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(54)名稱

ＤＬＬ３及ＣＤ３抗體構築體

(57)摘要

本發明係關於一種雙特異性抗體構築體，其包含結合於目標細胞表面上之人類 DLL3 的第一結合域及結合於 T 細胞表面上之人類 CD3 的第二結合域。此外，本發明提供一種編碼該抗體構築體之聚核苷酸、包含該聚核苷酸之載體及經該聚核苷酸或載體轉型或轉染之宿主細胞。此外，本發明提供一種用於產生本發明之抗體構築體的方法、該抗體構築體之醫療用途及包含該抗體構築體之套組。

The present invention relates to a bispecific antibody construct comprising a first binding domain which binds to human DLL3 on the surface of a target cell and a second binding domain which binds to human CD3 on the surface of a T cell. Moreover, the invention provides a polynucleotide encoding the antibody construct, a vector comprising said polynucleotide and a host cell transformed or transfected with said polynucleotide or vector. Furthermore, the invention provides a process for the production of the antibody construct of the invention, a medical use of said antibody construct and a kit comprising said antibody construct.

指定代表圖：

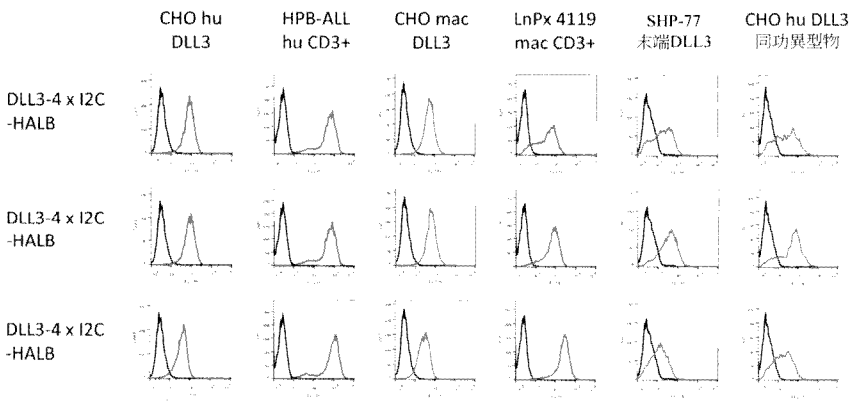
CHO hu DLL3
HPB-ALL hu CD3+
CHO mac DLL3
LnPx 4119 mac CD3+
SHP-77 末端DLL3
CHO hu DLL3 同功異型物
DLL3-4 x I2C -HALB
DLL3-4 x I2C -HALB
DLL3-4 x I2C -HALB

圖3

公告本

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發明摘要

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【發明名稱】

DLL3及CD3抗體構築體

ANTIBODY CONSTRUCTS FOR DLL3 AND CD3

【中文】

本發明係關於一種雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一結合域及結合於T細胞表面上之人類CD3的第二結合域。此外，本發明提供一種編碼該抗體構築體之聚核苷酸、包含該聚核苷酸之載體及經該聚核苷酸或載體轉型或轉染之宿主細胞。此外，本發明提供一種用於產生本發明之抗體構築體的方法、該抗體構築體之醫療用途及包含該抗體構築體之套組。

【英文】

The present invention relates to a bispecific antibody construct comprising a first binding domain which binds to human DLL3 on the surface of a target cell and a second binding domain which binds to human CD3 on the surface of a T cell. Moreover, the invention provides a polynucleotide encoding the antibody construct, a vector comprising said polynucleotide and a host cell transformed or transfected with said polynucleotide or vector. Furthermore, the invention provides a process for the production of the antibody construct of the invention, a medical use of said antibody construct and a kit comprising said antibody construct.

【代表圖】

【本案指定代表圖】：第（3）圖。

【本代表圖之符號簡單說明】：

無

【本案若有化學式時，請揭示最能顯示發明特徵的化學式】：

(無)

發明專利說明書

（本說明書格式、順序，請勿任意更動）

【發明名稱】

DLL3及CD3抗體構築體

ANTIBODY CONSTRUCTS FOR DLL3 AND CD3

本發明係關於一種雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一結合域及結合於T細胞表面上之人類CD3的第二結合域。此外，本發明提供一種編碼該抗體構築體之聚核苷酸、包含該聚核苷酸之載體及經該聚核苷酸或載體轉型或轉染之宿主細胞。此外，本發明提供一種用於產生本發明之抗體構築體的方法、該抗體構築體之醫療用途及包含該抗體構築體之套組。

小細胞肺癌(SCLC)為具有不良預後及有限的治療方案之肺癌之侵襲性形式，其占所有新近診斷之肺癌之約15%且每年在美國出現約25,000例新病例且在全世界範圍內出現180,000例新病例。在過去幾十年，存活率保持較低，其中僅5% SCLC患者存活五年，大部分歸因於缺乏可對抗此肺癌形式之新療法。大部分患者具有擴散期疾病，而約三分之一患者具有侷限期疾病，由僅一側胸腔中存在腫瘤且符合單輻射場定義。此等階段影響可用治療方案，其中侷限期疾病用化學療法及輻射治療且擴散期疾病用單獨的化學療法治療。具有淋巴瘤類特徵之散播性、轉移性腫瘤為SCLC之標誌。SCLC患者之第一例已知診斷將其描述為淋巴系統疾病，未識別為肺癌，直至1926年，其強調SCLC腫瘤與其他實體腫瘤相比之一些獨特性質。

患者通常對當前前線療法良好反應，該前線療法包括依託泊苷(etoposide)及順鉑(cisplatin)，但始終快速復發化療耐藥性疾病，其不

存在當前可用的治療方案。復發性頑抗性情形中之預後極其不良，其中存在快速疾病進程及小於六個月之短中值存活期。此外，SCLC患者具有高共患病率，包括高血壓、心肌疾病、糖尿病及副腫瘤症候群。與SCLC患者之通常較高年齡偶合，此等共患病影響患者耐受苛刻的化療方案的能力，進一步限制治療方案。

雙特異性抗體儀器治療，其包含識別表現於T細胞上之CD3的scFv及識別腫瘤相關抗原之另一scFv，已展示有前景的臨床功效，在諸如頑抗性B-ALL之血液學惡性病中具有高反應率(Topp, M.S.等人 *Blood*, 2012.120(26):第5185-5187頁)，引起Blincyto獲得批准。儘管在實體腫瘤適應症中尚未證明T細胞參與療法之功效，但鑒於疾病之散播性，SCLC可代表CD3 x腫瘤目標雙特異性抗體儀器治療之有前景的實體腫瘤適應症。因此，引導T細胞針對特異性腫瘤抗原之雙特異性T細胞接合分子呈現作為SCLC治療中之新治療方案的新機會。

藉由下一代測序，比較一組原發性患者腫瘤及正常組織之大型收集物中DLL3 mRNA之發病率，當前鑑別DLL3為SCLC特異性腫瘤抗原。SCLC腫瘤中之DLL3表現量為適中的，但極普遍，其中藉由RNA-seq所分析之腫瘤中之約90%展示DLL3表現之證據。與SCLC腫瘤相反，正常組織展示極低的DLL3轉錄物之表現，其中在睪丸、視神經及小腦中偵測到少量表現。藉由RNA-seq進行之SCLC細胞株與腫瘤之比較展示類似表現量，而SCLC細胞株上DLL3表現之細胞表面定量指示表現量低於5000 DLL3/細胞，其中典型表現量低於2000 DLL3/細胞。藉由IHC確認DLL3蛋白質之表現，其中86% SCLC腫瘤對DLL3展示陽性染色，具有均質及膜性染色圖案。除小腦中之極暗淡的染色以外，所有其他正常組織皆對DLL3染色呈陰性。

DLL3為非標準Notch配位體，以細胞自發方式發揮抑制Notch信號傳導、順式結合於Notch的功能，由此阻斷細胞與細胞的相互作用

及目標細胞中Notch之內化(標準Notch信號傳導之標誌)。DLL3之主要作用為在胚胎發育期間之體節發生。DLL3剔除小鼠在中軸骨及顱腦及神經元發育中展示部分缺陷。亦在具有某些生殖系DLL3突變的人類中發現Somitic圖案化缺陷，引起稱為脊椎肋骨發育不全之病狀。

除SCLC以外，先前已在使用抗體-藥物共軛物(ADC)之診斷及治療神經膠質瘤的方法中提出DLL3 (WO 2013/126746)。使用用於DLL3之基於ADC之方法可具有限制，得到細胞表面上蛋白質之低表現量以及降低之針對目標之ADC之效能及低表現。此外，ADC分子通常顯示與自由彈頭有關之毒性(可能為連接子降解之結果)，引起最大耐受劑量限制及與抗體之目標選擇無關的對功效之潛在影響。鑒於T細胞對其目標之所需敏感性，此對於T細胞接合雙特異性分子(經工程改造以同時接合DLL3及CD3)不大可能成為問題，且已在每個細胞表現數百目標蛋白質之細胞株上顯示高強效活體外細胞毒性。此外，由於DLL3與CD3目標之更有效接合，雙特異性T細胞接合抗體構築體與正常抗體(全長IgG)相比通常較小之尺寸可改良組織滲透及增加效能，引起T細胞與目標腫瘤細胞之間改良的突觸形成。

SCLC仍為顯著未滿足的醫學需求，且需要新的治療方案以改良此顯著患者群體之前景。上文論述之雙特異性抗體儀器治療經臨床驗證，且因此靶向DLL3及CD3之抗體構築體代表治療SCLC之有前景的新的可能及改良罹患此適應症之患者之存活期的機會。由於仍需要用於治療與DLL3之過表現有關的腫瘤或癌症疾病之其他可用方案，在此提供用於解決此問題之手段及方法，其呈雙特異性抗體構築體形式，其中一個結合域針對DLL3且第二結合域針對T細胞上之CD3。

因此，在第一態樣中，本發明提供雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一結合域及結合於T細胞表面上之人類CD3的第二結合域，其中第一結合域結合於包含於如SEQ

ID NO:260中所描繪之區域內的DLL3之抗原決定基。

必須注意，如本文所用，除非上下文另外明確指示，否則單數形式「一」及「該(the)」包括複數個提及物。因此，舉例而言，對「試劑」之參考包括此類不同試劑中之一或多者，且對「方法」之參考包括對一般熟習此項技術者已知的可針對本文中所述之方法修改或取代的等效步驟及方法之參考。

除非另外指示，否則在一系列要素之前的術語「至少」應理解為指系列中之每一要素。熟習此項技術者將認識到或能夠僅使用常規實驗確定本文中所描述之本發明之特定實施例之許多等效物。本發明意欲涵蓋此類等效物。

每當在本文中使用時，術語「及/或」包括「及」、「或」及「由該術語連接之要素的所有或任何其他組合」之含義。

如本文中所用，術語「約」或「大致」意謂在既定值或範圍之±20%內，較佳±15%內，更佳±10%內且最佳±5%內。

在本說明書通篇及隨後申請專利範圍中，除非上下文另有要求，否則詞語「包含(comprise)」及諸如「包含(comprises)」及「包含(comprising)」之變化形式應理解為暗示包括所述整數或步驟或整數或步驟之群，但不排除任何其他整數或步驟或整數或步驟之群。當在本文中使用時，術語「包含」可經術語「含有」或「包括」取代，或有時當在本文中使用時，經術語「具有」取代。

當在本文中使用時，「由.....組成」排除所主張要素中未規定之任何要素、步驟或成分。當在本文中使用時，「基本上由.....組成」不排除並不實質上影響技術方案之基本及新穎特徵之材料或步驟。

在本文中之各種情況下，術語「包含」、「基本上由.....組成」及「由.....組成」中之任一者可經其他兩個術語中之任一者替換。

術語「抗體構築體」係指其中結構及/或功能基於抗體(例如全長

或完整免疫球蛋白分子)之結構及/或功能之分子。因此，抗體構築體能夠結合於其特異性目標或抗原。此外，本發明之抗體構築體包含抗體之允許目標結合之最小結構需要。此最小需要可例如藉由存在至少三個輕鏈CDR (亦即VL區之CDR1、CDR2及CDR3)及/或三個重鏈CDR (亦即VH區之CDR1、CDR2及CDR3)，較佳所有六個CDR定義。本發明之構築體所基於之抗體包括例如單株、重組型、嵌合、去免疫、人類化及人類抗體。

包括駱駝抗體及藉由生物技術或蛋白質工程改造方法或製程產生之其他免疫球蛋白抗體之全長或完整抗體在本發明之「抗體構築體」之定義內。此等全長抗體可為例如單株、重組型、嵌合、去免疫、人類化及人類抗體。全長抗體之片段(諸如VH、VHH、VL、(s)dAb、 Fv、Fd、Fab、Fab'、F(ab')2或「r IgG」 (「半抗體」))亦在「抗體構築體」之定義內。本發明之抗體構築體亦可為抗體之經修飾片段，亦稱為抗體變異體，諸如scFv；di-scFv或bi(s)-scFv；scFv-Fc；scFv拉鏈；scFab；Fab2；Fab3；雙功能抗體；單鏈雙功能抗體；串聯雙功能抗體(Tandab)； 串聯di-scFv；串聯tri-scFv；「微型抗體」，其由如下結構例示：$(VH\text{-}VL\text{-}CH3)_2$、$(scFv\text{-}CH3)_2$、$((scFv)_2\text{-}CH3 + CH3)$、$((scFv)_2\text{-}CH3)$或$(scFv\text{-}CH3\text{-}scFv)_2$；多功能抗體，諸如三功能抗體或四功能抗體；及單域抗體，諸如奈米抗體，或僅包含一個可變域(其可為VHH、VH或VL)之獨立於其他V區或域而特異性結合抗原或抗原決定基的單可變域抗體。根據本發明之抗體構築體之更佳型式為交叉抗體、最大抗體(maxi bodies)、雜Fc構築體及單Fc構築體。此等型式之實例將描述於下文中。

結合域通常可包含抗體輕鏈可變區(VL)及抗體重鏈可變區(VH)；然而，其無需同時包含其兩者。舉例而言，Fd片段具有兩個VH區且通常保留完整抗原結合域之一些抗原結合功能。抗體片段、

抗體變異體或結合域之型式之其他實例包括(1) Fab片段，其為具有VL、VH、CL及CH1域之單價片段；(2) F(ab')2片段，其為具有兩個由二硫橋鍵在鉸鏈區連接之Fab片段之二價片段；(3) Fd片段，其具有兩個VH及CH1域；(4) Fv片段，其具有抗體之單個臂之VL及VH域；(5) dAb片段(Ward等人(1989) Nature 341:544-546)，其具有VH域；(6)分離之互補決定區(CDR)及(7)單鏈Fv(scFv)，後者為較佳的(例如來源於scFV文庫)。根據本發明之抗體構築體之實施例之實例例如描述於WO 00/006605、WO 2005/040220、WO 2008/119567、WO 2010/037838、WO 2013/026837、WO 2013/026833、US 2014/0308285、US 2014/0302037、WO2014/144722、WO 2014/151910及WO 2015/048272中。

此外，術語「抗體構築體」之定義包括單價、二價及多價(polyvalent/multivalent)構築體，且因此包括特異性結合於僅一種抗原結構之單特異性構築體以及經由不同結合域特異性結合超過一種抗原結構(例如兩種、三種或三種以上)之雙特異性及多特異性(polyspecific/multispecific)構築體。此外，術語「抗體構築體」之定義包括僅由一個多肽鏈組成之分子以及由超過一個多肽鏈組成之分子，該等鏈可相同(均二聚體、均三聚體或均寡聚物)或不同(雜二聚體、雜三聚體或雜寡聚物)。以上鑑別之抗體及其變異體或衍生物之實例尤其描述於Harlow及Lane, Antibodies a laboratory manual, CSHL Press (1988)；及Using Antibodies: a laboratory manual, CSHL Press (1999)；Kontermann及Dübel, Antibody Engineering, Springer, 第2版, 2010；及Little, Recombinant Antibodies for Immunotherapy, Cambridge University Press 2009中。

本發明之抗體構築體較佳為「活體外產生之抗體構築體」。此術語指根據上述定義之抗體構築體，其中所有或一部分可變區(例如至

少一個CDR)在非免疫細胞選擇(例如活體外噬菌體呈現)蛋白晶片或任何其他可測試候選序列結合於抗原之能力的方法中產生。因此，此術語較佳排除僅藉由在動物中在免疫細胞中進行基因組重排而產生的序列。「重組型抗體」為經由使用重組型DNA技術或遺傳工程改造製備之抗體。

如本文所用，術語「單株抗體」(mAb)或單株抗體構築體係指獲自實質上同種抗體之群的抗體，亦即構成該群之個別抗體除可少量存在之可能天然存在之突變及/或轉譯後修飾(例如異構化、醯胺化)以外為相同的。與通常包括針對不同決定子(或抗原決定基)之不同抗體的習知(多株)抗體製劑相比，單株抗體對抗原上之單一抗原位點或決定子具有高度特異性。除其特異性之外，單株抗體之有利之處在於其藉由融合瘤培養合成，因此未受其他免疫球蛋白污染。修飾語「單株」指示抗體之特徵為自實質上同種之抗體群體獲得，且不應理解為需要藉由任何特定方法產生該抗體。

為製備單株抗體，可使用提供藉由連續細胞株培養物製備之抗體的任何技術。舉例而言，所使用之單株抗體可藉由首先由Kohler等人, Nature, 256:495(1975)描述之融合瘤方法製得，或可藉由重組型DNA方法(參見例如美國專利第4,816,567號)製得。製備人類單株抗體之其他技術的實例包括三源融合瘤技術、人類B細胞融合瘤技術(Kozbor, Immunology Today 4 (1983), 72)及EBV融合瘤技術(Cole等人, Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc. (1985), 77-96)。

融合瘤可隨後使用標準方法篩選，諸如酶聯結免疫吸附分析法(ELISA)及表面電漿子共振(BIACORE™)分析，以鑑別一或多個產生與特定抗原特異性結合之抗體的融合瘤。相關抗原之任何形式可用作免疫原，例如重組型抗原、天然存在形式、其任何變異體或片段以及

其抗原肽。如BIAcore系統中所使用之表面電漿子共振可用於增加結合於目標抗原之抗原決定基(諸如DLL3或CD3ε)的噬菌體抗體的功效(Schier, Human Antibodies Hybridomas 7 (1996), 97-105；Malmborg, J. Immunol. Methods 183 (1995), 7-13)。

製備單株抗體之另一例示性方法包括篩選蛋白表現文庫，例如噬菌體呈現或核糖體呈現文庫。噬菌體呈現例如描述於Ladner等人，美國專利第5,223,409號；Smith (1985) Science 228:1315-1317，Clackson等人, Nature, 352: 624-628 (1991)及Marks等人, J. Mol. Biol., 222: 581-597 (1991)中。

除使用呈現文庫以外，可使用相關抗原使非人類動物，例如嚙齒動物(諸如小鼠、倉鼠、兔或大鼠)免疫。在一個實施例中，非人類動物包括人類免疫球蛋白基因之至少一部分。舉例而言，可用人類Ig(免疫球蛋白)基因座之大片段工程改造缺乏小鼠抗體產生之小鼠菌株。使用融合瘤技術，可製造及選擇來源於具有所需特異性之基因的抗原特異性單株抗體。參見例如XENOMOUSE™，Green等人 (1994) Nature Genetics 7:13-21、US 2003-0070185、WO 96/34096及WO 96/33735。

單株抗體亦可獲自非人類動物，且接著使用此項技術中已知的重組型DNA技術修飾，例如人類化、去免疫、使其嵌合等。經修飾之抗體構築體的實例包括非人類抗體之人類化變異體、「親和力成熟」抗體(參見例如Hawkins等人, J. Mol. Biol. 254, 889-896 (1992)及Lowman等人, Biochemistry 30, 10832-10837 (1991))及具有改變之效應功能的抗體突變體(參見例如美國專利5,648,260；Kontermann及Dübel (2010), 上述引文及Little(2009), 上述引文)。

在免疫學中，親和力成熟為可在免疫反應過程期間使B細胞產生對抗原具有增加之親和力的抗體的方法。在重複暴露於相同抗原下，

宿主將產生具有相繼增大之親和力的抗體。與天然原型類似，活體外親和力成熟係基於突變及選擇之原理。活體外親和力成熟成功地用於最佳化抗體、抗體構築體及抗體片段。CDR內部之無規突變使用射線、化學誘變劑或易錯PCR引入。此外，遺傳多樣性可藉由鏈改組而增加。使用呈現方法(如噬菌體呈現)之兩或三輪突變及選擇通常產生親和力在低奈莫耳範圍內之抗體片段。

抗體構築體之胺基酸取代變異之較佳類型包括取代親本抗體(例如人類化或人類抗體)之一或多個高變區殘基。通常，選擇用於進一步研究之所得變異體應相對於產生其之親本抗體具有經改良之生物特性。產生此類取代變異體之適宜方式涉及使用噬菌體呈現之親和力成熟。簡言之，使若干高變區位點(例如6-7個位點)突變以在各位點產生所有可能之胺基酸取代。因此產生之抗體變異體以單價方式自絲狀噬菌體粒子以與包裝在各粒子內之M13的基因III產物的融合物形式呈現。隨後如本文所揭示將噬菌體呈現之變異體針對其生物活性(例如結合親和力)進行篩選。為鑑別用於修飾之候選高變區位點，可進行丙胺酸掃描突變誘發以鑑別顯著有助於抗原結合之高變區殘基。或者或另外，分析抗原-抗體複合物的晶體結構以鑑別在結合域與例如人類FLT3之間的接觸點可為有益的。此類接觸殘基及相鄰殘基為根據本文中詳述之技術用於取代的候選物。在產生此等變異體後，如本文所述對變異體組進行篩選，且可在一或多個相關分析中選擇具有優良特性之抗體用於進一步研究。

本發明之單株抗體及抗體構築體尤其包括「嵌合」抗體(免疫球蛋白)，其中重鏈及/或輕鏈之一部分與來源於特定物種或屬於特定抗體類別或子類之抗體中的相應序列一致或同源，而鏈之其餘部分與來源於另一物種或屬於另一抗體類別或子類之抗體中的相應序列以及此類抗體之片段(只要其展現所需生物活性即可)一致或同源(美國專利第

4,816,567號；Morrison等人, Proc. Natl. Acad. Sci. USA, 81: 6851-6855 (1984))。本文中所關注之嵌合抗體包括「靈長類化」抗體，其包含來源於非人類靈長類動物(例如，舊世界猴、猿等)之可變域抗原結合序列及人類恆定區序列。已描述多種製備嵌合抗體之方法。參見例如Morrison等人, Proc. Natl. Acad. ScL U.S.A. 81:6851 , 1985；Takeda等人, Nature 314:452, 1985；Cabilly等人, 美國專利第4,816,567號；Boss等人, 美國專利第4,816,397號；Tanaguchi等人, EP 0171496；EP 0173494；及GB 2177096。

抗體、抗體構築體、抗體片段或抗體變異體亦可藉由例如WO 98/52976或WO 00/34317中所揭示之方法，藉由人類T細胞抗原決定基之特異性缺失(稱為「去免疫」之方法)來修飾。簡言之，可針對結合於II類MHC之肽分析抗體之重鏈及輕鏈可變域；此等肽表示潛在T細胞抗原決定基(如WO 98/52976及WO 00/34317中所定義)。為偵測潛在T細胞抗原決定基，可施用稱為「肽穿線」之電腦模型化法，且此外，可搜索人類II類MHC結合肽之資料庫中的VH及VL序列中所存在之基元，如WO 98/52976及WO 00/34317中所述。此等基元結合於18種主要II類MHC DR同種異型抗免疫球蛋白中之任一者，且因此構成潛在T細胞抗原決定基。所偵測之潛在T細胞抗原決定基可藉由取代可變域中之少數胺基酸殘基或較佳藉由單胺基酸取代基來消除。通常，進行保守取代。通常但非排他地，可使用對人類生殖系抗體序列中之位置常見的胺基酸。人類生殖系序列揭示於例如Tomlinson等人, (1992) J. MoI. Biol. 227:776-798；Cook, G.P.等人 (1995) Immunol. Today 第16卷 (5): 237-242；及Tomlinson等人 (1995) EMBO J. 14: 14:4628-4638中。V BASE目錄提供人類免疫球蛋白可變區序列之綜合目錄(由Tomlinson, LA.等人, MRC Centre for Protein Engineering, Cambridge, UK彙編)。此等序列可用作人類序列之來源，例如用於構

架區及CDR。亦可使用共同人類構架區，例如美國專利第6,300,064號中所述。

「人類化」抗體、抗體構築體、其變異體或片段(諸如Fv、Fab、Fab'、F(ab')2或抗體之其他抗原結合子序列)為大部分人類序列之抗體或免疫球蛋白，其含有來源於非人類免疫球蛋白之最小序列。在極大程度上，人類化抗體為人類免疫球蛋白(受體抗體)，其中來自受體高變區(亦為CDR)之殘基經來自非人類(例如嚙齒動物)物種(供體抗體)(諸如具有所需特異性、親和力及能力之小鼠、大鼠、倉鼠或兔)的高變區之殘基置換。在一些情況下，人類免疫球蛋白之Fv構架區(FR)殘基經相應非人類殘基置換。此外，如本文中所用之「人類化抗體」亦可包含未在受體抗體或供體抗體中發現之殘基。進行此等修飾以進一步優化且最佳化抗體效能。人類化抗體亦可包含免疫球蛋白恆定區(Fc)之至少一部分、通常人類免疫球蛋白之恆定區之至少一部分。對於進一步細節，參見Jones等人，Nature, 321: 522-525 (1986)；Reichmann等人，Nature, 332: 323-329 (1988)；及Presta, Curr. Op. Struct. Biol., 2: 593-596 (1992)。

人類化抗體或其片段可藉由用來自人類Fv可變域之等效序列置換不直接參與抗原結合之Fv可變域之序列產生。產生人類化抗體或其片段之例示性方法由以下文獻提供：Morrison (1985) Science 229:1202-1207；Oi等人，(1986) BioTechniques 4:214；及US 5,585,089；US 5,693,761；US 5,693,762；US 5,859,205；及US 6,407,213。此等方法包括分離、操控及表現編碼來自重鏈或輕鏈中之至少一者的免疫球蛋白Fv可變域之全部或一部分的核酸序列。此類核酸可獲自產生針對上述預定目標之抗體的融合瘤以及來自其他來源。可接著將編碼人類化抗體分子之重組型DNA選殖至適合的表現載體中。

人類化抗體亦可使用表現人類重鏈及輕鏈基因但不能表現內源性小鼠免疫球蛋白重鏈及輕鏈基因之轉殖基因動物(諸如小鼠)產生。Winter描述可用於製備本文所述之人類化抗體的例示性CDR移植方法(美國專利第5,225,539號)。特定人類抗體之全部CDR可用非人類CDR之至少一部分置換，或僅一些CDR可用非人類CDR置換。僅需要置換人類化抗體結合於預定抗原所需數目的CDR。

人類化抗體可藉由引入保守取代、共同序列取代、生殖系取代及/或回復突變來最佳化。此類經改變之免疫球蛋白分子可藉由此項技術中已知之若干技術中之任一者製備(例如Teng等人, Proc. Natl. Acad. Sci. U.S.A., 80: 7308-7312, 1983；Kozbor等人, Immunology Today, 4: 7279, 1983；Olsson等人, Meth. Enzymol., 92: 3-16, 1982及EP 239 400)。

術語「人類抗體」、「人類抗體構築體」及「人類結合域」包括具有實質上對應於此項技術中已知之人類生殖系免疫球蛋白序列之抗體區(諸如可變及恆定區或結構域)之抗體、抗體構築體及結合域，包括例如Kabat等人, (1991) (上述引文)所述者。本發明之人類抗體、抗體構築體或結合域可例如在CDR及尤其在CDR3中包括並非由人類生殖系免疫球蛋白序列編碼之胺基酸殘基(例如藉由活體外隨機或位點特異性突變誘發或藉由活體內體細胞突變引入的突變)。人類抗體、抗體構築體或結合域可具有至少一個、兩個、三個、四個、五個或更多個位置經不由人類生殖系免疫球蛋白序列編碼之胺基酸殘基置換。如本文所用之人類抗體、抗體構築體及結合域之定義亦涵蓋完全人類抗體，其僅包括抗體之非人工及/或遺傳改變之人類序列，其可藉由使用諸如Xenomouse之技術或系統獲得。

在一些實施例中，本發明之抗體構築體為「經分離」或「實質上純」的抗體構築體。「經分離」或「實質上純」在用於描述本文所

揭示之抗體構築體時意謂抗體構築體已自其製備環境之組分鑑別、分離及/或回收。抗體構築體較佳不或實質上不與來自其製備環境的所有其他組分締合。其製備環境之污染物組分(諸如由重組型轉染細胞產生的污染物組分)為通常干擾多肽之診斷性或治療性用途之物質，且可包括酶、激素及其他蛋白質或非蛋白質溶質。抗體構築體可例如占既定樣品中總蛋白質之至少約5重量%或至少約50重量%。應理解，視情況而定，經分離之蛋白質可占總蛋白質含量之5重量%至99.9重量%。多肽可經由使用誘導性啟動子或高表現啟動子以顯著較高濃度製備，以使得其以增加之濃度水準製備。定義包括在此項技術中已知之多種生物體及/或宿主細胞中製備抗體構築體。在較佳實施例中，抗體構築體(1)藉由使用轉杯式測序儀純化至一定程度以足以獲得N端或內部胺基酸序列之至少15個殘基，或(2)藉由SDS-PAGE在非還原或還原條件下使用考馬斯藍(Coomassie blue)或較佳銀染色純化至均質。通常，然而，經分離之抗體構築體藉由至少一個純化步驟製備。

根據本發明，術語「結合域」特徵在於分別(特異性)結合於目標分子(抗原)上之既定標目標原決定基或既定目標位點(此處： DLL3及CD3)/與其相互作用/識別其的域。第一結合域之結構及功能(識別DLL3)且較佳以及第二結合域之結構及/或功能(識別CD3)係基於抗體(例如全長或完全免疫球蛋白分子)之結構及/或功能。根據本發明，第一結合域由存在三個輕鏈CDR (亦即VL區之CDR1、CDR2及CDR3)及/或三個重鏈CDR (亦即VH區之CDR1、CDR2及CDR3)表徵。第二結合域較佳亦包含抗體之允許目標結合之最小結構需要。更佳地，第二結合域包含至少三個輕鏈CDR (亦即VL區之CDR1、CDR2及CDR3)及/或三個重鏈CDR (亦即VH區之CDR1、CDR2及CDR3)。據設想，第一及/或第二結合域藉由噬菌體呈現或文庫篩選方法產生或獲得而非藉由將來自預先存在之(單株)抗體之CDR序列移植於骨架中產生或獲得。

根據本發明，結合域呈一或多種多肽形式。此類多肽可包括蛋白質部分及非蛋白質部分(例如化學連接子或化學交聯劑，諸如戊二醛)。蛋白質(包括其片段，較佳生物活性片段及肽，通常具有少於30個胺基酸)包含兩個或更多個經由共價肽鍵彼此偶合之胺基酸(產生胺基酸之鏈)。如本文所用之術語「多肽」描述分子之群，其通常由超過30個胺基酸組成。多肽可進一步形成多聚體，諸如二聚體、三聚體以及更高級寡聚物，亦即由超過一個多肽分子組成。形成此類二聚體、三聚體等之多肽分子可相同或不相同。此類多聚體之相應高級結構因此稱為均二聚體或雜二聚體、均三聚體或雜三聚體等。雜多聚體之實例為抗體分子，其在其天然存在之形式下由兩個相同多肽輕鏈及兩個相同多肽重鏈組成。術語「肽」、「多肽」及「蛋白質」亦指經天然修飾之肽/多肽/蛋白質，其中修飾例如藉由轉譯後修飾(如糖基化、乙醯化、磷酸化及其類似修飾)進行。「肽」、「多肽」或「蛋白質」在本文提及時亦可經化學修飾，諸如聚乙二醇化。此類修飾在此項技術中為吾人所熟知且描述於下文中。

結合於DLL3之結合域及/或結合於CD3之結合域較佳為人類結合域。包含至少一個人類結合域之抗體及抗體構築體避免一些與具有非人類(諸如嚙齒動物，例如鼠類、大鼠、倉鼠或兔)可變及/或恆定區之抗體或抗體構築體有關的問題。此類嚙齒動物衍生之蛋白質的存在可引起抗體或抗體構築體之快速清除或可引起患者針對抗體或抗體構築體產生免疫反應。為避免使用源自嚙齒動物之抗體或抗體構築體，人類或完全人類抗體/抗體構築體可經由向嚙齒動物中引入人類抗體功能以使得嚙齒動物產生全人類抗體來產生。

在YAC中選殖及重建構兆鹼基大小之人類基因座且將其引入小鼠生殖系中的能力提供一種闡明極大或粗略定位之基因座之功能組分以及產生人類疾病之適用模型的有力方法。此外，使用此類技術用人類

等效物取代小鼠基因座可提供對發育期間人類基因產物之表現及調節，其與其他系統之聯繫及其參與疾病誘發及進展的獨到見解。

此類策略之一個重要實際應用為「人類化」小鼠體液免疫系統。於內源Ig基因已不活化之小鼠中引入人類免疫球蛋白(Ig)基因座提供研究漸進式表現及組裝抗體之潛在機制以及其在B細胞開發中之作用的機會。此外，此類策略可提供產生完全人類單株抗體(mAb)的理想來源，其為朝向實現人類疾病之抗體療法之前景的重要里程碑。完全人類抗體或抗體構築體預期使小鼠mAb或小鼠衍生之mAb固有的免疫原性及過敏反應達最小，因此提高所投與抗體/抗體構築體之功效及安全性。使用完全人類抗體或抗體構築體可預期在治療需要重複化合物投藥之慢性及復發性人類疾病(諸如發炎、自體免疫及癌症)中提供實質性優勢。

朝向此目標之一種方法為用人類Ig基因座之大片段工程改造小鼠抗體產生缺陷型小鼠菌株以預測此類小鼠將在小鼠抗體不存在下產生大譜系之人類抗體。大人類Ig片段將保持大可變基因多樣性以及適當調節抗體產生及表現。藉由使用小鼠機構進行抗體多樣化及選擇及對人類蛋白之缺乏免疫耐受性，此等小鼠品系中再產生之人類抗體譜將針對任何相關抗原(包括人類抗原)產生高親和力抗體。使用融合瘤技術，可容易地產生及選擇具有所需特異性之抗原特異性人類mAb。此通用策略結合第一XenoMouse小鼠菌株的產生加以展現(參見Green等人, Nature Genetics 7:13-21 (1994))。用分別含有人類重鏈基因座及κ輕鏈基因座之245 kb及190 kb大小之生殖系構型片段的酵母人造染色體(YAC)工程改造XenoMouse菌株，該等染色體含有核心可變及恆定區序列。證明含人類Ig之YAC與小鼠系統相容以用於抗體重排與表現且能夠取代不活化之小鼠Ig基因。此藉由其誘導B細胞發育、產生完全人類抗體之成人樣人類譜系及產生抗原特異性人類mAb之能力展

現。此等結果亦表明引入含有較大量V基因之人類Ig基因座之較大部分、其他調節元件及人類Ig恆定區可實質上再現特徵為對感染及免疫之人類體液反應的完整譜系。Green等人之研究近年來延伸至經由分別引入人類重鏈基因座及κ輕鏈基因座之兆鹼基大小之生殖系構型YAC片段來引入大於約80%人類抗體譜系。參見Mendez等人, Nature Genetics 15:146-156 (1997)及美國專利申請案第08/759,620號。

XenoMouse小鼠之產生進一步論述且描繪於美國專利申請案第07/466,008號、第07/610,515號、第07/919,297號、第07/922,649號、第08/031,801號、第08/112,848號、第08/234,145號、第08/376,279號、第08/430,938號、第08/464,584號、第08/464,582號、第08/463,191號、第08/462,837號、第08/486,853號、第08/486,857號、第08/486,859號、第08/462,513號、第08/724,752號及第08/759,620號；及美國專利第6,162,963號；第6,150,584號；第6,114,598號；第6,075,181號及第5,939,598號及日本專利第3 068 180 B2號、第3 068 506 B2號及第3 068 507 B2號中。亦參見Mendez等人 Nature Genetics 15:146-156 (1997)以及Green及Jakobovits J. Exp. Med. 188:483-495 (1998)、EP 0 463 151 B1、WO 94/02602、WO 96/34096、WO 98/24893、WO 00/76310及WO 03/47336。

在替代方法中，包括GenPharm International, Inc.之其他人已使用「微型基因座」方法。在微型基因座方法中，經由包括來自Ig基因座之碎片(個別基因)來模擬外源Ig基因座。因此，一或多個VH基因、一或多個DH基因、一或多個JH基因、μ恆定區及第二恆定區(較佳為γ恆定區)形成用於插入動物中之構築體。此方法描述於頒予Surani等人之美國專利第5,545,807號及各自頒予Lonberg及Kay之美國專利第5,545,806號；第5,625,825號；第5,625,126號；第5,633,425號；第5,661,016號；第5,770,429號；第5,789,650號；第5,814,318號；第

5,877,397號；第5,874,299號；及第6,255,458號，頒予Krimpenfort及Berns之美國專利第5,591,669號及第6,023,010號，頒予Berns等人之美國專利第5,612,205號；第5,721,367號；及第5,789,215號，及頒予Choi及Dunn之美國專利第5,643,763號，及GenPharm國際美國專利申請案第07/574,748號、第07/575,962號、第07/810,279號、第07/853,408號、第07/904,068號、第07/990,860號、第08/053,131號、第08/096,762號、第08/155,301號、第08/161,739號、第08/165,699號、第08/209,741號中。亦參見EP 0 546 073 B1、WO 92/03918、WO 92/22645、WO 92/22647、WO 92/22670、WO 93/12227、WO 94/00569、WO 94/25585、WO 96/14436、WO 97/13852及WO 98/24884及美國專利第5,981,175號。亦參見Taylor等人 (1992)，Chen等人 (1993)，Tuaillon等人 (1993)，Choi等人 (1993)，Lonberg等人 (1994)，Taylor等人 (1994)及Tuaillon等人 (1995)，Fishwild等人 (1996)。

Kirin亦已證明由小鼠產生人類抗體，在該小鼠中已經由微細胞融合引入染色體之大碎片或完整染色體。參見歐洲專利申請案第773 288號及第843 961號。Xenerex Biosciences正在研發可能產生人類抗體的技術。在此技術中，SCID小鼠用人類淋巴細胞(例如B細胞及/或T細胞)重建。隨後用抗原使小鼠免疫且該等小鼠可產生針對該抗原之免疫反應。參見美國專利第5,476,996號；第5,698,767號及第5,958,765號。

人類抗小鼠抗體(HAMA)反應引導工業上製備嵌合或其他人類化抗體。然而，預期將觀測到某些人類抗嵌合抗體(HACA)反應，尤其在抗體之長期或多劑量利用中。因此，需要提供包含針對DLL3之人類結合域及/或針對CD3之人類結合域的抗體構築體，以消除HAMA或HACA反應的問題及/或效應。

根據本發明，術語「(特異性)結合於」、「(特異性)識別」、「(特異性)針對」及「(特異性)反應」意謂結合域與目標分子(抗原)(此處：分別為DLL3及CD3)上之既定抗原決定基或既定目標位點相互作用或特異性相互作用。

術語「抗原決定基」係指與結合域、抗體或免疫球蛋白、或抗體或免疫球蛋白之衍生物、片段或變異體特異性結合的抗原上之位點。「抗原決定基」為抗原，且因此術語抗原決定基有時在本文中亦稱為「抗原結構」或「抗原決定子」。因此，結合域為「抗原相互作用位點」。該結合/相互作用亦理解為定義「特異性識別」。

「抗原決定基」可由藉由蛋白質之三級摺疊並列之鄰接胺基酸或非鄰接胺基酸形成。「線性抗原決定基」為胺基酸一級序列包含所識別之抗原決定基的抗原決定基。線性抗原決定基在獨特序列中通常包括至少3個或至少4個，且更通常至少5個或至少6個或至少7個，例如約8至約10個胺基酸。

與線性抗原決定基相比，「構形抗原決定基」為如下抗原決定基，其中構成抗原決定基之胺基酸的一級序列並非所識別抗原決定基之唯一指定組分(例如抗原決定基，其中胺基酸之一級序列並非必須由結合域識別)。通常，構形抗原決定基相對於線性抗原決定基包含增加數目之胺基酸。關於識別構形抗原決定基，結合域識別抗原、較佳地肽或蛋白質或其片段之三維結構(在本發明之上下文中，針對第一結合域之抗原結構包含在DLL3蛋白質內)。舉例而言，當蛋白質分子摺疊以形成三維結構時，形成構形抗原決定基之某些胺基酸及/或多肽主鏈變得毗鄰，使抗體能夠識別抗原決定基。確定抗原決定基之構形的方法包括(但不限於) x射線結晶學、二維核磁共振(2D-NMR)光譜法及定點旋轉標記及電子順磁共振(EPR)光譜法。

下文描述一種抗原決定基定位方法：當人類DLL3蛋白質中之區

域(相鄰胺基酸延伸子)與非人類及非靈長類動物DLL3抗原(例如小鼠DLL3，但亦可設想其他物種，諸如雞、大鼠、倉鼠、兔等)之其對應區域互換/置換時，預期發生結合域之結合降低，除非結合域對所使用之非人類、非靈長類動物DLL3具有交叉反應性。與結合於人類DLL3蛋白質中之相應區相比，該減少較佳為至少10%、20%、30%、40%或50%；更佳為至少60%、70%或80%，且最佳90%、95%或甚至100%，其中與人類DLL3蛋白質中相應區之結合設定為100%。據設想，前述人類DLL3/非人類DLL3嵌合體表現於CHO細胞中。亦設想，人類DLL3/非人類DLL3嵌合體與不同膜結合蛋白質(諸如EpCAM)之跨膜域及/或細胞質域融合。

在抗原決定基定位之替代性或其他方法中，可產生若干截短形式之人類DLL3細胞外域以確定藉由結合域識別之特異性區域。在此等截短版本中，以N端起始，逐步刪除不同細胞外DLL3域/子域或區。在本發明之情形下產生及使用之截短之DLL3版本描繪於圖1中。據設想，截短DLL3版本表現於CHO細胞中。亦設想，截短DLL3版本與不同膜結合蛋白質(諸如EpCAM)之跨膜域及/或細胞質域融合。亦設想，截短DLL3版本涵蓋其N端之信號肽域，例如來源於小鼠IgG重鏈信號肽之信號肽。此外設想，截短DLL3形式涵蓋其N端之v5域(在信號肽之後)，其使得檢驗細胞表面上之其恰當表現。預期在此等截短DLL3版本下會出現結合之減小或缺失，該等版本不再涵蓋由結合域識別之DLL3區。結合之降低較佳為至少10%、20%、30%、40%、50%；更佳為至少60%、70%、80%且最佳90%、95%或甚至100%，藉此與全部人類DLL3蛋白質(或其胞外區或結構域)之結合設定為100%。測試此結合損失之方法描述於實例2中。

另一種測定目標抗原之特異性殘基對抗體構築體或結合域之識別的方法為丙胺酸掃描(參見例如Morrison KL及Weiss GA. Cur Opin

Chem Biol. 2001年6月;5(3):302-7)，其中待分析的各殘基由丙胺酸藉由，例如經由定點突變誘發。丙胺酸由於其非龐大的化學上惰性甲基官能基而使用，然而，仍模擬許多其他胺基酸具有的二級結構參考物。有時，諸如纈胺酸或白胺酸之龐大胺基酸可用於需要保留突變殘基大小的情況。丙胺酸掃描為已使用一段較長時間的成熟技術。

結合域與抗原決定基或包含抗原決定基之區之間的相互作用暗示結合域對特定蛋白或抗原(此處：分別為DLL3及CD3)上之抗原決定基/包含抗原決定基之區展現可觀親和力，且通常不與除DLL3或CD3外之蛋白或抗原展現顯著反應性。「明顯親和力」包括以約10^{-6} M (KD)或更強之親和力結合。較佳地，當結合親和力為約10^{-12} M至10^{-8} M、10^{-12} M至10^{-9} M、10^{-12} M至10^{-10} M、10^{-11} M至10^{-8} M、較佳約10^{-11} M至10^{-9} M時，結合視為特異性的。結合域是否與目標特異性反應或特異性結合於目標可尤其易於藉由比較該結合域與目標蛋白或抗原的反應與該結合域與除DLL3或CD3以外之蛋白質或抗原的反應來測試。較佳地，本發明之結合域基本上或大體上不結合於除DLL3或CD3外之蛋白或抗原(亦即第一結合域不能夠結合於除DLL3以外之蛋白質且第二結合域不能夠結合於除CD3外之蛋白質)。

術語「基本上/大體上不結合」或「不能夠結合」意謂本發明之結合域不結合除DLL3或CD3外之蛋白質或抗原，亦即展示與除DLL3或CD3外之蛋白質或抗原不超過30%、較佳不超過20%、更佳不超過10%、尤其較佳不超過9%、8%、7%、6%或5%的反應性，藉此與DLL3或CD3之結合分別設定為100%。

亦設想本發明之抗體構築體結合於具有以下DLL3點突變中之一者或兩者之人類DLL3同功異型物：F172C及L218P。參見實例5。

咸信特異性結合由結合域之胺基酸序列中的特異性基元及抗原實現。因此，結合藉由其一級、二級及/或三級結構以及該等結構之

二級修飾的結果達成。抗原相互作用位點與其特異性抗原之特異性相互作用可使該位點與抗原簡單結合。此外，抗原-相互作用-位點與其特異性抗原之特異性相互作用可替代地或另外地使信號開始，例如由於誘導抗原之構形變化、抗原之寡聚等。

根據本發明之抗體構築體結合於DLL3之抗原決定基，該抗原決定基包含於如SEQ ID NO:260中所描繪之區域內，對應於涵蓋區域EGF-3及EGF-4之胺基酸延伸子。亦產生抗-DLL3結合子之其他群且在抗原決定基定位期間鑑別其DLL3結合特異性(參見實例2)。

所產生之結合子之最大群識別DSL域內之抗原決定基。然而，此等抗體構築體中無一者滿足初始18小時基於^{51}Cr之細胞毒性分析中之足夠的細胞毒活性的準則，其中受刺激之人類CD8+ T細胞作為效應細胞且經hu DLL3轉染之CHO細胞作為目標細胞。

在另一個初始48小時基於FACS之細胞毒性分析(使用未受刺激之人類PBMC作為效應細胞及經hu DLL3轉染之CHO細胞作為目標細胞)，此等識別蛋白質之N端內之DLL3抗原決定基的結合子具有1455與1580 pM之間的EC50值。在本文中，不認為此等值對於雙特異性抗體為足夠的，該等雙特異性抗體係提供用於引導針對癌細胞之患者之免疫系統，更特定言之T細胞之細胞毒活性方面的治療用途。

最終，產生另一結合子群且在多種分析中針對其細胞毒活性進行表徵。此等結合子之抗原決定基定位顯示針對EGF-5區域內所包含之DLL3抗原決定基及對亦在EGF-6區域內的某一延伸子的特異性(關於細節，參見實例2)。此等名為DLL3-18、DLL3-19、DLL3-20及DLL3-21之結合子之不同細胞毒性分析(參見實例8.3、8.5、8.6及8.7)中產生之資料之整體情況揭示如下：儘管並非所有的結合子在所有分析中在有利的EC50值方面不合格，但若與本發明之抗體構築體相比，整個群明顯表現不佳。此觀測結果由表6-9中展示之結果之更深

的陰影突出顯示。

總而言之，可明確陳述目前為止，本發明之抗體構築體(其結合於如SEQ ID NO:260中所描繪之區域內所包含之DLL3之抗原決定基)與具有不同抗原決定基特異性之DLL3結合子之多種其他群相比展示最佳活性效能。換言之，本發明之抗體構築體呈現有利的抗原決定基活性關係，因此支持強效雙特異性抗體構築體介導之細胞毒活性。

在另一態樣中，本發明提供雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一結合域及結合於T細胞表面上之人類CD3的第二結合域，其中第一結合域結合於如SEQ ID NO:258中所描繪之區域內所包含的DLL3之抗原決定基。

本發明之雙特異性抗體構築體之第一結合域較佳包含有選自由以下組成之群的包含CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區：

a)如SEQ ID NO:31中所描繪之CDR-H1、如SEQ ID NO:32中所描繪之CDR-H2、如SEQ ID NO:33中所描繪之CDR-H3、如SEQ ID NO:34中所描繪之CDR-L1、如SEQ ID NO:35中所描繪之CDR-L2及如SEQ ID NO:36中所描繪之CDR-L3；

b)如SEQ ID NO:41中所描繪之CDR-H1、如SEQ ID NO:42中所描繪之CDR-H2、如SEQ ID NO:43中所描繪之CDR-H3、如SEQ ID NO:44中所描繪之CDR-L1、如SEQ ID NO:45中所描繪之CDR-L2及如SEQ ID NO:46中所描繪之CDR-L3；

c)如SEQ ID NO:51中所描繪之CDR-H1、如SEQ ID NO:52中所描繪之CDR-H2、如SEQ ID NO:53中所描繪之CDR-H3、如SEQ ID NO:54中所描繪之CDR-L1、如SEQ ID NO:55中所描繪之CDR-L2及如SEQ ID NO:56中所描繪之CDR-L3；

d)如SEQ ID NO:61中所描繪之CDR-H1、如SEQ ID NO:62中所描

繪之CDR-H2、如SEQ ID NO:63中所描繪之CDR-H3、如SEQ ID NO:64中所描繪之CDR-L1、如SEQ ID NO:65中所描繪之CDR-L2及如SEQ ID NO:66中所描繪之CDR-L3；

e)如SEQ ID NO:71中所描繪之CDR-H1、如SEQ ID NO:72中所描繪之CDR-H2、如SEQ ID NO:73中所描繪之CDR-H3、如SEQ ID NO:74中所描繪之CDR-L1、如SEQ ID NO:75中所描繪之CDR-L2及如SEQ ID NO:76中所描繪之CDR-L3；

f)如SEQ ID NO:81中所描繪之CDR-H1、如SEQ ID NO:82中所描繪之CDR-H2、如SEQ ID NO:83中所描繪之CDR-H3、如SEQ ID NO:84中所描繪之CDR-L1、如SEQ ID NO:85中所描繪之CDR-L2及如SEQ ID NO:86中所描繪之CDR-L3；

g)如SEQ ID NO:91中所描繪之CDR-H1、如SEQ ID NO:92中所描繪之CDR-H2、如SEQ ID NO:93中所描繪之CDR-H3、如SEQ ID NO:94中所描繪之CDR-L1、如SEQ ID NO:95中所描繪之CDR-L2及如SEQ ID NO:96中所描繪之CDR-L3；

h)如SEQ ID NO:101中所描繪之CDR-H1、如SEQ ID NO:102中所描繪之CDR-H2、如SEQ ID NO:103中所描繪之CDR-H3、如SEQ ID NO:104中所描繪之CDR-L1、如SEQ ID NO:105中所描繪之CDR-L2及如SEQ ID NO:106中所描繪之CDR-L3；及

i)如SEQ ID NO:111中所描繪之CDR-H1、如SEQ ID NO:112中所描繪之CDR-H2、如SEQ ID NO:113中所描繪之CDR-H3、如SEQ ID NO:114中所描繪之CDR-L1、如SEQ ID NO:115中所描繪之CDR-L2及如SEQ ID NO:116中所描繪之CDR-L3。

術語「可變」係指抗體或免疫球蛋白域之部分在其序列中展現可變性且參與決定特定抗體之特異性及結合親和力(亦即為「可變域」)。可變重鏈(VH)與可變輕鏈(VL)一起配對形成單一抗原結合位

點。

可變性並不均勻地分佈於抗體之整個可變域中；其集中於各重鏈及輕鏈可變區之子域中。此等子域稱為「高變區」或「互補決定區」(CDR)。可變域之更保守性(亦即非高變)部分稱為「構架」區(FRM或FR)，且在三維空間中為六個CDR提供骨架以形成抗原結合表面。天然存在之重鏈及輕鏈的可變域各包含四個FRM區(FR1、FR2、FR3及FR4)，其主要採用β片構型，藉由三個高變區連接，從而形成連接β片結構且在一些情形下形成β片結構之一部分的環。各鏈中之高變區藉由FRM與另一鏈之高變區緊密結合在一起，促成抗原結合位點之形成(參見Kabat等人，上述引文)。

術語「CDR」及其複數「CDRs」係指互補決定區，其中三者組成輕鏈可變區之結合特徵(CDR-L1、CDR-L2及CDR-L3)，且三者組成重鏈可變區之結合特徵(CDR-H1、CDR-H2及CDR-H3)。CDR含有負責抗體與抗原之特異性相互作用之殘基中的大多數，因此促成抗體分子之功能活性：其為抗原特異性之主要決定因素。

使精確界定的CDR界限及長度經歷不同分類及編號系統。CDR可因此藉由Kabat、Chothia、觸點或任何其他邊界定義(包括本文所述之編號系統)提及。儘管邊界不同，但此等系統中之每一者在構成可變序列內所謂「高變區」之要素方面具有一些程度之重疊。因此，根據此等系統之CDR定義的長度及相對於相鄰構架區之界限區域可不同。參見例如Kabat (基於種間交叉序列可變性之方法)、Chothia (基於抗原-抗體複合物之結晶學研究的方法)及/或MacCallum (Kabat等人，上述引文；Chothia等人, J. MoI. Biol, 1987, 196: 901-917；及MacCallum等人, J. MoI. Biol, 1996, 262: 732)。另一用於表徵抗原結合位點之標準為由Oxford Molecular's AbM抗體模型化軟體使用之AbM定義。參見例如Protein Sequence and Structure Analysis of Antibody Variable

Domains. 在Antibody Engineering Lab Manual (編: Duebel, S.及Kontermann, R., Springer-Verlag, Heidelberg)中。在兩種殘基鑑別技術定義重疊區域但非相同區域之程度上，其可組合以定義混合CDR。然而，根據所謂Kabat系統編號為較佳。

通常，CDR形成可分類為標準結構的環結構。術語「標準結構」係指由抗原結合(CDR)環採用之主鏈構形。由比較結構研究發現六個抗原結合環中有五個僅具有有限譜系之可用構形。各標準結構之特徵可為多肽主鏈之扭轉角。因此，抗體之間的對應環可具有極類似三維結構，儘管在環之大部分中具有高胺基酸序列可變性(Chothia及Lesk, J. MoI. Biol., 1987, 196: 901；Chothia等人, Nature, 1989, 342: 877；Martin及Thornton, J. MoI. Biol, 1996, 263: 800)。此外，在所採用之環形結構與其周圍之胺基酸序列之間存在關係。特定標準類別之構形由環之長度及位於環內以及保守構架內(亦即環外)關鍵位置處之胺基酸殘基決定。可因此基於此等關鍵胺基酸殘基之存在進行分配至特定標準類別。

術語「標準結構」亦可包括關於例如Kabat (Kabat等人，上述引文)所編錄之抗體之線性序列的考慮因素。Kabat編號方案(系統)為廣泛採用之以一致方式對抗體可變域之胺基酸殘基編號的標準且亦如本文他處所提及為本發明中所用之較佳方案。其他結構考慮因素亦可用於確定抗體之標準結構。舉例而言，Kabat編號不能完全反映之差異可由Chothia等人之編號系統描述及/或由其他技術(例如結晶學及二維或三維電腦模型化)揭示。因此，既定抗體序列可歸於標準類別，其尤其允許鑑別適當框架序列(例如基於在庫中包括多種標準結構的需要)。如由Chothia等人，上述引文所描述的抗體胺基酸序列之Kabat編號及結構考慮因素及其對於構築抗體結構之典型態樣的推論描述於該文獻中。不同類別之免疫球蛋白的子單元結構及三維構型為此項技術

中所熟知的。抗體結構之綜述參見Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Harlow等人編, 1988。

輕鏈之CDR3及尤其重鏈之CDR3可構成輕鏈及重鏈可變區內抗原結合的最重要決定子。在一些抗體構築體中，重鏈CDR3似乎構成抗原與抗體之間的主要接觸區域。可使用僅CDR3變化之活體外選擇流程來改變抗體之結合特性或確定促成抗原結合之殘基。因此，CDR3通常為抗體結合位點內分子多樣性之最大來源。舉例而言，H3可短至兩個胺基酸殘基或大於26個胺基酸。

在經典全長抗體或免疫球蛋白中，各輕(L)鏈藉由一個共價二硫鍵連接至重(H)鏈，而兩個H鏈視H鏈同型而定藉由一或多個二硫鍵彼此連接。最接近於VH之CH域通常稱為CH1。恆定域(「C」)不直接參與抗原結合，但展現各種效應功能，諸如抗體依賴性細胞介導之細胞毒性及補體活化。抗體之Fc區包含在重鏈恆定域內且例如能夠與細胞表面位Fc受體相互作用。

組裝及體細胞突變後之抗體基因之序列高度變化，且此等變化之基因估計編碼10^{10}個不同抗體分子(Immunoglobulin Genes, 第2版, Jonio等人編, Academic Press, San Diego, CA, 1995)。因此，免疫系統提供免疫球蛋白之譜系。術語「譜系」係指至少一個完全或部分來源於至少一個編碼至少一種免疫球蛋白之序列的核苷酸序列。該(該等)序列可藉由重鏈之V、D及J區段及輕鏈之V及J區段之活體內重排產生。或者，該(該等)序列可回應於重排發生之因素(例如活體外刺激)自細胞產生。或者，部分或所有序列可藉由DNA拼接、核苷酸合成、突變誘發及其他方法獲得，參見例如美國專利5,565,332。譜系可僅包括一個序列或可包括複數個序列，包括遺傳性多樣之集合中的序列。

本發明之較佳抗體構築體亦可定義為雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一(較佳人類)結合域及結

合於T細胞表面上之人類CD3的第二結合域，其中該第一結合域與選自由DLL3-4、DLL3-5、DLL3-6、DLL3-7、DLL3-8、DLL3-9及DLL3-10組成之群的抗體結合於DLL3之相同抗原決定基，亦即包含有包含選自由以下組成之群的CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區的抗體：

a)如SEQ ID NO:31中所描繪之CDR-H1、如SEQ ID NO:32中所描繪之CDR-H2、如SEQ ID NO:33中所描繪之CDR-H3、如SEQ ID NO:34中所描繪之CDR-L1、如SEQ ID NO:35中所描繪之CDR-L2及如SEQ ID NO:36中所描繪之CDR-L3；

b)如SEQ ID NO:41中所描繪之CDR-H1、如SEQ ID NO:42中所描繪之CDR-H2、如SEQ ID NO:43中所描繪之CDR-H3、如SEQ ID NO:44中所描繪之CDR-L1、如SEQ ID NO:45中所描繪之CDR-L2及如SEQ ID NO:46中所描繪之CDR-L3；

c)如SEQ ID NO:51中所描繪之CDR-H1、如SEQ ID NO:52中所描繪之CDR-H2、如SEQ ID NO:53中所描繪之CDR-H3、如SEQ ID NO:54中所描繪之CDR-L1、如SEQ ID NO:55中所描繪之CDR-L2及如SEQ ID NO:56中所描繪之CDR-L3；

d)如SEQ ID NO:61中所描繪之CDR-H1、如SEQ ID NO:62中所描繪之CDR-H2、如SEQ ID NO:63中所描繪之CDR-H3、如SEQ ID NO:64中所描繪之CDR-L1、如SEQ ID NO:65中所描繪之CDR-L2及如SEQ ID NO:66中所描繪之CDR-L3；

e)如SEQ ID NO:71中所描繪之CDR-H1、如SEQ ID NO:72中所描繪之CDR-H2、如SEQ ID NO:73中所描繪之CDR-H3、如SEQ ID NO:74中所描繪之CDR-L1、如SEQ ID NO:75中所描繪之CDR-L2及如SEQ ID NO:76中所描繪之CDR-L3；

f)如SEQ ID NO:81中所描繪之CDR-H1、如SEQ ID NO:82中所描

繪之CDR-H2、如SEQ ID NO:83中所描繪之CDR-H3、如SEQ ID NO:84中所描繪之CDR-L1、如SEQ ID NO:85中所描繪之CDR-L2及如SEQ ID NO:86中所描繪之CDR-L3；及

g)如SEQ ID NO:91中所描繪之CDR-H1、如SEQ ID NO:92中所描繪之CDR-H2、如SEQ ID NO:93中所描繪之CDR-H3、如SEQ ID NO:94中所描繪之CDR-L1、如SEQ ID NO:95中所描繪之CDR-L2及如SEQ ID NO:96中所描繪之CDR-L3。

