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(54)名稱

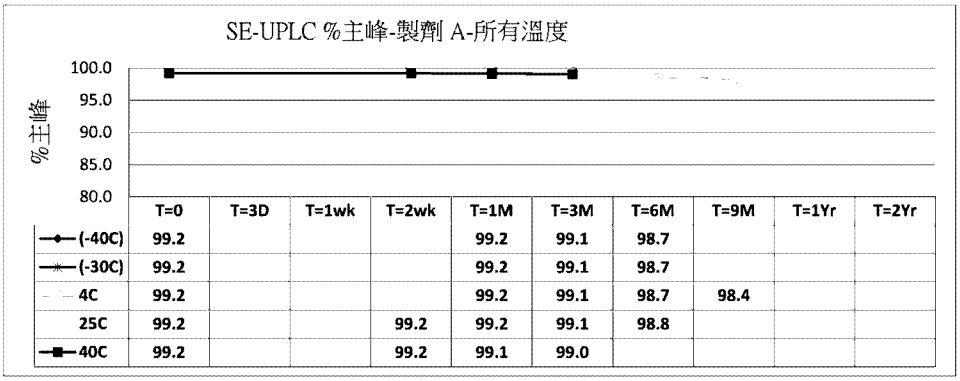
低 PH 藥物製劑

(57)摘要

本揭露描述了低 pH 製劑，所述製劑包含例如結合 CD3 的抗原結合蛋白、至少一種緩衝劑、至少一種糖和至少一種表面活性劑。

The present disclosure describes low pH formulations comprising, e.g., an antigen-binding protein that binds CD3, at least one buffer agent, at least one saccharide and at least one surfactant.

指定代表圖：



	T=0	T=3D	T=1wk	T=2wk	T=1M	T=3M	T=6M	T=9M	T=1Yr	T=2Yr
(-40C)	99.2				99.2	99.1	98.7			
(-30C)	99.2				99.2	99.1	98.7			
4C	99.2				99.2	99.1	98.7	98.4		
25C	99.2			99.2	99.2	99.1	98.8			
40C	99.2			99.2	99.1	99.0				

【圖 22A】

公告本

I860988

【發明摘要】

【中文發明名稱】

低PH藥物製劑

【英文發明名稱】

LOW PH PHARMACEUTICAL FORMULATION

【中文】

本揭露描述了低pH製劑，所述製劑包含例如結合CD3的抗原結合蛋白、至少一種緩衝劑、至少一種糖和至少一種表面活性劑。

【英文】

The present disclosure describes low pH formulations comprising, e.g., an antigen-binding protein that binds CD3, at least one buffer agent, at least one saccharide and at least one surfactant.

【指定代表圖】

圖22A

【代表圖之符號簡單說明】

無

【發明說明書】

【中文發明名稱】

低PH藥物製劑

【英文發明名稱】

LOW PH PHARMACEUTICAL FORMULATION

【技術領域】

【先前技術】

【0001】基於蛋白質的藥物係臨床（前）開發和商業產品中增長最快的治療劑之一。與小化學藥物相比，蛋白質藥物在相對低的濃度下具有高特異性和活性，並且典型地提供對高影響疾病的治療，所述疾病係例如各種癌症、自身免疫疾病、和代謝障礙（Roberts, Trends Biotechnol.[生物技術趨勢] 2014年7月；32(7):372-80，Wang, Int J Pharm.[國際藥劑學雜誌] 1999年8月20；185(2):129-88）。

【0002】由於商業規模純化方法的進步，現在可以在首次製造時以高純度獲得基於蛋白質的藥物，例如重組蛋白質。然而，蛋白質僅臨界穩定（marginally stable）並且極易受到化學和物理降解二者的影響。化學降解係指涉及共價鍵的修飾，例如脫醯胺化、氧化、裂解或形成新的二硫橋鍵、水解、異構化或去糖基化。物理降解包括蛋白質去折疊、對表面的不希望的吸附、和聚集。處理該等物理和化學不穩定性係蛋白質藥物開發中最具挑戰性的任務之一（Chi等人, Pharm Res [藥物研究], 第20卷，第9期, 2003年9月, 第1325-1336頁, Roberts, Trends Biotechnol.[生物技術趨勢] 2014年7月；32(7):372-80）。

【0003】蛋白質聚集代表蛋白質物理不穩定性的主要事件，並且其

發生歸因於使溶劑和疏水蛋白質殘基之間的熱力學上不利的相互作用最小化的固有傾向。這係特別成問題的，因為在重折疊、純化、滅菌、運輸和儲存過程中經常遇到。即使在蛋白質天然狀態在熱力學上高度有利（例如，中性pH和37°C）並且沒有應激的溶液條件下也會發生聚集（Chi等人, Pharm Res [藥物研究], 第20卷，第9期, 2003年9月, 第1325-1336頁, Roberts, Trends Biotechnol.[生物技術趨勢] 2014年7月；32(7):372-80, Wang, Int J Pharm.[國際藥學雜誌] 1999年8月20日；185(2):129-88, Mahler J Pharm Sci.[藥物科學雜誌] 2009年9月；98(9):2909-34）。

【0004】此外，還必須保護半衰期延長的抗體構建體，例如包含半衰期延長模式的雙特異性T細胞接合器（engager）（例如Fc分子），以防止蛋白質聚集和/或其他降解事件。蛋白質聚集係有問題的，因為它會損害治療性蛋白質的生物活性。此外，蛋白質的聚集導致不期望的藥物產品外觀，並且由於從終產物中除去聚集體所需的複雜的純化步驟而降低了產物產率。最近，人們還越來越關注並且有越來越多的證據證明聚集蛋白（甚至係人源化或全人源蛋白質）的存在可以顯著增加患者對活性蛋白質單體產生免疫應答的風險，導致形成中和抗體和抗藥性，或其他不良副作用（Mahler J Pharm Sci.[藥物科學雜誌] 2009年9月；98(9):2909-34）。

【0005】總的來說，文獻中已經報導了藉由多種機制使蛋白質聚集最小化的若干努力。藉由修飾蛋白質的一級結構，可以穩定蛋白質並且因此防止聚集體形成和其他化學變化，從而增加內部疏水性並且降低外部疏水性。然而，蛋白質的基因工程化可能導致功能受損和/或免疫原性增加。另一種方法集中於聚集體的解離（稱為“解聚”），以藉由使用多種機制如溫度、壓力、pH和鹽來恢復功能性天然單體。目前，蛋白質聚集體

主要在下游加工的精製步驟中作為雜質被除去。然而，在高水平的高分子量（HMW）的情況下，去除大量的HMW不僅導致顯著的產量損失，而且使得設計穩健的下游加工具有挑戰性（Chi等人, Pharm Res [藥物研究], 第20卷，第9期, 2003年9月, 第1325-1336頁）。

【0006】在生物學和生物技術應用中保持蛋白質穩定性和活性帶來嚴重挑戰。本領域存在對優化的藥物組成物之需求，所述藥物組成物提供治療性蛋白質的增強的穩定性並減少在配製、填充、運輸、儲存和給藥期間的聚集和變性或降解，從而防止功能喪失和不良免疫原性反應。

【發明內容】

【0007】在一個方面，本文描述了藥物組成物，該藥物組成物包含本文描述的抗原結合蛋白、至少一種緩衝劑、至少一種表面活性劑和至少一種糖，其中該藥物組成物的pH範圍為從3.5至5。

【0008】在一些實施方式中，抗原結合蛋白係抗體。在一些實施方式中，抗體係雙特異性抗體，例如結合CD3的雙特異性抗體。

【0009】在一些實施方式中，抗原結合蛋白係結合CD3的異源二聚體抗體。在一些實施方式中，異源二聚體抗體包含 a) 包含第一Fc結構域和抗CD3 scFv的第一單體，該抗CD3 scFv包含 (i) 包含如SEQ ID NO: 15所示的vlCDR1、如SEQ ID NO: 16所示的vlCDR2、和如SEQ ID NO: 17所示的vlCDR3的scFv可變輕結構域，和 (ii) 包含如SEQ ID NO: 11所示的vhCDR1、如SEQ ID NO: 12所示的vhCDR2、和如SEQ ID NO: 13所示的vhCDR3的scFv可變重結構域，其中使用結構域接頭將所述scFv共價附接至所述Fc結構域的N末端；b) 第二單體，其包含 i)如SEQ ID NO: 65所示的vhCDR1、如SEQ ID NO: 66所示的vhCDR2、和如SEQ ID NO:

67所示的vhCDR3的抗CD38重可變結構域，和 ii) 包含第二Fc結構域的重恒定結構域；和 c) 包含恒定結構域和抗CD38可變輕結構域的輕鏈，該抗CD38可變輕結構域包含如SEQ ID NO: 69所示的vlCDR1、如SEQ ID NO: 70所示的vlCDR2、和如SEQ ID NO: 71所示的vlCDR3，並且其中藥物組成物的pH範圍為從3.5至5。

【0010】在一些實施方式中，抗CD3 scFv包含與SEQ ID NO: 18中所示的胺基酸序列至少90%、至少95%或100%相同的胺基酸序列。

【0011】在一些實施方式中，抗CD38可變輕結構域包含與SEQ ID NO: 68中所示的胺基酸序列至少90%、至少95%或100%相同的胺基酸序列。

【0012】在一些實施方式中，抗CD38重可變結構域包含與SEQ ID NO: 64中所示的胺基酸序列至少90%、至少95%或100%相同的胺基酸序列。

【0013】在一些實施方式中，第一單體包含與SEQ ID NO: 335中所示的胺基酸序列至少90%、至少95%或100%相同的胺基酸序列。

【0014】在一些實施方式中，第二單體包含與SEQ ID NO: 337中所示的胺基酸序列至少90%、至少95%或100%相同的胺基酸序列。

【0015】在一些實施方式中，輕鏈包含與SEQ ID NO: 336中所示的胺基酸序列至少90%、至少95%或100%相同的胺基酸序列。

【0016】在多個方面，抗原結合蛋白係異源二聚體抗體，該抗體包含 a) 包含第一重鏈的第一單體，該第一重鏈包含 1) 第一可變重結構域；2) 包含第一CH1結構域和第一Fc結構域的第一恒定重結構域；和 3) 結合人CD3並且包含如下的scFv：(i) scFv可變輕結構域，其包含SEQ ID

NO:387中所示的vlCDR1、SEQ ID NO: 388中所示的vlCDR2、和SEQ ID NO: 389中所示的vlCDR3，(ii) scFv接頭，和 (iii) scFv可變重結構域，其包含SEQ ID NO: 383中所示的vhCDR1、SEQ ID NO: 384中所示的vhCDR2、和SEQ ID NO: 385中所示的vhCDR3；其中使用一個或多個結構域接頭將所述scFv共價附接至所述CH1結構域的C末端和所述第一Fc結構域的N末端之間。異源二聚體抗體進一步包含 b) 第二單體，其包含第二重鏈，該第二重鏈包含第二可變重結構域和第二恒定重鏈，該第二恒定重鏈包含第二Fc結構域；和 c) 包含可變輕結構域和恒定輕結構域的共同輕鏈。第一可變重結構域和可變輕結構域結合人STEAP1，並且第二可變重結構域和可變輕結構域結合人STEAP1。第一可變重結構域和第二可變重結構域包含重鏈CDR，該重鏈CDR包含SEQ ID NO: 360中所示的vhCDR1、SEQ ID NO: 361或SEQ ID NO: 363中所示的vhCDR2、和SEQ ID NO: 362中所示的vhCDR3，並且該可變輕結構域包含輕鏈CDR，該輕鏈CDR包含SEQ ID NO: 357中所示的vlCDR1、SEQ ID NO: 358中所示的vlCDR2、和SEQ ID NO: 359中所示的vlCDR3。可替代地，第一可變重結構域和第二可變重結構域包含重鏈CDR，該重鏈CDR包含SEQ ID NO: 368中所示的vhCDR1、SEQ ID NO: 369中所示的vhCDR2、和SEQ ID NO: 370中所示的vhCDR3，並且該可變輕結構域包含輕鏈CDR，該輕鏈CDR包含SEQ ID NO: 371中所示的vlCDR1、SEQ ID NO: 372中所示的vlCDR2、和SEQ ID NO: 373中所示的vlCDR3。在多個實施方式中，第一可變重結構域和第二可變重結構域包含與SEQ ID NO: 377或379至少90%相同（例如，至少95%相同或100%相同）的胺基酸序列，和/或可變輕結構域包含與SEQ ID NO: 378至少90%相同（例

如，至少95%相同或100%相同）的胺基酸序列。可替代地，第一可變重結構域和第二可變重結構域包含與SEQ ID NO: 380至少90%相同（例如，至少95%相同或100%相同）的胺基酸序列，和/或可變輕結構域包含與SEQ ID NO: 381至少90%相同（例如，至少95%相同或100%相同）的胺基酸序列。scFv視需要包含SEQ ID NO: 382和SEQ ID NO:383的可變重區和可變輕區。scFv接頭視需要包含SEQ ID NO: 391。在多個方面，scFv包含SEQ ID NO: 390的序列。在多個方面，a) 第一單體包含SEQ ID NO: 366或SEQ ID NO: 367的序列，第二單體包含SEQ ID NO:365的序列，且共同輕鏈包含SEQ ID NO:364的序列；或 b) 第一單體包含SEQ ID NO: 376的序列，第二單體包含SEQ ID NO:375的序列，且共同輕鏈包含SEQ ID NO:374的序列。

【0017】本揭露的藥物組成物包含至少一種緩衝劑。在一些實施方式中，緩衝劑係選自由以下各項組成之群組之酸：乙酸鹽、谷胺酸鹽、檸檬酸鹽、琥珀酸鹽、酒石酸鹽、富馬酸鹽、馬來酸鹽、組胺酸、磷酸鹽、和2-(N-味啉基)乙磺酸鹽或其組合。在一些實施方式中，至少一種緩衝劑在組成物中以從約5 mM至約200 mM（或約10 mM至約50 mM）的濃度範圍存在。

【0018】本揭露的藥物組成物包含至少一種糖。在一些實施方式中，糖選自由以下各項組成之群組：單糖、二糖、環狀多糖、糖醇、線性支鏈型聚葡糖（linear branched dextran）和線性非支鏈型聚葡糖（linear non-branched dextran）。在一些實施方式中，糖係糖醇（例如山梨糖醇）。在一些實施方式中，糖係選自由以下各項組成之群組之二糖：蔗糖、海藻糖、甘露糖醇和山梨糖醇或其組合。在一些實施方式中，至少一

種糖以約從1%至約15%（w/V）（或約9%至約12%（w/V）或約5%至約12%（w/V）或約7%至約12%（w/V））的濃度範圍存在於組成物中。

【0019】本揭露的藥物組成物包含至少一種表面活性劑。在一些實施方式中，表面活性劑選自由以下各項組成之群組：聚山梨醇酯20、聚山梨醇酯40、聚山梨醇酯60、聚山梨醇酯80、泊洛沙姆（poloxamer）188、普朗尼克（pluronic）F68、曲拉通（triton）X-100、聚氧乙烯3和PEG 3350、PEG 4000、或其組合。在一些實施方式中，至少一種表面活性劑以從0.004%至約0.5%（w/V）（或約0.001%至約0.01%（w/V）、或約0.001%至約0.5%（w/V）或約0.004%至約0.01%（w/V））的濃度範圍存在於組成物中。

【0020】在一些實施方式中，組成物的pH範圍為從4.0至5.0。在一些實施方式中，組成物的pH係4.2。

【0021】在一些實施方式中，組成物的滲透壓範圍為約150 mOsm至約500 mOsm。

【0022】本揭露的藥物組成物可視需要進一步包含選自由以下各項組成之群組之賦形劑：多元醇和胺基酸。在一些實施方式中，賦形劑以約0.1%至約15%（w/V）的濃度範圍存在。

【0023】在一些實施方式中，藥物組成物包含10 mM谷胺酸、9%（w/V）蔗糖和0.01%（w/V）聚山梨醇酯80，並且其中液體藥物組成物的pH為4.2。在一些實施方式中，異源二聚體抗體以從約0.1 mg/mL至約8 mg/mL的濃度範圍存在於組成物中。在一些實施方式中，異源二聚體抗體以從約0.1 mg/mL至約20 mg/mL的濃度範圍存在於組成物中。在一些實施方式中，異源二聚體抗體以1 mg/mL、5 mg/mL、10 mg/mL或20

mg/mL的濃度存在於組成物中。在一些實施方式中，異源二聚體抗體以從約50 μg至約200 mg的量範圍存在於組成物中。

【0024】本揭露的藥物組成物可以係凍乾組成物或液體組成物。在一些實施方式中，藥物組成物係凍乾組成物或重構的凍乾組成物。

【0025】在另一個方面，本文描述了治療有需要的受試者的癌症之方法，該方法包括向受試者給予本揭露的組成物。在一些實施方式中，癌症係多發性骨髓瘤。在一些實施方式中，癌症係前列腺癌。

【0026】應理解，雖然說明書中的多個實施方式係使用“包含”語言呈現的，但在多種情況下，也可以使用“由……組成”或“基本上由……組成”來描述相關的實施方式。本揭露設想了被描述為“包含”一種特徵的實施方式，以包括“由所述特徵組成”的實施方式。應注意，術語“一種/一個”係指一種/一個或多種/多個，例如，“一種/一個免疫球蛋白分子”應理解為代表一種/一個或多種/多個免疫球蛋白分子。同樣地，術語“一種/一個”、“一種或多種/一個或多個”以及“至少一種/至少一個”可以互換地使用。

【0027】還應理解，當描述值範圍時，所描述的特徵可以是在該範圍內找到的單個值。例如，“從約pH 4至約pH 6的pH”可以是但不限於，pH 4、4.2、4.6、5.1、5.5等，以及該等值之間的任何值。另外，“從約pH 4至約pH 6的pH”不應被解釋為意指所述製劑的pH在儲存期間在pH 4至pH 6的範圍內變化2個pH單位，而是指溶液的pH可以在該範圍內挑選值，並且pH在該pH下保持緩衝。在一些實施方式中，當使用術語“約”時，其意指所列舉數字加上或減去所列舉數字的5%、10%、15%或更多。預期的實際變化可從上下文確定。

【0028】在本文描述的任何範圍內，該範圍的端點包括在該範圍內。然而，該描述還考慮了排除較低和/或較高端點的相同範圍。從本申請的整體，包括附圖和具體實施方式，本發明的另外的特徵和變化對於熟悉該項技術者而言將是顯而易見的，並且所有該等特徵都旨在作為本發明的方面。同樣，在此描述的本發明的特徵可以重組成另外的實施方式，該等實施方式也旨在作為本發明的方面，無論該等特徵的組合是否在上文作為本發明的一個方面或實施方式具體提及。而且，只有本文描述為對本發明至關重要的該等限制才應被視為這樣的限制；在此未描述為關鍵的、本發明的缺少限制的變化旨在作為本發明的方面。

【0029】本文引用的所有參考文獻藉由引用併入本文。

【圖式簡單說明】

【0030】[圖1A和1B]描繪了若干種型式（format）的異源二聚體抗體。描繪了兩種形式的“開瓶器（bottle opener）”型式，一種具有包含scFv的抗CD3抗原結合結構域和包含Fab（如抗原結合結構域的實例）的抗CD38抗原結合結構域，並且另一種具有該等的顛倒。示出了所有mAb-Fv、mAb-scFv、中心scFv（或“XmAb^{2+1}”型式）和中心Fv型式。此外，示出了其中一個單體僅包含Fc結構域的“單臂”型式，為單臂中心scFv和單臂中心Fv兩者。還示出了雙scFv型式。

【0031】[圖2]描繪了“高-中＃1”抗CD3_H1.32_L1.47構建體的序列，包括可變重和輕結構域（CDR加底線），以及單獨的vl和vhCDR，以及具有帶電荷的接頭（加雙底線）的scFv構建體。與圖中描繪的所有序列一樣，根據需要，該帶電荷的接頭可以被不帶電荷的接頭或不同的帶電荷的接頭取代。

【0032】[圖3]描繪了中CD38: OKT10_H1L1.24構建體的序列，包括可變重和輕結構域（CDR加底線），以及單獨的vl和vhCDR，以及具有帶電荷的接頭（雙底線）的scFv構建體。

【0033】[圖4]描繪了低CD38: OKT10_H1L1構建體的序列，包括可變重和輕結構域（CDR加底線），以及單獨的vl和vhCDR，以及具有帶電荷的接頭（加雙底線）的scFv構建體。

【0034】[圖5]描繪了XENP18971的序列。CDR加底線。

【0035】[圖6]描繪了XENP18969的序列。CDR加底線。

【0036】[圖7]描繪了人CD3 ε的序列（SEQ ID NO: 130）。

【0037】[圖8]描繪了人CD38蛋白質的全長（SEQ ID NO:131）和胞外結構域（ECD；SEQ ID NO:132）。

【0038】[圖9A-9E]描繪了有用的異源二聚化變體組對（包括偏斜（skew）變體和pI變體）。

【0039】[圖10]描繪了電子等排（isosteric）變體抗體恒定區及其各自取代的列表。pI_(-)指示較低pI的變體，而pI_(+)指示較高pI的變體。該等可以視需要且獨立地與本發明的其他異源二聚化變體（以及如本文所概述的其他變體類型）組合。

【0040】[圖11]描繪了消融FcγR結合的有用消融變體（有時稱為“敲除”或“KO”變體）。

【0041】[圖12]顯示了本揭露的抗體的兩個實施方式。

【0042】[圖13A和13B]描繪了許多帶電荷的scFv接頭，其可用於增加或降低利用一種或多種scFv作為組分的異源二聚體抗體的pI。具有單個電荷的單個先前技術scFv接頭被稱為“惠特洛（Whitlow）”，來自

Whitlow等人, Protein Engineering [蛋白質工程] 6(8):989-995 (1993)。應注意，該接頭用於減少scFv中的聚集和增強蛋白水解穩定性。

【0043】[圖14]描繪了工程化異源二聚體-偏斜Fc變體、連同異源二聚體產率（藉由HPLC-CIEX確定）和熱穩定性（藉由DSC確定）的列表。未確定的熱穩定性由“n.d”指示。

【0044】[圖15A和15B]描繪了穩定性優化的人源化抗CD3變體scFv。相對於H1_L1.4 scFv序列給出取代。胺基酸編號係卡巴特（Kabat）編號。

【0045】[圖16A和16B]描繪了穩定性優化的人源化抗CD3變體scFv的胺基酸序列。CDR加底線。對於每個重鏈/輕鏈組合，列出了四個序列：(i) 具有C末端6xHis標籤的scFv，(ii) 僅scFv，(iii) 僅VH，(iv) 僅VL。

【0046】[圖17]描繪了XENP18971的序列。CDR加底線。

【0047】[圖18]描繪了XENP18969的序列。CDR加底線。

【0048】[圖19]顯示實施方式的可能組合的矩陣。“A”意指所引用的CD3序列的CDR可以與左側的CD38構建體的CDR組合。即，例如對於左上角的儲存格，來自可變重鏈CD3 H1.30序列的vhCDR和來自CD3 L1.47序列的可變輕鏈的vlCDR可以與來自CD38 OKT10 H1.77序列的vhCDR和來自OKT10L1.24序列的vlCDR組合。“B”意指來自CD3構建體的CDR可以與來自CD38構建體的可變重和輕結構域組合。即，例如對於左上角的儲存格，來自可變重鏈CD3 H1.30序列的vhCDR和來自CD3 L1.47序列的可變輕鏈的vlCDR可以與可變重結構域CD38 OKT10 H1.77序列和OKT10L1.24序列組合。顛倒“C”，使得來自CD3序列的可變重結構域和

可變輕結構域與CD38序列的CDR一起使用。“D”係來自每個的可變重鏈和可變輕鏈兩者組合的情況。“E”係指CD3的scFv與CD38抗原結合結構域構建體的CDR一起使用的情況，並且“F”係CD3的scFv與CD38抗原結合結構域的可變重和可變輕結構域一起使用的情況。

【0049】[圖20]描繪了XmAb18968的序列，在本文中也稱為抗體A。CDR加底線。

【0050】[圖21]係將各個CDR序列、可變區序列、重鏈和輕鏈序列、scFv序列、主鏈序列等與本申請所附序列表中列出的序列標識符聯繫在一起的表。關於所提到的若干種開瓶器型式的主鏈（SEQ ID NO: 347-354），未提供該等序列的Fv序列（例如，scFv和Fab側的vh和vl）。如熟悉該項技術者所理解和以下概述的，該等序列可與本文概述的任何vh和vl對一起使用，其中一種單體包括scFv（視需要包括帶電荷的scFv接頭）並且另一種單體包擴Fab序列（例如，附接至“Fab側重鏈”的vh和附接至“恒定輕鏈”的vl）。scFv可以是抗CD3或抗CD38，另一種是Fab。（“Fab”係指包含VH、CH1、VL、和CL免疫球蛋白結構域的部分。）即，例如，本文概述的CD3和CD38的任何Fv序列能以任何組合摻入該等主鏈中。

【0051】[圖22A和22B]顯示藉由SE-UHPLC確定的當以製劑A（圖22A）和製劑B（圖22B）配製時抗體A的主峰損失。

【0052】[圖23]顯示藉由SE-UHPLC確定的當以製劑C配製時抗體A的主峰損失。

【0053】[圖24A和24B]顯示藉由CE-HPLC確定的當以製劑A（圖24A）和製劑B（圖24B）配製時抗體A的主峰損失。

【0054】[圖25]顯示藉由CE-HPLC確定的當以製劑C配製時抗體A的主峰損失。

【0055】[圖26]顯示藉由rCE確定的當以製劑A配製時抗體A在-30°C的主峰損失。

【0056】[圖27]顯示藉由rCE確定的當以製劑B配製時抗體A在40°C的主峰損失。

【0057】[圖28]顯示藉由rCE確定的當以製劑C配製時抗體A的主峰損失。

【0058】[圖29]顯示藉由MAM確定的，當以製劑B和C配製時，在4°C、2°C、和40°C持續三個月，抗體A的脫醯胺化百分比。

【0059】[圖30]顯示藉由MAM確定的，當以製劑D配製時，在40°C持續0週、兩週和四週，抗體A的脫醯胺化百分比。

【0060】[圖31]顯示藉由MAM確定的，當以製劑B和C配製時，在40°C持續一個月，抗體A的脫醯胺化百分比。

【實施方式】

相關申請的交叉引用

【0061】本申請要求於2018年2月8日提交的美國臨時申請案號62/628,267和2019年1月31日提交的美國臨時申請案號62/799,577的優先權之權益，所述申請的揭露內容藉由引用以其整體併入本文。

藉由引用結合

【0062】本申請藉由引用併入2015年11月25日提交的國際專利公開案號WO 2016/086196；2015年11月25日提交的美國專利公開案號20160215063；2016年11月23日提交的國際專利公開案號WO

2017/091656；和2015年3月30日提交的美國專利案號9,822,186，所述公開以其整體明確地併入本文，特別是對其中的圖、圖例和申請專利範圍的引用。

【0063】藉由引用以其整體併入與本文同時提交的電腦可讀的核苷酸/胺基酸序列表，並且標識如下：名稱為“52588P_Seqlisting.txt”的ASCII（文本）檔，創建於2019年2月5日，大小為756,646位元組。

【0064】本揭露描述了包含結合CD3的抗原結合蛋白的低pH製劑。

【0065】在一些實施方式中，抗原結合蛋白係抗體，例如雙特異性抗體（例如，結合CD3的雙特異性抗體）。在一些實施方式中，抗原結合蛋白係異源二聚體抗體，其以這樣的方式共接合CD3和CD38，以將惡性細胞與T細胞暫態連接，從而誘導所結合惡性細胞的T細胞介導的殺死。在其他實施方式中，抗原結合蛋白係共接合CD3和STEAP1的異源二聚體抗體。

【0066】特定的基於蛋白質的藥物在較長時間段內在液體製劑中不穩定，並且特別是4°C及以上的製冷溫度下不穩定。本發明基於的總體概念係發現包含根據本發明的抗原結合蛋白的液體藥物組成物的膠體穩定性在低pH下得到改進。

【0067】製劑的各個方面描述如下。節標題的使用僅僅是為了便於閱讀，而不是意圖限制本身。整個文件旨在被視為統一的揭露，並且應理解，可以考慮本文描述的特徵的所有組合。

【0068】在一個方面，本文描述了藥物組成物，該藥物組成物包含本文描述的抗原結合蛋白、至少一種緩衝劑、至少一種表面活性劑和至少一種糖，其中該藥物組成物的pH範圍為從3.5至5。

【0069】*緩衝液*

【0070】本發明的藥物組成物包含緩衝劑，其視需要可選自由以下各項組成之群組：乙酸鹽、谷胺酸鹽、檸檬酸鹽、琥珀酸鹽、酒石酸鹽、富馬酸鹽、馬來酸鹽、組胺酸、磷酸鹽、2-(N-味啉基)乙磺酸鹽、磷酸鉀、乙酸/乙酸鈉、檸檬酸/檸檬酸鈉、琥珀酸/琥珀酸鈉、酒石酸/酒石酸鈉、組胺酸/組胺酸鹽酸鹽、甘胺酸、Tris、谷胺酸鹽及其組合。在一些實施方式中，藥物組成物包含至少一種選自由以下各項組成之群組之緩衝液：乙酸鹽、谷胺酸鹽、檸檬酸鹽、琥珀酸鹽、酒石酸鹽、富馬酸鹽、馬來酸鹽、組胺酸、磷酸鹽、2-(N-味啉基)乙磺酸鹽及其組合。

【0071】通常採用緩衝劑來控制製劑中的pH。在一些實施方式中，以一定濃度添加緩衝液使製劑的pH保持在約3.5至5、或約4至5，或約4.2。pH對製劑的影響可以使用若干種途徑中的任何一種或多種來表徵，例如加速穩定性研究和量熱篩選研究（Remmele R.L. Jr., 等人, Biochemistry [生物化學], 38(16): 5241-7 (1999)）。

【0072】有機酸、磷酸鹽和Tris係蛋白質製劑中的合適緩衝液（表1）。緩衝種類的緩衝容量在等於pKa的pH下最大，並且隨著pH從這個值增加或減小而降低。百分之九十的緩衝能力存在於其pKa的一個pH單位內。緩衝容量也隨緩衝液濃度的增加而成比例增加。

【0073】選擇緩衝液時典型地會考慮若干個因素。例如，緩衝液種類及其濃度應基於其pKa和所希望的製劑pH來定義。同樣重要的是確保緩衝液與蛋白質藥物、其他製劑賦形劑相容，並且不催化任何降解反應。最近，已示出聚陰離子羧酸鹽緩衝劑例如檸檬酸鹽和琥珀酸鹽與蛋白質的側鏈殘基形成共價加合物。要考慮的第三個方面係緩衝液可能誘導的刺痛和

刺激感。例如，已知檸檬酸鹽在注射時引起刺痛（Laursen T, 等人, Basic Clin Pharmacol Toxicol.[基礎臨床藥理學與毒理學], 98(2): 218-21 (2006)）。對於經由SC或IM途徑給予的藥物，刺激和刺激的潛力更大，其中藥物溶液在該位點保留的時間比藉由IV途徑給予的時間段相對更長，其中製劑在給予後迅速稀釋到血液中。對於藉由直接IV輸注給予的製劑，需要監測緩衝液（和任何其他製劑組分）的總量。例如，據報導，以磷酸鉀緩衝液形式給予的鉀離子可以在患者中誘導心血管效應（Hollander-Rodriguez JC, 等人, Am. Fam. Physician.[美國家庭醫師], 73(2): 283-90 (2006)）。

[表1]：緩衝劑及其pK_a值

緩衝液	pK_a	實例藥物產品
乙酸鹽	4.8	Neupogen、Neulasta
琥珀酸鹽	pK_{a1} = 4.8，pK_{a2} = 5.5	Actimmune
檸檬酸鹽	pK_{a1} = 3.1，pK_{a2} = 4.8，pK_{a3} = 6.4	修美樂（Humira）
組胺酸（咪唑）	6.0	Xolair
磷酸鹽	pK_{a1} = 2.15，pK_{a2} = 7.2，pK_{a3} = 12.3	Enbrel（液體製劑）
Tris	8.1	Leukine

【0074】選擇製劑中存在的緩衝液系統以在生理學上相容並保持所希望的pH。

【0075】緩衝液能以適於將製劑的pH維持在預定水平的任何量存在。緩衝液可以按約0.1 mM和約1000 mM（1 M）之間、或約5 mM和約200 mM之間、或約5 mM至約100 mM之間、或約10 mM和約50 mM之間的濃度存在。合適的緩衝液濃度涵蓋約200 mM或更低的濃度。在一些實

施方式中，製劑中的緩衝液以約190 mM、約180 mM、約170 mM、約160 mM、約150 mM、約140 mM、約130 mM、約120 mM、約110 mM、約100 mM、約80 mM、約70 mM、約60 mM、約50 mM、約40 mM、約30 mM、約20 mM、約10 mM或約5 mM的濃度存在。在一些實施方式中，緩衝液的濃度為至少0.1、0.5、0.7、0.8、0.9、1.0、1.2、1.5、1.7、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、30、40、50、60、70、80、90、100、200、500、700、或900 mM。在一些實施方式中，緩衝液的濃度為在1、1.2、1.5、1.7、2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、30、40、50、60、70、80、或90 mM和100 mM之間。在一些實施方式中，緩衝液的濃度為在5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、30、或40 mM和50 mM之間。在一些實施方式中，緩衝液的濃度為約10 mM。

【0076】用於緩衝本文列出的製劑的其他示例性pH緩衝劑包括但不限於甘胺酸、谷胺酸鹽、琥珀酸鹽、磷酸鹽、乙酸鹽和天冬胺酸。胺基酸例如組胺酸和谷胺酸也可用作緩衝劑。

【0077】*表面活性劑*

【0078】這裡描述的藥物組成物包含至少一種表面活性劑。表面活性劑通常用於蛋白質製劑中以防止表面誘導的降解。表面活性劑係兩親性分子，具有與蛋白質競爭介面位置的能力。表面活性劑分子的疏水部分佔據介面位置（例如，空氣/液體），而分子的親水部分保持朝向主體溶劑定向。在足夠的濃度下（典型地在洗滌劑的臨界膠束濃度附近），表面活性劑分子的表面層用於防止蛋白質分子吸附在介面處。因此，表面誘導的

降解被最小化。表面活性劑包括例如山梨糖醇聚乙氧基化物的脂肪酸酯，即聚山梨醇酯20和聚山梨醇酯80（參見例如Avonex®、Neupogen®、Neulasta®）。兩者的不同之處僅在於脂族鏈的長度，它們分別賦予分子C-12和C-18疏水特徵。因此，聚山梨醇酯80比聚山梨醇酯20具有更高的表面活性並且具有更低的臨界膠束濃度。表面活性劑泊洛沙姆188也已用於若干種市售的液體產品，例如Gonal-F®、Norditropin®、和Ovidrel®。

