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(71)申請人：新加坡商全民疫苗私人有限公司 (新加坡) VAC4ALL PTE. LTD. (SG)

新加坡

(72)發明人：德呂耶 皮耶 DRUILHE, PIERRE (FR)

(74)代理人：陳長文

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審查人員：吳思嫻

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(54)名稱

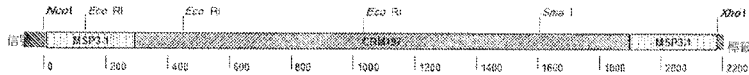
作為抗瘧疾疫苗之生物融合蛋白

(57)摘要

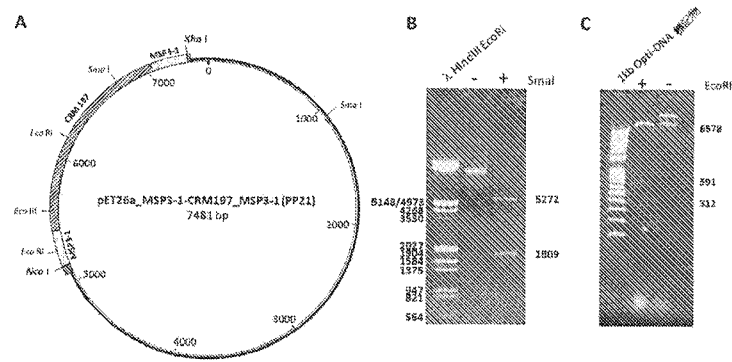
本發明係關於包括至少一個融合至載體異源蛋白序列之抗原性胺基酸序列之融合蛋白，其中該抗原性序列包括瘧原蟲屬(Plasmodium)蛋白之表位序列且該載體異源蛋白序列係在人類中具有免疫原性之序列。該等蛋白質可用作抗瘧疾疫苗。

The invention relates to fusion proteins which comprise at least one antigenic amino acid sequence fused to a carrier heterologous protein sequence, wherein the antigenic sequence comprises an epitopic sequence of a Plasmodium protein and the carrier heterologous protein sequence is a sequence that is immunogenic in humans. The proteins are useful as anti-malaria vaccines.

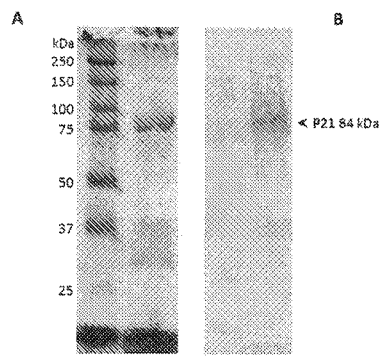
指定代表圖：



【圖 1】



【圖 2】



【圖 3】



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【發明摘要】

IPC分類:

【中文發明名稱】

作為抗瘧疾疫苗之生物融合蛋白

【英文發明名稱】

BIOFUSION PROTEINS AS ANTI-MALARIA VACCINES

【中文】

本發明係關於包括至少一個融合至載體異源蛋白序列之抗原性胺基酸序列之融合蛋白，其中該抗原性序列包括瘧原蟲屬(Plasmodium)蛋白之表位序列且該載體異源蛋白序列係在人類中具有免疫原性之序列。該等蛋白質可用作抗瘧疾疫苗。

【英文】

The invention relates to fusion proteins which comprise at least one antigenic amino acid sequence fused to a carrier heterologous protein sequence, wherein the antigenic sequence comprises an epitopic sequence of a Plasmodium protein and the carrier heterologous protein sequence is a sequence that is immunogenic in humans. The proteins are useful as anti-malaria vaccines.

【指定代表圖】

圖1

【代表圖之符號簡單說明】

無

【發明說明書】

【中文發明名稱】

作為抗瘧疾疫苗之生物融合蛋白

【英文發明名稱】

BIOFUSION PROTEINS AS ANTI-MALARIA VACCINES

【技術領域】

本發明係關於對抗瘧疾之保護，更特定而言係關於包括融合蛋白之瘧疾疫苗。

【先前技術】

造成人類瘧疾之寄生蟲(尤其包含惡性瘧原蟲(*Plasmodium falciparum*))在人類宿主中展現不同形態且隨其在所感染宿主之生物體中之定位而表現不同抗原。該等寄生蟲在人類生命循環期間之形態及抗原性差異使得能夠具有至少4個不同發育階段。寄生蟲在人類中之最初發育階段對應於藉由寄生蟲之昆蟲載體之叮咬引入宿主血液中的子孢子形式。第二階段對應於寄生蟲通過肝且感染肝細胞，其中寄生蟲發育形成肝裂殖體，該等肝裂殖體在其成熟(例如在子孢子侵入之後第6天之惡性瘧原蟲情形)時藉由破裂釋放肝裂殖子。第三階段之特徵在於在成熟時釋放游離裂殖子之寄生蟲之無性形式(血液階段裂殖體)感染血液紅血球；此紅細胞發育階段對應於疾病之病原期。第四階段對應於形成具有性潛力之形式(或配子母細胞)，該等形式在蚊子中變成細胞外性形式或配子。