抗體構築體是否與另一種既定抗體構築體結合於相同之DLL3抗原決定基可例如藉由用嵌合或截短目標分子進行抗原決定基定位來量測，例如如上文及實例2中所描述。

本發明之較佳抗體構築體亦可定義為雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一(較佳人類)結合域及結合於T細胞表面上之人類CD3的第二結合域，其中該第一結合域與選自由DLL3-4、DLL3-5、DLL3-6、DLL3-7、DLL3-8、DLL3-9及DLL3-10組成之群的抗體競爭結合，亦即包含有包含選自由上述組成之群的CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區的抗體。

抗體構築體是否與另一種既定抗體構築體競爭結合可在競爭分析，諸如競爭性ELISA或基於細胞之競爭分析中量測。亦可使用抗生素蛋白偶合微米粒子(珠粒)。與塗覆抗生素蛋白之ELISA盤類似，當與經生物素標記之蛋白反應時，各此等珠粒可用作可進行分析之受質。抗原塗覆於珠粒上且接著用第一抗體預塗。添加第二抗體且測定任何額外結合。經由流式細胞測量術進行讀出。

在本發明之一個實施例中，本發明之抗體構築體之第一結合域包含VH區，其選自由以下各者中描繪之VH區組成之群：SEQ ID NO:37、SEQ ID NO:47、SEQ ID NO:57、SEQ ID NO:67、SEQ ID

NO:77、SEQ ID NO:87、SEQ ID NO:97、SEQ ID NO:107、SEQ ID NO:117、SEQ ID NO:435及SEQ ID NO:529。

在另一實施例中，本發明之抗體構築體之第一結合域包含VL區，其選自由以下各者中描繪之VL區組成之群：SEQ ID NO:38、SEQ ID NO:48、SEQ ID NO:58、SEQ ID NO:68、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:98、SEQ ID NO:108、SEQ ID NO:118、SEQ ID NO:436及SEQ ID NO:530。

在另一實施例中，本發明之抗體構築體之第一結合域包含VH區及VL區，其選自由以下各者中所描繪之VH區及VL區之配對組成之群：SEQ ID NO:37+38、SEQ ID NO:47+48；SEQ ID NO:57+58；SEQ ID NO:67+68；SEQ ID NO:77+78 SEQ ID NO:87+88；SEQ ID NO:97+98；SEQ ID NO:107+108；SEQ ID NO:117+118；SEQ ID NO:435+436；及SEQ ID NO:529+530。

在另一實施例中，本發明之抗體構築體之第一結合域包含選自由以下各者中描繪之多肽組成之群的多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:437及SEQ ID NO:531。

以上第一結合域(其由其CDR、VH區及VL區及其組合指定)表徵為結合於如SEQ ID NO:258中所描繪之區域內所包含之DLL3抗原決定基的結合域。

如本文所用之術語「雙特異性」係指「至少雙特異性」之抗體構築體，亦即其至少包含第一結合域及第二結合域，其中該第一結合域結合於一種抗原或目標(此處：DLL3)，且該第二結合域結合於另一種抗原或目標(此處：CD3)。因此，本發明之抗體構築體包含針對至少兩種不同抗原或目標之特異性。本發明之術語「雙特異性抗體構築

體」亦涵蓋多特異性抗體構築體，諸如三特異性抗體構築體，後者包括三個結合域，或具有超過三個(例如四個、五個.....)特異性之構築體。

鑒於本發明之抗體構築體為(至少)雙特異性的，其不會天然存在且其顯著不同於天然存在之產物。因此，「雙特異性」抗體構築體或免疫球蛋白為具有至少兩個具有不同特異性之不同結合位點的人工雜交抗體或免疫球蛋白。雙特異性抗體構築體可藉由包括融合瘤融合或Fab'片段連接的多種方法產生。參見例如Songsivilai及Lachmann, Clin. Exp. Immunol. 79:315-321 (1990)。

本發明抗體構築體之至少兩個結合域及可變域可包含或可不包含肽連接子(間隔肽)。根據本發明，術語「肽連接子」包含使本發明之抗體構築體之一個(可變及/或結合)域及另一(可變及/或結合)域之胺基酸序列彼此連結之胺基酸序列。此類肽連接子之基本技術特徵在於其不包括任何聚合活性。適合的肽連接子描述於美國專利第4,751,180號及第4,935,233號或WO 88/09344中。亦可使用肽連接子以使其他域或模組或區(諸如半衰期延伸域)連接至本發明之抗體構築體。

在使用連接子之情況下，此連接子較佳具有一定長度及序列以足以確保第一及第二結構域中之每一者可彼此獨立地保留其不同結合特異性。對於連接本發明之抗體構築體中至少兩個結合域(或兩個可變域)之肽連接子，較佳為僅包含少數胺基酸殘基(例如12個胺基酸殘基或更少)之肽連接子。因此，12、11、10、9、8、7、6或5個胺基酸殘基之肽連接子為較佳的。設想之具有少於5個胺基酸之肽連接子包含4、3、2或一個胺基酸，其中富含Gly之連接子為較佳的。該「肽連接子」之情形下的尤其較佳「單一」胺基酸為Gly。因此，該肽連接子可由單一胺基酸Gly組成。肽連接子之另一個較佳實施例由胺基酸序列Gly-Gly-Gly-Gly-Ser，亦即Gly_4Ser (SEQ ID NO:286)，或其聚合

物，亦即$(Gly_4Ser)x$表徵，其中x為1或更大的整數(例如2或3)。較佳連接子描繪於SEQ ID NO:285-293中。該肽連接子之特徵(其包含不存在促二級結構)為此項技術中已知的，且例如描述於Dall'Acqua等人(Biochem. (1998) 37, 9266-9273)；Cheadle等人 (Mol Immunol (1992) 29, 21-30)及Raag及Whitlow (FASEB (1995) 9(1), 73-80)中。此外不促進任何二級結構之肽連接子為較佳的。該等結構域彼此之連接可由例如遺傳工程改造提供，如實例中所述。用於製備融合及可操作地連接雙特異性單鏈構築體及在哺乳動物細胞或細菌中表現其之方法為此項技術中熟知的(例如WO 99/54440或Sambrook等人，Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 2001)。

如本文上文所描述，本發明提供一個較佳實施例，其中該抗體構築體呈選自由以下組成之群的型式：$(scFv)_2$、scFv-單結構域mAb、雙功能抗體及前述型式中之任一者的寡聚物。術語「呈.....型式」不排除如本文所描述，構築體可藉由例如連接或融合至其他部分而進一步經修飾。

根據一個尤其較佳實施例且如隨附實例中所記錄，本發明之抗體構築體為「雙特異性單鏈抗體構築體」，更佳雙特異性「單鏈Fv」(scFv)。儘管Fv片段之兩個結構域(VL及VH)由單獨的基因編碼，但其可使用重組方法藉由合成連接子接合，如上文所描述，該等合成連接子使其能夠製成單一蛋白質鏈，其中VL及VH區配對以形成單價分子；參見例如Huston等人 (1988) Proc. Natl. Acad. Sci USA 85:5879-5883。此等抗體片段使用熟習此項技術者已知的習知技術獲得，且以與完整或全長抗體相同之方式評估片段之功能。單鏈可變片段(scFv)因此為通常用約十至約25個胺基酸、較佳約15至20個胺基酸之短連接子肽連接的免疫球蛋白之重鏈(VH)及輕鏈(VL)可變區的融合蛋白。連

接子通常富含甘胺酸以具有可撓性，以及絲胺酸或蘇胺酸以具有可溶性，且可連接VH之N端與VL之C端，或反之亦然。此蛋白保留原始免疫球蛋白之特異性，但去除恆定區且引入連接子。

雙特異性單鏈分子為此項技術中已知且描述於WO 99/54440, Mack, J. Immunol. (1997), 158, 3965-3970, Mack, PNAS, (1995), 92, 7021-7025, Kufer, Cancer Immunol. Immunother., (1997), 45, 193-197, Löffler, Blood, (2000), 95, 6, 2098-2103, Brühl, Immunol., (2001), 166, 2420-2426, Kipriyanov, J. Mol. Biol., (1999), 293, 41-56中。關於單鏈抗體產生所述之技術(尤其參見美國專利4,946,778；Kontermann及Dübel (2010), 上述引文及Little (2009), 上述引文)可適合於產生特異性識別所選目標之單鏈抗體構築體。

具有型式$(scFv)_2$之二價(亦稱為二價(divalent))或雙特異性單鏈可變片段(bi-scFvs或di-scFvs)可藉由連接兩個scFv分子(例如由如上文所描之連接子)工程改造。若此兩個scFv分子具有相同結合特異性，則所得$(scFv)_2$分子較佳稱為二價(亦即對於相同目標抗原決定基其具有兩個價數)。若兩個scFv分子具有不同結合特異性，則所得$(scFv)_2$分子較佳稱為雙特異性的。連接可藉由產生具有兩個VH區及兩個VL區之單一肽鏈進行，得到串聯scFv (參見例如Kufer P.等人, (2004) Trends in Biotechnology 22(5):238-244)。另一可能性為產生具有連接肽之scFv分子，該等連接肽對於兩個可變區摺疊在一起過短(例如約五個胺基酸)，從而迫使scFv二聚。此類型稱為雙功能抗體(參見例如Hollinger, Philipp等人, (1993年7月) Proceedings of the National Academy of Sciences of the United States of America 90 (14): 6444-8.)。

根據本發明之抗體構築體之另一較佳實施例，結合域(結合於目標抗原DLL3或CD3)之重鏈(VH)及輕鏈(VL)不經由如上文所描述之肽

連接子直接連接，但如關於雙功能抗體所描述形成結合域。因此，CD3結合域之VH可經由肽連接子融合於DLL3結合域之VL，且DLL3結合域之VH經由此類肽連接子與CD3結合域之VL融合。

單域抗體僅包含一個(單體)抗體可變域，其能夠獨立於其他V區或結構域選擇性結合於特異性抗原。第一單域抗體自駱駝中發現之重鏈抗體工程改造，且其稱為V_HH片段。軟骨魚亦具有重鏈抗體(IgNAR)，可自該等重鏈抗體獲得稱為V_{NAR}片段之單域抗體。替代性方法為將來自常見免疫球蛋白(例如來自人類或嚙齒動物)之二聚可變域分裂為單體，從而獲得單域Ab形式之VH或VL。儘管目前對獲得單域抗體之大多數研究基於重鏈可變域，但來源於輕鏈之奈米抗體亦展示特異性結合於目標抗原決定基。單結構域抗體之實例稱為sdAb、奈米抗體或單一可變域抗體。

因此，(單域mAb)$_2$為由(至少)兩個單域單株抗體構成之單株抗體構築體，該等單域單株抗體個別地選自包含VH、VL、V_HH及V_{NAR}之群。連接子較佳為肽連接子形式。類似地，「scFv單結構域mAb」為由至少一個上述單結構域抗體及一個上述scFv分子組成之單株抗體構築體。又，連接子較佳為肽連接子形式。

此外設想，本發明提供一種雙特異性抗體構築體，其包含結合於目標細胞表面之人類DLL3的第一結合域及結合於T細胞表面之人類CD3的第二結合域，其中第一結合域結合於包含在如SEQ ID NO:259中所描繪之區域內之DLL3之抗原決定基。

因此，在本發明之另一態樣中，雙特異性抗體構築體之第一結合域包含有選自由以下組成之群的包含CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區：

a)如SEQ ID NO:121中所描繪之CDR-H1、如SEQ ID NO:122中所描繪之CDR-H2、如SEQ ID NO:123中所描繪之CDR-H3、如SEQ ID

NO:124中所描繪之CDR-L1、如SEQ ID NO:125中所描繪之CDR-L2及如SEQ ID NO:126中所描繪之CDR-L3；

b)如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:134中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

c)如SEQ ID NO:141中所描繪之CDR-H1、如SEQ ID NO:142中所描繪之CDR-H2、如SEQ ID NO:143中所描繪之CDR-H3、如SEQ ID NO:144中所描繪之CDR-L1、如SEQ ID NO:145中所描繪之CDR-L2及如SEQ ID NO:146中所描繪之CDR-L3；

d)如SEQ ID NO:151中所描繪之CDR-H1、如SEQ ID NO:152中所描繪之CDR-H2、如SEQ ID NO:153中所描繪之CDR-H3、如SEQ ID NO:154中所描繪之CDR-L1、如SEQ ID NO:155中所描繪之CDR-L2及如SEQ ID NO:156中所描繪之CDR-L3；及

e)如SEQ ID NO:161中所描繪之CDR-H1、如SEQ ID NO:162中所描繪之CDR-H2、如SEQ ID NO:163中所描繪之CDR-H3、如SEQ ID NO:164中所描繪之CDR-L1、如SEQ ID NO:165中所描繪之CDR-L2及如SEQ ID NO:166中所描繪之CDR-L3；

f)如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:439中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:134中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

g)如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:440中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:134中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

h)如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:441中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

i) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:442中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

j) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:443中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

k)如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:444中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

l) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:439中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:441中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；及

m) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:440中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:442中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3。

在一個實施例中，本發明之抗體構築體之第一結合域包含選自由以下各者中描繪之VH區組成之群的VH區：SEQ ID NO:127、SEQ

ID NO:137、SEQ ID NO:147、SEQ ID NO:157、SEQ ID NO:167、SEQ ID NO:445、SEQ ID NO:446、SEQ ID NO:447、SEQ ID NO:448、SEQ ID NO:449、SEQ ID NO:450、SEQ ID NO:451、SEQ ID NO:452、SEQ ID NO:453、SEQ ID NO:454及SEQ ID NO:455。

在另一實施例中，本發明之抗體構築體之第一結合域包含選自由以下各者中描繪之VL區組成之群的VL區：SEQ ID NO:128、SEQ ID NO:138、SEQ ID NO:148、SEQ ID NO:158、SEQ ID NO:168、SEQ ID NO:456、SEQ ID NO:457、SEQ ID NO:458、SEQ ID NO:459、SEQ ID NO:460、SEQ ID NO:461、SEQ ID NO:462、SEQ ID NO:463、SEQ ID NO:464、SEQ ID NO:465、SEQ ID NO:466、SEQ ID NO:467、SEQ ID NO:468、SEQ ID NO:469及SEQ ID NO:470。

在另一實施例中，本發明之抗體構築體之第一結合域包含VH區及VL區，其選自由如以下各者中所描繪之VH區及VL區之配對組成之群：SEQ ID NO:127+128；SEQ ID NO:137+138；SEQ ID NO:147+148；SEQ ID NO:157+158；SEQ ID NO:167+168；SEQ ID NO;137+456；SEQ ID NO;137+457；SEQ ID NO:137+458；SEQ ID NO:137+459；SEQ ID NO:137+460；SEQ ID NO:445+138；SEQ ID NO:446+138；SEQ ID NO:447+138；SEQ ID NO:445+460；SEQ ID NO:448+461；SEQ ID NO:449+462；SEQ ID NO:450+463；SEQ ID NO:450+464；SEQ ID NO:450+465；SEQ ID NO:450+466；SEQ ID NO:450+467；SEQ ID NO:450+468；SEQ ID NO:451+463；SEQ ID NO:452+463；SEQ ID NO:453+463；SEQ ID NO:451+468；SEQ ID NO:454+469；及SEQ ID NO:455+470。

在另一實施例中，本發明之抗體構築體之第一結合域包含選自由以下各者中描繪之多肽組成之群的多肽：SEQ ID NO:129、SEQ ID

NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492及SEQ ID NO:493。

以上第一結合域(其由其CDR、VH區及VL區及其組合指定)表徵為結合於如SEQ ID NO:259中所描繪之區域內所包含之DLL3抗原決定基的結合域。

本發明之另一較佳抗體構築體亦可定義為雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一(較佳人類)結合域及結合於T細胞表面上之人類CD3的第二結合域，其中該第一結合域結合於與選自由DLL3-13、DLL3-14及DLL3-15組成之群的抗體相同之DLL3之抗原決定基，亦即包含有選自由以下組成之群的包含CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區的抗體：

a)如SEQ ID NO:121中所描繪之CDR-H1、如SEQ ID NO:122中所描繪之CDR-H2、如SEQ ID NO:123中所描繪之CDR-H3、如SEQ ID NO:124中所描繪之CDR-L1、如SEQ ID NO:125中所描繪之CDR-L2及如SEQ ID NO:126中所描繪之CDR-L3；

b)如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:134中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；及

c)如SEQ ID NO:141中所描繪之CDR-H1、如SEQ ID NO:142中所描繪之CDR-H2、如SEQ ID NO:143中所描繪之CDR-H3、如SEQ ID NO:144中所描繪之CDR-L1、如SEQ ID NO:145中所描繪之CDR-L2及如SEQ ID NO:146中所描繪之CDR-L3。

本發明之較佳抗體構築體亦可定義為雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一(較佳人類)結合域及結合於T細胞表面上之人類CD3的第二結合域，其中該第一結合域與選自由DLL3-13、DLL3-14及DLL3-15組成之群的抗體競爭結合，亦即包含有選自由上述組成之群的包含CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區的抗體。

亦設想本發明之抗體構築體除其結合於目標分子DLL3及CD3之功能外亦具有另一功能。在此型式中，抗體構築體為藉由經由結合於DLL3靶向目標細胞、經由CD3結合調節細胞毒性T細胞活性及經由募集如NK細胞之效應細胞提供諸如調節抗體依賴性細胞毒性之完全功能性Fc恆定域的三功能或多功能抗體構築體；標記(螢光等)；諸如毒素或放射性核種之治療劑及/或增強血清半衰期的方式等。

延長本發明抗體構築體之血清半衰期之方式的實例包括融合或以其他方式連接至抗體構築體之蛋白的肽、蛋白或結構域。肽、蛋白質或蛋白質結構域之群包括結合於人體中具有較佳藥物動力學概況之其他蛋白質(諸如血清白蛋白)的肽(參見WO 2009/127691)。此類半衰期延長之肽的替代性概念包括結合於新生兒Fc受體(FcRn，參見WO 2007/098420)之肽，其亦可用於本發明之構築體中。連接蛋白質之較大結構域或完整蛋白質的概念包括例如融合人類血清白蛋白、人類血清白蛋白之變異體或突變體(參見WO 2011/051489、WO 2012/059486、WO 2012/150319、WO 2013/135896、WO 2014/072481、WO 2013/075066)或其結構域以及融合免疫球蛋白(Fc

結構域)及其變異體之恆定區。Fc結構域之此類變異體可經最佳化/修飾以允許二聚體或多聚體的所需配對，消除Fc受體結合(例如Fcγ受體)或用於其他原因。此項技術中已知的延長小型蛋白質化合物在人體中之半衰期的另一個概念為諸如本發明之抗體構築體的化合物的聚乙二醇化。

在一個較佳實施例中，本發明之雙特異性抗體構築體可與融合搭配物(諸如蛋白質或多肽或肽)連接(例如經由肽鍵)，例如用於延長構築體之血清半衰期的目的。此等融合搭配物可選自人類血清白蛋白(「HSA」或「HALB」)以及其序列變異體、結合於HSA之肽、結合於FcRn之肽(「FcRn BP」)或包含(抗體源性)Fc區之構築體。此等融合搭配物之例示性序列描繪於SEQ ID NO:295-341中。通常，融合搭配物可直接(例如經由肽鍵)或經由諸如$(GGGGS)_n$(其中「n」為2或更大的整數，例如2或3或4)之肽連接子連接至本發明之雙特異性抗體構築體之N端或C端。適合之肽連接子描繪於SEQ ID NO:285-293中。

因此，根據本發明之較佳抗體構築體包含：

(a) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ

ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及SEQ ID NO:531；

• 具有選自由SEQ ID NO:285-293組成之群之胺基酸序列的肽連接子；及

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；及

• 視情況存在之His標籤，諸如SEQ ID NO:294中所描繪者；

(b) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及SEQ ID NO:531；

• 具有選自由SEQ ID NO:285-293組成之群之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ

ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；

• 視情況存在之具有選自由SEQ ID NO:285-293組成之群之胺基酸序列的肽連接子；

• 具有選自由SEQ ID NO:295及301-330組成之群之胺基酸序列的多肽；及

• 視情況存在之His標籤，諸如SEQ ID NO:294中所描繪者；

(c) 多肽，其以N端起始按以下次序包含：

• 具有胺基酸序列QRFVTGHFGGLX$_1$PANG (SEQ ID NO:296)之多肽，其中X$_1$為Y或H；及

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及SEQ ID NO:531；

• 具有選自由SEQ ID NO:285-293組成之群之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ

ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；

• 具有胺基酸序列QRFVTGHFGGLHPANG (SEQ ID NO:298)或QRFCTGHFGGLHPCNG (SEQ ID NO:300)之多肽；及

• 視情況存在之His標籤，諸如SEQ ID NO:294中所描繪者；

(d) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:348、SEQ ID NO:357、SEQ ID NO:366、SEQ ID NO:375、SEQ ID NO:384、SEQ ID NO:393、SEQ ID NO:402、SEQ ID NO:411、SEQ ID NO:420、SEQ ID NO:429及SEQ ID NO:432；

• 具有SEQ ID NO:292中所描繪之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:38、SEQ ID NO:48、SEQ ID NO:58、SEQ ID NO:68、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:98、SEQ ID NO:108、SEQ ID NO:118、SEQ ID NO:128、SEQ ID NO:138、SEQ ID NO:148、SEQ ID NO:158、SEQ ID NO:168、SEQ ID NO:436、SEQ ID NO:456、SEQ ID NO:457、SEQ ID NO:458、SEQ ID NO:459、SEQ ID NO:460、SEQ ID NO:461、SEQ ID NO:462、SEQ ID NO:463、SEQ ID NO:464、SEQ ID NO:465、SEQ ID NO:466、SEQ ID NO:467、SEQ ID NO:468、SEQ ID NO:469、SEQ ID NO:470及SEQ ID NO:530，接著C端處之絲胺酸殘基；

• 具有SEQ ID NO:331中所描繪之胺基酸序列的多肽；及

多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:37、SEQ ID NO:47、SEQ ID NO:57、SEQ ID NO:67、SEQ ID NO:77、SEQ ID NO:87、SEQ ID NO:97、SEQ ID NO:107、SEQ ID

NO:117、SEQ ID NO:127、SEQ ID NO:137、SEQ ID NO:147、SEQ ID NO:157、SEQ ID NO:167、SEQ ID NO:435、SEQ ID NO:445、SEQ ID NO:446、SEQ ID NO:447、SEQ ID NO:448、SEQ ID NO:449、SEQ ID NO:450、SEQ ID NO:451、SEQ ID NO:452、SEQ ID NO:453、SEQ ID NO:454及SEQ ID NO:455，及SEQ ID NO:529；

• 具有SEQ ID NO:292中所描繪之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:349、SEQ ID NO:358、SEQ ID NO:367、SEQ ID NO:376、SEQ ID NO:385、SEQ ID NO:394、SEQ ID NO:403、SEQ ID NO:412、SEQ ID NO:421、SEQ ID NO:430及SEQ ID NO:433，接著C端處之絲胺酸殘基；及

• 具有SEQ ID NO:332所描繪之胺基酸序列之多肽；

(e) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:348、SEQ ID NO:357、SEQ ID NO:366、SEQ ID NO:375、SEQ ID NO:384、SEQ ID NO:393、SEQ ID NO:402、SEQ ID NO:411、SEQ ID NO:420、SEQ ID NO:429及SEQ ID NO:432；

• 具有SEQ ID NO:292中所描繪之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:38、SEQ ID NO:48、SEQ ID NO:58、SEQ ID NO:68、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:98、SEQ ID NO:108、SEQ ID NO:118、SEQ ID NO:128、SEQ ID NO:138、SEQ ID NO:148、SEQ ID NO:158、SEQ ID NO:168、SEQ ID NO:436、SEQ ID NO:456、SEQ ID NO:457、SEQ ID NO:458、SEQ ID NO:459、SEQ ID NO:460、SEQ ID NO:461、SEQ ID NO:462、SEQ ID NO:463、SEQ ID NO:464、SEQ ID NO:465、SEQ ID NO:466、SEQ ID NO:467、

SEQ ID NO:468、SEQ ID NO:469、SEQ ID NO:470及SEQ ID NO:530；及

• 具有SEQ ID NO:333中所描繪之胺基酸序列的多肽；及

多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:37、SEQ ID NO:47、SEQ ID NO:57、SEQ ID NO:67、SEQ ID NO:77、SEQ ID NO:87、SEQ ID NO:97、SEQ ID NO:107、SEQ ID NO:117、SEQ ID NO:127、SEQ ID NO:137、SEQ ID NO:147、SEQ ID NO:157、SEQ ID NO:167、SEQ ID NO:435、SEQ ID NO:445、SEQ ID NO:446、SEQ ID NO:447、SEQ ID NO:448、SEQ ID NO:449、SEQ ID NO:450、SEQ ID NO:451、SEQ ID NO:452、SEQ ID NO:453、SEQ ID NO:454及SEQ ID NO:455，及SEQ ID NO:529；

• 具有SEQ ID NO:292中所描繪之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:349、SEQ ID NO:358、SEQ ID NO:367、SEQ ID NO:376、SEQ ID NO:385、SEQ ID NO:394、SEQ ID NO:403、SEQ ID NO:412、SEQ ID NO:421、SEQ ID NO:430及SEQ ID NO:433，接著C端處之絲胺酸殘基；及

• 具有SEQ ID NO:334中所描繪之胺基酸序列的多肽；

(f) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID

NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及SEQ ID NO:531；

• 具有選自由SEQ ID NO:285-293組成之群之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；

• 具有SEQ ID NO:335中所描繪之胺基酸序列的多肽；及

具有SEQ ID NO:336所描繪之胺基酸序列之多肽；

(g) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及

SEQ ID NO:531；及

• 具有SEQ ID NO:337中所描繪之胺基酸序列的多肽；及

多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；及

• 具有SEQ ID NO:338所描繪之胺基酸序列之多肽；

(h) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及SEQ ID NO:531；及

• 具有SEQ ID NO:339中所描繪之胺基酸序列的多肽；及

多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、

SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；及

• 具有SEQ ID NO:340所描繪之胺基酸序列之多肽；或

(i) 多肽，其以N端起始按以下次序包含：

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及SEQ ID NO:531；

• 具有選自由SEQ ID NO:285-293組成之群之胺基酸序列的肽連接子；

• 具有選自由以下組成之群的胺基酸序列之多肽：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；及

• 具有SEQ ID NO:341所描繪之胺基酸序列之多肽。

舉例而言，本發明之較佳雙特異性抗體構築體包含選自由以下各者中描繪之多肽組成之群的多肽或由其組成：SEQ ID NO:224、SEQ ID NO:225、SEQ ID NO:226、SEQ ID NO:227、SEQ ID NO:228、SEQ ID NO:229、SEQ ID NO:230、SEQ ID NO:231、SEQ

ID NO:232、SEQ ID NO:233、SEQ ID NO:234、SEQ ID NO:235、SEQ ID NO:236、SEQ ID NO:237、SEQ ID NO:242、SEQ ID NO:243、SEQ ID NO:244、SEQ ID NO:245、SEQ ID NO:246、SEQ ID NO:247、SEQ ID NO:248、SEQ ID NO:249、SEQ ID NO:250及SEQ ID NO:251。

如上文所述，本發明之若干較佳抗體構築體藉由與另一部分(諸如白蛋白或白蛋白變異體)融合而經修飾。若此等融合構築體針對其特性(諸如詳言之，其目標親和力或細胞毒活性)進行表徵，則熟習此項技術者將察覺到，可預期類似融合構築體或未經修飾之雙特異性抗體構築體具有類似(或可能甚至較佳)特性。舉例而言，若與白蛋白融合之雙特異性抗體構築體具有可觀或所需細胞毒活性或目標親和力，則可預期，對於無白蛋白之相同構築體將觀測到相同/類似或甚至更高之細胞毒活性/目標親和力。

根據另一個較佳實施例，本發明之雙特異性抗體構築體包含(除兩個結合域以外)包含兩個多肽單體之第三結構域，該等多肽單體各自包含鉸鏈、CH2及CH3結構域，其中該兩個多肽(或多肽單體)經由肽連接子彼此融合。該第三域較佳以N至C端次序包含：鉸鏈-CH2-CH3-連接子-鉸鏈-CH2-CH3。該第三結構域之較佳胺基酸序列描繪於SEQ ID NO:541-548中。該等多肽單體中之每一者較佳具有選自由SEQ ID NO:533-540組成之群或與此等序列至少90%一致的胺基酸序列。在另一較佳實施例中，本發明之雙特異性抗體構築體之第一及第二結合域經由肽連接子與第三結構域融合，該肽連接子例如選自由SEQ ID NO:285、286、288、289、290、292及293組成之群。

根據本發明，「鉸鏈」為IgG鉸鏈區。此區域可藉由類似地使用Kabat編號鑑別，參見Kabat位置223-243。根據上文，對「鉸鏈」之最小需要為與根據Kabat編號之D231至P243之IgG_1序列延伸子對應之

胺基酸殘基。術語CH2及CH3係指免疫球蛋白重鏈恆定區2及3。此等區域亦可藉由類似地使用Kabat編號鑑別，參見CH2之Kabat位置244-360及CH3之Kabat位置361-478。應理解，就其IgG_1 Fc區、IgG_2 Fc區、IgG_3 Fc區、IgG_4 Fc區、IgM Fc區、IgA Fc區、IgD Fc區及IgE Fc區而言，在免疫球蛋白之間存在一些變化(參見例如Padlan, Molecular Immunology, 31(3), 169-217 (1993))。術語Fc單體係指IgA、IgD及IgG之最後兩個重鏈恆定區，及IgE及IgM之最後三個重鏈恆定區。Fc單體亦可包括此等結構域之可撓鉸鏈N端。對於IgA及IgM，Fc單體可包括J鏈。對於IgG，Fc部分包含免疫球蛋白域CH2及CH3及前兩個結構域與CH2之間的鉸鏈。儘管免疫球蛋白之Fc部分之邊界可不同，但用於包含功能性鉸鏈、CH2及CH3域之人類IgG重鏈Fc部分之實例可定義為例如包含分別用於IgG_4之殘基(鉸鏈結構域之) D231至(CH3域C端之) P476 或D231至L476，其中編號根據Kabat。

本發明之抗體構築體因此可按N端至C端次序包含：

(a) 第一結合域；

(b) 具有選自由SEQ ID NO:286、292及293組成之群之胺基酸序列的肽連接子；

(c) 第二結合域；

(d) 具有選自由以下組成之群的胺基酸序列之肽連接子：SEQ ID NO:285、286、288、289、290、292及293；

(e) 第三結構域(包含鉸鏈、CH2及CH3域)之第一多肽單體；

(f) 具有選自由SEQ ID NO:550、551、552及553組成之群之胺基酸序列的肽連接子；及

(g) 第三結構域(包含鉸鏈、CH2及CH3域)之第二多肽單體。

本發明之抗體構築體亦較佳按N端至C端次序包含：

- 具有選自由以下組成之群的胺基酸序列之第一結合域：SEQ

ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:437、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492、SEQ ID NO:493及SEQ ID NO:531；

- 具有選自由SEQ ID NO:286、292及293組成之群之胺基酸序列的肽連接子；

- 具有選自由以下組成之群的胺基酸序列之第二結合域：SEQ ID NO:350、SEQ ID NO:359、SEQ ID NO:368、SEQ ID NO:377、SEQ ID NO:386、SEQ ID NO:395、SEQ ID NO:404、SEQ ID NO:413、SEQ ID NO:422、SEQ ID NO:431及SEQ ID NO:434；

- 具有選自由以下組成之群的胺基酸序列之肽連接子：SEQ ID NO:285、286、288、289、290、292及293；及

- 具有選自由SEQ ID NO:541-548組成之群之胺基酸序列的第三結構域。

因此，在一個較佳實施例中，本發明之抗體構築體包含選自由以下各者中描繪之多肽組成之群的多肽或由其組成：SEQ ID NO:517、SEQ ID NO:518、SEQ ID NO:519、SEQ ID NO:520、SEQ ID NO:521、SEQ ID NO:522、SEQ ID NO:523、SEQ ID NO:524、SEQ ID NO:525、SEQ ID NO:526、SEQ ID NO:527及SEQ ID

NO:528。

序列表(表18)亦提供名為DLL3-4及DLL3-14之結合子之序列變化。根據各別scFv分子內此突變之位置來鑑別插入此等序列變異體中之點突變。應理解，視參考物(其亦可為CDR區或VH/VL區)之多肽而定，鑑別此等位置之替代性方式亦為有可能的。舉例而言，名為DLL3-4-001之變異體在其scFv分子(SEQ ID NO:437)中具有G44C-G243C雙重突變。此轉譯成相應VH鏈(SEQ ID NO:435)中之G44C突變及相應VL鏈(SEQ ID NO:436)中之G101C突變。

抗體構築體之共價修飾亦包括在本發明之範疇內，且通常但未必總在轉譯後進行。舉例而言，藉由使抗體構築體之特定胺基酸殘基與能夠與所選側鏈或N端或C端殘基反應的有機衍生劑反應而將抗體構築體之數種類型之共價修飾引入分子中。

半胱胺醯基殘基最常與α-鹵代乙酸酯(及相對應的胺)(諸如氯乙酸或氯乙醯胺)反應以產生羧甲基或羧醯胺基甲基衍生物。半胱胺醯基殘基亦藉由與溴三氟丙酮、α-溴-β-(5-咪唑基)丙酸、氯乙醯基磷酸酯、N-烷基順丁烯二醯亞胺、3-硝基-2-吡啶基二硫化物、甲基2-吡啶基二硫化物、對氯汞基苯甲酸鹽、2-氯汞基-4-硝基苯酚或氯-7-硝基苯并-2-氧雜-1,3-二唑反應而衍生。

組胺醯基殘基藉由在pH 5.5-7.0下與焦碳酸二乙酯反應而衍生，此係因為此試劑對組胺醯基側鏈具有相對特異性。對溴苯甲醯甲基溴化物亦有用；反應物較佳在pH 6.0下用0.1 M二甲胂酸鈉進行。離胺醯基及胺基末端殘基與丁二酸或其他羧酸酐反應。用此等試劑進行衍生作用具有逆轉離胺醯基殘基之電荷的作用。其他適用於衍生含有α-胺基之殘基的試劑包括醯亞胺酯，諸如吡啶甲醯亞胺酸甲酯；磷酸吡哆醛；吡哆醛；氯硼氫化物；三硝基苯磺酸；O-甲基異脲；2,4-戊二酮及轉胺酶催化之與乙醛酸酯之反應。

精胺醯基殘基藉由與一種或數種習知試劑(其中有苯基乙二醛、2,3-丁二酮、1,2-環己二酮及茚滿三酮)反應而進行修飾。由於胍官能基具有高pKa，因此精胺酸殘基之衍生化需要反應在鹼性條件下進行。此外，此等試劑可與離胺酸之基團以及精胺酸ε-胺基反應。

可對酪胺醯基殘基進行特定修飾，其中尤其關注藉由與芳族重氮化合物或四硝基甲烷反應而將光譜標記引入酪胺醯基殘基中。最通常分別使用N-乙醯基咪唑及四硝基甲烷來形成O-乙醯基酪胺醯基物質及3-硝基衍生物。酪胺醯基殘基使用^{125}I或^{131}I碘化以製備用於放射免疫分析之經標記蛋白質，上文所描述之氯胺T方法為適合的。

羧基側基(天冬胺醯基或麩胺醯基)藉由與碳化二亞胺(R'-N=C=N--R')反應而選擇性地修飾，其中R及R'為視情況選用之不同烷基，諸如1-環己基-3-(2-嗎啉基-4-乙基)碳化二亞胺或1-乙基-3-(4-氮鎓-4,4-二甲基戊基)碳化二亞胺。此外，天冬胺醯基及麩胺醯基殘基藉由與銨離子反應而轉化成天冬醯胺醯基及麩醯胺醯基殘基。

用雙功能試劑衍生化適用於使本發明之抗體構築體交聯成多種方法中所用的不溶於水之支撐基質或表面。常用交聯劑包括例如1,1-雙(重氮乙醯基)-2-苯乙烷、戊二醛、N-羥基丁二醯亞胺酯(例如與4-疊氮水楊酸之酯)、同雙官能醯亞胺酯(包括二丁二醯亞胺基酯，諸如3,3'-二硫代雙(丁二醯亞胺基丙酸酯)及雙功能順丁烯二醯亞胺(諸如雙-N-順丁烯二醯亞胺-1,8-辛烷)。諸如3-[(對疊氮苯基)二硫基]丙醯亞胺甲酯之衍生劑產生能夠在光存在下形成交聯之可光活化中間物。或者，如美國專利第3,969,287號、第3,691,016號、第4,195,128號、第4,247,642號、第4,229,537號及第4,330,440號中所描述之反應性水不溶性基質(諸如溴化氰活化之碳水化合物)及反應性基板用於蛋白固定。

常使麩醯胺醯基及天冬醯胺醯基殘基脫醯胺以分別形成對應的

麩胺醯基及天冬胺醯基殘基。或者，此等殘基在適度酸性條件下脫去醯胺基。此等殘基之任一形式皆屬於本發明範疇內。

其他修飾包括脯胺酸及離胺酸之羥基化；絲胺醯基或蘇胺醯基殘基之羥基之磷酸化；離胺酸、精胺酸及組胺酸側鏈之α-胺基之甲基化(T. E. Creighton, Proteins: Structure and Molecular Properties, W. H. Freeman & Co., San Francisco, 1983, 第79-86頁)；N端胺之乙醯化；及任何C端羧基之醯胺化。

本發明範疇內包括的抗體構築體之另一類共價修飾包含改變蛋白質之糖基化模式。如此項技術中已知，糖基化模式可取決於蛋白質之序列(例如存在或不存在特定糖基化胺基酸殘基，下文論述)，或產生蛋白質之宿主細胞或生物體。下文論述特定表現系統。

多肽之糖基化通常為N-鍵聯或O-鍵聯的。N-鍵聯係指碳水化合物部分附接至天冬醯胺殘基之側鏈。三肽序列天冬醯胺酸-X-絲胺酸及天冬醯胺酸-X-蘇胺酸(其中X為除脯胺酸外之任何胺基酸)為碳水化合物部分酶促結合於天冬醯胺酸側鏈之識別序列。因此，在多肽中存在任一此等三肽序列皆可產生潛在糖基化位點。O連接之糖基化係指糖N-乙醯基半乳胺糖、半乳糖或木糖中之一者與羥胺基酸(雖然亦可使用5-羥基脯胺酸或5-羥基離胺酸但最常使用絲胺酸或蘇胺酸)連接。

向抗體構築體添加糖基化位點藉由改變胺基酸序列以使得其含有上述三肽序列中之一或多者而便利地實現(對於N連接之糖基化位點)。亦可藉由向起始序列中添加一或多個絲胺酸或蘇胺酸殘基或由其取代來進行改變(對於O連接之糖基化位點)。出於簡易性，抗體構築體之胺基酸序列較佳經由DNA水準改變，尤其藉由使編碼多肽之DNA在預先選擇之鹼基處突變以使得產生將轉譯為所需胺基酸之密碼子而改變。

增加抗體構築體上碳水化合物部分之數目的另一種手段為藉由

醣苷與蛋白質之化學或酶促偶合。此等程序為有利的，因為其不需要在具有糖基化能力之宿主細胞中產生蛋白質來進行N連接及O連接之糖基化。視所用偶聯模式而定，糖可連接至(a)精胺酸及組胺酸，(b)游離羧基，(c)游離硫氫基，諸如半胱胺酸之硫氫基，(d)游離羥基，諸如絲胺酸、蘇胺酸或羥基脯胺酸之羥基，(e)芳族殘基，諸如苯丙胺酸、酪胺酸或色胺酸之芳族殘基，或(f)麩醯胺酸之醯胺基。此等方法描述於WO 87/05330及Aplin及Wriston, 1981, CRC Crit. Rev. Biochem., 第259-306頁中。

存在於起始抗體構築體上之碳水化合物部分之移除可以化學或酶促方式實現。化學脫糖基化作用需要將蛋白質暴露於化合物三氟甲磺酸或等效化合物中。此處理使得除連接糖(N-乙醯葡萄胺糖或N-乙醯基半乳胺糖)外之大多數或所有糖裂解，而留下完整的多肽。化學脫糖基化由Hakimuddin等人, 1987, *Arch. Biochem. Biophys.* 259:52及Edge等人, 1981, *Anal. Biochem.* 118:131描述。多肽上碳水化合物部分之酶促裂解可藉由使用如由Thotakura等人, 1987, *Meth. Enzymol.* 138:350所述之各種內醣苷酶及外醣苷酶來達成。在潛在糖基化位點處之糖基化可藉由使用如由Duskin等人, 1982, J.Biol.Chem. 257:3105所描述之化合物衣黴素來阻止。衣黴素阻斷蛋白-N-醣苷鍵形成。

抗體構築體之其他修飾亦涵蓋於本文中。舉例而言，抗體構築體之另一類共價修飾包含將抗體構築體以美國專利第4,640,835號；第4,496,689號；第4,301,144號；第4,670,417號；第4,791,192號或第4,179,337號中所闡述之方式連接於各種非蛋白質聚合物，包括(但不限於)各種多元醇，諸如聚乙二醇、聚丙二醇、聚氧化烯或聚乙二醇與聚丙二醇之共聚物。此外，如此項技術中已知，可在抗體構築體內多個位置進行胺基酸取代，例如以促進聚合物(諸如PEG)之加成。

在一些實施例中，本發明抗體構築體之共價修飾包含添加一或

多個標記。標記基團可經由各種長度之間隔臂與抗體構築體偶合以降低潛在位阻。標記蛋白質之各種方法為此項技術中已知且可用於執行本發明。術語「標記」或「標記基團」係指任何可偵測標記。一般而言，標記屬於多種類別，視偵測標記之分析而定，以下實例包括(但不限於)：

a)同位素標記，其可為放射性或重同位素，諸如放射性同位素或放射性核種(例如^{3}H、^{14}C、^{15}N、^{35}S、^{89}Zr、^{90}Y、^{99}Tc、^{111}In、^{125}I、^{131}I)

b)磁性標記(例如磁性粒子)

c)氧化還原活性部分

d)光學染料(包括(但不限於)發色團、磷光體及螢光團)，諸如螢光基團(例如FITC、若丹明(rhodamine)、鑭系磷光體)、化學發光基團及可為「小分子」螢光或蛋白螢光之螢光團

e)酶類基團(例如辣根過氧化酶、β-半乳糖苷酶、螢光素酶、鹼磷酸酶)

f)經生物素標記之基團

g)由二級報導子識別之預定多肽抗原決定基(例如白胺酸拉鏈配對序列、二級抗體之結合位點、金屬結合域、抗原決定基標籤等)

「螢光標記物」意謂可經由固有螢光特性偵測之任何分子。適合螢光標籤包含但不限於螢光素、若丹明、四甲基若丹明、伊紅、赤藻紅、香豆素、甲基香豆素、芘、Malacite綠、芪、螢光黃(Lucifer Yellow)、Cascade Blue J、德克薩斯紅(Texas Red)、IAEDANS、EDANS、BODIPY FL、LC Red 640、Cy 5、Cy 5.5、LC Red 705、Oregon綠、Alexa-Fluor染料(Alexa Fluor 350、Alexa Fluor 430、Alexa Fluor 488、Alexa Fluor 546、Alexa Fluor 568、Alexa Fluor 594、Alexa Fluor 633、Alexa Fluor 660、Alexa Fluor 680)、Cascade Blue、

Cascade Yellow及R-藻紅素(PE)(Molecular Probes, Eugene, OR)、FITC、若丹明及德克薩斯紅(Pierce, Rockford, IL)、Cy5、Cy5.5、Cy7(Amersham Life Science, Pittsburgh, PA)。適合光學染料(包括螢光團)描述於Richard P. Haugland之Molecular Probes Handbook中。

適合蛋白螢光標記亦包括(但不限於)綠色螢光蛋白，包括GFP之海腎(Renilla)、海筆(Ptilosarcus)或多管水母(Aequorea)物種(Chalfie等人, 1994, Science 263:802-805)、EGFP (Clontech Laboratories, Inc., Genbank Accession Number U55762)、藍色螢光蛋白(BFP, Quantum Biotechnologies, Inc. 1801 de Maisonneuve Blvd. West, 8th Floor, Montreal, Quebec, Canada H3H 1J9；Stauber, 1998, Biotechniques 24:462-471；Heim等人, 1996, Curr. Biol. 6:178-182)、增強之黃色螢光蛋白(EYFP，Clontech Laboratories, Inc.)、螢光素酶(Ichiki等人, 1993, J. Immunol. 150:5408-5417)、β半乳糖(Nolan等人, 1988, Proc. Natl. Acad. Sci. U.S.A. 85:2603-2607)及海腎(WO92/15673、WO95/07463、WO98/14605、WO98/26277、WO99/49019、美國專利第5,292,658號；第5,418,155號；第5,683,888號；第5,741,668號；第5,777,079號；第5,804,387號；第5,874,304號；第5,876,995號；第5,925,558號)。

白胺酸拉鏈域為促進可發現該等白胺酸拉鏈域之蛋白質之寡聚的肽。白胺酸拉鏈最初在若干DNA結合蛋白中鑑別出(Landschulz等人, 1988, *Science* 240:1759)，且此後已在多種不同蛋白質中發現。已知白胺酸拉鏈包括二聚或三聚之天然存在之肽及其衍生物。適用於產生可溶性寡聚蛋白之白胺酸拉鏈域的實例描述於PCT申請案WO 94/10308中，且來源於肺表面活性蛋白D (SPD)之白胺酸拉鏈描述於Hoppe等人, 1994, *FEBS Letters* 344:191中。經修飾之白胺酸拉鏈允許與其融合之異源蛋白質穩定三聚的用途描述於Fanslow等人, 1994,

Semin. Immunol. 6:267-78中。在一種方法中，包含與白胺酸拉鏈肽融合之DLL3抗體片段或衍生物的重組融合蛋白表現於適合之宿主細胞中，且所形成之可溶性寡聚DLL3抗體片段或衍生物自培養物上清液回收。

本發明之抗體構築體亦可包含其他結構域，其例如有助於分離分子或與分子之經調適藥物動力學概況有關。有助於分離抗體構築體之域可選自肽基元或二次引入之部分，其可在分離方法(例如分離管柱)中捕捉。此類其他結構域之非限制性具體實例包含肽動機，稱為Myc標籤、HAT標籤、HA標籤、TAP標籤、GST標籤、幾丁質結合域(CBD標籤)、麥芽糖結合蛋白質(MBP標籤)、Flag標籤、Strep標籤及其變異體(例如StrepII標籤)及His標籤。由所鑑別之CDR表徵的所有本文所揭示之抗體構築體較佳包含His標籤域，其一般稱為分子之胺基酸序列中連續His殘基之重複序列，較佳五個，且更佳六個His殘基(六組胺酸)。His標籤可位於例如抗體構築體之N端或C端，其較佳位於C端。最佳為六組胺酸標籤(HHHHHH)經由肽鍵連接至本發明之抗體構築體之C端。

本發明抗體構築體之第一結合域結合於目標細胞表面上之人類DLL3。較佳人類DLL3之胺基酸序列由SEQ ID NO:252表示。應理解，在本發明之上下文中，術語「表面上」意謂結合域特異性結合於包含在DLL3細胞外域內之抗原決定基(DLL3 ECD)。因此，當本發明之第一結合域由天然表現細胞或細胞株及/或用DLL3轉型或(穩定/暫時)轉染之細胞或細胞株表現時，其較佳結合於DLL3。在一個較佳實施例中，當DLL3在諸如BIAcore或Scatchard之活體外結合分析中用作「目標」或「配位體」分子時，第一結合域亦結合於DLL3。「目標細胞」可為任何在其表面上表現DLL3之原核或真核細胞；較佳目標細胞為作為人類或動物體之一部分的細胞，諸如特異性DLL3表現癌或

腫瘤細胞。

術語「DLL3 ECD」係指DLL3之一種形式，其基本上不含DLL3之跨膜及細胞質域。熟習此項技術者應理解，針對本發明之DLL3多肽所鑑別之跨膜結構域依照此項技術中常規用於鑑別疏水性結構域類型之準則來鑑別。跨膜結構域之精確界限可變化，但最可能在本文中特定提及之結構域的任一端處變化不超過約5個胺基酸。較佳人類DLL3 ECD展示於SEQ ID NO:253中。

人類DLL3之第一結合域的親和力較佳為≤20 nM，更佳≤10 nM，甚至更佳≤5 nM，甚至更佳≤2 nM，甚至更佳≤1 nM，甚至更佳≤0.6 nM，甚至更佳≤0.5 nM，且最佳≤0.4 nM。親和力可例如在BIAcore分析中或在Scatchard分析中加以量測，如例如實例中所描述。測定親和力之其他方法亦為熟習此項技術者所熟知的。

T細胞或T淋巴球為在細胞介導之免疫性中起中心作用的一類淋巴球(其自身為一類白血球)。存在若干種T細胞亞群，各具有不同功能。T細胞可藉由細胞表面上T細胞受體(TCR)之存在而區別於其他淋巴球，諸如B細胞及NK細胞。TCR負責識別結合於主要組織相容複合體(MHC)分子之抗原且由兩個不同蛋白鏈組成。在95%的T細胞中，TCR由α及β鏈組成。當TCR與抗原肽及MHC (肽/MHC複合物)嚙合時，T淋巴球經由相關酶、輔助受體、特定接附分子及活化或釋放之轉錄因子介導的一系列生物化學事件活化。

CD3受體複合物為一種蛋白複合物且由四個鏈構成。在哺乳動物中，複合物含有CD3γ鏈、CD3δ鏈及兩個CD3ε鏈。此等鏈與T細胞受體(TCR)及所謂ζ鏈結合以形成T細胞受體CD3複合物且在T淋巴球中產生活化信號。CD3γ、CD3δ及CD3ε鏈為含有單一細胞外免疫球蛋白結構域之免疫球蛋白超家族之高度相關細胞表面蛋白。CD3分子之胞內尾部含有稱為基於免疫受體酪胺酸之活化基元或簡稱為ITAM的單一

保守基元，其對TCR之信號傳導能力為至關重要的。CD3ε分子為在人類中由位於染色體11上之*CD3E*基因編碼的多肽。CD3ε之最佳抗原決定基包含在人類CD3ε細胞外域之胺基酸殘基1-27內。

經由多特異性、至少雙特異性抗體構築體募集T細胞再導引目標細胞之溶解參與細胞溶解突觸形成及傳遞穿孔素及顆粒酶。嚙合之T細胞能夠進行連續目標細胞溶解，且不受干擾肽抗原加工及呈現或純系T細胞分化的免疫逃逸機制影響；參見例如WO 2007/042261。

由DLL3xCD3雙特異性抗體構築體介導之細胞毒性可以各種方式量測。參見實例8.1至8.7。效應細胞可為例如經刺激增濃之(人類)CD8陽性T細胞或未刺激之(人類)周邊血液單核細胞(PBMC)。若目標細胞為獼猴來源或表現獼猴DLL3或經獼猴DLL3轉染，則效應細胞亦應具有獼猴來源，諸如獼猴T細胞株，例如4119LnPx。標靶細胞應表現DLL3 (至少其胞外域)，例如人類或獼猴DLL3。目標細胞可為用DLL3 (例如人類或獼猴DLL3)穩定或暫時轉染之細胞株(諸如CHO)。或者，目標細胞可為DLL3陽性天然表現細胞株，諸如人類肺癌瘤細胞株SHP-77。通常，預期細胞表面上表現較高水準之DLL3的標靶細胞株的EC50值較低。效應子:目標細胞(E:T)比率通常為約10:1，但亦可變化。DLL3xCD3雙特異性抗體構築體之細胞毒活性可在51-鉻釋放分析(培育時間約18小時)或基於FACS之細胞毒性分析(培育時間約48小時)中量測。修改分析培育時間(細胞毒性反應)亦為可能的。量測細胞毒性之其他方法為熟習此項技術者所熟知的且包含MTT或MTS分析、基於ATP之分析(包括生物發光分析)、磺醯若丹明B (SRB)分析、WST分析、細胞群落分析及ECIS技術。

由本發明之DLL3xCD3雙特異性抗體構築體介導之細胞毒活性較佳在基於細胞之細胞毒性分析中量測。亦可在51-鉻釋放分析中進行量測。其由EC_{50}值表示，該值對應於一半最大有效濃度(誘導為基線

與最大值之間的一半的細胞毒性反應的抗體構築體之濃度)。較佳地，DLL3xCD3雙特異性抗體構築體之EC_{50}值為≤5000 pM或≤4000 pM，更佳為≤3000 pM或≤2000 pM，甚至更佳≤1000 pM或≤500 pM，甚至更佳≤400 pM或≤300 pM，甚至更佳≤200 pM，甚至更佳≤100 pM，甚至更佳≤50 pM，甚至更佳≤20 pM或≤10 pM，且最佳≤5 pM。

以上既定EC_{50}值可以不同分析量測。熟習此項技術者察覺到，預期與未刺激之PBMC相比，在經刺激/增濃之CD8+ T細胞用作效應細胞時EC_{50}值可較低。此外，可預期與低目標表現大鼠相比，當目標細胞表現大量目標抗原時EC_{50}值較低。舉例而言，當刺激性/增濃人類CD8+ T細胞用作效應細胞(且經DLL3轉染之細胞(諸如CHO細胞)或DLL3陽性人類肺癌瘤細胞株SHP-77用作目標細胞)時，DLL3 xCD3雙特異性抗體構築體之EC_{50}值較佳為≤1000 pM，更佳為≤500 PM，甚至更佳≤250 pM，甚至更佳≤100 pM，甚至更佳≤50 pM，甚至更佳≤10 pM，且最佳≤5 pM。當人類PBMC用作效應細胞時，DLL3xCD3雙特異性抗體構築體之EC_{50}值較佳為≤5000 pM或≤4000 pM (詳言之當目標細胞為DLL3陽性人類肺癌瘤細胞株SHP-77時)，更佳為≤2000 pM (詳言之當目標細胞為經DLL3轉染之細胞，諸如CHO細胞時)，更佳為≤1000 pM或≤500 pM，甚至更佳≤200 pM，甚至更佳≤150 pM，甚至更佳≤100 pM，且最佳≤50 pM或更低。當諸如LnPx4119之獼猴T細胞株用作效應細胞且諸如CHO細胞之獼猴DLL3經轉染細胞株用作目標細胞株時，DLL3xCD3雙特異性抗體構築體之EC_{50}值較佳為≤2000 pM或≤1500 pM，更佳為≤1000 pM或≤500 pM，甚至更佳≤300 pM或≤250 pM，甚至更佳≤100 pM，且最佳≤50 pM。

本發明之DLL3xCD3雙特異性抗體構築體較佳不誘導/介導DLL3陰性細胞(諸如CHO細胞)之溶解或不實質上誘導/介導DLL3陰性細胞之溶解。術語「不誘導溶解」、「不實質上誘導溶解」、「不介導溶解」

或「不實質上介導溶解」意謂本發明之抗體構築體不誘導或介導超過30%，較佳不超過20%，更佳不超過10%，尤其較佳不超過9%、8%、7%、6%或5% DLL3陰性細胞溶解，藉此DLL3陽性人類肺癌瘤細胞株SHP-77 (參見上文)之溶解設定為100%。此通常適用於高達500 nM之抗體構築體濃度。熟習此項技術者知曉如何在無需再費周折的情況下量測細胞溶解。此外，本發明教示如何量測細胞溶解之特別說明。

個別DLL3xCD3雙特異性抗體構築體之單體與二聚同功異型物之間的細胞毒活性差異稱為「效能差」。此效能差可例如計算為分子之單體與二聚形式之EC_{50}值之間的比率，參見實例15。本發明之DLL3xCD3雙特異性抗體構築體之效能差較佳為≤5，更佳≤4，甚至更佳≤3，甚至更佳≤2且最佳≤1。

本發明之抗體構築體之第一及/或第二(或任何其他)結合域較佳為對於靈長類動物之哺乳動物綱之成員具有特異性的種間交叉結合域。跨物種特異性CD3結合域例如描述於WO 2008/119567中。根據一個實施例，第一及/或第二結合域除分別結合於人類DLL3及人類CD3之外，亦將結合於靈長類動物之DLL3/CD3，該等靈長類動物包括(但不限於)新世界靈長類動物(諸如白鬢狨(*Callithrix jacchus*)、棉冠狨(*Saguinus Oedipus*)或松鼠猴(*Saimiri sciureus*))、舊世界靈長類動物(諸如狒狒及獼猴)、長臂猿、猩猩及非人類人亞科(*hominidae*)。據設想，本發明之抗體構築體之第一結合域(其結合於目標細胞表面上之人類DLL3)亦至少結合獼猴DLL3，及/或第二結合域(其結合於T細胞表面上之人類CD3)亦至少結合獼猴CD3。較佳獼猴為食蟹猴(*Macaca fascicularis*)。亦設想為恆河猴(*Macaca mulatta*；Rhesus)。

本發明之較佳雙特異性抗體構築體包含結合於標靶細胞表面上之人類DLL3的第一結合域及結合於T細胞表面上之人類CD3及至少獼猴CD3的第二結合域。在此實施例之一個態樣中，第一結合域結合於

包含在如SEQ ID NO:260中所描繪之區域內的DLL3之抗原決定基。

在本發明之一個態樣中，第一結合域結合於人類DLL3且進一步結合於獼猴DLL3 (諸如食蟹猴之DLL3)，且更佳結合於獼猴DLL3 ECD。較佳食蟹猴DLL3描繪於SEQ ID NO:271中。較佳獼猴DLL3 ECD描繪於SEQ ID NO:272中。獼猴DLL3之第一結合域的親和力較佳為≤15 nM，更佳≤10 nM，甚至更佳≤5 nM，甚至更佳≤1 nM，甚至更佳≤0.5 nM，甚至更佳≤0.1 nM，且最佳≤0.05 nM或甚至≤0.01 nM。

本發明之抗體構築體對結合獼猴DLL3對比人類DLL3的親和力差[ma DLL3:hu DLL3] (如例如藉由BiaCore或藉由Scatchard分析所測定)較佳在0.1與10之間，更佳在0.2與5之間，甚至更佳在0.3與4之間，甚至更佳在0.5與3之間或在0.5與2.5之間，且最佳在0.5與2之間或在0.6與2之間。參見實例3及4。