【0079】洗滌劑還可以影響蛋白質的熱力學構象穩定性。在此同樣地，給定賦形劑的作用將是蛋白質特異性的。例如，已示出聚山梨醇酯降低一些蛋白質的穩定性並增加其他蛋白質的穩定性。蛋白質的洗滌劑不穩定可以根據洗滌劑分子的疏水性尾部來合理解釋，該等洗滌劑分子能以部分或完全去折疊的蛋白質狀態進行特異性結合。該等類型的相互作用可以引起構象平衡向更擴展的蛋白質狀態的轉變（即，增加蛋白質分子的疏水部分的暴露以補充結合聚山梨醇酯）。或者，如果蛋白質天然狀態展現出一些疏水表面，則與天然狀態結合的洗滌劑可穩定該構象。

【0080】聚山梨醇酯的另一方面係它們固有地易受氧化降解的影響。通常，作為原料，它們含有足夠量的過氧化物以引起蛋白質殘基側鏈的氧化，尤其是甲硫胺酸。添加穩定劑引起的氧化損傷的可能性強調了製劑中應使用最低有效濃度的賦形劑。對於表面活性劑，給定蛋白質的有效濃度將取決於穩定機制。已經假定，如果表面活性劑穩定的機制與防止表面變性有關，則有效濃度將在洗滌劑的臨界膠束濃度附近。相反，如果穩定機制與特定的蛋白質-洗滌劑相互作用相關，則有效的表面活性劑濃度將與蛋白質濃度和相互作用的化學計量有關（Randolph T.W., 等人, *Pharm Biotechnol.* [藥物生物技術], 13:159-75 (2002)）。

【0081】還能以適當的量添加表面活性劑以防止在冷凍和乾燥過程中表面相關的聚集現象（Chang, B, J. Pharm. Sci.[藥物科學雜誌] 85:1325, (1996)）。示例性表面活性劑包括陰離子表面活性劑、陽離子表面活性劑、非離子表面活性劑、兩性離子表面活性劑、和兩性表面活性劑，包括衍生自天然存在的胺基酸的表面活性劑。陰離子表面活性劑包括但不限於十二烷基硫酸鈉、丁二酸二辛基磺酸鈉和二辛基磺酸鈉、鵝去氧膽酸（chenodeoxycholic acid）、N-月桂醯肌胺酸鈉鹽、十二烷基硫酸鋰、1-辛烷磺酸鈉鹽、膽酸鈉水合物、去氧膽酸鈉、和甘胺去氧膽酸鈉鹽。陽離子表面活性劑包括但不限於氯化苄烷銨或氯化本索寧、氯化十六烷基吡啶一水合物和溴化十六烷基三甲銨。兩性離子表面活性劑包括但不限於CHAPS、CHAPSO、SB3-10、和SB3-12。非離子表面活性劑包括但不限於毛地黃皂苷（digitonin）、曲拉通（Triton）X-100、曲拉通X-114、吐溫20和吐溫80。在另一個實施方式中，表面活性劑包括聚桂醇400；聚氧乙烯40硬脂酸酯；聚氧乙烯氫化蓖麻油10、40、50和60；甘油單硬脂酸酯；聚山梨醇酯40、60、65和80；大豆卵磷脂和其他磷脂例如DOPC、DMPG、DMPC、和DOPG；蔗糖脂肪酸酯；甲基纖維素和羧甲基纖維素。

【0082】本文描述的藥物組成物包含單獨的或呈不同比率的混合物的至少一種表面活性劑。在一些實施方式中，組成物包含濃度為約0.001%至約5% w/v（或約0.004%至約0.5% w/v或約0.001%至約0.01% w/v或約0.004%至約0.01% w/v）的表面活性劑。在一些實施方式中，組成物包含濃度為至少0.001% w/v、至少0.002% w/v、至少0.003% w/v、至少0.004% w/v、至少0.005% w/v、至少0.007% w/v、至少0.01%

w/v、至少0.05% w/v、至少0.1% w/v、至少0.2% w/v、至少0.3% w/v、至少0.4% w/v、至少0.5% w/v、至少0.6% w/v、至少0.7% w/v、至少0.8% w/v、至少0.9% w/v、至少1.0% w/v、至少1.5% w/v、至少2.0% w/v、至少2.5% w/v、至少3.0% w/v、至少3.5% w/v、至少4.0% w/v、或至少4.5% w/v的表面活性劑。在一些實施方式中，組成物包含濃度為約0.004% w/v至約0.5% w/v的表面活性劑。在一些實施方式中，組成物包含濃度為約0.004% w/v至約0.5% w/v的表面活性劑。在一些實施方式中，組成物包含濃度為約0.001% w/v至約0.01% w/v的表面活性劑。在一些實施方式中，組成物包含濃度為約0.004% w/v至約0.01% w/v的表面活性劑。在一些實施方式中，組成物包含濃度為約0.004% w/v、約0.005% w/v、約0.007% w/v、約0.01% w/v、約0.05% w/v、約0.1% w/v、約0.2% w/v、約0.3% w/v、約0.4% w/v至約0.5% w/v的表面活性劑。在一些實施方式中，組成物包含以約0.001% w/v至約0.01% w/v的濃度摻入的表面活性劑。在一些實施方式中，表面活性劑係聚山梨醇酯80，聚山梨醇酯80以約0.01% w/v的濃度存在。

【0083】*糖*

【0084】本文描述的藥物組成物包含至少一種糖。可以添加糖作為穩定劑或膨脹劑。如本文使用的術語“穩定劑”係指能夠防止聚集或其他物理降解以及水和固態的化學降解（例如，自溶、脫醯胺化、氧化等）的賦形劑。應用於藥物組成物中的穩定劑包括但不限於蔗糖、海藻糖、甘露糖、麥芽糖、乳糖、葡萄糖、棉子糖、纖維二糖、龍膽二糖、異麥芽糖、阿拉伯糖、葡糖胺、果糖、甘露糖醇、山梨糖醇、甘胺酸、精胺酸HCL、多羥基化合物（包括多糖例如聚葡糖、澱粉、羥乙基澱粉、環糊精、N-甲

基吡咯啶、纖維素和透明質酸）、和氯化鈉（Carpenter等人, Develop. Biol. Standard [生物標準化的發展] 74:225, (1991)）。

【0085】在一些實施方式中，所述至少一種糖選自由以下各項組成之群組：單糖、二糖、環狀多糖、糖醇、線性支鏈型聚葡糖和線性非支鏈型聚葡糖，及其組合。在一些實施方式中，至少一種糖係選自由以下各項組成之群組之二糖：蔗糖、海藻糖、甘露糖醇和山梨糖醇或其組合。

【0086】在一些實施方式中，藥物組成物包含濃度為約0.01% w/v至約40% w/v、或約0.01% w/v至約20% w/v、或約1% w/v至約15% w/v的至少一種糖。在一些實施方式中，藥物組成物包含濃度為至少0.5% w/v、至少1% w/v、至少2% w/v、至少3% w/v、至少4% w/v、至少5% w/v、至少6% w/v、至少7% w/v、至少8% w/v、至少9% w/v、至少10% w/v、至少11% w/v、至少12% w/v、至少13% w/v、至少14% w/v、至少15% w/v、至少16% w/v、至少17% w/v、至少18% w/v、至少19% w/v、至少20% w/v、至少30% w/v、或至少40% w/v的至少一種糖。在一些實施方式中，藥物組成物包含濃度為約1% w/v、約2% w/v、約3% w/v、約4% w/v、約5% w/v、約6% w/v、約7% w/v、約8% w/v、約9% w/v、約10% w/v、約11% w/v、約12% w/v、約13% w/v、約14% w/v至約15% w/v的至少一種糖。在一些實施方式中，藥物組成物包含濃度為約1% w/v至約15% w/v的至少一種糖。在又另一個實施方式中，藥物組成物包含濃度為約9% w/v、約9.5% w/v、約10% w/v、約10.5% w/v、約11% w/v、約11.5% w/v、或約12% w/v的至少一種糖。在一些實施方式中，藥物組成物包含濃度為約9% w/v至約12% w/v的至少一種糖。在一些實施方式中，該至少一種糖在組成物中的濃度為約9% w/v。在一些實施方式中，該至

少一種糖選自由以下各項組成之群組：蔗糖、海藻糖、甘露糖醇和山梨糖醇或其組合。在一些實施方式中，糖係山梨糖醇，並且在組成物中以從約9% w/v至約12% w/v的範圍存在。

【0087】如果希望，製劑還包括適於形成凍乾的“餅”的適量的膨脹和滲透壓調節劑，例如糖。

【0088】在較佳的實施方式中，藥物組成物包含10 mM谷胺酸、9%（w/V）蔗糖和0.01%（w/V）聚山梨醇酯80，其中藥物組成物的pH為4.2。

【0089】*其他考慮*

【0090】如本文使用的，術語“藥物組成物”涉及適於向有需要的受試者給予的組成物。術語“受試者”或“個體”或“動物”或“患者”在本文中可互換地使用，係指任何希望給予本發明藥物組成物的受試者，特別是哺乳動物受試者。哺乳動物受試者包括人、非人靈長類動物、狗、貓、豚鼠、兔、大鼠、小鼠、馬、牛、母牛等，較佳的是人。本發明的藥物組成物係穩定的和藥學上可接受的，即能夠引發所希望的治療效果，而不會在給予藥物組成物的受試者中引起顯著不希望的局部或全身性作用。本發明的藥學上可接受的組成物可以是無菌的和/或藥學上惰性的。具體地，術語“藥學上可接受的”可以意指由管理機構或其他受普遍承認的藥典批准在動物中使用，並且更特別地在人中使用。

【0091】本揭露提供的製劑包含本文描述的抗原結合蛋白（例如，異源二聚體抗體）。在一些實施方式中，提供了治療有效量的異源二聚體抗體。“治療有效量”係指所述異源二聚體抗體的引發所希望的治療效果的量。治療效果和毒性可以藉由標準藥物方法在細胞培養物中或實驗性動

物，例如ED50（在群體的50%中治療有效的劑量）和LD50（對群體的50%致死的劑量）來確定。治療和毒性作用之間的劑量比為治療指數，並且它能以ED50/LD50比表示。通常較佳的是展現出大治療指數的製劑。

【0092】蛋白質製劑通常腸胃外給予。腸胃外給予時，它們必須是無菌的。無菌稀釋劑包括藥學上可接受的液體（對人給予係安全且無毒的）並且有用於製備液體製劑，例如凍乾後重構的製劑。示例性的稀釋劑包括無菌水、注射用抑菌水（BWFI）、pH緩衝溶液（例如磷酸鹽緩衝鹽水）、無菌鹽水溶液、林格氏溶液或右旋糖溶液。稀釋劑可包括鹽和/或緩衝液的水溶液。

【0093】賦形劑係包括在製劑中的添加劑，因為它們賦予或增強藥物產品的穩定性、遞送和可製造性。無論其包含的原因如何，賦形劑都是藥物產品的整體組分，並且因此需要安全且患者耐受良好。對於蛋白質藥物，賦形劑的選擇特別重要，因為它們可以影響藥物的功效和免疫原性兩者。因此，需要在適當選擇賦形劑的情況下開發蛋白質製劑，該賦形劑提供合適的穩定性、安全性和適銷性。

【0094】本文描述的賦形劑藉由它們的化學類型或它們在製劑中的功能性作用來組織。當討論每種賦形劑類型時，提供了穩定模式的簡要說明。鑒於本文提供的教導和指導，熟悉該項技術者將能夠容易地改變賦形劑的量或範圍，而不會將黏度增加至不希望的水平。可以選擇賦形劑以實現最終溶液的所希望的滲透壓（即等滲、低滲或高滲）、pH、所希望的穩定性、抗聚集或抗降解或抗沈澱、在冷凍、凍乾或高溫條件下的保護、或其他性質。本領域已知各種類型的賦形劑。示例性賦形劑包括鹽、胺基酸、其他張度劑、表面活性劑、穩定劑、膨脹劑、冷凍保護劑、凍乾保護

劑、抗氧化劑、金屬離子、螯合劑和/或防腐劑。

【0095】此外，當以例如百分比（%）w/v報告在製劑中的特定賦形劑時，熟悉該項技術者將認識到也考慮了該賦形劑的當量莫耳濃度。

【0096】*其他穩定劑和膨脹劑*

【0097】穩定劑包括一類可用作冷凍保護劑、凍乾保護劑、和玻璃形成劑的化合物。冷凍保護劑用於在低溫下在冷凍期間或在冷凍狀態穩定蛋白質。藉由在冷凍乾燥的脫水階段期間保留蛋白質的天然樣構象性質，凍乾保護劑穩定冷凍乾燥的固體劑型中的蛋白質。玻璃態性質根據其作為溫度的函數的鬆弛性質被分類為“強”或“易碎”。重要的是，冷凍保護劑、凍乾保護劑和玻璃形成劑與蛋白質保持相同的相以賦予穩定性。糖、聚合物、和多元醇落入這一類別，並且有時可以發揮三種作用。

【0098】多元醇涵蓋一類賦形劑，其包括糖（例如甘露糖醇、蔗糖、或山梨糖醇）和其他多元醇（例如甘油和丙二醇）。聚合物聚乙二醇（PEG）包括在這個類別中。多元醇通常用作液體和凍乾的腸胃外蛋白質製劑兩者中的穩定賦形劑和/或等張劑。多元醇可以保護蛋白質免受物理和化學降解途徑的影響。

【0099】示例性的C_3-C_6多元醇包括丙二醇、甘油（丙三醇）、蘇糖、蘇糖醇、赤蘚糖、赤蘚糖醇、核糖、阿拉伯糖、阿拉伯糖醇、來蘇糖、麥芽糖醇、山梨糖醇、山梨糖、葡萄糖、甘露糖、甘露糖醇、左旋糖、右旋糖、麥芽糖、海藻糖、果糖、木糖醇、肌醇、半乳糖、木糖、果糖、蔗糖、1,2,6-己三醇等。高級糖包括聚葡糖、丙二醇或聚乙二醇。與非還原糖相比，還原糖，例如果糖、麥芽糖或半乳糖更容易氧化。糖醇的另外的實例係葡糖醇、麥芽糖醇、乳糖醇或異麥芽酮糖。另外的示例性凍

乾保護劑包括甘油和明膠，以及蜜二糖、松三糖、棉子糖、甘露三糖和水蘇糖。還原糖的實例包括葡萄糖、麥芽糖、乳糖、麥芽酮糖、異麥芽酮糖和乳果糖。非還原糖的實例包括選自糖醇和其他直鏈多元醇的多羥基化合物的非還原糖苷。單糖苷包括藉由還原例如乳糖、麥芽糖、乳果糖和麥芽酮糖的二糖而獲得的化合物。

【0100】胺基酸

【0101】在一些實施方式中，本文描述的藥物組成物進一步包含一種或多種胺基酸。胺基酸已被發現多用於蛋白質製劑中作為緩衝液、膨脹劑、穩定劑和抗氧化劑。採用組胺酸和谷胺酸來緩衝蛋白質製劑，pH範圍分別為5.5 – 6.5和4.0 – 5.5。組胺酸的咪唑基團的pKa = 6.0，並且谷胺酸側鏈的羧基基團的pKa為4.3，這使得它們適合於在各自的pH範圍內緩衝。谷胺酸發現於一些製劑中（例如，Stemgen®）。組胺酸通常發現於市售蛋白質製劑中（例如，Xolair®、Herceptin®、Recombinate®）。它提供了檸檬酸鹽的良好替代物，已知檸檬酸鹽係一在注射時引起刺痛的緩衝液。有趣的是，據報導，組胺酸在液體和凍乾呈遞兩者中以高濃度使用時也具有穩定作用（Chen B, 等人, *Pharm Res*.[藥物研究], 20(12): 1952-60 (2003)）。還觀察到組胺酸（高達60 mM）降低高濃度抗體製劑的黏度。然而，在同一項研究中，作者觀察到在不銹鋼容器中抗體的凍融研究期間含有組胺酸的製劑中聚集和變色增加。作者將此歸因於鋼容器腐蝕引起的鐵離子的影響。組胺酸的另一個注意事項係它在金屬離子存在下經歷光氧化（Tomita M, 等人, *Biochemistry* [生物化學], 8(12): 5149-60 (1969)）。在製劑中使用甲硫胺酸作為抗氧化劑似乎很有前景；已經觀察到它對多種氧化應激有效（Lam XM, 等人, *J Pharm Sci*.[藥物科學雜誌],

86(11): 1250-5 (1997)）。

【0102】胺基酸甘胺酸、脯胺酸、絲胺酸和丙胺酸穩定蛋白質。甘胺酸也是凍乾製劑中常用的膨脹劑（例如，Neumega®、Genotropin®、Humatrope®）。精胺酸已示出是有效抑制聚集的試劑，並已用於液體製劑和凍乾製劑兩者（例如，Activase®、Avonex®、Enbrel®液體）。

【0103】抗氧化劑

【0104】在一些實施方式中，本文描述的藥物組成物進一步包含一種或多種抗氧化劑。蛋白質殘餘物的氧化來自許多不同的來源。除了添加特定的抗氧化劑之外，防止氧化蛋白質損害涉及在整個生產過程和產品儲存中仔細控制許多因素，例如大氣氧、溫度、光暴露和化學污染。最常用的藥物抗氧化劑係還原劑、氧/自由基清除劑或螯合劑。治療性蛋白質製劑中的抗氧化劑必須是水溶性的並且在整個產品保質期內保持活性。還原劑和氧/自由基清除劑藉由消融溶液中的活性氧種類起作用。藉由結合促進自由基形成的痕量金屬污染物，例如EDTA的螯合劑可以是有效的。例如，EDTA用於酸性成纖維細胞生長因子的液體製劑中，以抑制金屬離子催化的半胱胺酸殘基的氧化。EDTA已用於市售的產品，像Kineret®和Ontak®。

【0105】然而，抗氧化劑本身可以誘導蛋白質的其他共價或物理變化。文獻中已經報導了許多這樣的情況。還原劑（例如麩胱甘肽）可引起分子內二硫鍵的破壞，這可導致二硫化物改組。在過渡金屬離子存在下，抗壞血酸和EDTA已示出可以促進許多蛋白質和多肽中的甲硫胺酸氧化（Akers MJ, 和 Defelippis MR. Peptides and Proteins as Parenteral Solutions.[肽和蛋白質作為腸胃外溶液] 在：Pharmaceutical Formulation

Development of Peptides and Proteins [肽和蛋白質的藥物製劑開發]. Sven Frokjaer, Lars Hovgaard, 編輯. Pharmaceutical Science [藥物科學]. Taylor和Francis, UK (1999)）；Fransson J.R., *J. Pharm. Sci.*[藥物科學雜誌] 86(9): 4046-1050 (1997)；Yin J, 等人, *Pharm Res.*[藥物研究], 21(12): 2377-83 (2004)）中。據報導，硫代硫酸鈉可降低rhuMab HER2中光和溫度誘導的甲硫胺酸氧化水平；然而，在該研究中也報導了硫代硫酸鹽-蛋白質加合物的形成（Lam XM, Yang JY, 等人, *J Pharm Sci.*[藥物科學雜誌] 86(11): 1250-5 (1997)）。根據蛋白質的特定應激和敏感性選擇合適的抗氧化劑。

【0106】金屬離子

【0107】在一些實施方式中，藥物組成物進一步包含一種或多種金屬離子。通常，過渡金屬離子在蛋白質製劑中是不希望的，因為它們可以催化蛋白質中的物理和化學降解反應。然而，當它們係蛋白質的輔助因子且在蛋白質的懸浮液製劑中時，特定金屬離子包括在製劑中，其中它們形成配位錯合物（例如胰島素的鋅懸浮液）。最近，已經提出使用鎂離子（10 –120 mM）來抑制天冬胺酸異構化成異天冬胺酸（國際專利公開案號WO 2004/039337）。

【0108】金屬離子賦予蛋白質穩定性或活性增加的兩個實例係人去氧核糖核酸酶（rhDNA酶，Pulmozyme®）和因子VIII。在rhDNA酶的情況下，Ca^{+2}離子（高達100 mM）藉由特異性結合位點增加酶的穩定性（Chen B, 等人, *J Pharm Sci.*[藥物科學雜誌], 88(4): 477-82 (1999)）。事實上，用EGTA從溶液中除去鈣離子引起脫醯胺化和聚集的增加。然而，僅用Ca^{+2}離子觀察到這種效應；觀察到其他二價陽離子 – Mg^{+2}、

Mn^{+2}和Zn^{+2}使rhDNA酶不穩定。在因子VIII中觀察到相似的效果。Ca^{+2}和Sr^{+2}離子使蛋白質穩定，而其他像Mg^{+2}、Mn^{+2}和Zn^{+2}、Cu^{+2}和Fe^{+2}使酶不穩定（Fatouros, A., 等人, *Int. J. Pharm.*[國際製藥雜誌], 155, 121–131 (1997)）。在使用因子VIII的單獨的研究中，觀察到在Al^{+3}離子存在下聚集速率的顯著增加（Derrick TS, 等人, *J. Pharm. Sci.*[藥物科學雜誌], 93(10): 2549-57 (2004)）。作者注意到其他賦形劑像緩衝鹽通常被Al^{+3}離子污染，並說明需要在配製產品中使用適當品質的賦形劑。

【0109】防腐劑

【0110】在一些實施方式中，該藥物組成物進一步包含一種或多種防腐劑。當開發涉及從相同容器中多次提取的多次使用腸胃外製劑時，防腐劑係必需的。它們的主要功能係在藥物產品的整個保質期或使用期限內抑制微生物生長並確保產品無菌。常用的防腐劑包括苯酚、苯甲醇、間甲酚、烷基對羥基苯甲酸酯（例如羥苯甲酸甲酯或羥基苯甲酸丙酯）、氯化苄烷銨和氯化本索寧。具有抗微生物保護活性的化合物的其他實例包括十八烷基二甲基苄基氯化銨、氯化六烴季銨。其他類型的防腐劑包括芳香醇，例如丁醇、苯酚、苯甲醇；鄰苯二酚、間苯二酚、環己醇、3-戊醇。儘管防腐劑具有長期使用歷史，但包含防腐劑的蛋白質製劑的開發可能具有挑戰性。防腐劑幾乎總是對蛋白質產生不穩定作用（聚集），並且這已成為限制其在多劑量蛋白質製劑中使用的主要因素（Roy S, 等人, *J Pharm Sci.*[藥物科學雜誌], 94(2): 382-96 (2005)）。

【0111】多次使用注射筆呈遞包含經防腐處理的製劑。例如，目前市場上可獲得經防腐處理的hGH製劑。Norditropin®（液體，諾和諾德公司（Novo Nordisk））、Nutropin AQ®（液體，基因泰克公司

（Genentech））和健豪寧（Genotropin）（凍乾 - 雙室藥筒，法瑪西亞普強公司（Pharmacia & Upjohn））含有苯酚，而Somatrope®（禮來公司（Eli Lilly））用間甲酚進行配製。

【0112】在經防腐處理的劑型的製劑開發期間考慮了若干個方面。防腐劑濃度的優化涉及在劑型中測試給定的防腐劑，其濃度範圍賦予抗微生物有效性而不損害蛋白質穩定性。例如，使用差示掃描量熱法（DSC），在開發用於白細胞介素-1受體（I型）的液體製劑中成功篩選了三種防腐劑。基於防腐劑在市售產品中常用濃度下對穩定性的影響，對防腐劑進行排序（Remmele RL Jr., 等人, *Pharm Res.*[藥物研究], 15(2): 200-8 (1998)）。

【0113】一些防腐劑會引起注射位點反應，這係選擇防腐劑時需要考慮的另一個因素。在專注於評估Norditropin中防腐劑和緩衝液的臨床試驗中，與含有間甲酚的製劑相比，觀察到含有苯酚和苯甲醇的製劑的疼痛感覺降低（Kappelgaard A.M., *Horm Res.*[激素研究] 62 增刊 3:98-103 (2004)）。有趣的是，在常用的防腐劑中，苯甲醇具有麻醉性質（Minogue SC, 和Sun DA., *Anesth Analg.*[麻醉與鎮痛], 100(3): 683-6 (2005)）。

【0114】然而，本揭露還考慮了不包含任何防腐劑的藥物組成物。

【0115】抗原結合蛋白

【0116】“抗原結合蛋白”係包含結合特定靶標抗原（例如CD3和/或CD38）的部分的蛋白質。抗原結合蛋白包含支架或框架部分，其允許抗原結合部分採用促進抗原結合蛋白與抗原結合的構象。在示例性方面，抗原結合蛋白係抗體或免疫球蛋白，或抗原結合抗體片段，或抗體蛋白質產

物。

【0117】術語“抗體”係指完整的抗原結合免疫球蛋白。“抗體”係一種抗原結合蛋白。抗體可以是IgA、IgD、IgE、IgG、或IgM抗體，包括IgG1、IgG2、IgG3或IgG4中的任何一種。在多個實施方式中，完整抗體包含兩條全長重鏈和兩條全長輕鏈。抗體具有可變區和恒定區。在IgG型式中，可變區通常為約100-110或更多個胺基酸，包含三個互補決定區（CDR），主要負責抗原識別，並且與結合不同抗原的其他抗體差異很大。可變區典型地包含至少三個重鏈或輕鏈CDR（Kabat等人, 1991, Sequences of Proteins of Immunological Interest [免疫相關蛋白質序列], Public Health Service [公共衛生署] N.I.H., 貝塞斯達, 馬里蘭州；還參見Chothia和Lesk, 1987, J. Mol. Biol.[分子生物學雜誌] 196:901-917；Chothia等人, 1989, Nature [自然] 342: 877-883），位於框架區內（由Kabat等人, 1991指定框架區1-4、FR1、FR2、FR3、和FR4；還參見Chothia和Lesk, 1987, 同上）。恒定區允許抗體募集免疫系統的細胞和分子。

【0118】在多個方面，抗體係單株抗體。在某些方面，抗體係人抗體。在某些方面，抗體（或其他抗原結合蛋白）係嵌合的或人源化的。術語“嵌合”係指含有來自兩種或更多種不同抗體的結構域的抗體。嵌合抗體可以例如含有來自一個物種的恒定結構域，和來自第二物種的可變結構域，或更一般地，可以含有來自至少兩個物種的胺基酸序列的區段。“嵌合”和“人源化”兩者通常是指組合來自多於一個物種的區域的抗原結合蛋白。嵌合抗體還可以含有同一物種內的兩種或更多種不同抗體的結構域。在一個實施方式中，嵌合抗體係CDR接枝抗體。

【0119】當與抗原結合蛋白相關使用時，術語“人源化”係指如下抗原結合蛋白（例如，抗體），其至少具有來自非人來源的CDR區，並且被工程化為具有比原始來源的抗體更相似於真實的人抗體的結構和免疫功能。例如，人源化可涉及將來自非人抗體（例如小鼠抗體）的CDR接枝到人框架區中。通常，在人源化抗體中，除CDR之外的整個抗體由人起源的多核苷酸編碼或與這種抗體相同（其CDR內除外）。CDR（部分或全部由源自非人生物體的核酸編碼）被接枝到人抗體可變區的β-折疊框架中以產生抗體，其特異性由接枝的CDR決定。這種抗體的產生描述於例如國際專利公開案號WO 92/11018；Jones, 1986, Nature [自然] 321:522-525；和Verhoeyen 等人, 1988, Science [科學] 239:1534-1536，所述公開均藉由引用整體併入。通常採用選擇的受體框架殘基向相應的供體殘基的“回復突變”，以重新獲得在初始接枝的構建體中喪失的親和力（參見例如，美國專利案號5530101；5585089；5693761；5693762；6180370；5859205；5821337；6054297；和6407213，均藉由引用整體併入）。人源化抗體視需要還包含免疫球蛋白（典型地是人免疫球蛋白）恒定區的至少一部分，並且因此典型地包含人Fc區。

【0120】視需要，組成物的抗體係雙特異性抗體，即結合兩種不同靶標的抗體（例如，CD3和不同第二靶標）。在多個方面，組成物的抗體係異源二聚體抗體。

【0121】在一些實施方式中，本文描述的組成物包含異源二聚體抗體，該異源二聚體抗體包含第一單體，該第一單體包含第一Fc結構域和抗CD3 scFv。異源二聚體抗體進一步包含第二單體，該第二單體包含抗CD38重可變結構域和包含第二Fc結構域的重恒定結構域。異源二聚體抗

體還包含輕鏈，該輕鏈包含恒定結構域和抗CD38可變輕結構域。以下進一步描述單體的特徵。

【0122】scFv包含可變重鏈、scFv接頭和可變輕結構域。視需要，可變輕鏈的C末端附接至scFv接頭的N末端，該接頭的C末端附接至可變重鏈的N末端（N-vh-接頭-vl-C），雖然可以轉換構型（N-vl-接頭-vh-C）。因此，scFv的描繪和說明中具體包括的是任一取向的scFv。在多個方面，scFv結構域接頭係帶電荷的接頭。可以使用許多合適的scFv接頭，並且許多在附圖中列出。可採用帶電荷的scFv接頭以促進第一和第二單體之間的pI分離。即，藉由摻入帶電荷的scFv接頭，正的或負的（或者在對不同單體使用scFv的支架的情況下兩者），這允許包含帶電荷的接頭的單體改變pI而不進一步改變Fc結構域。

【0123】使用結構域接頭將scFv共價附接至Fc結構域的N末端。“結構域接頭”將本文概述的任何兩個結構域連接在一起。如果希望，可以使用帶電荷的結構域接頭。帶電荷的結構域接頭也可以例如增加本揭露的單體的pI分離，並且因此附圖中包括的那些可以用於本文中利用接頭的任何實施方式中。

【0124】接頭肽可主要包括以下胺基酸殘基：Gly、Ser、Ala、或Thr。接頭肽應具有適於連接兩個分子的長度，使得它們相對於彼此呈現正確的構象，使得這兩個分子保持所希望的活性。在一個實施方式中，接頭長度為從約1至50個胺基酸，較佳的是長度為約1至30個胺基酸。在一個實施方式中，發現可以使用長度為1至20個胺基酸的接頭，在一些實施方式中使用從約5至約10個胺基酸。有用的接頭包括甘胺酸-絲胺酸聚合物（包括例如(GS)n、(GSGGS)n（SEQ ID NO:332）、(GGGGS)n（SEQ

ID NO:333）、和(GGGS)n（SEQ ID NO:334），其中n係至少一個（通常為從3至4）的整數），甘胺酸-丙胺酸聚合物，丙胺酸-絲胺酸聚合物和其他柔性接頭。可替代地，各種非蛋白質聚合物，包括但不限於聚乙二醇（PEG）、聚丙二醇、聚伸氧烷、或聚乙二醇和聚丙二醇的共聚物，可用作接頭。

【0125】其他接頭序列可包括CL/CH1結構域的任何長度（但不包括CL/CH1結構域的所有殘基）的任何序列；例如，CL/CH1結構域的前5-12個胺基酸殘基。接頭可以衍生自免疫球蛋白輕鏈，例如Cκ或Cλ。接頭可以衍生自任何同種型的免疫球蛋白重鏈，包括例如Cγ1、Cγ2、Cγ3、Cγ4、Cα1、Cα2、Cδ、Cε、和Cμ。接頭序列還可以衍生自其他蛋白質，例如Ig樣蛋白質（例如，TCR、FcR、KIR），鉸鏈區衍生的序列和來自其他蛋白質的其他天然序列。

【0126】抗CD3 scFv包含 (i) 包含如SEQ ID NO: 15所示的vlCDR1、如SEQ ID NO: 16所示的vlCDR2、和如SEQ ID NO: 17所示的vlCDR3的scFv可變輕結構域，和 (ii) 包含如SEQ ID NO: 11所示的vhCDR1、如SEQ ID NO: 12所示的vhCDR2、和如SEQ ID NO: 13所示的vhCDR3的scFv可變重結構域。視需要，抗CD3 scFv包含可變重結構域，該可變重結構域包含與SEQ ID NO: 10中所示的胺基酸序列至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。還視需要，抗CD3 scFv包含可變輕結構域，該可變輕結構域包含與SEQ ID NO: 14中所示的胺基酸序列至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。就此而言，在多個實施方式中，抗

CD3 scFv包含SEQ ID NO: 10的可變重結構域和SEQ ID NO: 14的可變輕結構域。視需要，可變重和可變輕結構域藉由包含序列GKPGSGKPGSGKPGSGKPGS（SEQ ID NO: 158）的scFv結構域接頭連接。就此而言，在多個實施方式中，抗CD3 scFv包含與SEQ ID NO: 18（抗體A的scFv）中所示的胺基酸序列至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在多個方面，引起與參考序列的百分比同一性小於100%的序列變異表示CDR序列外的修飾。在多個方面，scFv包含本文所示的、屬於抗CD3_H1.32_L1.47（對應於抗體A）的序列。

【0127】“Fc”或“Fc區”或“Fc結構域”係指包含抗體恒定區的多肽，該抗體不包括第一恒定區免疫球蛋白結構域，並且在一些情況下是鉸鏈的一部分。因此，“Fc結構域”係指IgA、IgD和IgG的最後兩個恒定區免疫球蛋白結構域、IgE和IgM的最後三個恒定區免疫球蛋白結構域、和在該等結構域的N末端的柔性鉸鏈。對於IgA和IgM，Fc可以包括J鏈。對於IgG，Fc結構域包含免疫球蛋白結構域Cγ2和Cγ3（Cγ2和Cγ3）以及Cγ1（Cγ1）和Cγ2（Cγ2）之間的下鉸鏈區。異源二聚體抗體較佳的是IgG抗體（其包括若干個亞類，包括但不限於IgG1、IgG2、IgG3、和IgG4）。儘管Fc區的邊界可以變化，人IgG重鏈Fc區通常定義為在其羧基末端包括殘基C226或P230，其中如在Kabat中根據歐洲索引進行編號。在一些實施方式中，對Fc區進行胺基酸修飾，例如，以改變與一種或多種FcγR受體或FcRn受體的結合。

【0128】在多個方面，第一單體（即，第一Fc結構域和抗CD3 scFv）包含與SEQ ID NO:335中所示的胺基酸序列至少90%相同（例如，

與SEQ ID NO: 335（對應於抗體A）中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。

【0129】異源二聚體抗體視需要進一步包含第二單體，該第二單體包含 i) 抗CD38重可變結構域和 ii) 包含第二Fc結構域的重恒定結構域。抗CD38重可變結構域包含以下CDR序列：如SEQ ID NO: 65所示的可變重鏈（vh）CDR1、如SEQ ID NO: 66所示的vhCDR2、和如SEQ ID NO: 67所示的vhCDR3。視需要，抗CD38重可變結構域包含與SEQ ID NO: 64中所示的胺基酸序列至少90%相同（例如，與SEQ ID NO: 64中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在多個方面，第二單體（即，抗CD38重可變結構域和包含第二Fc結構域的重恒定結構域）包含與SEQ ID NO: 82中所示的胺基酸序列至少90%相同（例如，與SEQ ID NO: 82（對應於抗體A）中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。

【0130】在多個方面，異源二聚體抗體進一步包含輕鏈，該輕鏈包含恒定結構域和抗CD38可變輕（vl）結構域。抗CD38可變輕結構域包含以下CDR：如SEQ ID NO: 69所示的vlCDR1、如SEQ ID NO: 70所示的vlCDR2、和如SEQ ID NO: 71所示的vlCDR3。視需要，抗CD38可變輕結構域包含與SEQ ID NO: 68中所示的胺基酸序列至少90%相同（例如，與SEQ ID NO: 68（對應於抗體A）中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在一些實施方式中，輕鏈（包含恒定結構域和抗CD38可變輕結構