並無引入臨床實踐中之實踐或有效疫苗。

瘧疾亞單位疫苗迄今為止已展示免疫原性之重大缺陷。所觀察到之免疫反應效價低且持續時間短。已探究各種方式來解決此缺陷，包含選擇

佐劑、於諸如病毒樣顆粒(VLP)、腺病毒載體等複合載體中表現及設置複雜初免-加強方案。即使使用來自惡性瘧原蟲瘧疾寄生蟲之紅血球前環子孢子蛋白(CSP)及B型肝炎病毒(HBsAg)之病毒套膜蛋白中之重複序列及T細胞表位的基因及複雜佐劑(例如AS01)所改造之RTS,S/AS01疫苗(Mosquirix®)亦受困於瘧疾特異性免疫反應之極短持續時間(而B型肝炎反應長時間保持較高)。

亦揭示瘧原蟲屬(Plasmodium)抗原至載體蛋白之化學偶聯。舉例而言，包括偶聯至銅綠假單胞菌(Pseudomonas aeruginosa)胞外蛋白A(repA)之去毒形式之瘧原蟲屬蛋白Pfs25H之疫苗正處於評估中。

然而，化學偶聯具有若干缺點。其在技術上較為吃力，難以再現，且相當昂貴。

仍亟需展示良好免疫原性及對抗瘧疾之保護而易於複製並負擔得起之疫苗產品。

【發明內容】

本發明提供源於由與載體蛋白(例如CRM197)融合之瘧原蟲屬多肽組成之新穎構築體之改良免疫原性的優點。並非以化學方式使瘧原蟲屬分子偶合至載體蛋白，發明者研發一種新穎方式，其中將寄生蟲蛋白與載體蛋白一起編碼為融合蛋白，從而製備「生物偶聯之融合產物」，其在本文中亦稱為「生物融合分子」且可以重組方式在(例如)大腸桿菌(E. coli)中產生。

更特定而言，本發明提供包括至少一個融合於載體異源蛋白序列之N-末端及/或C-末端之抗原性胺基酸序列之融合蛋白，其中抗原性序列包括瘧原蟲屬蛋白之表位序列且載體異源蛋白序列係在人類中具有免疫原性

之序列。

抗原性序列可為由紅血球階段之瘧原蟲屬所表現之抗原性蛋白或其表位片段。

或者，抗原性序列可為由紅血球前階段之瘧原蟲屬所表現之抗原性蛋白或其表位片段。

本發明之另一目標係編碼如本文所定義之融合蛋白之核酸構築體。

亦提供包括表現盒中之核酸構築體之載體以及插入載體之宿主細胞。

另外闡述製備融合蛋白之活體外方法，該方法包括使宿主細胞在誘導表現核酸構築體之條件下繁殖，且收集如此表現之融合蛋白。

根據本發明，提供一種疫苗，其包括該融合蛋白或至少兩種融合蛋白(其分別包括至少兩種不同抗原性胺基酸序列)之組合或編碼該(等)融合蛋白之核酸構築體與生理上可接受之媒劑。

該疫苗可用於向人類個體接種疫苗，來對抗瘧疾。

【圖式簡單說明】

圖1係PP21 (亦稱為「生物融合體MSP3-1」)之編碼序列之代表圖。鹼基對之標度自Nco I位點開始展示於下文中。

圖2展示pET26a-PP21質體圖(A)、藉由限制酶消解使用Sma I (B)或Eco R I (C)進行之小量製備分析。

圖3：藉由IMAC純化之重組蛋白PP21。(A)藉由電泳在變性條件及考馬斯藍色染(Coomassie blue)下進行之分析。(B)藉由西方印漬(Western blotting)使用鼠類抗MSP3免疫血清在1:1000稀釋下評價之抗原性。所觀察上區帶與全長PP21之84 kDa之理論分子量一致。37 kDa處之另一帶(在

較小程度上由抗MSP3免疫血清充分識別)可對應於PP21之降解片段。

圖4：藉由西方印漬使用抗MSP3-1 mAb RAM1在1:1000稀釋下所評價在不同儲存溫度下之PP21穩定性之時間量表。

圖5：與陽性對照MSP3-LSP相比所測定之PP21抗原含量。藉由與大量人類及動物抗MSP3血清(包含人類重組抗體)之反應性來測定臨床前PP21之抗原性。抗原含量提供反應性表位之量之較精確量度。其係藉由用於Elisa分析中之塗層之抗原連續稀釋液來實施且藉由充分定義之陽性對照(此處係藉由MSP3之C-末端區域免疫化之大鼠之集合)予以揭示。PP21之反應性與MSP3合成及重組構築體相同。

圖6：在藉由生物融合體MSP3-1偶聯物免疫化2次後於小鼠中所誘導之特異性抗體反應與當前MSP3-1-LSP相比之顯著改良。使用於Montanide ISA720中之僅1 μ g生物融合體MSP3-1或10 μ g MSP3-1 LSP在第0、14及28天對5隻(BALB/c)或4隻(C57BL/6)小鼠之組免疫化。在第2注射之後一週(亦即在第21天) (A)及在第3免疫化之後一週(亦即在第35天)收集血樣。藉由ELISA測定特異性MSP3-1 LSP抗體效價。單獨展示每一小鼠(1至5)之結果(此處係在僅兩次免疫化之後)。

圖7：在藉由生物融合體MSP3-1免疫化2次及3次後於小鼠中所誘導之抗體反應與當前MSP3-1-LSP之對比。第三注射加強抗體反應且證實生物融合體MSP3-1在C57Bl/6小鼠及Balb/c小鼠中之較佳免疫原性。藉由1 μ g生物融合體MSP3-1之3次注射誘導之MSP3-1-LSP特異性抗體之平均效價在C57Bl/6及Balb/c中分別達到 3×10^5 及 2×10^5 ；而10 μ g MSP3-1-LSP之3次注射在C57Bl/6及Balb/c小鼠中分別誘導最大 10^5 及 2.5×10^4 之平均效價。