在本發明之抗體構築體的一個實施例中，第二結合域結合於人類CD3ε及白鬢狨、棉冠狨或松鼠猴CD3ε。第二結合域較佳結合於此等CD3ε鏈之細胞外抗原決定基。亦設想，第二結合域結合於人類及恆河猴CD3ε鏈之細胞外抗原決定基。CD3ε之最佳抗原決定基包含在人類CD3ε細胞外域之胺基酸殘基1-27內。甚至更特定言之，抗原決定基至少包含胺基酸序列Gln-Asp-Gly-Asn-Glu。白鬢狨及棉冠狨均為屬於狨猴科(*Callitrichidae*)的新世界靈長類動物，而松鼠猴為屬於卷尾猴科(*Cebidae*)的新世界靈長類動物。

對於本發明之抗體構築體，結合於T細胞表面上之人類CD3的第二結合結構域包含具有選自以下之CDR-L1、CDR-L2及CDR-L3的VL區尤其較佳：

(a) 如WO 2008/119567之SEQ ID NO: 27中所描繪的CDR-L1、如WO 2008/119567之SEQ ID NO: 28中所描繪的CDR-L2及如WO 2008/119567之SEQ ID NO: 29中所描繪的CDR-L3；

(b) 如WO 2008/119567之SEQ ID NO:117中所描繪之CDR-L1、如WO 2008/119567之SEQ ID NO:118中所描繪之CDR-L2及如WO 2008/119567之SEQ ID NO:119中所描繪之CDR-L3；及

(c) 如WO 2008/119567之SEQ ID NO:153中所描繪的CDR-L1、如WO 2008/119567之SEQ ID NO:154中所描繪的CDR-L2及如WO 2008/119567之SEQ ID NO:155中所描繪的CDR-L3。

在本發明抗體構築體之一個替代性較佳實施例中，結合於T細胞表面上之人類CD3的第二結合域包含有包含選自以下之CDR-H1、CDR-H2及CDR-H3的VH區：

(a) 如WO 2008/119567之SEQ ID NO:12中所描繪之CDR-H1、如WO 2008/119567之SEQ ID NO:13中所描繪之CDR-H2及如WO 2008/119567之SEQ ID NO:14中所描繪之CDR-H3；

(b) WO 2008/119567之SEQ ID NO:30中所描繪之CDR-H1、WO 2008/119567之SEQ ID NO:31中所描繪之CDR-H2及WO 2008/119567之SEQ ID NO:32中所描繪之CDR-H3；

(c) 如WO 2008/119567之SEQ ID NO:48中所描繪之CDR-H1、如WO 2008/119567之SEQ ID NO:49中所描繪之CDR-H2及如WO 2008/119567之SEQ ID NO:50中所描繪之CDR-H3；

(d) 如WO 2008/119567之SEQ ID NO: 66中所描繪之CDR-H1、如WO 2008/119567之SEQ ID NO: 67中所描繪之CDR-H2及如WO 2008/119567之SEQ ID NO: 68中所描繪之CDR-H3；

(e) WO 2008/119567之SEQ ID NO:84中所描繪之CDR-H1、WO 2008/119567之SEQ ID NO:85中所描繪之CDR-H2及WO 2008/119567之SEQ ID NO:86中所描繪之CDR-H3；

(f) WO 2008/119567之SEQ ID NO:102中所描繪之CDR-H1、WO 2008/119567之SEQ ID NO:103中所描繪之CDR-H2及WO

2008/119567之SEQ ID NO:104中所描繪之CDR-H3；

(g) 如WO 2008/119567之SEQ ID NO:120中所描繪的CDR-H1、如WO 2008/119567之SEQ ID NO:121中所描繪的CDR-H2及如WO 2008/119567之SEQ ID NO:122中所描繪的CDR-H3；

(h) 如WO 2008/119567之SEQ ID NO:138中所描繪的CDR-H1、如WO 2008/119567之SEQ ID NO:139中所描繪的CDR-H2及如WO 2008/119567之SEQ ID NO:140中所描繪的CDR-H3；

(i) WO 2008/119567之SEQ ID NO:156中所描繪之CDR-H1、WO 2008/119567之SEQ ID NO:157中所描繪之CDR-H2及WO 2008/119567之SEQ ID NO:158中所描繪之CDR-H3；及

(j) 如WO 2008/119567之SEQ ID NO:174中所描繪之CDR-H1、如WO 2008/119567之SEQ ID NO:175中所描繪之CDR-H2及如WO 2008/119567之SEQ ID NO:176中所描繪之CDR-H3。

對於本發明之抗體構築體更佳的是，結合於T細胞表面上之人類CD3的第二結合域包含選自由以下組成之群的VL區：如WO 2008/119567之SEQ ID NO: 35、39、125、129、161或165中所描繪的VL區。

替代性較佳的是，結合於T細胞表面上之人類CD3的第二結合域包含選自由以下組成之群的VH區：如WO 2008/119567之SEQ ID NO: 15、19、33、37、51、55、69、73、87、91、105、109、123、127、141、145、159、163、177或181中所描繪的VH區。

更佳地，本發明之抗體構築體由結合於T細胞表面上之人類CD3的第二結合域表徵，該第二結合域包含選自由以下組成之群的VL區及VH區：

(a) 如WO 2008/119567之SEQ ID NO:17或21中所描繪之VL區及如WO 2008/119567之SEQ ID NO:15或19中所描繪之VH區；

(b) 如WO 2008/119567之SEQ ID NO:35或39中所描繪之VL區及如WO 2008/119567之SEQ ID NO:33或37中所描繪之VH區；

(c) 如WO 2008/119567之SEQ ID NO:53或57中所描繪之VL區及如WO 2008/119567之SEQ ID NO:51或55中所描繪之VH區；

(d) 如WO 2008/119567之SEQ ID NO:71或75中所描繪之VL區及如WO 2008/119567之SEQ ID NO:69或73中所描繪之VH區；

(e) 如WO 2008/119567之SEQ ID NO:89或93中所描繪之VL區及如WO 2008/119567之SEQ ID NO:87或91中所描繪之VH區；

(f) 如WO 2008/119567之SEQ ID NO:107或111中所描繪之VL區及如WO 2008/119567之SEQ ID NO:105或109中所描繪之VH區；

(g) 如WO 2008/119567之SEQ ID NO:125或129中所描繪之VL區及如WO 2008/119567之SEQ ID NO:123或127中所描繪之VH區；

(h) 如WO 2008/119567之SEQ ID NO:143或147中所描繪之VL區及如WO 2008/119567之SEQ ID NO:141或145中所描繪之VH區；

(i) 如WO 2008/119567之SEQ ID NO:161或165中所描繪之VL區及如WO 2008/119567之SEQ ID NO:159或163中所描繪之VH區；及

(j) 如WO 2008/119567之SEQ ID NO:179或183中所描繪之VL區及如WO 2008/119567之SEQ ID NO:177或181中所描繪之VH區。

根據本發明之抗體構築體之一個較佳實施例，結合域且尤其第二結合域(其結合於T細胞表面上之人類CD3)具有以下型式： VH區及VL區之配對呈單鏈抗體(scFv)型式。VH及VL區按VH-VL或VL-VH次序排列。較佳地，VH區以N端定位於連接子序列且VL區以C端定位於連接子序列。

上述本發明之抗體構築體的一個較佳實施例之特徵為結合於T細胞表面上之人類CD3的第二結合結構域包含選自由以下組成之群的胺基酸序列：WO 2008/119567之SEQ ID NOs: 23、25、41、43、59、

61、77、79、95、97、113、115、131、133、149、151、167、169、185或187。

因此，在一個實施例中，本發明之抗體構築體包含選自由以下各者中描繪之多肽組成之群的多肽：SEQ ID NO:40、SEQ ID NO:50、SEQ ID NO:60、SEQ ID NO:70、SEQ ID NO:80、SEQ ID NO:90、SEQ ID NO:100、SEQ ID NO:110、SEQ ID NO:120、SEQ ID NO:211、SEQ ID NO:212、SEQ ID NO:213、SEQ ID NO:214、SEQ ID NO:215、SEQ ID NO:216、SEQ ID NO:217、SEQ ID NO:438及SEQ ID NO:532。此等抗體構築體具有第一結合域，其結合於包含於如SEQ ID NO:258中所描繪之區域內的DLL3之抗原決定基。

在一個替代性實施例中，本發明之抗體構築體包含選自由以下各者中描繪之多肽組成之群的多肽：SEQ ID NO:130、SEQ ID NO:140、SEQ ID NO:150、SEQ ID NO:160、SEQ ID NO:170、SEQ ID NO:218、SEQ ID NO:219、SEQ ID NO:220、SEQ ID NO:494、SEQ ID NO:495、SEQ ID NO:496、SEQ ID NO:497、SEQ ID NO:498、SEQ ID NO:499、SEQ ID NO:500、SEQ ID NO:501、SEQ ID NO:502、SEQ ID NO:503、SEQ ID NO:504、SEQ ID NO:505、SEQ ID NO:506、SEQ ID NO:507、SEQ ID NO:508、SEQ ID NO:509、SEQ ID NO:510、SEQ ID NO:511、SEQ ID NO:512、SEQ ID NO:513、SEQ ID NO:514、SEQ ID NO:515及SEQ ID NO:516。此等抗體構築體具有第一結合域，其結合於包含於如SEQ ID NO:259中所描繪之區域內的DLL3之抗原決定基。

亦涵蓋本文所描述之抗體構築體的胺基酸序列修飾。舉例而言，可能需要改良抗體構築體之結合親和力及/或其他生物特性。抗體構築體之胺基酸序列變異體藉由向抗體構築體核酸中引入適當核苷酸變化或藉由肽合成來製備。所有下述胺基酸序列修飾應產生仍保留

未經修飾親本分子之所需生物活性(結合於DLL3及結合於CD3)的抗體構築體。

術語「胺基酸」或「胺基酸殘基」通常係指具有技術公認定義之胺基酸，諸如選自由以下組成之群的胺基酸：丙胺酸(Ala或A)；精胺酸(Arg或R)；天冬醯胺(Asn或N)；天冬胺酸(Asp或D)；半胱胺酸(Cys或C)；麩醯胺(Gln或Q)；麩胺酸(Glu或E)；甘胺酸(Gly或G)；組胺酸(His或H)；異白胺酸(He或I)；白胺酸(Leu或L)；離胺酸(Lys或K)；甲硫胺酸(Met或M)；苯丙胺酸(Phe或F)；脯胺酸(Pro或P)；絲胺酸(Ser或S)；蘇胺酸(Thr或T)；色胺酸(Trp或W)；酪胺酸(Tyr或Y)；及纈胺酸(Val或V)，但可視需要使用經修飾、合成或罕見的胺基酸。一般而言，胺基酸可分組為具有非極性側鏈(例如Ala、Cys、He、Leu、Met、Phe、Pro、Val)；帶負電側鏈(例如Asp、Glu)；帶正電側鏈(例如Arg、His、Lys)；或不帶電極性側鏈(例如Asn、Cys、Gln、Gly、His、Met、Phe、Ser、Thr、Trp及Tyr)。

胺基酸修飾包括例如抗體構築體之胺基酸序列內的殘基缺失及/或插入及/或取代。進行缺失、插入及取代之任何組合以獲得最終構築體，其限制條件為該最終構築體具有所需特徵。胺基酸變化亦可改變抗體構築體之轉譯後過程，諸如改變糖基化位點之數目或位置。

舉例而言，CDR中之每一者中可插入或缺失1、2、3、4、5或6個胺基酸(當然，視其長度而定)，而FR中之每一者中可插入或缺失1、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20或25個胺基酸。較佳地，胺基酸序列插入物包括向含有一百個或一百個以上殘基之多肽插入的長度為1、2、3、4、5、6、7、8、9或10個殘基之胺基及/或羧基端融合物，以及具有單個或多個胺基酸殘基之內部序列插入物。本發明抗體構築體之插入變異體包括與針對酶之抗體構築體之N端或C端的融合物或與延長抗體構築體之血清半

衰期的多肽的融合物。

取代型突變誘發之最受關注位點包括重鏈及/或輕鏈之CDR，尤其高變區，但亦涵蓋重鏈及/或輕鏈中之FR變化。取代較佳為如本文所描述之保守取代。較佳地，視CDR或FR之長度而定，可取代CDR中1、2、3、4、5、6、7、8、9或10個胺基酸，而可取代構架區(FR)中之1、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20或25個胺基酸。舉例而言，若CDR序列涵蓋6個胺基酸，則可設想取代此等胺基酸中之一者、兩者或三者。類似地，若CDR序列涵蓋15個胺基酸，則可設想取代此等胺基酸中之一者、兩者、三者、四者、五者或六者。

鑑別抗體構築體中作為突變誘發之較佳位置的特定殘基或區域之適用方法稱為「丙胺酸掃描突變誘發」，其如Cunningham及Wells, Science, 244: 1081-1085 (1989)所述。在本文中，鑑別抗體構築體內之目標殘基之殘基或基團(例如帶電殘基，諸如arg、asp、his、lys及glu)且經中性或帶負電胺基酸(最佳丙胺酸或聚丙胺酸)置換以影響胺基酸與抗原決定基之相互作用。

隨後，藉由在取代位點處或為取代位點引入其他變異體以優化對取代展現功能敏感性之彼等胺基酸位置。因此，在預先確定引入胺基酸序列變化之位點或區域時，突變本身之性質無需預先確定。舉例而言，為分析或最佳化既定位點之突變的效能，可在標靶密碼子或區進行丙胺酸掃描或隨機突變誘發，且針對所需活性之最佳組合篩選所表現之抗體構築體變異體。在具有已知序列之DNA的預定位點處進行取代突變之技術為所熟知的，例如M13引子突變誘發及PCR突變誘發。使用抗原結合活性之分析(諸如DLL3或CD3結合)進行突變體之篩選。

一般而言，若取代重鏈及/或輕鏈之一或多個或全部CDR中之胺

基酸，則較佳隨後獲得之「經取代」序列與「原始」CDR序列至少60%或65%、更佳70%或75%、甚至更佳80%或85%且尤其較佳90%或95%一致。此意謂與「經取代」序列一致的程度取決於CDR的長度。舉例而言，具有5個胺基酸之CDR與其經取代之序列較佳80%一致以有至少一個胺基酸經取代。因此，抗體構築體之CDR可與其經取代之序列具有不同程度之一致性，例如CDRL1可具有80%，而CDRL3可具有90%。

較佳取代(或置換)為保守取代。然而，可設想任何取代(包括非保守取代或下表1中所列之「例示性取代」中之一或多者)，只要抗體構築體保留其經由第一結合域結合於DLL3且經由第二結合域結合於CD3或CD3ε之能力及/或其CDR與隨後經取代序列具有一致性(與「原始」CDR序列至少60%或65%、更佳70%或75%、甚至更佳80%或85%、且尤其較佳90%或95%一致)即可。

保守取代以標題「較佳取代」展示於表1中。若此類取代引起生物活性變化，則可引入表1中稱為「例示性取代」或如下文提及胺基酸類別時之進一步描述的更實質變化且針對所要特徵篩選產物。

表1：胺基酸取代

原始	例示性取代	較佳取代
Ala (A)	val、leu、ile	val
Arg (R)	lys、gln、asn	lys
Asn (N)	gln、his、asp、lys、arg	gln
Asp (D)	glu、asn	glu
Cys (C)	ser、ala	ser
Gln (Q)	asn、glu	asn
Glu (E)	asp、gln	asp
Gly (G)	Ala	ala
His (H)	asn、gln、lys、arg	arg
Ile (I)	leu、val、met、ala、phe	leu
Leu (L)	正白胺酸、ile、val、met、ala	ile
Lys (K)	arg、gln、asn	arg
Met (M)	leu、phe、ile	leu
Phe (F)	leu、val、ile、ala、tyr	tyr

Pro (P)	Ala	ala
Ser (S)	Thr	thr
Thr (T)	Ser	ser
Trp (W)	tyr、phe	tyr
Tyr (Y)	trp、phe、thr、ser	phe
Val (V)	ile、leu、met、phe、ala	leu

本發明抗體構築體之生物特性的實質改變可藉由選擇取代實現，該等取代在其對維持(a)取代區域中多肽主鏈之結構，例如片或螺旋構形，(b)目標位點處分子之電荷或疏水性或(c)側鏈之體積的作用上顯著不同。天然存在之殘基可根據常見側鏈的特性加以分組：(1)疏水性：正白胺酸、met、ala、val、leu、ile；(2)中性親水性：cys、ser、thr；(3)酸性：asp、glu；(4)鹼性：asn、gin、his、lys、arg；(5)影響鏈取向之殘基：gly、pro；及(6)芳族：trp、tyr、phe。

非保守取代係意味將此等類別中之一者之成員換成另一類別。沒有參與維持抗體構築體之恰當構形之任何半胱胺酸殘基一般可經絲胺酸取代，以提高分子之氧化穩定性及防止異常交聯。反之，可在抗體中添加半胱胺酸鍵以改良其穩定性(尤其在抗體為諸如Fv片段之抗體片段的情況下)。

對於胺基酸序列，序列一致性及/或相似性係藉由使用此項技術中已知的標準技術測定，包括(但不限於)Smith及Waterman, 1981, *Adv. Appl. Math.* 2:482之局部序列一致性算法；Needleman及Wunsch, 1970, *J. Mol. Biol.* 48:443之序列一致性比對算法；Pearson及Lipman, 1988, *Proc. Nat. Acad. Sci. U.S.A.* 85:2444之相似性探索方法；此等算法之電腦化實施(Wisconsin Genetics軟體套件, Genetics Computer Group, 575 Science Drive, Madison, Wis.中之GAP、BESTFIT、FASTA及TFASTA)；由Devereux等人, 1984, *Nucl. Acid Res.* 12:387-395所述之最佳擬合序列程序，較佳使用預設或藉由檢查。較佳地，一致性百分比藉由FastDB基於以下參數計算：錯配罰分1；空隙罰分1；空隙尺寸

罰分0.33；及接合罰分30，「Current Methods in Sequence Comparison and Analysis,」 Macromolecule Sequencing and Synthesis, Selected Methods and Applications, 第127-149頁 (1988), Alan R. Liss, Inc。

適用演算法之一個實例為PILEUP。PILEUP使用漸進式成對比對方式來產生一組相關序列之多序列比對。其亦可繪製展示用於產生比對之叢集關係的樹形圖。PILEUP使用Feng及Doolittle, 1987, *J. Mol. Evol.* 35:351-360之漸進比對方法之簡化方法；該方法類似於Higgins and Sharp, 1989, *CABIOS* 5:151-153所述。適用PILEUP參數包括預設空隙權重3.00、預設空隙長度權重0.10及加權末端空隙。

適用算法之另一個實例為BLAST算法，描述於：Altschul等人, 1990, *J. Mol. Biol.* 215:403-410；Altschul等人, 1997, *Nucleic Acids Res.* 25:3389-3402；及Karin等人, 1993, *Proc. Natl. Acad. Sci. U.S.A.* 90:5873-5787中。特別適用之BLAST程序為WU-BLAST-2程序，其自Altschul等人, 1996, *Methods in Enzymology* 266:460-480獲得。WU-BLAST-2使用數個檢索參數，其中之大多數設定成預設值。使用以下值設定可調節的參數：重疊間隔=1、重疊分數=0.125、詞閾值(T)=II。HSP S及HSP S2參數為動態值且藉由程式本身視特定序列之組成及相關序列檢索之特定資料庫之組成而確立；然而可調節該等值以提高敏感性。

另一種適用算法為由Altschul等人, 1993, *Nucl. Acids Res.* 25:3389-3402報導之空隙BLAST。空隙BLAST使用BLOSUM-62取代計分；臨限值T參數設定為9； 兩命中點法用於觸發無空隙延伸部分，電荷空隙長度k，代價為10+k；Xu設定為16，且對於資料庫檢索階段Xg設定為40，且對於算法之輸出階段設定為67。空隙比對藉由對應於約22比特之分值觸發。

通常，個別變異體CDR之間的胺基酸同源性、類似性或一致性為

本文所描繪之序列的至少60%，且更通常具有至少65%或70%之較佳增加之同源性或一致性，更佳至少75%或80%，甚至更佳至少85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%，及幾乎100%。以類似方式，相對於本文所鑑別之結合蛋白的核酸序列的「核酸序列一致性百分比(%)」定義為候選序列中與抗體構築體之編碼序列中之核苷酸殘基一致的核苷酸殘基之百分比。特定方法使用設定為預設參數之WU-BLAST-2的BLASTN模組，其中重疊間隔及重疊分數分別設定為1及0.125。

通常，編碼個別變異體CDR之核苷酸序列與本文所描繪之核苷酸序列之間的核酸序列同源性、類似性或一致性為至少60%，且更通常具有至少65%、70%、75%、80%、81%、82%、83%、84%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%或99%的較佳增加之同源性或一致性，及幾乎100%。因此，「變異型CDR」為相對於本發明之親本CDR具有特定同源性、相似性或一致性的CDR，且享有親本CDR之生物功能，包括(但不限於)至少60%、65%、70%、75%、80%、81%、82%、83%、84%、85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%或99%之特異性及/或活性。

一個實施例中，與本發明抗體構築體之人類生殖系之一致性百分比為≥ 70%或≥ 75%，更佳≥ 80%或≥ 85%，甚至更佳≥ 90%，且最佳≥ 91%、≥ 92%、≥ 93%、≥ 94%、≥ 95%或甚至≥ 96%。參見實例7。與人類抗體生殖系基因產物之一致性被認為是在治療期間降低治療蛋白引起患者針對藥物之免疫反應之風險的重要特徵。Hwang及Foote(「Immunogenicity of engineered antibodies」; Methods 36 (2005) 3-10)證明藥物抗體構築體之非人類部分的減少在治療期間導致誘導患者之抗藥物抗體的風險會降低。藉由比較大量臨床上評估之抗體藥物

及各別免疫原性資料，顯示人類化抗體之V區使蛋白質之免疫原性(平均5.1%患者)低於帶有未改變之非人類V區之抗體(平均23.59%患者)的趨勢。因此，與人類序列具有較高程度的一致性對基於V區之蛋白質療法之抗體構築體形式是有需要的。出於確定生殖系一致性之此目的，可使用Vector NTI軟體將VL之V區與人類生殖系V區段及J區段之胺基酸序列比對(http://vbase.mrc-cpe.cam.ac.uk/)，且胺基酸序列藉由將一致胺基酸殘基除以VL之胺基酸殘基之總數計算(%)。同樣可用於VH區段(http://vbase.mrc-cpe.cam.ac.uk/)，除了可能由於VH CDR3之高多樣性及缺乏現有人類生殖系VH CDR3比對搭配物而排除在外。可隨後使用重組技術提高與人類抗體生殖系基因之序列一致性。

在另一實施例中，本發明之雙特異性抗體構築體在標準研究規模條件下(例如在標準兩步純化方法中)展現出高單體產量。較佳地，本發明抗體構築體之單體產量≥0.25 mg/L上清液，更佳≥0.5 mg/L，甚至更佳≥1 mg/L，且最佳≥3 mg/L上清液。

同樣，可測定二聚抗體構築體同功異型物之產量及因此抗體構築體之單體百分比(亦即單體:(單體+二聚體))。單體及二聚抗體構築體之生產率及所計算之單體百分比可例如在來自滾瓶中之標準化研究規模製備之培養物上清液的SEC純化步驟中獲得。在一個實施例中，抗體構築體之單體百分比為≥80%，更佳≥85%，甚至更佳≥90%，且最佳≥95%。

在一個實施例中，抗體構築體較佳血漿穩定性(有血漿下之EC50與無血漿下之EC50的比率)≤5或≤4，更佳≤3.5或≤3，甚至更佳≤2.5或≤2，且最佳≤1.5或≤1。抗體構築體之血漿穩定性可藉由將構築體在37℃下在人類血漿中培育24小時，繼而在51-鉻釋放細胞毒性分析中測定EC50來測試。細胞毒性分析中之效應細胞可為經刺激增濃之人類CD8陽性T細胞。目標細胞可為例如經人類DLL3轉染之CHO細胞。效應子:目

標細胞(E:T)比率可選擇為10:1。用於此目的之人類血漿庫獲自藉由塗佈EDTA之注射器收集的健康供體之血液。藉由離心移除細胞組分，收集上部血漿相且隨後彙集。作為對照，稀釋抗體構築體，隨後立即在RPMI-1640培養基中進行細胞毒性分析。血漿穩定性以EC50(血漿培育後)與EC50(對照)之比率的形式計算。參見實例11。

此外較佳的是，本發明抗體構築體的單體向二聚體之轉化率較低。轉化率可在不同條件下量測且藉由高效尺寸排阻層析分析。參見實例9。舉例而言，培育抗體構築體之單體同功異型物可在37℃下執行7天且在培育箱中達到例如100 μg / ml或250 μg / ml之濃度。在此等條件下，本發明抗體構築體展示二聚體百分比較佳≤5%，更佳≤4%，甚至更佳≤3%，甚至更佳≤2.5%，甚至更佳≤2%，甚至更佳≤1.5%，且最佳≤1%或≤0.5%，或甚至0%。

本發明之雙特異性抗體構築體亦較佳在多個凍/融循環後呈現極低二聚體轉化率。舉例而言，將抗體構築體單體例如在通用調配緩衝液中調節至250 μg/ml之濃度且進行三個凍/融循環(在-80℃下冷凍30分鐘，繼而在室溫下融化30分鐘)，繼而進行高效SEC以測定已轉化成二聚抗體構築體之最初單體抗體構築體的百分比。雙特異性抗體構築體例如在三個凍/融循環後之二聚體百分比為較佳≤5%，更佳≤4%，甚至更佳≤3%，甚至更佳≤2.5%，甚至更佳≤2%，甚至更佳≤1.5%，且最佳≤1%或≤0.5%。

本發明之雙特異性抗體構築體較佳展示有利的熱穩定性，其中聚集溫度≥45℃或≥50℃，更佳≥52℃或≥54℃，甚至更佳≥56℃或≥57℃，且最佳≥58℃或≥59℃。熱穩定性參數可如下依據抗體聚集溫度來確定：將濃度為250 μg/ml之抗體溶液轉移至單次使用光析槽中且置放於動態光散射(DLS)裝置中。樣品以0.5℃/分鐘之加熱速率自40℃加熱至70℃，其中持續獲取量測半徑。使用指示蛋白熔融及聚集之半徑增加

計算抗體之聚集溫度。參見實例10。

或者，溫度熔融曲線可藉由差示掃描熱量測定(DSC)確定，確定抗體構築體之固有生物物理學蛋白穩定性。此等實驗使用MicroCal LLC (Northampton, MA, U.S.A) VP-DSC器件執行。與僅含有調配緩衝液之樣品相比，自20℃至90℃記錄含有抗體構築體之樣品的能量吸收。將抗體構築體例如在SEC操作緩衝液中調節至250 μg/ml之最終濃度。為記錄各別熔融曲線，逐步提高整個樣品溫度。在各溫度T下，記錄樣品及調配緩衝液參考物之能量吸收。相對於各別溫度繪製樣品減去參考物之能量吸收Cp (kcal/mole/℃)之差值的圖。熔融溫度定義為能量吸收之第一最大值之溫度。

此外設想本發明之DLL3xCD3雙特異性抗體構築體不與人類DLL3旁系同源物DLL1及/或DLL4交叉反應(亦即不實質上結合)。此外，設想本發明之DLL3xCD3雙特異性抗體構築體不與獼猴/食蟹獼猴DLL3旁系同源物DLL1及/或DLL4交叉反應(亦即不實質上結合)。參見實例6。

亦設想，本發明之DLL3 xCD3雙特異性抗體構築體之濁度(如在純化單體抗體構築體濃縮至2.5 mg/ml且隔夜培育之後藉由OD340所量測)≤0.2，較佳≤0.15，更佳≤0.12，甚至更佳≤0.1，且最佳≤0.08。參見實例12。

亦設想，本發明之DLL3xCD3雙特異性抗體構築體不由目標細胞內化或不由目標細胞進行顯著內化。可例如如實例16中所描述分析內化率。較佳內化率(例如量測為細胞毒性之降低)在抗體構築體與目標細胞一起培育2小時(預先)之後≤20%，更佳≤15%，甚至更佳≤10%且最佳≤5%。

此外設想排出或可溶性DLL3不顯著削弱本發明之DLL3xCD3雙特異性抗體構築體之功效或生物活性。此可例如在細胞毒性分析法中

量測，其中向分析法中以增加之濃度，例如以0 nM-0.3 nM-0.7 nM-1 nM-3 nM-7 nM-12 nM添加可溶性DLL3。所測試之抗體構築體之EC50值不應在可溶性DLL3存在下顯著增加。參見實例17。

在另一個實施例中，本發明之抗體構築體在酸性pH值下穩定。在非生理pH值(諸如pH 5.5，例如操作陽離子交換層析所需之pH值)下，抗體構築體表現得愈具有耐受性，相對於所負載之蛋白質之總量自離子交換管柱溶離之抗體構築體之回收率愈高。在pH 5.5下自離子(例如陽離子)交換管柱之抗體構築體回收率為較佳≥30%，更佳≥40%，更佳≥ 50%，甚至更佳≥ 60%，甚至更佳≥ 70%，甚至更佳≥80%，甚至更佳≥ 90%，甚至更佳≥ 95%且最佳≥ 99%。參見實例13。

此外，據設想本發明之雙特異性抗體構築體展現治療功效或抗腫瘤活性。此可例如在以下晚期人類腫瘤異種移植模型之實例中所揭示的研究中評定：

在研究之第1天，將人類DLL3陽性癌細胞株(例如SHP-77)之5×10^6個細胞皮下注射於雌性NOD/SCID小鼠之背部右側。當平均腫瘤體積達到約100 mm^3時，將活體外擴增之人類CD3陽性T細胞移植於小鼠中，其藉由將約2×10^7個細胞注射於動物之腹膜腔中達成。媒劑對照組1之小鼠不接受效應細胞且用作未移植對照來與媒劑對照組2 (接受效應細胞)比較以監測單獨的T細胞對腫瘤生長之影響。抗體處理在平均腫瘤體積達到約200 mm^3時開始。處理開始之日各處理組之平均腫瘤尺寸不應在統計學上不同於任何其他組(變異數分析)。小鼠藉由靜脈內快速注射用每日0.5 mg/kg DLL3xCD3雙特異性抗體構築體處理約15至20天。在研究期間藉由測徑規量測腫瘤且藉由組間比較腫瘤體積(TV)評估進展。藉由以T/C% = 100 × (分析組之中值TV) / (對照組2之中值TV)形式計算TV確定腫瘤生長抑制T/C[%]。

熟習此項技術者知曉如何修改或調整此研究之特定參數，諸如

所注射腫瘤細胞之數目、注射位點、所移植人類T細胞之數目、欲投與之雙特異性抗體構築體之量及時刻表，而仍達成有意義且可複製之結果。較佳地，腫瘤生長抑制T/C[%]為≤70或≤60，更佳≤50或≤40，甚至更佳≤30或≤20且最佳≤10或≤5或甚至≤2.5。

本發明另外提供一種編碼本發明之抗體構築體的聚核苷酸/核酸分子。

聚核苷酸為由13個或更多個共價鍵結於鏈中之核苷酸單體構成的生物聚合物。DNA (諸如cDNA)及RNA (諸如mRNA)為具有不同生物功能之聚核苷酸的實例。核苷酸為充當核酸分子(如DNA或RNA)之單體或子單元的有機分子。核酸分子或聚核苷酸可為雙股及單股、線性及環形的。其較佳包含於載體中，該載體較佳包含於宿主細胞中。該宿主細胞例如在用本發明之載體或聚核苷酸轉型或轉染後能夠表現抗體構築體。出於該目的，聚核苷酸或核酸分子與控制序列可操作地連接。

遺傳密碼為遺傳物質(核酸)內編碼之資訊轉譯成蛋白質所用之規則之組。活細胞中之生物學解碼藉由核糖體實現，核糖體使用tRNA分子運載胺基酸且同時讀取mRNA之三個核苷酸而以由mRNA規定之次序連接胺基酸。該代碼定義此等核苷酸三聯體(稱為密碼子)之序列如何規定在蛋白質合成期間隨後添加哪個胺基酸。核酸序列中三個核苷酸之密碼子規定單一胺基酸，但有一些例外情形。因為絕大部分基因用完全相同之代碼編碼，故此特定代碼通常稱為標準遺傳密碼。遺傳密碼決定既定編碼區之蛋白質序列，而其他基因組區可影響此等蛋白質產生之時間及位置。

此外，本發明提供一種載體，其包含本發明之聚核苷酸/核酸分子。

載體為用作將(外來)遺傳物質轉移至細胞中之運載工具的核酸分

子。術語「載體」涵蓋(但不限於)質體、病毒、黏質體及人造染色體。一般而言，工程改造載體包含複製起點、多選殖位點及可選標記物。載體本身通常為核苷酸序列，通常DNA序列，其包含插入序列(轉殖基因)及充當載體之「主鏈」的較大序列。現今載體可包含除轉殖基因插入序列及主鏈以外之其他特徵：啟動子、遺傳標記、抗生素抗性序列、報導基因、靶向序列、蛋白質純化標籤。稱為表現載體(表現構築體)之載體特異於在目標細胞中表現轉殖基因，且通常具有控制序列。

術語「控制序列」係指在特定宿主生物體中表現可操作地連接之編碼序列所需之DNA序列。適用於原核生物之控制序列例如包括啟動子、視情況選用之操縱序列及核糖體結合位點。已知真核細胞利用啟動子、聚腺苷酸化信號及增強子。

核酸在其置放為與另一個核酸序列具有功能關係時「可操作地連接」。舉例而言，若前序列或分泌性前導序列之DNA表現為參與多肽分泌之前蛋白，則其與該多肽之DNA可操作地連接；若啟動子或增強子影響編碼序列之轉錄，則其與該序列可操作地連接；或若核糖體結合位點經定位以便有助於轉譯，則其與編碼序列可操作地連接。一般而言，「可操作地連接」意謂所連接之DNA序列相鄰且在分泌性前導序列之情況下，相鄰且在閱讀相(reading phase)中。然而，增強子不必為相鄰的。連接係藉由在適宜限制性位點處接合來實現。若此類位點不存在，則根據習知實踐使用合成寡核苷酸接附子或連接子。

「轉染」為向目標細胞中故意引入核酸分子或聚核苷酸(包括載體)的過程。該術語主要用於真核細胞中之非病毒方法。轉導通常用於描述病毒介導之核酸分子或聚核苷酸之轉移。動物細胞之轉染通常包括在細胞膜中打開短暫的孔或「洞」以使得可吸收物質。轉染可使用磷酸鈣、藉由電致孔、藉由細胞擠壓或藉由混合陽離子脂質與產生

脂質體(其與細胞膜融合且使其負載沈積於內部)之物質來執行。

術語「轉型」用於描述核酸分子或聚核苷酸(包括載體)向細菌以及非動物真核細胞(包括植物細胞)中之非病毒轉移。因此，轉型為細菌或非動物真核細胞之基因改變，其由經由細胞膜自其環境直接吸收且隨後併入外源遺傳物質(核酸分子)引起。轉型可由人工方式實現。為使轉型發生，細胞或細菌必須處於感受態，其可隨著對環境條件(諸如饑餓及細胞密度)之時間限制性反應而發生。

此外，本發明提供一種用聚核苷酸/核酸分子或用本發明之載體轉型或轉染之宿主細胞。

如本文所用，術語「宿主細胞」或「接受者細胞」意欲包括可為載體、外源核酸分子及編碼本發明抗體構築體之聚核苷酸之接受者；及/或抗體構築體本身之接受者的任何個別細胞或細胞培養物。將各別物質引入細胞中借助於轉型、轉染及其類似方法執行。術語「宿主細胞」亦意欲包括單個細胞之後代或可能後代。因為後續代中由於天然、偶然或故意突變或由於環境影響可能發生某些修飾，故實際上此類後代可能不與親本細胞完全相同(形態或基因組或總DNA互補序列)，但仍包括在如本文所用之術語之範疇內。適合宿主細胞包括原核或真核細胞，且亦包括(但不限於)細菌、酵母細胞、真菌細胞、植物細胞及動物細胞，諸如昆蟲細胞及哺乳動物細胞，例如鼠類、大鼠、獼猴或人類。

本發明之抗體構築體可在細菌中產生。在表現之後，本發明之抗體構築體以可溶性部分自大腸桿菌細胞漿料分離且可經由例如親和層析及/或尺寸排阻純化。可類似於純化例如CHO細胞中表現之抗體的方法來進行最終純化。

除原核生物以外，真核微生物(諸如絲狀真菌或酵母)為本發明之抗體構築體的適合選殖或表現宿主。在低級真核宿主微生物中最常使

用釀酒酵母(*Saccharomyces cerevisiae*)或普通麵包酵母。然而，多種其他屬、種及菌株通常可用且適用於本文，諸如粟酒裂殖酵母(*Schizosaccharomyces pombe*)；克魯維酵母屬(Kluyveromyce)宿主，諸如乳酸克魯維酵母(*K. lactis*)、脆壁克魯維酵母(*K. fragilis*) (ATCC 12424)、保加利亞克魯維酵母(*K. bulgaricus*) (ATCC 16045)、威克克魯維酵母(*K. wickeramii*) (ATCC 24178)、克魯維雄酵母(*K. waltii*) (ATCC 56500)、果妮克魯維酵母(*K. drosophilarum*) (ATCC 36906)、耐熱克魯維酵母(*K. thermotolerans*)及馬克斯克魯維酵母(*K. marxianus*)；耶氏酵母屬(yarrowia)(EP 402 226)；甲醇酵母(*Pichia pastoris*)(EP 183 070)；假絲酵母屬(Candida)；里氏木黴(*Trichoderma reesia*)(EP 244 234)；粗厚神經胞子菌(*Neurospora crassa*)；施氏酵母屬(Schwanniomyce)，諸如西方施氏酵母(*Schwanniomyces occidentalis*)；及絲狀真菌，諸如紅黴菌屬(Neurospora)、青黴菌屬(Penicillium)、彎頸黴屬(Tolypocladium)及麴菌屬(Aspergillus)宿主，諸如構巢麴菌(*A. nidulans*)及黑麴菌(*A. niger*)。

用於表現本發明之糖基化抗體構築體之適合宿主細胞來源於多細胞生物體。無脊椎動物細胞之實例包括植物及昆蟲細胞。已鑑別多種桿狀病毒株及變異體以及來自諸如草地黏蟲(*Spodoptera frugiperda*)(毛蟲)、埃及伊蚊(*Aedes aegypti*) (蚊子)、白紋伊蚊(*Aedes albopictus*)(蚊子)、黑腹果蠅(*Drosophila melanogaster*) (果蠅)及家蠶(*Bombyx mori*)之宿主的對應之容許性昆蟲宿主細胞。用於轉染之多種病毒株公開可得，例如苜蓿銀紋夜蛾(*Autographa californica*) NPV之L-1變異體及家蠶NPV之Bm-5病毒株，且根據本發明此類病毒可用作本文中之病毒，尤其用於轉染草地黏蟲細胞。

棉花、玉米、馬鈴薯、大豆、矮牽牛、番茄、芥菜及菸草之植物細胞培養物亦可用作宿主。適用於在植物細胞培養物中產生蛋白質

之選殖及表現載體為熟習此項技術者已知。參見(例如) Hiatt等人，Nature (1989) 342: 76-78，Owen等人(1992) Bio/Technology 10: 790-794，Artsaenko等人(1995) The Plant J 8: 745-750，及Fecker等人(1996) Plant Mol Biol 32: 979-986。

然而，脊椎動物細胞最受關注，且脊椎動物細胞於培養物(組織培養物)中之繁殖已成為常規程序。適用哺乳動物宿主細胞株之實例為由SV40轉型之猴腎CV1株(COS-7，ATCC CRL 1651)；人胚腎株(次選殖以用於在懸浮培養物中生長之293或293細胞，Graham等人，J. Gen Virol. 36：59 (1977))；幼倉鼠腎細胞(BHK，ATCC CCL 10)；中國倉鼠卵巢細胞/-DHFR (CHO，Urlaub等人，Proc. Natl. Acad. Sci. USA 77: 4216 (1980))；小鼠塞特利氏細胞(mouse sertoli cell，TM4，Mather, Biol. Reprod. 23: 243-251 (1980))；猴腎細胞(CVI ATCC CCL 70)；非洲綠猴腎細胞(VERO-76，ATCC CRL1587)；人類子宮頸癌細胞(HELA，ATCC CCL 2)；犬腎細胞(MDCK，ATCC CCL 34)；布法羅大鼠肝細胞(buffalo rat liver cell，BRL 3A，ATCC CRL 1442)；人類肺細胞(W138，ATCC CCL 75)；人類肝細胞(Hep G2，1413 8065)；小鼠乳房腫瘤(MMT 060562，ATCC CCL5 1)；TRI細胞(Mather等人，Annals N. Y Acad. Sci. (1982) 383: 44-68)；MRC 5細胞；FS4細胞；及人類肝癌株(Hep G2)。

在另一個實施例中，本發明提供一種產生本發明抗體構築體之方法，該方法包含在使得本發明之抗體構築體表現之條件下培養本發明之宿主細胞，及自培養物回收產生之抗體構築體。

如本文所用，術語「培養」係指在適合條件下在培養基中活體外維持細胞、使其分化、生長、增殖及/或繁殖。術語「表現」包括參與產生本發明抗體構築體之任何步驟，包括(但不限於)轉錄、轉錄後修飾、轉譯、轉譯後修飾及分泌。

當使用重組技術時，抗體構築體可於細胞內、周質間隙中產生或直接分泌於培養基中。若抗體構築體於細胞內產生，則作為第一步驟，例如藉由離心或超濾移除宿主細胞或已溶解片段之顆粒碎片。Carter等人, Bio/Technology 10: 163-167 (1992)描述分離分泌至大腸桿菌之周質間隙的抗體的程序。簡言之，在乙酸鈉(pH 3.5)、EDTA及苯基甲基磺醯基氟(PMSF)存在下經約30分鐘融化細胞漿料。可藉由離心移除細胞碎片。在抗體分泌至培養基中之情況下，通常首先使用市售蛋白質濃縮過濾器(例如Amicon或Millipore Pellicon超濾單元)濃縮此類表現系統之上清液。任一個前述步驟中可包括諸如PMSF之蛋白酶抑制劑以抑制蛋白分解，且可包括抗生素以防止外來污染物生長。

自宿主細胞製備之本發明之抗體構築體可使用例如羥磷灰石層析、凝膠電泳、透析及親和層析回收或純化。亦可視欲回收抗體而利用其他用於蛋白質純化之技術，諸如離子交換管柱分級分離、乙醇沈澱、逆相HPLC、二氧化矽層析、肝素SEPHAROSE™層析、陰離子或陽離子交換樹脂(諸如聚天冬胺酸管柱)層析、層析聚焦、SDS-PAGE及硫酸銨沈澱。若本發明之抗體構築體包含CH3域，則Bakerbond ABX樹脂(J.T. Baker, Phillipsburg, NJ)適用於純化。

親和層析為較佳純化技術。親和配位體所附接之基質最常為瓊脂糖，但其他基質為可用的。與用瓊脂糖可達成之流動速率及處理時間相比，機械穩定性基質(諸如受控微孔玻璃或聚(苯乙烯二乙烯基)苯)流動速率更快且處理時間更短。

此外，本發明提供一種醫藥組合物，其包含本發明之抗體構築體或根據本發明方法產生之抗體構築體。

如本文所用，術語「醫藥組合物」係關於適用於向患者(較佳人類患者)投與之組合物。本發明之尤其較佳的醫藥組合物包含較佳治療有效量之一種或複數種本發明之抗體構築體。較佳地，醫藥組合物

另外包含一或多種(醫藥學上有效之)載劑、安定劑、賦形劑、稀釋劑、增溶劑、界面活性劑、乳化劑、防腐劑及/或佐劑的適合調配物。組合物可接受之組分較佳在所採用之劑量及濃度下對受體無毒性。本發明之醫藥組合物包括(但不限於)液體、冷凍及凍乾組合物。

本發明組合物可包含醫藥學上可接受之載劑。一般而言，如本文所用，「醫藥學上可接受之載劑」意謂與醫藥投與(詳言之非經腸投與)相容之任何及全部水性及非水性溶液、無菌溶液、溶劑、緩衝液(例如磷酸鹽緩衝鹽水(PBS)溶液)、水、懸浮液、乳液(諸如油/水乳液)、各種類型之濕潤劑、脂質體、分散培養基及包衣。此類介質及試劑在醫藥組合物中之用途為此項技術中所熟知的，且包含此類載劑之組合物可藉由熟知之習知方法調配。

某些實施例提供包含本發明之抗體構築體及另外一或多種賦形劑(諸如此部分及本文別處中所說明性描述之賦形劑)的醫藥組合物。在此方面，賦形劑在本發明中可用於廣泛多種目的，諸如調節調配物之物理、化學或生物特性，諸如調節黏度及或本發明之方法以改良有效性及或穩定此類調配物及針對由於例如在製造、運送、儲存、使用前製備、投與及此後期間出現的應力而降解及腐敗的方法。

在某些實施例中，醫藥組合物可含有調配物材料以用於調節、維持或保持例如組合物的pH值、容積滲透濃度、黏度、澄清度、顏色、等滲性、氣味、無菌性、穩定性、溶解或釋放速率、吸收或滲透的目的(參見REMINGTON'S PHARMACEUTICAL SCIENCES, 第18版, (A.R. Genrmo編), 1990, Mack Publishing Company)。在此類實施例中，適合的調配物材料可包括(但不限於)：

- 胺基酸，諸如甘胺酸、丙胺酸、麩醯胺、天冬醯胺、蘇胺酸、脯胺酸、2-苯丙胺酸，包含帶電胺基酸，較佳離胺酸、乙酸離胺酸、精胺酸、麩胺酸酯及/或組胺酸

- 抗菌劑，諸如抗細菌劑及抗真菌劑
- 抗氧化劑，諸如抗壞血酸、甲硫胺酸、亞硫酸鈉或亞硫酸氫鈉；
- 緩衝液、緩衝系統及緩衝劑，其用於使組合物維持在生理pH值或略微較低的pH值下，通常在約5至約8或9之pH值範圍內；緩衝劑之實例為硼酸鹽、碳酸氫鹽、Tris-HCl、檸檬酸鹽、磷酸鹽或其他有機酸、丁二酸鹽、磷酸鹽、組胺酸及乙酸鹽；例如約pH 7.0-8.5之Tris緩衝液或約pH 4.0-5.5之乙酸鹽緩衝液；
- 非水性溶劑，諸如丙二醇、聚乙二醇、植物油(諸如橄欖油)及可注射有機酯(諸如油酸乙酯)；
- 水性載劑，包括水、醇/水溶液、乳液或懸浮液，包括鹽水及緩衝介質；
- 可生物降解聚合物，諸如聚酯；
- 增積劑，諸如甘露醇或甘胺酸；
- 螯合劑，諸如乙二胺四乙酸(EDTA)；
- 等滲及吸收延遲劑；
- 複合劑，諸如咖啡鹼、聚乙烯吡咯啶酮、β-環糊精或羥丙基-β-環糊精)
- 填充劑；
- 單醣；雙醣；及其他碳水化合物(諸如葡萄糖、甘露糖或糊精)；碳水化合物可為非還原糖，較佳海藻糖、蔗糖、八硫酸鹽、山梨醇或木糖醇；
- (低分子量)蛋白質、多肽或蛋白質載劑，諸如人類或牛血清白蛋白、明膠或免疫球蛋白，較佳來源於人類；
- 著色劑及調味劑；
- 含硫還原劑，諸如麩胱甘肽、硫辛酸、硫乙醇酸鈉、硫代甘

油、[α]-單硫代甘油及硫代硫酸鈉

- 稀釋劑；
- 乳化劑；
- 親水性聚合物，諸如聚乙烯吡咯啶酮)
- 成鹽相對離子，諸如鈉；
- 防腐劑，諸如抗菌劑、抗氧化劑、螯合劑、惰性氣體及其類似物；實例為：氯化苯甲烴銨、苯甲酸、水楊酸、硫柳汞、苯乙基醇、對羥基苯甲酸甲酯、對羥基苯甲酸丙酯、氯己定、山梨酸或過氧化氫)；
- 金屬錯合物，諸如Zn-蛋白質錯合物；
- 溶劑及共溶劑(諸如甘油、丙二醇或聚乙二醇)；
- 糖及糖醇，諸如海藻糖、蔗糖、八硫酸鹽、甘露醇、山梨醇或木糖醇水蘇糖、甘露糖、山梨糖、木糖、核糖、肌糖、半乳糖、乳糖醇、核糖醇、肌醇(myoinisitol)、半乳糖醇、丙三醇、環醇(例如肌醇(inositol))、聚乙二醇；及多羥基糖醇；
- 懸浮劑；
- 界面活性劑或濕潤劑，諸如普朗尼克(pluronic)、PEG、脫水山梨醇酯、聚山梨醇酯(諸如聚山梨醇酯20、聚山梨醇酯)、曲拉通(triton)、緩血酸胺、卵磷脂、膽固醇、泰洛沙泊(tyloxapal)；界面活性劑可為分子量較佳>1.2 KD之清潔劑及/或分子量較佳>3 KD之聚醚；較佳清潔劑之非限制性實例為Tween 20、Tween 40、Tween 60、Tween 80及Tween 85；較佳聚醚之非限制性實例為PEG 3000、PEG 3350、PEG 4000及PEG 5000；
- 穩定性增強劑，諸如蔗糖或山梨醇；
- 滲性增強劑，諸如鹼金屬鹵化物(較佳氯化鈉或氯化鉀)、甘露醇山梨醇；

• 非經腸遞送媒劑，包括氯化鈉溶液、林格氏右旋糖(Ringer's dextrose)、右旋糖及氯化鈉、乳酸林格氏溶液或不揮發性油；

• 靜脈內傳遞媒劑，包括流體及營養補充劑、電解質補充劑(諸如基於林格氏右旋糖之補充劑)。

對於熟習此項技術者顯而易見的是醫藥組合物之不同組分(例如以上列出之組分)可具有不同效應，例如胺基酸可充當緩衝劑、穩定劑及/或抗氧化劑；甘露醇可充當增積劑及/或張力增強劑；氯化鈉可充當遞送媒介及/或張力增強劑；等。

設想，除本文所定義之本發明多肽之外，本發明之組合物可包含其他生物學活性劑，視組合物之預期用途而定。此類藥劑可為作用於胃腸系統之藥物、充當細胞生長抑制劑之藥物、預防高尿酸血之藥物、抑制免疫反應之藥物(例如皮質類固醇)、調節發炎性反應之藥物、作用於循環系統之藥物及/或諸如此項技術中已知的細胞激素之藥劑。亦設想，本發明之抗體構築體應用於共同療法，亦即與另一抗癌藥劑組合。

最佳的醫藥組合物將由熟習此項技術者視例如預期投與途徑、傳遞型式及所需劑量確定。參見例如 REMINGTON'S PHARMACEUTICAL SCIENCES，見上文。在某些實施例中，此類組合物可影響本發明之抗體構築體的物理狀態、穩定性、活體內釋放率及活體內清除率。在某些實施例中，醫藥組合物中之主要媒劑或載劑本質上可為水性或非水性的。舉例而言，適合的媒劑或載劑可為注射用水、生理鹽水溶液或人工腦脊髓液，其中可能補充有供非經腸投與之組合物中所常見之其他物質。中性緩衝鹽水或與血清白蛋白混合之鹽水為另外的例示性媒劑。在某些實施例中，本發明之抗體構築體組合物可藉由以凍乾濾餅或水性溶液形式混合具有所需純度之所選擇的組合物與視情況選用之調配劑(REMINGTON'S PHARMACEUTICAL

SCIENCES，見上文)來準備用於儲存。另外，在某些實施例中，本發明之抗體構築體可使用適當賦形劑(諸如蔗糖)調配為凍乾物。

當涵蓋非經腸投與時，本發明所用的治療性組合物可以在醫藥學上可接受之媒劑中包含所需本發明之抗體構築體的無熱原質、非經腸可接受之水溶液形式提供。特別適用於非經腸注射之媒劑為無菌蒸餾水，本發明之抗體構築體在其中調配為恰當保存之無菌、等滲溶液。在某些實施例中，製備可涉及所需分子與諸如可注射微球、生物易侵蝕粒子、聚合化合物(諸如聚乳酸或聚乙醇酸)、珠粒或脂質體之試劑一起調配，該試劑可提供可經由積存注射傳遞之產物的控制或持續釋放。在某些實施例中，亦可使用玻尿酸，其具有促進循環之持久性持續的作用。在某些實施例中，可使用可植入藥物遞送裝置以引入所需抗體構築體。

額外醫藥組合物應對熟習此項技術者顯而易見，包括在持續或受控遞送/釋放調配物中包括本發明之抗體構築體的調配物。用於調配多種其他持續或控制遞送方式(諸如脂質體載劑、生物可侵蝕微粒或多孔珠粒及儲槽式注射劑)的技術亦為熟習此項技術者所知。參見例如國際專利申請案第PCT/US93/00829號，其描述用於遞送醫藥組合物之多孔聚合物微粒的控制釋放。持續釋放製劑可包括呈成形物品(例如膜或微囊)形式之半滲透性聚合物基質。持續釋放基質可包括聚酯、水凝膠、聚乳酸交酯(如美國專利第3,773,919號及歐洲專利申請公開案第EP 058481號中所揭示)、L-麩胺酸及L-麩胺酸γ-乙酯之共聚物(Sidman等人, 1983, Biopolymers 2:547-556)、聚(2-羥乙基-甲基丙烯酸酯) (Langer等人, 1981, J. Biomed. Mater. Res. 15:167-277及Langer, 1982, Chem. Tech. 12:98-105)、乙烯乙酸乙烯酯(Langer等人, 1981，同前文獻)或聚-D(-)-3-羥基丁酸(歐洲專利申請公開案第EP 133,988號)。持續釋放組合物亦可包括可藉由此項技術中已知之若干方法中

之任一者製備之脂質體。參見例如Eppstein等人，1985, Proc. Natl. Acad. Sci. U.S.A. 82:3688-3692；歐洲專利申請公開案第EP 036,676號；第EP 088,046號及第EP 143,949號。

抗體構築體亦可包覆於例如藉由凝聚技術或藉由界面聚合製備之微膠囊(分別例如羥甲基纖維素或明膠微膠囊及聚(甲基丙烯酸甲酯)微膠囊)中、膠體藥物遞送系統(例如脂質體、白蛋白微球、微乳液、奈米粒子及奈米膠囊)或巨乳液中。此類技術揭示於Remington's Pharmaceutical Sciences, 第16版, Oslo, A.編, (1980)中。

用於活體內投藥之醫藥組合物通常以無菌製劑形式提供。可藉由經無菌過濾膜過濾來實現滅菌。當組合物經凍乾時，使用此方法之滅菌可在凍乾及復原之前或之後進行。用於非經腸投藥之組合物可以凍乾形式或溶液形式儲存。非經腸組合物一般置放於具有無菌存取孔口之容器中，例如具有可用皮下注射針頭刺穿之塞子的靜脈內溶液袋或瓶。

本發明之另一個態樣包括本發明抗體構築體之自緩衝調配物，其可用作醫藥組合物，如國際專利申請案WO 06138181A2 (PCT/US2006/022599)中所描述。可獲得關於蛋白質穩定及調配物材料及適用於此方面之方法的多種闡述，諸如Arakawa等人，「Solvent interactions in pharmaceutical formulations」, Pharm Res. 8(3): 285-91 (1991)；Kendrick等人，「Physical stabilization of proteins in aqueous solution」, RATIONAL DESIGN OF STABLE PROTEIN FORMULATIONS: THEORY AND PRACTICE, Carpenter及Manning編, Pharmaceutical Biotechnology. 13: 61-84 (2002)及Randolph等人，「Surfactant-protein interactions」, Pharm Biotechnol. 13: 159-75 (2002)，特別參見與賦形劑及其用於本發明之自動緩衝蛋白質調配物之方法切合的部分，尤其關於蛋白質醫藥產品及用於獸醫學及/或人

類醫學用途之方法。

鹽可根據本發明之某些實施例用於例如調節調配物之離子強度及/或等張性及/或改良本發明組合物之蛋白質或其他成分的溶解性及/或物理穩定性。如所熟知，離子可藉由結合於蛋白質表面上之帶電殘基及藉由遮蔽蛋白質中之帶電及極性基團且減小其靜電相互作用、吸引及排斥相互作用的強度而使天然狀態之蛋白質穩定。離子亦可藉由結合於詳言之蛋白質之變性肽鍵(--CONH)而使變性狀態之蛋白質穩定。此外，離子與蛋白質中之帶電基團及極性基團的相互作用亦可減小分子間靜電相互作用，由此預防或減少蛋白質凝聚及不可溶性。

離子種類在其對蛋白質之效應方面有顯著差異。已完善可用於調配本發明之醫藥組合物的許多類別等級的離子及其對蛋白質之效應。一個實例為霍夫梅斯特序列(Hofmeister series)，其藉由對蛋白質在溶液中之構形穩定性的效應排列離子及極性非離子溶質。使溶質穩定稱為「親液的」。使溶質去穩定化稱為「離液的(chaotropic)」。親液劑通常在高濃度(例如>1莫耳濃度硫酸銨)下使用以使蛋白自溶液沈澱(「鹽析」)。離液劑通常用於使蛋白變性及/或溶解(「鹽溶」)。離子對「鹽溶」及「鹽析」之相對有效性定義其在霍夫梅斯特序列中之位置。

游離胺基酸可在根據本發明之各種實施例之本發明之抗體構築體調配物中用作增積劑、穩定劑及抗氧化劑以及其他標準用途。離胺酸、脯胺酸、絲胺酸及丙胺酸可用於使調配物中之蛋白質穩定。甘胺酸適用於凍乾以確保正確凍乾塊結構及特性。精胺酸可適用於在液體及凍乾調配物中抑制蛋白質凝聚。甲硫胺酸適用作抗氧化劑。

多元醇包括糖，例如甘露醇、蔗糖及山梨糖醇及諸如丙三醇及丙二醇之多元醇及(出於本文論述之目的)聚乙二醇(PEG)及相關之物質。多元醇為親液的。其為在液體及凍乾調配物中適用的穩定劑，保

護蛋白質免受物理及化學降解過程影響。多元醇亦適用於調節調配物之滲性。適用於本發明之所選實施例的多元醇為甘露醇，常用於確保凍乾調配物中凍乾塊之結構穩定性。其確保凍乾塊之結構穩定性。其一般與凍乾保護劑(例如蔗糖)一起使用。山梨醇及蔗糖為當中用於調節滲性之較佳藥劑且充當在運輸期間避免凍融應力或在製造過程期間避免製備塊體的穩定劑。還原糖(其含有自由醛基或酮基)，諸如葡萄糖及乳糖，可使表面離胺酸及精胺酸殘基糖化。因此，其一般不在根據本發明使用之較佳多元醇當中。另外，形成此類反應物質之糖，諸如在酸性條件下水解成果糖及葡萄糖且因此引起糖基化之蔗糖，在此方面亦不在本發明之較佳多元醇當中。PEG適用於使蛋白質穩定及充當低溫保護劑且在此方面可用於本發明。