域）包含與SEQ ID NO: 84中所示的胺基酸序列至少90%相同（例如，與SEQ ID NO: 84（對應於抗體A）中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。

【0131】在較佳的實施方式中，異源二聚體抗體係抗體A並且包含含有抗CD3 scFv的第一單體，該抗CD3 scFv包含含有SEQ ID NO: 14的胺基酸序列的抗CD3可變輕結構域和含有SEQ ID NO: 10的胺基酸序列的抗CD3可變重結構域；第二單體，其包含含有SEQ ID NO: 64的胺基酸序列的抗CD38可變重結構域，和含有SEQ ID NO: 68的胺基酸序列的可變輕結構域的輕鏈。例如，在一個實施方式中，異源二聚體抗體包含含有SEQ ID NO: 335的胺基酸序列的第一單體，含有SEQ ID NO: 82的胺基酸序列的第二單體，和含有SEQ ID NO: 84的胺基酸序列的輕鏈。

【0132】在一些實施方式中，本文描述的組成物包含結合CD3和STEAP1的異源二聚體抗體。STEAP1係包含六個跨膜結構域的339個胺基酸的蛋白質，產生三個胞外環和兩個胞內環。人STEAP1的胺基酸序列在本文中示為SEQ ID NO: 356。胞外環的估計位置係胺基酸92-118（胞外環1）、胺基酸185-217（胞外環2）和胺基酸279-290（胞外環3）。與正常組織相比，STEAP1在前列腺癌中差異表現，並且與原發性前列腺癌樣品相比，觀察到骨和淋巴結前列腺癌轉移灶中的表現增加。STEAP1代表用於診斷和基於抗體的治療的理想靶標，例如雙特異性抗STEAP1/抗CD3 T細胞募集抗體，以例如觸發T細胞依賴性細胞毒性或前列腺癌細胞的重定向裂解。本揭露的抗原結合蛋白視需要在第二胞外環的外部區域結合STEAP1。在至少一個實施方式中，抗原結合蛋白結合胺基酸92-118

（胞外環1）和/或胺基酸279-290（胞外環3）內的STEAP1區。還視需要，抗原結合蛋白不結合STEAP2（UniProtKB號Q8NFT2；SEQ ID NO: 177）。本揭露提供了包含抗原結合蛋白的組成物，該抗原結合蛋白以本文描述的任何型式結合STEAP1和CD3，視需要以圖1A中的“開瓶器”或圖1B中的中心scFv型式（也稱為“$XmAb^{2+1}$型式”）。

【0133】在一些實施方式中，本文描述的組成物包含異源二聚體抗體，該異源二聚體抗體包含含有第一Fc結構域和抗CD3 scFv的第一單體，並且進一步包含含有抗STEAP1重可變結構域和含有第二Fc結構域的重恒定結構域的第二單體。異源二聚體抗體還包含輕鏈，該輕鏈包含恒定結構域和抗STEAP1可變輕結構域。構成支架的單體的示例性方面如上描述。在該實施方式中，異源二聚體抗體進一步包含第二單體，該第二單體包含 i) 抗STEAP1重可變結構域和 ii) 包含第二Fc結構域的重恒定結構域。抗STEAP1重可變結構域視需要包含如SEQ ID NO:360所示的可變重（vh）CDR1、如SEQ ID NO:361或SEQ ID NO: 363所示的vhCDR2、和如SEQ ID NO:362的vhCDR3。輕鏈的抗STEAP1可變輕結構域包含如SEQ ID NO: 357所示的vlCDR1、如SEQ ID NO: 358所示的vlCDR2、和如SEQ ID NO: 359所示的vlCDR3。可替代地，抗STEAP1可變重結構域包含如SEQ ID NO: 368所示的vhCDR1、如SEQ ID NO: 369所示的vhCDR2、和如SEQ ID NO: 370所示的vhCDR3；並且可變輕結構域包含如SEQ ID NO: 371所示的vlCDR1、如SEQ ID NO: 372所示vlCDR2、和如SEQ ID NO: 373所示的vlCDR3。

【0134】視需要，抗STEAP1重可變結構域包含與SEQ ID NO: 377或SEQ ID NO:379中所示的胺基酸序列至少90%相同（例如，與SEQ ID

NO: 377或SEQ ID NO:379中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。視需要，抗STEAP1可變輕結構域包含與SEQ ID NO:378中所示的胺基酸序列至少90%相同（例如，與SEQ ID NO: 378中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在較佳的實施方式中，抗STEAP1可變重結構域包含SEQ ID NO: 380或SEQ ID NO: 379，並且抗STEAP1可變輕結構域包含SEQ ID NO: 378。

【0135】還視需要，抗STEAP1重可變結構域包含與SEQ ID NO:380中所示的胺基酸序列至少90%相同（例如，與SEQ ID NO: 380中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。視需要，抗STEAP1可變輕結構域包含與SEQ ID NO:381中所示的胺基酸序列至少90%相同（例如，與SEQ ID NO: 381中所示的胺基酸序列91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在較佳的實施方式中，抗STEAP1可變重結構域包含SEQ ID NO: 380，並且抗STEAP1可變輕結構域包含SEQ ID NO: 381。

【0136】在一些實施方式中，例如其中抗原結合蛋白係結合CD3和STEAP1的異源二聚體抗體的實施方式，則CD3結合結構域（視需要如上文討論的scFv）包含含有重鏈CDR的可變重結構域，該重鏈CDR包含SEQ ID NO: 383中所示的vhCDR1、SEQ ID NO: 384中所示的vhCDR2、和SEQ ID NO: 385中所示的vhCDR3；和可變輕結構域，該可變輕結構域包含輕鏈CDR，該輕鏈CDR包含SEQ ID NO: 387中所示的

vlCDR1、SEQ ID NO: 388中所示的vlCDR2、和SEQ ID NO: 389中所示的vlCDR3。例如，本揭露提供了包含多特異性（例如雙特異性）構建體的組成物，該構建體包含抗CD3可變重結構域和/或抗CD3可變輕結構域，該抗CD3可變重結構域包含與SEQ ID NO:382至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列，該抗CD3可變輕結構域包含與SEQ ID NO:386至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在多個方面，異源二聚體抗體包含含有SEQ ID NO: 390的抗CD3 scFv。以上更詳細地描述了scFv，並且上文描述的scFv的特徵也適用於此。

【0137】在多個實施方式中，抗原結合蛋白係圖1B中示出的中心scFv或“XmAb^{2+1}”型式的異源二聚體抗體。該型式依賴於使用插入的scFv結構域，形成第三抗原結合結構域，其中兩個單體的Fab部分結合一個靶標，並且“額外”scFv結構域結合另一個。將scFv結構域插入該等單體中的一個的Fc結構域和CH1-Fv區之間，因此提供第三抗原結合結構域。在該實施方式中，一種單體包含第一重鏈，該第一重鏈包含第一可變重結構域、CH1結構域（和視需要的接頭/鉸鏈）和Fc結構域，其中scFv包含scFv可變輕結構域、scFv接頭和scFv可變重結構域。使用視需要的結構域接頭將scFv共價附接至重恒定結構域的CH1結構域的C末端和第一Fc結構域的N末端之間（VH1-CH1-[視需要的結構域接頭] -VH2-scFv接頭-VL2-[包括鉸鏈的視需要的結構域接頭]-CH2-CH3，或scFv的相反取向VH1 -CH1 -[視需要的結構域接頭] -VL2-scFv接頭-VH2-[包括鉸鏈的視需要的結構域接頭] -CH2-CH3）。在一些實施方式中，第一單體係VH1-CH1結

構域接頭-VH2-scFv接頭-VL2-結構域接頭-CH2-CH3。其他單體係標準Fab側（即VH1-CH1-結構域接頭（例如，鉸鏈）-CH2-CH3）。該實施方式進一步利用包含可變輕結構域和恒定輕結構域的共同輕鏈，其與重鏈結合以形成結合靶標的兩個同一的Fab。對於本文的許多實施方式，該等構建體包括所希望的和如本文和國際專利公開案號WO 2017/21870中描述的偏斜變體、pI變體、消融變體、另外的Fc變體等。

【0138】在一些方面，抗原結合蛋白係“$XmAb^{2+1}$”型式的異源二聚體抗體，其結合CD3和STEAP1，並且CD3結合結構域（視需要如上文討論的scFv）包含含有重鏈CDR的可變重結構域（該重鏈CDR包含SEQ ID NO: 383中所示的vhCDR1、SEQ ID NO: 384中所示的vhCDR2、和SEQ ID NO: 385中所示的vhCDR3）和含有輕鏈CDR的可變輕結構域（該輕鏈CDR包含SEQ ID NO: 387中所示的vlCDR1、SEQ ID NO: 388中所示的vlCDR2、和SEQ ID NO: 389中所示的vlCDR3）。例如，該構建體視需要包含抗CD3可變重結構域和/或抗CD3可變輕結構域，該可變重結構域包含與SEQ ID NO:380至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列，該抗CD3可變輕結構域包含與SEQ ID NO:381至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在多個方面，scFv接頭包含SEQ ID NO: 391的胺基酸序列。在多個方面，異源二聚體抗體包含含有SEQ ID NO: 390的抗CD3 scFv。

【0139】在多個方面，抗原結合蛋白係$XmAb^{2+1}$型式的異源二聚體抗體，其包含結合STEAP1的兩個Fab。就此而言，在一些實施方式中，異源二聚體抗體的第一可變重結構域和第二可變重結構域包含SEQ ID

NO: 360中所示的vhCDR1、SEQ ID NO: 361或SEQ ID NO: 363中所示的vhCDR2、和SEQ ID NO: 362中所示的vhCDR3，並且可變輕結構域包含SEQ ID NO: 357中所示的vlCDR1、SEQ ID NO: 358中所示的vlCDR2、和SEQ ID NO: 359中所示的vlCDR3。可替代地，第一可變重結構域和第二可變重結構域包含SEQ ID NO: 368中所示的vhCDR1、SEQ ID NO: 369中所示的vhCDR2、和SEQ ID NO: 370中所示的vhCDR3；並且可變輕結構包含SEQ ID NO: 371中所示的vlCDR1、SEQ ID NO: 372中所示的vlCDR2、和SEQ ID NO: 373中所示的vlCDR3。在較佳的實施方式中，第一可變重結構域和第二可變重結構域包含與SEQ ID NO: 377（對應於抗體B）或SEQ ID NO: 379至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列，和/或可變輕結構域包含與SEQ ID NO: 378（對應於抗體B）至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。可替代地，第一可變重結構域和第二可變重結構域包含與SEQ ID NO: 380至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列，和/或可變輕結構域包含與SEQ ID NO: 381至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。如上所述，與參考序列相比導致小於100%的序列同一性的、本文描述的任何可變結構域序列（或全長單體序列）的變異較佳的是在CDR區外發生。

【0140】因此，本揭露提供了包含異源二聚體抗體的藥物組成物，該藥物組成物包含 (a) 包含第一重鏈的第一單體，該第一重鏈包含 1) 第

一可變重鏈結構域；2) 第一恒定重鏈，其包含第一CH1結構域和第一Fc結構域；和 3) 結合人CD3的scFv。scFv包含 (i) scFv可變輕結構域，其包含SEQ ID NO:387中所示的vlCDR1、SEQ ID NO:388中所示的vlCDR2、和SEQ ID NO:389中所示的vlCDR3；(ii) scFv接頭；和 (iii) scFv可變重結構域，其包含SEQ ID NO: 383中所示的vhCDR1、SEQ ID NO: 384中所示的vhCDR2、和SEQ ID NO: 385中所示的vhCDR3。使用一個或多個結構域接頭將scFv共價附接至所述CH1結構域的C末端和所述第一Fc結構域的N末端之間。異源二聚體抗體進一步包含 b) 包含第二重鏈的第二單體，該第二重鏈包含第二可變重結構域和包含第二Fc結構域的第二恒定重鏈，和 c) 包含可變輕結構域和恒定輕結構域的共同輕鏈；其中第一可變重結構域和可變輕結構域結合人STEAP1，並且第二可變重結構域和可變輕結構域結合人STEAP1。在一些方面，第一可變重結構域和第二可變重結構域包含重鏈CDR，該重鏈CDR包含SEQ ID NO: 360中所示的vhCDR1、SEQ ID NO: 361或SEQ ID NO: 363中所示的vhCDR2、和SEQ ID NO: 362中所示的vhCDR3。可變輕結構域視需要包含輕鏈CDR，該輕鏈CDR包含SEQ ID NO: 357中所示的vlCDR1、SEQ ID NO: 358中所示的vlCDR2、和SEQ ID NO: 359所示的vlCDR3。可替代地，第一可變重結構域和第二可變重結構域包含重鏈CDR，該重鏈CDR包含SEQ ID NO: 368中所示的vhCDR1、SEQ ID NO: 369中所示的vhCDR2、和SEQ ID NO: 370中所示的vhCDR3。可變輕結構域視需要包含輕鏈CDR，該輕鏈CDR包含SEQ ID NO: 371中所示的vlCDR1、SEQ ID NO: 372中所示的vlCDR2、和SEQ ID NO: 373中所示的vlCDR3。視需要，第一可變重結構域和第二可變重結構域包含與SEQ ID NO: 377

（對應於抗體B）或379至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列，和/或可變輕結構域包含與SEQ ID NO: 378（對應於抗體B）至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。scFv視需要包含可變重區和可變輕區，該可變重區和可變輕區具有分別與SEQ ID NO: 382和SEQ ID NO: 386至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列，並且scFv接頭視需要包含SEQ ID NO: 391。在多個實施方式中，scFv包含SEQ ID NO: 390的序列。

【0141】在本揭露的多個方面，抗CD3/抗STEAP1抗原結合蛋白係$XmAb^{2+1}$型式的異源二聚體抗體，該異源二聚體抗體包含第一單體，該第一單體包含與SEQ ID NO: 366或367至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列；第二單體，該第二單體包含與SEQ ID NO: 365至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列；和共同輕鏈，該共同輕鏈包含與SEQ ID NO: 364至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。在一些實施方式中，抗CD3/抗STEAP1抗原結合蛋白係$XmAb^{2+1}$型式的異源二聚體抗體，該異源二聚體抗體包含第一單體，該第一單體包含與SEQ ID NO: 366至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列；第二單體，該第二單體包含與SEQ ID NO: 365至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、

98%、99%、或100%相同）的胺基酸序列；和共同輕鏈，該共同輕鏈包含與SEQ ID NO: 364（對應於抗體B）至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。可替代地，抗CD3/抗STEAP1抗原結合蛋白係$XmAb^{2+1}$型式的異源二聚體抗體，該異源二聚體抗體包含第一單體，該第一單體包含與SEQ ID NO: 376至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列；第二單體，該第二單體包含與SEQ ID NO: 375至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列；和共同輕鏈，該共同輕鏈包含與SEQ ID NO: 374至少90%相同（例如，91%、92%、93%、94%、95%、96%、97%、98%、99%、或100%相同）的胺基酸序列。

【0142】在多個方面，抗原結合蛋白包含第一重鏈，該第一重鏈包含VH1-CH1-[結構域接頭] -VH2-scFv接頭-VL2-[結構域接頭（視需要包括鉸鏈）]-CH2-CH3；第二重鏈，該第二重鏈包含VH1-CH1-結構域接頭-CH2-CH3；和包含VL1的共同輕鏈；其中VH1和VL1結合STEAP1，並且VH2和VL2結合CD3。在該型式中，VH2視需要包含SEQ ID NO: 383（CDR1）、SEQ ID NO: 384（CDR2）、和SEQ ID NO: 385（CDR3）的CDR序列，而VL2包含SEQ ID NO: 387（CDR1）、SEQ ID NO: 388（CDR2）、和SEQ ID NO:389（CDR3）的CDR序列。VH1包含SEQ ID NO: 360（CDR1）、SEQ ID NO: 361或363（CDR2）、和SEQ ID NO: 362（CDR3）的CDR序列；並且VL1包含SEQ ID NO: 357（CDR1）、SEQ ID NO: 358（CDR2）、和SEQ ID NO:359（CDR3）的CDR序列。

可替代地，VH1包含SEQ ID NO: 368（CDR1）、SEQ ID NO: 369（CDR2）、和SEQ ID NO: 370（CDR3）的CDR序列；並且VL1包含SEQ ID NO: 371（CDR1）、SEQ ID NO: 372（CDR2）、和SEQ ID NO:373（CDR3）的CDR序列。視需要，抗原結合蛋白包含第一重鏈中的修飾，所述修飾包括但不限於E233P、delL234、L235V、G236A、S267K、r292c、n297g、v302c、E357Q、和S364K（EU編號，小寫字母指示本文進一步描述的SEFL2取代），並且第二重鏈包含修飾，所述修飾包括但不限於N208D、E233P、delL234、L235V、G236A、S267K、r292c、Q295E、n297g、v302c、L368D、K370S、N384D、Q418E、和N421D（EU編號，小寫字母指示本文進一步描述的SEFL2取代）。用於本實施方式的上下文的接頭視需要為GKPGSGKPGSGKPGSGKPGS（SEQ ID NO: 391）。

【0143】中心scFv型式的Fc結構域視需要包含偏斜變體（例如，選自由以下各項組成之群組：S364K/E357Q：L368D/K370S；L368D/K370S：S364K；L368E/K370S：S364K；T411T/E360E/Q362E：D401K；L368D/K370S：S364K/E357L，K370S：S364K/E357Q，T366S/L368A/Y407V：T366W 和 T366S/L368A/Y407V/Y349C：T366W/S354C），視需要包含消融變體，視需要包含帶電荷的scFv接頭，和包含pI變體的重鏈。在一些實施方式中，中心scFv型式包括偏斜變體、pI變體、和消融變體。因此，一些實施方式包括以下型式，該型式包含：a) 第一單體，該第一單體包含偏斜變體S364K/E357Q、消融變體E233P/L234V/L235A/G236del/S267K、和第一可變重鏈結構域（該第一可變重鏈結構域與輕鏈的第一可變輕結構域構成結合第一靶標的Fv）與第

二可變重鏈結構域；b) 第二單體，該第二單體包含偏斜變體L368D/K370S、pI變體N208D/Q295E/N384D/Q418E/N421D、消融變體E233P/L234V/L235A/G236del/S267K、和第一可變重鏈結構域（該第一可變重鏈結構域與第一可變輕結構域構成結合第一靶標的Fv）與第二可變輕鏈，該第二可變輕鏈與第二可變重鏈一起形成結合第二靶標的Fv；和c) 包含第一可變輕結構域和恒定輕結構域的輕鏈。

【0144】多特異性抗原結合蛋白的不同結合區獨立地展示其各自抗原（例如，CD3和STEAP1或CD3和CD38）的KD，所述KD小於或等於10^{-4} M、小於或等於10^{-5} M、小於或等於10^{-6} M、小於或等於10^{-7} M、小於或等於10^{-8} M、小於或等於10^{-9} M、小於或等於10^{-10} M、小於或等於10^{-11} M、或小於或等於10^{-12} M、或小於或等於10^{-13} M（例如10^{-7} M至10^{-12} M），其中KD係指特定抗體-抗原相互作用的解離速率。STEAP1結合區（或CD38結合區）不需要以與例如CD3結合區結合CD3相同的親和力結合STEAP1（或CD38）。

【0145】在一些實施方式中，製劑包含本文描述的抗原結合蛋白（例如，抗體），其量的範圍為從約50 μg至約200 mg（或從約500 μg至約150 mg、或從約50 mg至約200 mg、或從約50 mg至約150 mg、或從約50 mg至約100 mg、或從約50 mg至約75 mg）。在一些實施方式中，製劑包含抗體，其量為約50 μg、約100 μg、約150 μg、約200 μg、約250 μg、約300 μg、約350 μg、約400 μg、約450 μg、約500 μg、約550 μg、約600 μg、約650 μg、約700 μg、約750 μg、約800 μg、約850 μg、約900 μg、約950 μg、約1 mg、約5 mg、約10 mg、約15 mg、約20 mg、約25 mg、約30 mg、約35 mg、約40 mg、約45 mg、約50 mg、約

55 mg、約60 mg、約65 mg、約70 mg、約75 mg、約80 mg、約85 mg、約90 mg、約95 mg、約100 mg、約105 mg、約110 mg、約115 mg、約120 mg、約125 mg、約130 mg、約135 mg、約140 mg、約145 mg、約150 mg、約155 mg、約160 mg、約165 mg、約170 mg、約175 mg、約180 mg、約185 mg、約190 mg、約195 mg或約200 mg。

【0146】在一些實施方式中，製劑包含濃度範圍為從約0.1 mg/mL至約20mg/mL（或從約0.5 mg/mL至約10 mg/mL、或從約1 mg/mL至約10 mg/mL、或從約1 mg/mL至約20 mg/mL、或從約10 mg/mL至約20 mg/mL）的抗原結合蛋白（例如抗體）。在一些實施方式中，製劑包含濃度為約0.1 mg/mL、約0.5 mg/mL、約1 mg/mL、約2 mg/mL、約3 mg/mL、約4 mg/mL、約5 mg/mL、約6 mg/mL、約7 mg/mL、約8 mg/mL、約9 mg/mL、約10 mg/mL、約11 mg/mL、約12 mg/mL、約13 mg/mL、約14 mg/mL、約15 mg/mL、約16 mg/mL、約17 mg/mL、約18 mg/mL、約19 mg/mL、或約20 mg/mL的抗原結合蛋白（例如抗體，例如本文描述的異源二聚體抗體中的任一個）。

【0147】在一些實施方式中，製劑包含濃度範圍為從約0.1 mg/mL至約8 mg/mL（或從約0.5 mg/mL至約5 mg/mL或從約1 mg/mL至約5 mg/mL、或從約3至約6 mg/mL）的抗原結合蛋白（例如抗體）。在一些實施方式中，製劑包含濃度為約0.1 mg/mL、約0.5 mg/mL、約1 mg/mL、約2 mg/mL、約3 mg/mL、約4 mg/mL、約5 mg/mL、約6 mg/mL、約7 mg/mL、或約8 mg/mL的抗原結合蛋白（例如抗體，例如本文描述的異源二聚體抗體中的任一個）。

【0148】異源二聚體抗體型式進一步描述於國際專利公開案號WO

2017/218707中，所述公開藉由引用整體併入本文，並且特別地是關於附圖和圖例。在一個較佳的方面，異源二聚體抗體採用圖1A中稱為“開瓶器”的結構。“開瓶器”型式的一條重鏈含有scFv，並且另一條重鏈係“常規”Fab型式，包含傳統的重鏈和輕鏈。藉由使用促進異源二聚體抗體形成的恒定區（例如，Fc結構域、CH1結構域和/或鉸鏈區）中的胺基酸變體將兩條重鏈結合在一起。“開瓶器”格式具有若干個明顯的優點。依賴於兩種scFv構建體的抗體類似物通常具有穩定性和聚集問題，這藉由添加“常規”重鏈和輕鏈配對而在本揭露中得到緩解。另外，與依賴於兩條重鏈和兩條輕鏈的型式相反，重鏈和輕鏈的不正確配對（例如，重1與輕2配對等）不產生問題。

【0149】在多個方面，與野生型抗體結構域序列相比，異源二聚體抗體包括促進異源二聚體抗體形成（即，降低同二聚化）、調節抗體功能等的修飾。修飾通常集中在Fc結構域中（儘管這不是必需的）。藉由相對於天然序列的取代、缺失或插入的胺基酸位置提及修飾。例如，N434S或434S係相對於親本Fc多肽在位置434的絲胺酸的Fc結構域取代，其中根據EU索引編號。同樣，M428L/N434S定義了相對於親本Fc多肽具有取代M428L和N434S的Fc修飾。野生型胺基酸的同一性可以是未指明的，在這種情況下，前述變體稱為428L/434S。提供的取代的順序係任意的，也就是說，例如，428L/434S與M428L/N434S相同，等等。對於所討論的與抗體有關的所有位置，除非另外指出，胺基酸位置編號係根據EU索引進行。EU指數或如在Kabat或EU編號方案中的EU指數係指EU抗體的編號（Edelman 等人, 1969, Proc Natl Acad Sci USA [美國科學院院刊] 63:78-85, 將其整體藉由引用併入本文）。修飾可以是添加、缺失、或取

代。取代可包括天然存在的胺基酸，並且在某些情況下，可包括合成胺基酸。實例包括美國專利案號6,586,207；美國專利公開案號2004-0214988A1；國際專利公開案號WO 98/48032；WO 03/073238；WO 05/35727A2；WO 05/74524A2；WO 17/218707；J. W. Chin 等人, (2002), Journal of the American Chemical Society [美國化學學會雜誌] 124:9026-9027；J. W. Chin, 和P. G. Schultz, (2002), ChemBioChem [化學生物化學] 11:1135-1137；J. W. Chin, 等人, (2002), PICAS United States of America[PICAS美利堅合眾國] 99:11020-11024；和L. Wang, 和P. G. Schultz, (2002), Chem.[化學] 1-10, 均藉由引用整體併入。

【0150】有許多機制可用於產生異源二聚體蛋白質。導致異源二聚體產生的胺基酸變體被稱為“異二聚化變體”。異源二聚化變體可包括空間變體（例如，下文描述的“杵臼（knobs and holes）”變體或“偏斜”變體和下文描述的“電荷對”變體）以及“pI變體”，該等變體允許同源二聚體與異源二聚體的分離純化。如國際專利公開案號WO 2014/145806和WO 2017/218707中總體描述的（所述公開藉由引用以其整體併入本文並且特別用於討論“異源二聚化變體”），異二聚化的有用機制包括如描述於WO2014/145806中的“杵臼（knobs and holes）”（“KIH”；本文有時稱作“偏斜”變體）、“靜電轉向”或“電荷對”、描述於WO2014/145806中的pI變體、和於WO2014/145806和本文中概述的另外的常規Fc變體。

【0151】有若干種基本機制可以導致異源二聚體抗體的純化的簡化；一種依賴於使用pI變體，使得每種單體具有不同的pI，因此允許A-A、A-B和B-B二聚體蛋白的等電純化。可替代地，一些支架型式，例如“開瓶器”型式，也允許基於尺寸進行分離。也可能使相對於同源二聚體

“偏向”異源二聚體的形成。因此，發現空間異二聚化變體和pI或電荷對變體的組合在本發明中特別有用。

A. pI（等電點）變體

【0152】對於pI變體，可以將胺基酸修飾引入單體多肽的一種或兩種中；即，其中一種單體（本文簡稱為“單體A”）的pI可以遠離單體B工程化，或者單體A和B兩者都可以被改變，單體A的pI增加且單體B的pI減少。可以藉由去除或添加帶電荷的殘基（例如，中性胺基酸被帶正電荷或帶負電荷的胺基酸殘基替換，例如甘胺酸替換為谷胺酸）來完成任一種或兩種單體的pI變化，將帶電荷的殘基從正或負變為相反電荷（天冬胺酸變為賴胺酸）或將帶電荷的殘基改變為中性殘基（例如，電荷的喪失；賴胺酸變為絲胺酸）。許多該等變體示出於圖中。該等修飾在至少一種單體中產生pI的足夠變化，使得異二聚體可以與同源二聚體分離。如熟悉該項技術者所理解的，這可以藉由使用“野生型”重鏈恒定區和變體區來實現，所述變體區已被工程化為增加或減少其pI（wt A-+B或wt A - -B），或藉由增加一個區域並減少其他區域（A+ -B-或A- B+）來實現。

【0153】因此，在多個方面，異源二聚體抗體在一個或多個恒定區中包含一個或多個修飾以藉由將胺基酸取代（“pI變體”或“pI取代”）摻入一種或兩種單體中來改變異二聚體蛋白質的至少一種（如果不是兩種）單體的等電點（pI）以形成“pI抗體”。如果兩種單體的pI相差少至0.1個pH單位，則0.2、0.3、0.4和0.5或更大都是合適的，可以實現異源二聚體與兩種同源二聚體的分離。

【0154】為了實現良好分離，包括在每種或兩種單體上的pI變體的數量部分取決於組分的起始pI，例如，抗CD3 scFv和抗CD38 Fab的起始

pI。即，為了確定要工程化的單體或“方向”（例如更正或更負），計算兩個結構域的Fv序列並由此做出決定。不同的Fv將具有可被利用的不同起始pI。在一些實施方式中，使用美國專利公開案號2014/0370013的圖19中的圖表，基於變體重鏈恒定結構域計算pI的變化。可替代地，可以比較每種單體的pI。通常，將pI工程化為導致每種單體的總pI差異為至少約0.1 log，較佳的是0.2至0.5。

【0155】pI變體的較佳的組合示出於圖10中。該等變化相對於IgG1示出，但所有同種型以及同種型雜合體都可以藉由這種方式改變。在重鏈恒定結構域來自IgG2-4的情況下，也可以使用R133E和R133Q。

【0156】在一個實施方式中，Fab單體（陰性側）包含取代208D/295E/384D/418E/421D (N208D/Q295E/N384D/Q418E/N421D（相對於人IgG1）且scFv單體（陽性側）包含帶正電荷的scFv接頭，包括$(GKPGS)_4$。

【0157】調節pI的修飾也可以在輕鏈中進行。用於降低輕鏈pI的胺基酸取代包括但不限於K126E、K126Q、K145E、K145Q、N152D、S156E、K169E、S202E、K207E和在輕鏈的C末端添加DEDE肽。基於恒定λ輕鏈的該類別的變化包括R108Q、Q124E、K126Q、N138D、K145T和Q199E處的一個或多個取代。此外，還可以增加輕鏈的pI。

B. 偏斜/空間變體

【0158】存在許多合適的異二聚化偏斜變體組對。該等變體以“組”“對”的形式出現。即，對中的一組摻入到第一單體中，並且對的另一組摻入到第二單體中。應注意，該等組不一定表現為“杵臼”變體（其中一個單體上的殘基與另一個單體上的殘基之間具有一對一的對應）；即，該

等組對在兩個單體之間形成了介面，促進異源二聚體的形成並阻礙同源二聚體的形成，使得在生物條件下自發形成的異源二聚體的百分比超過90%，而不是預期的50%（25%同源二聚體A/A:50%異源二聚體A/B:25%同源二聚體B/B）。

【0159】在一些實施方式中，藉由添加空間變體促進異源二聚體的形成。即，藉由改變每條重鏈中的胺基酸，不同的重鏈更可能聯合以形成異源二聚體結構而不是形成具有相同Fc胺基酸序列的同源二聚體。圖9中包括空間變體的合適實例。

【0160】也可視需要使用本領域通常稱為“杵臼”的一種機制，其指的是產生空間影響以促進異源二聚體形成且不利於同源二聚體形成的胺基酸工程化。這進一步描述於美國專利公開案號20130205756, Ridgway 等人, Protein Engineering [蛋白質工程] 9(7):617 (1996)；Atwell 等人, J. Mol. Biol.[分子生物學雜誌] 1997 270:26；美國專利案號8,216,805，將其全部以其整體藉由引用併入本文。附圖鑒別了許多依賴於“杵臼”的“單體A – 單體B”對。此外，如描述於Merchant 等人, Nature Biotech.[自然生物技術] 16:677 (1998)，該等“杵臼”突變可以與二硫鍵組合，使形成偏向異二聚化。

【0161】發現用於生成異源二聚體的另一種機制有時被稱為“靜電轉向”，如描述於Gunasekaran 等, J. Biol. Chem.[生物化學雜誌] 285(25):19637 (2010)中，將其整體藉由引用併入本文。這有時在本文中稱為“電荷對”。在該實施方式中，靜電用於使形成偏向異二聚化。如熟悉該項技術者將理解的，該等也可能對pI有影響，並且因此對純化也有影響，並且因此在某些情況下也可以考慮pI變體。然而，由於產生該等以強

制異二聚化並且不用作純化工具，因此它們被歸類為“空間變體”。該等包括但不限於D221E/P228E/L368E，與D221R/P228R/K409R配對（即，該等係單體對應組）；和C220E/P228E/368E，與C220R/E224R/P228R/K409R配對。

【0162】另外的單體A和單體B變體可以任何量視需要和獨立地與其他變體組合，例如本文概述的pI變體或美國專利公開案號2012/0149876的圖37中示出的其他空間變體，該圖和圖例及其SEQ ID NO藉由引用明確地併入本文。

【0163】在一些實施方式中，本文概述的空間變體可以視需要和獨立地與任何pI變體（或其他變體，例如Fc變體，FcRn變體等）一起摻入一種或兩種單體中，並且可以獨立地和視需要包括於本發明的蛋白質中或自本發明的蛋白質排除。

【0164】合適的偏斜變體列表可發現於圖9和圖12中。在許多實施方式中特別有用的是如下組對，包括但不限於，S364K/E357Q：L368D/K370S；L368D/K370S：S364K；L368E/K370S：S364K；T411T/E360E/Q362E：D401K；L368D/K370S：S364K/E357L和K370S：S364K/E357Q。就命名而言，“S364K/E357Q：L368D/K370S”對意指其中一種單體具有雙變體組S364K/E357Q，並且另一種單體具有雙變體組L368D/K370S。

C. 用於調整功能的另外的Fc變體

【0165】存在許多有用的Fc胺基酸修飾，其可以由於各種原因而製備，包括但不限於，改變與一種或多種FcγR受體的結合、改變與FcRn受體的結合等。

【0166】可以進行許多有用的Fc取代以改變與一種或多種FcγR受體的結合。導致增加的結合以及降低的結合的取代可能是有用的。例如，已知增加與FcγRIIIa的結合通常導致ADCC增加（抗體依賴性細胞介導的細胞毒性；細胞介導的反應，其中表現FcγR的非特異性細胞毒性細胞識別靶標細胞上的結合抗體並且隨後引起靶標細胞的裂解）。類似地，在某些情況下，與FcγRIIb（抑制性受體）的結合降低也是有益的。發現本發明中有用的胺基酸取代包括美國專利公開案號2006/0024298（特別是圖41）、2006/0121032、2006/0235208、2007/0148170中列出的那些，所述公開全部藉由引用明確地併入本文，並且特別是其中揭露的變體。可以使用的特定變體包括但不限於236A、239D、239E、332E、332D、239D/332E、267D、267E、328F、267E/328F、236A/332E、239D/332E/330Y、239D、332E/330L、243A、243L、264A、264V和299T。

【0167】此外，發現另外的Fc取代，其可用於增加與FcRn受體的結合和增加血清半衰期，如美國專利公開案號2009/0163699中具體揭露的，所述公開藉由引用以其整體併入本文，所述取代包括但不限於434S、434A、428L、308F、259I、428L/434S、259I/308F、436I/428L、436I或V/434S、436V/428L和259I/308F/428L。

【0168】另一類別的功能性變體係“FcγR消融變體”或“Fc敲除（FcKO或KO）”變體。對於一些治療應用，期望減少或去除Fc結構域與一種或多種或全部Fcγ受體（例如，FcγR1、FcγRIIa、FcγRIIb、FcγRIIIa等）的正常結合，以避免另外的作用機制。即，例如，特別是在使用單價結合CD3的雙特異性抗體時，可能希望消融FcγRIIIa結合以消除