圖8：藉由生物融合體MSP3-1在小鼠中所誘導之MSP3-1特異性抗體之持續時間與當前MSP3-1-LSP相比之重大改良。

A及B：生物融合體MSP3-CRM與MSP3-1-LSP之對比：使用於Montanide ISA720中之僅1 μg生物融合體MSP3-1或10 μg MSP3-1 LSP在第0、14及28天對BALB/c (A-上左圖)及C57BL/6 (B-上右圖)小鼠免疫化。在隨訪中之不同日期收集血樣。藉由ELISA測定特異性MSP3-1 LSP抗體效價。所展示結果對應於在不同日期於每一組小鼠中所獲得之抗MSP3-1 LSP抗體效價之幾何平均值。在160天隨訪之後，生物融合體-MSP3-1偶聯物免疫小鼠中之平均抗體效價在C57bl/6及Balb/c中分別為 1.5×10^5 及 10^5 ，其至少高於藉由MSP3-1-LSP誘導且在第一免疫化之後第160天量測之抗體之平均效價10倍。

C及D：藉由MSP3-CRM誘發之免疫反應之長期持久性：藉由在第0、14及103天經皮下注射在Montanide ISA 720佐劑(v/v)中佐劑化之1μg生物融合體MSP3-CRM來對Balb/c及C57B16小鼠(4至5隻小鼠/組)之組免疫化。在不同日期收集血樣。藉由ELISA測定特異性MSP3抗體效價。結果展示，在兩次免疫化之後效價顯著增加且在第49天達到最大，而第三抗原注射(實施於第103天)不誘導抗體反應量值之任何可檢測增加。該等特異性抗體僅隨時間略微降低，且即使在免疫化之後第540天仍可以高效價檢測到。

E：在僅2次免疫化之後藉由MSP3-CRM誘發之免疫反應之長期持久性。就在僅兩次免疫化之後觀察之滿意反應而言，在藉由皮下注射僅在第0及14天使用2μg在Montanide ISA 720 (v/v)中佐劑化之生物融合體MSP3-CRM免疫化之其他17隻Balb/c小鼠中分析此免疫化方案。在不同

日期收集血樣。藉由ELISA測定特異性MSP3-1-LSP抗體效價。結果展示，MSP3抗體效價在兩個抗原注射之後有所增加且在所有小鼠中於第42與72天之間達到最大，且展示在380天實驗隨訪中免疫反應僅適當降低。

圖9：與MSP3-1-LSP相比，在使用生物融合體MSP3-1免疫化之小鼠中誘導之抗體對MSP3-1 ADCI (Ab依賴性細胞抑制)靶表位之改良識別。在MSP3-1-LSP中，肽「b」、「c」及「d」定義由在ADCI分析中有效之抗體靶向之不同B細胞表位，其與抗MSP3-1抗體之保護效應相關。為評估生物融合體MSP3-1誘導抗體靶向該等表位之能力，藉由ELISA測定抗體對血清中之肽a、b、c及d之效價。因此，由新穎調配物識別之ADCI靶數相當大且具有較高效價。使用於Montanide ISA720中之僅1 µg生物融合體MSP3-1或10 µg MSP3-1 LSP在第0、14及28天對BALB/c及C57BL/6小鼠免疫化。在第3免疫化之後一週(亦即在第35天)收集血樣。以1/400稀釋小鼠血清且藉由ELISA測定不同MSP3-1肽(a、b、c及d)之特異性抗體之效價。所展示結果對應於使用每一測試小鼠之血清獲得之光學密度。

圖10：使用1 µg生物融合體MSP3-1、10 µg當前MSP3-1 LSP或10 µg MSP3-1 C-末端重組蛋白免疫化之HIMM模型(人類免疫原性小鼠模型)中之人類抗體反應。向NOD.Cg - Prkdc^{scid} - IL2rg^{tm1Wjl}/SzJ (NSG)小鼠中植入在活體外經1 µg/ml抗原(4隻小鼠/組)刺激或未刺激之人類脾細胞。使每一NSG小鼠接受 30×10^6 個經抗原引發或未引發之脾細胞之腹膜腔內注射(ip)。在第7及21天，使用1 µg生物融合體MSP3-1或10 µg MSP3-1-LSP或10 µg MSP3-1 C-末端重組蛋白加強重構小鼠。使用Montanide ISA 720 (v/v)將所有抗原佐劑化且經腹膜腔內(ip)進行注射。使用未引發脾細胞重構之小鼠僅接受佐劑。在每一免疫化之後一週收集血樣。藉由總

IgG及特異性IgG ELISA來分析特異性抗體。使用下式計算經調節特異性抗體效價： $(\text{抗原特異性抗體效價}/\text{總人類IgG濃度}) \times 10$ (10 mg/ml可視為平均人類總IgG濃度)。表示出ELISA效價之幾何平均值(95 % CI)。

圖11：使用1 μg 生物融合體MSP3-1、10 μg 當前MSP3-1 LSP或10 μg MSP3-1 C-末端重組蛋白免疫化之HIMM模型(Hu淋巴NSG小鼠)中之人類IFN- γ 細胞反應。免疫化條件與上文相同。藉由IFN- γ ELISPOT評估細胞反應。在第28天，回收每一組小鼠之脾細胞，彙集且在活體外使用或不使用抗原刺激進行培養。所展示結果對應於使用每一組小鼠獲得之特異性斑點形成細胞(SFC)。

