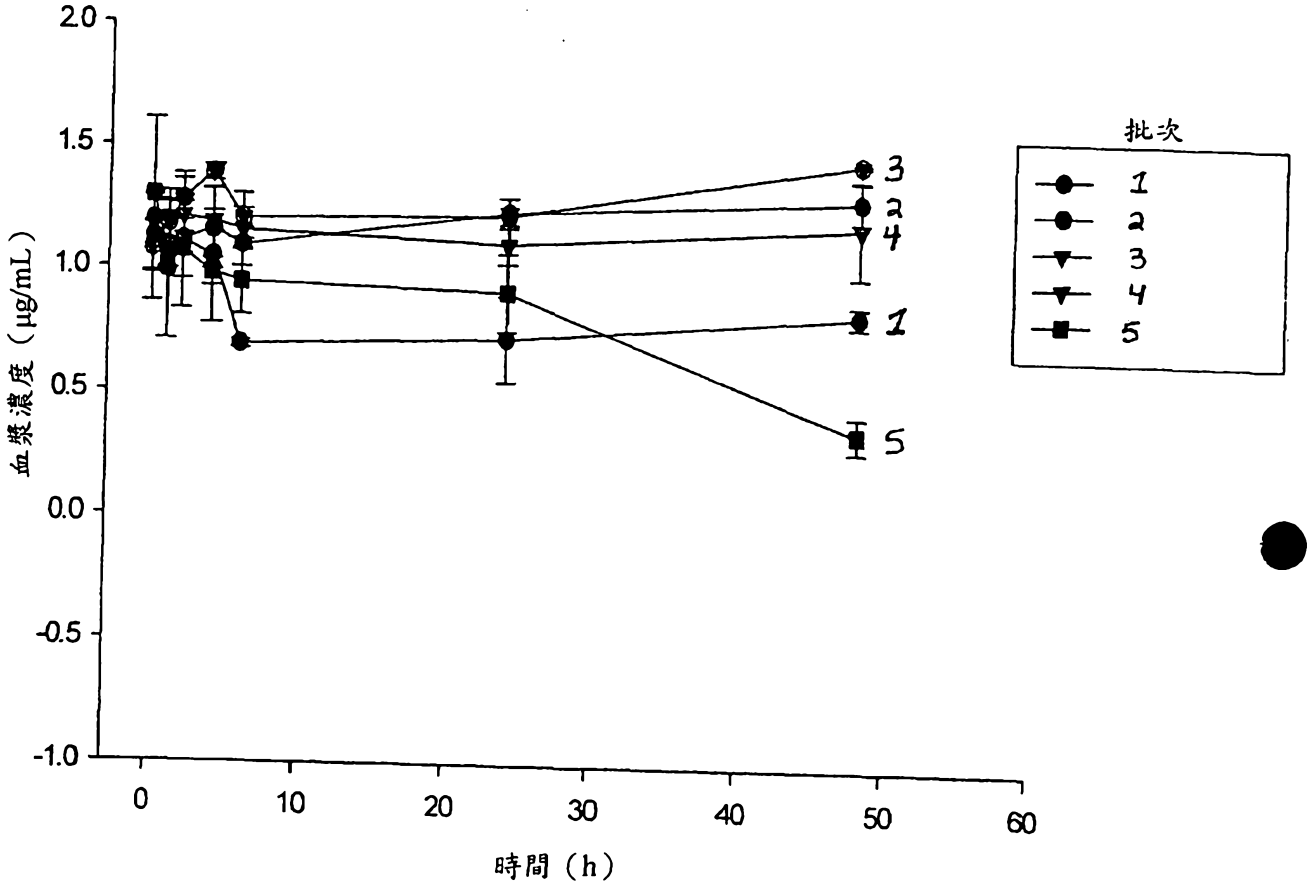


圖11B

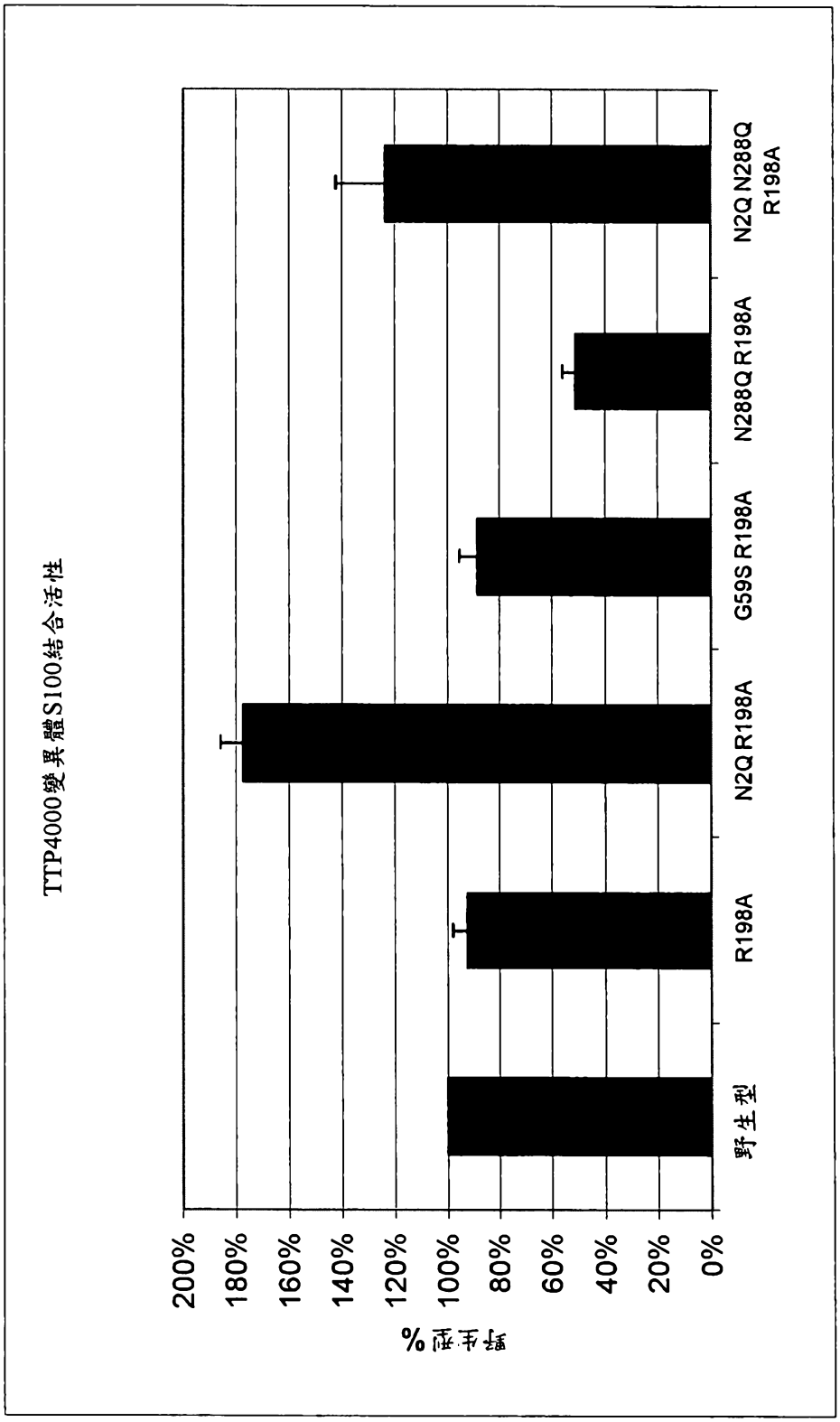

TTP4000變異體S100結合活性
野生型%
200%
180%
160%
140%
120%
100%
80%
60%
40%
20%
0%
野生型
R198A
N2Q R198A
G59S R198A
N288Q R198A
N2Q N288Q R198A

圖12

四、指定代表圖：

(一)本案指定代表圖為：第（12）圖。

(二)本代表圖之元件符號簡單說明：

（無元件符號說明）

五、本案若有化學式時，請揭示最能顯示發明特徵的化學式：

（無）