或顯著降低ADCC活性。考慮任何水平的降低（例如，結合或活性降低50%、60%、70%、80%、90%、或100%）。消融變體修飾的實例描繪於圖11中，並且每個可以獨立地和視需要包括或排除，較佳的方面利用選自由以下各項組成之群組之消融變體：G236R/L328R、E233P/L234V/L235A/G236del/S239K、E233P/L234V/L235A/G236del/S267K、E233P/L234V/L235A/G236del/S239K/A327G、E233P/L234V/L235A/G236del/S267K/A327G和E233P/L234V/L235A/G236del。應注意，本文引用的消融變體消除FcγR結合，但通常不消除FcRn結合。

D. 另外的抗體考慮

【0169】本揭露考慮了在本文描述的製劑中使用其他異源二聚體抗體。例如，可變重和輕序列，以及上文描述的scFv序列（和包含該等可變重和輕序列的Fab序列）能以其他型式使用，例如國際專利公開案號2014/145806的圖2或國際專利公開案號2017/218707的圖1中描繪的那些（其圖、格式和圖例藉由引用明確地併入本文），連同圖1A和1B。此外，CD3結合區和CD38結合區的胺基酸序列（例如，CDR序列、可變輕鏈和可變重鏈序列、和/或全長重鏈和輕鏈序列）在一併提供的序列表中提供並總結在圖21中。本文考慮了圖21中引用的序列的任何組合，只要所得的異源二聚體抗體與CD3和CD38兩者接合。抗CD3/抗CD38抗體進一步參考國際專利公開案號WO 2016/086196；美國專利公開案號20160215063；國際專利公開案號WO 2017/091656；和美國專利案號9,822,186進行描述，所述參考以其整體藉由引用併入本文，並且特別是關於抗CD3/抗CD38抗體及其胺基酸和核酸序列、序列表和圖的說明。

【0170】關於CD3結合，異源二聚體抗體可包含對CD3具有中或“中

等”親和力的抗CD3抗原結合結構域。就此而言，異源二聚體抗體與CD3結合的親和力（KD）為約15-50 nM（例如，約16-50 nM、15-45 nM、約20-40 nM、約25-40 nM、或約30-40 nM），視需要，使用美國專利公開案號20160215063和國際專利公開案號WO 2017/091656中描述的測定法測量親和力，所述公開藉由引用併入本文。

【0171】在另一個方面，該方法的異源二聚體抗體包含抗CD3抗原結合結構域，其是CD3的“強”或“高親和力”結合劑（例如，一個實例係描繪為H1.30_L1.47（視需要包括適當的帶電荷的接頭）的重和輕可變結構域）。在多個實施方式中，抗體構建體以約3-15 nM（例如，3-10 nM或4-7 nM）的親和力（KD）結合CD3，視需要，使用美國專利公開案號20160215063和國際專利公開案號WO 2017/091656中描述的測定法測量親和力，所述公開藉由引用併入本文。在其他實施方式中，該方法採用包含抗CD3抗原結合結構域的異源二聚體抗體，該抗CD3抗原結合結構域係CD3的“輕”或“低親和力”結合劑。就此而言，視需要異源二聚體抗體與CD3結合的親和力（KD）為約51 nM或更多（例如，約51-100 nM），視需要，使用美國專利公開案號20160215063和國際專利公開案號WO 2017/091656中描述的測定法測量親和力，所述公開藉由引用併入本文。異源二聚體抗體還結合例如CD38或STEAP1。

【0172】雙特異性抗體對CD38的親和力也對抗體靶向表現CD38的細胞的功效有影響。對CD38具有“中等”或“低”親和力的雙特異性抗體能夠在體外和體內有效殺死靶標細胞，同時具有降低的毒性譜。在多個實施方式中，對CD38證明“高”親和力的雙特異性抗體以例如低於1 nM的親和力（KD）結合CD38；對CD38證明“中等”或“中”親和力的雙特異性抗體

以例如約1-10 nM（例如2-8 nM或3-7 nM）的親和力（KD）結合CD38；對CD38證明“低”或“輕”親和力的雙特異性抗體以例如約11 nM或更多（例如11-100 nM）的親和力（KD）結合CD38，全部親和力視需要使用美國專利公開案號20160215063和國際專利公開案號WO 2017/091656中所示的方法測量，所述公開藉由引用併入本文。

【0173】通常，特異性結合可以展現為，例如，抗體對抗原具有至少約10^{-4} M、至少約10^{-5} M、至少約10^{-6} M、至少約10^{-7} M、至少約10^{-8} M、至少約10^{-9} M，可替代地至少約10^{-10} M、至少約10^{-11} M、至少約10^{-12} M或更高的KD，其中KD係指特定抗體-抗原相互作用的解離速率。典型地，特異性結合抗原的抗體相對於抗原具有對照分子的20倍、50倍、100倍、500倍、1000倍、5,000倍、10,000倍或更多倍的KD。同樣，特定抗原的特異性結合可以展現為，例如，相對於對照，抗體對抗原具有如下抗原或表位KA或Ka：至少20倍、50倍、100倍、500倍、1000倍、5,000倍、10,000倍或更多，其中KA或Ka係指特定抗體-抗原相互作用的解離率。應理解，與抗體有關的揭露也適用於抗原結合蛋白。

【0174】視需要，異源二聚體抗體在位置220處包含半胱胺酸取代絲胺酸；通常，這係在異源二聚體抗體的“scFv單體”側，儘管它也可以在“Fab單體”側或兩者上，以減少二硫化物的形成。本文序列中具體包括該等取代的半胱胺酸中的一個或兩個（C220S）。

E.片段

【0175】本揭露還考慮使用抗體片段（與構成抗體的天然生物形式的全長抗體不同，所述抗體片段包括可變區和恒定區，所述區通常包括Fab和Fc結構域以及視需要的額外抗原結合結構域，例如scFv）。抗體片

段含有至少一個恒定結構域，其可以被工程化以產生異源二聚體，例如pI工程化。可以使用的其他抗體片段包括含有一個或多個已經過pI工程化的本發明的CH1、CH2、CH3、鉸鏈和CL結構域的片段。

F.嵌合/人源化

【0176】異源二聚體抗體可以是來自不同物種的混合物，例如嵌合抗體和/或人源化抗體。通常，“嵌合抗體”和“人源化抗體”均指組合來自一種以上物種的區域的抗體。例如，“嵌合抗體”傳統上包含來自小鼠（或在一些情況下為大鼠）和來自人的一個或多個恒定區的一個或多個可變區。“人源化抗體”通常是指非人抗體，其具有與人抗體中發現的序列交換的可變域框架區。通常，在人源化抗體中，除CDR之外的整個抗體由人起源的多核苷酸編碼或與這種抗體相同（其CDR內除外）。CDR（部分或全部由源自非人生物體的核酸編碼）被接枝到人抗體可變區的β-折疊框架中以產生抗體，其特異性由接枝的CDR決定。這種抗體的產生描述於例如國際專利公開案號WO 92/11018，Jones, 1986, Nature [自然] 321:522-525，和Verhoeyen 等人, 1988, Science [科學] 239:1534-1536，所述公開均藉由引用整體併入。通常需要選擇的受體框架殘基向相應的供體殘基的“回復突變”，以重新獲得在初始接枝的構建體中喪失的親和力（美國專利案號5530101；5585089；5693761；5693762；6180370；5859205；5821337；6054297；和6407213，均藉由引用整體併入）。人源化抗體還包含免疫球蛋白（典型地是人免疫球蛋白）恒定區的至少一部分，並且因此典型地包含人Fc區。使用具有基因工程化免疫系統的小鼠也可以產生人源化抗體。Roque 等人, 2004, Biotechnol. Prog.[生物技術進展] 20:639-654, 藉由引用整體併入。用於人源化和重構型非人抗體的多種技

術和方法係本領域熟知的（參見Tsurushita和Vasquez, 2004, Humanization of Monoclonal Antibodies[單株抗體的人源化], Molecular Biology of B Cells [B細胞的分子生物學], 533-545, Elsevier Science（愛思唯爾科學出版社）（美國），和其中引用的參考文獻，全部藉由引用併入本文）。人源化方法包括但不限於描述於Jones 等人, 1986, Nature [自然] 321:522-525；Riechmann 等人,1988; Nature [自然] 332:323-329；Verhoeyen 等人, 1988, Science [科學], 239:1534-1536；Queen 等人, 1989, Proc Natl Acad Sci, USA [美國科學院院刊] 86:10029-33；He 等人, 1998, J. Immunol.[免疫學雜誌] 160: 1029-1035；Carter 等人, 1992, Proc Natl Acad Sci USA [美國科學院院刊] 89:4285-9, Presta 等人, 1997, Cancer Res.[癌症研究] 57(20):4593-9；Gorman 等人, 1991, Proc. Natl. Acad. Sci. USA [美國科學院院刊] 88:4181-4185；O'Connor 等人, 1998, Protein Eng [蛋白質工程] 11:321-8的方法，全部藉由引用併入本文。降低非人抗體可變區的免疫原性的人源化或其他方法可包括表面重修方法，如例如描述於Roguska 等人, 1994, Proc. Natl. Acad. Sci. USA [美國科學院院刊] 91:969-973中，藉由引用整體併入。

【0177】劑量

【0178】術語"有效給藥"或"有效劑量"被定義為足以達到或至少部分達到所希望效果的量。術語"治療有效劑量"被定義為足以在已經患有該疾病的患者中治癒或至少部分地停滯疾病及其併發症的量。對該用途有效的量或劑量將取決於待治療的病症（適應症）、遞送的抗體構建體、治療背景和目標、疾病的嚴重程度、在先治療、患者的臨床病史和對治療劑的應答、給予途徑、患者的大小（體重、體表或器官大小）、和/或狀況

（年齡和一般健康狀況），以及患者自身免疫系統的一般狀態。可以根據主治醫師的判斷調整適當的劑量，使得其可以一次或在一系列給藥後給予患者，並且是為了獲得最佳治療效果。

【0179】治療有效量的抗原結合蛋白（例如抗體）較佳的是導致疾病症狀的嚴重程度降低，無疾病症狀期的頻率或持續時間的增加或由於疾病折磨而預防損傷或殘疾。為了治療表現靶標細胞抗原的腫瘤，治療有效量的抗原結合蛋白（例如抗體），例如抗靶標細胞抗原/抗CD3抗體構建體，相對於未治療的患者較佳的是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%。可以在預測功效的動物模型中評估分子抑制腫瘤生長的能力。

【0180】術語“有效和無毒劑量”係指可耐受劑量的抗原結合蛋白（例如，抗體），其足夠高以引起病理細胞的耗竭、腫瘤消除、腫瘤縮小或疾病穩定而沒有或基本上沒有主要毒性作用。這種有效和無毒劑量可以例如藉由本領域描述的劑量遞增研究來確定，並且應該低於誘導嚴重不良反應的劑量（劑量限制性毒性，DLT）。

【0181】如本文使用的術語“毒性”係指在不良事件或嚴重不良事件中顯現的藥物的毒性作用。該等不良反應可能是指給藥後缺乏系統性藥物耐受性和/或缺乏局部耐受性。毒性還可能包括由藥物引起的致畸或致癌作用。

【0182】術語“安全性”、“體內安全性”或“耐受性”限定了藥物的施用在施用後當時（局部耐受）和在較長的該藥物應用時間段期間不會誘導嚴重的不良事件。可以例如在治療期間和隨訪期間定期評估“安全性”、“體內安全性”或“耐受性”。測量包括臨床評估，例如器官表現，以及實驗

室異常的篩選。可以進行臨床評估，並根據NCI-CTC和/或MedDRA標準記錄/編碼與正常發現的偏差。器官表現可包括例如過敏/免疫學、血液/骨髓、心律失常、凝血等的標準，如例如在不良事件的通用術語標準（Common Terminology Criteria for adverse events）v3.0（CTCAE）中所示。可以測試的實驗室參數包括例如血液學、臨床化學、凝血曲線和尿分析以及其他體液的檢查，例如血清、血漿、淋巴或脊髓液、流體等。因此可以評估安全性，例如藉由身體檢查，成像技術（即，超音波、X射線、CT掃描、磁共振成像（MRI）），藉由測量實驗室參數和記錄不良事件採用技術裝置（即心電圖）、生命徵象進行的其他測量。例如，可以藉由組織病理學和/或組織化學方法檢查根據本發明的用途和方法的非黑猩猩靈長類動物中的不良事件。

【0183】上述術語也在如下中有提及：例如生物技術衍生藥物S6的臨床前安全性評估[Preclinical safety evaluation of biotechnology-derived pharmaceuticals S6]；ICH三方協調指南[ICH Harmonised Tripartite Guideline]；於1997年7月16日舉行的ICH指導委員會會議[ICH Steering Committee meeting]。

【0184】取決於上述因素，典型的劑量範圍可以為從約0.1 μg/kg至高達約30 mg/kg或更高。在具體的實施方式中，劑量範圍可以為從1.0 μg/kg至約20 mg/kg，視需要為從10 μg/kg至高達約10 mg/kg或從100 μg/kg至高達約5 mg/kg。可以提供製劑使得異二聚體抗體以單位劑量提供，例如，以實現每千克體重0.1-50 mg抗體的劑量（僅計算蛋白質的質量，無化學修飾）。

【0185】製劑的治療用途

【0186】本文描述的製劑有用於治療、緩解和/或防止本文描述病理醫學病症的藥物組成物，用於有需要的患者。術語“治療”係指治療性治療和預防性或者防治性措施二者。治療包括將製劑應用或施用於來自患有疾病/障礙、具有疾病/障礙的症狀或易患疾病/障礙的患者的身體、分離的組織、或細胞，目的係治療、治癒、緩解、減輕、改變、補救、改善、改進或影響疾病、疾病的症狀、或易患病傾向。

【0187】如本文使用的，術語“改善”係指藉由將包含本文描述的抗原結合蛋白的組成物給予有需要的受試者，對患有如下文指明的腫瘤或癌症或轉移性癌症的患者的疾病狀態的任何改進。這種改進還可以被視為減緩或停止患者的腫瘤或癌症或轉移性癌症的進展。本文使用的術語“防止”意指藉由將包含本文描述的抗原結合蛋白（即抗體構建體）的組成物給予有需要的受試者，避免患有如下文所述的腫瘤或癌症或轉移性癌症的患者的發病或復發。

【0188】在一個實施方式中，本發明提供治療或緩解增殖性疾病、腫瘤性疾病、病毒性疾病或免疫障礙之方法，該方法包括向有需要的受試者給予本文描述的製劑的步驟。術語“疾病”係指將受益於用本文描述的藥物組成物進行的治療的任何病症。這包括慢性和急性障礙或疾病，包括使哺乳動物易於罹患所討論的疾病的那些病理狀態。術語“病毒性疾病”描述了為受試者的病毒感染結果的疾病。在本文中使用的術語“免疫障礙”與本術語的通用定義一致，其包括免疫障礙，例如自身免疫疾病、超敏反應、免疫缺陷。

【0189】“瘤”係組織的異常生長，通常但並不總是形成腫塊。當還形成腫塊時，通常將其稱為“腫瘤”。瘤或腫瘤或可以是良性的、潛在惡性

的（癌前的）或惡性的。惡性瘤通常被稱為癌症。它們通常侵入並破壞周圍組織並可能形成轉移，即它們擴散到身體的其他部位、組織或器官。因此，術語“轉移性癌症”涵蓋轉移到除原始腫瘤之外的其他組織或器官。淋巴瘤和白血病係淋巴腫瘤。出於本發明的目的，它們也涵蓋在術語“腫瘤”或“癌症”中。術語“有需要的受試者”或“需要治療”的受試者包括已經患有該障礙的受試者，以及其中需防止該障礙的受試者。有需要的受試者或“患者”包括接受預防性或治療性治療的人和其他哺乳動物受試者。

【0190】給藥途徑

【0191】示例性給藥途徑包括但不限於局部途徑（例如表皮、吸入、鼻、眼、耳/耳部、陰道、黏膜）；腸途徑（例如口腔、胃腸、舌下、唇下、頰、直腸）；和腸胃外途徑（例如靜脈內、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、管腔內）。較佳的是，藥物製劑藉由胃腸外給予，例如靜脈內、皮下、或肌肉內給予。腸胃外給藥可以藉由注射，例如推注注射，或藉由輸注，例如連續輸注來實現。給藥可經由貯庫實現長期釋放。在一些實施方式中，藉由初始推注、隨後連續輸注以維持藥物產品的治療循環水平靜脈內給予製劑。在一些實施方式中，製劑以一次性劑量給予。可以使用醫療裝置給予藥物組成物。用於給予藥物組成物的醫療裝置的實例描述於美國專利案號4,475,196；4,439,196；4,447,224；4,447, 233；4,486,194；4,487,603；4,596,556；4,790,824；4,941,880；5,064,413；5,312,335；5,312,335；5,383,851；和5,399,163中。

【0192】特別地，本發明提供了合適組成物的不間斷給藥。作為非

限制性實例，可以藉由患者佩戴的小泵系統實現不間斷或基本上不間斷的給藥，即連續給藥，所述小泵系統用於計量治療劑進入患者體內的流入量。藥物組成物可以藉由使用所述泵系統給予。這種泵系統通常是本領域中已知的，並且通常依賴於含有待輸注的治療劑的藥筒的週期性交換。當在這種泵系統中交換藥筒時，可能會暫時中斷本應流入患者體內的治療劑的不間斷流動。在這種情況下，藥筒更換前的給藥階段和藥筒置換後的給藥階段仍將被認為在本發明的藥物裝置與方法的含義內，一起構成這種治療劑的一種“不間斷給藥”。

【0193】製劑的連續或不間斷給藥可以藉由流體遞送裝置或小泵系統進行靜脈內或皮下給藥，該流體遞送裝置或小泵系統包括用於驅動流體離開儲存器的流體驅動機制和用於致動該驅動機制的致動機制。用於皮下給藥的泵系統可包括針或套管，用於穿透患者的皮膚並將合適的組成物遞送到患者體內。所述泵系統可以獨立於靜脈、動脈或血管直接固定或附接至患者的皮膚，從而允許泵系統和患者皮膚之間的直接接觸。泵系統可以附接至患者的皮膚上24小時至長達若干天。泵系統可以是小尺寸的，具有小體積的儲存器。作為非限制性實例，待給予的合適的藥物組成物的儲存器體積可以為0.1和50 ml之間。

【0194】連續給藥也可以藉由佩戴在皮膚上並定期更換的貼劑的方式進行透皮給藥。熟悉該項技術者知道適用於該目的的用於藥物遞送的貼劑系統。應注意，透皮給藥特別適合於不間斷給藥，因為第一次用盡貼劑的交換可以有利地與更換新的第二貼劑同時完成，例如在緊鄰第一次用盡貼劑的皮膚表面上且在去除第一個耗竭的貼劑之前立即更換。不會出現流動中斷或動力細胞失效的問題。

【0195】如果藥物組成物已經凍乾，則凍乾材料在給藥前首先在合適的液體中重構。凍乾物質可以在例如抑菌型注射用水（BWFI）、生理鹽水、磷酸鹽緩衝鹽水（PBS）、或與凍乾前蛋白質所在製劑相同的製劑中重構。藥物組成物可以作為單獨的治療劑給予，或者與另外的療法例如需要時的抗癌療法（例如，其他蛋白質和非蛋白質藥物）組合給予。該等藥物可以與如本文定義的本發明的組成物同時給予，或者在給予所述製劑之前或之後以及時定義的間隔和劑量分別給予。

【0196】套組

【0197】作為一個另外的方面，本文描述的是包含一種或多種本文描述的藥物組成物的套組（kit），所述藥物組成物以利於用於給予受試者的方式包裝。在一個實施方式中，此類套組包括本文描述的製劑（例如，包含其中描述抗體的組成物），所述製劑包裝在容器中，例如在密封瓶、小管、單次使用或多次使用的小瓶、預填充式注射器、或預填充式注射裝置中，所述套組視需要具有貼附於容器上或包括在包裝中的標籤，該標籤描述了化合物或組成物在實踐該方法中的用途。在一個方面，該組成物被包裝為一個單位劑型。該套組可以進一步包括適於根據特定的給藥途徑給予該組成物的裝置。較佳的是，套組含有描述本文描述的抗體或本文描述的製劑的用途的標籤。

【0198】本文描述的藥物組成物能以多種形式配製，例如，以固體、液體、冷凍、氣體或凍乾形式，並且尤其可以是軟膏、乳膏、透皮貼劑、凝膠、粉末、片劑、溶液，氣溶膠、顆粒、丸劑、懸浮液、乳液、膠囊、糖漿、液體、酏劑、提取物、酊劑或流體提取物形式。

【0199】通常，對於本發明的藥物組成物，可以想到多種儲存和/或

劑型，這取決於預期的給藥途徑、遞送型式和所希望的劑量（參見，例如，Remington's Pharmaceutical Sciences [雷明頓藥物科學], 第22版, Oslo, A., 編輯, (2012)）。技術人員將意識到，特定劑型的這種選擇可以例如影響抗體的物理狀態、穩定性、體內釋放速率和體內清除速率。

【0200】例如，藥物組成物中的主要媒介物或載體在自然界中可以是水性或非水性的。合適的媒介物或載體可以是注射用水、生理鹽水溶液或人造腦脊液，可能補充有組成物中常見的用於腸胃外給藥的其他物質。中性緩衝鹽水或與血清白蛋白混合的鹽水係另外的示例性媒介物。

實例

【0201】材料與方法

【0202】*SE-UHPLC*（尺寸排阻超高效液相層析法）係一種定量分析重組單株抗體（mAb）或X-mAb的方法。SE-UHPLC基於其流體動力學體積的差異分離蛋白質。具有較高流體動力學體積的分子比具有較小體積的分子更先洗脫。將樣品載入到SE-UHPLC柱（BEH200，4.6 x 300 mm，（沃特斯公司（Waters Corporation），186005226））上，等度分離並藉由UV吸光度監測洗脫液。藉由計算每個分離的組分與總積分面積相比的百分比來確定純度。SE-UHPLC設置如下：流速：0.4 mL/min，執行時間：12 min，UV檢測：280 nm，柱溫度：環境，靶標蛋白質載入：6 μg，蛋白質相容流動細胞：5 mm。

【0203】陽離子交換高效液相層析法（CEX）係一種對帶電荷的變體分佈進行定量純度分析之方法。固定相A：1x CX-1 pH梯度緩衝液A，pH 5.6（10x CX-1 pH梯度緩衝液A，pH 5.6，250 mL和流動相B：1x CX-1 pH梯度緩衝液，pH 10.2。

【0204】*CE-HPLC*（陽離子交換高效液相層析法）係一種對帶電荷的變體分佈進行定量純度分析之方法。流動相A：25 mM磷酸鈉，10%乙腈，pH 6.7，和固定相B：25 mM磷酸鈉，500 mM氯化鈉，10%乙腈，pH 6.7。用於抗體A CE-HPLC的柱係Bio Mab NP -5，4.6 x 250 mm，5 µm（安捷倫科技有限公司（Agilent Technology），5190-2407）。CE-HPLC方法設置如下：流速：0.75 mL/min，執行時間：60 min，柱溫設置值：30°C ± 5°C, 檢測器波長：280 nm，靶標蛋白質載入：20 µg。用於抗體B CE-HPLC方法的柱係YMC BioPro SP-F，4.6 x 100 mm，5 µm（YMC有限公司（YMC Co., Ltd.），SF00S05-1046WP）。CE-HPLC方法設置如下：流速：1.0 mL/min，執行時間：45分鐘，自動進樣器溫度設置值：5°C ± 3°C，柱溫設置值：30°C ± 2°C, 檢測器波長：280 nm，靶標樣品蛋白質載入：70 ± 10 ug。

【0205】*rCE-SDS*（還原毛細管電泳 - 十二烷基硫酸鈉）係一種在變性和還原條件下進行定量純度分析的方法。

【0206】*MAM*（多屬性方法）係使用Thermo Scientific Orbitrap型質譜儀和Chromeleaon軟體進行多種產品品質屬性（PQA）（氧化、異構化、脫醯胺化和糖化作用）的方法。使用肽作圖測量熱應激（在40°C孵育）下的化學修飾。酶促消化蛋白質，並使用反相層析法分離所得肽。蛋白質用鹽酸胍變性，並且然後用二硫蘇糖醇（DTT）還原。在DTT中孵育後，藉由添加碘乙酸使游離的半胱胺酸殘基烷基化。然後將樣品緩衝交換到50 mM Tris-HCl，20 mM甲硫胺酸，pH 7.8中，用於消化。將胰蛋白酶和彈性蛋白酶添加至各反應管中（酶與蛋白質的比率為1:20）。將樣品分別在37°C下消化60 min和在37°C下消化30 min。藉由添加鹽酸胍，250

mM乙酸鹽，pH4.7淬滅消化。

【0207】凍乾藥物產品的水分含量藉由用烘箱進行量熱滴定法來確定。凍乾藥物產品的水分限制為2%。Karl Fischer方法的原理係基於藉由量熱滴定法確定的樣品中的水含量。藉由在烘箱中加熱樣品來釋放水。乾燥空氣或惰性氣體（例如氮氣）將蒸發的水分帶到滴定儀。存在的水量藉由測量滴定期間產生的庫侖（電流/時間）的量來確定。當藉由滴定消耗了所有的水時，會發生碘過量。藉由向雙Pt電極應用恒定強度的交流電流來體積指示終點。這導致Pt接線指示電極之間的電壓差，其在最小量的游離碘存在下急劇降低。該電壓差用於確定滴定的終點。

實例1 –低pH製劑中的抗體穩定性

【0208】以下實例描述了在多個不同溫度（4°C、25°C、40°C、-30°C和-40°C）下，在不同蛋白質濃度（即1 mg/mL和5 mg/mL）的液體製劑或凍乾製劑中驗證本文描述的異源二聚體抗體長達3年的穩定性的測定。使用以下測定分析異源二聚體抗體的穩定性：外觀（經由在每個時間點目測20個小瓶）、pH、滲透壓、CE-HPLC、rCE、MAM（多屬性方法）和卡爾·費歇爾（Karl Fischer）（水分含量）。驗證研究樣品係在5cc小瓶中的1.3 mL填充物。異源二聚體抗體DS（無聚山梨醇酯80的材料）為10.6 mg/mL，並用緩衝液（G42Su）稀釋至5 mg/mL和1 mg/mL。所述製劑在G42SuT製劑中是等滲的，滲透壓值為326 mOsm/kg。

【0209】異源二聚體抗體的穩定性在以下製劑中評估：

【0210】**製劑A**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的1 mg/mL異源二聚體抗體凍乾製劑；

【0211】**製劑B**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%

（w/v）聚山梨醇酯80、pH 4.2中的5 mg/mL異源二聚體抗體凍乾製劑；

【0212】**製劑C**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的5 mg/mL異源二聚體抗體液體製劑；以及

【0213】**製劑D**：在10 mM 乙酸鹽、9%（w/v）蔗糖、0.01%聚山梨醇酯80、pH 5.2中的1 mg/mL異源二聚體抗體液體製劑。

【0214】*結果：*

【0215】當以製劑C配製時，在40°C下3個月後，經由SE-UHPLC確定抗體A具有13.4%的主峰損失。參見圖23。相反，當分別在製劑A（圖22A）和製劑B（圖22B）中配製時，經由SE-UHPLC確定抗體A具有0.2%和0.0%的主峰損失。當以製劑C配製時，在40°C下3個月後，經由CE-HPLC確定抗體A具有58.2%的主峰損失。參見圖25。相反，當分別在製劑A（圖24A）和製劑B（圖24B）中配製時，經由CE-HPLC確定抗體A具有10.5%和0.5%的主峰損失。

【0216】當以製劑A配製時，在-30°C下3個月後，經由rCE顯示抗體A的2.9%的主峰損失（圖26）。當以製劑C配製時，在40°C下3個月後，經由rCE顯示抗體A的19.9%的主峰損失。參見圖28。然而，抗體A在製劑A中在40°C下3個月後經由rCE顯示0.6%的主峰損失（圖26），並且當以製劑B配製時經由rCE顯示0.0%的主峰損失。參見圖27。

【0217】當以製劑C配製時，抗體A在40°C下3個月後經由MAM在N103（CD3 scFv-FC）顯示9.1%脫醯胺化。參見圖29，最後一欄。相反，當以製劑B配製時，抗體A經由MAM顯示0.3%脫醯胺化。參見圖29，右側第二欄。當以製劑D配製時，抗體A在40°C下4週後經由MAM在

N103（CD3 scFV-FC）顯示13.8%脫醯胺化（參見圖30），並且當以製劑C配製時，在40°C下1個月後經由MAM在N103（CD3 scFv-Fc）顯示3.7%脫醯胺化。參見圖31。相反，當以製劑B配製時，在40°C下1個月後抗體A經由MAM顯示0.4%脫醯胺化。參見圖31。

【0218】本文提供的數據證明，由於液體製劑中脫醯胺化的高風險，凍乾製劑A和凍乾製劑B比液體製劑C和液體製劑D更穩定。

實例2 –低pH製劑中的抗體穩定性

【0219】以下實例描述了在不同蛋白質濃度（例如1 mg/mL、5 mg/mL和20 mg/mL）的液體或凍乾製劑中，在多個不同溫度（4°C、25°C、40°C、-30°C和-40°C）在不同時間點驗證本文描述的異源二聚體抗體的穩定性的測定。異源二聚體抗體的穩定性在以下製劑中評估：

【0220】**製劑E**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的1 mg/mL異源二聚體抗體凍乾製劑；

【0221】**製劑F**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的5 mg/mL異源二聚體抗體凍乾製劑；

【0222】**製劑G**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的20 mg/mL異源二聚體抗體凍乾製劑；

【0223】**製劑H**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的1 mg/mL異源二聚體抗體液體製劑；

【0224】**製劑I**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的5 mg/mL異源二聚體抗體液體製劑；以及

【0225】**製劑J**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%

（w/v）聚山梨醇酯80、pH 4.2中的20 mg/mL異源二聚體抗體液體製劑。

【0226】將凍乾製劑E-G的穩定性與液體製劑H-J的穩定性進行比較。

【0227】使用以下測定分析異源二聚體抗體的穩定性：外觀（經由在每個時間點目測20個小瓶）、pH、滲透壓、CE-HPLC、rCE、MAM（多屬性方法）和卡爾·費歇爾（Karl Fischer）（水分含量）。驗證研究樣品係在5cc小瓶中的1.3 mL填充物。製劑E-G係等滲的，其滲透壓值分別為314 mOsm/kg和311 mOsm/kg。在任何測試的製劑中均未觀察到蛋白質顆粒。

【0228】異源二聚體抗體的穩定性在以下製劑中評估：

【0229】*結果：*

【0230】當以製劑J配製時，在40°C下3個月後，經由CEX確定抗體A具有34.7%的主峰損失。相反，當以製劑G配製時，在相同的條件下，經由CEX確定抗體A具有2.8%的主峰損失。參見表2。

【0231】[表2].如藉由CEX確定的製劑G和J的%主峰。

溫度	時間點	製劑J	製劑G
40°C	0	74.8	74.4
	1周	70.7	74.5
	2週	67.4	73.6
	1個月	68.4	74.8
	3個月	40.1	71.6
25°C	0	74.8	74.4
	1週	74.3	N/A
	2週	74.0	75.5
	1個月	73.2	75.2
	3個月	68.7	74.3
4°C	0	74.8	74.4
	1個月	74.9	75.1
	3個月	75.2	73.8

【0232】當以製劑J配製時，在40°C下3個月後，經由SE-UHPLC確定抗體A具有15.3%的主峰損失。相反，當以製劑G配製時，在相同的條件下，經由SE-UHPLC確定抗體A具有1.6%的主峰損失。參見表3。

【0233】[表3].如藉由SE-UHPLC確定的製劑G和J的%主峰。

溫度	時間點	製劑J	製劑G
40°C	0	98.6	98.6
	1週	98.3	98.6
	2週	98.4	99.1
	1個月	97.4	99.1
	3個月	83.3	97.0
25°C	0	98.6	98.6
	1週	98.6	N/A
	2週	98.9	99.0
	1個月	99.8	99.1
	3個月	95.9	97.0
4°C	0	98.6	98.6
	1個月	99.1	99.1
	3個月	97.0	97.1

【0234】當以製劑J配製時，在40°C下3個月後，經由rCE顯示抗體A的3.7%的主峰損失。然而，當以製劑G中時，在40°C下3個月後，經由rCE顯示抗體A的0.0%的主峰損失。參見表4。

【0235】[表4].如藉由rCE確定的製劑G和J的%主峰。

溫度	時間點	製劑J	製劑G
40°C	0	99.7	99.7
	1週	99.4	99.6
	1個月	96.9	99.5
	3個月	96.0	99.5
25°C	0	99.7	99.7
	1週	99.6	N/A
	1個月	99.2	99.5
	3個月	98.8	99.5

4°C	0	99.7	99.7
	1個月	99.5	99.5
	3個月	99.4	99.4

【0236】當以製劑G配製時，預期抗體A顯示與上文實例1中描述的製劑B相同的%脫醯胺化。

【0237】本文提供的數據證明凍乾製劑G比液體製劑J更穩定，如藉由在測試時間點在製劑G中觀察到的降低的%主峰損失所證明的。此外，確定具有20 mg/mL異源二聚體抗體濃度的製劑J具有與製劑A（異源二聚體抗體1 mg/mL）和B（異源二聚體抗體5 m/mL）相似的主峰損失%，這係令人驚訝的，因為製劑J中存在較高的異源二聚體抗體濃度（20 mg/mL）。

實例3 - 低pH製劑中的抗體穩定性

【0238】以下實例描述了在10 mg/mL的蛋白質濃度的液體或凍乾製劑中，在多個不同溫度（4°C、25°C、40°C、-30°C和-40°C）在長達3年的時間驗證本文描述的異源二聚體抗體的穩定性的測定。異源二聚體抗體的穩定性在以下製劑中評估：

【0239】**製劑K**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的10 mg/mL異源二聚體抗體凍乾製劑；以及

【0240】**製劑L**：在10 mM L-谷胺酸、9%（w/v）蔗糖、0.01%（w/v）聚山梨醇酯80、pH 4.2中的10 mg/mL異源二聚體抗體液體製劑。

【0241】將凍乾製劑K的穩定性與液體製劑L的穩定性進行比較。在該研究中利用抗體B。

【0242】使用以下測定分析異源二聚體抗體的穩定性：外觀（經由在每個時間點目測20個小瓶）、pH、滲透壓、SE-HPLC、rCE、MAM

（多屬性方法）和卡爾·費歇爾（Karl Fischer）（水分含量）。驗證研究樣品係在5cc小瓶中的1.3 mL填充物。製劑K係等滲的，其滲透壓值為305 mOsm/kg。在任何測試的製劑中均未觀察到蛋白質顆粒。

【0243】異源二聚體抗體的穩定性在以下製劑中評估：

【0244】結果：

【0245】當以製劑L配製時，在40°C下3個月後，經由CEX確定抗體B具有34.5%的主峰損失。相反，當以製劑K配製時，在相同的條件下，經由CEX確定抗體B具有0.7%的主峰損失。參見表5。

【0246】[表5].如藉由CEX確定的製劑K和L的%主峰。

溫度	時間點	製劑L	製劑K
40°C	0	95.0	94.9
	1週	91.6	94.6
	2週	89.2	94.9
	1個月	83.3	94.8
	3個月	60.5	94.2
25°C	0	95.0	94.9
	1週	94.7	94.7
	2週	95.1	95.1
	1個月	95.0	95.0
	3個月	94.6	94.6
4°C	0	95.0	94.9
	1週	94.7	94.8
	2週	95.2	95.0
	1個月	95.5	95.0
	3個月	94.5	94.8
-30°C	0	95.0	94.9
	1週	94.8	94.7
	2週	95.3	95.2
	1個月	95.8	95.0
	3個月	94.8	94.7

【0247】當以製劑L配製時，在40°C下3個月後，經由SE-HPLC確定抗體B具有22.5%的主峰損失。相反，當以製劑K配製時，在相同的條件下，經由CEX確定抗體B具有0.7%的主峰損失。參見表6的SE-HPLC數據。

【0248】[表6].如藉由SE-HPLC確定的製劑K和L的%主峰。

溫度	時間點	製劑L	製劑K
40°C	0	98.8	98.8
	1週	92.2	97.3
	2週	92.6	98.5
	1個月	91.7	98.7
	3個月	76.3	97.1
25°C	0	98.8	98.8
	1週	96.9	97.4
	2週	96.7	98.6
	1個月	98.7	98.7
	3個月	97.2	97.2
4°C	0	98.8	98.8
	1週	97.6	97.1
	2週	97.9	98.6
	1個月	98.5	98.7
	3個月	96.7	97.0
-30°C	0	98.8	98.8
	1週	97.7	97.7
	2週	98.0	98.0
	1個月	98.7	98.7
	3個月	96.8	97.5

【0249】當以製劑L配製時，抗體B在40°C下3個月後經由MAM顯示6.8%脫醯胺化。參見表7。相反，當以製劑K配製時，抗體B經由MAM顯示<0.6%脫醯胺化。

【0250】[表7].如藉由MAM確定的製劑K和L的%脫醯胺化。

溫度	時間點	製劑L	製劑K
40°C	0	< 0.6%	< 0.6%
	1個月	2.4%	< 0.6%
	3個月	6.8%	< 0.6%
25°C	0	< 0.6%	< 0.6%
	1個月	< 0.6%	< 0.6%
	3個月	1.0%	< 0.6%
4°C	0	< 0.6%	< 0.6%
	1個月	< 0.6%	< 0.6%
	3個月	< 0.6%	< 0.6%
-30°C	0	< 0.6%	< 0.6%
	1個月	< 0.6%	< 0.6%
	3個月	< 0.6%	< 0.6%

【0251】本文提供的數據證明，由於液體製劑中脫醯胺化的高風險，凍乾製劑K比液體製劑L更穩定。

【序列表】

<110> 美商安進公司(AMGEN INC.)