圖12：HIMM中之T細胞反應：藉由1 μg 生物偶聯物PP21或10 μg MSP3-LSP免疫化之小鼠中之移植人類淋巴球中之CD4-Th1反應的顯著改良。

圖13：在使用生物融合體MSP3-1免疫化之HIMM模型中誘發之人類抗體對寄生蟲天然蛋白之改良識別。向NSG小鼠中植入人類脾細胞且使用1 μg 生物融合體MSP3-1、10 μg 當前MSP3-1 LSP或10 μg MSP3-1 C-末端重組蛋白免疫化(如圖6中所闡述)。藉由免疫螢光抗體測試(IFAT)在3D7惡性瘧原蟲(Pf)感染之紅血球上評估第28天小鼠血清中之人類抗體與寄生蟲蛋白之反應性(其係在瘧疾攻擊期間活化ADCI防禦機制之關鍵特徵)。所展示結果對應於使用每一組小鼠獲得之效價範圍。

圖14：使用1 μg 生物融合體MSP3-1免疫化之HIMM模型中所誘發之人類抗體反應不取決於疫苗製劑中所使用之佐劑。(A)向NSG小鼠中植入衍生自兩個不同供體且使用1 μg 經Montanide ISA720佐劑化之生物融合體MSP3-1進行刺激或並不刺激之人類脾細胞(如圖6中所闡述) (4隻小鼠/

組/供體)。(B)向NSG小鼠中植入使用1 μ g經MF59而非Montanide ISA720佐劑化之生物融合體MSP3-1進行刺激(9隻小鼠)或並不刺激(8隻小鼠)之人類脾細胞(如圖6中所闡述，但使用來自不同供體之人類淋巴球)。在兩種情形下，藉由ELISA在第28天測定特異性MSP3-1 LSP抗體效價。所展示結果對應於使用每一組小鼠獲得之ELISA效價之平均值 $\pm$ SD。

圖15：使用經Montanide ISA720佐劑化之生物融合體MSP3-1免疫化之HIMM模型中之人類淋巴球中所誘發人類IgG抗體之抗體子類。向NSG小鼠中植入使用1 μ g MSP3生物融合體刺激或並不刺激之人類脾細胞(如圖10中所闡述)。以1/20稀釋在第28天收集之小鼠血清。藉由子類IgG ELISA測定特異性MSP3-1 LSP抗體效價。所展示結果對應於使用經免疫化小鼠及未免疫化小鼠獲得之光學密度之平均值 $\pm$ SD。

圖16：使用經MF59佐劑化之生物融合體MSP3-1免疫化之HIMM模型中所誘發人類IgG抗體之子類。向NSG小鼠中植入使用1 μ g經MF59佐劑化之生物融合體MSP3-1刺激或並不刺激之人類脾細胞(如圖14中所闡述)。以1/20稀釋在第28天收集之小鼠血清。藉由子類IgG ELISA在具反應小鼠之血清中測定特異性MSP3-1 LSP抗體效價。所展示結果對應於使用經免疫化小鼠及未免疫化小鼠獲得之光學密度之平均值 $\pm$ SD。兩種佐劑皆獲得嗜細胞子類IgG1之主導性。

圖17：0.2 μ g或1 μ g PP21在Balbc小鼠 PP21-montanide (上左及上右)或相同劑量在C57b1小鼠(下圖左及下右圖)中之免疫原性。如圖6-8中來測定抗MSP3-1-LSP抗體效價之演變。

圖18：藉由PP21誘發之抗MSP3-1抗體與MSP3蛋白質家族之其他成員之交叉反應性(藉由ELISA測得之OD值)。使C57B1/6 (C)及Balb/c (B)

小鼠接受2次注射(J0、J14)之4 μ g PP21。在第63天收集試樣。

圖19：在C57BL(C)及Balb/C小鼠(B)中由氫氧化鋁佐劑化之PP21在1 μ g劑量/免疫化下之免疫原性。展示在2次免疫化或3次免疫化後藉由ELISA在C57BL (C)及Balb/C小鼠(B)中測得之抗體效價。未測試高於25:600之稀釋度。應注意，氫氧化鋁在人類中係產生高Th1反應之強力佐劑，與之相反，其在齧齒類動物中通常係較差佐劑，且仍與PP21一起誘導強力反應。

圖20.南美松鼠猴中之生物融合體偶聯物PP21之高免疫原性。藉由1 μ g由MontanideI Isa 720佐劑化之PP21 (在第0、28及112天經皮下投與)對出生於Primate Center of Belem, Brasil之動物屋中之籠中之南美松鼠猴免疫化(虛線，與僅接受Montanide之對照(直線)相比)。藉由ELISA針對MSP3-LSP抗原以及藉由IFAT及WB測定抗體(未展示)。即使在每次免疫化僅使用0.1 μ g抗原時，免疫反應約低5倍，亦即仍極顯著(未展示)。

圖 21：藉由LSA3-CRM (PP25)與LSA3-729在接受1 μ g PP25與Montanide ISA720或10 μ g LSA3-729與Montanide ISA720之Balb/C小鼠中所誘發之抗體反應。在第0、7、28天免疫化，在第45天收集血清。