本發明之抗體構築體調配物的實施例進一步包含界面活性劑。蛋白質分子可易於吸附於表面上及變性且隨後在氣-液、固-液及液-液界面凝聚。此等作用一般與蛋白質濃度成反比。此等有害相互作用一般與蛋白質濃度成反比且通常藉由諸如在產品運送及操作期間產生的物理攪動而加劇。界面活性劑常規用於預防、最小化或減少表面吸附。在此方面，本發明中適用之界面活性劑包括聚山梨醇酯20、聚山梨醇酯80、脫水山梨醇聚乙氧基化物之其他脂肪酸酯及泊洛沙姆188(poloxamer 188)。界面活性劑亦常用於控制蛋白質構形穩定性。在此方面，界面活性劑之用途具有蛋白質特異性，因為任何既定界面活性劑通常將使一些蛋白質穩定且使其他蛋白質不穩定。

聚山梨醇酯易於氧化降解且常常在供應時含有足夠數量的過氧化物以引起蛋白質殘基側鏈(尤其甲硫胺酸)氧化。因此，聚山梨醇酯應謹慎使用且當使用時，應在其最低有效濃度下使用。在此方面，聚山梨醇酯例示賦形劑應以其最低有效濃度使用的通用規則。

本發明之抗體構築體調配物的實施例進一步包含一或多種抗氧

化劑。在一定程度上，可藉由維持適當水準之環境氧氣及溫度及藉由避免曝光而在醫藥調配物中預防蛋白質的有害氧化。亦可使用抗氧化劑賦形劑來預防蛋白質之氧化降解。在此方面，適用之抗氧化劑為還原劑、氧/自由基清除劑及螯合劑。適用於本發明之治療性蛋白質調配物的抗氧化劑較佳為水溶性的且在產品之整個存放期中維持其活性。在此方面，EDTA為本發明之較佳抗氧化劑。抗氧化劑可損害蛋白質。舉例而言，還原劑(詳言之，諸如麩胱甘肽)可破壞分子內二硫鍵。因此，選擇適用於本發明之抗氧化劑以尤其消除或充分降低其自身損傷調配物中之蛋白質的可能性。

本發明之調配物可包括金屬離子，其為蛋白質輔助因子且為形成蛋白質配位複合物所需，諸如形成某些胰島素懸浮液所需的鋅。金屬離子亦可抑制一些降解蛋白質之過程。然而，金屬離子亦催化降解蛋白質之物理及化學過程。鎂離子(10-120 mM)可用於抑制天冬胺酸異構化成異天冬胺酸。Ca^{+2}離子(至多100 mM)可增加人類去氧核糖核酸酶之穩定性。然而，Mg^{+2}、Mn^{+2}及Zn^{+2}可使rhDNase去穩定化。類似地，Ca^{+2}及Sr^{+2}可使因子VIII穩定，因子VIII可藉由Mg^{+2}、Mn^{+2}及Zn^{+2}、Cu^{+2}及Fe^{+2}不穩定，且其凝聚可藉由Al^{+3}離子增加。

本發明之抗體構築體調配物的實施例另外包含一或多種防腐劑。當研發多劑量非經腸調配物涉及多於一次自相同容器提取時，需要防腐劑。其主要功能為抑制微生物生長且在整個存放期或藥品使用時期確保產品無菌性。常用防腐劑包括苯甲醇、苯酚及間甲酚。雖然防腐劑具有較長的與小分子注射劑一起使用之歷史，但研發包括防腐劑之蛋白質調配物可能具有挑戰性。防腐劑幾乎始終具有對蛋白質之不穩定化效應(凝聚)且此已變成限制其在多劑量蛋白質調配物中使用的主要因素。迄今，已調配大多數蛋白質藥物僅用於單次使用。然而，當多劑量調配物為可能的時，其具有使得患者能夠方便且增加可

銷售性的附加優勢。良好實例為人類生長激素(hGH)，其中防腐調配物的研發已使得更加方便的多次使用注射筆呈現商業化。目前市場上可獲得至少四種含有hGH防腐調配物的此類筆裝置。Norditropin (液體，Novo Nordisk)、Nutropin AQ (液體，Genentech)及Genotropin (凍乾--雙腔藥筒，Pharmacia & Upjohn)含有苯酚，而Somatrope (Eli Lilly)與間甲酚一起調配。在防腐劑型之調配及研發期間需要考慮若干態樣。藥品中之有效防腐劑濃度必須經最佳化。此需要測試劑型中之既定防腐劑，使得濃度範圍賦予抗微生物有效性而不損害蛋白質穩定性。

如可預期，研發含有防腐劑之液體調配物比凍乾調配物更具挑戰性。冷凍乾燥之產品可在無防腐劑的情況下凍乾且在使用時用含有防腐劑之稀釋劑復原。此縮短防腐劑與蛋白質接觸的時間，使相關穩定性風險顯著減至最小。在液體調配物之情況下，應經整個產品存放期(約18至24個月)維持防腐劑有效性及穩定性。注意的重點為防腐劑有效性應展現在含有活性藥物及全部賦形劑組分之最終調配物中。

本文所揭示之抗體構築體亦可調配為免疫脂質體。「脂質體」為由各種類型之脂質、磷脂及/或適用於向哺乳動物遞送藥物之界面活性劑構成的小微脂粒。脂質體之組分通常排列為雙層形式，類似於生物膜之脂質排列。含有抗體構築體之脂質體藉由此項技術中已知之方法製備，諸如Epstein等人，Proc. Natl. Acad. Sci. USA, 82: 3688 (1985)；Hwang等人，Proc. Natl Acad. Sci. USA, 77: 4030 (1980)；美國專利第4,485,045號及第4,544,545號；及W0 97/38731中所描述之方法。循環時間增加之脂質體揭示於美國專利第5,013, 556號中。尤其適用之脂質體可藉由逆相蒸發法用包含磷脂醯膽鹼、膽固醇及PEG衍生化之磷脂醯乙醇胺(PEG-PE)的脂質組合物產生。脂質體經具有界定孔徑之過濾器擠出以產生具有所需直徑之脂質體。本發明之抗體構築

體的Fab'片段可如Martin等人 J. Biol. Chem. 257: 286-288 (1982)中所述經由二硫鍵互換反應與脂質體結合。脂質體內視情況含有化學治療劑。參見Gabizon等人 J. National Cancer Inst. 81 (19) 1484 (1989)。

一旦醫藥組合物已調配，即可將其以溶液、懸浮液、凝膠、乳液、固體、晶體或脫水或凍乾散劑形式儲存於無菌小瓶中。此類調配物可以即用形式或在投與前復原之形式(例如，凍乾形式)儲存。

本文所定義之醫藥組合物的生物活性可例如藉由細胞毒性分析測定，如以下實例WO 99/54440或由Schlereth等人(Cancer Immunol. Immunother. 20 (2005), 1-12)中所描述。如本文所用之「功效」或「活體內功效」係指使用例如標準化NCI反應準則對藉由本發明之醫藥組合物之療法的反應。使用本發明之醫藥組合物之療法的功效或活體內功效指代用於其預期目的之組合物之有效性，亦即組合物引起其所需效應(亦即病理性細胞，例如腫瘤細胞之耗盡)的能力。活體內功效可藉由對相應疾病實體建立之標準方法來監測，包括(但不限於)白血球計數、差異、螢光活化細胞分選、骨髓抽吸。此外，可使用各種疾病特異性臨床化學參數及其他已建立之標準方法。此外，可使用電腦輔助斷層攝影術、X射線、核磁共振斷層攝影術(例如，用於基於國家癌症學會準則之反應評定[Cheson BD, Horning SJ, Coiffier B, Shipp MA, Fisher RI, Connors JM, Lister TA, Vose J, Grillo-Lopez A, Hagenbeek A, Cabanillas F, Klippensten D, Hiddemann W, Castellino R, Harris NL, Armitage JO, Carter W, Hoppe R, Canellos GP. Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. J Clin Oncol. 1999年4月；17(4):1244])、正電子發射斷層攝影掃描、白血球計數、差異、螢光活化細胞分選、骨髓抽吸、淋巴結活檢/組織學及各種淋巴瘤特異性臨床化學參數(例如，乳酸脫氫酶)及其他已建

立之標準方法。

藥物(諸如本發明之醫藥組合物)之研發中的另一個主要挑戰為藥物動力學特性之可預測調節。為此目的，可形成候選藥物之藥物動力學概況，亦即影響特定藥物治療給定病狀之能力之藥代動力學參數之概況。影響藥物治療一定疾病實體之能力的藥物之藥物動力學參數包括(但不限於)：半衰期、分佈體積、肝首過代謝及血清結合程度。給定藥劑之功效可受上文所提及之參數中之每一者影響。

「半衰期」意謂50%投與藥物經由(例如)代謝、排泄等之生物過程消除之時間。由「肝首過代謝」意謂在首次與肝接觸之後，亦即在其首次穿過肝期間待代謝之藥物之傾向。「分佈體積」意謂遍及身體之多個腔室之滯留量，例如細胞內及細胞外空間、組織及器官等，及此等腔室內藥物之分佈。「血清結合程度」意謂藥物與血清蛋白(諸如白蛋白)相互作用且結合導致藥物之生物活性降低或損失之傾向。

藥物動力學參數亦包括給定量的投與藥物之生物可用性、滯後時間(Tlag)、Tmax、吸收速率、更加起效及/或Cmax。「生物可用性」意謂藥物在血液隔室中之量。「滯後時間」意謂藥物投藥與其在血液或血漿中之偵測及可測性之間的時間延遲。「Tmax」為達到藥物最大血液濃度後的時間，且「Cmax」為使用既定藥物最大限度獲得的血液濃度。達到藥物生物效果所需的藥物之血液或組織濃度的時間受所有參數影響。展現跨物種特異性之雙特異性抗體構築體的藥物動力學參數(可如上文所概述在非黑猩猩靈長類動物之臨床前動物測試中測定)亦闡述於例如Schlereth等人之出版物(Cancer Immunol. Immunother. 20 (2005), 1-12)中。

一個實施例提供本發明之抗體構築體或根據本發明方法產生之抗體構築體，其用於預防、治療或改善腫瘤或癌症疾病或轉移性癌症疾病。

本文所述之調配物適用作治療、改善及/或預防有需要之患者之如本文所述之病理性醫學病狀的醫藥組合物。術語「治療」指代治療性治療及預防性或防治性措施兩者。治療包括以治癒、治療、減輕、降低、改變、補救、改善、改良或影響疾病、疾病症狀或疾病之傾向為目的，向來自患有疾病/病症、具有疾病/病症之症狀或易患疾病/病症之患者的身體、分離組織或細胞施用或投與調配物。

如本文所用之術語「改善」係指患有如下文所說明之腫瘤或癌症或轉移性癌症之患者的疾病病況之任何改良，其藉由向有需要之個體投與本發明之抗體構築體來進行。此類改良亦可視為患者之腫瘤或癌症或轉移性癌症的進程減緩或停止。如本文所用之術語「預防」意謂避免出現或再出現患有如下文所說明之腫瘤或癌症或轉移性癌症的患者，其藉由向有需要之個體投與本發明之抗體構築體來進行。

術語「疾病」係指受益於用本文所描述之抗體構築體或醫藥組成物治療的任何病狀。其包括慢性及急性病症或疾病，包括使哺乳動物易患所述疾病之彼等病理病狀。

「贅瘤」為組織之異常生長，通常會但未必總會形成腫塊。當亦形成腫塊時，一般稱為「腫瘤」。贅瘤或腫瘤可為良性的、潛在惡性的(癌前)或惡性的。惡性贅瘤一般稱為癌症。其通常侵入且破壞周圍組織且可形式癌轉移，亦即其擴展至身體之其他部分、組織或器官。因此，術語「轉移性癌症」涵蓋至除原始腫瘤外之其他組織或器官之癌轉移。淋巴瘤及白血病為淋巴贅瘤。出於本發明之目的，亦藉由術語「腫瘤」或「癌症」涵蓋。

在本發明之一較佳實施例中，腫瘤或癌症疾病選自包括(但不限於)以下之群(或由以下組成)：肺癌，較佳為SCLC、乳房、子宮頸、結腸、結腸直腸、子宮內膜、頭部及頸部、肝、卵巢、胰腺、前列腺、皮膚、胃、睪丸、甲狀腺、腎上腺、腎、膀胱、子宮、食道、尿

道上皮及腦腫瘤或癌症，淋巴瘤、癌瘤及肉瘤，及來源於前述任一者之轉移性癌症疾病。

更特定言之，腫瘤或癌症疾病可選自由以下組成之群：小細胞肺癌(SCLC)、非小細胞肺癌(NSCLC)、神經膠質瘤、神經膠母細胞瘤、黑素瘤、神經內分泌前列腺癌、神經內分泌胰臟癌、肝母細胞瘤及肝細胞癌。轉移性癌症疾病可源自前述疾病中之任一者。

本發明亦提供一種用於治療或改善腫瘤或癌症疾病或轉移性癌症疾病之方法，其包含向有需要之個體投與本發明之抗體構築體或根據本發明方法產生之抗體構築體的步驟。

術語「有需要之個體」或「需要治療」之個體包括已患病症之個體以及預防病症之個體。有需要之個體或「患者」包括接受預防性或治療性治療之人類及其他哺乳動物個體。

本發明之抗體構築體一般將經設計以尤其在一定生物可用性及持久性範圍下用於特定投藥途徑及方法，特定投藥劑量及頻率，特定疾病之特定治療。組合物之材料較佳以投藥位點可接受之濃度調配。

因此，可根據本發明設計調配物及組合物以藉由任何適合之投藥途徑遞送。在本發明之上下文中，投藥途徑包括(但不限於)

- 局部途徑(諸如經上表皮、吸入、經鼻、經眼、經耳、經陰道、經黏膜)；
- 腸內途徑(諸如經口、經胃腸、舌下、唇下、經頰、經直腸)；及
- 非經腸途徑(諸如靜脈內、動脈內、骨內、肌肉內、腦內、腦室內、硬膜外、鞘內、皮下、腹膜內、羊膜外、關節內、心內、皮內、病灶內、子宮內、膀胱內、玻璃體內、經皮、鼻內、經黏膜、滑膜內、邊緣內)。

本發明之醫藥組合物及抗體構築體尤其適用於非經腸投藥，例

如皮下或靜脈內傳遞，例如藉由注射(諸如快速注射)，或藉由輸注(諸如連續輸注)。醫藥組合物可使用醫療裝置投與。用於投與醫藥組合物之醫療裝置的實例描述於美國專利第4,475,196號；第4,439,196號；第4,447,224號；第4,447, 233號；第4,486,194號；第4,487,603號；第4,596,556號；第4,790,824號；第4,941,880號；第5,064,413號；第5,312,335號；第5,312,335號；第5,383,851號；及第5,399,163號中。

特定言之，本發明提供適合組合物之不間斷投與。作為非限制性實例，不間斷或大體上不間斷，亦即連續投與可藉由患者帶有之小泵系統計量治療劑向患者身體中之流入來實現。包含本發明抗體構築體之醫藥組合物可藉由使用該等泵系統投與。此類泵系統通常為此項技術中已知，且通常依賴於定期更換容納欲輸注治療劑之濾筒。在更換此類泵系統中之濾筒時，可繼而暫時中斷治療劑向患者身體之流動，否則該流動為不間斷的。在此情況下，在本發明之醫藥手段及方法之含義內，濾筒更換前之投藥階段及濾筒更換後之投藥階段仍認為一起構成此類治療劑之一次「不間斷投與」。

連續或不間斷投與本發明之抗體構築體可為靜脈內或皮下投與，其借助於包括用於驅動流體離開儲集器之流體驅動機構及用於致動驅動機構之致動機構的流體遞送裝置或小泵系統。用於皮下投與之泵系統可包括用於穿過患者皮膚且向患者身體傳遞適合組合物之針或導管。該等泵系統可直接獨立於靜脈、動脈或血管固定或連接於患者之皮膚，從而使得泵系統與患者之皮膚之間可直接接觸。泵系統可連接於患者之皮膚24小時至數天。在小體積儲集器之情況下，泵系統可具有小尺寸。作為一個非限制性實例，用於投與適合醫藥組合物之儲集器之體積可在0.1與50 ml之間。

連續投藥亦可為借助於皮膚上穿戴之貼片經皮投與且以一定時

間間隔更換。熟習此項技術者已知適用於此目的之用於藥物傳遞之貼片系統。值得注意地，經皮投藥尤其適於不間斷投藥，因為更換第一耗盡貼片可藉由例如在緊鄰第一耗盡貼片之皮膚之表面上放置新第二貼片且隨後立即移除第一耗盡貼片而同時有利地實現。不會發生流動中斷或電源電池故障之問題。

若醫藥組合物已凍乾，則經凍乾物質首先在適當液體中復原，隨後投與。經凍乾物質可在(例如)注射用抑菌水(BWFI)、生理食鹽水、磷酸鹽緩衝生理食鹽水(PBS)或蛋白質在凍乾之前所處之相同調配物中復原。

本發明之組合物可以適合劑量向個體投與，該適合劑量可例如藉由劑量遞增研究藉由向非黑猩猩靈長類動物(例如獼猴)投與增加劑量的展現跨物種特異性之本發明抗體構築體來確定。如上文所闡述，展現本文所描述之跨物種特異性的本發明抗體構築體可有利地以相同形式用於非黑猩猩靈長類動物之臨床前測試及人類之藥物。給藥方案將由主治醫師及臨床因素判定。如醫學技術中所熟知，對於任何一個患者，劑量視許多因素而定，包括患者之體型、體表面積、年齡、待投與之特定化合物、性別、投藥時間及途徑、一般健康狀況及同時投與之其他藥物。

術語「有效劑量」或「有效劑量」定義為足以達成或至少部分達成所需作用之量。術語「治療有效劑量」定義為足以治癒或至少部分遏止已患有疾病之患者之疾病及其併發症之量。有效用於此用途之量或劑量將以下而定：視待治療之病狀(適應症)、遞送之抗體構築體、治療情形及目標、疾病之嚴重性、先前療法、患者之臨床病史及對治療劑之反應、投藥路徑、患者之體型(體重、身體表面或器官尺寸)及/或條件(年齡及一般健康狀況)及患者自身免疫系統之一般狀態。適當劑量可根據主治醫師之判斷調節以使得其可向患者投與一次

或經一系列投藥向患者投與，且以獲得最佳治療作用。

典型劑量可在約0.1 μg/kg至高達約30 mg/kg或更高之範圍內變化，視上文所提及之因素而定。在特定實施例中，劑量可在1.0 μg/kg至約20 mg/kg、視情況10 μg/kg至約10 mg/kg或100 μg/kg至約5 mg/kg範圍內。

治療性有效量之本發明抗體構築體較佳使疾病症狀之嚴重性降低，無疾病症狀期之頻率或持續時間提高或預防疾病病痛所致之損傷或失能。關於治療DLL3表現性腫瘤，治療有效量之本發明抗體構築體(例如抗DLL3/抗CD3抗體構築體)相對於未經治療之患者較佳抑制細胞生長或腫瘤生長至少約20%、至少約40%、至少約50%、至少約60%、至少約70%、至少約80%或至少約90%。可在預測在人類腫瘤中之功效的動物模型中評估化合物抑制腫瘤生長的能力。

醫藥組合物可作為唯一治療劑投與或與其他療法(諸如視需要抗癌療法，例如其他蛋白質及非蛋白質藥物)組合投與。此等藥物可以適時定義之時間間隔及劑量與如本文所定義之包含本發明抗體構築體之組合物同時投與，或分別在投與該抗體構築體之前或之後投與。

如本文中所用之術語「有效且無毒劑量」係指本發明抗體構築體之可耐受劑量，其足夠高以引起病理性細胞消除、腫瘤去除、腫瘤縮小或疾病穩定而無或基本上無大的毒性作用。此類有效且無毒劑量可例如藉由此項技術中描述之劑量遞增研究確定且應低於誘導嚴重不良側面事件之劑量(劑量限制性毒性(dose limiting toxicity；DLT))。

如本文中所用之術語「毒性」係指體現在不良事件或嚴重不良事件中之藥物的毒性作用。此等側面事件可指一般缺乏藥物耐受性及/或投藥之後缺乏局部耐受性。毒性亦可包括由藥物引起之致畸或致癌作用。

如本文所用之術語「安全性」、「活體內安全性」或「耐受性」

定義投與藥物而不會在投與後立即誘導嚴重不良事件(局部耐受性)及不會在藥物之較長期施用期間誘導嚴重不良事件。「安全性」、「活體內安全性」或「耐受性」可在治療及追蹤階段期間(例如)以常規間隔進行評估。量測包括臨床評估，例如器官表現，及實驗室異常之篩檢。臨床評估可進行且偏向根據NCI-CTC及/或MedDRA標準所記錄/編碼之正常研究結果。器官表現可包括諸如過敏/免疫學、血液/骨髓、心律不整、凝血及其類似者之標準，如闡述於例如不良事件之通用術語標準v3.0 (Common Terminology Criteria for adverse events v3.0；CTCAE)中。可測試之實驗室參數包括例如血液學、臨床化學、凝血概況及尿液分析及諸如血清、血漿、淋巴或脊髓液、液體及其類似物之其他體液的檢查。因此，安全性可(例如)藉由身體檢查、成像技術(亦即超音波、x射線、CT掃描、磁共振成像(MRI)、藉由技術器件之其他測量(亦即心電圖))、生命體征、藉由量測實驗室參數及記錄不良事件來評定。舉例而言，在本發明之用途及方法中，非黑猩猩靈長類動物中之不良事件可藉由組織病理學及/或組織化學方法檢查。

以上術語亦例如在Preclinical safety evaluation of biotechnology-derived pharmaceuticals S6; ICH Harmonised Tripartite Guideline; ICH Steering Committee meeting, 1997年7月16日中提及。

在另一實施例中，本發明提供一種套組，其包含本發明之抗體構築體、根據本發明方法產生之抗體構築體、本發明之多肽、本發明之載體及/或本發明之宿主細胞。

在本發明之情形下，術語「套組」意謂一起包裝於容器、或其他物件中的兩種或更多種組分，其中之一對應於本發明之抗體構築體、醫藥組合物、載體或宿主細胞。因此，套組可描述為足以達成某一目標之一組產品及/或用具，其可作為單個單元出售。

套組可包含一或多個任何適合形狀、尺寸及材料(較佳防水，例如塑膠或玻璃)之接收器(諸如小瓶、安瓿、容器、針筒、瓶子、袋子)，其含有適用於投藥之劑量的本發明之抗體構築體或醫藥組合物(參見上文)。套組可另外含有使用說明(例如小冊或說明手冊形式)、投與本發明之抗體構築體的構件(諸如注射器、泵、輸注器或其類似物)、復原本發明之抗體構築體的構件及/或稀釋本發明之抗體構築體的構件。

本發明亦提供用於單次劑量投藥單位的套組。本發明之套組亦可含有包含經乾燥/凍乾之抗體構築體的第一容器及包含水性調配物之第二容器。在本發明之某些實施例中，提供含有單室及多室預填充注射器(例如液體注射器及冷凍乾燥物注射器)的套組。

【圖式簡單說明】

圖1

用於抗原決定基定位之表現於CHO細胞上之DLL3 ECD/截短DLL3構築體之示意圖。跨膜及胞內域來源於EpCAM。參見實例1。

圖2

抗DLL3抗體構築體之抗原決定基定位。如藉由抗原決定基定位偵測之分別識別EGF-3結構域及EGF -4結構域之雙特異性抗體構築體之實例。x軸描繪PE-A (PE=藻紅素，A=信號面積)，且y軸描繪計數。參見實例2。

圖3

如由流式細胞測量術偵測之抗DLL3抗體構築體之交叉反應性：結合於人類及獼猴DLL3及CD3。x軸描繪FL2-H，且y軸描繪計數。參見實例5。

圖4

藉由流式細胞測量術進行之抗DLL3抗體構築體之分析：不結合

於人類旁系同源物DLL1及DLL4。x軸描繪FL1-H，且y軸描繪計數。參見實例6。

圖5

在人類血漿中培育96小時之後，抗DLL3抗體構築體之穩定性。參見實例11。

圖6

抗DLL3抗體構築體之單體及二聚同功異型物之間的效能差。參見實例15。

圖7

活體外內化分析法，如實例16中所描述進行。在不存在T細胞之情況下，在目標細胞(SHP-77)上預先培育抗體構築體，以量測由內化引起之抗體構築體之缺失。結果表明未發生顯著內化。獲得結果，其中在右側展示對照目標(其內化為熟知的)以用於對比。

圖8

SHP-77模型(圖8A)及WM266-4模型(圖8B)之小鼠異種移植功效研究之結果。針對時間標繪腫瘤體積。參見實例18。

圖9

實例20中測定不同HLE抗體構築體(圖9A中之白蛋白融合物及圖9B中之Fc融合物)之藥物動力學。

實例：

以下實例說明本發明。此等實例不應理解為限制本發明之範疇。本發明僅受申請專利範圍限制。

實例1

產生表現野生型及截短DLL3之CHO細胞

在實例1及2中，DLL3抗原之細胞外結構域可再分成由以下胺基酸位置界定之不同子結構域或區域：

信號肽：1-26

N端：27-175

DSL：176-215

EGF-1：216-249

EGF-2：274-310

EGF-3：312-351

EGF-4：353-389

EGF-5：391-427

EGF-6：429-465

對於構築用於抗原決定基定位之截短DLL3分子，自N端開始，逐步自抗原刪除人類DLL3之各別八個細胞外結構域(信號肽加N端、DSL、EGF1、EGF2、EGF3、EGF4、EGF5及EGF6)之序列。產生以下分子；亦參見圖1：

- Hu DLL3 ECD/完全ECD SEQ ID NO:263
- Hu DLL3 ECD/至DSL SEQ ID NO:264
- Hu DLL3 ECD/至EGF-1 SEQ ID NO:265
- Hu DLL3 ECD/至EGF-2 SEQ ID NO:266
- Hu DLL3 ECD/至EGF-3 SEQ ID NO:267
- Hu DLL3 ECD/至EGF-4 SEQ ID NO:268
- Hu DLL3 ECD/至EGF-5 SEQ ID NO:269
- Hu DLL3 ECD/僅EGF-6 SEQ ID NO:270

對於產生表現人類、食蟹猴(「cyno」)及截短人類N端V5標記之DLL3之CHO細胞，將人類DLL3-ECD (SEQ ID NO:253；亦參見GenBank寄存編號NM_016941)、食蟹猴DLL3至ECD (SEQ ID NO:272)及七個截短人類N端V5標記之DLL3-ECD版本(參見上文)之各別編碼序列選殖至稱為pEF-DHFR之質體中(pEF-DHFR描述於Raum等人

Cancer Immunol Immunother 50 (2001) 141-150中)。對於人類及食蟹猴DLL3之細胞表面表現，使用原始信號肽，且對於截短人類N端DLL3之細胞表面表現，使用小鼠IgG重鏈信號肽，接著V5標籤。所有所提及之DLL3-ECD序列框內後接有人工Ser/Gly-連接子之編碼序列，接著為來源於人類EpCAM之跨膜/胞內域之結構域(序列之胺基酸266-314，如GenBank寄存編號NM_002354中所公佈)。所有選殖程序根據標準方案進行(Sambrook, Molecular Cloning; A Laboratory Manual, 第3版, Cold Spring Harbour Laboratory Press, Cold Spring Harbour, New York (2001))。對於各構築體，將對應質體轉染至用於真核表現之缺乏DHFR之CHO細胞中，如Kaufman R.J. (1990) Methods Enzymol. 185, 537-566所述。

使用單株小鼠IgG2b抗人類DLL3抗體，在FACS分析法中檢驗CHO細胞上人類及食蟹猴DLL3之表現。使用單株小鼠IgG2a抗-v5標籤抗體檢驗人類DLL3-ECD之七個截短版本之表現。結合單株抗體用抗小鼠IgG Fc-γ-PE偵測。作為陰性對照，將細胞與同型對照抗體而非第一抗體一起培育。樣品藉由流式細胞測量術量測。

實例2

抗DLL3抗體構築體之抗原決定基定位

經人類DLL3及截短人類DLL3分子轉染之細胞(參見實例1)在PBS/1.5% FCS中用粗物質(與人類白蛋白(變異體1)融合之含有雙特異性DLL3xCD3抗體構築體(其中CD3結合域命名為I2C)之非經稀釋之周質提取物)染色。結合分子用內部小鼠單株抗CD3結合域抗體(50 µl)，之後用抗小鼠IgG Fc-γ-PE (1:100，50 µl；Jackson Immunoresearch號115-116-071)偵測。所有抗體均在PBS/1.5% FCS中稀釋。作為陰性對照，將細胞與PBS/2% FCS而非周質提取物一起培育。樣品藉由流式細胞測量術量測。

藉由相應DLL3結合域識別之區示於序列表(表18)中。對位於DLL3之N端、DSL結構域及不同的EGF結構域內之抗原決定基具有特異性之結合子進行定位。

圖2展示兩個例示性結合子，其結合於EGF-3區域內所包含之DLL3抗原決定基(在不包含EGF-3之各別截短DLL3構築體中缺失FACS信號)。圖2亦展示例示性結合子，其結合於EGF-3區域內所包含之DLL3抗原決定基(在不包含EGF-4之各別截短DLL3構築體中損失FACS信號)。

一些結合子描述為對由稱為EGF-5/[6]之區域定位的抗原決定基具有特異性。方括號意指對於僅具有左側EGF-6結構域之截短DLL3構築體(圖1中最後一個構築體)，結合子之FACS信號降低(亦即，既不完全存在，亦不完全缺失)。

以下實例中使用之雙特異性DLL3xCD3構築體選自具有「I2C」作為CD3結合域且具有與野生型人類血清白蛋白之C端融合物的構築體，參見例如SEQ ID NO:224-230、233-235、238-241。

實例3

基於Biacore確定與人類及食蟹猴DLL3之抗體親和力

Biacore分析實驗使用有雞白蛋白之重組型人類/食蟹猴DLL3-ECD融合蛋白進行，以確定本發明抗體構築體之目標結合。

詳言之，CM5感測子晶片(GE Healthcare)用大致600-800 RU相應重組型抗原使用乙酸鹽緩衝液(pH 4.5)根據製造商之手冊來固定。DLL3xCD3雙特異性抗體構築體樣品以以下濃度之稀釋系列裝載：在HBS-EP操作緩衝液(GE Healthcare)中稀釋之50 nM、25 nM、12.5 nM、6.25 nM及3.13 nM。流動速率為30 µl/min持續3分鐘，隨後又在30 µl/ml之流動速率下施用HBS-EP操作緩衝液持續8分鐘至20分鐘。晶片之再生使用10 mM甘胺酸、10 mM NaCl (pH 1.5)溶液進行。使用

BiaEval軟體分析資料集。一般進行兩個獨立實驗。

本發明之DLL3xCD3雙特異性抗體構築體展示針對人類DLL3之次奈莫耳範圍之極高親和力(除具有在極低的一個數位奈莫耳範圍內之KD值的DLL3-13以外)。平衡與獼猴DLL3之結合，亦展示類似範圍內之親和力。親和力值以及親和力差計算值展示於表2中。

表2：DLL3xCD3雙特異性抗體構築體對人類及獼猴DLL3之親和力，如藉由Biacore分析所測定，以及所計算之種間親和力差。

DLL3xCD3雙特異性抗體構築體	**KD hu DLL3 [nM]**	**KD cyno DLL3 [nM]**	**親和力差 KD mac/KD hu**
DLL3-4	0.41	0.55	1.34
DLL3-5	0.82	1.03	1.26
DLL3-6	0.55	0.75	1.36
DLL3-7	0.19	0.29	1.52
DLL3-8	0.69	0.96	1.39
DLL3-9	0.35	0.54	1.54
DLL3-10	0.24	0.33	1.38
DLL3-13	1.74	5.55	3.19
DLL3-14	0.47	0.86	1.83
DLL3-15	0.45	0.69	1.53

此外，在Biacore分析中證實雙特異性抗體構築體與人類CD3及獼猴CD3之結合在較低的2數位奈莫耳範圍內(資料未展示)。

實例4

基於Scatchard分析DLL3xCD3雙特異性抗體構築體與目標抗原陽性細胞上人類及獼猴DLL3之親和力，且確定種間親和力差

DLL3xCD3雙特異性抗體構築體與用人類或獼猴DLL3轉染之CHO細胞之親和力亦藉由作為量測人類與獼猴DLL3之間的潛在親和力差的最可靠方法的Scatchard分析確定。對於Scatchard分析，使用單價偵測系統進行飽和結合實驗以準確確定DLL3xCD3雙特異性抗體構築體與各別細胞株之單價結合。

相應細胞株之2×10^4個細胞(以重組方式表現人類DLL3之CHO細胞株，以重組方式表現獼猴DLL3之CHO細胞株)各與50 µl以10-20 nM

起始之三倍稀釋系列(以1:2進行十二次稀釋)之相應DLL3xCD3雙特異性抗體構築體(直至達到飽和)一起培育，之後在4℃下在攪拌下培育16 h及一個剩餘洗滌步驟。接著，再將細胞與30 µl CD3xALEXA488結合物溶液一起培育一小時。在一個洗滌步驟之後，使細胞再懸浮於150 µl含有3.5%甲醛之FACS緩衝液中，再培育15 min，離心，再懸浮於FACS緩衝液中且使用FACS CantoII機及FACS Diva軟體進行分析。自兩個獨立實驗組，各使用三份，得到資料。計算相應Scatchard分析以推知最大結合(Bmax)。確定半最大結合下DLL3xCD3雙特異性抗體構築體之濃度，反映相應KD。三份量測之值繪製成雙曲線及S形曲線，以表明極小至最佳結合範圍內之適當濃度。

表3中描繪之值來源於每個DLL3xCD3雙特異性抗體構築體之兩個獨立實驗。基於細胞之Scatchard分析證實本發明之DLL3xCD3雙特異性抗體構築體對人類DLL3及mac DLL3具有次奈莫耳親和力，且呈現約為1之小型食蟹猴/人類種間親和力差。

表3：DLL3xCD3雙特異性抗體構築體之親和力(KD)，如在基於細胞之Scatchard分析中測定，及所計算之親和力差KD獼猴DLL3/KD人類DLL3。在兩個獨立實驗中量測抗體構築體，各使用三份。

DLL3xCD3雙特異性抗體構築體	基於細胞之親和力 **hu DLL3 [nM]**	基於細胞之親和力 **mac DLL3 [nM]**	親和力差 **KD mac/KD hu**
DLL3-4	0.39	0.24	0.6
DLL3-5	0.33	0.22	0.7
DLL3-6	0.33	0.23	0.7
DLL3-7	0.21	0.33	1.6
DLL3-8	0.18	0.34	1.9
DLL3-9	0.30	0.49	1.6
DLL3-10	0.37	0.32	0.8
DLL3-13	0.24	0.29	1.2
DLL3-14	0.53	0.51	1.0
DLL3-15	0.25	0.50	2.0

實例5

雙特異性結合及種間交叉反應性

為確認結合於人類DLL3及CD3及食蟹獼猴DLL3及CD3，藉由流式細胞術使用以下各物測試本發明之雙特異性抗體構築體：

- CHO細胞分別用人類DLL3、人工人類DLL3同功異型物(由點突變F172C及L218P表徵)及獼猴DLL3轉染，
- 人類DLL3陽性人類肺癌瘤細胞株SHP-77，
- 表現CD3之人類T細胞白血病細胞株HPB-all (DSMZ, Braunschweig, ACC483)，及
- 表現食蟹猴CD3之T細胞株LnPx 4119

對於流式細胞測量術，在4℃下使相應細胞株之200,000個細胞與50 µl濃度為5 µg/ml之純化雙特異性抗體構築體一起培育60分鐘。細胞在4℃下用PBS/2% FCS洗滌兩次且接著與對雙特異性抗體構築體之CD3結合部分具有特異性的內部小鼠抗體(2 µg/ml)一起培育30分鐘。在洗滌之後，在4℃下結合之小鼠抗體用山羊抗小鼠Fcγ-PE (1:100)偵測30分鐘。樣品藉由流式細胞測量術量測。使用未轉染之CHO細胞作為陰性對照。

結果展示於圖3中。本發明之DLL3xCD3雙特異性抗體構築體將經人類DLL3、人工DLL3同功異型物及食蟹猴DLL3轉染之CHO細胞染色，且其亦將人類DLL3陽性人類肺癌瘤細胞株SHP-77 (天然表現物)染色。亦藉由雙特異性抗體構築體識別表現CD3之人類及食蟹猴T細胞株。此外，不存在陰性對照細胞(未經轉染之CHO，資料展示於實例6中)之染色。

實例6

確認不存在與人類旁系同源物之結合

將人類DLL3旁系同源物DLL1及DLL4穩定轉染至CHO細胞中。在序列表(SEQ ID NO:283及284)中鑑別本發明實例中所使用的旁系同源物之序列。在FACS分析中用對各別旁系同源物具有特異性之抗體

確認蛋白質表現：對於DLL4，抗體為抗人類DLL1 MAB1818 (R&D；5 μg/ml)，及抗人類DLL4 MAB1506 (R&D；5 μg/ml)。

如實例5中所描述進行流式細胞測量術分析，不同之處在於用山羊抗小鼠FITC (1:100)偵測所結合之小鼠抗體。結果展示於圖4中。分析證實本發明之DLL3xCD3雙特異性抗體構築體皆不與人類DLL3旁系同源物DLL1及DLL4交叉反應。

實例7

與人類生殖系之一致性

為分析抗體構築體與人類抗體生殖系基因之序列之一致性/相似性，本發明之DLL3結合域如下對準：將包括所有CDR之完整VL對準；將包括CDR 1及2但不包括CDR3之完整VH針對人類抗體生殖系基因(Vbase)對準。更多細節可現於本申請案之說明書中。結果展示於以下表4中：

表4：VH及VL與人類生殖系之一致性

DLL3xCD3雙特異性抗體構築體	與人類生殖系之一致性% [VH/VL]
DLL3-4	96.9 / 93.3
DLL3-5	96.9 / 96.6
DLL3-6	96.9 / 96.6
DLL3-7	93.9 / 96.6
DLL3-8	94.8 / 96.6
DLL3-9	96.9 / 95.5
DLL3-10	91.9 / 95.5
DLL3-13	95.9 / 95.7
DLL3-14	94.9 / 94.6
DLL3-15	93.9 / 94.6

實例8

細胞毒活性

在五個活體外細胞毒性分析中分析本發明之DLL3xCD3雙特異性抗體構築體對將效應子T細胞再引導至表現DLL3之目標細胞之效能：

- 在18小時51鉻釋放分析中量測DLL3xCD3雙特異性抗體構築體

對將刺激性人類CD8+效應子T細胞再引導至人類DLL3轉染之CHO細胞之效能。

• 在18小時51-鉻釋放分析中量測DLL3xCD3雙特異性抗體構築體再引導刺激性人類CD8+效應子T細胞針對DLL3陽性人類肺癌瘤細胞株SHP-77之效能。

• 在48小時基於FACS之細胞毒性分析中量測DLL3xCD3雙特異性抗體構築體對將非刺激性人類PBMC中之T細胞再引導至人類DLL3轉染之CHO細胞之效能。

• 在48小時基於FACS之細胞毒性分析中量測DLL3xCD3雙特異性抗體構築體再引導未刺激性人類PBMC中之T細胞針對DLL3陽性人類細胞株SHP-77之效能。

• 對於確認交叉反應性DLL3xCD3雙特異性抗體構築體能夠再引導獼猴T細胞針對經獼猴DLL3轉染之CHO細胞，用獼猴T細胞株作為效應子T細胞進行48小時基於FACS之細胞毒性分析。

實例8.1

使用刺激性人類T細胞之鉻釋放分析

如下文所述獲得富集$CD8^+$ T細胞之刺激性T細胞。在37℃下用最終濃度1 μg/ml之市售抗CD3特異性抗體(OKT3，Orthoclone)塗佈皮氏培養皿(petri dish)(直徑145 mm，Greiner bio-one GmbH, Kremsmünster)1小時。藉由一個用PBS洗滌之步驟移除未結合蛋白。將3-5×10^7個人類PBMC添加至預塗佈之皮氏培養皿中於120 ml具有穩定麩醯胺酸/10% FCS / IL-2 20 U/ml (Proleukin®，Chiron)之 RPMI 1640中且刺激2天。在第三天，收集細胞且用RPMI 1640洗滌一次。添加IL-2至最終濃度為20 U/ml且在與上文相同之細胞培養基中再培養細胞一天。使用Dynal-Beads根據製造商之方案藉由消耗$CD4^+$ T細胞及$CD56^+$ NK細胞$CD8^+$細胞使毒性T淋巴球(CTL)富集。

經食蟹猴DLL3或人類DLL3轉染之CHO目標細胞用PBS洗滌兩次且在37℃下在最終體積100 µl之具有50%FCS之RPMI中用11.1 MBq ^{51}Cr標記60分鐘。隨後，經標記之目標細胞用5 ml RPMI洗滌3次，且接著用於細胞毒性分析中。在96孔盤中於總體積200 µl之E:T比率10:1之補充型RPMI中進行分析。使用起始濃度0.01-1 µg/ml之純化雙特異性抗體構築體及其三倍稀釋液。分析之培育時間為18小時。細胞毒性經確定為上清液中釋放之鉻相對於最大溶解(添加Triton-X)及自發溶解(無效應細胞)之差值之相對值。一式四份進行所有量測。上清液中鉻活性之量測在Wizard 3" γ計數器中進行(Perkin Elmer Life Sciences GmbH, Köln, Germany)。對結果之分析用Windows用之Prism 5進行(5.0版，GraphPad Software Inc., San Diego, California, USA)。使用藉由分析程式由S形劑量反應曲線計算之EC50值比較細胞毒活性。

實例8.2

再引導刺激性人類效應子T細胞針對經人類DLL3轉染之CHO細胞之效能

在51-鉻(^{51}Cr)釋放細胞毒性分析中使用用人類DLL3轉染之CHO細胞作為目標細胞及刺激性人類CD8+ T細胞作為效應細胞來分析本發明之DLL3xCD3雙特異性抗體構築體之細胞毒活性。如實例8.1中所述進行實驗。

結果展示於表5中。DLL3xCD3雙特異性抗體構築體展示1數位皮莫耳範圍內之極有效之對經人類DLL3轉染之CHO細胞之細胞毒活性。

表5：使用經人類DLL3轉染之CHO細胞作為目標細胞及刺激性人類CD8 T細胞作為效應細胞之51-鉻(^{51}Cr)釋放細胞毒性分析中分析之DLL3xCD3雙特異性抗體構築體之EC50值[pM]。

DLL3xCD3雙特異性抗體構築體	EC50 [pM]
DLL3-4	3.8
DLL3-5	4.2
DLL3-6	2.1
DLL3-7	2.2
DLL3-8	1.2
DLL3-9	1.2
DLL3-10	1.4
DLL3-13	1.8
DLL3-14	5.4
DLL3-15	9.8

實例8.3

再引導刺激性人類效應子T細胞針對DLL3陽性人類肺癌瘤細胞株SHP-77之效能

在51-鉻(^{51}Cr)釋放細胞毒性分析中使用DLL3陽性人類肺癌瘤細胞株SHP至77作為目標細胞來源及刺激性人類CD8+ T細胞作為效應細胞來分析DLL3xCD3雙特異性抗體構築體之細胞毒活性。如實例8.1中所述進行分析。

根據使用刺激性富集之人類CD8+T淋巴球作為效應細胞及人類DLL3轉染之CHO細胞作為目標細胞之51-鉻釋放分析之結果，本發明之DLL3xCD3雙特異性抗體構築體對天然表現目標細胞亦具有有效細胞毒活性(參見表6)。

表6：在DLL3陽性人類肺癌瘤細胞株SHP-77作為目標細胞來源且刺激性富集人類CD8 T細胞作為效應細胞情況下，在18小時51-鉻(^{51}Cr)釋放細胞毒性分析中分析之DLL3xCD3雙特異性抗體構築體之EC50值[pM]。

列1-10：本發明之抗體構築體，其結合於如SEQ ID NO:260中所描繪之區域內所包含之DLL3抗原決定基(列1-7：結合於EGF-3區域內所包含之DLL3抗原決定基的抗體構築體。列8-10：結合於EGF-4區域內所包含之DLL3抗原決定基之抗體構築體)。列11-14：結合於EGF-

5/[EGF-6]區域內所包含之DLL3抗原決定基之抗體構築體。

列	DLL3xCD3雙特異性抗體構築體	EC50 [pM]
1	DLL3-4	27
2	DLL3-5	26
3	DLL3-6	18
4	DLL3-7	23
5	DLL3-8	39
6	DLL3-9	18
7	DLL3-10	31
8	DLL3-13	22
9	DLL3-14	31
10	DLL3-15	36
11	DLL3-18	38
12	DLL3-19	142
13	DLL3-20	171
14	DLL3-21	324

實例8.4

使用未刺激性人類PBMC之基於FACS之細胞毒性分析

分離效應細胞

藉由Ficoll密度梯度離心，自富集淋巴細胞之製劑(白血球層)(收集輸注用血液之血庫之副產物)製備人類周邊血液單核細胞(PBMC)。白血球層藉由本地血庫提供且在與血液收集同一天製備PBMC。在Ficoll密度離心及用達爾伯克氏PBS (Gibco)大規模洗滌之後，經由與紅血球溶解緩衝液(155 mM NH_4Cl、10 mM $KHCO_3$、100 μM EDTA)一起培育自PBMC移除剩餘紅血球。在100 x g下離心PBMC時，經由上清液移除血小板。剩餘淋巴球主要涵蓋B及T淋巴球、NK細胞及單核細胞。保持PBMC在37℃/5% CO_2下於具有10%FCS (Gibco)之RPMI培養基(Gibco)中培養。

消耗$CD14^+$及$CD56^+$細胞

對於$CD14^+$細胞之消耗，使用人類CD14 MicroBeads (Milteny Biotec, MACS, 編號130-050-201)，對於NK細胞之消耗，使用人類CD56 MicroBeads (MACS, 編號130-050-401)。對PBMC進行計數且在

室溫下用300 x g離心10分鐘。將上清液丟棄且細胞集結粒再懸浮於MACS分離緩衝液[80 μL/ 10^7個細胞；PBS (Invitrogen, 編號20012-043)、0.5% (v/v) FBS (Gibco, 編號10270-106)、2 mM EDTA (Sigma-Aldrich, 編號E-6511)]中。添加CD14 MicroBeads及CD56 MicroBeads(20 μL/10^7個細胞)且在4-8℃下培育15分鐘。用MACS分離緩衝液(1-2 mL/10^7個細胞)洗滌細胞。在離心(參見上文)之後，將上清液丟棄且細胞再懸浮於MACS分離緩衝液(500 μL/10^8個細胞)中。接著使用LS管柱(Miltenyi Biotec, 編號130-042-401)分離CD14/CD56陰性細胞。在培育箱中，在37℃下在補充有10% FBS (Biochrom AG，#S0115)、1x非必需胺基酸(Biochrom AG，#K0293)、10 mM Hepes緩衝液(Biochrom AG，#L1613)、1 mM丙酮酸鈉(Biochrom AG，#L0473)及100 U/mL青黴素/鏈黴素(Biochrom AG，#A2213)之RPMI完全培養基(亦即RPMI1640，Biochrom AG，#FG1215)中培養具有或不具有CD14+/CD56+細胞之PBMC直至需要。

目標細胞標記

對於用流式細胞測量術分析分析細胞溶解，使用作為目標細胞之螢光膜染料$DiOC_{18}$ (DiO) (Molecular Probes, 編號V22886)標記人類DLL3或獼猴DLL3轉染之CHO細胞且使其與效應細胞不同。簡言之，收集細胞，用PBS洗滌一次且於含有2% (v/v) FBS及膜染料DiO (5微升/10^6個細胞)之PBS中調節至10^6個細胞/毫升。在37℃下培育3分鐘後，用完全RPMI培養基洗滌細胞兩次且將細胞數調節至1.25×10^5個細胞/毫升。使用0.5% (v/v)等張EosinG溶液(Roth, #45380)測定細胞活力。

基於流動式細胞測量術之分析

此分析經設計以定量在DLL3雙特異性抗體構築體之連續稀釋液存在下經食蟹獼猴或人類DLL3轉染之CHO細胞的溶解。混合等體積

之DiO標記之目標細胞及效應細胞(亦即無$CD14^+$細胞之PBMC)，從而產生10:1之E:T細胞比率。將160 μl此懸浮液轉移至96孔盤之各孔中。添加40 μL DLL3xCD3雙特異性抗體構築體之連續稀釋液及陰性對照雙特異性(識別不相關目標抗原之基於CD3之雙特異性抗體構築體)或RPMI完全培養基作為額外陰性對照。雙特異性抗體介導之細胞毒性反應在7% CO_2含濕氣培育箱中進行48小時。隨後將細胞轉移至新96孔盤，且藉由添加最終濃度為1 μg/mL之碘化丙錠(PI)監測標靶細胞膜完整性之損失。PI為膜不可滲透性染料，其通常為活細胞所排斥，而死細胞吸收其且變得可由螢光發射鑑別。

藉由流式細胞術在FACSCanto儀器上量測樣品且藉由FACSDiva軟體(均來自Becton Dickinson)分析。目標細胞鑑別為DiO陽性細胞。將PI陰性目標細胞分類為活目標細胞。根據下式計算細胞毒性之百分比：

$$\text{細胞毒性}[\%] = \frac{n_{\text{死目標細胞}}}{n_{\text{目標細胞}}} \times 100$$

n=事件數

使用GraphPad Prism 5軟體(Graph Pad Software, San Diego)，相對於相應雙特異性抗體濃度繪製細胞毒性百分比之圖。用四參數邏輯回歸模型分析劑量反應曲線以評估具有固定之希爾斜率(hill slope)之S型劑量反應曲線且計算EC_{50}值。

實例8.5

將刺激性人類PBMC再引導至人類DLL3轉染之CHO細胞之效能

在基於FACS之細胞毒性分析中使用用人類DLL3轉染之CHO細胞作為目標細胞及非刺激性人類PBMC作為效應細胞來分析DLL3xCD3雙特異性抗體構築體之細胞毒活性。如以上實例8.4中所述進行分析。

非刺激性人類PBMC作為效應細胞且經人類DLL3轉染之CHO細胞作為目標之基於FACS之細胞毒性分析之結果展示於表7中。

表7：用非刺激性人類PBMC作為效應細胞且經人類DLL3轉染之CHO細胞作為目標細胞，在48小時基於FACS之細胞毒性分析中量測之DLL3xCD3雙特異性抗體構築體之EC50值[pM]。

列1-10：本發明之抗體構築體，其結合於如SEQ ID NO:260中所描繪之區域內所包含之DLL3抗原決定基(列1-7：結合於EGF-3區域內所包含之DLL3抗原決定基的抗體構築體。列8-10：結合於EGF-4區域內所包含之DLL3抗原決定基之抗體構築體)。列11-14：結合於EGF-5/[EGF-6]區域內所包含之DLL3抗原決定基之抗體構築體。

列	**DLL3xCD3雙特異性抗體構築體**	**EC50 [pM]**
1	DLL3-4	53
2	DLL3-5	36
3	DLL3-6	44
4	DLL3-7	40
5	DLL3-8	43
6	DLL3-9	43
7	DLL3-10	40
8	DLL3-13	116
9	DLL3-14	66
10	DLL3-15	57
11	DLL3-18	169
12	DLL3-19	107
13	DLL3-20	171
14	DLL3-21	85

預計與使用刺激性人類CD8+ T細胞之細胞毒性分析相比，在使用非刺激性PBMC作為效應細胞之細胞毒性分析中EC50值通常較高(參見實例8.2)。

實例8.6

再引導非刺激性人類PBMC針對DLL3陽性肺癌瘤細胞株SHP-77之效能

使用DLL3陽性人類肺癌瘤細胞株SHP-77作為目標細胞來源及非

刺激性人類PBMC作為效應細胞，在基於FACS之細胞毒性分析中進一步分析DLL3xCD3雙特異性抗體構築體之細胞毒活性。如以上實例8.4中所述進行分析。結果展示於表8中。

表8：用非刺激性人類PBMC作為效應細胞及人類細胞株SHP-77作為目標細胞來源，在48小時基於FACS之細胞毒性分析中量測之DLL3xCD3雙特異性抗體構築體之EC50值[pM]。

列1-10：本發明之抗體構築體，其結合於如SEQ ID NO:260中所描繪之區域內所包含之DLL3抗原決定基(列1-7：結合於EGF-3區域內所包含之DLL3抗原決定基的抗體構築體。列8-10：結合於EGF-4區域內所包含之DLL3抗原決定基之抗體構築體)。列11-14：結合於EGF-5/[EGF-6]區域內所包含之DLL3抗原決定基之抗體構築體。

列	**DLL3xCD3雙特異性抗體構築體**	**EC50 [pM]**
1	DLL3-4	44
2	DLL3-5	65
3	DLL3-6	31
4	DLL3-7	30
5	DLL3-8	24
6	DLL3-9	33
7	DLL3-10	32
8	DLL3-13	49
9	DLL3-14	65
10	DLL3-15	66
11	DLL3-18	76
12	DLL3-19	180
13	DLL3-20	1540
14	DLL3-21	770

實例8.7

獼猴T細胞再引導至表現獼猴DLL3之CHO細胞之效能

最終，在基於FACS之細胞毒性分析中使用用獼猴(食蟹猴)DLL3轉染之CHO細胞作為目標細胞及獼猴T細胞株4119LnPx (Knappe等人 Blood 95:3256-61 (2000))作為效應細胞來源來分析DLL3xCD3雙特異性抗體構築體之細胞毒活性。如上文所述進行獼猴DLL3轉染之CHO

細胞之目標細胞標記及細胞毒活性之基於流式細胞測量術之分析。

結果展示於表9中。藉由本發明之DLL3xCD3雙特異性抗體構築體誘導來自細胞株4119LnPx之獼猴T細胞有效殺死經獼猴DLL3轉染之CHO細胞。在此分析法中，抗體構築體有效呈現2數位皮莫耳EC50值，證實其在獼猴系統中活性極高。

表9：用獼猴T細胞株4119LnPx作為效應細胞及經獼猴DLL3轉染之CHO細胞作為目標細胞，在48小時基於FACS之細胞毒性分析中量測之DLL3xCD3雙特異性抗體構築體之EC50值[pM]。

列1-10：本發明之抗體構築體，其結合於如SEQ ID NO:260中所描繪之區域內所包含之DLL3抗原決定基(列1-7：結合於EGF-3區域內所包含之DLL3抗原決定基的抗體構築體。列8-10：結合於EGF-4區域內所包含之DLL3抗原決定基之抗體構築體)。列11-14：結合於EGF-5/[EGF-6]區域內所包含之DLL3抗原決定基之抗體構築體。

列	**DLL3xCD3雙特異性抗體構築體**	**EC50 [pM]**
1	DLL3-4	36
2	DLL3-5	42
3	DLL3-6	40
4	DLL3-7	101
5	DLL3-8	44
6	DLL3-9	58
7	DLL3-10	42
8	DLL3-13	65
9	DLL3-14	28
10	DLL3-15	32
11	DLL3-18	134
12	DLL3-19	66
13	DLL3-20	231
14	DLL3-21	86

實例9

在250 μg/ml下(i)三個凍/融循環及(ii)培育7天後單體至二聚體之轉化

使雙特異性DLL3xCD3抗體單體構築體依序經受不同應力條件、高性能SEC，以確定已轉化為二聚抗體構築體之最初單體抗體構築體

之百分比。

(i) 用通用調配物緩衝液將25 μg單體抗體構築體調節至濃度為250 μg/ml，且接著在-80℃下冷凍30分鐘，之後在室溫下解凍30分鐘。三個凍/融循環之後，藉由HP-SEC確定二聚體含量。

(ii) 用通用調配物緩衝液將25 μg單體抗體構築體調節至濃度為250 μg/ml，之後在37℃下培育7天。二聚體含量藉由HP-SEC確定。

將高解析度SEC管柱TSK Gel G3000 SWXL (Tosoh, Tokyo-Japan)連接至配備有A905自動取樣器之Äkta Purifier 10 FPLC (GE Lifesciences)。管柱平衡及操作緩衝液由100 mM KH2PO4 - 200 mM Na2SO4 (調節至pH 6.6)組成。將抗體溶液(25 μg蛋白質)施用於平衡管柱且在7 MPa之最大壓力下以0.75 ml/min之流動速率進行溶離。在280、254及210 nm光學吸光度下監測整個操作。藉由Äkta Unicorn軟體操作評估表中記錄之210 nm信號之峰積分進行分析。二聚體含量藉由二聚體峰之面積除以單體加二聚體峰之總面積來計算。

結果展示於以下表10中。本發明之DLL3xCD3雙特異性抗體構築體在三個凍/融循環之後呈現0.0%之二聚體百分比，且在37℃下培育7天之後具有≤2%之二聚體百分比。

表10：如藉由高效尺寸排阻層析(HP-SEC)測定之單體對比二聚DLL3xCD3雙特異性抗體構築體之百分比

DLL3xCD3雙特異性抗體構築體	**在三個凍/融循環之後的二聚體百分比**	**在37℃下培育7天之後的二聚體百分比**
DLL3-4	0.7	0.0
DLL3-5	1.5	0.0
DLL3-6	1.3	0.0
DLL3-7	1.2	0.0
DLL3-8	1.5	0.0
DLL3-9	1.8	0.0
DLL3-10	0.6	0.0
DLL3-13	1.6	0.0
DLL3-14	0.4	0.0
DLL3-15	1.2	0.0

實例10

熱穩定性

抗體聚集溫度如下確定：40 μl抗體構築體溶液以250 μg/ml轉移至單次使用光析槽中且置放於Wyatt動態光散射裝置DynaPro Nanostar (Wyatt)中。樣品以0.5℃/分鐘之加熱速率自40℃加熱至70℃，其中持續獲取量測半徑。DLS裝置遞送之套裝軟體使用指示蛋白及聚集熔融之半徑之增加以計算抗體構築體之聚集溫度。

所有測試之本發明之DLL3xCD3雙特異性抗體構築體展示聚集溫度≥45℃之熱穩定性，如以下表11中所示。結合於EGF-4區域(如SEQ ID NO:259中所描繪)內所包含之DLL3之抗原決定基的抗體構築體之群甚至具有≥50℃，更精確而言，≥54℃之熱穩定性。

表11：如藉由DLS (動態光散射)所測定之雙特異性抗體構築體之熱穩定性

DLL3xCD3雙特異性抗體構築體	**熱穩定性(DLS，℃，聚集)**
DLL3-4	59.3
DLL3-5	45.4
DLL3-6	58.8
DLL3-7	58.2
DLL3-8	49.8
DLL3-9	49.6
DLL3-10	52.9
DLL3-13	54.0
DLL3-14	57.0
DLL3-15	56.3

實例11

在人類血漿中培育24小時後之穩定性

純化之雙特異性抗體構築體在37℃下在人類血漿池中以1:5之比率在2-20 μg/ml之最終濃度下培育96小時。在血漿培育之後，在使用起始濃度為0.01-0.1 μg/ml之刺激性增濃之人類CD8+ T細胞及人類DLL3轉染之CHO細胞及10:1之效應子與目標細胞(E:T)之比率之51-鉻

釋放分析中比較抗體構築體(如實例8.1中所述之分析)。包括非培育性新近解凍之雙特異性抗體構築體作為對照物。

為展示於以下表12中，兩個抗體構築體DLL-4及DLL-14之例示性結果亦展示於圖5中。所有測試之抗體構築體具有≤2.5之極有利血漿穩定性(EC_{50}血漿/EC_{50}對照物)。結合於EGF-4區域(如SEQ ID NO:259中所描繪)內所包含之DLL3之抗原決定基的抗體構築體之群甚至具有≤1.5，更精確而言，≤1.1之血漿穩定性。