<120> 低PH藥物製劑

<130> 32512/52588/PC

<140> TW 108104516
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
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Val Lys Gly

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Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
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His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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Gly Thr Asn Lys Arg Ala Pro
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1 5

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

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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1               5                   10                  15

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

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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Val Lys Gly

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<400> 13

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr
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Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
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Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

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

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
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Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
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Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
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Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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Val Lys Gly

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Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

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1               5                  10                  15

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

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
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Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
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Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
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Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
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Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
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Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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Val Lys Gly

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Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
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His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 37
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 可變重 (vh) 結構域

<400> 37

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 38
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> vhCDR1

<400> 38

Thr Tyr Ala Met Asn
1 5

<210> 39
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> vhCDR2

<400> 39

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Gly

<210> 40
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> vhCDR3

<400> 40

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Asp Tyr
1 5 10

<210> 41
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 可變輕 (vl) 結構域

<400> 41

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 42
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> vlCDR1

<400> 42

Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
1 5 10

<210> 43
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> vlCDR2

<400> 43

Gly Thr Asn Lys Arg Ala Pro
1 5

<210> 44
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> vlCDR3

<400> 44

Ala Leu Trp Tyr Ser Asn His Trp Val
1 5

<210> 45
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> scFv（包括帶電荷的接頭）

<400> 45

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

〈210〉 46
〈211〉 125
〈212〉 PRT
〈213〉 人工序列

<220>
<223> 可變重 (vh) 結構域

<400> 46

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 47
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> vhCDR1

<400> 47

Thr Tyr Ala Met Ser
1 5

<210> 48
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> vhCDR2

<400> 48

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Gly

<210> 49
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> vhCDR3

<400> 49

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 50
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 可變輕 (vl) 結構域

<400> 50

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 51
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> v1CDR1

<400> 51

Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
1 5 10

<210> 52
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> v1CDR2

<400> 52

Gly Thr Asn Lys Arg Ala Pro
1 5

<210> 53
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> v1CDR3

<400> 53

Ala Leu Trp Tyr Ser Asn His Trp Val
1 5

<210> 54
<211> 254
<212> PRT
<213> 人工序列

〈220〉
〈223〉 scFv（包括帶電荷的接頭）

〈400〉 54

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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 Ser Thr Tyr
            20                  25                  30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205
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Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 55
<211> 116
<212> PRT
<213> 人工序列

<220>
<223> 可變重 (vh) 結構域

<400> 55

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 56
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> vhCDR1

<400> 56

Tyr Ser Trp Met Asn
1 5

<210> 57
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> vhCDR2

<400> 57

Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val Lys
1 5 10 15

Gly

<210> 58
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> vhCDR3

<400> 58

Tyr Gly Asn Trp Phe Pro Tyr
1 5

<210> 59
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 可變輕 (vl) 結構域

<400> 59

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

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

<210> 60
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> vlCDR1

<400> 60

Arg Ala Ser Gln Asn Val Asp Thr Trp Val Ala
1 5 10

<210> 61
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> vlCDR2

<400> 61

Ser Ala Ser Tyr Arg Tyr Ser
1 5

<210> 62
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> vlCDR3

<400> 62

Gln Gln Tyr Asp Ser Tyr Pro Leu Thr
1 5

<210> 63
<211> 243
<212> PRT
<213> 人工序列

<220>
<223> scFv（包括帶電荷的接頭）

<400> 63

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys
115 120 125

Pro Gly Ser Gly Lys Pro Gly Ser Asp Ile Val 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 Asn Val Asp Thr Trp Val Ala Trp Tyr Gln Gln Lys Pro
165 170 175

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

Gly Val Pro Asp Arg Phe Thr 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 Phe Cys
210 215 220

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

Glu Ile Lys

<210> 64
<211> 116
<212> PRT
<213> 人工序列

<220>
<223> 可變重 (vh) 結構域

<400> 64

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 65
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> vhCDR1

<400> 65

Arg Ser Trp Met Asn
1 5

<210> 66
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> vhCDR2

<400> 66

Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val Lys
1 5 10 15

Gly

<210> 67
<211> 7
<212> PRT
<213> 人工序列

<220>

<223> vhCDR3

<400> 67

Tyr Gly Asn Trp Phe Pro Tyr
1 5

<210> 68
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 可變輕 (vl) 結構域

<400> 68

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

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

<210> 69
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> vlCDR1

<400> 69

Arg Ala Ser Gln Asn Val Asp Thr Trp Val Ala
1 5 10

<210> 70
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> vlCDR2

<400> 70

Ser Ala Ser Tyr Arg Tyr Ser
1 5

<210> 71
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> vlCDR3

<400> 71

Gln Gln Tyr Asp Ser Tyr Pro Leu Thr
1 5

<210> 72
<211> 243
<212> PRT
<213> 人工序列

<220>
<223> scFv（包括帶電荷的接頭）

<400> 72

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys
115 120 125

Pro Gly Ser Gly Lys Pro Gly Ser Asp Ile Val 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 Asn Val Asp Thr Trp Val Ala Trp Tyr Gln Gln Lys Pro
165 170 175

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

Gly Val Pro Asp Arg Phe Thr 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 Phe Cys
210 215 220

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

Glu Ile Lys

<210> 73
<211> 116
<212> PRT
<213> 人工序列

<220>

<223> 可變重（vh）結構域

<400> 73

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 74
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> vhCDR1

<400> 74

Arg Ser Trp Met Asn
1 5

<210> 75
<211> 17
<212> PRT
<213> 人工序列

<220>

<223> vhCDR2

<400> 75

Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr Ser Val Lys
1 5 10 15

Gly

<210> 76
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> vhCDR3

<400> 76

Tyr Gly Asn Trp Phe Pro Tyr
1 5

<210> 77
<211> 116
<212> PRT
<213> 人工序列

<220>
<223> 可變輕 (vl) 結構域

<400> 77

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser
115

<210> 78
<211> 11
<212> PRT
<213> 人工序列

<220>
<223> vlCDR1

<400> 78

Arg Ala Ser Gln Asn Val Asp Thr Asn Val Ala
1 5 10

<210> 79
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> vlCDR2

<400> 79

Ser Ala Ser Tyr Arg Tyr Ser
1 5

<210> 80
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> vlCDR3

<400> 80

Gln Gln Tyr Asp Ser Tyr Pro Leu Thr
1 5

<210> 81
<211> 252

〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 scFv（包括帶電荷的接頭）

〈400〉 81

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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 Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys
        115                 120                 125

Pro Gly Ser Gly Lys Pro Gly Ser Glu Val Gln Leu Val Glu Ser Gly
    130                 135                 140

Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala
145                 150                 155                 160

Ser Gly Phe Asp Phe Ser Arg Ser Trp Met Asn Trp Val Arg Gln Ala
                165                 170                 175

Pro Gly Lys Gly Leu Glu Trp Val Ser Glu Ile Asn Pro Asp Ser Ser
            180                 185                 190
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Thr Ile Asn Tyr Ala Thr Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
195 200 205

Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala
210 215 220

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Gly Asn Trp Phe Pro
225 230 235 240

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
245 250

<210> 82
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP13551 HC-Fab

<400> 82

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 83
<211> 485
<212> PRT
<213> 人工序列

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<400> 83

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 84
<211> 214
<212> PRT
<213> 人工序列

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<223> XENP13551 LC

〈400〉 84

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Asp Ile Val 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 Asn Val Asp Thr Trp
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
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<210> 85
<211> 445
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<223> XENP13243 HC-Fab

<400> 85

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 86
<211> 485
<212> PRT
<213> 人工序列

<220>
<223> XENP13243 HC-scFv

<400> 86

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 87
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP13243 LC

<400> 87

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 88
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP14702抗CD38

<400> 88

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 89
<211> 485

<212> PRT
<213> 人工序列

<220>
<223> XENP14702抗CD38

<400> 89

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 90
<211> 214
<212> PRT
<213> 人工序列

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<223> XENP14702抗CD38

<400> 90

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 91
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP15426抗CD38

<400> 91

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 92
<211> 485
<212> PRT
<213> 人工序列

<220>
<223> XENP15426抗CD38

<400> 92

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 93
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP15426抗CD38

<400> 93

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 94
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP14701抗CD38

<400> 94

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

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<400> 95

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
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<400> 97

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

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<400> 98

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<400> 99

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Lys Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

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<223> XENP13243抗CD38

<400> 100

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 101
<211> 485

<212> PRT
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<400> 101

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 103
<211> 445
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<400> 103

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

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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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<400> 105

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 106
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<400> 106

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 107
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<400> 107

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 108
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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
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<400> 109

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 110
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<400> 110

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<400> 111

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 112
<211> 445
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<400> 112

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 113
<211> 485

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<400> 113

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<400> 114

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 115
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<400> 115

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 116
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<400> 116

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 117
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<400> 117

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 118
<211> 445
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<400> 118

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 119
<211> 485
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<400> 119

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 120
<211> 214
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〈400〉 120

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
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<210> 121
<211> 445
<212> PRT
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<220>
<223> XENP15055抗CD38

<400> 121

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 122
<211> 485
<212> PRT
<213> 人工序列

<220>
<223> XENP15055抗CD38

<400> 122

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 123
<211> 214
<212> PRT
<213> 人工序列

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<223> XENP15055抗CD38

<400> 123

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 124
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP13544抗CD38

<400> 124

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

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
        195                 200                 205

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

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225                 230                 235                 240
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Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 125
<211> 485

<212> PRT
<213> 人工序列

<220>
<223> XENP13544抗CD38

<400> 125

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Cys Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 126
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP13544抗CD38

<400> 126

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 127
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP13694抗CD38

<400> 127

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 128
<211> 485
<212> PRT
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<400> 128

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Cys Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 129
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP13694抗CD38

<400> 129

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 130
<211> 207
<212> PRT
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<400> 130

Met Gln Ser Gly Thr His Trp Arg Val Leu Gly Leu Cys Leu Leu Ser
1 5 10 15

Val Gly Val Trp Gly Gln Asp Gly Asn Glu Glu Met Gly Gly Ile Thr
20 25 30

Gln Thr Pro Tyr Lys Val Ser Ile Ser Gly Thr Thr Val Ile Leu Thr
35 40 45

Cys Pro Gln Tyr Pro Gly Ser Glu Ile Leu Trp Gln His Asn Asp Lys
50 55 60

Asn Ile Gly Gly Asp Glu Asp Asp Lys Asn Ile Gly Ser Asp Glu Asp
65 70 75 80

His Leu Ser Leu Lys Glu Phe Ser Glu Leu Glu Gln Ser Gly Tyr Tyr
85 90 95

Val Cys Tyr Pro Arg Gly Ser Lys Pro Glu Asp Ala Asn Phe Tyr Leu
100 105 110

Tyr Leu Arg Ala Arg Val Cys Glu Asn Cys Met Glu Met Asp Val Met
115 120 125

Ser Val Ala Thr Ile Val Ile Val Asp Ile Cys Ile Thr Gly Gly Leu
130 135 140

Leu Leu Leu Val Tyr Tyr Trp Ser Lys Asn Arg Lys Ala Lys Ala Lys
145 150 155 160

Pro Val Thr Arg Gly Ala Gly Ala Gly Gly Arg Gln Arg Gly Gln Asn
165 170 175

Lys Glu Arg Pro Pro Pro Val Pro Asn Pro Asp Tyr Glu Pro Ile Arg
180 185 190

Lys Gly Gln Arg Asp Leu Tyr Ser Gly Leu Asn Gln Arg Arg Ile
195 200 205

<210> 131
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<400> 131

Met Ala Asn Cys Glu Phe Ser Pro Val Ser Gly Asp Lys Pro Cys Cys
1 5 10 15

Arg Leu Ser Arg Arg Ala Gln Leu Cys Leu Gly Val Ser Ile Leu Val
20 25 30

Leu Ile Leu Val Val Val Leu Ala Val Val Val Pro Arg Trp Arg Gln
35 40 45

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

Ala Arg Cys Val Lys Tyr Thr Glu Ile His Pro Glu Met Arg His Val
65 70 75 80

Asp Cys Gln Ser Val Trp Asp Ala Phe Lys Gly Ala Phe Ile Ser Lys
85 90 95

```
His Pro Cys Asn Ile Thr Glu Glu Asp Tyr Gln Pro Leu Met Lys Leu
            100                 105                 110

Gly Thr Gln Thr Val Pro Cys Asn Lys Ile Leu Leu Trp Ser Arg Ile
        115                 120                 125

Lys Asp Leu Ala His Gln Phe Thr Gln Val Gln Arg Asp Met Phe Thr
    130                 135                 140

Leu Glu Asp Thr Leu Leu Gly Tyr Leu Ala Asp Asp Leu Thr Trp Cys
145                 150                 155                 160

Gly Glu Phe Asn Thr Ser Lys Ile Asn Tyr Gln Ser Cys Pro Asp Trp
                165                 170                 175

Arg Lys Asp Cys Ser Asn Asn Pro Val Ser Val Phe Trp Lys Thr Val
            180                 185                 190

Ser Arg Arg Phe Ala Glu Ala Ala Cys Asp Val Val His Val Met Leu
        195                 200                 205

Asn Gly Ser Arg Ser Lys Ile Phe Asp Lys Asn Ser Thr Phe Gly Ser
    210                 215                 220

Val Glu Val His Asn Leu Gln Pro Glu Lys Val Gln Thr Leu Glu Ala
225                 230                 235                 240

Trp Val Ile His Gly Gly Arg Glu Asp Ser Arg Asp Leu Cys Gln Asp
                245                 250                 255

Pro Thr Ile Lys Glu Leu Glu Ser Ile Ile Ser Lys Arg Asn Ile Gln
            260                 265                 270

Phe Ser Cys Lys Asn Ile Tyr Arg Pro Asp Lys Phe Leu Gln Cys Val
        275                 280                 285

Lys Asn Pro Glu Asp Ser Ser Cys Thr Ser Glu Ile
    290                 295                 300
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<210> 132
<211> 258
<212> PRT
<213> 人工序列

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〈223〉 ECD結構域

〈400〉 132

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Val Pro Arg Trp Arg Gln Gln Trp Ser Gly Pro Gly Thr Thr Lys Arg
1               5                  10                  15

Phe Pro Glu Thr Val Leu Ala Arg Cys Val Lys Tyr Thr Glu Ile His
            20                  25                  30

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

Gly Ala Phe Ile Ser Lys His Pro Cys Asn Ile Thr Glu Glu Asp Tyr
    50                  55                  60

Gln Pro Leu Met Lys Leu Gly Thr Gln Thr Val Pro Cys Asn Lys Ile
65                  70                  75                  80

Leu Leu Trp Ser Arg Ile Lys Asp Leu Ala His Gln Phe Thr Gln Val
                85                  90                  95

Gln Arg Asp Met Phe Thr Leu Glu Asp Thr Leu Leu Gly Tyr Leu Ala
            100                 105                 110

Asp Asp Leu Thr Trp Cys Gly Glu Phe Asn Thr Ser Lys Ile Asn Tyr
        115                 120                 125

Gln Ser Cys Pro Asp Trp Arg Lys Asp Cys Ser Asn Asn Pro Val Ser
    130                 135                 140

Val Phe Trp Lys Thr Val Ser Arg Arg Phe Ala Glu Ala Ala Cys Asp
145                 150                 155                 160

Val Val His Val Met Leu Asn Gly Ser Arg Ser Lys Ile Phe Asp Lys
                165                 170                 175

Asn Ser Thr Phe Gly Ser Val Glu Val His Asn Leu Gln Pro Glu Lys
            180                 185                 190

Val Gln Thr Leu Glu Ala Trp Val Ile His Gly Gly Arg Glu Asp Ser
        195                 200                 205
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Arg Asp Leu Cys Gln Asp Pro Thr Ile Lys Glu Leu Glu Ser Ile Ile
210 215 220

Ser Lys Arg Asn Ile Gln Phe Ser Cys Lys Asn Ile Tyr Arg Pro Asp
225 230 235 240

Lys Phe Leu Gln Cys Val Lys Asn Pro Glu Asp Ser Ser Cys Thr Ser
245 250 255

Glu Ile

<210> 133
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 133

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 134
<211> 18
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 134

Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15

Lys Gly

<210> 135
<211> 14
<212> PRT
<213> 人工序列

<220>

<223> 帶正電荷的scFv接頭

<400> 135

Ile Arg Pro Arg Ala Ile Gly Gly Ser Lys Pro Arg Val Ala
1 5 10

<210> 136
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 136

Gly Lys Gly Gly Ser Gly Lys Gly Gly Ser Gly Lys Gly Gly Ser
1 5 10 15

<210> 137
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 137

Gly Gly Lys Gly Ser Gly Gly Lys Gly Ser Gly Gly Lys Gly Ser
1 5 10 15

<210> 138
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 138

Gly Gly Gly Lys Ser Gly Gly Gly Lys Ser Gly Gly Gly Lys Ser
1 5 10 15

<210> 139
<211> 15
<212> PRT
<213> 人工序列

<220>

<223> 帶正電荷的scFv接頭

<400> 139

Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser
1 5 10 15

<210> 140
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 140

Gly Gly Gly Lys Ser Gly Gly Lys Gly Ser Gly Lys Gly Gly Ser
1 5 10 15

<210> 141
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 141

Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser
1 5 10 15

<210> 142
<211> 20
<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 142

Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly
1 5 10 15

Lys Pro Gly Ser
20

<210> 143
<211> 20

<212> PRT
<213> 人工序列

<220>
<223> 帶正電荷的scFv接頭

<400> 143

Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly
1 5 10 15

Lys Gly Lys Ser
20

<210> 144
<211> 20
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 144

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> 145
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 145

Ser Thr Ala Gly Asp Thr His Leu Gly Gly Glu Asp Phe Asp
1 5 10

<210> 146
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 146

Gly Glu Gly Gly Ser Gly Glu Gly Gly Ser Gly Glu Gly Gly Ser
1 5 10 15

<210> 147
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 147

Gly Gly Glu Gly Ser Gly Gly Glu Gly Ser Gly Gly Glu Gly Ser
1 5 10 15

<210> 148
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 148

Gly Gly Gly Glu Ser Gly Gly Gly Glu Ser Gly Gly Gly Glu Ser
1 5 10 15

<210> 149
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 149

Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser
1 5 10 15

<210> 150
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 150

Gly Gly Gly Glu Ser Gly Gly Glu Gly Ser Gly Glu Gly Gly Ser
1 5 10 15

<210> 151
<211> 20
<212> PRT
<213> 人工序列

<220>
<223> 帶負電荷的scFv接頭

<400> 151

Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser Gly Glu Gly Glu Ser Gly
1 5 10 15

Glu Gly Glu Ser
20

<210> 152
<211> 15
<212> PRT
<213> 人工序列

<220>
<223> scFv接頭

<400> 152

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 153
<211> 20
<212> PRT
<213> 人工序列

<220>
<223> scFv接頭

<400> 153

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> 154
<211> 18
<212> PRT
<213> 人工序列

<220>
<223> scFv接頭

<400> 154

Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15

Lys Gly

<210> 155
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> scFv接頭

<400> 155

Pro Arg Gly Ala Ser Lys Ser Gly Ser Ala Ser Gln Thr Gly Ser Ala
1 5 10 15

Pro Gly Ser

<210> 156
<211> 19
<212> PRT
<213> 人工序列

<220>
<223> scFv接頭

<400> 156

Gly Thr Ala Ala Ala Gly Ala Gly Ala Ala Gly Gly Ala Ala Ala Gly
1 5 10 15

Ala Ala Gly

<210> 157
<211> 19

<212> PRT
<213> 人工序列

<220>
<223> scFv接頭

<400> 157

Gly Thr Ser Gly Ser Ser Gly Ser Gly Ser Gly Gly Ser Gly Ser Gly
1 5 10 15

Gly Gly Gly

<210> 158
<211> 20
<212> PRT
<213> 人工序列

<220>
<223> scFv接頭

<400> 158

Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly
1 5 10 15

Lys Pro Gly Ser
20

<210> 159
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP14419抗CD38

<400> 159

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 160
<211> 714
<212> PRT
<213> 人工序列

<220>
<223> XENP14419抗CD38

<400> 160

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly
565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

<210> 161
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP14419抗CD38

<400> 161

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 162
<211> 585
<212> PRT
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<220>
<223> XENP14420抗CD38

<400> 162

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

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His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Leu Val Thr Val Ser Ser
            580                 585
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<210> 163
<211> 569
<212> PRT
<213> 人工序列

<220>
<223> XENP14420抗CD38

<400> 163

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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 Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140
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Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ala Val Val
450 455 460

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

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
485 490 495

Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly
500 505 510

Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser Leu
515 520 525

Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp
530 535 540

Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val Phe
545 550 555 560

Gly Gly Gly Thr Lys Leu Thr Val Leu
565

<210> 164
<211> 214
<212> PRT
<213> 人工序列

〈220〉
〈223〉 XENP14420抗CD38

〈400〉 164

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
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Phe Asn Arg Gly Glu Cys
210

<210> 165
<211> 445
<212> PRT
<213> 人工序列

<220>
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<400> 165

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 166
<211> 718
<212> PRT
<213> 人工序列

<220>
<223> XENP14421抗CD38

<400> 166

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 167
<211> 214
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<213> 人工序列

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<223> XENP14421抗CD38

<400> 167

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 168
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> XENP14422抗CD38

〈400〉 168

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Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1               5                  10                  15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            20                  25                  30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        35                  40                  45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
    50                  55                  60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65                  70                  75                  80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                85                  90                  95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
            100                 105                 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
        115                 120                 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
    130                 135                 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145                 150                 155                 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
                165                 170                 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
            180                 185                 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
        195                 200                 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
    210                 215                 220
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Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 169
<211> 718
<212> PRT
<213> 人工序列

<220>
<223> XENP14422抗CD38

<400> 169

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 170
<211> 214
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<213> 人工序列

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<400> 170

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 171
<211> 589
<212> PRT
<213> 人工序列

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<223> XENP14423抗CD38

<400> 171

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His Thr
355 360 365

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
370 375 380

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
385 390 395 400

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
405 410 415

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
420 425 430

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
435 440 445

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
450 455 460

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
465 470 475 480

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
485 490 495

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
500 505 510

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
515 520 525

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
530 535 540

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
545 550 555 560

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
565 570 575

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
580 585

<210> 172
<211> 573
<212> PRT
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<400> 172

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr
225 230 235 240

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly
245 250 255

Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly
260 265 270

Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly
275 280 285

Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
290 295 300

Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
305 310 315 320

Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
325 330 335

Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His Thr
340 345 350

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
355 360 365

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
370 375 380

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
385 390 395 400

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
405 410 415

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
420 425 430

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
435 440 445

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
450 455 460

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
485 490 495

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
500 505 510

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
515 520 525

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
530 535 540

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
545 550 555 560

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
565 570

<210> 173
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<212> PRT
<213> 人工序列

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<400> 173

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 174
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> XENP15427抗CD38

<400> 174

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 175
<211> 714
<212> PRT
<213> 人工序列

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<223> XENP15427抗CD38

<400> 175

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Ser Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly
565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

<210> 176
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP15427抗CD38

<400> 176

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 177
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> XENP15428抗CD38

<400> 177

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 178
<211> 714
<212> PRT
<213> 人工序列

<220>
<223> XENP15428抗CD38

<400> 178

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Asp Tyr Trp Gly
565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

<210> 179
<211> 214
<212> PRT
<213> 人工序列

<220>

<223> XENP15428抗CD38

<400> 179

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
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Phe Asn Arg Gly Glu Cys
210

<210> 180
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> XENP15429抗CD38

<400> 180

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 181
<211> 714
<212> PRT
<213> 人工序列

<220>
<223> XENP15429抗CD38

<400> 181

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

```
His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
            580                 585                 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
        595                 600                 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
    610                 615                 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625                 630                 635                 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
                645                 650                 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
            660                 665                 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
        675                 680                 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
    690                 695                 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705                 710
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<210> 182
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP15429抗CD38

<400> 182

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30
```

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 183
<211> 231
<212> PRT
<213> 人工序列

<220>

<223> XENP15430抗CD38

<400> 183

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 184
<211> 718
<212> PRT
<213> 人工序列

<220>
<223> XENP15430抗CD38

<400> 184

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 185
<211> 214
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<213> 人工序列

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<400> 185

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 186
<211> 231
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<400> 186

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 187
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<212> PRT
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<400> 187

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 188
<211> 214
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<213> 人工序列

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<400> 188

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 189
<211> 231
<212> PRT
<213> 人工序列

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<223> XENP15432抗CD38

<400> 189

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 190
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<212> PRT
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<400> 190

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

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
    210                 215                 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225                 230                 235                 240
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Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 191
<211> 214
<212> PRT
<213> 人工序列

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<223> XENP15432抗CD38

<400> 191

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 192
<211> 445
<212> PRT
<213> 人工序列

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<223> XENP15433抗CD38

<400> 192

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 193
<211> 714
<212> PRT
<213> 人工序列

<220>
<223> XENP15433抗CD38

<400> 193

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Ser Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly
565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

<210> 194
<211> 214
<212> PRT
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〈223〉 XENP15433抗CD38

〈400〉 194

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
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Phe Asn Arg Gly Glu Cys
210

<210> 195
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP15434抗CD38

<400> 195

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
                405                 410                 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445
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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 Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125
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Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Asp Tyr Trp Gly
565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

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Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 198
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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 Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220
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Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

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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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys
355 360 365

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

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

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

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly
435 440 445

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu
450 455 460

Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu
465 470 475 480

Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp
485 490 495

Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg
500 505 510

Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly
515 520 525

Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu Gln
530 535 540

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg
545 550 555 560

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly
565 570 575

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly Lys
580 585 590

Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala Val
595 600 605

Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr
610 615 620

Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala
625 630 635 640

Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile Gly
645 650 655

Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
660 665 670

Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro Glu
675 680 685

Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp Val
690 695 700

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
705 710

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Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 201
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<400> 201

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

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<400> 202

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

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
    210                 215                 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225                 230                 235                 240
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Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

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<400> 203

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 204
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<400> 204

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 205
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<400> 205

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 206
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP15437抗CD38

<400> 206

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
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Phe Asn Arg Gly Glu Cys
210

<210> 207
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> XENP15438抗CD38

<400> 207

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 208
<211> 718
<212> PRT
<213> 人工序列

<220>
<223> XENP15438抗CD38

<400> 208

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

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

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
225 230 235 240

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
245 250 255

Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
260 265 270

Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
275 280 285

Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp
290 295 300

Asp Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
305 310 315 320

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser
325 330 335

Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
340 345 350

Ser Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
355 360 365

Ser Gly Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu
370 375 380

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
385 390 395 400

Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro
405 410 415

Gly Lys Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro
420 425 430

Gly Val Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
435 440 445

Leu Thr Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys
450 455 460

Ala Leu Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu
465 470 475 480

Thr Val Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
500 505 510

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
515 520 525

Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val
530 535 540

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
545 550 555 560

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
565 570 575

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
580 585 590

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
595 600 605

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
610 615 620

Ser Arg Glu Gln Met Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val
625 630 635 640

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
645 650 655

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
660 665 670

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
675 680 685

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
690 695 700

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 209
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> XENP15438抗CD38

<400> 209

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 210
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

〈400〉 210

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 211
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 211

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

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

<220>
<223> 抗CD3序列

<400> 212

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 213
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 213

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

〈210〉 214
〈211〉 262
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 214

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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 Ser Thr Tyr
            20                  25                  30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
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Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 215
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 215

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 216
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 216

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 217
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 217

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 218
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 218

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 219
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 219

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 220
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 220

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 221
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 221

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 222
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 222

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 223
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 223

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 224
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 224

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 225
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 225

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 226
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 226

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

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Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
                245                 250                 255

His His His His His His
            260
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<210> 227
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 227

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 228
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 228

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 229
<211> 109
<212> PRT
<213> 人工序列

<220>

<223> 抗CD3序列

<400> 229

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 230
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 230

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Pro Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 231
<211> 254

〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 231

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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 Ser Thr Tyr
            20                  25                  30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Pro Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
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Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 232
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 232

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Pro Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 233
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 233

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 234
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 234

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 235
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 235

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 236
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 236

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

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

<210> 237
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 237

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 238
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

〈400〉 238

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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 Ser Thr Tyr
            20                  25                  30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
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Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 239
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 239

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 240
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 240

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

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

<210> 241
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 241

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

〈210〉 242
〈211〉 262
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 242

```
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 Ser Thr Tyr
            20                  25                  30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
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Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 243
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 243

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 244
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 244

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 245
<211> 109
<212> PRT
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<220>
<223> 抗CD3序列

<400> 245

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 246
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 246

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 247
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 247

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 248
<211> 125
<212> PRT
<213> 人工序列

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<223> 抗CD3序列

<400> 248

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 249
<211> 109
<212> PRT
<213> 人工序列

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<223> 抗CD3序列

<400> 249

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 250
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 250

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Glu Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

〈210〉 251
〈211〉 254
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 251

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Glu Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 252
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 252

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Glu Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 253
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 253

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 254
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 254

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

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Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225                 230                 235                 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
                245                 250                 255

His His His His His His
            260
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<210> 255
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 255

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 256
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 256

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 257
<211> 109
<212> PRT
<213> 人工序列

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<223> 抗CD3序列

<400> 257

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 258
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 258

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 259
<211> 254

<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 259

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 260
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 260

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

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

<210> 261
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 261

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 262
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 262

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 263
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 263

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 264
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 264

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110

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

<210> 265
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 265

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 266
<211> 262
<212> PRT
<213> 人工序列

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<223> 抗CD3序列

〈400〉 266

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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 Ser Thr Tyr
            20                  25                  30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
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Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 267
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 267

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 268
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 268

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 269
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 269

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

〈210〉 270
〈211〉 262
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 270

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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 Ser Thr Tyr
            20                  25                  30

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

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
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Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 271
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 271

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 272
<211> 125
<212> PRT
<213> 人工序列

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<223> 抗CD3序列

<400> 272

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 273
<211> 109
<212> PRT
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<223> 抗CD3序列

<400> 273

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 274
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 274

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 275
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 275

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 276
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 276

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 277
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 277

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 278
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 278

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 279
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 279

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 280
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 280

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 281
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 281

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 282
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 282

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

〈210〉 283
〈211〉 254
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 283

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 284
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 284

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
100 105 110

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

<210> 285
<211> 109
<212> PRT
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<223> 抗CD3序列

<400> 285

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 286
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 286

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 287
<211> 254

<212> PRT
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<220>
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<400> 287

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 288
<211> 125
<212> PRT
<213> 人工序列

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<400> 288

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Asn Tyr Val Ser Trp Phe
100 105 110

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

<210> 289
<211> 109
<212> PRT
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<400> 289

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 290
<211> 262
<212> PRT
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<400> 290

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 291
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 291

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 292
<211> 125
<212> PRT
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<400> 292

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

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

<210> 293
<211> 109
<212> PRT
<213> 人工序列

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<223> 抗CD3序列

<400> 293

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 294
<211> 262
<212> PRT
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<220>
<223> 抗CD3序列

〈400〉 294

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 295
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 295

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 296
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 296

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Gln Tyr Val Ser Trp Phe
100 105 110

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

<210> 297
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 297

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

〈210〉 298
〈211〉 262
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 298

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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 Ser Thr Tyr
            20                  25                  30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
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Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 299
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 299

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 300
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 300

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 301
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 301

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 302
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 302

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 303
<211> 254
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<220>
<223> 抗CD3序列

<400> 303

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 304
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 304

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Ala Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 305
<211> 109
<212> PRT
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<400> 305

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 306
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 306

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

<210> 307
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 307

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 308
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 308

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 309
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 309

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 310
<211> 262
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 310

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser
245 250 255

His His His His His His
260

〈210〉 311
〈211〉 254
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 311

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 312
<211> 125
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 312

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

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

<210> 313
<211> 109
<212> PRT
<213> 人工序列

<220>

<223> 抗CD3序列

<400> 313

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 314
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 314

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 Ser Tyr Ser
20 25 30

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

Ser Glu Ile Asn Pro Gln Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 315
<211> 485
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 315

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 316
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 316

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 317
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 317

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 318
<211> 485
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 318

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 Ser Thr Tyr
20 25 30

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

Gly Arg Ile Arg Ser Lys Ala 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 319
<211> 214
<212> PRT
<213> 人工序列

<220>

〈223〉 抗CD3序列

〈400〉 319

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
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Phe Asn Arg Gly Glu Cys
210