圖22：LSA3-CRM (PP25)與LSA3-729免疫化Balb/C小鼠(在活體外藉由DG 729攻擊)中所誘發之IFN γ (ELISPOT)。

圖23：HIMM中之抗LSA3-729人類抗體反應及結果之改良再現性：使用來自兩個人類供體«A»及«B»之淋巴球在HIMM中對LSA3-CRM構築體PP25之抗LSA3-729人類抗體反應

圖24：藉由PP25誘發之免疫反應之持續時間之改良。

圖25：研發用於HuH7.5中之惡性瘡原蟲肝階段發育之新穎宿主細胞

且與人類原代肝細胞(HPH)進行比較。該圖展示在感染孢子之後第4、5及7天肝裂殖體之經小鼠多株抗PfHsp-70免疫染色之代表性試樣。放大率：400倍，比例尺：10 μm 。在第7天於HPH中難以發現滿意LS。然後將此肝細胞瘤模型用於功能分析中以量測能夠抑制孢子侵襲至肝細胞中之抗體。

圖26：抗Pf LSA3抗體對Hu7.5肝細胞瘤細胞中之孢子侵襲之抑制(ILSDA)。展示天然蛋白質上之抗LSA3反應性之間之關聯(藉由IFAT分析)以及肝階發育期抑制分析(ILSDA)中之功能抑制效應。較小圖形展示使用抗環孢子mAb 2A10之相同分析。

圖27：在HIMM模型中所移植之人類淋巴球中藉由構築體PP23(MSP3-2-CRMP97-MSP3-3)誘發強B及T細胞反應。上圖(A)展示抗體反應，中間圖(B)展示同型分佈，其主要係IgG1種類，主要嗜細胞種類能夠與ADCI機制中之單核球協同作用。下圖(C)展示藉由在活體外藉由MSP3-2或MSP3-3再刺激之IFN- γ 之分泌評估之T細胞反應。

圖28：BALb/c小鼠(n=5)中之1 μg 與10 μg 劑量之生物融合體LSA5-CRM/Montanide ISA720之免疫原性。實驗條件類似於圖8中所闡述者。在第0、14及28天(箭頭)藉由生物融合體LSA5-CRM/Montanide ISA720免疫化。藉由ELISA滴定利用LSA5-LSP作為抗原使用在第0、7、21、42天收集之血清來實施血清抗體檢測。

【實施方式】

定義

「疫苗」應理解為意指用以產生免疫性，以用於預防及/或治療疾病之組合物。因此，疫苗係包括抗原之藥劑，且計畫用於人類或動物中，藉

由接種疫苗而產生特定防禦及保護性物質。本文所用之「疫苗」意指能夠誘發之部分或完全保護之免疫原性組合物。疫苗可在受感染個體中用於預防感染及/或治療感染。

術語「免疫原性」意指所提及組合物或蛋白質能夠在投與時誘發免疫反應。個體中之「免疫反應」係指對抗原產生適應性及/或先天性免疫反應，包含體液免疫反應、細胞免疫反應或體液與細胞免疫反應。「體液免疫反應」係指由抗體所調介者。

本文件中所用之術語「保護」或「預防」係指在與瘧原蟲屬寄生蟲接觸之後不會出現症狀或出現之疾病症狀減少。特定而言，術語「預防瘧疾」係指所治療個體在與造成瘧疾之瘧原蟲屬接觸之後，不會出現症狀或出現之症狀減少。

「患者」或「個體」通常係哺乳動物個體，較佳係人類個體。個體可為雄性或雌性、兒童或成人。個體可為先前已診斷或鑑別為患有瘧疾者。或者，個體亦可為過去未曾被診斷患有瘧疾但處於發生該病症之風險下(例如因感染或因在瘧疾流行之區域內旅行)者。舉例而言，個體可為具有一或多種瘧疾症狀者。

舉例而言，個體可感染惡性瘧原蟲或間日瘧原蟲(*Plasmodium vivax*)。

原始多肽之「同源」或「實質上同源」序列通常係如下序列：其與原始多肽序列或原始多肽之免疫原性或表位片段具有至少約80%一致性，且實質上保留該原始多肽對預期靶之期望效應(亦即誘發免疫原性反應或被抗體識別)。在越佳之實施例中，同源序列與原始多肽序列或其免疫原性或表位片段具有至少約85%、90%、95%、97%或99%之一致性。

「免疫原性片段」通常具有至少5個胺基酸之長度。更佳地，免疫原性片段之長度為至少7、9、11、13、15、17及19個胺基酸。「表位」通常具有至少5個胺基酸，較佳為至少7至14個胺基酸之長度。「表位片段」包括該表位且因此可以更長。

在本發明之上下文中，術語「融合或生物融合」意指在重組蛋白中，載體蛋白係直接連接至抗原性瘡原蟲屬序列，或藉由肽連接體連接至抗原性瘡原蟲屬序列。肽連接體可為1至35個胺基酸，較佳為5至20個胺基酸，仍較佳為5至10個胺基酸之序列。在較佳實施例中，連接體肽係 $(\text{Gly-Gly-Gly-Gly-Ser})_n$ 、 $(\text{Gly})_n$ 或 $(\text{EAAAK})_n$ ，其中 n 為1至4，較佳為1至3。在任一實施例中，形成單一多肽。