表12：在存在及不存在血漿培育情況下之抗體構築體之EC50值及所計算之血漿/對照物值

DLL3xCD3雙特異性抗體構築體	**EC_{50} [pM]**		**血漿與對照物比率(EC_{50}血漿/EC_{50}對照物)**
	具有血漿	不具有血漿	
DLL3-4	3.6	3.8	0.9
DLL3-5	5.4	4.2	1.3
DLL3-6	4.8	2.1	2.3
DLL3-7	2.7	2.2	1.2
DLL3-8	1.0	1.2	0.8
DLL3-9	1.2	1.2	1.0
DLL3-10	2.5	1.4	1.8
DLL3-13	2.0	1.8	1.1
DLL3-14	4.8	5.4	0.9
DLL3-15	7.8	9.8	0.8

實例12

2500 μg/ml抗體濃度下之渾濁度

藉由旋轉濃縮單元將1 ml濃度250 μg/ml之純化之抗體構築體溶液濃縮至2500 μg/ml。在5℃下存儲16小時之後，抗體溶液之濁度藉由針對通用調配物緩衝液之OD340 nm光學吸收量測來確定。

結果展示於以下表13中。除一個構築體具有稍微高於0.1之渾濁度以外，所有測試之抗體構築體具有≤0.1之極有利渾濁度。結合於EGF-4區域(如SEQ ID NO:259中所描繪)內所包含之DLL3之抗原決定基的抗體構築體之群甚至具有≤0.08之渾濁度。

表13：在濃縮至2.5 mg/ml隔夜之後抗體構築體之渾濁度

DLL3xCD3雙特異性抗體構築體	2500 μg/ml下之渾濁度 [OD340]
DLL3-4	0.073
DLL3-5	0.106
DLL3-6	0.080
DLL3-7	0.089
DLL3-8	0.069
DLL3-9	0.085
DLL3-10	0.091
DLL3-13	0.075
DLL3-14	0.073
DLL3-15	0.078

實例13

藉由高解析度陽離子交換層析得到之蛋白均質性

藉由高解析度陽離子交換層析CIEX分析本發明抗體構築體之蛋白均質性。

50 μg抗體構築體單體用50 ml結合緩衝液A (20 mM磷酸二氫鈉、30 mM NaCl、0.01%辛酸鈉，pH 5.5)稀釋且將40 ml此溶液施用於連接至Äkta Micro FPLC裝置(GE Healthcare, Germany)之1 ml BioPro SP-F管柱(YMC, Germany)中。在樣品結合之後，再用結合緩衝液實施洗滌步驟。對於蛋白溶離，施用超過10倍管柱體積之使用緩衝液B (20 mM磷酸二氫鈉、1000 mM NaCl、0.01%辛酸鈉，pH 5.5)高達50%緩衝液B之線性增加之鹽梯度。在280、254及210 nm光學吸光度下監測整個操作。藉由Äkta Unicorn軟體操作評估表中記錄之280 nm信號之峰積分進行分析。

結果展示於以下表14中。所有測試抗體構築體之極有利之均質性≥80% (主峰之曲線下面積(=AUC))。結合於EGF-3區域(如SEQ ID NO:258)中所描繪內所包含之DLL3之抗原決定基的抗體構築體之群甚至具有≥90%之均質性。

表14：抗體構築體之蛋白質均質性(主峰之AUC%)

DLL3xCD3雙特異性抗體構築體	蛋白質均質性主峰之AUC%
DLL3-4	96
DLL3-5	100
DLL3-6	95
DLL3-7	93
DLL3-8	100
DLL3-9	93
DLL3-10	90
DLL3-13	100
DLL3-14	100
DLL3-15	83

實例14

如藉由HIC Butyl所量測之表面疏水性

疏水性相互作用層析HIC中以流通模式測試本發明之雙特異性抗體構築體之表面疏水性。

將50 μg抗體構築體單體用通用調配物緩衝液稀釋至最終體積為500 μl (10 mM檸檬酸、75 mM離胺酸鹽酸鹽、4%海藻糖，pH 7.0)且施加於連接至Äkta Purifier FPLC系統(GE Healthcare, Germany)之1 ml Butyl Sepharose FF管柱(GE Healthcare, Germany)。在280、254及210 nm光學吸光度下監測整個操作。藉由Äkta Unicorn軟體操作評估表中記錄之280 nm信號之峰積分進行分析。溶離行為藉由比較蛋白信號之面積及升高及降低速度來評估，由此指示BiTE白蛋白融合物與基質之交互作用之強度。

抗體構築體具有良好溶離性質，其大部分為快速及完全的。

實例15

雙特異性抗體構築體之單體與二聚同功異型物之間的效能差

為確定個別DLL3xCD3雙特異性抗體構築體之單體與二聚同功異型物之間的細胞毒活性差(稱為效能差)，如上文所述用純化之雙特異性抗體構築體單體及二聚體進行18小時51-鉻釋放細胞毒性分析(實例8.1)。效應細胞為刺激性增濃之人類CD8+ T細胞。目標細胞為hu

DLL3經轉染之CHO細胞。效應子與目標細胞(E:T)之比率為10:1。效能差計算為EC50值之間的比率。

結果展示於以下表15中；兩個抗體構築體DLL-4及DLL-14之例示性結果亦展示於圖6中。所測試之DLL3xCD3雙特異性抗體構築體之效能差在0.2與1.0之間。因此與其各別單體相比，不存在實質上活性更高的二聚體。

表15：單體與二聚同功異型物之間的效能差

DLL3xCD3雙特異性抗體構築體	**EC_{50} [pM] 單體**	**EC_{50} [pM] 二聚體**	**比率 EC_{50}單體/EC_{50}二聚體**
DLL3-4	3.8	5.7	0.7
DLL3-5	4.2	11	0.4
DLL3-6	2.1	13	0.2
DLL3-7	2.2	4.2	0.5
DLL3-8	1.2	3.4	0.4
DLL3-9	1.2	3.8	0.3
DLL3-10	1.4	1.4	1.0
DLL3-13	1.8	3.0	0.6
DLL3-14	5.4	8.7	0.6
DLL3-15	9.8	25	0.4

實例16

活體外內化分析

在沒有T細胞存在下，量測隨著於目標細胞上預培育構築體而變化的DLL3xCD3雙特異性抗體構築體之效力變化。若抗體構築體進行內化，則其應經歷溶酶體降解作用。有效濃度應隨時間降低，且因此表觀效能亦應降低。觀測其他目標之作用(其中此為已知現象)，但未在DLL3xCD3雙特異性抗體構築體情況下觀測到影響。如下進行分析：

對T細胞進行計數且在分析培養基中稀釋至1×10^5個/毫升之濃度。對SHP-77細胞進行計數且以2500個細胞/孔(cpw)塗佈。抗體構築體在100 nM之起始濃度下以1:2(與Bravo一起)連續稀釋。向培養物分析盤中添加抗體構築體，允許培育0小時、1小時或2小時，隨後添加T

細胞。接著在25000 cpw下塗佈T細胞，且在37℃下培育分析物48小時。用Steady-Glo®系統(25微升/孔)分析SHP-77細胞存活期。結果展示於圖7中且未顯示抗體構築體DLL3-4 x CD3(I2C)之顯著內化。

實例17

排出研究

為了分析本發明之DLL3xCD3雙特異性抗體構築體之細胞毒活性是否因存在排出DLL顯著減弱，進行以下分析：對T細胞進行計數且在分析培養基中稀釋至1×10^5個/毫升之濃度。對SHP-77細胞進行計數且在具有0.3 nM與12 nM之間的增加之濃度之可溶性DLL3的分析培養基中稀釋至1.25×10^5個/毫升之濃度。SHP-77細胞以2500個細胞/孔(cpw)塗佈，且T細胞以25000 cpw添加。以1:2 (與Bravo一起)連續稀釋抗體構築體，且添加至分析培養物中(與Bravo一起)。在37℃下培育48小時。用Steady-Glo®系統(25微升/孔)分析SHP-77細胞存活期。

實例18

小鼠異種移植功效研究

在雌性NOD/SCID小鼠之模型中測試HLE DLL3xCD3雙特異性抗體構築體(SEQ ID NO:517)之抗腫瘤活性，該小鼠在研究第1天皮下注射5×10^6個人類DLL3陽性SCLC (SHP-77 luc)或5×10^6個人類DLL3陽性黑素瘤(WM 266-4)細胞。在第12天腹膜內注射效應細胞(2×10^7個活體外擴增及活化之活人類CD3+ T細胞)。處理在第16天(WM 266-4)或第18天(SHP-77 luc)開始。藉由靜脈內推注每五天投與四次(q5d×4)抗體構築體。處理組如下：

- SCLC模型(SHP-77 luc)/7隻小鼠/組
  - 具有T細胞之媒劑處理組
  - DLL3xCD3雙特異性抗體構築體：每次投藥10 mg/kg
- 黑素瘤模型(WM266-4)/9隻小鼠/組

- 具有T細胞之媒劑處理組
- DLL3xCD3雙特異性抗體構築體：每次投藥10 mg/kg
- DLL3xCD3雙特異性抗體構築體：每次投藥2 mg/kg

在研究期間藉由測徑規量測腫瘤且藉由組間比較腫瘤體積(TV)評估進展。藉由以T/C(%)=100×(分析組之中值TV)/(對照組之中值TV)形式計算腫瘤體積來測定第x天之腫瘤生長抑制T/C[%]，且計算值描繪於以下表16中：

表16:具有SHP-77 luc細胞及WM266-4細胞之小鼠異種移植研究之T/C值

研究天數	T/C (%) SHP-77模型 10 mg/kg	T/C (%) WM266-4模型 10 mg/kg	T/C (%) WM266-4模型 2 mg/kg
15	103	101	101
17	92	76	77
20	64	42	47
23	50	36	38
26	52	31	35
29	34	46	40
31	33	56	55
33	30	64	75
36	24	*n.a*	*n.a*
38	19	*n.a*	*n.a*

結果亦展示於圖8A及8B中。在兩個腫瘤模型及在2及10 mg/kg之測試劑量下皆展示顯著腫瘤生長抑制。

實例19

食蟹猴探索性毒理學研究

用非半衰期延長之DLL3xCD3雙特異性抗體構築體(SEQ ID NO:554)進行探索性毒理學研究。三隻雌性食蟹猴經由連續靜脈內輸注給藥16天(5、15及45微克/公斤/天各持續3天，接著100微克/公斤/天持續7天)。未觀測到與測試物相關之臨床觀測結果、體溫、食物消耗或體重變化。

符合對DLL3xCD3雙特異性抗體構築體之藥理學之預期，循環T

淋巴細胞群體(總T-淋巴細胞、T-輔助細胞及T-細胞毒性淋巴細胞、NK細胞、B-淋巴細胞及CD25+活化T-淋巴細胞)在給藥第一天降低且在所有動物中之研究持續時間內始終保持較低。活化標記物(經活化之T細胞上之CD69及CD25)在第1天增加，但在研究中之稍後時間點未增加。

總而言之，DLL3xCD3雙特異性抗體構築體即使在最高測試劑量(100微克/公斤/天，>300×EC_{50})下亦極良好耐受。

實例20

食蟹猴PK研究

用未經處理之雄性食蟹猴進行食蟹猴PK研究。三種不同白蛋白融合DLL3xCD3(I2C)雙特異性抗體構築體(DLL3-4、DLL3-6及DLL3-14)以靜脈內單次推注形式以12 μg/kg之濃度投與。對於每個分子，每組使用兩隻動物。

在相同條件下進行單獨的食蟹猴PK研究，但以不同Fc融合版本形式使用DLL3-4。

在給藥前及在給藥後0.05、0.5、1、4、8、24、48、72、120、168、240及336小時收集血液樣品。製備血清用於測定免疫分析中分子之血清濃度。藉由經由抗體構築體之目標部分捕獲抗體構築體來進行分析，而針對構築體之CD3結合部分之抗體用於偵測。使用血清濃度-時間概況測定PK參數。使用標準非間隔分析(NCA)法測定藥物動力學參數。評估以下PK參數：AUC_{inf} (血清濃度-時間曲線下面積)、V_{ss} (穩定狀態下之分佈體積)、CL (全身清除率)及終末$t_{1/2}$ (終末半衰期)。對於所有抗體構築體，在其投藥之後，所有動物中在所有時間點時的血清含量為可定量的。未在任何經處理之動物中進行臨床觀測。

所測試之抗體構築體之藥物動力學展示於圖9中，且PK參數在以

下表17中概述為n=2之平均值。

白蛋白融合構築體展示符合人類患者中每週一次或兩次給藥時程之有利的PK概況。在Fc融合構築體(scFc)情況下觀測到甚至更有利的支持每週一次給藥或甚至每隔一週給藥的PK概況。

表17：食蟹猴中DLL3xCD3雙特異性抗體構築體之HLE變異體之藥物動力學參數

抗體構築體	**AUC_{inf} [ng×h/mL]**	**V_{SS} [mL/kg]**	**CL [mL/h/kg]**	**$t_{1/2}$ [h]**
DLL3-4 x I2C HALB	20,669	70	0.58	98
DLL3-6 x I2C HALB	20,228	67	0.59	103
DLL3-14 x I2C HALB	21,597	107	0.55	154
DLL3-4 x I2C scFc	29,746	118	0.40	213
DLL3-4 (cc) x I2C scFc	24,769	144	0.48	234
DLL3-4 x I2C hetero Fc	14,639	166	0.82	173

表18：序列表

SEQ ID NO	DLL3 抗原決定基	名稱	型式/來源	胺基酸序列
1		**DLL3-1**	VH CDR1	DYGIH
2		**DLL3-1**	VH CDR2	VISYHGSNKYYARSVKG
3		**DLL3-1**	VH CDR3	EIPFGMDV
4		**DLL3-1**	VL CDR1	RSSQSLLHSDGYNYLD
5		**DLL3-1**	VL CDR2	LGSNRAS
6		**DLL3-1**	VL CDR3	MQALQTPLT
7		**DLL3-1**	VH	QVQLVESGGGVVQSGRSLRLSCAASGFTFSDYGIHWVRQAPGKGLEWVAVISYHGSNKYYARSVKGRFTVSRDNSKNTLYLQMNSLRAEDTAVYYCAREIPFGMDVWGQGTTVTVSS
8		**DLL3-1**	VL	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHSDGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLTISRVEAEDVGVYYCMQALQTPLTFGGGTKVDIK
9	**N端.**	**DLL3-1**	scFv	QVQLVESGGGVVQSGRSLRLSCAASGFTFSDYGIHWVRQAPGKGLEWVAVISYHGSNKYYARSVKGRFTVSRDNSKNTLYLQMNSLRAEDTAVYYCAREIPFGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSDGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLTISRVEAEDVGVYYCMQALQTPLTFGGGTKVDIK
10		**DLL3-1 xI2C**	雙特異性分子	QVQLVESGGGVVQSGRSLRLSCAASGFTFSDYGIHWVRQAPGKGLEWVAVISYHGSNKYYARSVKGRFTVSRDNSKNTLYLQMNSLRAEDTAVYYCAREIPFGMDVWGQGTTVTVSSGGGGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSDGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLTISRVEAEDVGVYYCMQALQTPLTFGGGTKVDIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
11		**DLL3-2**	VH CDR1	GYYMH
12		**DLL3-2**	VH CDR2	WINPNSGDTNYAQKFQG
13		**DLL3-2**	VH CDR3	DANIAALDAFEI
14		**DLL3-2**	VL CDR1	RASQSISSYLN
15		**DLL3-2**	VL CDR2	AASSLQS
16		**DLL3-2**	VL CDR3	QQSYSTPLT
17		**DLL3-2**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRVTMTRDTSISTAYMELSRLTSDDTAVYYCARDANIAALDAFEIWGQGTMVTVSS

18		**DLL3-2**	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK
19	**N端.**	**DLL3-2**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGDTNY AQKFQGRVTMTRDTSISTAYMELSRLTSDDTAVYYCARDANIAALDAFEIWGQGTMVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIK
20		**DLL3-2 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGDTNY AQKFQGRVTMTRDTSISTAYMELSRLTSDDTAVYYCARDANIAALDAFEIWGQGTMVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKSGGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYA DSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVS SGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAP RGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTV L
21		**DLL3-3**	VH CDR1	SYGMH
22		**DLL3-3**	VH CDR2	VISYHGRDTYYARSVKG
23		**DLL3-3**	VH CDR3	DGATVTSYYYSGMDV
24		**DLL3-3**	VL CDR1	RASQGISNYLA
25		**DLL3-3**	VL CDR2	LASSLQS
26		**DLL3-3**	VL CDR3	QQYNFYPFT
27		**DLL3-3**	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYHGRDTYYA RSVKGRFTISRDNSKNTLYLHMNSLRAEDTAVYYCARDGATVTSYYYSGMDVWGQGTTVTV SSK
28		**DLL3-3**	VL	DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWFQQKPGKAPKSLIYLASSLQSGVPSKFSGS GSGTDFTLTISSLQPEDFATYYCQQYNFYPFTFGPGTKVDIK
29	**EGF-1**	**DLL3-3**	scFv	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYHGRDTYYA RSVKGRFTISRDNSKNTLYLHMNSLRAEDTAVYYCARDGATVTSYYYSGMDVWGQGTTVTV SSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWFQQKPGKAPKS LIYLASSLQSGVPSKFSGSGSGTDFTLTISSLQPEDFATYYCQQYNFYPFTFGPGTKVDIK
30		**DLL3-3 xI2C**	雙特異性分子	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYHGRDTYYA RSVKGRFTISRDNSKNTLYLHMNSLRAEDTAVYYCARDGATVTSYYYSGMDVWGQGTTVTV SSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWFQQKPGKAPKS LIYLASSLQSGVPSKFSGSGSGTDFTLTISSLQPEDFATYYCQQYNFYPFTFGPGTKVDIKSGGG GSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYA TYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTL

				VTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKP GQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGT KLTVL
31		**DLL3-4**	VH CDR1	SYYWS
32		**DLL3-4**	VH CDR2	YVYYSGTTNYNPSLKS
33		**DLL3-4**	VH CDR3	IAVTGFYFDY
34		**DLL3-4**	VL CDR1	RASQRVNNNYLA
35		**DLL3-4**	VL CDR2	GASSRAT
36		**DLL3-4**	VL CDR3	QQYDRSPLT
37		**DLL3-4**	VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSS
38		**DLL3-4**	VL	EIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIK
39	**EGF-3**	**DLL3-4**	scFv	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIK
40		**DLL3-4 xI2C**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
41		**DLL3-5**	VH CDR1	SYYWS
42		**DLL3-5**	VH CDR2	YIYYSGRTNYYPSLKS
43		**DLL3-5**	VH CDR3	IAVAGFFFDY
44		**DLL3-5**	VL CDR1	RASQSVNKNYLA
45		**DLL3-5**	VL CDR2	GASSRAT
46		**DLL3-5**	VL CDR3	QQYDRSPLT
47		**DLL3-5**	VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYYSGRTNYYPSLK SRVTISIDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSS
48		**DLL3-5**	VL	EIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIK
49	**EGF-3**	**DLL3-5**	scFv	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYYSGRTNYYPSLK

				SRVTISIDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIK
50		**DLL3-5 xI2C**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYYSGRTNYYPSLK SRVTISIDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
51		**DLL3-6**	VH CDR1	SFYWS
52		**DLL3-6**	VH CDR2	YIYYSGTTNYNPSLKS
53		**DLL3-6**	VH CDR3	IAVAGFFFDY
54		**DLL3-6**	VL CDR1	RASQSVNKNYLA
55		**DLL3-6**	VL CDR2	GASSRAT
56		**DLL3-6**	VL CDR3	QQYDRSPLT
57		**DLL3-6**	VH	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSS
58		**DLL3-6**	VL	EIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIK
59	**EGF-3**	**DLL3-6**	scFv	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIK
60		**DLL3-6 xI2C**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
61		**DLL3-7**	VH CDR1	SFYWS
62		**DLL3-7**	VH CDR2	YIYYSGTTNYNPSLKS
63		**DLL3-7**	VH CDR3	IAVAGFFFDY

64		**DLL3-7**	VL CDR1	RASQSVNKNYLA
65		**DLL3-7**	VL CDR2	GASSRAT
66		**DLL3-7**	VL CDR3	QQYDRSPLT
67		**DLL3-7**	VH	QVQLQESGPGLVKPSQTLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSS
68		**DLL3-7**	VL	EIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIK
69	**EGF-3**	**DLL3-7**	scFv	QVQLQESGPGLVKPSQTLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIK
70		**DLL3-7 xI2C**	雙特異性分子	QVQLQESGPGLVKPSQTLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
71		**DLL3-8**	VH CDR1	SFYWS
72		**DLL3-8**	VH CDR2	YIYYSGTTNYNPSLKS
73		**DLL3-8**	VH CDR3	IAVAGFFFDY
74		**DLL3-8**	VL CDR1	RASQSVNKNYLA
75		**DLL3-8**	VL CDR2	GASSRAT
76		**DLL3-8**	VL CDR3	QQYDRSPLT
77		**DLL3-8**	VH	QVQLQEWGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLK SRVTISVDTSKNQLSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSK
78		**DLL3-8**	VL	EIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVDIK
79	**EGF-3**	**DLL3-8**	scFv	QVQLQEWGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLK SRVTISVDTSKNQLSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVDIK
80		**DLL3-8 xI2C**	雙特異性分子	QVQLQEWGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLK SRVTISVDTSKNQLSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG

				IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVDIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
81		**DLL3-9**	VH CDR1	SFYWS
82		**DLL3-9**	VH CDR2	YIYYSGTTNYNPSLKS
83		**DLL3-9**	VH CDR3	IAVAGFFFDY
84		**DLL3-9**	VL CDR1	RASQSVNKNYLA
85		**DLL3-9**	VL CDR2	GASSRAT
86		**DLL3-9**	VL CDR3	QQYDRSPLT
87		**DLL3-9**	VH	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSS
88		**DLL3-9**	VL	EIVLTQSPGTLSLSPGESATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSG SGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTRLEIK
89	**EGF-3**	**DLL3-9**	scFv	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGESATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTRLEIK
90		**DLL3-9** **xI2C**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGESATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTRLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
91		**DLL3-10**	VH CDR1	SYYWS
92		**DLL3-10**	VH CDR2	YIFYNGITNYNPSLKS
93		**DLL3-10**	VH CDR3	IHSGSFSFDY
94		**DLL3-10**	VL CDR1	RASQSVSRGYLA
95		**DLL3-10**	VL CDR2	GASSRAT
96		**DLL3-10**	VL CDR3	QQYDTSPIT
97		**DLL3-10**	VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIFYNGITNYNPSLKS RVTISLDTSKNQFSLKLSSVTAADTAKYYCARIHSGSFSFDYWDQGTLVTVSS
98		**DLL3-10**	VL	EIVMTQSPGTLSLSPGERATLSCRASQSVSRGYLAWYQQKPGQAPRLLIYGASSRATDIPDRFS

				GSGSGTDFTLTISRLEPEDFAVYYCQQYDTSPITFGQGTKVEIK
99	**EGF-3**	**DLL3-10**	scFv	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIFYNGITNYNPSLKS RVTISLDTSKNQFSLKLSSVTAADTAKYYCARIHSGSFSFDYWDQGTLVTVSSGGGGSGGGGS GGGGSEIVMTQSPGTLSLSPGERATLSCRASQSVSRGYLAWYQQKPGQAPRLLIYGASSRATDI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDTSPITFGQGTKVEIK
100		**DLL3-10 xI2C**	雙特異性分子	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIFYNGITNYNPSLKS RVTISLDTSKNQFSLKLSSVTAADTAKYYCARIHSGSFSFDYWDQGTLVTVSSGGGGSGGGGS GGGGSEIVMTQSPGTLSLSPGERATLSCRASQSVSRGYLAWYQQKPGQAPRLLIYGASSRATDI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDTSPITFGQGTKVEIKSGGGGSEVQLVESGGG LVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFT ISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSGG GGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKF LAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
101		**DLL3-11**	VH CDR1	NAGMS
102		**DLL3-11**	VH CDR2	RIKNKIDGGTTDFAAPVKG
103		**DLL3-11**	VH CDR3	RGWYGDYFDY
104		**DLL3-11**	VL CDR1	RSSQSLLHSNGYNYLD
105		**DLL3-11**	VL CDR2	LGSNRAS
106		**DLL3-11**	VL CDR3	MQALQTPFT
107		**DLL3-11**	VH	EVQLVESGGGLVKPGGSLRLSCAASGFIFNNAGMSWVRQAPGKGLEWVGRIKNKIDGGTTDF AAPVKGRFTISRDDSKNTLYLQMNSLKAEDTAVYYCTARGWYGDYFDYWGQGTLVTVSS
108		**DLL3-11**	VL	DIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVP DRFSGSGSGTDFTLKISRVEAEDVGIYYCMQALQTPFTFGPGTKVEIK
109	**EGF-3**	**DLL3-11**	scFv	EVQLVESGGGLVKPGGSLRLSCAASGFIFNNAGMSWVRQAPGKGLEWVGRIKNKIDGGTTDF AAPVKGRFTISRDDSKNTLYLQMNSLKAEDTAVYYCTARGWYGDYFDYWGQGTLVTVSSGG GGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQL LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGIYYCMQALQTPFTFGPGTKVEIK
110		**DLL3-11 xI2C**	雙特異性分子	EVQLVESGGGLVKPGGSLRLSCAASGFIFNNAGMSWVRQAPGKGLEWVGRIKNKIDGGTTDF AAPVKGRFTISRDDSKNTLYLQMNSLKAEDTAVYYCTARGWYGDYFDYWGQGTLVTVSSGG GGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQL LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGIYYCMQALQTPFTFGPGTKVEIKSGGG GSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYA TYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTL VTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKP GQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGT KLTVL

111		**DLL3-12**	VH CDR1	SYDIH
112		**DLL3-12**	VH CDR2	VISSHGSNKNYARSVKG
113		**DLL3-12**	VH CDR3	DGYSGNDPFYYYYHGMDV
114		**DLL3-12**	VL CDR1	RASQSISSYLN
115		**DLL3-12**	VL CDR2	AASSLQS
116		**DLL3-12**	VL CDR3	QQSFTTPLT
117		**DLL3-12**	VH	QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYDIHWVRQAPGKGLEWVAVISSHGSNKNYAR SVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCARDGYSGNDPFYYYYHGMDVWGQGTTV TVSS
118		**DLL3-12**	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS GSGTDFSLTISSLQPEDFATYYCQQSFTTPLTFGGGTKVEIK
119	**EGF-3/[4]**	**DLL3-12**	scFv	QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYDIHWVRQAPGKGLEWVAVISSHGSNKNYAR SVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCARDGYSGNDPFYYYYHGMDVWGQGTTV TVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFSLTISSLQPEDFATYYCQQSFTTPLTFGGGTKVEIK
120		**DLL3-12 xI2C**	雙特異性分子	QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYDIHWVRQAPGKGLEWVAVISSHGSNKNYAR SVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCARDGYSGNDPFYYYYHGMDVWGQGTTV TVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFSLTISSLQPEDFATYYCQQSFTTPLTFGGGTKVEIKSGG GGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNY ATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGT LVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQK PGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGG TKLTVL
121		**DLL3-13**	VH CDR1	SYYMH
122		**DLL3-13**	VH CDR2	IINPSDGSTNYAQNFQG
123		**DLL3-13**	VH CDR3	GGNSAFYSYYDMDV
124		**DLL3-13**	VL CDR1	RSSQSLVYRDGNTYLS
125		**DLL3-13**	VL CDR2	KVSNWQS
126		**DLL3-13**	VL CDR3	MQGTHWPPT
127		**DLL3-13**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSDGSTNYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
128		**DLL3-13**	VL	DVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVEIK
129	**EGF-4**	**DLL3-13**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSDGSTNYA

				QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVE IK
130		**DLL3-13 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSDGSTNYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
131		**DLL3-14**	VH CDR1	NYYMH
132		**DLL3-14**	VH CDR2	IINPSDGSTSYAQKFQG
133		**DLL3-14**	VH CDR3	GGNSAFYSYYDMDV
134		**DLL3-14**	VL CDR1	RSSQSLVYRDGNTYLS
135		**DLL3-14**	VL CDR2	KVSNWQS
136		**DLL3-14**	VL CDR3	MQGTHWPPT
137		**DLL3-14**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
138		**DLL3-14**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK
139	**EGF-4**	**DLL3-14**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIK
140		**DLL3-14 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW

				VFGGGTKLTVL
141		**DLL3-15**	VH CDR1	GYYIH
142		**DLL3-15**	VH CDR2	IINPSDGSTSYGQNFQG
143		**DLL3-15**	VH CDR3	GGNSAFYSYYDMDV
144		**DLL3-15**	VL CDR1	RSSQSLAYRDGNTYLS
145		**DLL3-15**	VL CDR2	KVSNWQS
146		**DLL3-15**	VL CDR3	MQGTHWPPT
147		**DLL3-15**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYIHWVRQAPGQGLEWMGIINPSDGSTSYGQNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVSS
148		**DLL3-15**	VL	DVVMTQSPLSLPVTLGQPASISCRSSQSLAYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVEIK
149	**EGF-4**	**DLL3-15**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYIHWVRQAPGQGLEWMGIINPSDGSTSYGQNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVSSGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLAYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVEIK
150		**DLL3-15 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYIHWVRQAPGQGLEWMGIINPSDGSTSYGQNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVSSGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLAYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVEIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
151		**DLL3-16**	VH CDR1	GHYMH
152		**DLL3-16**	VH CDR2	IINPSDGSTNYAQKFQG
153		**DLL3-16**	VH CDR3	GTTVVHYSYYDMDV
154		**DLL3-16**	VL CDR1	RSSQSLVYRDGNTYLT
155		**DLL3-16**	VL CDR2	KVSNWQS
156		**DLL3-16**	VL CDR3	MQGTHWPPT
157		**DLL3-16**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGHYMHWVRQAPGQGLEWMGIINPSDGSTNYAQKFQGRVTMTRDTSTSTVYMELRSLRSEDTAVYYCTRGTTVVHYSYYDMDVWGQGTTVTVSS
158		**DLL3-16**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLTWFQQRPGQSPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGGGTKVEIK

159	**EGF-4**	**DLL3-16**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGHYMHWVRQAPGQGLEWMGIINPSDGSTNYA QKFQGRVTMTRDTSTSTVYMELRSLRSEDTAVYYCTRGTTVVHYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLTWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGGGTKVE IK
160		**DLL3-16 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGHYMHWVRQAPGQGLEWMGIINPSDGSTNYA QKFQGRVTMTRDTSTSTVYMELRSLRSEDTAVYYCTRGTTVVHYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLTWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGGGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
161		**DLL3-17**	VH CDR1	NYFMH
162		**DLL3-17**	VH CDR2	IINPSDGSTSYAQNFQG
163		**DLL3-17**	VH CDR3	GGNSAFYSYYDMDV
164		**DLL3-17**	VL CDR1	RSSQSLVYRDGNTYLS
165		**DLL3-17**	VL CDR2	RVSNWQS
166		**DLL3-17**	VL CDR3	MQGTYWPPT
167		**DLL3-17**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYFMHWVRQAPGLGLEWMGIINPSDGSTSYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
168		**DLL3-17**	VL	DVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQSPRRLIYRVSNWQSGVP DRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTYWPPTFGQGTKVDIK
169	**EGF-4**	**DLL3-17**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYFMHWVRQAPGLGLEWMGIINPSDGSTSYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYRVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTYWPPTFGQGTKVD IK
170		**DLL3-17 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYFMHWVRQAPGLGLEWMGIINPSDGSTSYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYRVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTYWPPTFGQGTKVD IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW

				VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
171		**DLL3-18**	VH CDR1	NYGMH
172		**DLL3-18**	VH CDR2	VISHHGSSKYYARSVKG
173		**DLL3-18**	VH CDR3	DWWELVFDY
174		**DLL3-18**	VL CDR1	KSSQSLLHSDGKTFLY
175		**DLL3-18**	VL CDR2	EVSNRFS
176		**DLL3-18**	VL CDR3	LQGIHLPFT
177		**DLL3-18**	VH	QVQLVESGGGAVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAVISHHGSSKYYA RSVKGRFTISRDNSKNTLYLEMNSLRAEDTAVYYCARDWWELVFDYWGQGTLVTVSS
178		**DLL3-18**	VL	DIVMTQTPLSLSVTPGQPASISCKSSQSLLHSDGKTFLYWYLQKPGQPPQLLIYEVSNRFSGVPD RFSGSGSGTDFTLKISRVEAEDVGVYYCLQGIHLPFTFGPGTKVEIK
179	**EGF-5/[6]**	**DLL3-18**	scFv	QVQLVESGGGAVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAVISHHGSSKYYA RSVKGRFTISRDNSKNTLYLEMNSLRAEDTAVYYCARDWWELVFDYWGQGTLVTVSSGGGG SGGGGSGGGGSDIVMTQTPLSLSVTPGQPASISCKSSQSLLHSDGKTFLYWYLQKPGQPPQLLI YEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCLQGIHLPFTFGPGTKVEIK
180		**DLL3-18 xI2C**	雙特異性分子	QVQLVESGGGAVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAVISHHGSSKYYA RSVKGRFTISRDNSKNTLYLEMNSLRAEDTAVYYCARDWWELVFDYWGQGTLVTVSSGGGG SGGGGSGGGGSDIVMTQTPLSLSVTPGQPASISCKSSQSLLHSDGKTFLYWYLQKPGQPPQLLI YEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCLQGIHLPFTFGPGTKVEIKSGGGGS EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKL TVL
181		**DLL3-19**	VH CDR1	NSRMGVS
182		**DLL3-19**	VH CDR2	HIFSNDGKSYSTSLKS
183		**DLL3-19**	VH CDR3	YNYDSSGYYYSFFDY
184		**DLL3-19**	VL CDR1	RASQSISSYLN
185		**DLL3-19**	VL CDR2	AASSLQS
186		**DLL3-19**	VL CDR3	QQGYSSPFT
187		**DLL3-19**	VH	QVTLKESGPMLVKPTETLTLTCTVSGFSLSNSRMGVSWIRQPPGRALEWLAHIFSNDGKSYSTS LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYNYDSSGYYYSFFDYWGQGTLVTVSS
188		**DLL3-19**	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQGYSSPFTFGGGTKVEIK
189	**EGF-**	**DLL3-19**	scFv	QVTLKESGPMLVKPTETLTLTCTVSGFSLSNSRMGVSWIRQPPGRALEWLAHIFSNDGKSYSTS

	5/[6]			LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYNYDSSGYYYSFFDYWGQGTLVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGYSSPFTFGGGTKVEIK
190		**DLL3-19 xI2C**	雙特異性分子	QVTLKESGPMLVKPTETLTLTCTVSGFSLSNSRMGVSWIRQPPGRALEWLAHIFSNDGKSYSTS LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYNYDSSGYYYSFFDYWGQGTLVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGYSSPFTFGGGTKVEIKSGGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYA DSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVS SGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAP RGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTV L	
191		**DLL3-20**	VH CDR1	NARMGVS
192		**DLL3-20**	VH CDR2	HIFSTDEKSYSTSLKS
193		**DLL3-20**	VH CDR3	YYYDSSGYYYSFFDY
194		**DLL3-20**	VL CDR1	RASQSIRSYLN
195		**DLL3-20**	VL CDR2	GASNLQS
196		**DLL3-20**	VL CDR3	QQSYSSPFT
197		**DLL3-20**	VH	QVTLKESGPVLVKPTETLTLTCTVSGFSLSNARMGVSWLRQPPGKALEWLAHIFSTDEKSYSTS LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYYYDSSGYYYSFFDYWGQGTLVTVSS
198		**DLL3-20**	VL	DIQMTQSPSSLSASVGDRVTITCRASQSIRSYLNWYQQKPGKAPKLLIYGASNLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQSYSSPFTFGGGTKVEIK
199	**EGF-5/[6]**	**DLL3-20**	scFv	QVTLKESGPVLVKPTETLTLTCTVSGFSLSNARMGVSWLRQPPGKALEWLAHIFSTDEKSYSTS LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYYYDSSGYYYSFFDYWGQGTLVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSIRSYLNWYQQKPGKAPKLLIY GASNLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSSPFTFGGGTKVEIK
200		**DLL3-20 xI2C**	雙特異性分子	QVTLKESGPVLVKPTETLTLTCTVSGFSLSNARMGVSWLRQPPGKALEWLAHIFSTDEKSYSTS LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYYYDSSGYYYSFFDYWGQGTLVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSIRSYLNWYQQKPGKAPKLLIY GASNLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSSPFTFGGGTKVEIKSGGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTV SSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQA PRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLT VL
201		**DLL3-21**	VH CDR1	SYYIH

202		**DLL3-21**	VH CDR2	IINPSGGSKSYAQKFRG
203		**DLL3-21**	VH CDR3	SMSTVTSDAFDI
204		**DLL3-21**	VL CDR1	RASQSISNYLN
205		**DLL3-21**	VL CDR2	AASSLQS
206		**DLL3-21**	VL CDR3	QQSYSAPLT
207		**DLL3-21**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYAFTSYYIHWVRQAPGQGLEWMGIINPSGGSKSYAQ KFRGRVTMTRDTSTSTVYMELSSLTSEDTAVYYCARSMSTVTSDAFDIWGQGTMVTVSS
208		**DLL3-21**	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISNYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS GSGTEFTLTISSLQPEDFATYYCQQSYSAPLTFGGGTKVDIK
209	**EGF-5/[6]**	**DLL3-21**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYAFTSYYIHWVRQAPGQGLEWMGIINPSGGSKSYAQ KFRGRVTMTRDTSTSTVYMELSSLTSEDTAVYYCARSMSTVTSDAFDIWGQGTMVTVSSGGG GSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISNYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQSYSAPLTFGGGTKVDIK
210		**DLL3-21 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYAFTSYYIHWVRQAPGQGLEWMGIINPSGGSKSYAQ KFRGRVTMTRDTSTSTVYMELSSLTSEDTAVYYCARSMSTVTSDAFDIWGQGTMVTVSSGGG GSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISNYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQSYSAPLTFGGGTKVDIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSG GGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRG LIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
211	**EGF-3**	**DLL3-4 xF12Q**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
212	**EGF-3**	**DLL3-5 xF12Q**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYYSGRTNYYPSLK SRVTISIDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL

213	**EGF-3**	**DLL3-6 xF12Q**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
214	**EGF-3**	**DLL3-7 xF12Q**	雙特異性分子	QVQLQESGPGLVKPSQTLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
215	**EGF-3**	**DLL3-8 xF12Q**	雙特異性分子	QVQLQEWGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLK SRVTISVDTSKNQLSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVDIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
216	**EGF-3**	**DLL3-9 xF12Q**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGESATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTRLEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
217	**EGF-3**	**DLL3-10 xF12Q**	雙特異性分子	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIFYNGITNYNPSLKS RVTISLDTSKNQFSLKLSSVTAADTAKYYCARIHSGSFSFDYWDQGTLVTVSSGGGGSGGGGS GGGGSEIVMTQSPGTLSLSPGERATLSCRASQSVSRGYLAWYQQKPGQAPRLLIYGASSRATDI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDTSPITFGQGTKVEIKSGGGGSEVQLVESGGG LVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRFTI

				SRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGSGG GGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKF LAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
218	**EGF-4**	**DLL3-13 xF12Q**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSDGSTNYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
219	**EGF-4**	**DLL3-14 xF12Q**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWA YWGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYP NWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNR WVFGGGTKLTVL
220	**EGF-4**	**DLL3-15 xF12Q**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYIHWVRQAPGQGLEWMGIINPSDGSTSYGQ NFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVSS GGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLAYRDGNTYLSWFQQRPGQS PRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVEI KSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
221	**N端.**	**DLL3-1 xI2C-HALB 變異體 1**	雙特異性分子-HALB變異體1	QVQLVESGGGVVQSGRSLRLSCAASGFTFSDYGIHWVRQAPGKGLEWVAVISYHGSNKYYAR SVKGRFTVSRDNSKNTLYLQMNSLRAEDTAVYYCAREIPFGMDVWGQGTTVTVSSGGGGSG GGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSDGYNYLDWYLQKPGQSPQLLIYL GSNRASGVPDRFSGSGSGTDFTLTISRVEAEDVGVYYCMQALQTPLTFGGGTKVDIKSGGGGS EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQ

				APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKL TVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTC VADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRL VRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAAC LLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLT KVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADL PSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAA DPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVS RNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFS ALEVDETYVPKEFNAGTFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAAMDDFA AFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
222	N端.	**DLL3-2 xI2C-HALB 變異體 1**	雙特異性分子-HALB變異體1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGDTNY AQKFQGRVTMTRDTSISTAYMELSRLTSDDTAVYYCARDANIAALDAFEIWGQGTMVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGGGTKVEIKSGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYA DSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVS SGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAP RGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTV LPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVA DESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVR PEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLP KLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVH TECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLA ADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHE CYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLG KVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEV DETYVPKEFNAGTFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAAMDDFAAFVE KCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
223	EGF-1	**DLL3-3 xI2C-HALB**	雙特異性分子-HALB	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYHGRDTYYA RSVKGRFTISRDNSKNTLYLHMNSLRAEDTAVYYCARDGATVTSYYYSGMDVWGQGTTVTV SSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWFQQKPGKAPKS LIYLASSLQSGVPSKFSGSGSGTDFTLTISSLQPEDFATYYCQQYNFYPFTFGPGTKVDIKSGGG GSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYA TYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTL VTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKP GQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGT

			KLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAK TCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLP RLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKA ACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTD LTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPA DLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCA AADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVE VSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPC FSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDD FAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHHH
224	**EGF-3**	**DLL3-4 xl2C-HALB** 雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGS DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGLHHHHHH
225	**EGF-3**	**DLL3-5 xl2C-HALB** 雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYYSGRTNYYPSLK SRVTISIDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGS DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC

				DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGLHHHHHHH
226	**EGF-3**	**DLL3-6 xI2C-HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGS DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGLHHHHHHH
227	**EGF-3**	**DLL3-7 xI2C-HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSQTLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGS DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC

				TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGLHHHHHH
228	EGF-3	**DLL3-8 xI2C-HALB**	雙特異性分子-HALB	QVQLQEWGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLK SRVTISVDTSKNQLSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVDIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGS DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGLHHHHHH
229	EGF-3	**DLL3-9 xI2C-HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGESATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTRLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGS DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD

				EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGLHHHHHHH
230	**EGF-3**	**DLL3-10 xI2C-HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIFYNGITNYNPSLKS RVTISLDTSKNQFSLKLSSVTAADTAKYYCARIHSGSFSFDYWDQGTLVTVSSGGGSGGGGS GGGGSEIVMTQSPGTLSLSPGERATLSCRASQSVSRGYLAWYQQKPGQAPRLLIYGASSRATDI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDTSPITFGQGTKVEIKSGGGGSEVQLVESGGG LVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFT ISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSGG GGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKF LAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGSDA HKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENCDK SLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTA FHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEG KASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLL ECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDV CKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVFDEF KPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCCKH PEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFN AETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKE TCFAEEGKKLVAASQAALGLHHHHHHH
231	**EGF-3**	**DLL3-11 xI2C-HALB**	雙特異性分子-HALB	EVQLVESGGGLVKPGGSLRLSCAASGFIFNNAGMSWVRQAPGKGLEWVGRIKNKIDGGTTDF AAPVKGRFTISRDDSKNTLYLQMNSLKAEDTAVYYCTARGWYGDYFDYWGQGTLVTVSSGG GGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQL LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGIYYCMQALQTPFTFGPGTKVEIKSGGG GSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYA TYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTL VTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKP GQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGT KLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAK TCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLP RLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKA ACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTD

				LTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPA DLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCA AADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVE VSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPC FSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDD FAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
232	**EGF-3/[4]**	**DLL3-12 xI2C-HALB**	雙特異性分子-HALB	QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYDIHWVRQAPGKGLEWVAVISSHGSNKNYAR SVKGRFTISRDNSKNTLYLQMNSLKAEDTAVYYCARDGYSGNDPFYYYYHGMDVWGQGTTV TVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFSLTISSLQPEDFATYYCQQSFTTPLTFGGGTKVEIKSGG GGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNY ATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGT LVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQK PGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGG TKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFA KTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNL PRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKA ACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTD LTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPA DLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCA AADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVE VSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPC FSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDD FAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
233	**EGF-4**	**DLL3-13 xI2C-HALB**	雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSDGSTNYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYFCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEV TEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDD NPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQA ADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSK LVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDE

				MPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEK CCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPT LVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNR RPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV MDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
234	**EGF-4**	**DLL3-14 xI2C-HALB**	雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNE VTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKD DNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQ AADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVS KLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVEND EMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLE KCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTP TLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVN RRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV MDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
235	**EGF-4**	**DLL3-15 xI2C-HALB**	雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYIHWVRQAPGQGLEWMGIINPSDGSTSYGQ NFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVSS GGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLAYRDGNTYLSWFQQRPGQS PRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYFCMQGTHWPPTFGQGTKVEI KSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEV TEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDD NPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQA ADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSK LVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDE MPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEK

				CCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPT
				LVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNR
				RPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV
				MDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
236	EGF-4	DLL3-16 xI2C-HALB	雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGHYMHWVRQAPGQGLEWMGIINPSDGSTNYA
				QKFQGRVTMTRDTSTSTVYMELRSLRSEDTAVYYCTRGTTVVHYSYYDMDVWGQGTTVTVS
				SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLTWFQQRPGQ
				SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGGGTKVE
				IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK
				YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW
				GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW
				VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV
				FGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEV
				TEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDD
				NPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQA
				ADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSK
				LVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDE
				MPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEK
				CCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPT
				LVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNR
				RPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV
				MDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
237	EGF-4	DLL3-17 xI2C-HALB	雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYFMHWVRQAPGLGLEWMGIINPSDGSTSYA
				QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS
				SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ
				SPRRLIYRVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTYWPPTFGQGTKVD
				IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK
				YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW
				GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW
				VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV
				FGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEV
				TEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDD
				NPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQA
				ADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSK
				LVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDE
				MPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEK
				CCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPT

				LVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNR RPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV MDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
238	**EGF-5/[6]**	**DLL3-18 xI2C-HALB**	雙特異性分子-HALB	QVQLVESGGGAVQPGRSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAVISHHGSSKYYA RSVKGRFTISRDNSKNTLYLEMNSLRAEDTAVYYCARDWWELVFDYWGQGTLVTVSSGGGG SGGGGSGGGGSDIVMTQTPLSLSVTPGQPASISCKSSQSLLHSDGKTFLYWYLQKPGQPPQLLI YEVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCLQGIHLPFTFGPGTKVEIKSGGGGS EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKL TVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTC VADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRL VRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAAC LLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLT KVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADL PSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAA DPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVS RNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFS ALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFA AFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
239	**EGF-5/[6]**	**DLL3-19 xI2C-HALB**	雙特異性分子-HALB	QVTLKESGPMLVKPTETLTLTCTVSGFSLSNSRMGVSWIRQPPGRALEWLAHIFSNDGKSYSTS LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYNYDSSGYYYSFFDYWGQGTLVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYA ASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGYSSPFTFGGGTKVEIKSGGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYA DSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVS SGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAP RGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTV LPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVA DESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVR PEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLP KLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVH TECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLA ADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHE CYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLG KVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEV

				DETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVE KCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
240	**EGF-5/[6]**	**DLL3-20 xI2C-HALB**	雙特異性分子-HALB	QVTLKESGPVLVKPTETLTLTCTVSGFSLSNARMGVSWLRQPPGKALEWLAHIFSTDEKSYSTS LKSRLTISKDTSKSQVVLTMTNMDPVDTATYYCARYYYDSSGYYYSFFDYWGQGTLVTVSSG GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSIRSYLNWYQQKPGKAPKLLIY GASNLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSSPFTFGGGTKVEIKSGGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTV SSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQA PRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLT VLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCV ADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLV RPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLL PKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKV HTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSL AADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADP HECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRN LGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSAL EVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAF VEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHH
241	**EGF-5/[6]**	**DLL3-21 xI2C-HALB**	雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYAFTSYYIHWVRQAPGQGLEWMGIINPSGGSKSYAQ KFRGRVTMTRDTSTSTVYMELSSLTSEDTAVYYCARSMSTVTSDAFDIWGQGTMVTVSSGGG GSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISNYLNWYQQKPGKAPKLLIYAAS SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQSYSAPLTFGGGTKVDIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSG GGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRG LIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPG GGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADES AENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEV DVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKL DELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTE CCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAAD FVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECY AKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKV GSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDET YVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCC

				KADDKETCFAEEGKKLVAASQAALGLHHHHHH
242	**EGF-3**	**DLL3-4 xF12Q - HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGG SDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAEN CDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVM CTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELR DEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVES KDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKV FDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSK CCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGKKLVAASQAALGLHHHHHH
243	**EGF-3**	**DLL3-5 xF12Q - HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYYSGRTNYYPSLK SRVTISIDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGG SDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAEN CDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVM CTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELR DEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVES KDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKV FDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSK CCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGKKLVAASQAALGLHHHHHH

244	**EGF-3**	**DLL3-6 xF12Q - HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGG SDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAEN CDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVM CTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELR DEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVES KDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKV FDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSK CCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGKKLVAASQAALGLHHHHHH
245	**EGF-3**	**DLL3-7 xF12Q - HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSQTLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGG SDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAEN CDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVM CTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELR DEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVES KDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKV FDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSK CCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGKKLVAASQAALGLHHHHHH
246	**EGF-3**	**DLL3-8**	雙特異性分	QVQLQEWGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLK

		xF12Q - HALB	子-HALB	SRVTISVDTSKNQLSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVDIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGG SDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAEN CDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVM CTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELR DEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVES KDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKV FDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSK CCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGKKLVAASQAALGLHHHHHH
247	**EGF-3**	**DLL3-9 xF12Q - HALB**	雙特異性分子-HALB	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGESATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTRLEIKSGGGGSEVQLVESGG GLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRF TISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGS GGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGG SDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAEN CDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVM CTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELR DEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHG DLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVES KDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKV FDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSK CCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGKKLVAASQAALGLHHHHHH
248	**EGF-3**	**DLL3-10 xF12Q -**	雙特異性分子-HALB	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIFYNGITNYNPSLKS RVTISLDTSKNQFSLKLSSVTAADTAKYYCARIHSGSFSFDYWDQGTLVTVSSGGGGSGGGGS

		HALB	GGGGSEIVMTQSPGTLSLSPGERATLSCRASQSVSRGYLAWYQQKPGQAPRLLIYGASSRATDI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDTSPITFGQGTKVEIKSGGGGSEVQLVESGGG LVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKGRFTI SRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLVTVSSGGGGSGG GGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKF LAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLPGGGGSDA HKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENCDK SLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTA FHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEG KASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLL ECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDV CKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVFDEF KPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCCKH PEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFN AETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKE TCFAEEGKKLVAASQAALGLHHHHHHH
249	**EGF-4**	**DLL3-13 xF12Q HALB** - 雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSDGSTNYA QNFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNE VTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKD DNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQ AADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVS KLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVEND EMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLE KCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTP TLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVN RRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV MDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGLHHHHHHH
250	**EGF-4**	**DLL3-14 xF12Q HALB** - 雙特異性分子-HALB	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ

				SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV
				EIKSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRS
				KYNNYATYYADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWA
				YWGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYP
				NWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNR
				WVFGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVN
				EVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHK
				DDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECC
				QAADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEV
				SKLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVEN
				DEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTL
				EKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVST
				PTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLV
				NRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKA
				VMDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGL**HHHHHH**
251	**EGF-4**	**DLL3-15 xF12Q HALB** - 雙特異性分子-HALB		QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYIHWVRQAPGQGLEWMGIINPSDGSTSYGQ
				NFQGRVTMTRDTSTNTVYMELSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVSS
				GGGGSGGGGSGGGGSDVVMTQSPLSLPVTLGQPASISCRSSQSLAYRDGNTYLSWFQQRPGQS
				PRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCMQGTHWPPTFGQGTKVEI
				KSGGGGSEVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSK
				YNNYATYYADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAY
				WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN
				WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW
				VFGGGTKLTVLPGGGGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNE
				VTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKD
				DNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQ
				AADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVS
				KLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVEND
				EMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLE
				KCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTP
				TLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVN
				RRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAV
				MDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGL**HHHHHH**
252	-	人類**DLL3**	人類	MVSPRMSGLLSQTVILALIFLPQTRPAGVFELQIHSFGPGPGAPRSPCSARLPCRLFFRVCLKP
				GLSEEAAESPCALGAALSARGPVYTEQPGAPAPDLPLPDGLLQVPFRDAWPGTFSFIIETWREE
				LGDQIGGPAWSLLARVAGRRRLAAGGPWARDIQRAGAWELRFSYRARCEPPAVGTACTRLCR
				PRSAPSRCGPGLRPCAPLEDECEAPLVCRAGCSPEHGFCEQPGECRCLEGWTGPLCTVPVSTSS

				CLSPRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPRSFECTCPRGFYGLRCEVSGVTCADGP CFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAG FAGPRCEHDLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGR CYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYLLPPALGLLVAAGV AGAALLLVHVRRRGHSQDAGSRLLAGTPEPSVHALPDALNNLRTQEGSGDGPSSSVDWNRPE DVDPQGIYVISAPSIYAREVATPLFPPLHTGRAGQRQHLLFPYPSSILSVK
253	-	**人類DLL3 ECD**	人類	MVSPRMSGLLSQTVILALIFLPQTRPAGVFELQIHSFGPGPGPGAPRSPCSARLPCRLFFRVCLKP GLSEEAAESPCALGAALSARGPVYTEQPGAPAPDLPLPDGLLQVPFRDAWPGTFSFIIETWREE LGDQIGGPAWSLLARVAGRRRLAAGGPWARDIQRAGAWELRFSYRARCEPPAVGTACTRLCR PRSAPSRCGPGLRPCAPLEDECEAPLVCRAGCSPEHGFCEQPGECRCLEGWTGPLCTVPVSTSS CLSPRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPRSFECTCPRGFYGLRCEVSGVTCADGP CFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAG FAGPRCEHDLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGR CYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYL
254	-	**Hu DLL3 N端.**	人類	MVSPRMSGLLSQTVILALIFLPQTRPAGVFELQIHSFGPGPGPGAPRSPCSARLPCRLFFRVCLKP GLSEEAAESPCALGAALSARGPVYTEQPGAPAPDLPLPDGLLQVPFRDAWPGTFSFIIETWREE LGDQIGGPAWSLLARVAGRRRLAAGGPWARDIQRAGAWELRFSYR
255	-	**Hu DLL3 DSL dom**	人類	ARCEPPAVGTACTRLCRPRSAPSRCGPGLRPCAPLEDECE
256	-	**Hu DLL3 EGF-1**	人類	APLVCRAGCSPEHGFCEQPGECRCLEGWTGPLCT
257	-	**Hu DLL3 EGF-2**	人類	GPGPCDGNPCANGGSCSETPRSFECTCPRGFYGLRCE
258	-	**Hu DLL3 EGF-3**	人類	SGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFQGSNCE
259	-	**Hu DLL3 EGF-4**	人類	RVDRCSLQPCRNGGLCLDLGHALRCRCRAGFAGPRCE
260	-	**Hu DLL3 EGF-3+4**	人類	SGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGH ALRCRCRAGFAGPRCE
261	-	**Hu DLL3 EGF-5**	人類	DLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCR
262	-	**Hu DLL3 EGF-6**	人類	RADPCAARPCAHGGRCYAHFSGLVCACAPGYMGARCE
263	-	**人類 DLL3**	人工	MVSPRMSGLLSQTVILALIFLPQTRPAGVFELQIHSFGPGPGPGAPRSPCSARLPCRLFFRVCLKP GLSEEAAESPCALGAALSARGPVYTEQPGAPAPDLPLPDGLLQVPFRDAWPGTFSFIIETWREE LGDQIGGPAWSLLARVAGRRRLAAGGPWARDIQRAGAWELRFSYRARCEPPAVGTACTRLCR

		ECD x EpCAM		PRSAPSRCGPGLRPCAPLEDECEAPLVCRAGCSPEHGFCEQPGECRCLEGWTGPLCTVPVSTSS CLSPRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPRSFECTCPRGFYGLRCEVSGVTCADGP CFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAG FAGPRCEHDLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGR CYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYLSGGGGSGAGVIAVI VVVVIAIVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA
264	-	**V5 x hu DLL3-DSL x EpCAM**	人工	MGWSCIILFLVATATGVHSGKPIPNPLLGLDSTSGARCEPPAVGTACTRLCRPRSAPSRCGPGLR PCAPLEDECEAPLVCRAGCSPEHGFCEQPGECRCLEGWTGPLCTVPVSTSSCLSPRGPSSATTG CLVPGPGPCDGNPCANGGSCSETPRSFECTCPRGFYGLRCEVSGVTCADGPCFNGGLCVGGAD PDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAGFAGPRCEHDLDDC AGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGRCYAHFSGLVCACA PGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYLSGGGGSGAGVIAVIVVVVIAIVAGIVVL VISRKKRMAKYEKAEIKEMGEMHRELNA
265	-	**V5 x hu DLL3-EGF1 x EpCAM**	人工	MGWSCIILFLVATATGVHSGKPIPNPLLGLDSTSGAPLVCRAGCSPEHGFCEQPGECRCLEGWT GPLCTVPVSTSSCLSPRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPRSFECTCPRGFYGLRC EVSGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDL GHALRCRCRAGFAGPRCEHDLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADP CAARPCAHGGRCYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYLSG GGGSGAGVIAVIVVVVIAIVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA
266	-	**V5 x hu DLL3-EGF2 x EpCAM**	人工	MGWSCIILFLVATATGVHSGKPIPNPLLGLDSTSGGPGPCDGNPCANGGSCSETPRSFECTCPRG FYGLRCEVSGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNG GLCLDLGHALRCRCRAGFAGPRCEHDLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDC RERADPCAARPCAHGGRCYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAPPGLRPGDP QRYLSGGGGSGAGVIAVIVVVVIAIVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA
267	-	**V5 x hu DLL3-EGF3 x EpCAM**	人工	MGWSCIILFLVATATGVHSGKPIPNPLLGLDSTSGSGVTCADGPCFNGGLCVGGADPDSAYICH CPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAGFAGPRCEHDLDDCAGRACAN GGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGRCYAHFSGLVCACAPGYMGAR CEFPVHPDGASALPAAPPGLRPGDPQRYLSGGGGSGAGVIAVIVVVVIAIVAGIVVLVISRKKR MAKYEKAEIKEMGEMHRELNA
268	-	**V5 x hu DLL3-EGF4 x EpCAM**	人工	MGWSCIILFLVATATGVHSGKPIPNPLLGLDSTSGRVDRCSLQPCRNGGLCLDLGHALRCRCRA GFAGPRCEHDLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGG RCYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYLSGGGGSGAGVIA VIVVVVIAIVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA
269	-	**V5 x hu DLL3-EGF5 x EpCAM**	人工	MGWSCIILFLVATATGVHSGKPIPNPLLGLDSTSGDLDDCAGRACANGGTCVEGGGAHRCSCA LGFGGRDCRERADPCAARPCAHGGRCYAHFSGLVCACAPGYMGARCEFPVHPDGASALPAAP PGLRPGDPQRYLSGGGGSGAGVIAVIVVVVIAIVAGIVVLVISRKKRMAKYEKAEIKEMGEMH RELNA