<210> 320
<211> 445
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 320

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 Asp Phe Ser Arg Ser
20 25 30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

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

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

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

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

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

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

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

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

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

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

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 321
<211> 485
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 321

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 Ser Thr Tyr
20 25 30

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

Gly 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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

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

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

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 322
<211> 214
<212> PRT
<213> 人工序列

<220>
<223> 抗CD3序列

<400> 322

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

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

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

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

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

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

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

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

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<400> 323

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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 Asp Phe Ser Arg Ser
            20                  25                  30

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

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
        195                 200                 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220
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Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

〈210〉 324
〈211〉 485
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 抗CD3序列

〈400〉 324

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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 Ser Thr Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Gly 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190
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Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<400> 325

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 326
<211> 445
<212> PRT
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<400> 326

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 Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 327
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<400> 327

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 Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

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<400> 328

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

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<400> 329

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 Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 330
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<400> 330

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 Ser Thr Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 331
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〈223〉 抗CD3序列

〈400〉 331

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Asp Ile Val 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 Asn Val Asp Thr Asn
            20                  25                  30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
        35                  40                  45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
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Phe Asn Arg Gly Glu Cys
210

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Gly Ser Gly Gly Ser
1 5

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Gly Gly Gly Gly Ser
1 5

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<223> 有用的接頭

<400> 334

Gly Gly Gly Ser
1

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<400> 335

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 Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Arg Ser Lys Ala 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Glu Pro
245 250 255

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
260 265 270

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
275 280 285

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
290 295 300

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
305 310 315 320

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
325 330 335

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
340 345 350

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
355 360 365

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
370 375 380

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn Gln
385 390 395 400

Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
405 410 415

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
420 425 430

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
435 440 445

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
450 455 460

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
465 470 475 480

Leu Ser Pro Gly Lys
485

<210> 336
<211> 214
<212> PRT
<213> 人工序列

<220>
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<400> 336

Asp Ile Val 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 Asn Val Asp Thr Trp
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 337
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<220>
<223> XmAb18968 (412220) HC

<400> 337

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 Asp Phe Ser Arg Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala Thr 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 Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asp Thr
195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
210 215 220

Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu
405 410 415

Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 338
<211> 1449
<212> DNA
<213> 人工序列

<220>
<223> XmAb18968 (412220) ScFv-Fc

<400> 338
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gctgccagcg gattcacttt tagcacatat gcgatgaatt gggtcagaca ggctccaggc 120

aaagggctgg agtgggtggg acggatcaga agtaagtata ataattatgc cacctattat 180

gctgactccg tgaagggcag attcactatt tctagggacg attccaagaa cactctctac 240

ctgcaaatga attccctgag ggctgaggac accgcggtct actattgcgt gcggcacggc 300

aacttcggcg actcttacgt gtcttggttc gactattggg ggcaagggac tctcgtgaca 360

gtgagctccg gtaagcctgg tagcgggaaa ccaggcagcg gaaagcctgg cagcggtaaa 420

ccaggctccc aggccgtggt tacacaggaa ccctccttga ctgtgtcacc tgggggcaca 480

gtcactctta cctgcggcag ttccactggg gccgtaacaa cctctaacta tgcgaattgg 540

gttcagcaga agccaggtaa gagccctagg gggttgatag gtggaactaa taaacgggcc 600

cccggggtgc cagcccgctt cagtgggagt ttgctggggg gaaaggccgc cctcaccatc 660

tcaggggctc aacccgagga tgaggcagac tattactgcg ccctgtggta ctccaatcac 720

tgggtcttcg gcgggggtac aaagctgact gtgctggagc ccaaatctag cgacaaaact 780

cacacatgcc caccgtgccc ggcgcctcct gttgctggac cgtcagtctt cctcttcccc 840

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 900

gacgtgaagc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 960

cataatgcca agacaaagcc gcgggaggag cagtacaaca gcacgtaccg tgtggtcagc 1020

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 1080

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1140

gaaccacagg tgtatacccct gcccccatcc cgggagcaga tgaccaagaa ccaggtaaag 1200

ttgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1260

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1320

ttcctctata gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1380

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1440

ccgggtaaa 1449

<210> 339
<211> 642
<212> DNA
<213> 人工序列

<220>
<223> XmAb18968 (412220) LC

<400> 339
gacatcgtga tgacacagag tcccagctct ctctcagcga gcgttggcga tagggtgact 60

ataacatgca gagcatccca aaacgtggat acatgggtgg cttggtacca acagaagcca 120

ggtcagtctc ccaaggccct gatttatagc gcatcctatc gctacagtgg tgttcccgac 180

aggtttaccg ggtctggcag tggcaccgat tttaccctga ctatctcttc cctgcaaccc 240

gaggacttcg caacatattt ctgccagcag tatgattcct acccccctgac cttcggcgga 300

ggcaccaaac tcgaaattaa gcgtacggtg gccgcaccat ctgtcttcat cttcccgcca 360

tctgatgagc agttgaaatc tggaactgcc tctgttgtgt gcctgctgaa taacttctat 420

cccagagagg ccaaagtaca gtggaaggtg gataacgccc tccaatcggg taactcccag 480

gagagtgtca cagagcagga cagcaaggac agcacctaca gcctcagcag caccctgacg 540

ctgagcaaag cagactacga gaaacacaaa gtctacgcct gcgaagtcac ccatcagggc 600

ctgagctcgc ccgtcacaaa gagcttcaac aggggagagt gt 642

<210> 340
<211> 1329
<212> DNA
<213> 人工序列

<220>
<223> XmAb18968 (412220) LC

<400> 340
cagttggtgg agagcggggg cggcctcgtc cagccggggg gctcactgag gctctcctgt 60

gcagccagcg gattcgactt cagccgatca tggatgaatt gggtgagaca ggcacctggt 120

aagggccttg agtgggtctc tgagattaat ccagactcta gtaccattaa ttacgctact 180

tcagtcaagg gcaggtttac gatctcaaga gacaacagca agaatacgct gtacctccaa 240

atgaactctc ttagggctga agatactgca gtgtactact gtgcacgata tgggaactgg 300

tttccgtatt ggggccaggg cacgttggtg accgtgtctt ccgcaagcac taagggccca 360

tcggtcttcc ccctggcacc ctcctccaag agcacctctg ggggcacagc ggccctgggc 420

tgcctggtca aggactactt ccccgaaccg gtgacggtgt cgtggaactc aggcgccctg 480

accagcggcg tgcacacctt cccggctgtc ctacagtcct caggactcta ctccctcagc 540

agcgtggtga ccgtgccctc cagcagcttg ggcacccaga cctacatctg caacgtgaat 600

cacaagccca gcgacaccaa ggtggacaag aaagttgagc ccaaatcttg tgacaaaact 660

cacacatgcc caccgtgccc ggcgcctcct gttgctggac cgtcagtctt cctcttcccc 720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 780

gacgtgaagc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 840

cataatgcca agacaaagcc gcgggaggag gagtacaaca gcacgtaccg tgtggtcagc 900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtataccct gcccccatcc cgggaggaga tgaccaagaa ccaggtaagc 1080

ttgacctgcg acgtcagcgg cttctatccc agcgacatcg ccgtggagtg ggagagcgac 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctata gcaagctcac cgtggacaag agcaggtggg agcaggggga cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> 341
<211> 504
<212> PRT
<213> 人工序列

<220>
<223> XmAb18968 (412220) ScFv-Fc

<400> 341

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
85 90 95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val
115 120 125

Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
130 135 140

Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly
145 150 155 160

Lys Pro Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val
165 170 175

Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala
180 185 190

Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys
195 200 205

Ser Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val
210 215 220

Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr
225 230 235 240

Ile Ser Gly Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu
245 250 255

Trp Tyr Ser Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val
260 265 270

Leu Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro
275 280 285

Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
290 295 300

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
305 310 315 320

Val Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
325 330 335

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
340 345 350

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
355 360 365

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
370 375 380

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
385 390 395 400

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr
405 410 415

Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
420 425 430

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
435 440 445

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
450 455 460

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
465 470 475 480

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
485 490 495

Ser Leu Ser Leu Ser Pro Gly Lys
500

<210> 342
<211> 233
<212> PRT
<213> 人工序列

<220>
<223> XmAb18968 (412220) LC

<400> 342

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
20 25 30

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Val
35 40 45

Asp Thr Trp Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys
50 55 60

Ala Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg
65 70 75 80

Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
85 90 95

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Tyr Asp Ser
100 105 110

Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr
115 120 125

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
130 135 140

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
145 150 155 160

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
165 170 175

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
180 185 190

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
195 200 205

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
210 215 220

Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230

<210> 343
<211> 464
<212> PRT
<213> 人工序列

<220>
<223> XmAb18968 (412220) HC

<400> 343

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe
35 40 45

Ser Arg Ser Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Glu Ile Asn Pro Asp Ser Ser Thr Ile Asn Tyr Ala
65 70 75 80

Thr Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Tyr Gly Asn Trp Phe Pro Tyr Trp Gly Gln Gly
115 120 125

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
130 135 140

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
145 150 155 160

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
165 170 175

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
180 185 190

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
195 200 205

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
210 215 220

Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
225 230 235 240

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
245 250 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
260 265 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu Asp Pro
275 280 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
290 295 300

Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser Thr Tyr Arg Val Val
305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
405 410 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
420 425 430

Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser Val Met His Glu Ala
435 440 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455 460

<210> 344
<211> 1512
<212> DNA
<213> 人工序列

<220>
<223> XmAb18968 (412220) ScFv-Fc

<400> 344
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt acactccgaa 60

gttcagctcg tcgagtctgg aggtggcctc gtccagccag gcggtagtct gaggctctca 120

tgcgctgcca gcggattcac ttttagcaca tatgcgatga attgggtcag acaggctcca 180

ggcaaagggc tggagtgggt gggacggatc agaagtaagt ataataatta tgccacctat 240

tatgctgact ccgtgaaggg cagattcact atttctaggg acgattccaa gaacactctc 300

tacctgcaaa tgaattccct gagggctgag gacaccgcgg tctactattg cgtgcggcac 360

ggcaacttcg gcgactctta cgtgtcttgg ttcgactatt gggggcaagg gactctcgtg 420

acagtgagct ccggtaagcc tggtagcggg aaaccaggca gcggaaagcc tggcagcggt 480

aaaccaggct cccaggccgt ggttacacag gaaccctcct tgactgtgtc acctgggggc 540

acagtcactc ttacctgcgg cagttccact ggggccgtaa caacctctaa ctatgcgaat 600

tgggttcagc agaagccagg taagagccct agggggttga taggtggaac taataaacgg 660

gccccccgggg tgccagcccg cttcagtggg agtttgctgg ggggaaaggc cgccctcacc 720

atctcagggg ctcaacccga ggatgaggca gactattact gcgccctgtg gtactccaat 780

cactgggtct tcggcggggg tacaaagctg actgtgctgg agcccaaatc tagcgacaaa 840

actcacacat gcccaccgtg cccggcgcct cctgttgctg gaccgtcagt cttcctcttc 900

cccccaaaac ccaaggacac cctcatgatc tcccggaccc ctgaggtcac atgcgtggtg 960

gtggacgtga agcacgaaga ccctgaggtc aagttcaact ggtacgtgga cggcgtggag 1020

gtgcataatg ccaagacaaa gccgcgggag gagcagtaca acagcacgta ccgtgtggtc 1080

agcgtcctca ccgtcctgca ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc 1140

tccaacaaag ccctcccagc ccccatcgag aaaaccatct ccaaagccaa agggcagccc 1200

cgagaaccac aggtgtatac cctgccccca tcccgggagc agatgaccaa gaaccaggta 1260

aagttgacct gcctggtcaa aggcttctat cccagcgaca tcgccgtgga gtgggagagc 1320

aatgggcagc cggagaacaa ctacaagacc acgcctcccg tgctggactc cgacggctcc 1380

ttcttcctct atagcaagct caccgtggac aagagcaggt ggcagcaggg gaacgtcttc 1440

tcatgctccg tgatgcatga ggctctgcac aaccactaca cgcagaagag cctctccctg 1500

tctccgggta aa 1512

<210> 345
<211> 699
<212> DNA
<213> 人工序列

<220>
<223> XmAb18968 (412220) LC

<400> 345
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt ccacagcgac 60

atcgtgatga cacagagtcc cagctctctc tcagcgagcg ttggcgatag ggtgactata 120

acatgcagag catcccaaaa cgtggataca tgggtggctt ggtaccaaca gaagccaggt 180

cagtctccca aggccctgat ttatagcgca tcctatcgct acagtggtgt tcccgacagg 240

tttaccgggt ctggcagtgg caccgatttt accctgacta tctcttccct gcaacccgag 300

gacttcgcaa catatttctg ccagcagtat gattcctacc ccctgacctt cggcggaggc 360

accaaactcg aaattaagcg tacggtggcc gcaccatctg tcttcatctt cccgccatct 420

gatgagcagt tgaaatctgg aactgcctct gttgtgtgcc tgctgaataa cttctatccc 480

agagaggcca aagtacagtg gaaggtggat aacgccctcc aatcgggtaa ctcccaggag 540

agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg 600

agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg 660

agctcgcccg tcacaaagag cttcaacagg ggagagtgt 699

<210> 346
<211> 1392
<212> DNA
<213> 人工序列

<220>

<223> XmAb18968 (412220) LC

<400> 346
atgggatgga gctgtatcat cctcttcttg gtagcaacag ctacaggtgt ccactccgag 60

gttcagttgg tggagagcgg gggcggcctc gtccagccgg ggggctcact gaggctctcc 120

tgtgcagcca gcggattcga cttcagccga tcatggatga attgggtgag acaggcacct 180

ggtaagggcc ttgagtgggt ctctgagatt aatccagact ctagtaccat taattacgct 240

acttcagtca agggcaggtt tacgatctca agagacaaca gcaagaatac gctgtacctc 300

caaatgaact ctcttagggc tgaagatact gcagtgtact actgtgcacg atatgggaac 360

tggtttccgt attggggcca gggcacgttg gtgaccgtgt cttccgcaag cactaagggc 420

ccatcggtct tccccctggc accctcctcc aagagcacct ctgggggcac agcggccctg 480

ggctgcctgg tcaaggacta cttccccgaa ccggtgacgg tgtcgtggaa ctcaggcgcc 540

ctgaccagcg gcgtgcacac cttcccggct gtcctacagt cctcaggact ctactccctc 600

agcagcgtgg tgaccgtgcc ctccagcagc ttgggcaccc agacctacat ctgcaacgtg 660

aatcacaagc ccagcgacac caaggtggac aagaaagttg agcccaaatc ttgtgacaaa 720

actcacacat gcccaccgtg cccggcgcct cctgttgctg gaccgtcagt cttcctcttc 780

cccccaaaac ccaaggacac cctcatgatc tcccggaccc ctgaggtcac atgcgtggtg 840

gtggacgtga agcacgaaga ccctgaggtc aagttcaact ggtacgtgga cggcgtggag 900

gtgcataatg ccaagacaaa gccgcgggag gaggagtaca acagcacgta ccgtgtggtc 960

agcgtcctca ccgtcctgca ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc 1020

tccaacaaag ccctcccagc ccccatcgag aaaaccatct ccaaagccaa agggcagccc 1080

cgagaaccac aggtgtatac cctgccccca tcccgggagg agatgaccaa gaaccaggta 1140

agcttgacct gcgacgtcag cggcttctat cccagcgaca tcgccgtgga gtgggagagc 1200

gacgggcagc cggagaacaa ctacaagacc acgcctcccg tgctggactc cgacggctcc 1260

ttcttcctct atagcaagct caccgtggac aagagcaggt gggagcaggg ggacgtcttc 1320

tcatgctccg tgatgcatga ggctctgcac aaccactaca cgcagaagag cctctccctg 1380

tctccgggta aa 1392

<210> 347
<211> 329
<212> PRT
<213> 人工序列

〈220〉
〈223〉 Fab側HC（開瓶器主鏈1）

〈400〉 347

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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 Asp 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 Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        115                 120                 125

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    130                 135                 140

Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145                 150                 155                 160

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                165                 170                 175

Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            180                 185                 190

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        195                 200                 205
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Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
225 230 235 240

Thr Lys Asn Gln Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro
245 250 255

Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn
260 265 270

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
275 280 285

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val
290 295 300

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305 310 315 320

Lys Ser Leu Ser Leu Ser Pro Gly Lys
325

<210> 348
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> scFv HC（開瓶器主鏈1）

<400> 348

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys
130 135 140

Asn Gln Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 349
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 恒定LC（開瓶器主鏈1）

<400> 349

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 350
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> scFv HC（開瓶器主鏈2）

<400> 350

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 351
<211> 329
<212> PRT
<213> 人工序列

<220>
<223> Fab側HC（開瓶器主鏈3）

<400> 351

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 Asp 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 Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
115 120 125

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140

Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175

Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
225 230 235 240

Thr Lys Asn Gln Val Ser Leu Thr Cys Glu Val Ser Gly Phe Tyr Pro
245 250 255

Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn
260 265 270

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
275 280 285

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val
290 295 300

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305 310 315 320

Lys Ser Leu Ser Leu Ser Pro Gly Lys
325

<210> 352
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> scFv HC（開瓶器主鏈3）

<400> 352

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 353
<211> 330
<212> PRT
<213> 人工序列

<220>
<223> Fab側HC（開瓶器主鏈4）

<400> 353

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 Asp 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 Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
115 120 125

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140

Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175

Glu Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
225 230 235 240

Thr Glu Asn Glu Val Ser Leu Thr Cys Leu Val Lys Ser Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Glu Val Asp Lys Ser Arg Trp Glu Gln Gly Asp
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 354
<211> 231
<212> PRT
<213> 人工序列

<220>
<223> scFv HC（開瓶器主鏈4）

<400> 354

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
20 25 30

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
35 40 45

Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
50 55 60

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
65 70 75 80

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
85 90 95

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
100 105 110

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
115 120 125

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
130 135 140

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
145 150 155 160

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
165 170 175

Thr Thr Pro Pro Val Leu Asp Ser Lys Gly Ser Phe Phe Leu Tyr Ser
180 185 190

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
195 200 205

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
210 215 220

Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 355
<211> 107
<212> PRT
<213> 人工序列

<220>
<223> 可變輕 (vl) 結構域 (H1L1) CD38臂

<400> 355

Asp Ile Val 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 Asn Val Asp Thr Asn
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr 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 Phe Cys Gln Gln Tyr Asp Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 356
<211> 339
<212> PRT
<213> 智人

<400> 356

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
1 5 10 15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
20 25 30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
35 40 45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
50 55 60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
65 70 75 80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
85 90 95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
100 105 110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
115 120 125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
130 135 140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
145 150 155 160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
165 170 175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
180 185 190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
195 200 205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
210 215 220

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
225 230 235 240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
245 250 255

Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
260 265 270

Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
275 280 285

Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
290 295 300

Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
305 310 315 320

Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
325 330 335

Ser Gln Leu

<210> 357
<211> 10
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 357

Arg Ala Ser Ser Ser Val Ser Tyr Met His
1 5 10

<210> 358
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 358

Ser Thr Ser Asn Leu Ala Ser
1 5

<210> 359
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 359

Gln Gln Arg Arg Ser Phe Pro Tyr Thr
1 5

<210> 360
<211> 5
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 360

Thr Tyr Trp Ile Glu
1 5

<210> 361
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 361

Glu Ile Leu Pro Gly Ser Gly Asn Thr Asp Phe Asn Glu Lys Phe Gln
1 5 10 15

Gly

<210> 362
<211> 12
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 362

Trp Gly Tyr Tyr Gly Thr Arg Gly Tyr Phe Asn Val
1 5 10

<210> 363
<211> 17
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 363

Glu Ile Leu Pro Gly Ser Gly Gln Thr Asp Phe Asn Glu Lys Phe Gln
1 5 10 15

Gly

<210> 364
<211> 232
<212> PRT
<213> 人工序列

〈220〉
〈223〉 合成多肽

〈400〉 364

```
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1               5                  10                  15

Val His Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
            20                  25                  30

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val
        35                  40                  45

Ser Tyr Met His Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu
    50                  55                  60

Leu Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
65                  70                  75                  80

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
                85                  90                  95

Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Arg Ser Phe
            100                 105                 110

Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val
        115                 120                 125

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
    130                 135                 140

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
145                 150                 155                 160

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
                165                 170                 175

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
            180                 185                 190

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
        195                 200                 205
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Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
210 215 220

Lys Ser Phe Asn Arg Gly Glu Cys
225 230

<210> 365
<211> 469
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 365

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Ser Thr Tyr Trp Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
50 55 60

Glu Trp Met Gly Glu Ile Leu Pro Gly Ser Gly Asn Thr Asp Phe Asn
65 70 75 80

Glu Lys Phe Gln Gly Arg Val Thr Phe Thr Ala Asp Thr Ser Ser Asp
85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Thr Arg Trp Gly Tyr Tyr Gly Thr Arg Gly Tyr Phe Asn
115 120 125

Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly

145 150 155 160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
210 215 220

Val Asn His Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro
225 230 235 240

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
245 250 255

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
260 265 270

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
275 280 285

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
290 295 300

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser
305 310 315 320

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
325 330 335

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
340 345 350

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
355 360 365

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln

370 375 380

Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala
385 390 395 400

Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
405 410 415

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
420 425 430

Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser
435 440 445

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
450 455 460

Leu Ser Pro Gly Lys
465

<210> 366
<211> 742
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 366

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Ser Thr Tyr Trp Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
50 55 60

Glu Trp Met Gly Glu Ile Leu Pro Gly Ser Gly Asn Thr Asp Phe Asn
65 70 75 80

Glu Lys Phe Gln Gly Arg Val Thr Phe Thr Ala Asp Thr Ser Ser Asp
85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Thr Arg Trp Gly Tyr Tyr Gly Thr Arg Gly Tyr Phe Asn
115 120 125

Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
145 150 155 160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
210 215 220

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
225 230 235 240

Lys Ser Cys Gly Gly Gly Gly 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 Arg
260 265 270

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn
275 280 285

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly 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

Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu
325 330 335

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val
340 345 350

Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp
355 360 365

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly
370 375 380

Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala
385 390 395 400

Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val
405 410 415

Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr
420 425 430

Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile
435 440 445

Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly
450 455 460

Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro
465 470 475 480

Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp
485 490 495

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Ser
500 505 510

Gly Gly Gly Gly Ser Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
515 520 525

Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
530 535 540

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
545 550 555 560

Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
565 570 575

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
580 585 590

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
595 600 605

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
610 615 620

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
625 630 635 640

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn
645 650 655

Gln Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
660 665 670

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
675 680 685

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
690 695 700

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
705 710 715 720

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
725 730 735

Ser Leu Ser Pro Gly Lys
740

〈210〉 367
〈211〉 745
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 合成多肽

〈400〉 367

```
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1               5                  10                  15

Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu
            20                  25                  30

Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly
        35                  40                  45

Tyr Thr Phe Ser Thr Tyr Trp Ile Glu Trp Val Arg Gln Ala Pro Gly
    50                  55                  60

Gln Arg Leu Glu Trp Met Gly Glu Ile Leu Pro Gly Ser Gly Gln Thr
65                  70                  75                  80

Asp Phe Asn Glu Lys Phe Gln Gly Arg Val Thr Phe Thr Ala Asp Thr
                85                  90                  95

Ser Ser Asp Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp
            100                 105                 110

Thr Ala Val Tyr Tyr Cys Thr Arg Trp Gly Tyr Tyr Gly Thr Arg Gly
        115                 120                 125

Tyr Phe Asn Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
    130                 135                 140

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145                 150                 155                 160

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
                165                 170                 175

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
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180 185 190

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
195 200 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
210 215 220

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
225 230 235 240

Val Glu Pro Lys Ser Cys Gly Gly Gly Gly 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 Ser Thr Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Gly 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
370 375 380

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
385 390 395 400

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly

405 410 415

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
420 425 430

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
435 440 445

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
450 455 460

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
465 470 475 480

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
485 490 495

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly
500 505 510

Gly Gly Ser Gly Gly Gly Gly Ser Lys Thr His Thr Cys Pro Pro Cys
515 520 525

Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
530 535 540

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
545 550 555 560

Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
565 570 575

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Cys Glu Glu
580 585 590

Gln Tyr Gly Ser Thr Tyr Arg Cys Val Ser Val Leu Thr Val Leu His
595 600 605

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
610 615 620

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln

625 630 635 640

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met
645 650 655

Thr Lys Asn Gln Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
660 665 670

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
675 680 685

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
690 695 700

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
705 710 715 720

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
725 730 735

Lys Ser Leu Ser Leu Ser Pro Gly Lys
740 745

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<400> 368

Asn Tyr Gly Met Asn
1 5

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<400> 369

Trp Met Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe Gln

1 5 10 15

Gly

<210> 370
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<400> 370

Ala Gly Gly Gln Leu Arg Pro Gly Ala Met Asp Tyr
1 5 10

<210> 371
<211> 15
<212> PRT
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<223> 合成多肽

<400> 371

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Phe Met Asn
1 5 10 15

<210> 372
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 372

Val Ala Ser Asn Leu Glu Ser
1 5

<210> 373
<211> 9
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 373

Gln Gln Ser Asn Glu Glu Pro Pro Thr
1 5

<210> 374
<211> 237
<212> PRT
<213> 人工序列

<220>
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<400> 374

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Asp Ile Val Leu Thr Gln Thr Pro Leu Ser Leu Ser Val
20 25 30

Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Ser Val
35 40 45

Asp Tyr Asp Gly Asp Ser Phe Met Asn Trp Tyr Leu Gln Lys Pro Gly
50 55 60

Gln Pro Pro Gln Leu Leu Ile Tyr Val Ala Ser Asn Leu Glu Ser Gly
65 70 75 80

Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
85 90 95

Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln
100 105 110

Gln Ser Asn Glu Glu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu
115 120 125

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
130 135 140

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
145 150 155 160

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
165 170 175

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
180 185 190

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
195 200 205

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
210 215 220

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230 235

<210> 375
<211> 469
<212> PRT
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<220>
<223> 合成多肽

<400> 375

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asn Tyr Gly Met Asn Trp Val Gln Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Trp Met Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala
65 70 75 80

Asp Lys Phe Gln Gly Arg Val Thr Phe Thr Leu Asp Thr Ser Ala Arg
85 90 95

Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val

100 105 110

Tyr Phe Cys Ala Arg Ala Gly Gly Gln Leu Arg Pro Gly Ala Met Asp
115 120 125

Tyr Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
145 150 155 160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
210 215 220

Val Asn His Lys Pro Ser Asp Thr Lys Val Asp Lys Lys Val Glu Pro
225 230 235 240

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Pro
245 250 255

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
260 265 270

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
275 280 285

Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
290 295 300

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Glu Tyr Asn Ser
305 310 315 320

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

325 330 335

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
340 345 350

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
355 360 365

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
370 375 380

Val Ser Leu Thr Cys Asp Val Ser Gly Phe Tyr Pro Ser Asp Ile Ala
385 390 395 400

Val Glu Trp Glu Ser Asp Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
405 410 415

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
420 425 430

Thr Val Asp Lys Ser Arg Trp Glu Gln Gly Asp Val Phe Ser Cys Ser
435 440 445

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
450 455 460

Leu Ser Pro Gly Lys
465

<210> 376
<211> 742
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 376

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

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Pro Gly Ala Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45

Thr Asn Tyr Gly Met Asn Trp Val Gln Gln Ala Pro Gly Gln Gly Leu
    50                  55                  60

Glu Trp Met Gly Trp Met Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala
65                  70                  75                  80

Asp Lys Phe Gln Gly Arg Val Thr Phe Thr Leu Asp Thr Ser Ala Arg
                85                  90                  95

Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
            100                 105                 110

Tyr Phe Cys Ala Arg Ala Gly Gly Gln Leu Arg Pro Gly Ala Met Asp
        115                 120                 125

Tyr Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys
    130                 135                 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
145                 150                 155                 160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
                165                 170                 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
            180                 185                 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
        195                 200                 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
    210                 215                 220

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
225                 230                 235                 240

Lys Ser Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln
                245                 250                 255
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Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
260 265 270

Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn
275 280 285

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly 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

Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Leu Tyr Leu
325 330 335

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Val
340 345 350

Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr Trp
355 360 365

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro Gly Ser Gly
370 375 380

Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gln Ala
385 390 395 400

Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val
405 410 415

Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr
420 425 430

Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly Leu Ile
435 440 445

Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly
450 455 460

Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala Gln Pro
465 470 475 480

Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn His Trp
485 490 495

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Ser
500 505 510

Gly Gly Gly Gly Ser Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
515 520 525

Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
530 535 540

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
545 550 555 560

Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
565 570 575

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
580 585 590

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
595 600 605

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
610 615 620

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
625 630 635 640

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Gln Met Thr Lys Asn
645 650 655

Gln Val Lys Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
660 665 670

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
675 680 685

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
690 695 700

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
705 710 715 720

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
725 730 735

Ser Leu Ser Pro Gly Lys
740

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<400> 377

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 Ser Thr Tyr
20 25 30

Trp Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Glu Ile Leu Pro Gly Ser Gly Asn Thr Asp Phe Asn Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Phe Thr Ala Asp Thr Ser Ser Asp Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Trp Gly Tyr Tyr Gly Thr Arg Gly Tyr Phe Asn Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 378

〈211〉 106
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 合成多肽

〈400〉 378

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Arg Ser Phe Pro Tyr Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

〈210〉 379
〈211〉 121
〈212〉 PRT
〈213〉 人工序列

〈220〉
〈223〉 合成多肽

〈400〉 379

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 Ser Thr Tyr
20 25 30

Trp Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met

35 40 45

Gly Glu Ile Leu Pro Gly Ser Gly Gln Thr Asp Phe Asn Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Phe Thr Ala Asp Thr Ser Ser Asp Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Trp Gly Tyr Tyr Gly Thr Arg Gly Tyr Phe Asn Val Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 380
<211> 121
<212> PRT
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<400> 380

Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Gln Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Met Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Phe Thr Leu Asp Thr Ser Ala Arg Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Ala Gly Gly Gln Leu Arg Pro Gly Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 381
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<220>
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<400> 381

Asp Ile Val Leu Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Phe Met Asn Trp Tyr Leu Gln Lys Pro Gly Gln Pro Pro
35 40 45

Gln Leu Leu Ile Tyr Val Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
65 70 75 80

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Glu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 382
<211> 125
<212> PRT
<213> 人工序列

<220>
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<400> 382

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 Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 383
<211> 5
<212> PRT
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<220>
<223> 合成多肽

<400> 383

Thr Tyr Ala Met Asn
1 5

<210> 384
<211> 19
<212> PRT
<213> 人工序列

<220>
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<400> 384

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Gly

<210> 385
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 385

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 386
<211> 109
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 386

Gln Ala 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 Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 387
<211> 14
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 387

Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
1 5 10

<210> 388
<211> 7
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 388

Gly Thr Asn Lys Arg Ala Pro
1 5

<210> 389
<211> 9
<212> PRT
<213> 人工序列

<220>
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<400> 389

Ala Leu Trp Tyr Ser Asn His Trp Val
1 5

<210> 390
<211> 254
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 390

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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 Ser Thr Tyr
            20                  25                  30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Gly 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
                85                  90                  95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
            100                 105                 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
        115                 120                 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
    130                 135                 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145                 150                 155                 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
                165                 170                 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
            180                 185                 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
        195                 200                 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
    210                 215                 220
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Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 391
<211> 20
<212> PRT
<213> 人工序列

<220>
<223> 合成多肽

<400> 391

Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly
1 5 10 15

Lys Pro Gly Ser
20

【發明申請專利範圍】

【請求項1】

一種液體藥物組成物，該藥物組成物包含(a)結合CD3之異源二聚體抗體、(b)10至50 mM之量的谷胺酸鹽、(c)0.004至0.01%(w/V)之量的表面活性劑，其中該表面活性劑係聚山梨醇酯20、聚山梨醇酯40、聚山梨醇酯60、聚山梨醇酯80或其組合、和(d)9至12%(w/V)之量的糖，其中該藥物組成物的pH範圍為從4至5；