載體蛋白

載體異源蛋白序列可有利地選自由以下組成之群：白喉類毒素之交叉反應材料(CRM)、白喉類毒素(D)、銅綠假單胞菌胞外蛋白A之無毒突變重組體(repA)、腦膜炎球菌外膜蛋白複合物(OMPC)、破傷風類毒素(T)、流行性感嗜血桿菌蛋白D (H. influenza protein D, hiD)及其免疫原性片段。

在較佳實施例中，載體異源蛋白序列可為CRM197或其免疫原性片段，該片段較佳地選自由以下組成之群：CRM197之片段A、跨膜結構域T、受體結合結構域R、CRM197之胺基酸序列1-190及CRM197之胺基酸序列1-389。

白喉毒素之片段A自胺基酸1延伸至201。CRM197擁有酶促惰性片段A，該片段展示甘胺酸52經麩胺酸取代。

白喉毒素之片段B自胺基酸202延伸至535。

下表1展示關於特定載體之其他資訊。

載體	名稱	NCB: SEQ ID NO
白喉毒素	DIP_RS12515毒素 [白喉棒桿菌 (<i>Corynebacterium diphtheriae</i>) NCTC 13129]	NC_002935.2 SEQ ID NO: 81
CRM197		SEQ ID NO: 82
破傷風類毒素	破傷風毒素[破傷風梭菌 (<i>Clostridium tetani</i>)]	X04436.1 SEQ ID NO: 83
Hib蛋白質D	用於蛋白質D之流行性感冒嗜 血桿菌(3639)基因	Z35656 SEQ ID NO: 84

亦可使用實質上同源序列。

抗原性瘧原蟲屬序列

本發明之融合蛋白構築體包括至少一個包括瘧原蟲屬蛋白之表位序列之抗原性序列。

該抗原性序列可為來自任一瘧原蟲屬物種之任一瘧原蟲屬抗原之序列。

感染人類之寄生蟲之「瘧原蟲屬」包括(但不限於)惡性瘧原蟲、間日瘧原蟲、諾氏症原蟲(P. knowles)、卵形瘧原蟲(P. ovale)及三日瘧原蟲(P. malariae)。下文所列示之抗原主要係來自惡性瘧原蟲之抗原。然而，亦涵蓋其他瘧原蟲屬物種中之直向同源物。特定而言，間日瘧原蟲抗原與惡性瘧原蟲抗原展示相同之低免疫原性。

該抗原可表現於紅血球階段(亦稱為「血液階段」)或紅血球前階段(子孢子及肝階段)中。

可使用之抗原性序列之實例列示於下表2中。亦可使用實質上同源序列。

表現於紅血球階段中且作為Ab依賴性細胞抑制(ADCI)防禦機制之靶之抗原包含：

MSP3 (例如MSP3-1、MSP3-2、MSP3-3、MSP3-4、MSP3-7、MSP3-8)、11-1之PEBS子區(亦稱為LSA5)、Glurp R0及R2、SERP、P27及P27A、P45、P90及P77、P14、P181 (其係P77之組合)、MSP1-區2、MSP2 (兩個3D7及FC27等位基因，二者皆係二態及恆定區域)、GBP 130 (尤其N及C部分二者)、蛋白質332、蛋白質11-1、MSP4或其任一表位片段。

較佳地，融合蛋白中之抗原性序列係MSP3或其表位片段。

在另一較佳實施例中，融合蛋白中之抗原性序列係LSA5或其表位片段。

惡性瘧原蟲裂殖子表面蛋白3 (MSP-3)係已知無性血液階段瘧疾疫苗候選抗原(Sirima等人，N Engl J Med 2011, 365(11):1062-1064；Demanga等人，Infect Immun 2010, 78(1):486-494；Daher等人，Infect Immun 2010, 78(1):477-485；Rousillon等人、Roussilhon等人，PLoS Medicine，2007年11月4日，第11期，e320)。

特定而言，可使用6種MSP3蛋白中之任一者，較佳為MSP3-1以及蛋白質之肽a、b、c、d、e、f、重組體C-末端亦及全長及N-末端。在一較佳實施例中，抗原性序列係MSP3或其表位片段，該片段涵蓋選自MSP3-1、MSP3-2、MSP3-3、MSP3-4、MSP3-7、MSP3-8之瘧原蟲屬MSP3蛋白之C-末端區域之基序a、b、c、d、e及/或f。

涵蓋來自裂殖子表面之其他抗原、尤其鬆散附接或裂解且由此可自裂殖子表面釋放者。

表現於紅血球前階段中之抗原包含LSA3、PEBS、CS、Trap及Salsa及其任一表位片段。在惡性瘧原蟲中，肝階段抗原-3 (LSA-3)係表現於紅血球前階段之抗原(Toure-Balde等人：Infect Immun 2009, 77(3):1189-1196；Daubersies等人：Nat Med 2000, 6(11):1258-1263)。

亦涵蓋涉及其他階段或其他機制之抗原。彼等抗原包含涉及有性階段之抗原(例如Pf25或Pf45/48)及涉及紅血球中之裂殖子侵襲抑制之GIA機制的血液階段抗原(例如Rh5、AMA1、MSP1-19、MSP1-42、MSP2或MSP4-5)或涉及細胞黏附之抗原(例如Var CSA)。

表2：抗原性序列(惡性瘧原蟲)