270	-	**V5 x hu DLL3-EGF6 x EpCAM**	人工	MGWSCIILFLVATATGVHSGKPIPNPLLGLDSTSGRADPCAARPCAHGGRCYAHFSGLVCACA PGYMGARCEFPVHPDGASALPAAPPGLRPGDPQRYLSGGGGSGAGVIAVIVVVVIAIVAGIVVL VISRKKRMAKYEKAEIKEMGEMHRELNA
271	-	**短尾猴 DLL3**	食蟹猴	MVSPRMSRLLSQTVILALIFIPQARPAGVFELQIHSFGPGPGPGAPRSPCSARGPCRLFFRVCLKP GLSEEAAESPCALGAALSARGPVYTEQPEAPAPDLPLPNGLLQVPFRDAWPGTFSLIIETWREEL GDQIGGPAWSLLARVTRRRRLAAGGPWARDIQRAGAWELRFSYRARCELPAVGTACTRLCRP RSAPSRCGPGLRPCAPLEDECEAPPVCRAGCSLEHGFCEQPGECRCLEGWTGPLCMVPASTSSC LGLRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPGSFECTCPRGFYGLRCEVSGVTCADGPC FNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAGF AGPRCEHNLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGRC YAHFSGLVCACAPGYMGSRCEFPVHPDGVSALPAAPPGLRPGDPQRYLLPPALGLLVAAGVA GAALLLVHVRRRGHAQDAGSRLLAGTPEPSVHALPDALNNQRTQEGPGDVPSSSVDWNRPED VDSRGIYVISAPSIYAREA
272	-	**短尾猴 DLL3 ECD**	食蟹猴	MVSPRMSRLLSQTVILALIFIPQARPAGVFELQIHSFGPGPGPGAPRSPCSARGPCRLFFRVCLKP GLSEEAAESPCALGAALSARGPVYTEQPEAPAPDLPLPNGLLQVPFRDAWPGTFSLIIETWREEL GDQIGGPAWSLLARVTRRRRLAAGGPWARDIQRAGAWELRFSYRARCELPAVGTACTRLCRP RSAPSRCGPGLRPCAPLEDECEAPPVCRAGCSLEHGFCEQPGECRCLEGWTGPLCMVPASTSSC LGLRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPGSFECTCPRGFYGLRCEVSGVTCADGPC FNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAGF AGPRCEHNLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGRC YAHFSGLVCACAPGYMGSRCEFPVHPDGVSALPAAPPGLRPGDPQRYL
273	-	**Ma DLL3 N端.**	食蟹猴	MVSPRMSRLLSQTVILALIFIPQARPAGVFELQIHSFGPGPGPGAPRSPCSARGPCRLFFRVCLKP GLSEEAAESPCALGAALSARGPVYTEQPEAPAPDLPLPNGLLQVPFRDAWPGTFSLIIETWREEL GDQIGGPAWSLLARVTRRRRLAAGGPWARDIQRAGAWELRFSYR
274	-	**Ma DLL3 DSL dom.**	食蟹猴	ARCELPAVGTACTRLCRPRSAPSRCGPGLRPCAPLEDECE
275	-	**Ma DLL3 EGF-1**	食蟹猴	APPVCRAGCSLEHGFCEQPGECRCLEGWTGPLCM
276	-	**Ma DLL3 EGF-2**	食蟹猴	GPGPCDGNPCANGGSCSETPGSFECTCPRGFYGLRCE
277	-	**Ma DLL3 EGF-3**	食蟹猴	SGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFQGSNCE
278	-	**Ma DLL3 EGF-4**	食蟹猴	RVDRCSLQPCRNGGLCLDLGHALRCRCRAGFAGPRCE
279	-	**Ma DLL3**	食蟹猴	SGVTCADGPCFNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGH

		EGF-3+4		ALRCRCRAGFAGPRCE
280	-	**Ma DLL3 EGF-5**	食蟹猴	NLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCR
281	-	**Ma DLL3 EGF-6**	食蟹猴	RADPCAARPCAHGGRCYAHFSGLVCACAPGYMGSRCE
282	-	**Ma DLL3 ECD x EpCAM**	人工	MVSPRMSRLLSQTVILALIFIPQARPAGVFELQIHSFGPGPGPGAPRSPCSARGPCRLFFRVCLKP GLSEEAAESPCALGAALSARGPVYTEQPEAPAPDLPLPNGLLQVPFRDAWPGTFSLIIETWREEL GDQIGGPAWSLLARVTRRRRLAAGGPWARDIQRAGAWELRFSYRARCELPAVGTACTRLCRP RSAPSRCGPGLRPCAPLEDECEAPPVCRAGCSLEHGFCEQPGECRCLEGWTGPLCMVPASTSSC LGLRGPSSATTGCLVPGPGPCDGNPCANGGSCSETPGSFECTCPRGFYGLRCEVSGVTCADGPC FNGGLCVGGADPDSAYICHCPPGFQGSNCEKRVDRCSLQPCRNGGLCLDLGHALRCRCRAGF AGPRCEHNLDDCAGRACANGGTCVEGGGAHRCSCALGFGGRDCRERADPCAARPCAHGGRC YAHFSGLVCACAPGYMGSRCEFPVHPDGVSALPAAPPGLRPGDPQRYLSGGGGSGAGVIAVIV VVVIAIVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA
283	-	人類 **DLL1**	人類	MGSRCALALAVLSALLCQVWSSGVFELKLQEFVNKKGLLGNRNCCRGGAGPPPCACRTFFRV CLKHYQASVSPEPPCTYGSAVTPVLGVDSFSLPDGGGADSAFSNPIRFPFGFTWPGTFSLIIEALH TDSPDDLATENPERLISRLATQRHLTVGEEWSQDLHSSGRTDLKYSYRFVCDEHYYGEGCSVF CRPRDDAFGHFTCGERGEKVCNPGWKGPYCTEPICLPGCDEQHGFCDKPGECKCRVGWQGRY CDECIRYPGCLHGTCQQPWQCNCQEGWGGLFCNQDLNYCTHHKPCKNGATCTNTGQGSYTC SCRPGYTGATCELGIDECDPSPCKNGGSCTDLENSYSCTCPPGFYGKICELSAMTCADGPCFNG GRCSDSPDGGYSCRCPVGYSGFNCEKKIDYCSSSPCSNGAKCVDLGDAYLCRCQAGFSGRHCD DNVDDCASSPCANGGTCRDGVNDFSCTCPPGYTGRNCSAPVSRCEHAPCHNGATCHERGHRY VCECARGYGGPNCQFLLPELPPGPAVVDLTEKLEGQGGPFPWVAVCAGVILVLMLLLGCAAV VVCVRLRLQKHRPPADPCRGETETMNNLANCQREKDISVSIIGATQIKNTNKKADFHGDHSAD KNGFKARYPAVDYNLVQDLKGDDTAVRDAHSKRDTKCQPQGSSGEEKGTPTTLRGGEASER KRPDSGCSTSKDTKYQSVYVISEEKDECVIATEV
284	-	人類 **DLL4**	人類	MAAASRSASGWALLLLVALWQQRAAGSGVFQLQLQEFINERGVLASGRPCEPGCRTFFRVCL KHFQAVVSPGPCTFGTVSTPVLGTNSFAVRDDSSGGGRNPLQLPFNFTWPGTFSLIIEAWHAPG DDLRPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYYGDNCSRLCKK RNDHFGHYVCQPDGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGRLCNE CIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATCSNSGQRSYTCTCRP GYTGVDCELELSECDSNPCRNGGSCKDQEDGYHCLCPPGYYGLHCEHSTLSCADSPCFNGGSC RERNQGANYACECPPNFTGSNCEKKVDRCTSNPCANGGQCLNRGPSRMCRCRPGFTGTYCEL HVSDCARNPCAHGGTCHDLENGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRATCYTDLSTD TFVCNCPYGFVGSRCEFPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLRRPDDGS REAMNNLSDFQKDNLIPAAQLKNTNQKKELEVDCGLDKSNCGKQQNHTLDYNLAPGPLGRG TMPGKFPHSDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIATEV

285	-	連接子**1**	人工	GGGG
286	-	連接子**2**	人工	GGGGS
287	-	連接子**3**	人工	GGGGQ
288	-	連接子**4**	人工	SGGGGS
289	-	連接子**5**	人工	PGGGGS
290	-	連接子**6**	人工	PGGDGS
291	-	連接子**7**	人工	GGGGSGGGS
292	-	連接子**8**	人工	GGGGSGGGGS
293		連接子**9**	人工	GGGGSGGGGSGGGGS
294	-	**Hexa-his**	人工	HHHHHH
295	-	**Ab156**	人工	RDWDFDVFGGGTPVGG
296	-	線性 FcRn BP	人工	QRFVTGHFGGLXPANG
297	-	線性 FcRn BP-Y	人工	QRFVTGHFGGLYPANG
298	-	線性 FcRn BP-H	人工	QRFVTGHFGGLHPANG
299		核心 FcRn BP-H	人工	TGHFGGLHP
300		環狀 FcRn BP-H	人工	QRFCTGHFGGLHPCNG
301	-	**HALB**	人類	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGL
302	-	**HALB 變**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC

	異體 1		TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAAMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGL
303	- **HALB 變異體 2**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGPKLVAASQAALGL
304	- **HALB 變異體 3**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGPHLVAASKAALGL
305	- **HALB 變異體 4**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALGVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKA

			DDKETCFAEEGPKLVAASQAALGL
306	-	**HALB** 變異體 **5** 人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKA DDKETCFAEEGPKLVAASQAALGL
307	-	**HALB** 變異體 **6** 人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKAD DKETCFAEEGPHLVAASQAALGL
308	-	**HALB** 變異體 **7** 人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGPHLVAASKAALGL
309	-	**HALB** 變異體 **8** 人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF

				DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKAD DKETCFAEEGPKLVAASKAALGL
310	-	**HALB 變異體 9**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGPKLVAASKAALGL
311	-	**HALB 變異體 10**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGL
312	-	**HALB 變異體 11**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAGTFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAAMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGL
313	-	**HALB 變異體 12**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD

				EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGPKLVAASQAALGL
314	-	**HALB 變異體 13**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGPHLVAASKAALGL
315	-	**HALB 變異體 14**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALGVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKA DDKETCFAEEGPKLVAASQAALGL
316	-	**HALB 變異體 15**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKA DDKETCFAEEGPKLVAASQAALGL

317	-	**HALB 變異體 16**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKAD DKETCFAEEGPHLVAASQAALGL
318	-	**HALB 變異體 17**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGPHLVAASKAALGL
319	-	**HALB 變異體 18**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKAD DKETCFAEEGPKLVAASKAALGL
320	-	**HALB 變異體 19**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQSPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC

				CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGPKLVAASKAALGL
321	-	**HALB 變異體 20**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGL
322	-	**HALB 變異體 21**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAGTFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAAMDDFAAFVEKCCKAD DKETCFAEEGKKLVAASQAALGL
323	-	**HALB 變異體 22**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGPKLVAASQAALGL
324	-	**HALB 變異體 23**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD

				LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGPHLVAASKAALGL
325	-	**HALB 變異體 24**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALGVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKA DDKETCFAEEGPKLVAASQAALGL
326	-	**HALB 變異體 25**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKA DDKETCFAEEGPKLVAASQAALGL
327	-	**HALB 變異體 26**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKAD DKETCFAEEGPHLVAASQAALGL
328	-	**HALB 變**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC

	異體 27		DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKAD DKETCFAEEGPHLVAASKAALGL
329	- **HALB 變異體 28**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDKFAAFVEKCCKAD DKETCFAEEGPKLVAASKAALGL
330	- **HALB 變異體 29**	人工	DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQAPFEDHVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMC TAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRD EGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGD LLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESK DVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVF DEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKC CKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALDVDETYVP KEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKA DDKETCFAEEGPKLVAASKAALGL
331	- **交叉抗體 1 HC**	人工	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKG FYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFFLYSDLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK
332	- **交叉抗體 1 LC**	人工	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSN NKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECSDKTHTCPPCPAPELLGGPSVF

				LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRKEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFFLYSKLTVDKSRWQQGNVFSCSVM HEALHNHYTQKSLSLSPGK
333	-	交叉抗體2 **HC**	人工	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVEPKSSDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFFLYSDLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
334	-	交叉抗體2 **LC**	人工	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSN NKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECSEPKSSDKTHTCPPCPAPEAAG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRKEMTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
335	-	雜 **Fc** 結合子**Fc**	人工	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRKEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
336	-	雜 **Fc** 搭配物**Fc**	人工	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFFLYSD LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
337	-	最大抗體1目標**Fc**	人工	EPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSRKEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
338	-	最大抗體1 **CD3 Fc**	人工	EPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFF LYSDLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
339	-	最大抗體2目標**Fc**	人工	EPKSSDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSRKEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
340	-	最大抗體2	人工	EPKSSDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV

		CD3 Fc		DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFF LYSDLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
341	-	**單Fc**	人工	APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVTTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFFLYSDLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
342	-	F6A 之 CDR-L1	人工	GSSTGAVTSGYYPN
343		F6A 之 CDR-L2	人工	GTKFLAP
344		F6A 之 CDR-L3	人工	ALWYSNRWV
345		F6A 之 CDR-H1	人工	IYAMN
346		F6A 之 CDR-H2	人工	RIRSKYNNYATYYADSVKS
347		F6A 之 CDR-H3	人工	HGNFGNSYVSFFAY
348		F6A之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNIYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKSRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYVSFFAYWGQGTLVT VSS
349		F6A之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
350		F6A之VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNIYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKSRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYVSFFAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKL TVL
351		H2C 之 CDR-L1	人工	GSSTGAVTSGYYPN
352		H2C 之 CDR-L2	人工	GTKFLAP
353		H2C 之	人工	ALWYSNRWV

		CDR-L3		
354		H2C 之 CDR-H1	人工	KYAMN
355		H2C 之 CDR-H2	人工	RIRSKYNNYATYYADSVKD
356		H2C 之 CDR-H3	人工	HGNFGNSYISYWAY
357		H2C之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVT VSS
358		H2C之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
359		H2C之VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKL TVL
360		H1E 之 CDR-L1	人工	GSSTGAVTSGYYPN
361		H1E 之 CDR-L2	人工	GTKFLAP
362		H1E 之 CDR-L3	人工	ALWYSNRWV
363		H1E 之 CDR-H1	人工	SYAMN
364		H1E 之 CDR-H2	人工	RIRSKYNNYATYYADSVKG
365		H1E 之 CDR-H3	人工	HGNFGNSYLSFWAY
366		H1E之VH	人工	EVQLVESGGGLEQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTLVT VSS
367		H1E之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL

368	H1E之VH-VL	人工		EVQLVESGGGLEQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKL TVL
369	G4H之CDR-L1	人工	GSSTGAVTSGYYPN	
370	G4H之CDR-L2	人工	GTKFLAP	
371	G4H之CDR-L3	人工	ALWYSNRWV	
372	G4H之CDR-H1	人工	RYAMN	
373	G4H之CDR-H2	人工	RIRSKYNNYATYYADSVKG	
374	G4H之CDR-H3	人工	HGNFGNSYLSYFAY	
375	G4H之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSYFAYWGQGTLVT VSS
376	G4H之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL	
377	G4H之VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSYFAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKL TVL
378	A2J之CDR-L1	人工	RSSTGAVTSGYYPN	
379	A2J之CDR-L2	人工	ATDMRPS	
380	A2J之CDR-L3	人工	ALWYSNRWV	
381	A2J之	人工	VYAMN	

		CDR-H1		
382		A2J 之 CDR-H2	人工	RIRSKYNNYATYYADSVKK
383		A2J 之 CDR-H3	人工	HGNFGNSYLSWWAY
384		A2J之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNVYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKKRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSWWAYWGQGTLV TVSS
385		A2J之VL	人工	QTVVTQEPSLTVSPGGTVTLTCRSSTGAVTSGYYPNWVQQKPGQAPRGLIGATDMRPSGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
386		A2J 之 VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNVYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKKRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSWWAYWGQGTLV TVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCRSSTGAVTSGYYPNWVQQKPG QAPRGLIGATDMRPSGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTK LTVL
387		E1L 之 CDR-L1	人工	GSSTGAVTSGYYPN
388		E1L 之 CDR-L2	人工	GTKFLAP
389		E1L 之 CDR-L3	人工	ALWYSNRWV
390		E1L 之 CDR-H1	人工	KYAMN
391		E1L 之 CDR-H2	人工	RIRSKYNNYATYYADSVKS
392		E1L 之 CDR-H3	人工	HGNFGNSYTSYYAY
393		E1L之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKSRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYTSYYAYWGQGTLVT VSS
394		E1L之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
395		E1L之VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKSRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYTSYYAYWGQGTLVT

				VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
396		E2M 之 CDR-L1	人工	RSSTGAVTSGYYPN
397		E2M 之 CDR-L2	人工	ATDMRPS
398		E2M 之 CDR-L3	人工	ALWYSNRWV
399		E2M 之 CDR-H1	人工	GYAMN
400		E2M 之 CDR-H2	人工	RIRSKYNNYATYYADSVKE
401		E2M 之 CDR-H3	人工	HRNFGNSYLSWFAY
402		E2M之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNGYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKERFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHRNFGNSYLSWFAYWGQGTLVTVSS
403		E2M之VL	人工	QTVVTQEPSLTVSPGGTVTLTCRSSTGAVTSGYYPNWVQQKPGQAPRGLIGATDMRPSGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
404		E2M之VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNGYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKERFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHRNFGNSYLSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCRSSTGAVTSGYYPNWVQQKPGQAPRGLIGATDMRPSGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
405		F7O 之 CDR-L1	人工	GSSTGAVTSGYYPN
406		F7O 之 CDR-L2	人工	GTKFLAP
407		F7O 之 CDR-L3	人工	ALWYSNRWV
408		F7O 之 CDR-H1	人工	VYAMN

409	F7O 之 CDR-H2	人工	RIRSKYNNYATYYADSVKK
410	F7O 之 CDR-H3	人工	HGNFGNSYISWWAY
411	F7O之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNVYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKKRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISWWAYWGQGTLVT VSS
412	F7O之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKL TVL
413	F7O之VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNVYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKKRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISWWAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKL TVL
414	F12Q 之 CDR-L1	人工	GSSTGAVTSGNYPN
415	F12Q 之 CDR-L2	人工	GTKFLAP
416	F12Q 之 CDR-L3	人工	VLWYSNRWV
417	F12Q 之 CDR-H1	人工	SYAMN
418	F12Q 之 CDR-H2	人工	RIRSKYNNYATYYADSVKG
419	F12Q 之 CDR-H3	人工	HGNFGNSYVSWWAY
420	F12Q之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLV TVSS
421	F12Q之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
422	F12Q 之 VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLV TVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPG

				QAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTK LTVL
423		I2C 之 CDR-L1	人工	GSSTGAVTSGNYPN
424		I2C 之 CDR-L2	人工	GTKFLAP
425		I2C 之 CDR-L3	人工	VLWYSNRWV
426		I2C 之 CDR-H1	人工	KYAMN
427		I2C 之 CDR-H2	人工	RIRSKYNNYATYYADSVKD
428		I2C 之 CDR-H3	人工	HGNFGNSYISYWAY
429		I2C之VH	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVT VSS
430		I2C之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
431		I2C 之 VH-VL	人工	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVT VSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKL TVL
432		F12q之VH	人工	EVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLV TVSS
433		F12q之VL	人工	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
434		F12q 之 VH-VL	人工	EVQLVESGGGLVQPGGSLRLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWWAYWGQGTLV TVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPG QAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTK LTVL

435		**DLL3-4-001 (G44C)**	VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKCLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSS
436		**DLL3-4-001 (G234C)**	VL	EIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGCGTKLEIK
437		**DLL3-4-001 (G44C-G243C)**	scFv	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKCLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGCGTKLEIK
438		**DLL3-4-001 (CC) xI2C**	雙特異性分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKCLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGCGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
439		**DLL3-14 - D55E**	VH-CDR2	IINPSEGSTSYAQKFQG
440		**DLL3-14 - G56A**	VH-CDR2	IINPSDASTSYAQKFQG
441		**DLL3-14 - D171E**	VL-CDR1	RSSQSLVYREGNTYLS
442		**DLL3-14 - G172A**	VL-CDR1	RSSQSLVYRDANTYLS
443		**DLL3-14 - N173Q**	VL-CDR1	RSSQSLVYRDGQTYLS
444		**DLL3-14 - T174A**	VL-CDR1	RSSQSLVYRDGNAYLS
445		**DLL3-14 - L43Q**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVTS S

446		**DLL3-14 - D55E**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
447		**DLL3-14 - G56A**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
448		**DLL3-14 - L43Q-D55E**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
449		**DLL3-14 - L43Q-G56A**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS
450		**DLL3-14 - G44C**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
451		**DLL3-14 - L43Q-G44C**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
452		**DLL3-14 - G44C-D55E**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
453		**DLL3-14 - G44C-G56A**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
454		**DLL3-14 - L43Q-G44C-D55E**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
455		**DLL3-14 - L43Q-G44C-G56A**	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS S
456		**DLL3-14 - D171E**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQSPRRLIYKVSNWQSGVP DRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK

457		**DLL3-14 - G172A**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK
458		**DLL3-14 - N173Q**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGQTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK
459		**DLL3-14 - T174A**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNAYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK
460		**DLL3-14 - G208S**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK
461		**DLL3-14 - D171E-G208S**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQSPRRLIYKVSNWQSGVP DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK
462		**DLL3-14 G172A-G208S**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVEIK
463		**DLL3-14 - Q243C**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK
464		**DLL3-14 - D171E-Q243C**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQSPRRLIYKVSNWQSGVP DRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK
465		**DLL3-14 - G172A-Q243C**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK
466		**DLL3-14 - N173Q Q243C**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGQTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK
467		**DLL3-14 - T174A-Q243C**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNAYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK
468		**DLL3-14 - G208S-Q243C**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK
469		**DLL3-14 - D171E-G208S-**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQSPRRLIYKVSNWQSGVP DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK

		Q243C		
470		**DLL3-14 - G172A- G208S- Q243C**	VL	DVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQSPRRLIYKVSNWQSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVEIK
471		**DLL3-14 - 001**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIK
472		**DLL3-14 - 002**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIK
473		**DLL3-14 - 003**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGQTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTIIWPPTFGQGTKV EIK
474		**DLL3-14 - 004**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNAYLSWFQQRPG QSPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTK VEIK
475		**DLL3-14 - 005**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IK
476		**DLL3-14 - 006**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIK
477		**DLL3-14 -**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSEGSTSYA

	007		QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIK
478	**DLL3-14 - 008**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIK
479	**DLL3-14 - 009**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IK
480	**DLL3-14 - 010**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IK
481	**DLL3-14 - 011**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IK
482	**DLL3-14 - 012 (CC)**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIK
483	**DLL3-14 - 013**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIK
484	**DLL3-14 - 014**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ

				SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIK
485		**DLL3-14 - 015**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGQTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIK
486		**DLL3-14 - 016**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNAYLSWFQQRPG QSPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTK VEIK
487		**DLL3-14 - 017**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IK
488		**DLL3-14 - 018**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIK
489		**DLL3-14 - 019**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIK
490		**DLL3-14 - 020**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIK
491		**DLL3-14 - 021**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IK

492		**DLL3-14 - 022**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IK
493		**DLL3-14 - 023**	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IK
494		**DLL3-14 - 001 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
495		**DLL3-14 - 002 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
496		**DLL3-14 - 003 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGQTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW

			VFGGGTKLTVL
497	**DLL3-14 - 004 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNAYLSWFQQRPG QSPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTK VEIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIR SKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWA YWGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYP NWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNR WVFGGGTKLTVL
498	**DLL3-14 - 005 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
499	**DLL3-14 - 006 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
500	**DLL3-14 - 007 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL

501		**DLL3-14 - 008 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL	
502		**DLL3-14 - 009 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL	
503		**DLL3-14 - 010 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL	
504		**DLL3-14 - 011 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQGLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL	
505		**DLL3-14 -**	雙特異性分	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA

	012 (CC) xI2C	子	QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
506	**DLL3-14 - 013 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
507	**DLL3-14 - 014 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
508	**DLL3-14 - 015 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGQTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
509	**DLL3-14 - 016 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS

			SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNAYLSWFQQRPG QSPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTK VEIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIR SKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWA YWGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYP NWVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNR WVFGGGTKLTVL
510	**DLL3-14 - 017 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
511	**DLL3-14 - 018 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
512	**DLL3-14 - 019 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
513	**DLL3-14 - 020 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ

			SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVL
514	**DLL3-14 - 021 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
515	**DLL3-14 - 022 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSEGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYREGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
516	**DLL3-14 - 023 xI2C**	雙特異性分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGQCLEWMGIINPSDASTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDANTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKVE IKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSK YNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYW GQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWV FGGGTKLTVL
517	**DLL3-4 xI2C -scFc**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG

				IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
518		**DLL3-4 xI2C -scFc_delGK**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGGSGGGGSGGGGSG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
519		**DLL3-4-001 (CC) xI2C -scFc**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKCLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGCGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD

			KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
520	**DLL3-4-001 (CC) xI2C -scFc _delGK**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKCLEWIGYVYYSGTTNYNPSLK SRVTISVDTSKNQFSLKLSSVTAADTAVYYCASIAVTGFYFDYWGQGTLVTVSSGGGGSGGGG SGGGGSEIVLTQSPGTLSLSPGERVTLSCRASQRVNNNYLAWYQQRPGQAPRLLIYGASSRATG IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGCGTKLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
521	**DLL3-6 xI2C -scFc**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY

				VDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
522		**DLL3-6 xI2C -scFc_delGK**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKGLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGGGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGGSGGGGSGGGGSG GGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
523		**DLL3-6-001 (CC) xI2C -scFc**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKCLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGCGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGG SGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGS FFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
524		**DLL3-6-001 (CC)**	雙特異性HLE分子	QVQLQESGPGLVKPSETLSLTCTVSGASISSFYWSWIRQPPGKCLEWIGYIYYSGTTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCARIAVAGFFFDYWGQGTLVTVSSGGGGSGGGGS

	xI2C - scFc_delGK		GGGGSEIVLTQSPGTLSLSPGERATLSCRASQSVNKNYLAWYQQKPGQAPRLLIYGASSRATGI PDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYDRSPLTFGCGTKVEIKSGGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLVTVSSGGGGSG GGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGT KFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVLGGGGD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
525	**DLL3-14 xI2C -scFc**	雙特異性HLE分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW VFGGGTKLTVLGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGSGGG GSGGGGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
526	**DLL3-14 xI2C - scFc_delGK**	雙特異性HLE分子	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLGLEWMGIINPSDGSTSYA QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGQGTKV EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN

				WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW
				VFGGGTKLTVLGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE
				DPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKVSNKALP
				APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
				TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGGGGGGS
				GGGGSGGGGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
				VDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCKV
				SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQP
				ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
527	**DLL3-14 - 012 (CC) xI2C -scFc**	雙特異性HLE分子		QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA
				QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS
				SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ
				SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV
				EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS
				KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY
				WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN
				WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW
				VFGGGTKLTVLGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV
				TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGG
				GSGGGGSGGGGSGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV
				VVDVSHEDPEVKFNWYVDGVEVHNAKTKPCEEQYGSTYRCVSVLTVLHQDWLNGKEYKCK
				VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ
				PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
528	**DLL3-14 - 012 (CC) xI2C-scFc_delGK**	雙特異性HLE分子		QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYYMHWVRQAPGLCLEWMGIINPSDGSTSYA
				QKFQGRVTMTRDTSTNTVYMDLSSLRSEDTAVYYCARGGNSAFYSYYDMDVWGQGTTVTVS
				SGGGGSGGGGSGGGGSDVVMTQTPLSLPVTLGQPASISCRSSQSLVYRDGNTYLSWFQQRPGQ
				SPRRLIYKVSNWQSGVPDRFSGGGSGTDFTLKISRVEAEDVGVYYCMQGTHWPPTFGCGTKV
				EIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRS
				KYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAY
				WGQGTLVTVSSGGGGSGGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN
				WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRW
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【符號說明】

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【序列表】

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<120> DLL3及CD3抗體構築體

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Asp Ala Asn Ile Ala Ala Leu Asp Ala Phe Glu Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 18
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 18

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

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

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

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
85 90 95

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

<210> 19
<211> 243
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 19

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Asp Ala Asn Ile Ala Ala Leu Asp Ala Phe Glu Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys

<210> 20
<211> 498
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 20

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Asp Ala Asn Ile Ala Ala Leu Asp Ala Phe Glu Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
245 250 255

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala
260 265 270

Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln
275 280 285

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr
290 295 300

Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr
305 310 315 320

Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn
325 330 335

Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
340 345 350

Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr
355 360 365

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr
385 390 395 400

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly
405 410 415

Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly
420 425 430

Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly
435 440 445

Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
450 455 460

Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val
465 470 475 480

Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
485 490 495

Val Leu

<210> 21
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 21

Ser Tyr Gly Met His
1 5

<210> 22
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 22

Val Ile Ser Tyr His Gly Arg Asp Thr Tyr Tyr Ala Arg Ser Val Lys
1 5 10 15

Gly

<210> 23
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 23

Asp Gly Ala Thr Val Thr Ser Tyr Tyr Tyr Ser Gly Met Asp Val
1 5 10 15

<210> 24
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 24

Arg Ala Ser Gln Gly Ile Ser Asn Tyr Leu Ala
1 5 10

<210> 25
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 25

Leu Ala Ser Ser Leu Gln Ser
1 5

<210> 26
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 26

Gln Gln Tyr Asn Phe Tyr Pro Phe Thr
1 5

<210> 27
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 27

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

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

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

Ala Val Ile Ser Tyr His Gly Arg Asp Thr Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Ala Thr Val Thr Ser Tyr Tyr Tyr Ser Gly Met Asp
100 105 110

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

<210> 28
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 28

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

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

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
35 40 45

Tyr Leu Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Phe Tyr Pro Phe
85 90 95

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

<210> 29
<211> 246
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 29

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

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

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

Ala Val Ile Ser Tyr His Gly Arg Asp Thr Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Ala Thr Val Thr Ser Tyr Tyr Tyr Ser Gly Met Asp
100 105 110

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

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr Leu Ala Trp Phe Gln
165 170 175

Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile Tyr Leu Ala Ser Ser
180 185 190

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

195 200 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln Tyr Asn Phe Tyr Pro Phe Thr Phe Gly Pro Gly
225 230 235 240

Thr Lys Val Asp Ile Lys
245

<210> 30
<211> 501
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 30

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

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

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

Ala Val Ile Ser Tyr His Gly Arg Asp Thr Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Ala Thr Val Thr Ser Tyr Tyr Tyr Ser Gly Met Asp
100 105 110

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

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr Leu Ala Trp Phe Gln
165 170 175

Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile Tyr Leu Ala Ser Ser
180 185 190

Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln Tyr Asn Phe Tyr Pro Phe Thr Phe Gly Pro Gly
225 230 235 240

Thr Lys Val Asp Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
245 250 255

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

Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp
275 280 285

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg
290 295 300

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp
305 310 315 320

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln
325 330 335

Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
340 345 350

His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly
355 360 365

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro
385 390 395 400

Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser
405 410 415

Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln
420 425 430

Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu

435 440 445

Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys
450 455 460

Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr
465 470 475 480

Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr
485 490 495

Lys Leu Thr Val Leu
500

<210> 31
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 31

Ser Tyr Tyr Trp Ser
1 5

<210> 32
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 32

Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 33
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 33

Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr
1 5 10

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

<220>

<223> 合成肽

<400> 34

Arg Ala Ser Gln Arg Val Asn Asn Asn Tyr Leu Ala
1 5 10

<210> 35
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 35

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 36
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 36

Gln Gln Tyr Asp Arg Ser Pro Leu Thr
1 5

<210> 37
<211> 118
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 37

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

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

85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 38
<211> 108
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 38

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

Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Asn Asn Asn
20 25 30

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

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

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

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

Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 39
<211> 241
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 39

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys

<210> 40
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 40

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

1 5 10 15

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 41
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 41

Ser Tyr Tyr Trp Ser

1 5

<210> 42
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 42

Tyr Ile Tyr Tyr Ser Gly Arg Thr Asn Tyr Tyr Pro Ser Leu Lys Ser
1 5 10 15

<210> 43
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 43

Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr
1 5 10

<210> 44
<211> 12
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 44

Arg Ala Ser Gln Ser Val Asn Lys Asn Tyr Leu Ala
1 5 10

<210> 45
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 45

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 46
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 46

Gln Gln Tyr Asp Arg Ser Pro Leu Thr
1 5

<210> 47
<211> 118
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 47

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Arg Thr Asn Tyr Tyr Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser
115

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

<220>
<223> 合成肽

<400> 48

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

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

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu

35 40 45

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

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

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

Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 49
<211> 241
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 49

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Arg Thr Asn Tyr Tyr Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys

<210> 50
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 50

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Arg Thr Asn Tyr Tyr Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

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Ser Phe Tyr Trp Ser
1 5

<210> 52
<211> 16
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<220>
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<400> 52

Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

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Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr
1 5 10

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<400> 54

Arg Ala Ser Gln Ser Val Asn Lys Asn Tyr Leu Ala
1 5 10

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<400> 55

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 56
<211> 9
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<400> 56

Gln Gln Tyr Asp Arg Ser Pro Leu Thr
1 5

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<400> 57

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser
115

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<211> 108
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<400> 58

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

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

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

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

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

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

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

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<400> 59

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

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

<210> 60
<211> 496
<212> PRT
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<220>
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<400> 60

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

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

245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 61
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<400> 61

Ser Phe Tyr Trp Ser
1 5

<210> 62
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 62

Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 63
<211> 10
<212> PRT
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<400> 63

Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr
1 5 10

<210> 64
<211> 12
<212> PRT
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<400> 64

Arg Ala Ser Gln Ser Val Asn Lys Asn Tyr Leu Ala
1 5 10

<210> 65
<211> 7
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<220>
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<400> 65

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 66

<211> 9
<212> PRT
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<220>
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<400> 66

Gln Gln Tyr Asp Arg Ser Pro Leu Thr
1 5

<210> 67
<211> 118
<212> PRT
<213> 人工序列

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<400> 67

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser
115

<210> 68
<211> 108
<212> PRT
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<400> 68

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

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

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

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

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

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

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

<210> 69
<211> 241
<212> PRT
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<220>
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<400> 69

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

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<211> 496
<212> PRT
<213> 人工序列

<220>
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<400> 70

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 71
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<400> 71

Ser Phe Tyr Trp Ser
1 5

<210> 72
<211> 16
<212> PRT
<213> 人工序列

<220>
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<400> 72

Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 73
<211> 10
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<213> 人工序列

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<223> 合成肽

<400> 73

Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr
1 5 10

<210> 74
<211> 12
<212> PRT
<213> 人工序列

<220>
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<400> 74

Arg Ala Ser Gln Ser Val Asn Lys Asn Tyr Leu Ala
1 5 10

<210> 75
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 75

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 76
<211> 9
<212> PRT
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<220>
<223> 合成肽

<400> 76

Gln Gln Tyr Asp Arg Ser Pro Leu Thr
1 5

<210> 77
<211> 119
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 77

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Lys
115

<210> 78
<211> 108
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 78

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

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

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

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

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

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

Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105

<210> 79
<211> 241
<212> PRT
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<220>
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<400> 79

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
225 230 235 240

Lys

<210> 80
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 80

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

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

485 490 495

<210> 81
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<212> PRT
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<220>
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<400> 81

Ser Phe Tyr Trp Ser
1 5

<210> 82
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 82

Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 83
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 83

Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr
1 5 10

<210> 84
<211> 12
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 84

Arg Ala Ser Gln Ser Val Asn Lys Asn Tyr Leu Ala
1 5 10

<210> 85
<211> 7
<212> PRT
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<220>
<223> 合成肽

<400> 85

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 86
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 86

Gln Gln Tyr Asp Arg Ser Pro Leu Thr
1 5

<210> 87
<211> 118
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 87

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser
115

<210> 88
<211> 108
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 88

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

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

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

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

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

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

Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 89
<211> 241
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 89

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile
225 230 235 240

Lys

<210> 90
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 90

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu

65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 91
<211> 5
<212> PRT
<213> 人工序列

<220>
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<400> 91

Ser Tyr Tyr Trp Ser
1 5

<210> 92
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 92

Tyr Ile Phe Tyr Asn Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 93
<211> 10
<212> PRT
<213> 人工序列

<220>
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<400> 93

Ile His Ser Gly Ser Phe Ser Phe Asp Tyr
1 5 10

<210> 94
<211> 12
<212> PRT
<213> 人工序列

<220>
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<400> 94

Arg Ala Ser Gln Ser Val Ser Arg Gly Tyr Leu Ala
1 5 10

<210> 95
<211> 7
<212> PRT
<213> 人工序列

<220>
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<400> 95

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 96
<211> 9
<212> PRT
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<220>
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<400> 96

Gln Gln Tyr Asp Thr Ser Pro Ile Thr
1 5

<210> 97
<211> 118
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 97

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Phe Tyr Asn Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Lys Tyr Tyr Cys Ala
85 90 95

Arg Ile His Ser Gly Ser Phe Ser Phe Asp Tyr Trp Asp Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 98
<211> 108
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 98

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

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

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

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

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

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

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

100 105

<210> 99
<211> 241
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 99

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Phe Tyr Asn Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Lys Tyr Tyr Cys Ala
85 90 95

Arg Ile His Ser Gly Ser Phe Ser Phe Asp Tyr Trp Asp Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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

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

Ser Val Ser Arg Gly Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Asp Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Thr Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

<210> 100
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 100

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Phe Tyr Asn Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Lys Tyr Tyr Cys Ala
85 90 95

Arg Ile His Ser Gly Ser Phe Ser Phe Asp Tyr Trp Asp Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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

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

Ser Val Ser Arg Gly Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Asp Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Thr Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 101
<211> 5
<212> PRT
<213> 人工序列

<220>
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<400> 101

Asn Ala Gly Met Ser
1 5

<210> 102
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 102

Arg Ile Lys Asn Lys Ile Asp Gly Gly Thr Thr Asp Phe Ala Ala Pro
1 5 10 15

Val Lys Gly

<210> 103
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 103

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

<210> 104
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 104

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp

1 5 10 15

<210> 105
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 105

Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 106
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 106

Met Gln Ala Leu Gln Thr Pro Phe Thr
1 5

<210> 107
<211> 121
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 107

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

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

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

Gly Arg Ile Lys Asn Lys Ile Asp Gly Gly Thr Thr Asp Phe Ala Ala
50 55 60

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

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

Tyr Cys Thr Ala Arg Gly Trp Tyr Gly Asp Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 108
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 108

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala
85 90 95

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

<210> 109
<211> 248
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 109

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

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

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

Gly Arg Ile Lys Asn Lys Ile Asp Gly Gly Thr Thr Asp Phe Ala Ala

50 55 60

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

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

Tyr Cys Thr Ala Arg Gly Trp Tyr Gly Asp Tyr Phe Asp Tyr Trp Gly
100 105 110

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

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro
130 135 140

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

Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp
165 170 175

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly
180 185 190

Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val
210 215 220

Gly Ile Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Phe Thr Phe Gly
225 230 235 240

Pro Gly Thr Lys Val Glu Ile Lys
245

<210> 110
<211> 503
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 110

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

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

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

Gly Arg Ile Lys Asn Lys Ile Asp Gly Gly Thr Thr Asp Phe Ala Ala
50 55 60

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

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

Tyr Cys Thr Ala Arg Gly Trp Tyr Gly Asp Tyr Phe Asp Tyr Trp Gly
100 105 110

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

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro
130 135 140

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

Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp
165 170 175

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly
180 185 190

Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val
210 215 220

Gly Ile Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Phe Thr Phe Gly
225 230 235 240

Pro Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val
245 250 255

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

Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met
275 280 285

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

290 295 300

Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val
305 310 315 320

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr
325 330 335

Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
340 345 350

Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
355 360 365

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
370 375 380

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln
385 390 395 400

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
405 410 415

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val
420 425 430

Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys
435 440 445

Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
450 455 460

Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala
465 470 475 480

Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly
485 490 495

Gly Thr Lys Leu Thr Val Leu
500

<210> 111
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 111

Ser Tyr Asp Ile His
1 5

<210> 112
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 112

Val Ile Ser Ser His Gly Ser Asn Lys Asn Tyr Ala Arg Ser Val Lys
1 5 10 15

Gly

<210> 113
<211> 18
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 113

Asp Gly Tyr Ser Gly Asn Asp Pro Phe Tyr Tyr Tyr Tyr His Gly Met
1 5 10 15

Asp Val

<210> 114
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 114

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 115
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 115

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 116

<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 116

Gln Gln Ser Phe Thr Thr Pro Leu Thr
1 5

<210> 117
<211> 127
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 117

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

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

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

Ala Val Ile Ser Ser His Gly Ser Asn Lys Asn Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Tyr Ser Gly Asn Asp Pro Phe Tyr Tyr Tyr Tyr His
100 105 110

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 118
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 118

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

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

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

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Phe Thr Thr Pro Leu
85 90 95

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

<210> 119
<211> 249
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 119

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

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

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

Ala Val Ile Ser Ser His Gly Ser Asn Lys Asn Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Tyr Ser Gly Asn Asp Pro Phe Tyr Tyr Tyr Tyr His
100 105 110

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
130 135 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145 150 155 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
180 185 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
210 215 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Phe Thr Thr Pro Leu Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 120
<211> 504
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 120

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

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

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

Ala Val Ile Ser Ser His Gly Ser Asn Lys Asn Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Tyr Ser Gly Asn Asp Pro Phe Tyr Tyr Tyr Tyr His
100 105 110

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
130 135 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145 150 155 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
180 185 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
210 215 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Phe Thr Thr Pro Leu Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu
245 250 255

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

Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala
275 280 285

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
290 295 300

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
305 310 315 320

Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala
325 330 335

Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr
340 345 350

Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala
355 360 365

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
370 375 380

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr
385 390 395 400

Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr
405 410 415

Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp
420 425 430

Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr
435 440 445

Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu
450 455 460

Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu
465 470 475 480

Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly
485 490 495

Gly Gly Thr Lys Leu Thr Val Leu
500

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Ser Tyr Tyr Met His
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Ile Ile Asn Pro Ser Asp Gly Ser Thr Asn Tyr Ala Gln Asn Phe Gln
1 5 10 15

Gly

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Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
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Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu Ser
1 5 10 15

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Lys Val Ser Asn Trp Gln Ser
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<400> 126

Met Gln Gly Thr His Trp Pro Pro Thr
1 5

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

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

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

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

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu

210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

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

450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

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<400> 131

Asn Tyr Tyr Met His
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<400> 132

Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

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<400> 133

Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
1 5 10

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Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu Ser
1 5 10 15

<210> 135
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<400> 135

Lys Val Ser Asn Trp Gln Ser
1 5

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<400> 136

Met Gln Gly Thr His Trp Pro Pro Thr
1 5

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<400> 137

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

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<400> 138

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

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<400> 139

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

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

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

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<400> 141

Gly Tyr Tyr Ile His
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<210> 142
<211> 17
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<400> 142

Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Gly Gln Asn Phe Gln
1 5 10 15

Gly

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<211> 14
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<400> 143

Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
1 5 10

<210> 144
<211> 16
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<400> 144

Arg Ser Ser Gln Ser Leu Ala Tyr Arg Asp Gly Asn Thr Tyr Leu Ser
1 5 10 15

<210> 145
<211> 7
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<213> 人工序列

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<400> 145

Lys Val Ser Asn Trp Gln Ser
1 5

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<400> 146

Met Gln Gly Thr His Trp Pro Pro Thr
1 5

<210> 147
<211> 123
<212> PRT
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<400> 147

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Gly Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 148
<211> 112
<212> PRT
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<220>
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<400> 148

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly

1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Ala Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

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

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

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

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 149
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<400> 149

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Gly Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Ala Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

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<400> 150

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Gly Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Ala Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 151
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<400> 151

Gly His Tyr Met His
1 5

<210> 152
<211> 17
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<223> 合成肽

<400> 152

Ile Ile Asn Pro Ser Asp Gly Ser Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 153
<211> 14
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<400> 153

Gly Thr Thr Val Val His Tyr Ser Tyr Tyr Asp Met Asp Val
1 5 10

<210> 154
<211> 16
<212> PRT
<213> 人工序列

<220>
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<400> 154

Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu Thr
1 5 10 15

<210> 155
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<220>
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<400> 155

Lys Val Ser Asn Trp Gln Ser
1 5

<210> 156
<211> 9
<212> PRT
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<220>
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<400> 156

Met Gln Gly Thr His Trp Pro Pro Thr
1 5

<210> 157
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<400> 157

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly His
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Thr Arg Gly Thr Thr Val Val His Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 158
<211> 112
<212> PRT
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<223> 合成肽

<400> 158

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Thr Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 159
<211> 250
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<400> 159

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly His
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Thr Arg Gly Thr Thr Val Val His Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Thr Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
245 250

<210> 160
<211> 505
<212> PRT
<213> 人工序列

<220>
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<400> 160

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly His
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Thr Arg Gly Thr Thr Val Val His Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Thr Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr

180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 161
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 161

Asn Tyr Phe Met His
1 5

<210> 162
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 162

Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Asn Phe Gln
1 5 10 15

Gly

<210> 163
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 163

Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
1 5 10

<210> 164
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 164

Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu Ser
1 5 10 15

<210> 165
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 165

Arg Val Ser Asn Trp Gln Ser
1 5

<210> 166
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 166

Met Gln Gly Thr Tyr Trp Pro Pro Thr
1 5

<210> 167
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 167

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 168
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 168

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Arg Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

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

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

Thr Tyr Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105 110

<210> 169
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 169

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Arg Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr Tyr Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
245 250

<210> 170
<211> 505
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 170

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Arg Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr Tyr Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Asp Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 171
<211> 5
<212> PRT
<213> 人工序列

<220>

<223> 合成肽

<400> 171

Asn Tyr Gly Met His
1 5

<210> 172
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 172

Val Ile Ser His His Gly Ser Ser Lys Tyr Tyr Ala Arg Ser Val Lys
1 5 10 15

Gly

<210> 173
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 173

Asp Trp Trp Glu Leu Val Phe Asp Tyr
1 5

<210> 174
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 174

Lys Ser Ser Gln Ser Leu Leu His Ser Asp Gly Lys Thr Phe Leu Tyr
1 5 10 15

<210> 175
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 175

Glu Val Ser Asn Arg Phe Ser
1 5

<210> 176
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 176

Leu Gln Gly Ile His Leu Pro Phe Thr
1 5

<210> 177
<211> 118
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 177

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

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

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

Ala Val Ile Ser His His Gly Ser Ser Lys Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Trp Trp Glu Leu Val Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 178
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 178

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

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asp Gly Lys Thr Phe Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Pro
35 40 45

Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

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

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

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

<210> 179
<211> 245
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 179

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

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

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

Ala Val Ile Ser His His Gly Ser Ser Lys Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Trp Trp Glu Leu Val Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

115 120 125

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

Ser Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln
145 150 155 160

Ser Leu Leu His Ser Asp Gly Lys Thr Phe Leu Tyr Trp Tyr Leu Gln
165 170 175

Lys Pro Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg
180 185 190

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
210 215 220

Tyr Cys Leu Gln Gly Ile His Leu Pro Phe Thr Phe Gly Pro Gly Thr
225 230 235 240

Lys Val Glu Ile Lys
245

<210> 180
<211> 500
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 180

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

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

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

Ala Val Ile Ser His His Gly Ser Ser Lys Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Trp Trp Glu Leu Val Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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

Ser Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln
145 150 155 160

Ser Leu Leu His Ser Asp Gly Lys Thr Phe Leu Tyr Trp Tyr Leu Gln
165 170 175

Lys Pro Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg
180 185 190

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
210 215 220

Tyr Cys Leu Gln Gly Ile His Leu Pro Phe Thr Phe Gly Pro Gly Thr
225 230 235 240

Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val
245 250 255

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

Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val
275 280 285

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

Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg
305 310 315 320

Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met
325 330 335

Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His
340 345 350

Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln

355 360 365

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser
385 390 395 400

Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser
405 410 415

Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys
420 425 430

Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala
435 440 445

Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala
450 455 460

Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr
465 470 475 480

Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys
485 490 495

Leu Thr Val Leu
500

<210> 181
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 181

Asn Ser Arg Met Gly Val Ser
1 5

<210> 182
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 182

His Ile Phe Ser Asn Asp Gly Lys Ser Tyr Ser Thr Ser Leu Lys Ser
1 5 10 15

<210> 183
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 183

Tyr Asn Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe Asp Tyr
1 5 10 15

<210> 184
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 184

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 185
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 185

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 186
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 186

Gln Gln Gly Tyr Ser Ser Pro Phe Thr
1 5

<210> 187
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 187

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

1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Asn Ser
20 25 30

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

Trp Leu Ala His Ile Phe Ser Asn Asp Gly Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Asn Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

<210> 188
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 188

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

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

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

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

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

<210> 189
<211> 247
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 189

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

Thr Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Asn Ser
20 25 30

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

Trp Leu Ala His Ile Phe Ser Asn Asp Gly Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Asn Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
180 185 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Gly Tyr Ser Ser Pro Phe Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 190
<211> 502
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 190

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

Thr Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Asn Ser
20 25 30

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

Trp Leu Ala His Ile Phe Ser Asn Asp Gly Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Asn Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
180 185 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Gly Tyr Ser Ser Pro Phe Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln
245 250 255

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

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn
275 280 285

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile
290 295 300

Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys
305 310 315 320

Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu
325 330 335

Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val
340 345 350

Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp
355 360 365

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu
385 390 395 400

Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly
405 410 415

Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln
420 425 430

Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe
435 440 445

Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly
450 455 460

Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu
465 470 475 480

Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly
485 490 495

Thr Lys Leu Thr Val Leu
500

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<400> 191

Asn Ala Arg Met Gly Val Ser
1 5

<210> 192
<211> 16
<212> PRT
<213> 人工序列

<220>
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<400> 192

His Ile Phe Ser Thr Asp Glu Lys Ser Tyr Ser Thr Ser Leu Lys Ser
1 5 10 15

<210> 193
<211> 15
<212> PRT
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<400> 193

Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe Asp Tyr
1 5 10 15

<210> 194
<211> 11
<212> PRT
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<400> 194

Arg Ala Ser Gln Ser Ile Arg Ser Tyr Leu Asn
1 5 10

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<400> 195

Gly Ala Ser Asn Leu Gln Ser
1 5

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<400> 196

Gln Gln Ser Tyr Ser Ser Pro Phe Thr
1 5

<210> 197
<211> 125
<212> PRT
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<220>
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<400> 197

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

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

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

Trp Leu Ala His Ile Phe Ser Thr Asp Glu Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

<210> 198
<211> 107
<212> PRT
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<220>
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<400> 198

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

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

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

Tyr Gly Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

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

<210> 199
<211> 247
<212> PRT
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<220>
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<400> 199

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

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

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

Trp Leu Ala His Ile Phe Ser Thr Asp Glu Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Ser Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser
180 185 190

Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ser Pro Phe Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 200
<211> 502
<212> PRT
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<220>
<223> 合成肽

<400> 200

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

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

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

Trp Leu Ala His Ile Phe Ser Thr Asp Glu Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Ser Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser
180 185 190

Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ser Pro Phe Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln
245 250 255

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

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn
275 280 285

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile
290 295 300

Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys
305 310 315 320

Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu
325 330 335

Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val
340 345 350

Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp
355 360 365

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu
385 390 395 400

Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly
405 410 415

Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln
420 425 430

Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe
435 440 445

Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly
450 455 460

Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu
465 470 475 480

Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly
485 490 495

Thr Lys Leu Thr Val Leu
500

<210> 201
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 201

Ser Tyr Tyr Ile His
1 5

<210> 202
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 202

Ile Ile Asn Pro Ser Gly Gly Ser Lys Ser Tyr Ala Gln Lys Phe Arg
1 5 10 15

Gly

<210> 203
<211> 12
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 203

Ser Met Ser Thr Val Thr Ser Asp Ala Phe Asp Ile
1 5 10

<210> 204
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 204

Arg Ala Ser Gln Ser Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 205
<211> 7
<212> PRT
<213> 人工序列

<220>
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<400> 205

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 206
<211> 9
<212> PRT
<213> 人工序列

<220>

<223> 合成肽

<400> 206

Gln Gln Ser Tyr Ser Ala Pro Leu Thr
1 5

<210> 207
<211> 121
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 207

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Ser Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Gly Gly Ser Lys Ser Tyr Ala Gln Lys Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Ala Arg Ser Met Ser Thr Val Thr Ser Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 208
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 208

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

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

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

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ala Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105

<210> 209
<211> 243
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 209

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Ser Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Gly Gly Ser Lys Ser Tyr Ala Gln Lys Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Ala Arg Ser Met Ser Thr Val Thr Ser Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

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

Asp Ile Lys

<210> 210
<211> 498
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 210

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Ser Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Gly Gly Ser Lys Ser Tyr Ala Gln Lys Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Ala Arg Ser Met Ser Thr Val Thr Ser Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly

115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

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

Asp Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
245 250 255

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala
260 265 270

Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln
275 280 285

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr
290 295 300

Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr
305 310 315 320

Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn
325 330 335

Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
340 345 350

Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr
355 360 365

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr
385 390 395 400

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly
405 410 415

Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly
420 425 430

Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly
435 440 445

Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
450 455 460

Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val
465 470 475 480

Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
485 490 495

Val Leu

<210> 211
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 211

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 212
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 212

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Arg Thr Asn Tyr Tyr Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 213
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 213

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 214
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 214

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 215
<211> 496
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<220>
<223> 合成肽

<400> 215

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 216
<211> 496
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<400> 216

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 217
<211> 496
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<400> 217

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Phe Tyr Asn Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Lys Tyr Tyr Cys Ala
85 90 95

Arg Ile His Ser Gly Ser Phe Ser Phe Asp Tyr Trp Asp Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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

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

Ser Val Ser Arg Gly Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Asp Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Thr Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

<210> 218
<211> 505
<212> PRT
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<223> 合成肽

<400> 218

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val

100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 219
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<223> 合成肽

<400> 219

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 220
<211> 505
<212> PRT
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<400> 220

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Gly Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr

65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Ala Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 221
<211> 1096
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<400> 221

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

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

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

Ala Val Ile Ser Tyr His Gly Ser Asn Lys Tyr Tyr Ala Arg Ser Val

50 55 60

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

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

Ala Arg Glu Ile Pro Phe Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

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

Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
145 150 155 160

Leu Leu His Ser Asp Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys
165 170 175

Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

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

Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Asp Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu
245 250 255

Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys
260 265 270

Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg
275 280 285

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

Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe
305 310 315 320

Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn
325 330 335

Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly
340 345 350

Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly
355 360 365

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
370 375 380

Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu
385 390 395 400

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
405 410 415

Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro
420 425 430

Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro
435 440 445

Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
450 455 460

Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys
465 470 475 480

Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu
485 490 495

Thr Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val
500 505 510

Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val
515 520 525

Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His
530 535 540

Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala
545 550 555 560

Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly
565 570 575

Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met
580 585 590

Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu
595 600 605

Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu
610 615 620

Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu
625 630 635 640

Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala
645 650 655

Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu
660 665 670

Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp
675 680 685

Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys
690 695 700

Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala
705 710 715 720

Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val
725 730 735

Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His
740 745 750

Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr
755 760 765

Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys
770 775 780

Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn
785 790 795 800

Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu
805 810 815

Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu
820 825 830

Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val
835 840 845

Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys
850 855 860

Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp
865 870 875 880

Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn
885 890 895

Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu
900 905 910

Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu
915 920 925

Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys
930 935 940

His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val
945 950 955 960

Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp
965 970 975

Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys
980 985 990

Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn
995 1000 1005

Ala Gly Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu
1010 1015 1020

Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val
1025 1030 1035

Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Ala Met
1040 1045 1050

Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp
1055 1060 1065

Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala
1070 1075 1080

Ser Gln Ala Ala Leu Gly Leu His His His His His His
1085 1090 1095

<210> 222
<211> 1095
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 222

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Asp Ala Asn Ile Ala Ala Leu Asp Ala Phe Glu Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val
225 230 235 240

Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
245 250 255

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala
260 265 270

Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln
275 280 285

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr
290 295 300

Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr
305 310 315 320

Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn
325 330 335

Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
340 345 350

Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr
355 360 365

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr
385 390 395 400

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly
405 410 415

Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly
420 425 430

Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly
435 440 445

Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
450 455 460

Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val
465 470 475 480

Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
485 490 495

Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala
500 505 510

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu

515 520 525

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
530 535 540

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
545 550 555 560

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
565 570 575

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
580 585 590

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
595 600 605

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val
610 615 620

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
625 630 635 640

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
645 650 655

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
660 665 670

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
675 680 685

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
690 695 700

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
705 710 715 720

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
725 730 735

Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
740 745 750

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
755 760 765

Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
770 775 780

Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
785 790 795 800

Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
805 810 815

Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
820 825 830

Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
835 840 845

Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
850 855 860

Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
865 870 875 880

Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
885 890 895

Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
900 905 910

Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
915 920 925

Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
930 935 940

Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
945 950 955 960

Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
965 970 975

Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
980 985 990

Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
995 1000 1005

Gly Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys
1010 1015 1020

Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
1025 1030 1035

His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Ala Met Asp
1040 1045 1050

Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys
1055 1060 1065

Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
1070 1075 1080

Gln Ala Ala Leu Gly Leu His His His His His His
1085 1090 1095

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20 25 30

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

Ala Val Ile Ser Tyr His Gly Arg Asp Thr Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Ala Thr Val Thr Ser Tyr Tyr Tyr Ser Gly Met Asp
100 105 110

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

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr Leu Ala Trp Phe Gln
165 170 175

Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile Tyr Leu Ala Ser Ser
180 185 190

Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln Tyr Asn Phe Tyr Pro Phe Thr Phe Gly Pro Gly
225 230 235 240

Thr Lys Val Asp Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
245 250 255

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

Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp
275 280 285

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg
290 295 300

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp
305 310 315 320

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln
325 330 335

Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
340 345 350

His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly
355 360 365

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro
385 390 395 400

Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser
405 410 415

Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln
420 425 430

Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu
435 440 445

Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys
450 455 460

Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr
465 470 475 480

Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr
485 490 495

Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser
500 505 510

Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala
515 520 525

Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu
530 535 540

Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys
545 550 555 560

Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu
565 570 575

Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly
580 585 590

Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys
595 600 605

Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg
610 615 620

Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr
625 630 635 640

Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe
645 650 655

Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe
660 665 670

Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys
675 680 685

Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg
690 695 700

Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala
705 710 715 720

Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala
725 730 735

Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys
740 745 750

Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala
755 760 765

Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu
770 775 780

Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val
785 790 795 800

Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe
805 810 815

Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val
820 825 830

Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr
835 840 845

Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu
850 855 860

Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val
865 870 875 880

Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys
885 890 895

Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn
900 905 910

Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro
915 920 925

Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys
930 935 940

Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu
945 950 955 960

Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val
965 970 975

Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg

980 985 990

Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu
995 1000 1005

Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu
1010 1015 1020

Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu
1025 1030 1035

Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala
1040 1045 1050

Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
1055 1060 1065

Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
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Ala Ala Ser Gln Ala Ala Leu Gly Leu His His His His His His
1085 1090 1095

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Arg Thr Asn Tyr Tyr Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu

835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
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Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile

225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
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Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser

690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
65 70 75 80

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

85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser

545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Phe Tyr Asn Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Lys Tyr Tyr Cys Ala
85 90 95

Arg Ile His Ser Gly Ser Phe Ser Phe Asp Tyr Trp Asp Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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

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

Ser Val Ser Arg Gly Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Asp Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Thr Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