其中該異源二聚體抗體包含Fab、Fc及scFv。

【請求項2】

如請求項1之液體藥物組成物，其中該谷胺酸鹽以10 mM至30 mM的濃度範圍存在。

【請求項3】

如請求項1或2之液體藥物組成物，其中該糖以9%至11%（w/V）的濃度範圍存在。

【請求項4】

如請求項1或2之液體藥物組成物，其中該糖以9%至10.5%（w/V）的濃度範圍存在。

【請求項5】

如請求項4之液體藥物組成物，其中該糖以9%至10%（w/V）的濃度範圍存在。

【請求項6】

如請求項1或2之液體藥物組成物，其中該表面活性劑以0.005%至0.01%（w/V）的濃度範圍存在。

【請求項7】

如請求項1或2之液體藥物組成物，其中該至表面活性劑以0.007%至0.01%（w/V）的濃度範圍存在。

【請求項8】

如請求項7之液體藥物組成物，其中該表面活性劑以0.01%（w/V）的濃度存在。

【請求項9】

如請求項1或2之液體藥物組成物，其中該組成物的pH範圍為從4.2至4.6。

【請求項10】

如請求項9之液體藥物組成物，其中該組成物的pH為4.2。

【請求項11】

如請求項1之液體藥物組成物，其具有150 mOsm至500 mOsm的滲透壓範圍。

【請求項12】

如請求項1之液體藥物組成物，其進一步包含選自由以下各項組成之群組之賦形劑：多元醇和胺基酸。

【請求項13】

如請求項12之液體藥物組成物，其中所述賦形劑以0.1%至15%（m/V）的濃度範圍存在。

【請求項14】

如請求項1之液體藥物組成物，其包含10 mM谷胺酸、9%（w/V）蔗糖和0.01%（w/V）聚山梨醇酯80，並且其中液體藥物組成物的pH為

4.2。

【請求項15】

如請求項1之液體藥物組成物，其中該異源二聚體抗體以0.1 mg/ml至8 mg/ml的濃度範圍存在。

【請求項16】

如請求項1之液體藥物組成物，其中該異源二聚體抗體以0.1 mg/mL至20 mg/mL的濃度範圍存在。

【請求項17】

如請求項1之液體藥物組成物，其中該異源二聚體抗體以範圍從50 μg至200 mg的量存在。

【請求項18】

如請求項1之液體藥物組成物，其中該異源二聚體抗體以1 mg/mL存在。

【請求項19】

如請求項1之液體藥物組成物，其中該異源二聚體抗體以5 mg/mL存在。

【請求項20】

如請求項1之液體藥物組成物，其中該異源二聚體抗體以20 mg/mL存在。

【請求項21】

如請求項1之液體藥物組成物，其中該異源二聚體抗體以10 mg/mL存在。

【請求項22】

一種如請求項1至21中任一項之組成物之用途，其係用於製備治療癌症之醫藥品。

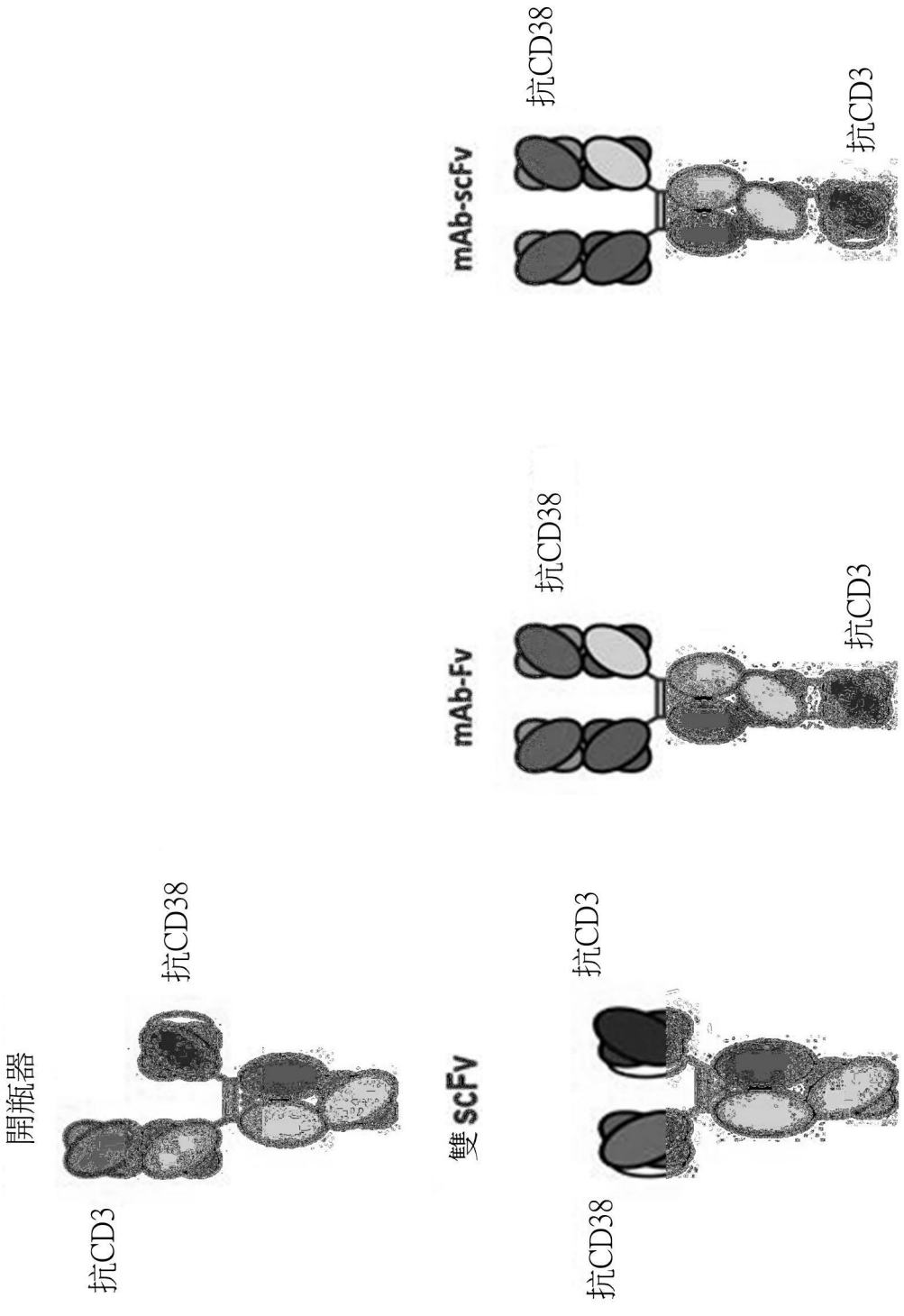
【請求項23】

如請求項22之用途，其中該癌症係多發性骨髓瘤。

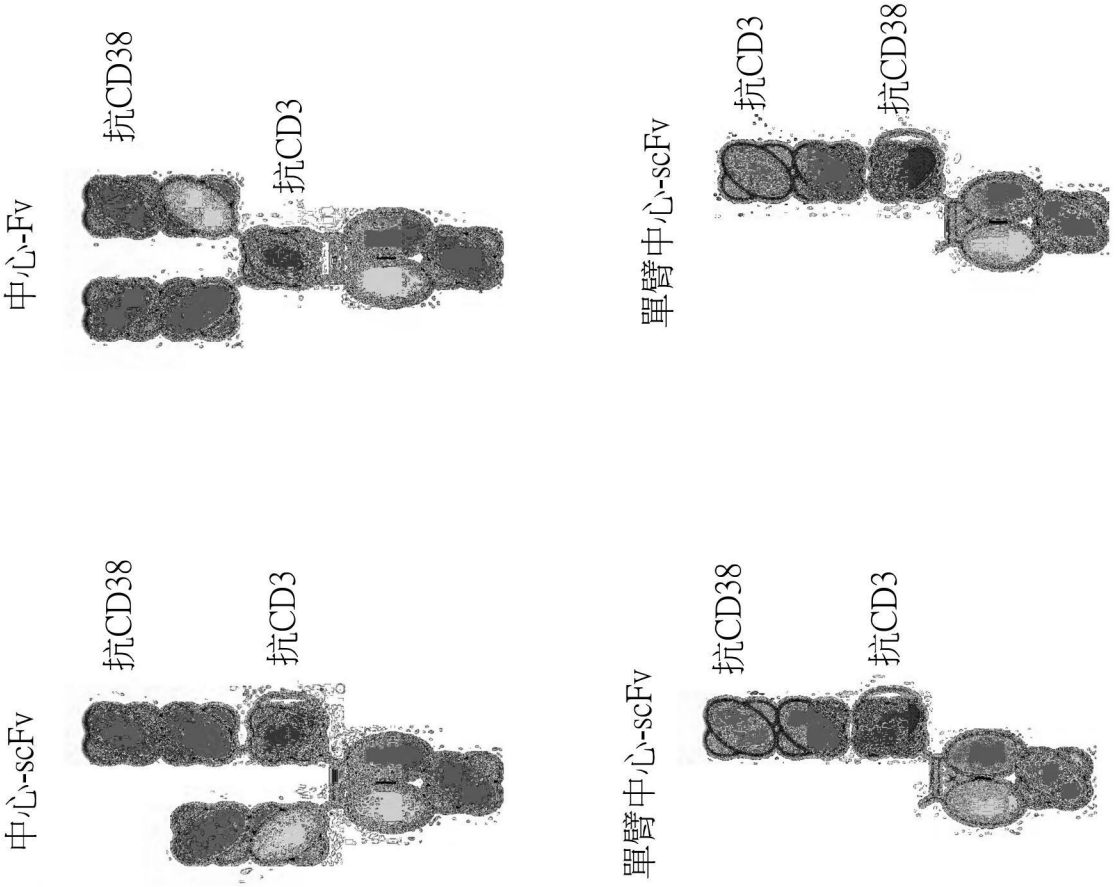
【請求項24】

如請求項22之用途，其中該癌症係前列腺癌。

【發明圖式】


開瓶器
抗CD38
抗CD3
雙 scFv
抗CD3
抗CD38
mAb-Fv
抗CD38
抗CD3
mAb-scFv
抗CD38
抗CD3

【圖 1A】


中心-Fv
抗CD38
抗CD3
單臂中心-scFv
抗CD3
抗CD38
中心-scFv
抗CD38
抗CD3
單臂中心-scFv
抗CD38
抗CD3

【圖 1B】

高-中 #1 CD3: 抗 CD3_H1.32_L1.47

項目	序列	SEQ ID NO:
可變重 (vh) 結構域	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS	10
vhCDR1	TYAMN	11
vhCDR2	RIRSKANNYATYYADSVKG	12
vhCDR3	HGNFGDSYVSWFAY	13
可變輕 (vl) 結構域	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPE DEADYYCALWYSNHWVFGGGTKLTVL	14
vlCDR1	GSSTGAVTTSNYAN	15
vlCDR2	GTNKRAP	16
vlCDR3	ALWYSNHWV	17
scFv （包括帶電荷的接頭）	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLY LQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGT VTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHW VFGGGTKLTVL	18

【圖 2】

中 CD38: OKT10_H1L1.24

項目	序列	SEQ ID NO:
可變重 (vh) 結構域	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS	64
vhCDR1	RSWMN	65
vhCDR2	EINPDSSTINYATSVKG	66
vhCDR3	YGNWFPY	67
可變輕 (vl) 結構域	DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFA TYFCQQYDSYPLTFGGGTKLEIK	68
vlCDR1	RASQNVDTWVA	69
vlCDR2	SASYRYS	70
vlCDR3	QQYDSYPLT	71
scFv （包括帶電荷的接頭）	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSDIVMTQSPSSLSASVGDRVTITCRASQ NVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK	72

【圖 3】

低 CD38: OKT10_H1L1

項目	序列	SEQ ID NO:
可變重 (vh) 結構域	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS	73
vhCDR1	RSWMN	74
vhCDR2	EINPDSSTINYATSVKG	75
vhCDR3	YGNWFPY	76
可變輕 (vl) 結構域	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS	77
vlCDR1	RASQNVDTNVA	78
vlCDR2	SASYRYS	79
vlCDR3	QQYDSYPLT	80
scFv （包括帶電荷的接頭）	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSEVQLVESGGGLVQPGGSLRLSCAASGF DFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYWG QGTLVTVSS	81

【圖 4】

XENP18971 抗CD38 (OKT10_H1L1) x 抗CD3 (SP34_H1.32_L1.47) mAb-scFv (抗體 B)

HC 1 (SEQ ID NO:106)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:107)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:108)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

【圖 5】

XENP18969 抗 CD38 (OKT10_H1L1.24) x 抗 CD3 (SP34_H1.33_L1.47) mAb-scFv

HC 1 (SEQ ID NO:109)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARYGNWFPYW
GQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPK
SCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYT
QKSLSLSPGK

HC 2 (SEQ ID NO:110)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGDS
YVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGS
LLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO:111)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYDSYPLTFGGGTKLEIK/RTV
AAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

【圖 6】

>sp|P07766|CD3E_人T細胞表面糖蛋白CD3 ε 鏈

(SEQ ID NO:130)

MQSGTHWRVLGLCLLSVGVWGQDGNEEMGGITQTPYKVSISGTTVILTCPQYPGSEILWQ

HNDKNIGGDEDDKNIGSDEDHLSLKEFSELEQSGYYVCYPRGSKPEDANFYLYLRARVCE

NCMEMDVMSVATIVIVDICITGGLLLLVYYWSKNRKAKAKPVTRGAGAGGRQRGQNKERP

PPVPNPDYEPIRKGQRDLYSGLNQRRI

【圖 7】

人CD38序列，“/”指示與胞外結構域（ECD）的接合

(SEQ ID NO:131)

MANCEFSPVSGDKPCCRLSRRAQLCLGVSILVLILVVVLAVV/VPRWRQQWSGPGTTKRFP

ETVLARCVKYTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLGTQTVPCN

KILLWSRIKDLAHQFTQVQRDMFTLEDTLLGYLADDLTWCGEFNTSKINYQSCPDWRKDC

SNNPVSVFWKTVSRRFAEAACDVVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQTLEA

WVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCKNIYRPDKFLQCVKNPEDSSCTSEI

ECD結構域 **(SEQ ID NO:132)**

VPRWRQQWSGPGTTKRFPETVLARCVKYTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLGTQTVPCNKI

LLWSRIKDLAHQFTQVQRDMFTLEDTLLGYLADDLTWCGEFNTSKINYQSCPDWRKDC

SNNPVSVFWKTVSRRFAEAACDVVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQTLEA

WVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCKNIYRPDKFLQCVKNPEDSSCTSEI

【圖 8】

單體 1	單體 2
F405A	T394F
S364D	Y349K
S364E	L368K
S364E	Y349K
S364F	K370G
S364H	Y349K
S364H	Y349T
S364Y	K370G
T411K	K370E
V397S/F405A	T394F
K370R/T411K	K370E/T411E
L351E/S364D	Y349K/L351K
L351E/S364E	Y349K/L351K
L351E/T366D	L351K/T366K
P395T/V397S/F405A	T394F
S364D/K370G	S364Y/K370R
S364D/T394F	Y349K/F405A
S364E/F405A	Y349K/T394F
S364E/F405S	Y349K/T394Y
S364E/T411E	Y349K/D401K
S364H/D401K	Y349T/T411E
S364H/F405A	Y349T/T394F
S364H/T394F	Y349T/F405A
Y349C/S364E	Y349K/S354C
L351E/S364D/F405A	Y349K/L351K/T394F
L351K/S364H/D401K	Y349T/L351E/T411E
S364E/T411E/F405A	Y349K/T394F/D401K
S364H/D401K/F405A	Y349T/T394F/T411E
S364H/F405A/T411E	Y349T/T394F/D401K

【圖 9A】

單體 1	單體 2
K370E/T411D	T411K
L368E/K409E	L368K
Y349T/T394F/S354C	S364H/F405A/Y349C
T411E	D401K
T411E	D401R/T411R
Q347E/K360E	Q347R
L368E	S364K
L368E/K370S	S364K
L368E/K370T	S364K
L368E/D401R	S364K
L368E/D401N	S364K
L368E	E357S/S364K
L368E	S364K/K409E
L368E	S364K/K409V
L368D	S364K
L368D/K370S	S364K
L368D/K370S	S364K/E357L
L368D/K370S	S364K/E357Q
T411E/K360E/Q362E	D401K
K370S	S364K
L368E/K370S	S364K/E357Q
K370S	S364K/E357Q
T411E/K360D	D401K
T411E/K360E	D401K
T411E/Q362E	D401K
T411E/N390D	D401K
T411E	D401K/Q347K
T411E	D401K/Q347R
T411E/K360D/Q362E	D401K

【圖 9B】

單體 1	單體 2
T411E/K360E/N390D	D401K
T411E/Q362E/N390D	D401K
T411E/Q347R	D401K/K360D
T411E/Q347R	D401K/K360E
T411E/K360	D401K/Q347K
T411E/K360D	D401K/Q347R
T411E/K360E	D401K/Q347K
T411E/K360E	D401K/Q347R
T411E/S364K	D401K/K370S
T411E/K370S	D401K/S364K
Q347E	E357Q
Q347E	E357Q/Q362K
K360D/Q362E	Q347R
K360D/Q362E	D401K
K360D/Q362E	Q347R/D401K
K360E/Q362E	Q347R
K360E/Q362E	D401K
K360E/Q362E	Q347R/D401K
Q362E/N390D	D401K
Q347E/K360D	D401N
K360D	Q347R/N390K
K360D	N390K/D401N
K360E	Y349H
K370S/Q347E	S364K
K370S/E357L	S364K
K370S/E357Q	S364K
K370S/Q347E/E357L	S364K
K370S/Q347E/E357Q	S364K

【圖 9C】

單體 1	單體 2
L368D/K370S/Q347E	S364K
L368D/K370S/E357L	S364K
L368D/K370S/E357Q	S364K
L368D/K370S/Q347E/E357L	S364K
L368D/K370S/Q347E/E357Q	S364K
L368E/K370S/Q347E	S364K
L368E/K370S/E357L	S364K
L368E/K370S/E357Q	S364K
L368E/K370S/Q347E/E357L	S364K
L368E/K370S/Q347E/E357Q	S364K
L368D/K370T/Q347E	S364K
L368D/K370T/E357L	S364K
L368D/K370T/E357Q	S364K
L368D/K370T/Q347E/E357L	S364K
L368D/K370T/Q347E/E357Q	S364K
L368E/K370T/Q347E	S364K
L368E/K370T/E357L	S364K
L368E/K370T/E357Q	S364K
L368E/K370T/Q347E/E357L	S364K
L368E/K370T/Q347E/E357Q	S364K
T411E/Q362E	D401K/T411K
T411E/N390D	D401K/T411K
T411E/Q362E	D401R/T411R
T411E/N390D	D401R/T411R
Y407T	T366Y
F405A	T394W
T366Y/F405A	T394W/Y407T
Y407A	T366W
T366S/L368A/Y407V	T366W
T366S/L368A/Y407V/Y349C	T366W/S354C

【圖 9D】

單體 1	單體 2
K392D/K409D	E356K/D399K
K370D/K392D/K409D	E356K/E357K/D399K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/N384S/K392N/V397M/Q419E/K447_	Q196K/I199T/N276K
N384S/K392N/V397M/Q419E	N276K
D221E/P228E/L368E	D221R/P228R/K409R
C220E/P228E/L368E	C220R/E224R/P228R/K409R
F405L	K409R
T366I/K392M/T394W	F405A/Y407V
T366V/K409F	L351Y/Y407A
T366A/K392E/K409F/T411E	D399R/S400R/Y407A
L351K	L351E
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/P217R/P228R/N276K
I199T/N203D/K247Q/R355Q/Q419E/K447_	Q196K/I199T/N276K
I199T N203D K274Q R355Q N384S K392N V397M Q419E DEL447	
N208D Q295E N384D Q418E N421D	
N208D Q295E Q418E N421D	
Q196K I199T P217R P228R N276K	
Q196K I199T N276K	
E269Q E272Q E283Q E357Q	
E269Q E272Q E283Q	
E269Q E272Q	
E269Q E283Q	
E272Q E283Q	
E269Q	

【圖 9E】

pI 變體

變體恒定區	取代
pI_ISO(-)	I199T N203D K274Q R355Q N384S K392N V397M Q419E DEL447
pI_(-)_電子等排_A	N208D Q295E N384D Q418E N421D
pI_(-)_電子等排_B	N208D Q295E Q418E N421D
pI_ISO(+RR)	Q196K I199T P217R P228R N276K
pI_ISO(+)	Q196K I199T N276K
pI_(+)_電子等排_A	E269Q E272Q E283Q E357Q
pI_(+)_電子等排_B	E269Q E272Q E283Q
pI_(+)_電子等排_E269Q/E272Q	E269Q E272Q
pI_(+)_電子等排_E269Q/E283Q	E269Q E283Q
pI_(+)_電子等排_E272Q/E283Q	E272Q E283Q
pI_(+)_電子等排_E269Q	E269Q

【圖 10】

消融變體

變體	變體，續
G236R	P329K
S239G	A330L
S239K	A330S/P331S
S239Q	I332K
S239R	I332R
V266D	V266D/A327Q
S267K	V266D/P329K
S267R	S267R/A327Q
H268K	S267R/P329K
E269R	G236R/L328R
299R	E233P/L234V/L235A/G236del/S239K
299K	E233P/L234V/L235A/G236del/S267K
K322A	E233P/L234V/L235A/G236del/S239K/A327G
A327G	E233P/L234V/L235A/G236del/S267K/A327G
A327L	E233P/L234V/L235A/G236del
A327N	S239K/S267K
A327Q	267K/P329K
L328E	
L328R	
P329A	
P329H	

【圖 11】

scFv 單體 (＋)	Fab 單體 (-)
異源二聚體pI變體 **S364K/E357Q**	異二聚化pI變體 **L368D/K370S**
視需要的scFv帶電荷的接頭，包括但不限於 $(GKPGS)_4$	等電pI取代 **N208D/Q295E/N384D/Q418E/N421D**
FcKO E233P/L234V/L235A/G236del/S267K	**FcKO E233P/L234V/L235A/G236del/S267K**
± 428L/434S，對於FcRn	**± 428L/434S**，對於FcRn
抗CD3的scFv	Fv序列，對於抗CD38

scFv 單體	Fab 單體
異源二聚體pI變體 **S364K/E357Q**	異二聚化pI變體 **L368D/K370S**
視需要的scFv帶電荷的接頭，包括但不限於 $(GKPGS)_4$	pI取代 **I199T N203D K274Q R355Q Q419E K447del**
FcKO E233P/L234V/L235A/G236del/S267K	**FcKO E233P/L234V/L235A/G236del/S267K**
± 428L/434S，對於FcRn（視需要的）	**± 428L/434S**，對於FcRn（視需要的）
抗CD3的scFv	抗CD38的scFv

【圖 12】

帶正電荷的scFv接頭

名稱	序列	長度	電荷	SEQ ID NO:
Gly-Ser 15	GGGGSGGGGSGGGGS	15	0	
惠特洛接頭	GSTSGSGKPGSGEGSTKG	18	+1	
6paxA_1 (+A)	IRPRAIGGSKPRVA	14	+4	
+B	GKGGSGKGGSGKGGS	15	+3	
+C	GGKGSGGKGSGGKGS	15	+3	
+D	GGGKSGGGKSGGGKS	15	+3	
+E	GKGKSGKGKSGKGKS	15	+6	
+F	GGGKSGGKGSGKGGS	15	+3	
+G	GKPGSGKPGSGKPGS	15	+3	
+H	GKPGSGKPGSGKPGSGKPGS	20	+4	
+I	GKGKSGKGKSGKGKSGKGKS	20	+8	

帶負電荷的scFv接頭

名稱	序列	長度	電荷	SEQ ID NO:
Gly-Ser 15	GGGGSGGGGSGGGGSGGGGS	20	0	
3hsc_2 (-A)	STAGDTHLGGEDFD	14	-4	
-B	GEGGSGEGGSGEGGS	15	-3	
-C	GGEGSGGEGSGGEGS	15	-3	
-D	GGGESGGGESGGGES	15	-3	
-E	GEGESGEGESGEGES	15	-6	
-F	GGGESGGEGSGEGGS	15	-3	

-G GEGESGEGESGEGESGEGES 20 -8

【圖 13A】

scFv接頭

GGGGSGGGGSGGGGS (SEQ ID NO: 152)

GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 153)

GSTSGSGKPGSGEGSTKG (SEQ ID NO: 154)

PRGASKSGSASQTGSAPGS (SEQ ID NO: 155)

GTAAAGAGAAGGAAAGAAG (SEQ ID NO: 156)

GTSGSSGSGSGGSGSGGGG (SEQ ID NO: 157)

GKPGSGKPGSGKPGSGKPGS (SEQ ID NO: 158)

【圖 13B】

XENP	異源二聚體-偏斜變體，鏈 1	異源二聚體-偏斜變體，鏈 2	異源二聚體產率(%)	CH3 Tm (°C)
12757	無	無	52.7	83.1
12758	L368D/K370S	S364K	94.4	76.6
12759	L368D/K370S	S364K/E357L	90.2	77.2
12760	L368D/K370S	S364K/E357Q	95.2	77.5
12761	T411E/K360E/Q362E	D401K	85.6	80.6
12496	L368E/K370S	S364K	91.5	n.d.
12511	K370S	S364K	59.9	n.d.
12840	L368E/K370S	S364K/E357Q	59.5	n.d.
12841	K370S	S364K/E357Q	90.4	n.d.
12894	L368E/K370S	S364K	41.0	n.d.
12895	K370S	S364K	49.3	n.d.
12896	L368E/K370S	S364K/E357Q	73.9	n.d.
12901	K370S	S364K/E357Q	87.9	n.d.

【圖 14】

VH ID	VL ID	VH 取代	VL 取代
H1	L1.4		
H1.30	L1.47	N30S/N100D	Q42K/A43S/L75I/E85D/L95H
H1.33	L1.47	N30S/N100D/A101D	Q42K/A43S/L75I/E85D/L95H
H1.31	L1.47	N30S/N35S/N100D	Q42K/A43S/L75I/E85D/L95H
H1.32	L1.47	N30S/Y52CA/N100D	Q42K/A43S/L75I/E85D/L95H
H1.88	L1.47	N30S/N100P	Q42K/A43S/L75I/E85D/L95H
H1.89	L1.47	N30S/N100D/S100AE	Q42K/A43S/L75I/E85D/L95H
H1.90	L1.47	N30S/N100D/S100AP	Q42K/A43S/L75I/E85D/L95H
H1.91	L1.47	N30S/Y52CA/N100D	Q42K/A43S/L75I/E85D/L95H
H1.92	L1.47	N30S/Y58A/N100D	Q42K/A43S/L75I/E85D/L95H
H1.93	L1.47	N30S/N100E	Q42K/A43S/L75I/E85D/L95H
H1.94	L1.47	N30S/N100Q	Q42K/A43S/L75I/E85D/L95H
H1.96	L1.47	N30S/N100D/S100AN	Q42K/A43S/L75I/E85D/L95H
H1.97	L1.47	N30S/N100D/S100AQ	Q42K/A43S/L75I/E85D/L95H
H1.98	L1.47	N30S/Y52CA/N100D/A101D	Q42K/A43S/L75I/E85D/L95H
H1.99	L1.47	N30S/Y58A/N100D/A101D	Q42K/A43S/L75I/E85D/L95H
H1.100	L1.47	N30S/N100A/A101D	Q42K/A43S/L75I/E85D/L95H
H1.101	L1.47	N30S/N100Q/A101D	Q42K/A43S/L75I/E85D/L95H
H1.102	L1.47	N30S/N100D/S100AE/A101D	Q42K/A43S/L75I/E85D/L95H
H1.103	L1.47	N30S/N100D/S100AN/A101D	Q42K/A43S/L75I/E85D/L95H
H1.104	L1.47	N30S/N100D/S100AP/A101D	Q42K/A43S/L75I/E85D/L95H
H1.105	L1.47	N30S/N100D/S100AQ/A101D	Q42K/A43S/L75I/E85D/L95H

【圖 15A】

VH ID	VL ID	VH 取代	VL 取代
H1.106	L1.47	N30S/Y52CA/Y58A/N100D	Q42K/A43S/L75I/E85D/L95H
H1.107	L1.47	N30S/Y52CA/Y58A/N100A	Q42K/A43S/L75I/E85D/L95H
H1.108	L1.47	N30S/Y52CA/Y58A/N100Q	Q42K/A43S/L75I/E85D/L95H
H1.109	L1.47	N30S/Y52CA/Y58A/N100D/A101D	Q42K/A43S/L75I/E85D/L95H

【圖 15B】

抗CD3序列

H1.33_L1.47

SEQ ID NO: 218

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 219

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 220

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS

SEQ ID NO: 221

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

【圖 16A】

H1.32_L1.47

SEQ ID NO: 226

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVLGSHHHHHH

SEQ ID NO: 227

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL

SEQ ID NO: 228

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS

SEQ ID NO: 229

QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTIS
GAQPEDEADYYCALWYSNHWVFGGGTKLTVL

【圖 16B】

XENP18971 抗CD38 (OKT10_H1L1) x 抗CD3 (SP34_H1.32_L1.47) mAb-scFv

HC 1 (SEQ ID NO: 317)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO: 318)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDS
KNTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQ
EPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDE
ADYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 319)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQP
EDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

【圖 17】

XENP18969 抗CD38 (OKT10_H1L1.24) x 抗CD3 (SP34_H1.33_L1.47) mAb-scFv

HC 1 (SEQ ID NO: 320)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNT
LYLQMNSLRAEDTAVYYCARYGNWFPYWGQGTLVTVSS/ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAG
PSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCDVSGFYPSDIAVEWESDGQPENNYKTTP
PVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

HC 2 (SEQ ID NO: 321)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSK
NTLYLQMNSLRAEDTAVYYCVRHGNFGDSYVSWFDYWGQGTLVTVSS/GKPGSGKPGSGKPGSGKPGS/QAVVTQE
PSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEA
DYYCALWYSNHWVFGGGTKLTVL/EPKSSDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

LC (SEQ ID NO: 322)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQ
PEDFATYFCQQYDSYPLTFGGGTKLEIK/RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN
SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

【圖 18】

	高 CD3	高-中 #1 CD3	高-中 #2 CD3	高-中 #3 CD3	中.CD3	低 CD3
	抗CD3	抗CD3	抗CD3	抗CD3	抗CD3	抗CD3
	H1.30_L1.47	H1.32_L1.47	H1.89_L1.47	H1.90_L1.47	H1.33_L1.47	H1.31_L1.47
高 CD38 OKT10 H1.77_L1.24	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
中 CD38 OKT10 H1L1.24	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F
低 CD38 OKT10 H1L1	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F	A, B, C, D, E. F

【圖 19】

XmAb18968－抗體 A

ScFv-Fc (SEQ ID NO: 335)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDT
AVYYCVRHGNFGDSYVSWFAYWGQGTLVTVSSGKPGSGKPGSGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQ
QKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCALWYSNHWVFGGGTKLTVLEPKSSDKTHTCPPCPAPPVAGPSV
FLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

輕鏈 (SEQ ID NO: 336)

DIVMTQSPSSLSASVGDRVTITCRASQNVDTWVAWYQQKPGQSPKALIYSASYRYSGVPDRFTGSGSGTDFTLTISSLQPEDFATYFCQQYD
SYPLTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADY
EKHKVYACEVTHQGLSSPVTKSFNRGEC

重鏈 (SEQ ID NO: 337)

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRSWMNWVRQAPGKGLEWVSEINPDSSTINYATSVKGRFTISRDNSKNTLYLQMNSLRAE
DTAVYYCARYGNWFPYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVK
FNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQV
SLTCDVSGFYPSDIAVEWESDGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWEQGDVFSCSVMHEALHNHYTQKSLSLSPGK

【圖 20】

序列標識符	分子	說明
1.	高 CD3: 抗 CD3_H1.30_L1.47	可變重 (vh) 結構域
2.		vhCDR1
3.		vhCDR2
4.		vhCDR3
5.		可變輕 (vl) 結構域
6.		vlCDR1
7.		vlCDR2
8.		vlCDR3
9.		scFv （包括帶電荷的接頭）
10.	高-中 #1 CD3: 抗 CD3_H1.32_L1.47	可變重 (vh) 結構域
11.		vhCDR1
12.		vhCDR2
13.		vhCDR3
14.		可變輕 (vl) 結構域
15.		vlCDR1
16.		vlCDR2
17.		vlCDR3
18.		scFv （包括帶電荷的接頭）
19.	高-中 #2 CD3: 抗 CD3_H1.89_L1.47	可變重 (vh) 結構域
20.		vhCDR1
21.		vhCDR2
22.		vhCDR3
23.		可變輕 (vl) 結構域

序列標識符	分子	說明
24.		vlCDR1
25.		vlCDR2
26.		vlCDR3
27.		scFv（包括帶電荷的接頭）
28.	高-中#3 CD3: 抗 CD3_H1.90_L1.47	可變重 (vh) 結構域
29.		vhCDR1
30.		vhCDR2
31.		vhCDR3
32.		可變輕 (vl) 結構域
33.		vlCDR1
34.		vlCDR2
35.		vlCDR3
36.		scFv（包括帶電荷的接頭）
37.	中 CD3: 抗 CD3_H1.33_L1.47	可變重 (vh) 結構域
38.		vhCDR1
39.		vhCDR2
40.		vhCDR3
41.		可變輕 (vl) 結構域
42.		vlCDR1
43.		vlCDR2
44.		vlCDR3
45.		scFv（包括帶電荷的接頭）
46.	低CD3: 抗 CD3_H1.31_L1.47	可變重 (vh) 結構域
47.		vhCDR1

序列標識符	分子	說明
48.		vhCDR2
49.		vhCDR3
50.		可變輕 (vl) 結構域
51.		vlCDR1
52.		vlCDR2
53.		vlCDR3
54.		scFv （包括帶電荷的接頭）
55.	高 CD38: OKT10_H1.77_L1.24	可變重 (vh) 結構域
56.		vhCDR1
57.		vhCDR2
58.		vhCDR3
59.		可變輕 (vl) 結構域
60.		vlCDR1
61.		vlCDR2
62.		vlCDR3
63.		scFv （包括帶電荷的接頭）
64.	中 CD38: OKT10_H1L1.24	可變重 (vh) 結構域
65.		vhCDR1
66.		vhCDR2
67.		vhCDR3
68.		可變輕 (vl) 結構域
69.		vlCDR1
70.		vlCDR2
71.		vlCDR3

序列標識符	分子	說明
72.		scFv（包括帶電荷的接頭）
73.	低CD38: OKT10_H1L1	可變重 (vh) 結構域
74.		vhCDR1
75.		vhCDR2
76.		vhCDR3
77.		可變輕 (vl) 結構域
78.		vlCDR1
79.		vlCDR2
80.		vlCDR3
81.		scFv（包括帶電荷的接頭）
82.	XENP15331	HC-Fab
83.		HC-scFv
84.		LC
85.	XENP13243	HC-Fab
86.		HC-scFv
87.		LC
88.	XENP14702 抗 CD38 x 抗 CD3 Fab-scFv-Fc	HC1 (Fab-Fc)
89.		HC2 (scFv-Fc)
90.		LC
91.	XENP15426 抗 CD38 (OKT10_H1.77_L1.24, CD38高) x 抗 CD3 (H1.33_L1.47, CD3中等) Fab-scFv-Fc	HC1 (Fab-Fc)
92.		HC2 (scFv-Fc)
93.		LC
94.	XENP14701 抗 CD38 x 抗 CD3 Fab-scFv-Fc	HC1 (Fab-Fc) (OKT10 H1)
95.		HC2 (scFv-Fc) (αCD3 H1.31_L1.47)

序列標識符	分子	說明
96.		LC (OKT10 L1)
97.	XENP14703 抗 CD38 x 抗 CD3 Fab-scFv-Fc	HC1 (Fab-Fc) (OKT10 H1)
98.		HC2 (scFv-Fc) (αCD3 H1.31_L1.47)
99.		LC (OKT10 L1.53)
100.	XENP13243 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.30_L1.47)	HC1 (Fab-Fc)
101.		HC2 (scFv-Fc)
102.		LC
103.	XENP18967 抗 CD38 (OKT10_H1.77_L1.24) x 抗 CD3 (SP34_H1.32_L1.47) mAb-scFv	HC1 (Fab-Fc)
104.		HC2 (scFv-Fc)
105.		LC
106.	XENP18971 抗 CD38 (OKT10_H1L1) x 抗 CD3 (SP34_H1.32_L1.47) mAb-scFv	HC1 (Fab-Fc)
107.		HC2 (scFv-Fc)
108.		LC
109.	XENP18969 抗 CD38 (OKT10_H1L1.24) x 抗 CD3 (SP34_H1.33_L1.47) mAb-scFv	HC1 (Fab-Fc)
110.		HC2 (scFv-Fc)
111.		LC
112.	XENP18970 抗 CD38 (OKT10_H1L1.24) x 抗 CD3 (SP34_H1.31_L1.47) mAb-scFv	HC1 (Fab-Fc)
113.		HC2 (scFv-Fc)
114.		LC
115.	XENP18972 抗 CD38 (OKT10_H1L1) x 抗 CD3 (SP34_H1.33_L1.47) mAb-scFv	HC1 (Fab-Fc)
116.		HC2 (scFv-Fc)
117.		LC
118.	XENP18973 抗 CD38 (OKT10_H1L1) x 抗 CD3 (SP34_H1.31_L1.47) mAb-scFv	HC1 (Fab-Fc)
119.		HC2 (scFv-Fc)

序列標識符	分子	說明
120.		LC
121.	XENP15055 抗 CD38 (OKT10_H1L1, CD38低) x 抗 CD3 (H1.33_L1.47, CD3中等) Fab-scFv-Fc	HC1 (Fab-Fc)
122.		HC2 (scFv-Fc)
123.		LC
124.	XENP13544 抗 CD38 (OKT10_H1L1, CD38低) x 抗 CD3 (H1.79_L1.48) Fab-scFv-Fc	HC1 (Fab-Fc)
125.		HC2 (scFv-Fc)
126.		LC
127.	XENP13694 抗 CD38 (OKT10_H1.77_L1.24, CD38高) x 抗 CD3 (H1.79_L1.48) Fab-scFv-Fc	HC1 (Fab-Fc)
128.		HC2 (scFv-Fc)
129.		LC
130.	>sp|P07766|CD3E_人T細胞表面糖蛋白CD3 ε鏈	人 CD3 ε (圖 7)
131.	人 CD38 序列	人 CD38 w/ECD(圖 8)
132.	人 CD38 序列	ECD 結構域
168.	XENP14422 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.30_L1.47) 單臂中心-scFv	HC1
169.		HC2
170.		LC
171.	XENP14423 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.30_L1.47) 中心-Fv	HC1
172.		HC2
173.		LC
174.	XENP15427 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.31_L1.47) 單臂 mAb-scFv	HC1
175.		HC2
176.		LC
177.	XENP15428 抗 CD38 (OKT10_H1L1) x 抗	HC1

序列標識符	分子	說明
178.	CD3 (H1.33_L1.47) 單臂 mAb-scFv	HC2
179.		LC
180.	XENP15429 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.30_L1.47) 單臂 mAb-scFv	HC1
181.		HC2
182.		LC
183.	XENP15430 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.31_L1.47) 單臂中心 -scFv	HC1
184.		HC2
185.		LC
186.	XENP15431 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.33_L1.47) 單臂中心 -scFv	HC1
187.		HC2
188.		LC
189.	XENP15432 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.30_L1.47) 單臂中心 -scFv	HC1
190.		HC2
191.		LC
192.	XENP15433 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.31_L1.47) mAb-scFv	HC1
193.		HC2
194.		LC
195.	XENP15434 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.33_L1.47) mAb-scFv	HC1
196.		HC2
197.		LC
198.	XENP15435 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.30_L1.47) mAb-scFv	HC1
199.		HC2
200.		LC
201.	XENP15436 抗 CD38 (OKT10_H1L1) x 抗	HC1

序列標識符	分子	說明
202.	CD3 (H1.31_L1.47) 中心 -scFv	HC2
203.		LC
204.	XENP15437 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.33_L1.47) 中心 -scFv	HC1
205.		HC2
206.		LC
207.	XENP15438 抗 CD38 (OKT10_H1L1) x 抗 CD3 (H1.30_L1.47) 中心 -scFv	HC1
208.		HC2
209.		LC
210.	抗 CD3 H1_L1.4	
211.		
212.		
213.		
214.	抗 CD3 H1.30_L147	
215.		
216.		
217.		
218.	抗 CD3 H1.33_L1.47	scFv w/ C末端6xHis標籤
219.	圖 16A	scFv
220.		VH
221.		VL
222.	抗 CD3 H1.31_L1.47	
223.		
224.		
225.		