抗原	名稱	PlasmodB		胺基酸序列	
Ag27	營養子輸出蛋白 1 (TEX1)	PFF0165C	PF3D7_0603400	SEQ ID NO: 1	
Ag27 (P27A)	#肽27A	#	#	SEQ ID NO: 2	
Ag27 (P27)	#肽27	#	#	SEQ ID NO: 3	
MSP1	裂殖子表面蛋白 1 (MSP1)肽區塊II	PFI1475w	PFI1475w	SEQ ID NO: 4	
MSP1-42	裂殖子表面蛋白 -1 42kDa 片段[合成構築體]	#		SEQ ID NO: 5	
MSP2	裂殖子表面蛋白 2 (MSP2)	PFB0300c	PF3D7_0206800	SEQ ID NO: 6	
MSP3-1	裂殖子表面蛋白3-1	PF10_0345	PF3D7_1035400	SEQ ID NO: 7	
MSP3-1CT	C-末端	#	#	SEQ ID NO: 8	

MSP3-1a	#肽a	#	#	SEQ ID NO: 9
MSP3-1b	#肽b	#	#	SEQ ID NO: 10
MSP3-1c	#肽c	#	#	SEQ ID NO: 11
MSP3-1d	#肽d	#	#	SEQ ID NO: 12
MSP3-1e	#肽e	#	#	SEQ ID NO: 13
MSP3-1f	#肽f	#	#	SEQ ID NO: 14
MSP3-2	裂殖子表面蛋白3-2	PF10_0346	PF3D7_1035500	SEQ ID NO: 15
MSP3-2CT	C-末端	#	#	SEQ ID NO: 16
MSP3-2a	#肽a	#	#	SEQ ID NO: 17
MSP3-2b	#肽b	#	#	SEQ ID NO: 18
MSP3-2c	#肽c	#	#	SEQ ID NO: 19
MSP3-2d	#肽d	#	#	SEQ ID NO: 20
MSP3-2e	#肽e	#	#	SEQ ID NO: 21
MSP3-2f	#肽f	#	#	SEQ ID NO: 22
MSP3-3	裂殖子表面蛋白3-3	PF10_0347	PF3D7_1035600	SEQ ID NO: 23
MSP3-3CT	C-末端	#	#	SEQ ID

				NO: 24
MSP3-3a	#肽a	#	#	SEQ ID
				NO: 25
MSP3-3b	#肽b	#	#	SEQ ID
				NO: 26
MSP3-3c	#肽c	#	#	SEQ ID
				NO: 27
MSP3-3d	#肽d	#	#	SEQ ID
				NO: 28
MSP3-3e	#肽e	#	#	SEQ ID
				NO: 29
MSP3-3f	#肽f	#	#	SEQ ID
				NO: 30
MSP3-4	裂殖子表面蛋白3-4	PF10_0348	PF3D7_1035700	SEQ ID
				NO: 31
MSP3-4CT	C-末端	#	#	SEQ ID
				NO: 32
MSP3-4a	#肽a	#	#	SEQ ID
				NO: 33
MSP3-4b	#肽b	#	#	SEQ ID
				NO: 34
MSP3-4c	#肽c	#	#	SEQ ID
				NO: 35
MSP3-4d	#肽d	#	#	SEQ ID
				NO: 36
MSP3-4e	#肽e	#	#	SEQ ID
				NO: 37
MSP3-4f	#肽f	#	#	SEQ ID
				NO: 38
MSP3-7	裂殖子表面蛋白3-7	PF10_0352	PF3D7_1036000	SEQ ID
				NO: 39

MSP3-7CT	C-末端	#	#	SEQ ID NO: 40
MSP3-7a	#肽a	#	#	SEQ ID NO: 41
MSP3-7b	#肽b	#	#	SEQ ID NO: 42
MSP3-7c	#肽c	#	#	SEQ ID NO: 43
MSP3-7d	#肽d	#	#	SEQ ID NO: 44
MSP3-7e	#肽e	#	#	SEQ ID NO: 45
MSP3-7f	#肽f	#	#	SEQ ID NO: 46
MSP3-8	裂殖子表面蛋白3-8	PF10_0355	PF3D7_1036300	SEQ ID NO: 47
MSP3-8CT	C-末端	#	#	SEQ ID NO: 48
MSP3-8a	#肽a	#	#	SEQ ID NO: 49
MSP3-8b	#肽b	#	#	SEQ ID NO: 50
MSP3-8c	#肽c	#	#	SEQ ID NO: 51
MSP3-8d	#肽d	#	#	SEQ ID NO: 52
MSP3-8e	#肽e	#	#	SEQ ID NO: 53
MSP3-8f	#肽f	#	#	SEQ ID NO: 54
MSP4	裂殖子表面蛋白4	PFB0310c	PF3D7_0207000	SEQ ID