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

1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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

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

Gly Arg Ile Lys Asn Lys Ile Asp Gly Gly Thr Thr Asp Phe Ala Ala
50 55 60

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

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

Tyr Cys Thr Ala Arg Gly Trp Tyr Gly Asp Tyr Phe Asp Tyr Trp Gly
100 105 110

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

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro
130 135 140

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

Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp
165 170 175

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly
180 185 190

Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val
210 215 220

Gly Ile Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Phe Thr Phe Gly
225 230 235 240

Pro Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val
245 250 255

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

Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met
275 280 285

Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg
290 295 300

Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val
305 310 315 320

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr
325 330 335

Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
340 345 350

Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
355 360 365

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
370 375 380

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln
385 390 395 400

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys

405 410 415

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val
420 425 430

Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys
435 440 445

Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
450 455 460

Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala
465 470 475 480

Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly
485 490 495

Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His
500 505 510

Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe
515 520 525

Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro
530 535 540

Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys
545 550 555 560

Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His
565 570 575

Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr
580 585 590

Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn
595 600 605

Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu
610 615 620

Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu
625 630 635 640

Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro
645 650 655

Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala
660 665 670

Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu
675 680 685

Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys
690 695 700

Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe
705 710 715 720

Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu
725 730 735

Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr
740 745 750

Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp
755 760 765

Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu
770 775 780

Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala
785 790 795 800

Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala
805 810 815

Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys
820 825 830

Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro
835 840 845

Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr
850 855 860

Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala
865 870 875 880

Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu
885 890 895

Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe
900 905 910

Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser
915 920 925

Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser
930 935 940

Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp
945 950 955 960

Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr
965 970 975

Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn
980 985 990

Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro
995 1000 1005

Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys
1010 1015 1020

Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
1025 1030 1035

Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
1040 1045 1050

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys
1055 1060 1065

Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
1070 1075 1080

Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His His His
1085 1090 1095

His His
1100

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

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

Ala Val Ile Ser Ser His Gly Ser Asn Lys Asn Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Gly Tyr Ser Gly Asn Asp Pro Phe Tyr Tyr Tyr Tyr His
100 105 110

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
130 135 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145 150 155 160

Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
180 185 190

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
210 215 220

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Phe Thr Thr Pro Leu Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu
245 250 255

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

Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala
275 280 285

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
290 295 300

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
305 310 315 320

Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala
325 330 335

Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr
340 345 350

Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala
355 360 365

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
370 375 380

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr
385 390 395 400

Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr
405 410 415

Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp
420 425 430

Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr
435 440 445

Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu
450 455 460

Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu
465 470 475 480

Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly
485 490 495

Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp Ala
500 505 510

His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn
515 520 525

Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys
530 535 540

Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala
545 550 555 560

Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu
565 570 575

His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu
580 585 590

Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg
595 600 605

Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg
610 615 620

Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn
625 630 635 640

Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His
645 650 655

Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys
660 665 670

Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu
675 680 685

Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala
690 695 700

Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala
705 710 715 720

Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala
725 730 735

Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His
740 745 750

Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala
755 760 765

Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys
770 775 780

Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile
785 790 795 800

Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala
805 810 815

Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala
820 825 830

Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His
835 840 845

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

850 855 860

Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr
865 870 875 880

Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn
885 890 895

Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys
900 905 910

Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val
915 920 925

Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly
930 935 940

Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu
945 950 955 960

Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys
965 970 975

Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val
980 985 990

Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val
995 1000 1005

Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
1010 1015 1020

Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
1025 1030 1035

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln
1040 1045 1050

Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
1055 1060 1065

Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
1070 1075 1080

Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His His
1085 1090 1095

His His His
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr

225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp
500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
1070 1075 1080

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His
1100

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp
500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys

675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
1070 1075 1080

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His
1100

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Gly Gln Asn Phe

50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Ala Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp
500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
1070 1075 1080

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His
1100

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly His
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Thr Arg Gly Thr Thr Val Val His Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Thr Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

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

500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
1070 1075 1080

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Arg Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr Tyr Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Asp Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp
500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala

945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
1070 1075 1080

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His
1100

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

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

Ala Val Ile Ser His His Gly Ser Ser Lys Tyr Tyr Ala Arg Ser Val
50 55 60

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

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

Ala Arg Asp Trp Trp Glu Leu Val Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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

Ser Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln
145 150 155 160

Ser Leu Leu His Ser Asp Gly Lys Thr Phe Leu Tyr Trp Tyr Leu Gln
165 170 175

Lys Pro Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg
180 185 190

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
210 215 220

Tyr Cys Leu Gln Gly Ile His Leu Pro Phe Thr Phe Gly Pro Gly Thr
225 230 235 240

Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val
245 250 255

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

Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val
275 280 285

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

Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg
305 310 315 320

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

325 330 335

Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His
340 345 350

Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln
355 360 365

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser
385 390 395 400

Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser
405 410 415

Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys
420 425 430

Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala
435 440 445

Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala
450 455 460

Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr
465 470 475 480

Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys
485 490 495

Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu
500 505 510

Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu
515 520 525

Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp
530 535 540

His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val
545 550 555 560

Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe
565 570 575

Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu
580 585 590

Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe
595 600 605

Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro
610 615 620

Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe
625 630 635 640

Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr
645 650 655

Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr
660 665 670

Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu
675 680 685

Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu
690 695 700

Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp
705 710 715 720

Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu
725 730 735

Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys
740 745 750

His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys
755 760 765

Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys
770 775 780

Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu
785 790 795 800

Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val
805 810 815

Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe
820 825 830

Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser
835 840 845

Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu
850 855 860

Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe
865 870 875 880

Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln
885 890 895

Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala
900 905 910

Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr
915 920 925

Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys
930 935 940

Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser
945 950 955 960

Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser
965 970 975

Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro
980 985 990

Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe
995 1000 1005

Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser
1010 1015 1020

Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu
1025 1030 1035

Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val
1040 1045 1050

Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp
1055 1060 1065

Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
1070 1075 1080

Ala Ser Gln Ala Ala Leu Gly Leu His His His His His His
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Thr Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Asn Ser
20 25 30

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

Trp Leu Ala His Ile Phe Ser Asn Asp Gly Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Asn Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser
180 185 190

Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Gly Tyr Ser Ser Pro Phe Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln
245 250 255

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

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn
275 280 285

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile
290 295 300

Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys
305 310 315 320

Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu
325 330 335

Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val
340 345 350

Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp
355 360 365

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu
385 390 395 400

Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly
405 410 415

Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln
420 425 430

Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe
435 440 445

Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly
450 455 460

Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu
465 470 475 480

Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly
485 490 495

Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His Lys
500 505 510

Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys
515 520 525

Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe
530 535 540

Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr
545 550 555 560

Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr
565 570 575

Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr
580 585 590

Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu
595 600 605

Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val
610 615 620

Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu
625 630 635 640

Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr
645 650 655

Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala
660 665 670

Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro
675 680 685

Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln
690 695 700

Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys
705 710 715 720

Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe
725 730 735

Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu
740 745 750

Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu
755 760 765

Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys
770 775 780

Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu

785 790 795 800

Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp
805 810 815

Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp
820 825 830

Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp
835 840 845

Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr
850 855 860

Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys
865 870 875 880

Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile
885 890 895

Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln
900 905 910

Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr
915 920 925

Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys
930 935 940

Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr
945 950 955 960

Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro
965 970 975

Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg
980 985 990

Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys
995 1000 1005

Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
1010 1015 1020

Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val
1025 1030 1035

Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
1040 1045 1050

Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
1055 1060 1065

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu
1070 1075 1080

Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His His His His
1085 1090 1095

His

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

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

Trp Leu Ala His Ile Phe Ser Thr Asp Glu Lys Ser Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Ser Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr Ser Phe Phe
100 105 110

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

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Arg Ser Tyr Leu Asn Trp Tyr

165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser
180 185 190

Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ser Pro Phe Thr Phe Gly Gly
225 230 235 240

Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln
245 250 255

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

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn
275 280 285

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile
290 295 300

Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys
305 310 315 320

Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu
325 330 335

Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val
340 345 350

Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp
355 360 365

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu
385 390 395 400

Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly
405 410 415

Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln
420 425 430

Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe
435 440 445

Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly
450 455 460

Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu
465 470 475 480

Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly
485 490 495

Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His Lys
500 505 510

Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys
515 520 525

Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe
530 535 540

Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr
545 550 555 560

Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr
565 570 575

Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr
580 585 590

Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu
595 600 605

Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val
610 615 620

Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu
625 630 635 640

Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr
645 650 655

Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala
660 665 670

Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro
675 680 685

Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln
690 695 700

Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys
705 710 715 720

Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe
725 730 735

Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu
740 745 750

Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu
755 760 765

Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys
770 775 780

Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu
785 790 795 800

Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp
805 810 815

Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp
820 825 830

Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp
835 840 845

Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr
850 855 860

Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys
865 870 875 880

Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile
885 890 895

Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln
900 905 910

Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr
915 920 925

Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys
930 935 940

Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr
945 950 955 960

Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro
965 970 975

Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg
980 985 990

Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys
995 1000 1005

Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr
1010 1015 1020

Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val
1025 1030 1035

Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
1040 1045 1050

Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
1055 1060 1065

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu
1070 1075 1080

Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His His His His His
1085 1090 1095

His

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<400> 241

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Ser Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Gly Gly Ser Lys Ser Tyr Ala Gln Lys Phe
50 55 60

Arg Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

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

Ala Arg Ser Met Ser Thr Val Thr Ser Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Ser Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
210 215 220

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

Asp Ile Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser
245 250 255

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala
260 265 270

Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln
275 280 285

Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr
290 295 300

Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr
305 310 315 320

Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn
325 330 335

Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
340 345 350

Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr
355 360 365

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
370 375 380

Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr
385 390 395 400

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly
405 410 415

Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly
420 425 430

Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly
435 440 445

Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
450 455 460

Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val
465 470 475 480

Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
485 490 495

Val Leu Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala
500 505 510

His Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu
515 520 525

Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val
530 535 540

Lys Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp
545 550 555 560

Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp
565 570 575

Lys Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala
580 585 590

Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln
595 600 605

His Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val

610 615 620

Asp Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys
625 630 635 640

Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro
645 650 655

Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys
660 665 670

Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu
675 680 685

Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys
690 695 700

Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val
705 710 715 720

Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser
725 730 735

Lys Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly
740 745 750

Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile
755 760 765

Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu
770 775 780

Lys Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp
785 790 795 800

Glu Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser
805 810 815

Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly
820 825 830

Met Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val
835 840 845

Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys
850 855 860

Cys Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu
865 870 875 880

Phe Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys
885 890 895

Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu
900 905 910

Val Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val
915 920 925

Glu Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His
930 935 940

Pro Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val
945 950 955 960

Leu Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg
965 970 975

Val Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe
980 985 990

Ser Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala
995 1000 1005

Glu Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys
1010 1015 1020

Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys
1025 1030 1035

His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp
1040 1045 1050

Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys
1055 1060 1065

Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser
1070 1075 1080

Gln Ala Ala Leu Gly Leu His His His His His His
1085 1090 1095

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

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala

1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Arg Thr Asn Tyr Tyr Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

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

465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
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Ala Leu Gly Leu His His His His His His
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Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu

930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
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Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys

325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
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Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met

785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

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

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

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

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile

180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu
645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
1070 1075 1080

Ala Leu Gly Leu His His His His His His
1085 1090

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

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Phe Tyr Asn Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

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

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Lys Tyr Tyr Cys Ala
85 90 95

Arg Ile His Ser Gly Ser Phe Ser Phe Asp Tyr Trp Asp Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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

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

Ser Val Ser Arg Gly Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Asp Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Thr Ser Pro Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Val Ser Trp Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Pro Gly Gly Gly Gly Ser Asp Ala His Lys Ser Glu Val Ala His Arg
500 505 510

Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala
515 520 525

Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu
530 535 540

Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser
545 550 555 560

Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu
565 570 575

Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys
580 585 590

Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys
595 600 605

Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val
610 615 620

Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr
625 630 635 640

Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu

645 650 655

Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln
660 665 670

Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg
675 680 685

Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser
690 695 700

Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg
705 710 715 720

Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu
725 730 735

Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu
740 745 750

Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu
755 760 765

Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro
770 775 780

Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met
785 790 795 800

Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp
805 810 815

Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe
820 825 830

Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu
835 840 845

Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala
850 855 860

Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys
865 870 875 880

Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu
885 890 895

Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg
900 905 910

Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val
915 920 925

Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu
930 935 940

Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn
945 950 955 960

Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr
965 970 975

Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala
980 985 990

Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr
995 1000 1005

Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
1010 1015 1020

Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys
1025 1030 1035

Pro Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe
1040 1045 1050

Ala Ala Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr
1055 1060 1065

Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala
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Ala Leu Gly Leu His His His His His His
1085 1090

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

35 40 45

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

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp
500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
1070 1075 1080

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

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

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

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

485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp
500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
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Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His
1100

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
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Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Gly Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

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

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

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

Cys Arg Ser Ser Gln Ser Leu Ala Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Phe Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Pro Gly Gly Gly Gly Ser Asp
500 505 510

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
515 520 525

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
530 535 540

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
545 550 555 560

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
565 570 575

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
580 585 590

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
595 600 605

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
610 615 620

Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
625 630 635 640

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
645 650 655

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
660 665 670

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys

675 680 685

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
690 695 700

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
705 710 715 720

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
725 730 735

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
740 745 750

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
755 760 765

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
770 775 780

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
785 790 795 800

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
805 810 815

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
820 825 830

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
835 840 845

His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
850 855 860

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
865 870 875 880

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
885 890 895

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
900 905 910

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
915 920 925

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
930 935 940

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
945 950 955 960

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
965 970 975

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
980 985 990

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
995 1000 1005

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
1010 1015 1020

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
1025 1030 1035

Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
1040 1045 1050

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
1055 1060 1065

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly
1070 1075 1080

Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu His His
1085 1090 1095

His His His His
1100

<210> 252
<211> 618
<212> PRT
<213> 智人

<400> 252

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

Ala Leu Ile Phe Leu Pro Gln Thr Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Leu Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Gly Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asp Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Phe Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Ala Gly Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg
145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala
165 170 175

Arg Cys Glu Pro Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg
180 185 190

Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala
195 200 205

Pro Leu Glu Asp Glu Cys Glu Ala Pro Leu Val Cys Arg Ala Gly Cys
210 215 220

Ser Pro Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu
225 230 235 240

Glu Gly Trp Thr Gly Pro Leu Cys Thr Val Pro Val Ser Thr Ser Ser
245 250 255

Cys Leu Ser Pro Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val
260 265 270

Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser
275 280 285

Cys Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe
290 295 300

Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro
305 310 315 320

Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala
325 330 335

Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys
340 345 350

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
355 360 365

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
370 375 380

Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys
385 390 395 400

Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser
405 410 415

Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro
420 425 430

Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe
435 440 445

Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys
450 455 460

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

Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Leu Pro Pro Ala
485 490 495

Leu Gly Leu Leu Val Ala Ala Gly Val Ala Gly Ala Ala Leu Leu Leu
500 505 510

Val His Val Arg Arg Arg Gly His Ser Gln Asp Ala Gly Ser Arg Leu
515 520 525

Leu Ala Gly Thr Pro Glu Pro Ser Val His Ala Leu Pro Asp Ala Leu
530 535 540

Asn Asn Leu Arg Thr Gln Glu Gly Ser Gly Asp Gly Pro Ser Ser Ser
545 550 555 560

Val Asp Trp Asn Arg Pro Glu Asp Val Asp Pro Gln Gly Ile Tyr Val
565 570 575

Ile Ser Ala Pro Ser Ile Tyr Ala Arg Glu Val Ala Thr Pro Leu Phe
580 585 590

Pro Pro Leu His Thr Gly Arg Ala Gly Gln Arg Gln His Leu Leu Phe
595 600 605

Pro Tyr Pro Ser Ser Ile Leu Ser Val Lys
610 615

<210> 253
<211> 492
<212> PRT
<213> 智人

<400> 253

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

Ala Leu Ile Phe Leu Pro Gln Thr Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Leu Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Gly Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asp Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Phe Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Ala Gly Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg
145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala
165 170 175

Arg Cys Glu Pro Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg
180 185 190

Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala
195 200 205

Pro Leu Glu Asp Glu Cys Glu Ala Pro Leu Val Cys Arg Ala Gly Cys
210 215 220

Ser Pro Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu
225 230 235 240

Glu Gly Trp Thr Gly Pro Leu Cys Thr Val Pro Val Ser Thr Ser Ser
245 250 255

Cys Leu Ser Pro Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val
260 265 270

Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser
275 280 285

Cys Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe
290 295 300

Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro
305 310 315 320

Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala
325 330 335

Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys
340 345 350

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
355 360 365

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
370 375 380

Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys
385 390 395 400

Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser
405 410 415

Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro
420 425 430

Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe
435 440 445

Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys
450 455 460

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

Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu

485 490

<210> 254
<211> 175
<212> PRT
<213> 智人

<400> 254

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

Ala Leu Ile Phe Leu Pro Gln Thr Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Leu Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Gly Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asp Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Phe Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Ala Gly Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg
145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg
165 170 175

<210> 255
<211> 40
<212> PRT
<213> 智人

<400> 255

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

Arg Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys
20 25 30

Ala Pro Leu Glu Asp Glu Cys Glu
35 40

<210> 256
<211> 34
<212> PRT
<213> 智人

<400> 256

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

Glu Gln Pro Gly Glu Cys Arg Cys Leu Glu Gly Trp Thr Gly Pro Leu
20 25 30

Cys Thr

<210> 257
<211> 37
<212> PRT
<213> 智人

<400> 257

Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser Cys
1 5 10 15

Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe Tyr
20 25 30

Gly Leu Arg Cys Glu
35

<210> 258
<211> 40
<212> PRT
<213> 智人

<400> 258

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

Val Gly Gly Ala Asp Pro Asp Ser Ala Tyr Ile Cys His Cys Pro Pro
20 25 30

Gly Phe Gln Gly Ser Asn Cys Glu
35 40

<210> 259
<211> 37
<212> PRT
<213> 智人

<400> 259

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
1 5 10 15

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
20 25 30

Gly Pro Arg Cys Glu
35

<210> 260
<211> 78
<212> PRT
<213> 智人

<400> 260

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

Val Gly Gly Ala Asp Pro Asp Ser Ala Tyr Ile Cys His Cys Pro Pro
20 25 30

Gly Phe Gln Gly Ser Asn Cys Glu Lys Arg Val Asp Arg Cys Ser Leu
35 40 45

Gln Pro Cys Arg Asn Gly Gly Leu Cys Leu Asp Leu Gly His Ala Leu
50 55 60

Arg Cys Arg Cys Arg Ala Gly Phe Ala Gly Pro Arg Cys Glu
65 70 75

<210> 261
<211> 37
<212> PRT
<213> 智人

<400> 261

Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys Ala Asn Gly Gly Thr Cys
1 5 10 15

Val Glu Gly Gly Gly Ala His Arg Cys Ser Cys Ala Leu Gly Phe Gly
20 25 30

Gly Arg Asp Cys Arg
35

<210> 262
<211> 37
<212> PRT
<213> 智人

<400> 262

Arg Ala Asp Pro Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys
1 5 10 15

Tyr Ala His Phe Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met
20 25 30

Gly Ala Arg Cys Glu
35

<210> 263
<211> 548
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 263

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

Ala Leu Ile Phe Leu Pro Gln Thr Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Leu Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Gly Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asp Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Phe Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Ala Gly Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg
145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala
165 170 175

Arg Cys Glu Pro Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg
180 185 190

Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala
195 200 205

Pro Leu Glu Asp Glu Cys Glu Ala Pro Leu Val Cys Arg Ala Gly Cys
210 215 220

Ser Pro Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu
225 230 235 240

Glu Gly Trp Thr Gly Pro Leu Cys Thr Val Pro Val Ser Thr Ser Ser
245 250 255

Cys Leu Ser Pro Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val
260 265 270

Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser
275 280 285

Cys Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe
290 295 300

Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro
305 310 315 320

Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala
325 330 335

Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys
340 345 350

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
355 360 365

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
370 375 380

Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys
385 390 395 400

Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser
405 410 415

Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro
420 425 430

Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe
435 440 445

Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys
450 455 460

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

Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Ser Gly Gly Gly
485 490 495

Gly Ser Gly Ala Gly Val Ile Ala Val Ile Val Val Val Val Ile Ala
500 505 510

Ile Val Ala Gly Ile Val Val Leu Val Ile Ser Arg Lys Lys Arg Met
515 520 525

Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu Met Gly Glu Met His Arg
530 535 540

Glu Leu Asn Ala
545

<210> 264
<211> 408
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 264

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

Val His Ser Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser
20 25 30

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

Arg Leu Cys Arg Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu
50 55 60

Arg Pro Cys Ala Pro Leu Glu Asp Glu Cys Glu Ala Pro Leu Val Cys
65 70 75 80

Arg Ala Gly Cys Ser Pro Glu His Gly Phe Cys Glu Gln Pro Gly Glu
85 90 95

Cys Arg Cys Leu Glu Gly Trp Thr Gly Pro Leu Cys Thr Val Pro Val
100 105 110

Ser Thr Ser Ser Cys Leu Ser Pro Arg Gly Pro Ser Ser Ala Thr Thr
115 120 125

Gly Cys Leu Val Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala
130 135 140

Asn Gly Gly Ser Cys Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys
145 150 155 160

Pro Arg Gly Phe Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys
165 170 175

Ala Asp Gly Pro Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp
180 185 190

Pro Asp Ser Ala Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser
195 200 205

Asn Cys Glu Lys Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn
210 215 220

Gly Gly Leu Cys Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg
225 230 235 240

Ala Gly Phe Ala Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala
245 250 255

Gly Arg Ala Cys Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala
260 265 270

His Arg Cys Ser Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu
275 280 285

Arg Ala Asp Pro Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys
290 295 300

Tyr Ala His Phe Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met
305 310 315 320

Gly Ala Arg Cys Glu Phe Pro Val His Pro Asp Gly Ala Ser Ala Leu
325 330 335

Pro Ala Ala Pro Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu
340 345 350

Ser Gly Gly Gly Gly Ser Gly Ala Gly Val Ile Ala Val Ile Val Val
355 360 365

Val Val Ile Ala Ile Val Ala Gly Ile Val Val Leu Val Ile Ser Arg
370 375 380

Lys Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu Met Gly
385 390 395 400

Glu Met His Arg Glu Leu Asn Ala
405

<210> 265
<211> 368
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 265

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

Val His Ser Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser
20 25 30

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

Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu Glu Gly Trp Thr
50 55 60

Gly Pro Leu Cys Thr Val Pro Val Ser Thr Ser Ser Cys Leu Ser Pro
65 70 75 80

Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val Pro Gly Pro Gly
85 90 95

Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser Cys Ser Glu Thr
100 105 110

Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe Tyr Gly Leu Arg
115 120 125

Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro Cys Phe Asn Gly
130 135 140

Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala Tyr Ile Cys His
145 150 155 160

Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys Arg Val Asp Arg
165 170 175

Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys Leu Asp Leu Gly
180 185 190

His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala Gly Pro Arg Cys
195 200 205

Glu His Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys Ala Asn Gly Gly
210 215 220

Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser Cys Ala Leu Gly
225 230 235 240

Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro Cys Ala Ala Arg
245 250 255

Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe Ser Gly Leu Val
260 265 270

Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys Glu Phe Pro Val
275 280 285

His Pro Asp Gly Ala Ser Ala Leu Pro Ala Ala Pro Pro Gly Leu Arg
290 295 300

Pro Gly Asp Pro Gln Arg Tyr Leu Ser Gly Gly Gly Gly Ser Gly Ala
305 310 315 320

Gly Val Ile Ala Val Ile Val Val Val Ile Ala Ile Val Ala Gly
325 330 335

Ile Val Val Leu Val Ile Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu
340 345 350

Lys Ala Glu Ile Lys Glu Met Gly Glu Met His Arg Glu Leu Asn Ala
355 360 365

<210> 266
<211> 310
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 266

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

Val His Ser Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser
20 25 30

Thr Ser Gly Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly
35 40 45

Gly Ser Cys Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg

50 55 60

Gly Phe Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp
65 70 75 80

Gly Pro Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp
85 90 95

Ser Ala Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys
100 105 110

Glu Lys Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly
115 120 125

Leu Cys Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly
130 135 140

Phe Ala Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala Gly Arg
145 150 155 160

Ala Cys Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg
165 170 175

Cys Ser Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala
180 185 190

Asp Pro Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala
195 200 205

His Phe Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala
210 215 220

Arg Cys Glu Phe Pro Val His Pro Asp Gly Ala Ser Ala Leu Pro Ala
225 230 235 240

Ala Pro Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Ser Gly
245 250 255

Gly Gly Gly Ser Gly Ala Gly Val Ile Ala Val Ile Val Val Val Val
260 265 270

Ile Ala Ile Val Ala Gly Ile Val Val Leu Val Ile Ser Arg Lys Lys
275 280 285

Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu Met Gly Glu Met
290 295 300

His Arg Glu Leu Asn Ala
305 310

<210> 267
<211> 272
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 267

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

Val His Ser Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser
20 25 30

Thr Ser Gly Ser Gly Val Thr Cys Ala Asp Gly Pro Cys Phe Asn Gly
35 40 45

Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala Tyr Ile Cys His
50 55 60

Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys Arg Val Asp Arg
65 70 75 80

Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys Leu Asp Leu Gly
85 90 95

His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala Gly Pro Arg Cys
100 105 110

Glu His Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys Ala Asn Gly Gly
115 120 125

Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser Cys Ala Leu Gly
130 135 140

Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro Cys Ala Ala Arg
145 150 155 160

Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe Ser Gly Leu Val
165 170 175

Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys Glu Phe Pro Val
180 185 190

His Pro Asp Gly Ala Ser Ala Leu Pro Ala Ala Pro Pro Gly Leu Arg
195 200 205

Pro Gly Asp Pro Gln Arg Tyr Leu Ser Gly Gly Gly Gly Ser Gly Ala
210 215 220

Gly Val Ile Ala Val Ile Val Val Val Val Ile Ala Ile Val Ala Gly

225 230 235 240

Ile Val Val Leu Val Ile Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu
245 250 255

Lys Ala Glu Ile Lys Glu Met Gly Glu Met His Arg Glu Leu Asn Ala
260 265 270

<210> 268
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 268

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

Val His Ser Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser
20 25 30

Thr Ser Gly Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly
35 40 45

Gly Leu Cys Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala
50 55 60

Gly Phe Ala Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala Gly
65 70 75 80

Arg Ala Cys Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His
85 90 95

Arg Cys Ser Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg
100 105 110

Ala Asp Pro Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr
115 120 125

Ala His Phe Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly
130 135 140

Ala Arg Cys Glu Phe Pro Val His Pro Asp Gly Ala Ser Ala Leu Pro
145 150 155 160

Ala Ala Pro Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Ser
165 170 175

Gly Gly Gly Gly Ser Gly Ala Gly Val Ile Ala Val Ile Val Val Val
180 185 190

Val Ile Ala Ile Val Ala Gly Ile Val Val Leu Val Ile Ser Arg Lys
195 200 205

Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu Met Gly Glu
210 215 220

Met His Arg Glu Leu Asn Ala
225 230

<210> 269
<211> 193
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 269

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

Val His Ser Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser
20 25 30

Thr Ser Gly Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys Ala Asn Gly
35 40 45

Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser Cys Ala Leu
50 55 60

Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro Cys Ala Ala
65 70 75 80

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

Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys Glu Phe Pro
100 105 110

Val His Pro Asp Gly Ala Ser Ala Leu Pro Ala Ala Pro Pro Gly Leu
115 120 125

Arg Pro Gly Asp Pro Gln Arg Tyr Leu Ser Gly Gly Gly Gly Ser Gly
130 135 140

Ala Gly Val Ile Ala Val Ile Val Val Val Val Ile Ala Ile Val Ala
145 150 155 160

Gly Ile Val Val Leu Val Ile Ser Arg Lys Lys Arg Met Ala Lys Tyr
165 170 175

Glu Lys Ala Glu Ile Lys Glu Met Gly Glu Met His Arg Glu Leu Asn
180 185 190

Ala

<210> 270
<211> 155
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 270

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

Val His Ser Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser
20 25 30

Thr Ser Gly Arg Ala Asp Pro Cys Ala Ala Arg Pro Cys Ala His Gly
35 40 45

Gly Arg Cys Tyr Ala His Phe Ser Gly Leu Val Cys Ala Cys Ala Pro
50 55 60

Gly Tyr Met Gly Ala Arg Cys Glu Phe Pro Val His Pro Asp Gly Ala
65 70 75 80

Ser Ala Leu Pro Ala Ala Pro Pro Gly Leu Arg Pro Gly Asp Pro Gln
85 90 95

Arg Tyr Leu Ser Gly Gly Gly Gly Ser Gly Ala Gly Val Ile Ala Val
100 105 110

Ile Val Val Val Val Ile Ala Ile Val Ala Gly Ile Val Val Leu Val
115 120 125

Ile Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys
130 135 140

Glu Met Gly Glu Met His Arg Glu Leu Asn Ala
145 150 155

<210> 271
<211> 587
<212> PRT
<213> 食蟹猴

<400> 271

Met Val Ser Pro Arg Met Ser Arg Leu Leu Ser Gln Thr Val Ile Leu

1 5 10 15

Ala Leu Ile Phe Ile Pro Gln Ala Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Gly Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Glu Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asn Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Thr Arg Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg
145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala
165 170 175

Arg Cys Glu Leu Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg
180 185 190

Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala
195 200 205

Pro Leu Glu Asp Glu Cys Glu Ala Pro Pro Val Cys Arg Ala Gly Cys
210 215 220

Ser Leu Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu
225 230 235 240

Glu Gly Trp Thr Gly Pro Leu Cys Met Val Pro Ala Ser Thr Ser Ser
245 250 255

Cys Leu Gly Leu Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val
260 265 270

Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser
275 280 285

Cys Ser Glu Thr Pro Gly Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe
290 295 300

Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro
305 310 315 320

Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala
325 330 335

Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys
340 345 350

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
355 360 365

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
370 375 380

Gly Pro Arg Cys Glu His Asn Leu Asp Asp Cys Ala Gly Arg Ala Cys
385 390 395 400

Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser
405 410 415

Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro
420 425 430

Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe
435 440 445

Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ser Arg Cys
450 455 460

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

Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Leu Pro Pro Ala
485 490 495

Leu Gly Leu Leu Val Ala Ala Gly Val Ala Gly Ala Ala Leu Leu Leu
500 505 510

Val His Val Arg Arg Arg Gly His Ala Gln Asp Ala Gly Ser Arg Leu
515 520 525

Leu Ala Gly Thr Pro Glu Pro Ser Val His Ala Leu Pro Asp Ala Leu
530 535 540

Asn Asn Gln Arg Thr Gln Glu Gly Pro Gly Asp Val Pro Ser Ser Ser
545 550 555 560

Val Asp Trp Asn Arg Pro Glu Asp Val Asp Ser Arg Gly Ile Tyr Val
565 570 575

Ile Ser Ala Pro Ser Ile Tyr Ala Arg Glu Ala
580 585

<210> 272
<211> 492
<212> PRT
<213> 食蟹猴

<400> 272

Met Val Ser Pro Arg Met Ser Arg Leu Leu Ser Gln Thr Val Ile Leu
1 5 10 15

Ala Leu Ile Phe Ile Pro Gln Ala Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Gly Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Glu Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asn Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Thr Arg Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg
145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala
165 170 175

Arg Cys Glu Leu Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg
180 185 190

Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala
195 200 205

Pro Leu Glu Asp Glu Cys Glu Ala Pro Pro Val Cys Arg Ala Gly Cys
210 215 220

Ser Leu Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu
225 230 235 240

Glu Gly Trp Thr Gly Pro Leu Cys Met Val Pro Ala Ser Thr Ser Ser
245 250 255

Cys Leu Gly Leu Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val
260 265 270

Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser
275 280 285

Cys Ser Glu Thr Pro Gly Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe
290 295 300

Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro
305 310 315 320

Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala
325 330 335

Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys
340 345 350

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
355 360 365

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
370 375 380

Gly Pro Arg Cys Glu His Asn Leu Asp Asp Cys Ala Gly Arg Ala Cys
385 390 395 400

Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser
405 410 415

Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro
420 425 430

Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe
435 440 445

Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ser Arg Cys
450 455 460

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

Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu
485 490

<210> 273
<211> 175
<212> PRT
<213> 食蟹猴

<400> 273

Met Val Ser Pro Arg Met Ser Arg Leu Leu Ser Gln Thr Val Ile Leu
1 5 10 15

Ala Leu Ile Phe Ile Pro Gln Ala Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Gly Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Glu Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asn Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Thr Arg Arg Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg
145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg
165 170 175

<210> 274
<211> 40
<212> PRT
<213> 食蟹猴

<400> 274

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

Arg Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys
20 25 30

Ala Pro Leu Glu Asp Glu Cys Glu
35 40

<210> 275
<211> 34
<212> PRT
<213> 食蟹猴

<400> 275

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

Glu Gln Pro Gly Glu Cys Arg Cys Leu Glu Gly Trp Thr Gly Pro Leu
20 25 30

Cys Met

<210> 276
<211> 37
<212> PRT
<213> 食蟹猴

<400> 276

Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser Cys
1 5 10 15

Ser Glu Thr Pro Gly Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe Tyr
20 25 30

Gly Leu Arg Cys Glu
35

<210> 277
<211> 40
<212> PRT
<213> 食蟹猴

<400> 277

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

Val Gly Gly Ala Asp Pro Asp Ser Ala Tyr Ile Cys His Cys Pro Pro
20 25 30

Gly Phe Gln Gly Ser Asn Cys Glu

35 40

<210> 278
<211> 37
<212> PRT
<213> 食蟹猴

<400> 278

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
1 5 10 15

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
20 25 30

Gly Pro Arg Cys Glu
35

<210> 279
<211> 78
<212> PRT
<213> 食蟹猴

<400> 279

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

Val Gly Gly Ala Asp Pro Asp Ser Ala Tyr Ile Cys His Cys Pro Pro
20 25 30

Gly Phe Gln Gly Ser Asn Cys Glu Lys Arg Val Asp Arg Cys Ser Leu
35 40 45

Gln Pro Cys Arg Asn Gly Gly Leu Cys Leu Asp Leu Gly His Ala Leu
50 55 60

Arg Cys Arg Cys Arg Ala Gly Phe Ala Gly Pro Arg Cys Glu
65 70 75

<210> 280
<211> 37
<212> PRT
<213> 食蟹猴

<400> 280

Asn Leu Asp Asp Cys Ala Gly Arg Ala Cys Ala Asn Gly Gly Thr Cys
1 5 10 15

Val Glu Gly Gly Gly Ala His Arg Cys Ser Cys Ala Leu Gly Phe Gly
20 25 30

Gly Arg Asp Cys Arg
35

<210> 281
<211> 37
<212> PRT
<213> 食蟹猴

<400> 281

Arg Ala Asp Pro Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys
1 5 10 15

Tyr Ala His Phe Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met
20 25 30

Gly Ser Arg Cys Glu
35

<210> 282
<211> 548
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 282

Met Val Ser Pro Arg Met Ser Arg Leu Leu Ser Gln Thr Val Ile Leu
1 5 10 15

Ala Leu Ile Phe Ile Pro Gln Ala Arg Pro Ala Gly Val Phe Glu Leu
20 25 30

Gln Ile His Ser Phe Gly Pro Gly Pro Gly Pro Gly Ala Pro Arg Ser
35 40 45

Pro Cys Ser Ala Arg Gly Pro Cys Arg Leu Phe Phe Arg Val Cys Leu
50 55 60

Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly
65 70 75 80

Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Glu Ala
85 90 95

Pro Ala Pro Asp Leu Pro Leu Pro Asn Gly Leu Leu Gln Val Pro Phe
100 105 110

Arg Asp Ala Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Thr Trp Arg
115 120 125

Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala
130 135 140

Arg Val Thr Arg Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg

145 150 155 160

Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala
165 170 175

Arg Cys Glu Leu Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg
180 185 190

Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala
195 200 205

Pro Leu Glu Asp Glu Cys Glu Ala Pro Pro Val Cys Arg Ala Gly Cys
210 215 220

Ser Leu Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu
225 230 235 240

Glu Gly Trp Thr Gly Pro Leu Cys Met Val Pro Ala Ser Thr Ser Ser
245 250 255

Cys Leu Gly Leu Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val
260 265 270

Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser
275 280 285

Cys Ser Glu Thr Pro Gly Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe
290 295 300

Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro
305 310 315 320

Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala
325 330 335

Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys
340 345 350

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
355 360 365

Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
370 375 380

Gly Pro Arg Cys Glu His Asn Leu Asp Asp Cys Ala Gly Arg Ala Cys
385 390 395 400

Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Gly Ala His Arg Cys Ser
405 410 415

Cys Ala Leu Gly Phe Gly Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro
420 425 430

Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe
435 440 445

Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ser Arg Cys
450 455 460

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

Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Ser Gly Gly Gly
485 490 495

Gly Ser Gly Ala Gly Val Ile Ala Val Ile Val Val Val Val Ile Ala
500 505 510

Ile Val Ala Gly Ile Val Val Leu Val Ile Ser Arg Lys Lys Arg Met
515 520 525

Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu Met Gly Glu Met His Arg
530 535 540

Glu Leu Asn Ala
545

<210> 283
<211> 723
<212> PRT
<213> 智人

<400> 283

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

Cys Gln Val Trp Ser Ser Gly Val Phe Glu Leu Lys Leu Gln Glu Phe
20 25 30

Val Asn Lys Lys Gly Leu Leu Gly Asn Arg Asn Cys Cys Arg Gly Gly
35 40 45

Ala Gly Pro Pro Pro Cys Ala Cys Arg Thr Phe Phe Arg Val Cys Leu
50 55 60

Lys His Tyr Gln Ala Ser Val Ser Pro Glu Pro Pro Cys Thr Tyr Gly
65 70 75 80

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

Gly Gly Gly Ala Asp Ser Ala Phe Ser Asn Pro Ile Arg Phe Pro Phe
100 105 110

Gly Phe Thr Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Ala Leu His
115 120 125

Thr Asp Ser Pro Asp Asp Leu Ala Thr Glu Asn Pro Glu Arg Leu Ile
130 135 140

Ser Arg Leu Ala Thr Gln Arg His Leu Thr Val Gly Glu Glu Trp Ser
145 150 155 160

Gln Asp Leu His Ser Ser Gly Arg Thr Asp Leu Lys Tyr Ser Tyr Arg
165 170 175

Phe Val Cys Asp Glu His Tyr Tyr Gly Glu Gly Cys Ser Val Phe Cys
180 185 190

Arg Pro Arg Asp Asp Ala Phe Gly His Phe Thr Cys Gly Glu Arg Gly
195 200 205

Glu Lys Val Cys Asn Pro Gly Trp Lys Gly Pro Tyr Cys Thr Glu Pro
210 215 220

Ile Cys Leu Pro Gly Cys Asp Glu Gln His Gly Phe Cys Asp Lys Pro
225 230 235 240

Gly Glu Cys Lys Cys Arg Val Gly Trp Gln Gly Arg Tyr Cys Asp Glu
245 250 255

Cys Ile Arg Tyr Pro Gly Cys Leu His Gly Thr Cys Gln Gln Pro Trp
260 265 270

Gln Cys Asn Cys Gln Glu Gly Trp Gly Gly Leu Phe Cys Asn Gln Asp
275 280 285

Leu Asn Tyr Cys Thr His His Lys Pro Cys Lys Asn Gly Ala Thr Cys
290 295 300

Thr Asn Thr Gly Gln Gly Ser Tyr Thr Cys Ser Cys Arg Pro Gly Tyr
305 310 315 320

Thr Gly Ala Thr Cys Glu Leu Gly Ile Asp Glu Cys Asp Pro Ser Pro
325 330 335

Cys Lys Asn Gly Gly Ser Cys Thr Asp Leu Glu Asn Ser Tyr Ser Cys
340 345 350

Thr Cys Pro Pro Gly Phe Tyr Gly Lys Ile Cys Glu Leu Ser Ala Met
355 360 365

Thr Cys Ala Asp Gly Pro Cys Phe Asn Gly Gly Arg Cys Ser Asp Ser
370 375 380

Pro Asp Gly Gly Tyr Ser Cys Arg Cys Pro Val Gly Tyr Ser Gly Phe
385 390 395 400

Asn Cys Glu Lys Lys Ile Asp Tyr Cys Ser Ser Ser Pro Cys Ser Asn
405 410 415

Gly Ala Lys Cys Val Asp Leu Gly Asp Ala Tyr Leu Cys Arg Cys Gln
420 425 430

Ala Gly Phe Ser Gly Arg His Cys Asp Asp Asn Val Asp Asp Cys Ala
435 440 445

Ser Ser Pro Cys Ala Asn Gly Gly Thr Cys Arg Asp Gly Val Asn Asp
450 455 460

Phe Ser Cys Thr Cys Pro Pro Gly Tyr Thr Gly Arg Asn Cys Ser Ala
465 470 475 480

Pro Val Ser Arg Cys Glu His Ala Pro Cys His Asn Gly Ala Thr Cys
485 490 495

His Glu Arg Gly His Arg Tyr Val Cys Glu Cys Ala Arg Gly Tyr Gly
500 505 510

Gly Pro Asn Cys Gln Phe Leu Leu Pro Glu Leu Pro Pro Gly Pro Ala
515 520 525

Val Val Asp Leu Thr Glu Lys Leu Glu Gly Gln Gly Gly Pro Phe Pro
530 535 540

Trp Val Ala Val Cys Ala Gly Val Ile Leu Val Leu Met Leu Leu Leu
545 550 555 560

Gly Cys Ala Ala Val Val Val Cys Val Arg Leu Arg Leu Gln Lys His
565 570 575

Arg Pro Pro Ala Asp Pro Cys Arg Gly Glu Thr Glu Thr Met Asn Asn
580 585 590

Leu Ala Asn Cys Gln Arg Glu Lys Asp Ile Ser Val Ser Ile Ile Gly
595 600 605

Ala Thr Gln Ile Lys Asn Thr Asn Lys Lys Ala Asp Phe His Gly Asp
610 615 620

His Ser Ala Asp Lys Asn Gly Phe Lys Ala Arg Tyr Pro Ala Val Asp
625 630 635 640

Tyr Asn Leu Val Gln Asp Leu Lys Gly Asp Asp Thr Ala Val Arg Asp
645 650 655

Ala His Ser Lys Arg Asp Thr Lys Cys Gln Pro Gln Gly Ser Ser Gly
660 665 670

Glu Glu Lys Gly Thr Pro Thr Thr Leu Arg Gly Gly Glu Ala Ser Glu
675 680 685

Arg Lys Arg Pro Asp Ser Gly Cys Ser Thr Ser Lys Asp Thr Lys Tyr
690 695 700

Gln Ser Val Tyr Val Ile Ser Glu Glu Lys Asp Glu Cys Val Ile Ala
705 710 715 720

Thr Glu Val

<210> 284
<211> 685
<212> PRT
<213> 智人

<400> 284

Met Ala Ala Ala Ser Arg Ser Ala Ser Gly Trp Ala Leu Leu Leu Leu
1 5 10 15

Val Ala Leu Trp Gln Gln Arg Ala Ala Gly Ser Gly Val Phe Gln Leu
20 25 30

Gln Leu Gln Glu Phe Ile Asn Glu Arg Gly Val Leu Ala Ser Gly Arg
35 40 45

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

Phe Gln Ala Val Val Ser Pro Gly Pro Cys Thr Phe Gly Thr Val Ser
65 70 75 80

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

Gly Gly Gly Arg Asn Pro Leu Gln Leu Pro Phe Asn Phe Thr Trp Pro
100 105 110

Gly Thr Phe Ser Leu Ile Ile Glu Ala Trp His Ala Pro Gly Asp Asp
115 120 125

Leu Arg Pro Glu Ala Leu Pro Pro Asp Ala Leu Ile Ser Lys Ile Ala
130 135 140

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

Thr Ser Thr Leu Thr Arg Leu Arg Tyr Ser Tyr Arg Val Ile Cys Ser
165 170 175

Asp Asn Tyr Tyr Gly Asp Asn Cys Ser Arg Leu Cys Lys Lys Arg Asn
180 185 190

Asp His Phe Gly His Tyr Val Cys Gln Pro Asp Gly Asn Leu Ser Cys
195 200 205

Leu Pro Gly Trp Thr Gly Glu Tyr Cys Gln Gln Pro Ile Cys Leu Ser
210 215 220

Gly Cys His Glu Gln Asn Gly Tyr Cys Ser Lys Pro Ala Glu Cys Leu
225 230 235 240

Cys Arg Pro Gly Trp Gln Gly Arg Leu Cys Asn Glu Cys Ile Pro His
245 250 255

Asn Gly Cys Arg His Gly Thr Cys Ser Thr Pro Trp Gln Cys Thr Cys
260 265 270

Asp Glu Gly Trp Gly Gly Leu Phe Cys Asp Gln Asp Leu Asn Tyr Cys
275 280 285

Thr His His Ser Pro Cys Lys Asn Gly Ala Thr Cys Ser Asn Ser Gly
290 295 300

Gln Arg Ser Tyr Thr Cys Thr Cys Arg Pro Gly Tyr Thr Gly Val Asp
305 310 315 320

Cys Glu Leu Glu Leu Ser Glu Cys Asp Ser Asn Pro Cys Arg Asn Gly
325 330 335

Gly Ser Cys Lys Asp Gln Glu Asp Gly Tyr His Cys Leu Cys Pro Pro
340 345 350

Gly Tyr Tyr Gly Leu His Cys Glu His Ser Thr Leu Ser Cys Ala Asp
355 360 365

Ser Pro Cys Phe Asn Gly Gly Ser Cys Arg Glu Arg Asn Gln Gly Ala
370 375 380

Asn Tyr Ala Cys Glu Cys Pro Pro Asn Phe Thr Gly Ser Asn Cys Glu
385 390 395 400

Lys Lys Val Asp Arg Cys Thr Ser Asn Pro Cys Ala Asn Gly Gly Gln

405 410 415

Cys Leu Asn Arg Gly Pro Ser Arg Met Cys Arg Cys Arg Pro Gly Phe
420 425 430

Thr Gly Thr Tyr Cys Glu Leu His Val Ser Asp Cys Ala Arg Asn Pro
435 440 445

Cys Ala His Gly Gly Thr Cys His Asp Leu Glu Asn Gly Leu Met Cys
450 455 460

Thr Cys Pro Ala Gly Phe Ser Gly Arg Arg Cys Glu Val Arg Thr Ser
465 470 475 480

Ile Asp Ala Cys Ala Ser Ser Pro Cys Phe Asn Arg Ala Thr Cys Tyr
485 490 495

Thr Asp Leu Ser Thr Asp Thr Phe Val Cys Asn Cys Pro Tyr Gly Phe
500 505 510

Val Gly Ser Arg Cys Glu Phe Pro Val Gly Leu Pro Pro Ser Phe Pro
515 520 525

Trp Val Ala Val Ser Leu Gly Val Gly Leu Ala Val Leu Leu Val Leu
530 535 540

Leu Gly Met Val Ala Val Ala Val Arg Gln Leu Arg Leu Arg Arg Pro
545 550 555 560

Asp Asp Gly Ser Arg Glu Ala Met Asn Asn Leu Ser Asp Phe Gln Lys
565 570 575

Asp Asn Leu Ile Pro Ala Ala Gln Leu Lys Asn Thr Asn Gln Lys Lys
580 585 590

Glu Leu Glu Val Asp Cys Gly Leu Asp Lys Ser Asn Cys Gly Lys Gln
595 600 605

Gln Asn His Thr Leu Asp Tyr Asn Leu Ala Pro Gly Pro Leu Gly Arg
610 615 620

Gly Thr Met Pro Gly Lys Phe Pro His Ser Asp Lys Ser Leu Gly Glu
625 630 635 640

Lys Ala Pro Leu Arg Leu His Ser Glu Lys Pro Glu Cys Arg Ile Ser
645 650 655

Ala Ile Cys Ser Pro Arg Asp Ser Met Tyr Gln Ser Val Cys Leu Ile
660 665 670

Ser Glu Glu Arg Asn Glu Cys Val Ile Ala Thr Glu Val
675 680 685

<210> 285
<211> 4
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 285

Gly Gly Gly Gly
1

<210> 286
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 286

Gly Gly Gly Gly Ser
1 5

<210> 287
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 287

Gly Gly Gly Gly Gln
1 5

<210> 288
<211> 6
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 288

Ser Gly Gly Gly Gly Ser
1 5

<210> 289
<211> 6
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 289

Pro Gly Gly Gly Gly Ser
1 5

<210> 290
<211> 6
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 290

Pro Gly Gly Asp Gly Ser
1 5

<210> 291
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 291

Gly Gly Gly Gly Ser Gly Gly Gly Ser
1 5

<210> 292
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 292

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 293
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 293

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 294
<211> 6
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 294

His His His His His His
1 5

<210> 295
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 295

Arg Asp Trp Asp Phe Asp Val Phe Gly Gly Gly Thr Pro Val Gly Gly
1 5 10 15

<210> 296
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<220>
<221> misc_feature
<222> (12)..(12)
<223> Xaa可為任何天然存在之胺基酸

<400> 296

Gln Arg Phe Val Thr Gly His Phe Gly Gly Leu Xaa Pro Ala Asn Gly
1 5 10 15

<210> 297
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 297

Gln Arg Phe Val Thr Gly His Phe Gly Gly Leu Tyr Pro Ala Asn Gly
1 5 10 15

<210> 298
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 298

Gln Arg Phe Val Thr Gly His Phe Gly Gly Leu His Pro Ala Asn Gly
1 5 10 15

<210> 299
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 299

Thr Gly His Phe Gly Gly Leu His Pro
1 5

<210> 300
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 300

Gln Arg Phe Cys Thr Gly His Phe Gly Gly Leu His Pro Cys Asn Gly
1 5 10 15

<210> 301
<211> 585
<212> PRT
<213> 智人

<400> 301

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

<210> 302
<211> 585
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 302

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Gly Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Ala Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys

545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

<210> 303
<211> 585
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 303

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His

450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

<210> 304
<211> 585
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 304

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu

355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

<210> 305
<211> 585
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 305

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser

260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Gly Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

<210> 306
<211> 585
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 306

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala

165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

<210> 307
<211> 585
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 307

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu

65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

<210> 308
<211> 585
<212> PRT

<213> 人工序列

<220>
<223> 合成肽

<400> 308

Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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20 25 30

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

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565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Gly Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Ala Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val

565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser

465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

370 375 380

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Gly Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
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Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
20 25 30

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His

275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
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Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
20 25 30

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser

180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
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Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
20 25 30

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro

85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1 5 10 15

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

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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

Gln Ser Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Gly Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Ala Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
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Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
20 25 30

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu

580 585

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

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

485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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1 5 10 15

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu

385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser

290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
580 585

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

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

195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro His Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu

100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Lys Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu

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

Gln Ala Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
100 105 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
115 120 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
130 135 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145 150 155 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
165 170 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
180 185 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
195 200 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
210 215 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225 230 235 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
245 250 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
260 265 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
275 280 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
290 295 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305 310 315 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
325 330 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
340 345 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
355 360 365

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

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385 390 395 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
405 410 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
420 425 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
435 440 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
450 455 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465 470 475 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Asp Val Asp Glu Thr
485 490 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
500 505 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
515 520 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
530 535 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545 550 555 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Pro Lys Leu Val
565 570 575

Ala Ala Ser Lys Ala Ala Leu Gly Leu
580 585

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

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

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

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

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

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

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

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu
165 170 175

Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Asp Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

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

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

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Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
1 5 10 15

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
20 25 30

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

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
50 55 60

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

65 70 75 80

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
85 90 95

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser Asp Lys Thr His Thr Cys
100 105 110

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
115 120 125

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
130 135 140

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
145 150 155 160

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
165 170 175

Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu
180 185 190

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
195 200 205

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
210 215 220

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
225 230 235 240

Arg Lys Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
245 250 255

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
260 265 270

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Lys Ser Asp Gly
275 280 285

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
305 310 315 320

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

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

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

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

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

Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Thr Val Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

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

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

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu

225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Asp Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

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

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

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Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
1 5 10 15

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
20 25 30

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

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
50 55 60

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
65 70 75 80

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
85 90 95

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser Glu Pro Lys Ser Ser Asp
100 105 110

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
115 120 125

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
130 135 140

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
145 150 155 160

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

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
180 185 190

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
195 200 205

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
210 215 220

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
225 230 235 240

Thr Leu Pro Pro Ser Arg Lys Glu Met Thr Lys Asn Gln Val Ser Leu
245 250 255

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
260 265 270

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
275 280 285

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

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
305 310 315 320

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
325 330 335

Gly Lys

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Lys Glu Met Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Lys Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Asp Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Asp Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

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<400> 337

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln
65 70 75 80

Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Lys Glu Met Thr
130 135 140

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

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Lys Thr Thr Pro Pro Val Leu Lys Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

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<400> 338

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln
65 70 75 80

Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
130 135 140

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

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Asp Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Asp Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys

225 230

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<400> 339

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Lys Glu Met Thr
130 135 140

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

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Lys Thr Thr Pro Pro Val Leu Lys Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

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<400> 340

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
130 135 140

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

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Asp Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Asp Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 341
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<400> 341

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95

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

Pro Arg Glu Pro Gln Val Thr Thr Leu Pro Pro Ser Arg Glu Glu Met
115 120 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145 150 155 160

Tyr Asp Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
165 170 175

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

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
210 215

<210> 342
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<400> 342

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 343
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<400> 343

Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 344
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<400> 344

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 345
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<400> 345

Ile Tyr Ala Met Asn
1 5

<210> 346
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<400> 346

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Ser

<210> 347
<211> 14
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<220>
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<400> 347

His Gly Asn Phe Gly Asn Ser Tyr Val Ser Phe Phe Ala Tyr
1 5 10

<210> 348
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<400> 348

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Phe Phe
100 105 110

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

<210> 349
<211> 109
<212> PRT
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<400> 349

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 350
<211> 249
<212> PRT
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<220>
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<400> 350

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Phe Phe
100 105 110

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

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

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 351
<211> 14
<212> PRT
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<400> 351

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 352
<211> 7
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<220>
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<400> 352

Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 353
<211> 9
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<400> 353

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 354
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<400> 354

Lys Tyr Ala Met Asn
1 5

<210> 355
<211> 19
<212> PRT
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<220>
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<400> 355

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Asp

<210> 356
<211> 14
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<220>
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<400> 356

His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr

1 5 10

<210> 357
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<212> PRT
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<220>
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<400> 357

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

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

<210> 358
<211> 109
<212> PRT
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<220>
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<400> 358

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 359
<211> 249
<212> PRT
<213> 人工序列

<220>
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<400> 359

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

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

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

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

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

165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 360
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<400> 360

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 361
<211> 7
<212> PRT
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<400> 361

Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 362
<211> 9
<212> PRT
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<400> 362

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 363
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<400> 363

Ser Tyr Ala Met Asn
1 5

<210> 364
<211> 19
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<220>
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<400> 364

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Gly

<210> 365
<211> 14
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<220>
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<400> 365

His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Phe Trp Ala Tyr
1 5 10

<210> 366
<211> 125
<212> PRT
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<220>
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<400> 366

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp

50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Phe Trp
100 105 110

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

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<211> 109
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<220>
<223> 合成肽

<400> 367

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

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<211> 249
<212> PRT
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<400> 368

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Phe Trp
100 105 110

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

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

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 369
<211> 14
<212> PRT

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<400> 369

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 370
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<400> 370

Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 371
<211> 9
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<400> 371

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

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<400> 372

Arg Tyr Ala Met Asn
1 5

<210> 373
<211> 19
<212> PRT
<213> 人工序列

<220>
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<400> 373

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Gly

<210> 374
<211> 14
<212> PRT
<213> 人工序列

<220>
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<400> 374

His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe Ala Tyr
1 5 10

<210> 375
<211> 125
<212> PRT
<213> 人工序列

<220>
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<400> 375

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe
100 105 110

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

<210> 376
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 376

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 377
<211> 249
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 377

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe
100 105 110

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

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

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 378
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 378

Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 379
<211> 7
<212> PRT
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<220>
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<400> 379

Ala Thr Asp Met Arg Pro Ser
1 5

<210> 380

<211> 9
<212> PRT
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<220>
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<400> 380

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 381
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<220>
<223> 合成肽

<400> 381

Val Tyr Ala Met Asn
1 5

<210> 382
<211> 19
<212> PRT
<213> 人工序列

<220>
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<400> 382

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Lys

<210> 383
<211> 14
<212> PRT
<213> 人工序列

<220>
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<400> 383

His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Trp Trp Ala Tyr
1 5 10

<210> 384
<211> 125
<212> PRT
<213> 人工序列

<220>
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<400> 384

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Trp Trp
100 105 110

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

<210> 385
<211> 109
<212> PRT
<213> 人工序列

<220>
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<400> 385

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

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

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 386
<211> 249
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 386

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Trp Trp
100 105 110

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

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

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

Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Ala
180 185 190

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

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 387
<211> 14
<212> PRT
<213> 人工序列

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<400> 387

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 388
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 388

Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 389
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 389

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 390
<211> 5
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<213> 人工序列

<220>
<223> 合成肽

<400> 390

Lys Tyr Ala Met Asn
1 5

<210> 391
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 391

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Ser

<210> 392
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 392

His Gly Asn Phe Gly Asn Ser Tyr Thr Ser Tyr Tyr Ala Tyr
1 5 10

<210> 393
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 393

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Thr Ser Tyr Tyr
100 105 110

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

<210> 394
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 394

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 395
<211> 249
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 395

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Thr Ser Tyr Tyr
100 105 110

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

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

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 396
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 396

Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 397
<211> 7
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<213> 人工序列

<220>
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<400> 397

Ala Thr Asp Met Arg Pro Ser
1 5

<210> 398
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 398

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 399
<211> 5
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<220>
<223> 合成肽

<400> 399

Gly Tyr Ala Met Asn
1 5

<210> 400
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 400

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Glu

<210> 401
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<220>
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<400> 401

His Arg Asn Phe Gly Asn Ser Tyr Leu Ser Trp Phe Ala Tyr
1 5 10

<210> 402
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 402

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Gly Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Glu Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Arg Asn Phe Gly Asn Ser Tyr Leu Ser Trp Phe
100 105 110

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

<210> 403
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 403

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

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

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

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

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 404
<211> 249
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 404

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Gly Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Glu Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Arg Asn Phe Gly Asn Ser Tyr Leu Ser Trp Phe
100 105 110

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

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

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu

145 150 155 160

Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Ala
180 185 190

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

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 405
<211> 14
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<213> 人工序列

<220>
<223> 合成肽

<400> 405

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
1 5 10

<210> 406
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 406

Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 407
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 407

Ala Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 408
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 408

Val Tyr Ala Met Asn
1 5

<210> 409
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 409

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Lys

<210> 410
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 410

His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Trp Trp Ala Tyr
1 5 10

<210> 411
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 411

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

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

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

35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Trp Trp
100 105 110

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

<210> 412
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 412

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 413
<211> 249
<212> PRT
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<220>

<223> 合成肽

<400> 413

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Trp Trp
100 105 110

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

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

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 414
<211> 14
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<213> 人工序列

<220>
<223> 合成肽

<400> 414

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
1 5 10

<210> 415
<211> 7
<212> PRT
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<220>
<223> 合成肽

<400> 415

Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 416
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 416

Val Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 417
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 417

Ser Tyr Ala Met Asn
1 5

<210> 418
<211> 19
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<400> 418

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Gly

<210> 419
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<400> 419

His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp Ala Tyr
1 5 10

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<400> 420

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
100 105 110

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

<210> 421
<211> 109
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<220>
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<400> 421

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

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<211> 249
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<220>
<223> 合成肽

<400> 422

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
100 105 110

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

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

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 423
<211> 14
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<213> 人工序列

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<400> 423

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
1 5 10

<210> 424
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<400> 424

Gly Thr Lys Phe Leu Ala Pro

1 5

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<400> 425

Val Leu Trp Tyr Ser Asn Arg Trp Val
1 5

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<400> 426

Lys Tyr Ala Met Asn
1 5

<210> 427
<211> 19
<212> PRT
<213> 人工序列

<220>
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<400> 427

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Asp

<210> 428
<211> 14
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<220>
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<400> 428