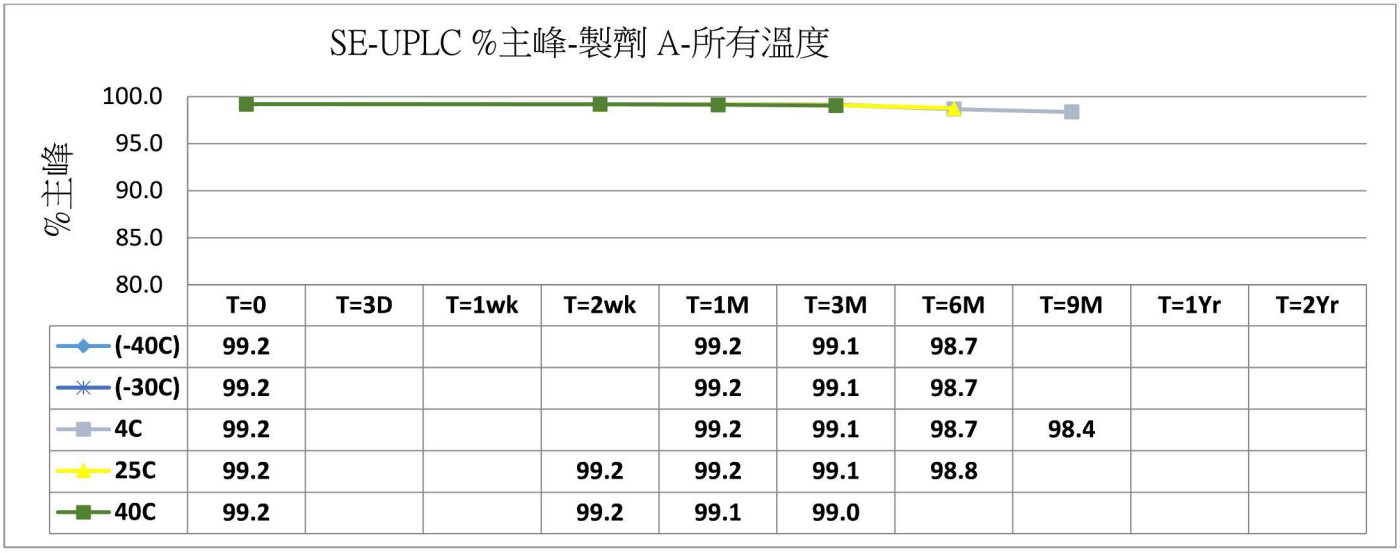
序列標識符	分子	說明
226.	抗 CD3 H1.32_L1.47	scFv w/ C末端6xHis標籤
227.		scFv
228.		VH
229.		VL
314.	XENP18967 抗 CD38 (OKT10_H1.77_L1.24) x 抗 CD3 (SP34_H1.32_L1.47) mAb-scFv	HC1
315.		HC2
316.		LC
317.	XENP18971 抗 CD38 (OKT10_H1L1) x 抗 CD3 (SP34_H1.32_L1.47) mAb-scFv	HC1
318.		HC2
319.		LC
320.	XENP18969 抗 CD38 (OKT10_H1L1.24) x 抗 CD3 (SP34_H1.33_L1.47) mAb-scFv	HC1
321.		HC2
322.		LC
323.	XENP18970 抗 CD38 (OKT10_H1L1.24) x 抗 CD3 (SP34_H1.31_L1.47) mAb-scFv	HC1
324.		HC2
325.		LC
326.	XENP18972 抗 CD38 (OKT10_H1L1) x 抗 CD3 (SP34_H1.33_L1.47) mAb-scFv	HC1
327.		HC2
328.		LC
329.	XENP18973 抗 CD38 (OKT10_H1L1) x 抗 CD3 (SP34_H1.31_L1.47) mAb-scFv	HC1
330.		HC2
331.		LC
332.	(GSGGS)n	接頭
333.	(GGGGS)n	接頭

序列標識符	分子	說明
334.	(GGGS)n	[0040]
335.	XmAb18968 (412220)	scFv-Fc
336.		輕鏈
337.		重鏈
347.	開瓶器主鏈 1	Fab側重鏈
348.		scFv 重鏈
349.		恒定輕鏈
350.	開瓶器主鏈 2 Fab側重鏈與主鏈1相同 恒定輕鏈與主鏈1相同	scFv 重鏈
351.	開瓶器主鏈 3	Fab側重鏈
352.	恒定輕鏈與主鏈1相同	scFv 重鏈
353.	開瓶器主鏈 4	Fab側重鏈
354.	恒定輕鏈與主鏈1相同	scFv 重鏈
355.		
356.	人 STEAP 1	
357.	2F3 Xmab 2+1	LCDR1
358.	2F3 Xmab 2+1	LCDR2
359.	2F3 Xmab 2+1	LCDR3
360.	2F3 Xmab 2+1	HCDR1
361.	2F3 Xmab 2+1	HCDR2
362.	2F3 Xmab 2+1	HCDR3
363.	2F3-N67Q Xmab 2+1	HCDR2

序列標識符	分子	說明
364.	2F3 Xmab 2+1	輕鏈
365.	2F3 Xmab 2+1	重鏈
366.	2F3 Xmab 2+1	XVHMx
367.	2F3-N67Q Xmab 2+1	XVHMx
368.	11C2 Xmab 2+1	HCDR1
369.	11C2 Xmab 2+1	HCDR2
370.	11C2 Xmab 2+1	HCDR3
371.	11C2 Xmab 2+1	LCDR1
372.	11C2 Xmab 2+1	LCDR2
373.	11C2 Xmab 2+1	LCDR3
374.	11C2 Xmab 2+1	輕鏈
375.	11C2 Xmab 2+1	重鏈
376.	11C2 Xmab 2+1	XMVHx
377.	2F3 Xmab 2+1	重可變
378.	2F3 Xmab 2+1/2F3-N67Q Xmab 2+1	輕可變
379.	2F3-N67Q Xmab 2+1	重可變
380.	11C2 Xmab 2+1	重可變
381.	11C2 Xmab 2+1	輕可變
382.	抗 CD3 (SS28641)	重可變
383.	抗 CD3 (SS28641)	HCDR1
384.	抗 CD3 (SS28641)	HCDR2
385.	抗 CD3 (SS28641)	HCDR3
386.	抗 CD3 (SS28641)	輕可變
387.	抗 CD3 (SS28641)	LCDR1

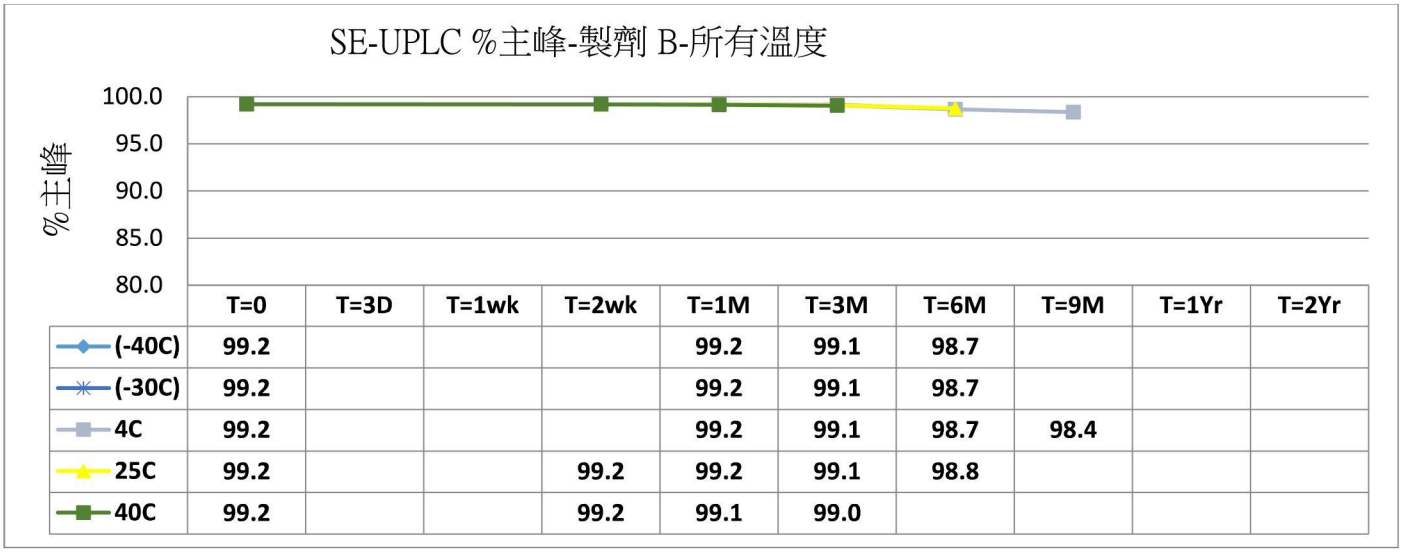
序列標識符	分子	說明
388.	抗 CD3 (SS28641)	LCDR2
389.	抗 CD3 (SS28641)	LCDR3
390.	抗 CD3 (H1.30_L1.47	scFv
391.	接頭	接頭

【圖 21】



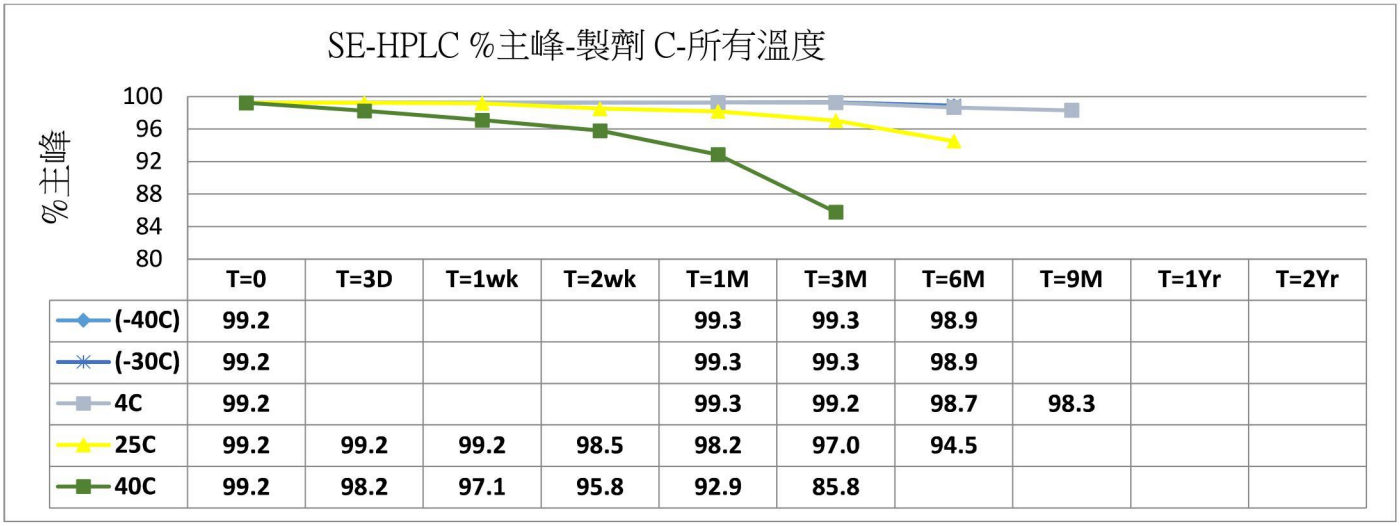
	T=0	T=3D	T=1wk	T=2wk	T=1M	T=3M	T=6M	T=9M	T=1Yr	T=2Yr
(-40C)	99.2				99.2	99.1	98.7			
(-30C)	99.2				99.2	99.1	98.7			
4C	99.2				99.2	99.1	98.7	98.4		
25C	99.2			99.2	99.2	99.1	98.8			
40C	99.2			99.2	99.1	99.0				

【圖 22A】



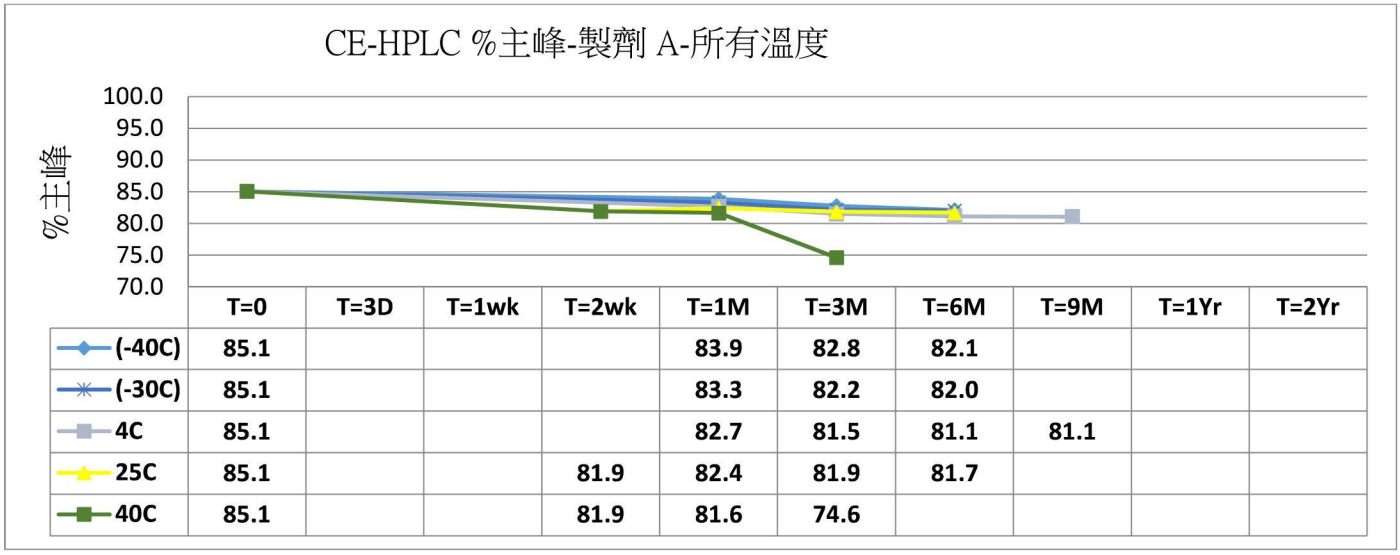
	T=0	T=3D	T=1wk	T=2wk	T=1M	T=3M	T=6M	T=9M	T=1Yr	T=2Yr
(-40C)	99.2				99.2	99.1	98.7			
(-30C)	99.2				99.2	99.1	98.7			
4C	99.2				99.2	99.1	98.7	98.4		
25C	99.2			99.2	99.2	99.1	98.8			
40C	99.2			99.2	99.1	99.0				

【圖 22B】



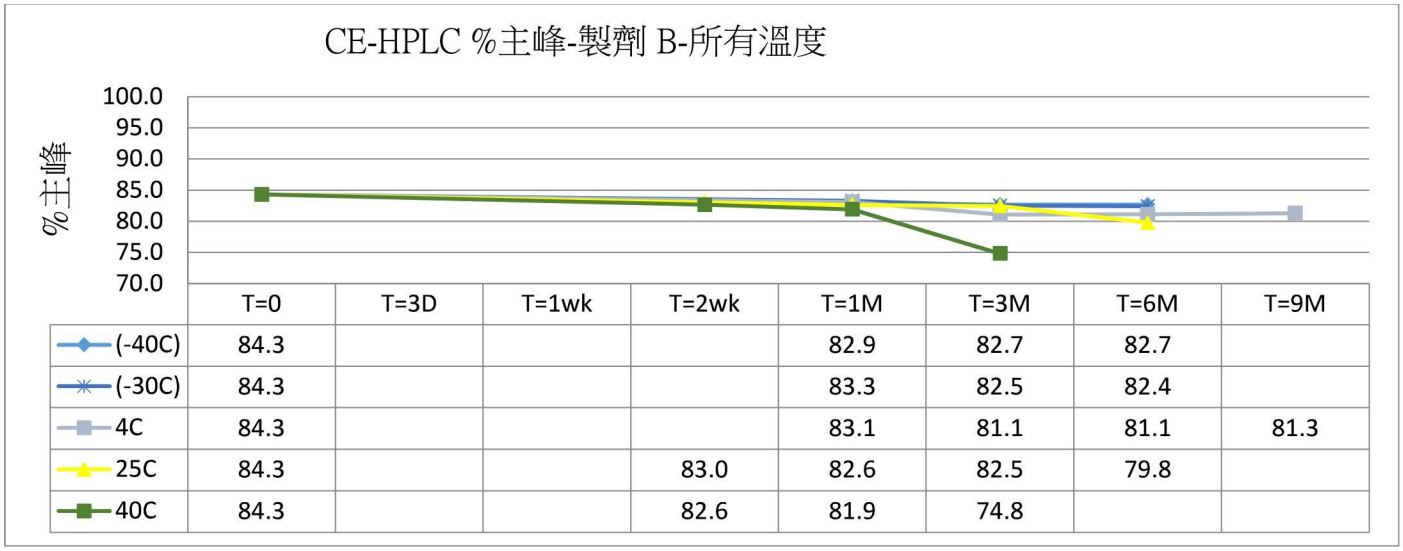
	T=0	T=3D	T=1wk	T=2wk	T=1M	T=3M	T=6M	T=9M	T=1Yr	T=2Yr
(-40C)	99.2				99.3	99.3	98.9			
(-30C)	99.2				99.3	99.3	98.9			
4C	99.2				99.3	99.2	98.7	98.3		
25C	99.2	99.2	99.2	98.5	98.2	97.0	94.5			
40C	99.2	98.2	97.1	95.8	92.9	85.8				

【圖 23】



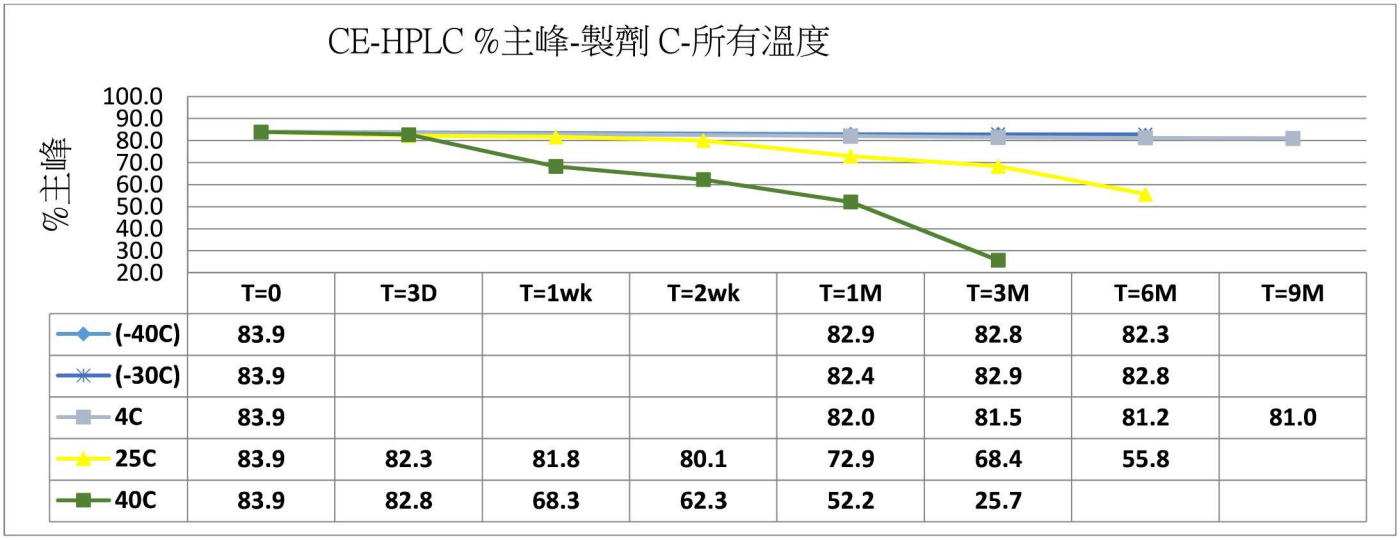
	T=0	T=3D	T=1wk	T=2wk	T=1M	T=3M	T=6M	T=9M	T=1Yr	T=2Yr
(-40C)	85.1				83.9	82.8	82.1			
(-30C)	85.1				83.3	82.2	82.0			
4C	85.1				82.7	81.5	81.1	81.1		
25C	85.1			81.9	82.4	81.9	81.7			
40C	85.1			81.9	81.6	74.6				

【圖 24A】



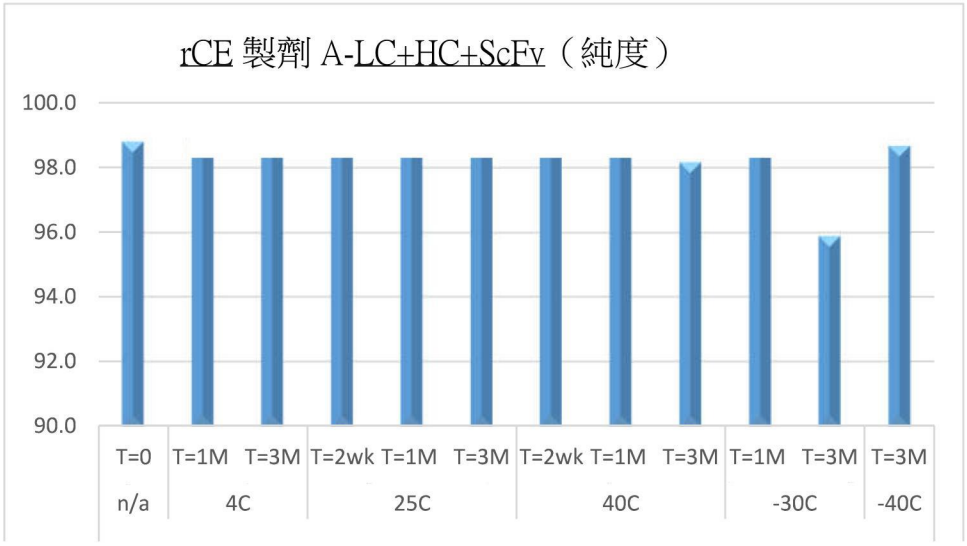
	T=0	T=3D	T=1wk	T=2wk	T=1M	T=3M	T=6M	T=9M
(-40C)	84.3				82.9	82.7	82.7	
(-30C)	84.3				83.3	82.5	82.4	
4C	84.3				83.1	81.1	81.1	81.3
25C	84.3			83.0	82.6	82.5	79.8	
40C	84.3			82.6	81.9	74.8		

【圖 24B】

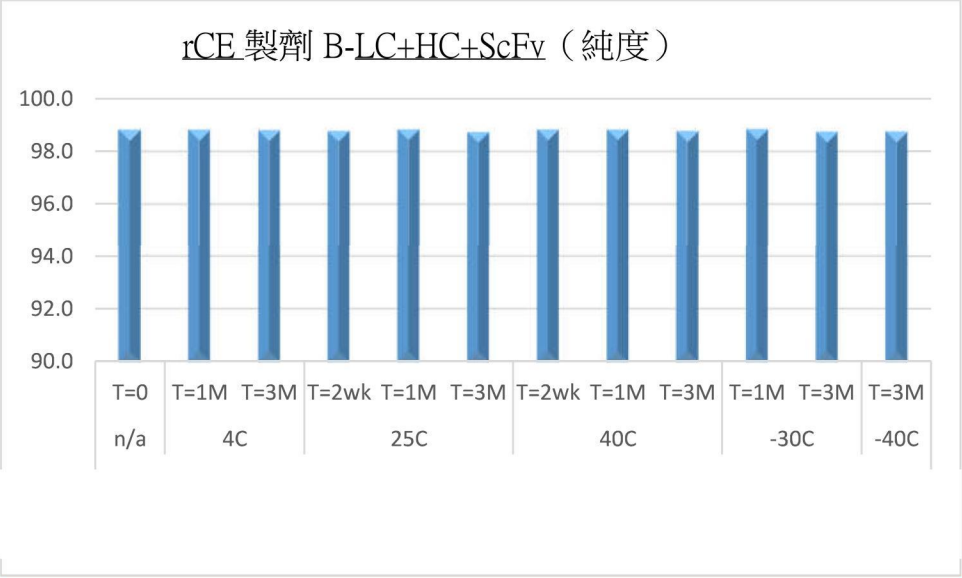


	T=0	T=3D	T=1wk	T=2wk	T=1M	T=3M	T=6M	T=9M
(-40C)	83.9				82.9	82.8	82.3	
(-30C)	83.9				82.4	82.9	82.8	
4C	83.9				82.0	81.5	81.2	81.0
25C	83.9	82.3	81.8	80.1	72.9	68.4	55.8	
40C	83.9	82.8	68.3	62.3	52.2	25.7		

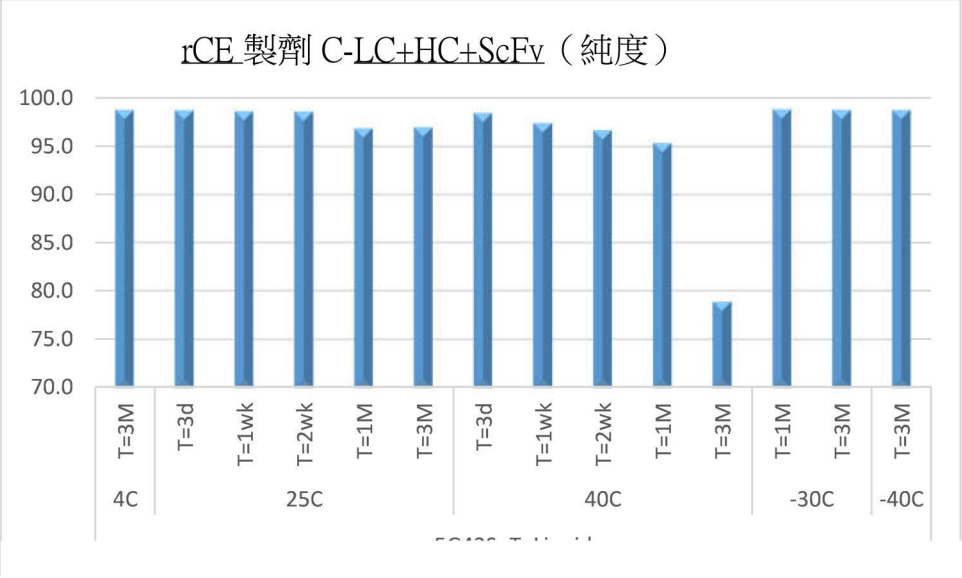
【圖 25】



【圖 26】


rCE 製劑 B-LC+HC+ScFv（純度）
100.0
98.0
96.0
94.0
92.0
90.0
T=0
n/a
T=1M
T=3M
4C
T=2wk
T=1M
T=3M
25C
T=2wk
T=1M
T=3M
40C
T=1M
T=3M
-30C
T=3M
-40C

【圖 27】


rCE 製劑 C-LC+HC+ScFv（純度）
100.0
95.0
90.0
85.0
80.0
75.0
70.0
T=3M
4C
T=3d
T=1wk
T=2wk
T=1M
T=3M
25C
T=3d
T=1wk
T=2wk
T=1M
T=3M
40C
T=1M
T=3M
-30C
T=3M
-40C

【圖 28】

	屬性					
			CD38_Lyo_4C_3MO	CD38_Lyo_25C_3MO	CD38_Lyo_40C_3MO	CD38_液體_40C_3MO
ScFv-Fc	CDR Trp 氧化	$(Trp^{111})^{CD3**}$	ND	ND	ND	ND
		$(Trp^{238})^{CD3}$	ND	ND	ND	ND
		$(Trp^{243})^{CD3}$	ND	ND	ND	ND
	CDR Met 氧化	$(M^{34})^{CD3}$	ND	ND	ND	ND
	CDR 異構化	$(D^{64})^{CD3}$	ND	ND	ND	ND
		$(D^{106})^{CD3**}$	ND	ND	ND	ND
	CDR 脫醯胺化	$(N^{56})^{CD3}$	ND	ND	ND	ND
		$(N^{57})^{CD3}$	ND	ND	ND	ND
		$(N^{103})^{CD3**}$	0.6%	0.5%	0.3%	9.1%
		$(N^{241})^{CD3}$	ND	ND	ND	ND
	CDR 糖化	$(K^{54})^{CD3}$	ND	ND	ND	ND
		$(K^{67})^{CD3}$	ND	ND	ND	ND
		$(K^{200})^{CD3}$	0.1%	0.1%	0.2%	3.5%
	總CD3 CDR水平		0.6%	0.6%	0.5%	12.6%
	羥基 Lys	$(K^{67})^{CD3}$	ND	ND	ND	ND
	D/P Frag.	$D^{308}P*$	0.1%	0.2%	0.3%	2.4%
	C末端 Lys***		21.5%	21.6%	20.8%	17.9%

【圖 29】

	屬性		靶標	製劑D中的抗體A			製劑D中的抗體B		
				T0	2wk	4wk	T0	2wk	4wk
ScFv-Fc	CDR Trp 氧化	$(Trp^{111})^{CD3*}$	≤5%	ND	ND	ND	ND	ND	ND
		$(Trp^{238})^{CD3*}$	≤5%	ND	ND	ND	0.1%	0.0%	ND
		$(Trp^{243})^{CD3*}$	≤5%	ND	ND	ND	0.0%	0.1%	0.1%
	CDR Met 氧化	$(M^{34})^{CD3*}$	≤5%	ND	ND	ND	ND	ND	ND
	CDR 異構化	$(D^{64})^{CD3*}$	≤5%	ND	ND	ND	ND	ND	ND
		$(D^{106})^{CD3*}$	≤5%	ND	ND	ND	ND	ND	ND
	CDR 脫醯胺化	$(N^{56})^{CD3*}$	≤5%	0.4%	0.3%	0.5%	0.3%	0.4%	0.4%
		$(N^{57})^{CD3*}$	≤5%	0.2%	0.2%	0.1%	0.2%	0.3%	0.1%
		$(N^{103})^{CD3}$	**≤5%**	**0.3%**	**7.9%**	**13.8%**	**0.7%**	**7.8%**	**12.3%**
		$(N^{241})^{CD3*}$	≤5%	0.2%	0.1%	0.5%	0.3%	0.5%	0.3%
	CDR 糖化	$(K^{54})^{CD3*}$	≤5%	ND	ND	ND	ND	ND	ND
		$(K^{67})^{CD3*}$	≤5%	0.2%	0.1%	0.3%	0.1%	0.1%	0.4%
		$(K^{200})^{CD3*}$	≤5%	0.2%	0.3%	0.2%	0.1%	0.2%	0.2%
	總CD3 CDR水平		**≤20**	**1.5%**	**9.0%**	**15.4%**	**1.8%**	**9.3%**	**13.7%**
	羥基 Lys	$(K^{67})^{CD3*}$		0.1%	0.1%	0.0%	0.1%	0.1%	0.0%
	D/P Frag.	$D^{308}P$		0.5%	1.3%	0.5%	0.8%	1.4%	0.4%

【圖 30】

	屬性		樣品					
			TS1 DS	Lyo_4C_T0	Lyo_4C_1MO	Lyo_25C_1MO	Lyo_40C_1MO	液體_40C_1MO
ScFv-Fc	CDR Trp 氧化	(Trp^{111}) CD3**	ND	ND	ND	ND	ND	ND
		(Trp^{238}) CD3	ND	ND	ND	ND	ND	ND
		(Trp^{243}) CD3	ND	ND	ND	ND	ND	ND
	CDR Met 氧化	(M^{34}) CD3	ND	ND	ND	ND	ND	ND
	CDR 異構化	(D^{64}) CD3	ND	ND	ND	ND	ND	ND
		(D^{106}) CD3**	ND	ND	ND	ND	ND	ND
	CDR 脫醯胺化	(N^{56}) CD3	ND	ND	ND	ND	ND	ND
		(N^{57}) CD3	ND	ND	ND	ND	ND	ND
		(N^{103}) CD3**	0.2%	0.4%	0.4%	0.5%	0.4%	3.7%
		(N^{241}) CD3	ND	ND	ND	ND	ND	ND
	CDR 糖化	(K^{54}) CD3	ND	ND	ND	ND	ND	ND
		(K^{67}) CD3	ND	ND	ND	ND	ND	ND
		(K^{200}) CD3	0.2%	0.2%	0.2%	0.2%	0.2%	1.3%
	總CD3 CDR水平		0.4%	0.6%	0.6%	0.7%	0.6%	5.0%
	羥基 Lys	(K^{67}) CD3	ND	ND	ND	ND	ND	ND
	D/P Frag.	$D^{308}P$*	0.0%	0.1%	0.1%	0.1%	0.2%	0.5%

【圖 31】