His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
1 5 10

<210> 429
<211> 125
<212> PRT
<213> 人工序列

<220>
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<400> 429

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

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

<210> 430
<211> 109
<212> PRT
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<220>
<223> 合成肽

<400> 430

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 431
<211> 249
<212> PRT
<213> 人工序列

<220>
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<400> 431

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

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

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

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 432
<211> 125
<212> PRT
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<220>
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<400> 432

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
100 105 110

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

<210> 433
<211> 109
<212> PRT
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<220>
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<400> 433

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

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 434
<211> 249
<212> PRT
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<220>
<223> 合成肽

<400> 434

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

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

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

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
100 105 110

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

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 435
<211> 118
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 435

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala

85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 436
<211> 108
<212> PRT
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<220>
<223> 合成肽

<400> 436

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Asn Asn Asn
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asp Arg Ser Pro
85 90 95

Leu Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 437
<211> 241
<212> PRT
<213> 人工序列

<220>
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<400> 437

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys

<210> 438
<211> 496
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 438

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

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<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 439

Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln

1 5 10 15

Gly

<210> 440
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 440

Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 441
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 441

Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu Ser
1 5 10 15

<210> 442
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 442

Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu Ser
1 5 10 15

<210> 443
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 443

Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Gln Thr Tyr Leu Ser
1 5 10 15

<210> 444
<211> 16
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 444

Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Ala Tyr Leu Ser
1 5 10 15

<210> 445
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 445

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 446
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 446

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 447
<211> 123
<212> PRT
<213> 人工序列

<220>
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<400> 447

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 448
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 448

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 449
<211> 122
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 449

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser
115 120

<210> 450
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 450

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 451
<211> 123

<212> PRT
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<220>
<223> 合成肽

<400> 451

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 452
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 452

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr

65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 453
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 453

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 454
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 454

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 455
<211> 123
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 455

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val

100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 456
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 456

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Glu Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 457
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 457

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Ala Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 458
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 458

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Gln Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 459
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 459

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Ala Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 460
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 460

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 461
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 461

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Glu Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 462
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 462

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Ala Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 463
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 463

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 464
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 464

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Glu Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 465
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 465

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Ala Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 466
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 466

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg

20 25 30

Asp Gly Gln Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 467
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 467

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Ala Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 468
<211> 112
<212> PRT
<213> 人工序列

<220>

<223> 合成肽

<400> 468

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 469
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 469

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Glu Gly Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys

100 105 110

<210> 470
<211> 112
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 470

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg
20 25 30

Asp Ala Asn Thr Tyr Leu Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Trp Gln Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 471
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 471

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 472
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 472

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met

35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 473
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 473

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Gln Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 474
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 474

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Ala Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 475
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 475

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 476
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 476

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 477
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 477

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu

165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 478
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 478

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

<210> 479
<211> 250
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 479

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe

50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
245 250

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<400> 482

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

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<400> 484

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Gln Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

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<400> 486

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Ala Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr

180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

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<400> 487

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

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<400> 488

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 489
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<400> 489

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

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<400> 490

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr

65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 491
<211> 250
<212> PRT
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<220>
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<400> 491

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 492
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<212> PRT
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<400> 492

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 493
<211> 250
<212> PRT
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<400> 493

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
245 250

<210> 494
<211> 505
<212> PRT
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<220>
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<400> 494

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 495
<211> 505
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<400> 495

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Gln Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Ala Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
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Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Gln Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Ala Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 514
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1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 515
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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Glu Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Glu Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 516
<211> 505
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<400> 516

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Ala Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Ala Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
500 505 510

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
515 520 525

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
530 535 540

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
545 550 555 560

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr
565 570 575

Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
580 585 590

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
595 600 605

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
610 615 620

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
625 630 635 640

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
645 650 655

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys

660 665 670

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
675 680 685

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
690 695 700

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
705 710 715 720

Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
725 730 735

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
740 745 750

Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
755 760 765

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
770 775 780

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
785 790 795 800

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
805 810 815

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln
820 825 830

Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln
835 840 845

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
850 855 860

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
865 870 875 880

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
885 890 895

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
900 905 910

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
915 920 925

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
930 935 940

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
945 950 955 960

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
965 970 975

Ser Leu Ser Leu Ser Pro Gly Lys
980

<210> 518
<211> 982
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<400> 518

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln

165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
500 505 510

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
515 520 525

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
530 535 540

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
545 550 555 560

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr
565 570 575

Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
580 585 590

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
595 600 605

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
610 615 620

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
625 630 635 640

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
645 650 655

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
660 665 670

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
675 680 685

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
690 695 700

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
705 710 715 720

Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
725 730 735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
740 745 750

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
755 760 765

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
770 775 780

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
785 790 795 800

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
805 810 815

Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly
820 825 830

Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp
835 840 845

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
850 855 860

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
865 870 875 880

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
885 890 895

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
900 905 910

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
915 920 925

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
930 935 940

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
945 950 955 960

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
965 970 975

Ser Leu Ser Pro Gly Lys
980

<210> 519
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<400> 519

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
500 505 510

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
515 520 525

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
530 535 540

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
545 550 555 560

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr
565 570 575

Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
580 585 590

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
595 600 605

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
610 615 620

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
625 630 635 640

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
645 650 655

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
660 665 670

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
675 680 685

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
690 695 700

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
705 710 715 720

Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
725 730 735

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

740 745 750

Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
755 760 765

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
770 775 780

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
785 790 795 800

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
805 810 815

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln
820 825 830

Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln
835 840 845

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
850 855 860

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
865 870 875 880

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
885 890 895

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
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Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
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Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
930 935 940

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
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Ser Leu Ser Leu Ser Pro Gly Lys
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Gly Tyr Val Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
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Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Thr Gly Phe Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
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Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Arg Val Asn Asn Asn Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly

245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
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Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
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Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
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Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
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Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
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Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
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Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
545 550 555 560

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr
565 570 575

Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
580 585 590

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
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Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
610 615 620

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
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Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
645 650 655

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
660 665 670

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
675 680 685

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
690 695 700

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
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Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
725 730 735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
740 745 750

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
755 760 765

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
770 775 780

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
785 790 795 800

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
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Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly
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Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp
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Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
850 855 860

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Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
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Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
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915 920 925

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
930 935 940

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
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35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
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Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
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Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
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Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
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Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
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Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
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Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
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Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
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Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
545 550 555 560

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565 570 575

Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
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Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
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Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
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Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
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Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
645 650 655

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
660 665 670

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
675 680 685

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
690 695 700

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
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Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
725 730 735

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
740 745 750

Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
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Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
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Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
785 790 795 800

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
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Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln

820 825 830

Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln
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Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
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Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
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Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
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Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
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Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
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Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
930 935 940

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
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Ser Leu Ser Leu Ser Pro Gly Lys
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Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
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Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
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Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
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Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

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145 150 155 160

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
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Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
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Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys

325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
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Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
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Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
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Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
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Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
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Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
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Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
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Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
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Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
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Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
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Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr
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Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
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Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
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Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
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Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
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Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
645 650 655

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
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Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
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Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
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Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
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725 730 735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
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Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
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Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
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Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
785 790 795 800

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
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Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly
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Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp
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Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
850 855 860

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
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Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
885 890 895

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
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Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
930 935 940

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
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Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
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Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
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Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
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Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
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Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
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Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
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Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
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Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
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Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
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Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
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Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
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Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
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Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
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Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
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Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
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Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
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Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
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Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
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Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
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Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
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Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
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Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
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Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
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Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
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Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
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Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
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Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
675 680 685

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
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Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
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Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
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Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
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Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
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Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
785 790 795 800

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
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Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln
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Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln
835 840 845

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
850 855 860

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
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Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
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Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser

900 905 910

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
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Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
930 935 940

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
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Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
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Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
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Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
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Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
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Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
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Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
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Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
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Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
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Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
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Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val

405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
500 505 510

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
515 520 525

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
530 535 540

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
545 550 555 560

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr
565 570 575

Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp
580 585 590

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
595 600 605

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
610 615 620

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
625 630 635 640

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
645 650 655

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
660 665 670

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
675 680 685

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
690 695 700

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
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Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
725 730 735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
740 745 750

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
755 760 765

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
770 775 780

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
785 790 795 800

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
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Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly
820 825 830

Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp
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Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
850 855 860

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
865 870 875 880

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
885 890 895

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
900 905 910

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
915 920 925

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
930 935 940

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
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35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
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Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys Thr
500 505 510

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
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Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
530 535 540

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
545 550 555 560

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
565 570 575

Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val
580 585 590

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
595 600 605

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
610 615 620

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
625 630 635 640

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
645 650 655

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
660 665 670

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
675 680 685

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
690 695 700

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
705 710 715 720

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
725 730 735

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
740 745 750

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys
755 760 765

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
770 775 780

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
785 790 795 800

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
805 810 815

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
820 825 830

Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys
835 840 845

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
850 855 860

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
865 870 875 880

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
885 890 895

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
900 905 910

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
915 920 925

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
930 935 940

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
945 950 955 960

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
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Lys

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Tyr Met His Trp Val Arg Gln Ala Pro Gly Leu Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp

465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys Thr
500 505 510

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
515 520 525

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
530 535 540

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
545 550 555 560

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
565 570 575

Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val
580 585 590

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
595 600 605

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
610 615 620

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
625 630 635 640

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
645 650 655

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
660 665 670

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
675 680 685

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
690 695 700

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
705 710 715 720

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
725 730 735

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
740 745 750

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His
755 760 765

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
770 775 780

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
785 790 795 800

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
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Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
820 825 830

Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser
835 840 845

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
850 855 860

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
865 870 875 880

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
885 890 895

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
900 905 910

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
915 920 925

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
930 935 940

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
945 950 955 960

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35 40 45

Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
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Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
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Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
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Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
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Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
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Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
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Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
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Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys Thr
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His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
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Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
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Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
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Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
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Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val
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Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
595 600 605

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
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Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
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Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
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Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
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Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
675 680 685

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
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Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
705 710 715 720

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
725 730 735

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
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Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys
755 760 765

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
770 775 780

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
785 790 795 800

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
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Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
820 825 830

Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys
835 840 845

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
850 855 860

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
865 870 875 880

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
885 890 895

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
900 905 910

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
915 920 925

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
930 935 940

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
945 950 955 960

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
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Gly Ile Ile Asn Pro Ser Asp Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Asn Thr Val Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
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Ala Arg Gly Gly Asn Ser Ala Phe Tyr Ser Tyr Tyr Asp Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln
130 135 140

Thr Pro Leu Ser Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Val Tyr Arg Asp Gly Asn Thr Tyr Leu
165 170 175

Ser Trp Phe Gln Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr
180 185 190

Lys Val Ser Asn Trp Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Gly
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Pro Thr
225 230 235 240

Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
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Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
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Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
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Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
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Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
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Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
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Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Asp Lys Thr
500 505 510

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
515 520 525

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg

530 535 540

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
545 550 555 560

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
565 570 575

Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val
580 585 590

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
595 600 605

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
610 615 620

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
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Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
645 650 655

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
660 665 670

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
675 680 685

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
690 695 700

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
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Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
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Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His
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Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
770 775 780

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
785 790 795 800

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
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Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
820 825 830

Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser
835 840 845

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
850 855 860

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
865 870 875 880

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
885 890 895

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
900 905 910

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
915 920 925

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
930 935 940

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
945 950 955 960

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35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Asn Lys Asn
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asp Arg Ser Pro
85 90 95

Leu Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys
100 105

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Ser Phe
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Ile Ala Val Ala Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Asp Arg Ser Pro Leu Thr Phe Gly Cys Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
245 250 255

Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser
260 265 270

Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro
275 280 285

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn
290 295 300

Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser
305 310 315 320

Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys
325 330 335

Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly
340 345 350

Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val
355 360 365

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
385 390 395 400

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
405 410 415

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
420 425 430

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
435 440 445

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
450 455 460

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
465 470 475 480

Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
485 490 495

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser

210 215 220

Pro
225

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

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<400> 536

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro
225

<210> 537
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<400> 537

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro

165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro
225

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 540
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<400> 540

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro
225

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<400> 541

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
245 250 255

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
260 265 270

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
275 280 285

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
290 295 300

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
305 310 315 320

Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr
325 330 335

Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
340 345 350

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
355 360 365

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
370 375 380

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
385 390 395 400

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
405 410 415

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
420 425 430

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
435 440 445

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
450 455 460

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
465 470 475 480

Ser Pro Gly Lys

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<400> 542

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
225 230 235 240

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
245 250 255

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
260 265 270

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
275 280 285

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
290 295 300

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
305 310 315 320

Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Gly Ser Thr Tyr Arg
325 330 335

Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
340 345 350

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
355 360 365

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
370 375 380

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
385 390 395 400

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
405 410 415

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
420 425 430

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
435 440 445

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
450 455 460

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
465 470 475 480

<210> 543
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<400> 543

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
245 250 255

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
260 265 270

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
275 280 285

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
290 295 300

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
305 310 315 320

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
325 330 335

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
340 345 350

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
355 360 365

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
370 375 380

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
385 390 395 400

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
405 410 415

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
420 425 430

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
435 440 445

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
450 455 460

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
465 470 475 480

Ser Pro Gly Lys

<210> 544
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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
225 230 235 240

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
245 250 255

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
260 265 270

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
275 280 285

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
290 295 300

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
305 310 315 320

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
325 330 335

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
340 345 350

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
355 360 365

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
370 375 380

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
385 390 395 400

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
405 410 415

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
420 425 430

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
435 440 445

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
450 455 460

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
465 470 475 480

<210> 545
<211> 484
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 545

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
245 250 255

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
260 265 270

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
275 280 285

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
290 295 300

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
305 310 315 320

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr
325 330 335

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
340 345 350

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
355 360 365

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
370 375 380

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
385 390 395 400

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
405 410 415

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
420 425 430

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
435 440 445

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
450 455 460

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
465 470 475 480

Ser Pro Gly Lys

<210> 546
<211> 480
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 546

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
225 230 235 240

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
245 250 255

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
260 265 270

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
275 280 285

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
290 295 300

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
305 310 315 320

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg
325 330 335

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
340 345 350

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
355 360 365

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
370 375 380

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
385 390 395 400

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
405 410 415

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
420 425 430

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
435 440 445

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
450 455 460

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
465 470 475 480

<210> 547
<211> 484
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 547

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
245 250 255

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
260 265 270

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
275 280 285

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
290 295 300

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
305 310 315 320

Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Asn Ser Thr
325 330 335

Tyr Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
340 345 350

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
355 360 365

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
370 375 380

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
385 390 395 400

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
405 410 415

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
420 425 430

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
435 440 445

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
450 455 460

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
465 470 475 480

Ser Pro Gly Lys

<210> 548
<211> 480
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 548

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
225 230 235 240

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
245 250 255

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
260 265 270

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
275 280 285

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
290 295 300

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
305 310 315 320

Asn Ala Lys Thr Lys Pro Cys Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
325 330 335

Cys Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
340 345 350

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
355 360 365

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
370 375 380

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
385 390 395 400

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
405 410 415

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
420 425 430

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
435 440 445

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
450 455 460

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
465 470 475 480

<210> 549
<211> 20
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 549

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 550
<211> 25
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 550

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25

<210> 551
<211> 30
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 551

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25 30

<210> 552
<211> 35
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 552

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser
35

<210> 553
<211> 40
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 553

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser
35 40

<210> 554
<211> 503
<212> PRT
<213> 人工序列

<220>
<223> 合成肽

<400> 554

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile Ser Ser Tyr
20 25 30

Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Ser Gln Phe Ser Leu

65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Ser Ile Ala Val Arg Gly Phe Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Gly Thr Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys Arg Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly
245 250 255

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala
260 265 270

Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala
275 280 285

Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn
290 295 300

Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile
305 310 315 320

Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu
325 330 335

Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe
340 345 350

Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu
355 360 365

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
370 375 380

Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val
385 390 395 400

Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala
405 410 415

Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln
420 425 430

Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr
435 440 445

Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr
450 455 460

Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu
465 470 475 480

Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val
485 490 495

Leu His His His His His His
500

申請專利範圍

1. 一種雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一結合域及結合於T細胞表面上之人類CD3及至少獼猴CD3的第二結合域，其中該第一結合域結合於包含於如SEQ ID NO:260中所描繪之區域內的DLL3之抗原決定基，其中該第一結合域結合於包含於如SEQ ID NO:258中所描繪之區域內的DLL3之抗原決定基，其中該第一結合域包含選自由以下組成之群的包含CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區：

a) 如SEQ ID NO:31中所描繪之CDR-H1、如SEQ ID NO:32中所描繪之CDR-H2、如SEQ ID NO:33中所描繪之CDR-H3、如SEQ ID NO:34中所描繪之CDR-L1、如SEQ ID NO:35中所描繪之CDR-L2及如SEQ ID NO:36中所描繪之CDR-L3；

b) 如SEQ ID NO:41中所描繪之CDR-H1、如SEQ ID NO:42中所描繪之CDR-H2、如SEQ ID NO:43中所描繪之CDR-H3、如SEQ ID NO:44中所描繪之CDR-L1、如SEQ ID NO:45中所描繪之CDR-L2及如SEQ ID NO:46中所描繪之CDR-L3；

c) 如SEQ ID NO:51中所描繪之CDR-H1、如SEQ ID NO:52中所描繪之CDR-H2、如SEQ ID NO:53中所描繪之CDR-H3、如SEQ ID NO:54中所描繪之CDR-L1、如SEQ ID NO:55中所描繪之CDR-L2及如SEQ ID NO:56中所描繪之CDR-L3；

d) 如SEQ ID NO:61中所描繪之CDR-H1、如SEQ ID NO:62中所描繪之CDR-H2、如SEQ ID NO:63中所描繪之CDR-H3、如SEQ ID NO:64中所描繪之CDR-L1、如SEQ ID NO:65中所描繪之CDR-L2及如SEQ ID NO:66中所描繪之CDR-L3；

e) 如SEQ ID NO:71中所描繪之CDR-H1、如SEQ ID NO:72中所描繪之CDR-H2、如SEQ ID NO:73中所描繪之CDR-H3、如SEQ ID NO:74中所描繪之CDR-L1、如SEQ ID NO:75中所描繪之CDR-L2及如SEQ ID NO:76中所描繪之CDR-L3；

f) 如SEQ ID NO:81中所描繪之CDR-H1、如SEQ ID NO:82中所描繪之CDR-H2、如SEQ ID NO:83中所描繪之CDR-H3、如SEQ ID NO:84中所描繪之CDR-L1、如SEQ ID NO:85中所描繪之CDR-L2及如SEQ ID NO:86中所描繪之CDR-L3；

g) 如SEQ ID NO:91中所描繪之CDR-H1、如SEQ ID NO:92中所描繪之CDR-H2、如SEQ ID NO:93中所描繪之CDR-H3、如SEQ ID NO:94中所描繪之CDR-L1、如SEQ ID NO:95中所描繪之CDR-L2及如SEQ ID NO:96中所描繪之CDR-L3；

h) 如SEQ ID NO:101中所描繪之CDR-H1、如SEQ ID NO:102中所描繪之CDR-H2、如SEQ ID NO:103中所描繪之CDR-H3、如SEQ ID NO:104中所描繪之CDR-L1、如SEQ ID NO:105中所描繪之CDR-L2及如SEQ ID NO:106中所描繪之CDR-L3；及

i) 如SEQ ID NO:111中所描繪之CDR-H1、如SEQ ID NO:112中所描繪之CDR-H2、如SEQ ID NO:113中所描繪之CDR-H3、如SEQ ID NO:114中所描繪之CDR-L1、如SEQ ID NO:115中所描繪之CDR-L2及如SEQ ID NO:116中所描繪之CDR-L3。

2. 如請求項1之抗體構築體，其中該第一結合域進一步結合於獼猴DLL3。

3. 如請求項2之抗體構築體，其中該第一結合域進一步結合於食蟹猴(*Macaca fascicularis*) DLL3。

4. 如請求項1至3中任一項之抗體構築體，其中該第二結合域結合於人類CD3ε及白鬢狨(*Callithrix jacchus*)、棉頂狨(*Saguinus*

Oedipus)或松鼠猴(*Saimiri sciureus*) CD3ε。

5. 如請求項1至3中任一項之抗體構築體，其中該抗體構築體呈選自由以下組成之群的型式：$(scFv)_2$、scFv-單域mAb、雙功能抗體及上述型式的寡聚物。

6. 如請求項1至3中任一項之抗體構築體，其中該第一結合域包含選自由以下各者中描繪之VH區組成之群的VH區：SEQ ID NO:37、SEQ ID NO:47、SEQ ID NO:57、SEQ ID NO:67、SEQ ID NO:77、SEQ ID NO:87、SEQ ID NO:97、SEQ ID NO:107、SEQ ID NO:117、SEQ ID NO:435及SEQ ID NO:529。

7. 如請求項1至3中任一項之抗體構築體，其中該第一結合域包含選自由以下各者中描繪之VL區組成之群的VL區：SEQ ID NO:38、SEQ ID NO:48、SEQ ID NO:58、SEQ ID NO:68、SEQ ID NO:78、SEQ ID NO:88、SEQ ID NO:98、SEQ ID NO:108、SEQ ID NO:118、SEQ ID NO:436及SEQ ID NO:530。

8. 如請求項1至3中任一項之抗體構築體，其中該第一結合域包含VH區及VL區，其選自由如以下各者中所描繪之VH區及VL區之配對組成之群：SEQ ID NO：37+38；SEQ ID NO:47+48；SEQ ID NO:57+58；SEQ ID NO:67+68；SEQ ID NO:77+78；SEQ ID NO:87+88；SEQ ID NO:97+98；SEQ ID NO:107+108；SEQ ID NO:117+118；SEQ ID NO:435+436；及SEQ ID NO:529+530。

9. 如請求項1至3中任一項之抗體構築體，其中該第一結合域包含選自由以下各者中描繪之多肽組成之群的多肽：SEQ ID NO:39、SEQ ID NO:49、SEQ ID NO:59、SEQ ID NO:69、SEQ ID NO:79、SEQ ID NO:89、SEQ ID NO:99、SEQ ID NO:109、SEQ ID NO:119、SEQ ID NO:437及SEQ ID NO:531。

10. 如請求項1至3中任一項之抗體構築體，其包含選自由以下各者

中描繪之多肽組成之群的多肽：SEQ ID NO:40、SEQ ID NO:50、SEQ ID NO:60、SEQ ID NO:70、SEQ ID NO:80、SEQ ID NO:90、SEQ ID NO:100、SEQ ID NO:110、SEQ ID NO:120、SEQ ID NO:211、SEQ ID NO:212、SEQ ID NO:213、SEQ ID NO:214、SEQ ID NO:215、SEQ ID NO:216、SEQ ID NO:217、SEQ ID NO:438及SEQ ID NO:532。

11. 一種雙特異性抗體構築體，其包含結合於目標細胞表面上之人類DLL3的第一結合域及結合於T細胞表面上之人類CD3及獼猴CD3的第二結合域，其中該第一結合域結合於包含於如SEQ ID NO:260中所描繪之區域內的DLL3之抗原決定基，其中該第一結合域結合於包含於如SEQ ID NO:259中所描繪之區域內的DLL3之抗原決定基，其中該第一結合域包含選自由以下組成之群的包含CDR-H1、CDR-H2及CDR-H3之VH區及包含CDR-L1、CDR-L2及CDR-L3之VL區：

a) 如SEQ ID NO:121中所描繪之CDR-H1、如SEQ ID NO:122中所描繪之CDR-H2、如SEQ ID NO:123中所描繪之CDR-H3、如SEQ ID NO:124中所描繪之CDR-L1、如SEQ ID NO:125中所描繪之CDR-L2及如SEQ ID NO:126中所描繪之CDR-L3；

b) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:134中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

c) 如SEQ ID NO:141中所描繪之CDR-H1、如SEQ ID NO:142中所描繪之CDR-H2、如SEQ ID NO:143中所描繪之CDR-H3、如SEQ ID NO:144中所描繪之CDR-L1、如SEQ ID NO:145中所描繪之CDR-L2及如SEQ ID NO:146中所描繪之CDR-L3；

d) 如SEQ ID NO:151中所描繪之CDR-H1、如SEQ ID NO:152中所描繪之CDR-H2、如SEQ ID NO:153中所描繪之CDR-H3、如SEQ ID NO:154中所描繪之CDR-L1、如SEQ ID NO:155中所描繪之CDR-L2及如SEQ ID NO:156中所描繪之CDR-L3；

e) 如SEQ ID NO:161中所描繪之CDR-H1、如SEQ ID NO:162中所描繪之CDR-H2、如SEQ ID NO:163中所描繪之CDR-H3、如SEQ ID NO:164中所描繪之CDR-L1、如SEQ ID NO:165中所描繪之CDR-L2及如SEQ ID NO:166中所描繪之CDR-L3；

f) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:439中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:134中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

g) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:440中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:134中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

h) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:441中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

i) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:442中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

j) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如

SEQ ID NO:443中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

k) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:132中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:444中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；

l) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:439中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:441中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3；及

m) 如SEQ ID NO:131中所描繪之CDR-H1、如SEQ ID NO:440中所描繪之CDR-H2、如SEQ ID NO:133中所描繪之CDR-H3、如SEQ ID NO:442中所描繪之CDR-L1、如SEQ ID NO:135中所描繪之CDR-L2及如SEQ ID NO:136中所描繪之CDR-L3。

12. 如請求項11之抗體構築體，其中該第一結合域進一步結合於獼猴DLL3。

13. 如請求項12之抗體構築體，其中該第一結合域進一步結合於食蟹猴(*Macaca fascicularis*) DLL3。

14. 如請求項11至13中任一項之抗體構築體，其中該第二結合域結合於人類CD3ε及白鬢狨(*Callithrix jacchus*)、棉頂狨(*Saguinus Oedipus*)或松鼠猴(*Saimiri sciureus*) CD3ε。

15. 如請求項11至13中任一項之抗體構築體，其中該抗體構築體呈選自由以下組成之群的型式：$(scFv)_2$、scFv-單域mAb、雙功能抗體及上述型式的寡聚物。

16. 如請求項11至13中任一項之抗體構築體，其中該第一結合域包含選自由以下各者中描繪之VH區組成之群的VH區：SEQ ID

NO:127、SEQ ID NO:137、SEQ ID NO:147、SEQ ID NO:157、SEQ ID NO:167、SEQ ID NO:445、SEQ ID NO:446、SEQ ID NO:447、SEQ ID NO:448、SEQ ID NO:449、SEQ ID NO:450、SEQ ID NO:451、SEQ ID NO:452、SEQ ID NO:453、SEQ ID NO:454及SEQ ID NO:455。

17. 如請求項11至13中任一項之抗體構築體，其中該第一結合域包含選自由以下各者中描繪之VL區組成之群的VL區：SEQ ID NO:128、SEQ ID NO:138、SEQ ID NO:148、SEQ ID NO:158、SEQ ID NO:168、SEQ ID NO:456、SEQ ID NO:457、SEQ ID NO:458、SEQ ID NO:459、SEQ ID NO:460、SEQ ID NO:461、SEQ ID NO:462、SEQ ID NO:463、SEQ ID NO:464、SEQ ID NO:465、SEQ ID NO:466、SEQ ID NO:467、SEQ ID NO:468、SEQ ID NO:469及SEQ ID NO:470。

18. 如請求項11至13中任一項之抗體構築體，其中該第一結合域包含VH區及VL區，其選自由如以下各者中所描繪之VH區及VL區之配對組成之群：SEQ ID NO:127+128；SEQ ID NO:137+138；SEQ ID NO:147+148；SEQ ID NO:157+158；SEQ ID NO:167+168；SEQ ID NO:137+456；SEQ ID NO:137+457；SEQ ID NO:137+458；SEQ ID NO:137+459；SEQ ID NO:137+460；SEQ ID NO:445+138；SEQ ID NO:446+138；SEQ ID NO:447+138；SEQ ID NO:445+460；SEQ ID NO:448+461；SEQ ID NO:449+462；SEQ ID NO:450+463；SEQ ID NO:450+464；SEQ ID NO:450+465；SEQ ID NO:450+466；SEQ ID NO:450+467；SEQ ID NO:450+468；SEQ ID NO:451+463；SEQ ID NO:452+463；SEQ ID NO:453+463；SEQ ID NO:451+468；SEQ ID NO:454+469；及SEQ ID NO:455+470。

19. 如請求項11至13中任一項之抗體構築體，其中該第一結合域包含選自由以下各者中描繪之多肽組成之群的多肽：SEQ ID NO:129、SEQ ID NO:139、SEQ ID NO:149、SEQ ID NO:159、SEQ ID NO:169、SEQ ID NO:471、SEQ ID NO:472、SEQ ID NO:473、SEQ ID NO:474、SEQ ID NO:475、SEQ ID NO:476、SEQ ID NO:477、SEQ ID NO:478、SEQ ID NO:479、SEQ ID NO:480、SEQ ID NO:481、SEQ ID NO:482、SEQ ID NO:483、SEQ ID NO:484、SEQ ID NO:485、SEQ ID NO:486、SEQ ID NO:487、SEQ ID NO:488、SEQ ID NO:489、SEQ ID NO:490、SEQ ID NO:491、SEQ ID NO:492及SEQ ID NO:493。

20. 如請求項11至13中任一項之抗體構築體，其包含選自由以下各者中描繪之多肽組成之群的多肽：SEQ ID NO:130、SEQ ID NO:140、SEQ ID NO:150、SEQ ID NO:160、SEQ ID NO:170、SEQ ID NO:218、SEQ ID NO:219、SEQ ID NO:220、SEQ ID NO:494、SEQ ID NO:495、SEQ ID NO:496、SEQ ID NO:497、SEQ ID NO:498、SEQ ID NO:499、SEQ ID NO:500、SEQ ID NO:501、SEQ ID NO:502、SEQ ID NO:503、SEQ ID NO:504、SEQ ID NO:505、SEQ ID NO:506、SEQ ID NO:507、SEQ ID NO:508、SEQ ID NO:509、SEQ ID NO:510、SEQ ID NO:511、SEQ ID NO:512、SEQ ID NO:513、SEQ ID NO:514、SEQ ID NO:515及SEQ ID NO:516。

21. 如請求項1至3中任一項之抗體構築體，其包含選自由以下各者中描繪之多肽組成之群的多肽或由其組成：SEQ ID NO:517、SEQ ID NO:518、SEQ ID NO:519、SEQ ID NO:520、SEQ ID NO:521、SEQ ID NO:522、SEQ ID NO:523、SEQ ID NO:524。

22. 如請求項11至13中任一項之抗體構築體，其包含選自由以下描繪

之多肽組成之群的多肽或由其組成：SEQ ID NO:525及SEQ ID NO:526。

23. 一種聚核苷酸，其編碼如請求項1至22中任一項之抗體構築體。

24. 一種載體，其包含如請求項23之聚核苷酸。

25. 一種宿主細胞，其用如請求項23之聚核苷酸或用如請求項24之載體轉型或轉染。

26. 一種用於製備如請求項1至22中任一項之抗體構築體之方法，該方法包含在允許該抗體構築體之表現的條件下培養如請求項25之宿主細胞及自該培養物回收該所產生之抗體構築體。

27. 一種醫藥組合物，其包含如請求項1至22中任一項之抗體構築體或根據如請求項26之方法產生的抗體構築體。

28. 如請求項1至3及11至13中任一項之抗體構築體，其係用於治療或改善腫瘤或癌症疾病或轉移性癌症疾病。

29. 一種如請求項1至22中任一項之抗體構築體或根據如請求26之方法產生之抗體構築體之用途，其係用於製備治療或改善腫瘤或癌症疾病或轉移性癌症疾病之醫藥品。

30. 如請求項29之用途，其中該腫瘤或癌症疾病選自由以下組成的群組：肺癌、乳房、子宮頸、結腸、結腸直腸、子宮內膜、頭部及頸部、肝、卵巢、胰腺、前列腺、皮膚、胃、睪丸、甲狀腺、腎上腺、腎、膀胱、子宮、食道、尿道上皮及腦腫瘤或癌症，淋巴瘤、癌瘤及肉瘤，以及來源於前述任一者之轉移性癌症疾病。

31. 如請求項29之用途，其中該腫瘤或癌症疾病選自由以下組成的群組：小細胞肺癌(SCLC)、非小細胞肺癌(SCLC)、神經膠質瘤、神經膠母細胞瘤、黑素瘤、神經內分泌前列腺癌、神經內分泌胰臟癌、肝母細胞瘤、肝細胞癌及源自前述疾病中任一者

之轉移性癌症。

32. 一種套組，其包含如請求項1至22中任一項之抗體構築體、根據如請求項26之方法產生之抗體構築體、如請求項23之聚核苷酸、如請求項24之載體及/或如請求項25之宿主細胞。

圖式

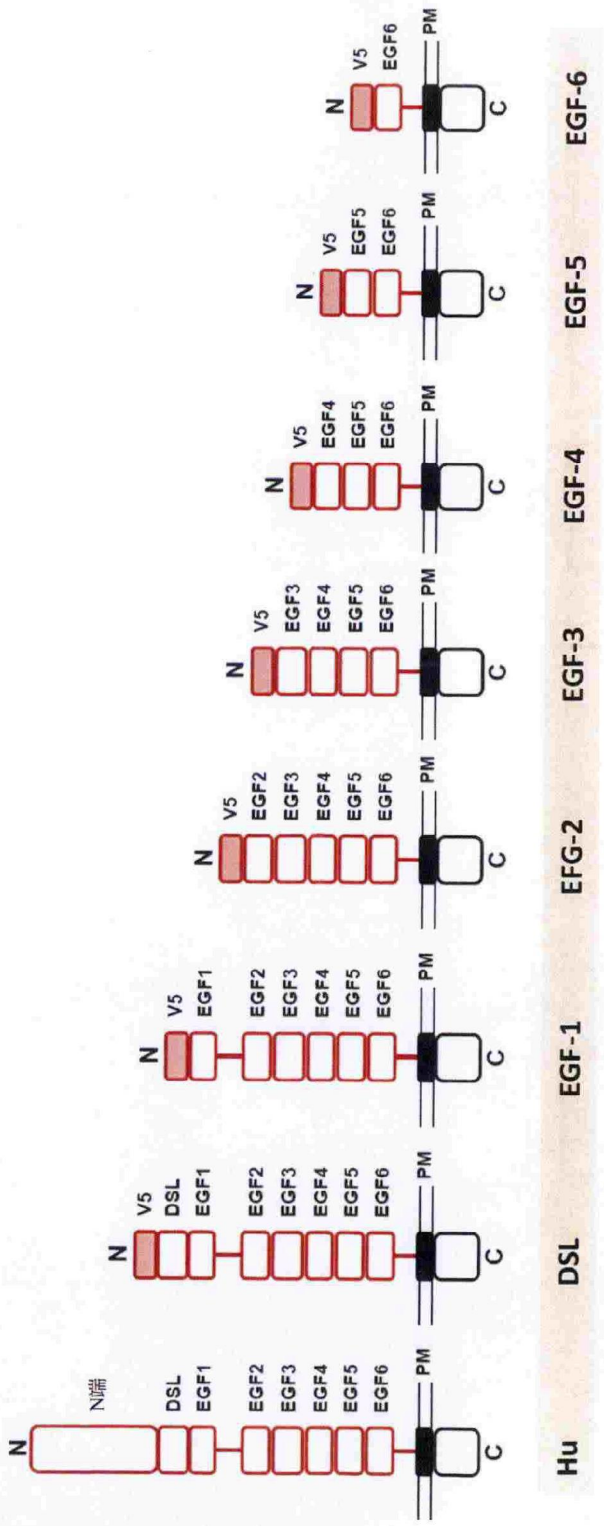
N端
DSL
EGF1
EGF2
EGF3
EGF4
EGF5
EGF6
V5
PM
N
C
Hu
DSL
EGF-1
EFG-2
EGF-3
EGF-4
EGF-5
EGF-6

圖1

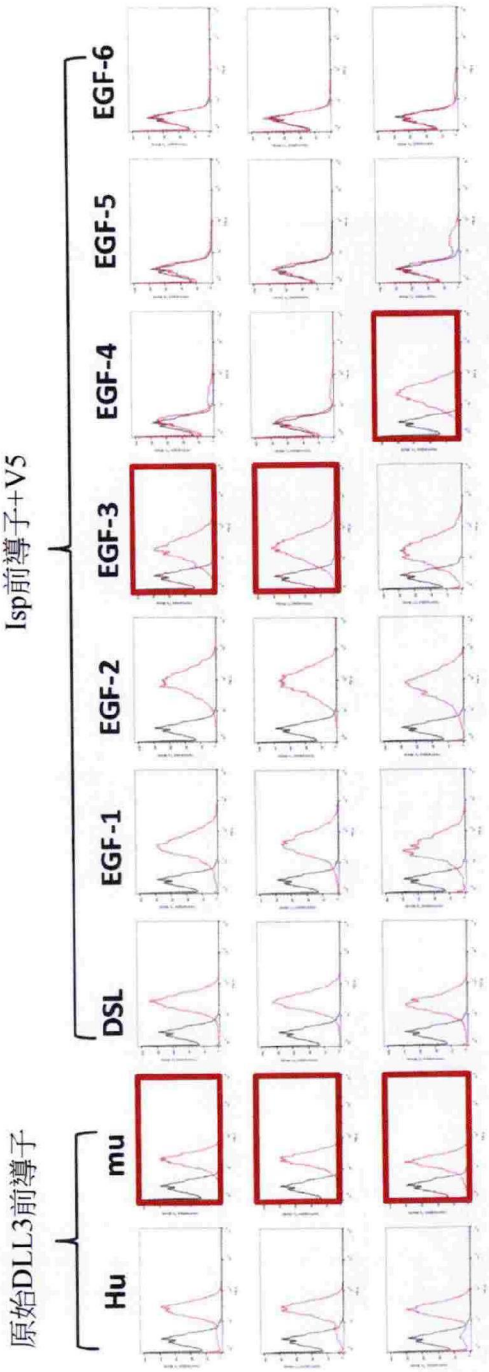
原始DLL3前導子
Isp前導子+V5
CHO DLL3
Hu
mu
DSL
EGF-1
EGF-2
EGF-3
EGF-4
EGF-5
EGF-6
DLL3-4 x I2C -HALB變異體1
DLL3-6 x I2C -HALB變異體1
DLL3-14 x I2C -HALB變異體1

圖2

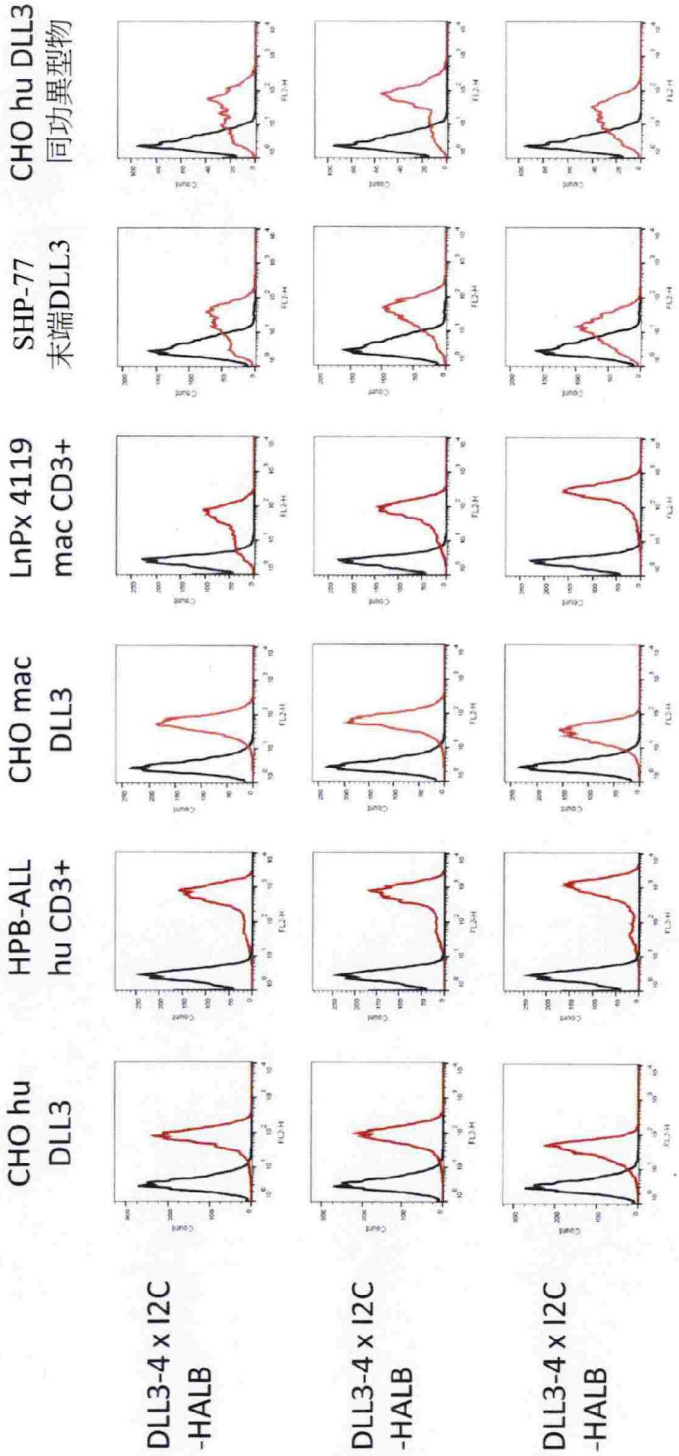
CHO hu DLL3
HPB-ALL hu CD3+
CHO mac DLL3
LnPx 4119 mac CD3+
SHP-77 末端DLL3
CHO hu DLL3 同功異型物
DLL3-4 x I2C -HALB
DLL3-4 x I2C -HALB
DLL3-4 x I2C -HALB

圖3

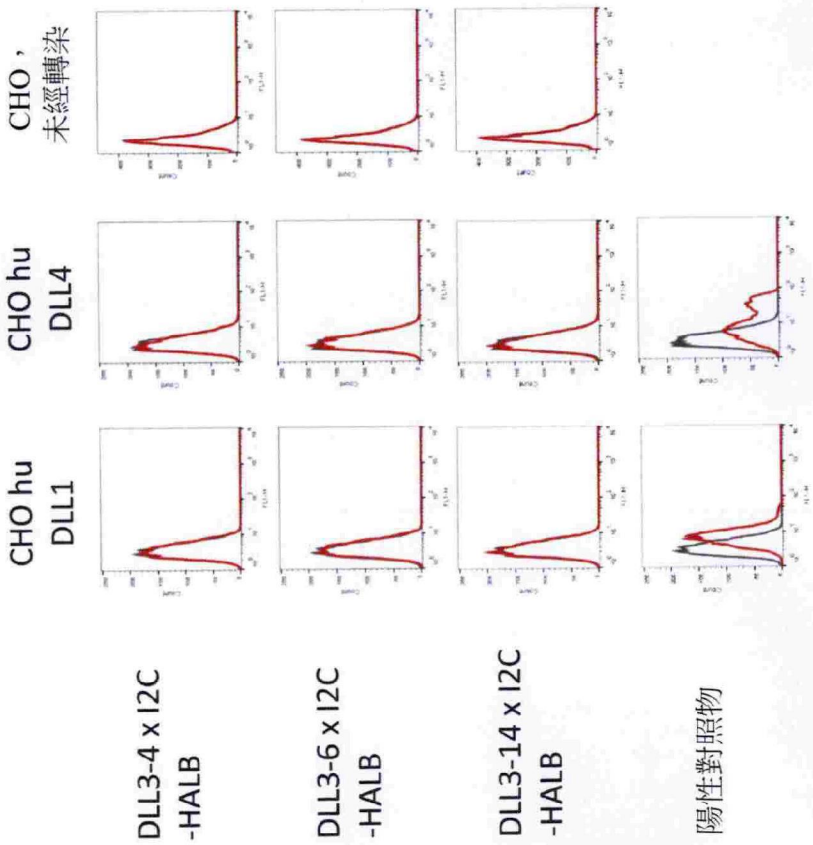
CHO hu DLL1
CHO hu DLL4
CHO，未經轉染
DLL3-4 x I2C -HALB
DLL3-6 x I2C -HALB
DLL3-14 x I2C -HALB
陽性對照物

圖4

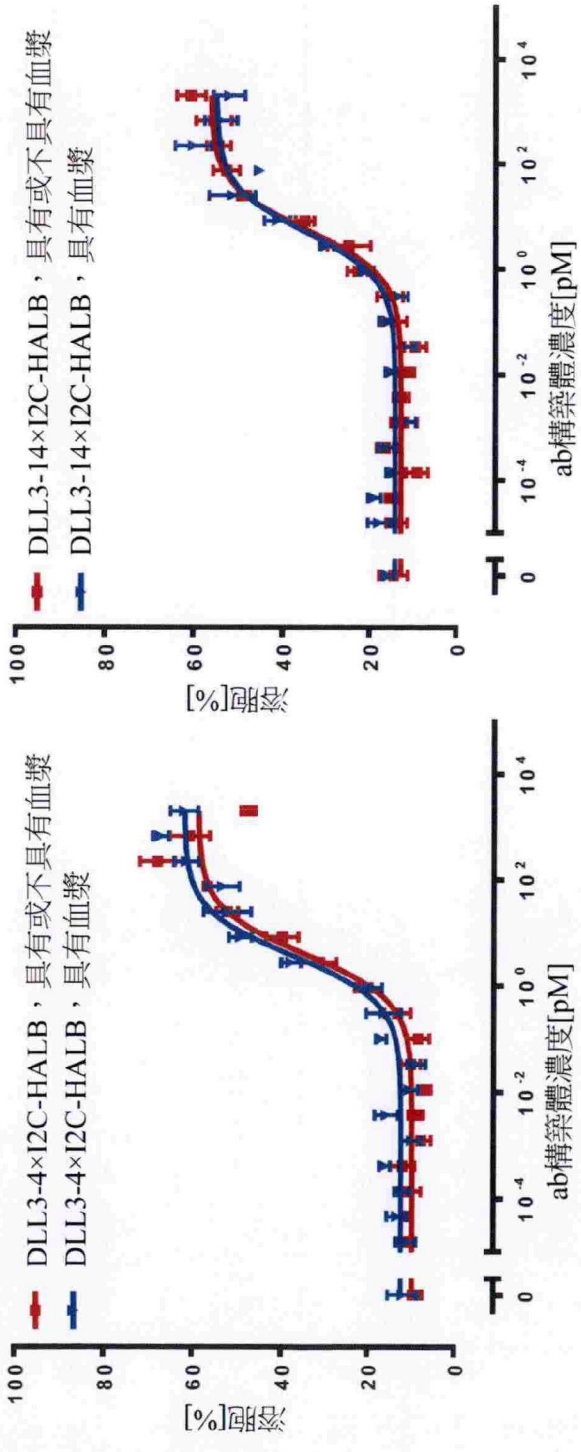
DLL3-14×I2C-HALB，具有或不具有血漿
DLL3-14×I2C-HALB，具有血漿
溶胞[%]
100
80
60
40
20
0
0
10 -4
10 -2
10 0
10 2
10 4
ab構築體濃度[pM]
DLL3-4×I2C-HALB，具有或不具有血漿
DLL3-4×I2C-HALB，具有血漿
溶胞[%]
100
80
60
40
20
0
0
10 -4
10 -2
10 0
10 2
10 4
ab構築體濃度[pM]

圖5

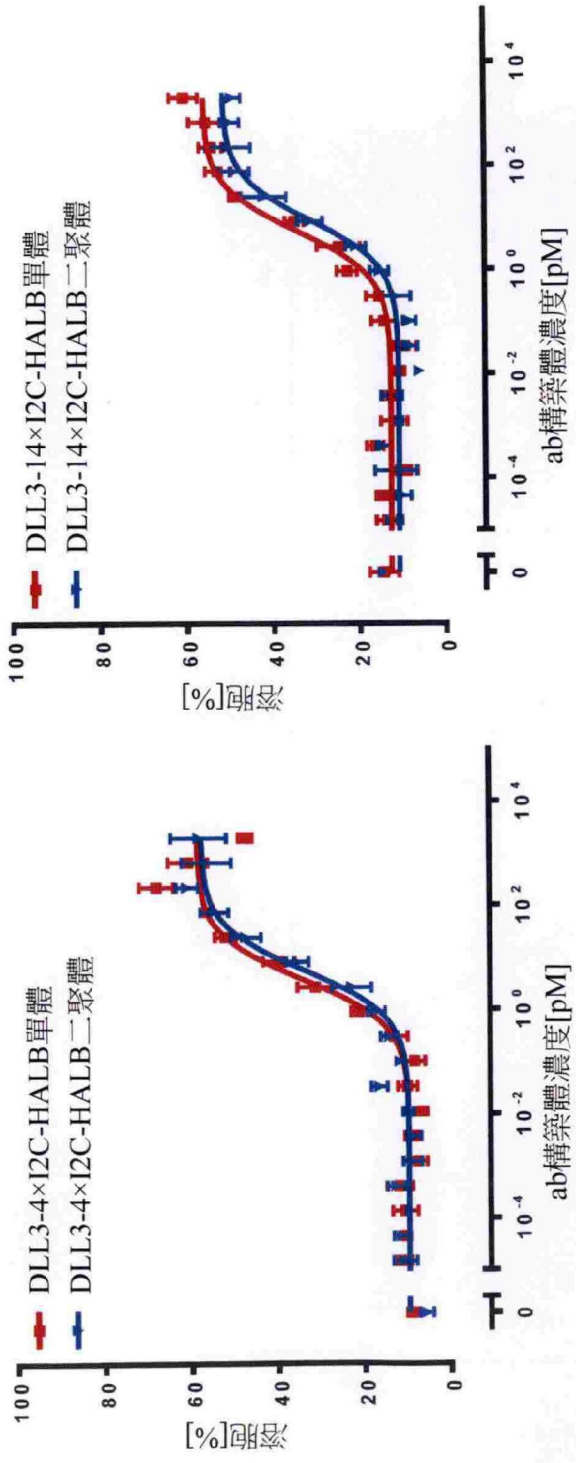
DLL3-14×I2C-HALB單體
DLL3-14×I2C-HALB二聚體
溶胞[%]
100
80
60
40
20
0
0
10⁻⁴
10⁻²
10⁰
10²
10⁴
ab構築體濃度[pM]
DLL3-4×I2C-HALB單體
DLL3-4×I2C-HALB二聚體
溶胞[%]
100
80
60
40
20
0
0
10⁻⁴
10⁻²
10⁰
10²
10⁴
ab構築體濃度[pM]

圖6

對照目標(左側)
DLL3 (右側)
2.5
2.0
1.5
1.0
0.5
0.0
相對EC50
0 hr
2 hr
100
50
0
特異性細胞毒性
-2
0
2
4
log[ab構築體]，pM
IC50
0 hrs
12.15
2 hrs
13.18

圖7

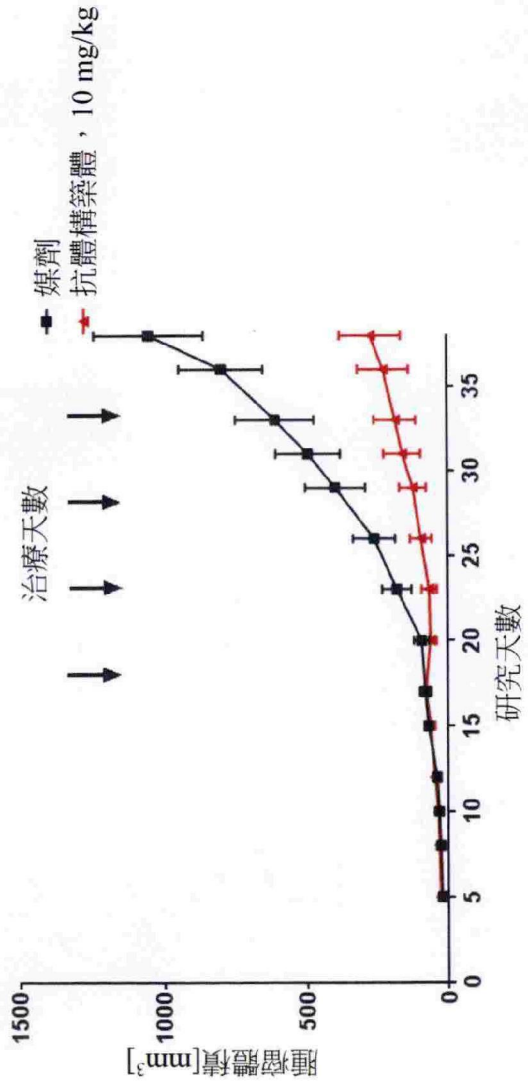
媒劑
抗體構築體，10 mg/kg
治療天數
腫瘤體積[mm³]
研究天數
0
500
1000
1500
0
5
10
15
20
25
30
35

圖8A

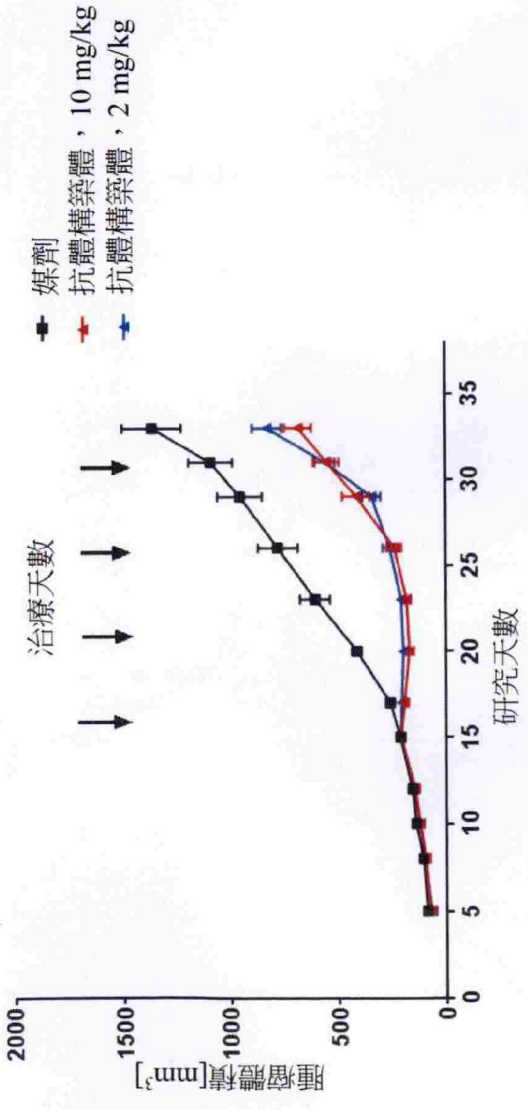
媒劑
抗體構築體，10 mg/kg
抗體構築體，2 mg/kg
治療天數
腫瘤體積[mm³]
研究天數
0
500
1000
1500
2000
0
5
10
15
20
25
30
35

圖8B

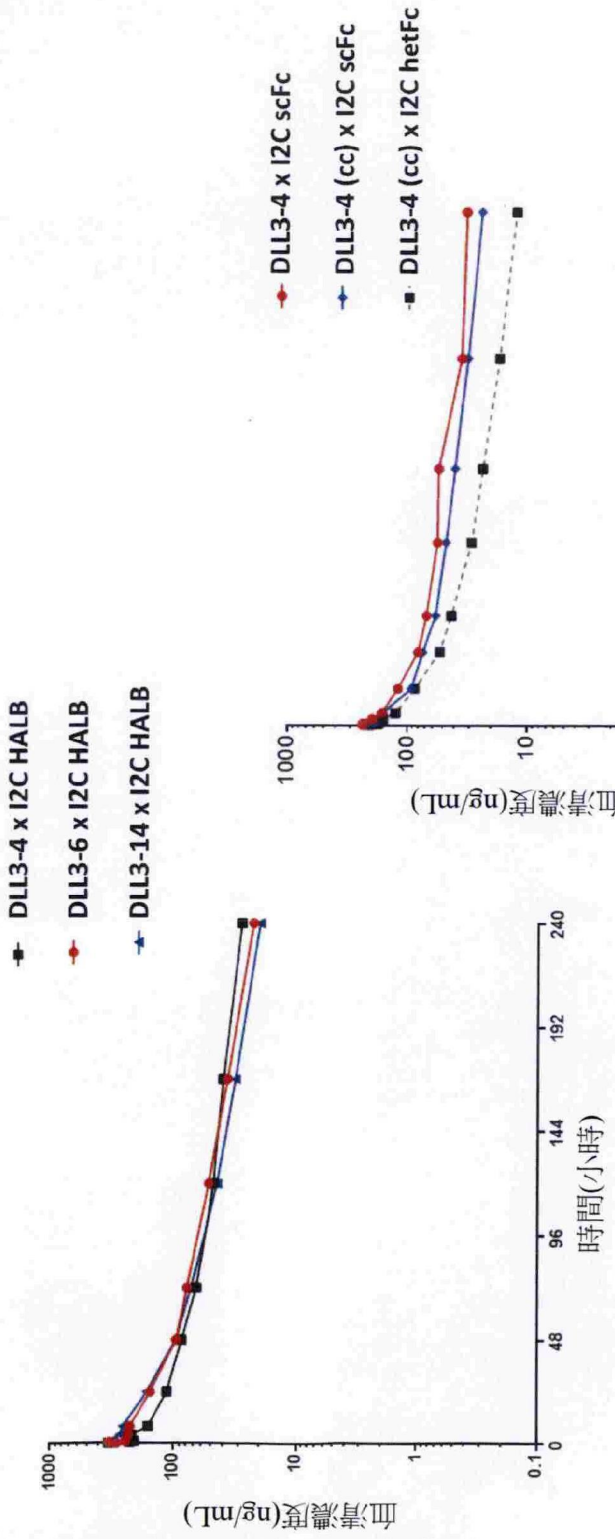
DLL3-4 x I2C HALB
DLL3-6 x I2C HALB
DLL3-14 x I2C HALB
血清濃度(ng/mL)
1000
100
10
1
0.1
0
48
96
144
192
240
時間(小時)

圖9A

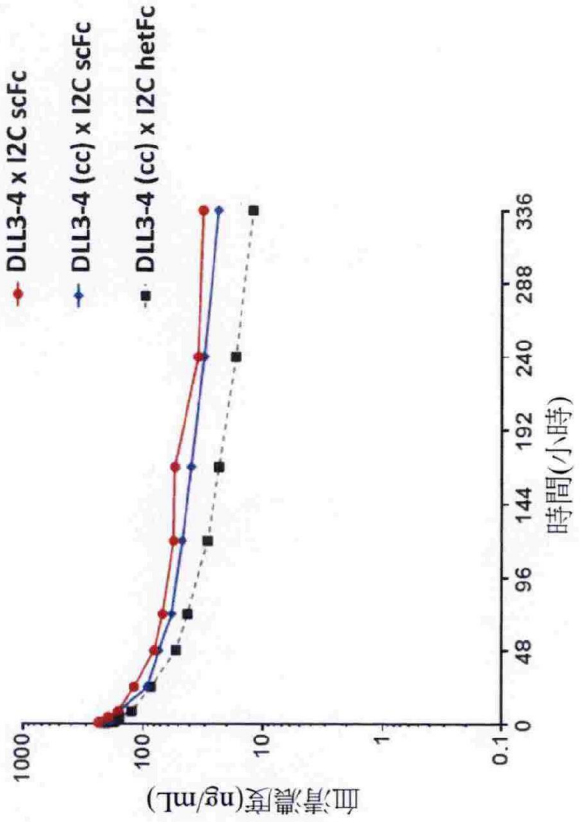
DLL3-4 x I2C scFc
DLL3-4 (cc) x I2C scFc
DLL3-4 (cc) x I2C hetFc
血清濃度(ng/mL)
1000
100
10
1
0.1
0
48
96
144
192
240
288
336
時間(小時)

圖9B