(SALSA)	(MSP4)			NO: 55
Pf11.1	配子母細胞特異性蛋白質(Pf11-1)	PF10_0374	PF3D7_1038400	SEQ ID NO: 56
Pf11.1	Pf11.1之子區域(亦稱為	#	#	SEQ ID NO: 57
(PEBS)	LSA5)			
Ag332	抗原332，DBL樣蛋白質(Pf332)	PF11_0356	PF3D7_1149000	SEQ ID NO: 58
SERP	絲胺酸重複抗原 1 (SERA1)	PFB0360c	PF3D7_0208000	SEQ ID NO: 59
	絲胺酸重複抗原 2 (SERA2)	PFB0355c	PF3D7_0207900	SEQ ID NO: 60
#	絲胺酸重複抗原 3 (SERA3)	PFB0350c	PF3D7_0207800	SEQ ID NO: 61
#	絲胺酸重複抗原 4 (SERA4)	PFB0345c	PF3D7_0207700	SEQ ID NO: 62
#	絲胺酸重複抗原 5 (SERA5)	PFB0340c	PF3D7_0207600	SEQ ID NO: 63
GLURP	富麩胺酸鹽蛋白質 (GLURP)	PF10_0344	PF3D7_1035300	SEQ ID NO: 64
GLURP-R0	肽R0	#	#	SEQ ID NO: 65
GLURP-R2	肽R2	#	#	SEQ ID NO: 66
Gbp130	血型糖蛋白結合蛋白質 (GBP)	PF10_0159	PF3D7_1016300	SEQ ID NO: 67
P14	保守瘧原蟲屬蛋白，未知功能肽14	PFC0245c	PF3D7_0305500	SEQ ID NO: 68
P45	保守瘧原蟲屬蛋白，未知功能肽45	PF11_0207	PF3D7_1120000	SEQ ID NO: 69
P77	Snf2相關CBP活化劑，假定(SRCAP)肽77	PF08_0048	PF3D7_0820000	SEQ ID NO: 70

P90	保守瘧原蟲屬蛋白，未知功能肽90	PFD0520c	PF3D7_0410500	SEQ ID NO: 71
RH5	網狀細胞結合蛋白同系物5 (RH5)	PFD1145c	PF3D7_0424100	SEQ ID NO: 72
AMA1	頂端膜抗原1 (AMA1)	PF11_0344	PF3D7_1133400	SEQ ID NO: 73
Pfs25	25 kDa動合子表面抗原前體(Pfs25)	PF10_0303	PF3D7_1031000	SEQ ID NO: 74
VAR	紅血球膜蛋白1，PfEMP1 (VAR)	PFA0005w	PF3D7_0100100	SEQ ID NO: 75
LSA3	肝階段抗原3	PFB0915w	PF3D7_0220000	SEQ ID NO: 76
LSA3 (DG729)	肽DG729	#	#	SEQ ID NO: 77
CS	環子孢子(CS)蛋白	PFC0210c	PF3D7_0304600	SEQ ID NO: 78
TRAP	(凝血酶敏感蛋白相關匿名蛋白(TRAP)	PF13_0201	PF3D7_1335900	SEQ ID NO: 79
SALSA	裂殖子表面蛋白4 (MSP4)	PFB0310c	PF3D7_0207000	SEQ ID NO: 80

#係指與上一列相同之參考

融合構築體

在一特定實施例中，融合蛋白包括融合至CRM197或其免疫原性片段(作為載體序列)之MSP3 (較佳地MSP3-1)、LSA3、LSA5 (亦稱為PEBS)或其表位片段(作為抗原性序列)或由其組成。

在一較佳態樣中，融合蛋白包括兩個抗原性序列，該等抗原性序列各自位於載體蛋白序列之C-末端及N-末端，或二者皆位於同一末端，其中兩個抗原性序列彼此相同或不同。

在一較佳實施例中，抗原性序列與載體序列之間之融合係直接融合。

在另一實施例中，至少一個胺基酸序列可藉由肽連接體連接於載體異源蛋白序列之N-末端及/或C-末端，其中肽連接體較佳係1至35個胺基酸，較佳為5至20個胺基酸之序列。在一較佳態樣中，肽連接體係(Gly-Gly-Gly-Gly-Ser)_n、(Gly)_n或(EAAAK)_n，其中n為1至4，較佳為1至3。

核酸、載體及宿主細胞

可藉由任一重組技術來製備本發明融合蛋白。因此，本發明之另一態樣係關於含有編碼該融合蛋白之核酸之載體，較佳為表現載體。

本發明中所使用之表現載體可提供活體外及/或活體內表現(例如在適宜宿主細胞、宿主生物體及/或表現系統中)。其通常包括如上文所定義之多核苷酸序列及調控序列(例如適宜啟動子、增強子、終止子等)，從而容許將蛋白質產物表現(例如轉錄及轉譯)於宿主細胞或宿主生物體中。

本發明載體可呈載體形式，例如質體、黏粒、YAC、病毒載體或轉座子。

在一較佳但非限制性態樣中，本發明載體包括i)至少一個如上文所闡述之核酸；其可操作地連結至ii)一或多個調控元件，例如啟動子及視情況選用之適宜終止子；及亦視情況選用之iii)一或多個基因構築體之其他元件，例如3'-或5'-UTR序列、前導序列、選拔標記物、表現標記物/報導子基因及/或可促進或增加轉變或整合(效率)之元件。

較佳宿主細胞係大腸桿菌。然而，可使用任一原核或真核表現系統，例如細菌、酵母、絲狀真菌、昆蟲、植物細胞及哺乳動物細胞。

較佳載體、啟動子及宿主細胞皆係能夠表現醣基化或非醣基化重組

蛋白之載體、啟動子及宿主細胞，例如：用於原核表現之pET26a (具有T7啟動子)或pTrcHis2 (具有trp lac啟動子)質體、用於轉移之pUC19、pUC 57或 pCR4 TOPO質體、及用於蛋白質表現之大腸桿菌BL21 (DE3)或大腸桿菌NiCo21宿主細胞、或僅用於質體擴增之大腸桿菌Top 10。

疫苗調配物

將融合蛋白與生理上可接受之媒劑一起、視情況與佐劑組合調配於醫藥組合物中。

由此提供包括融合蛋白或至少兩種融合蛋白(其分別包括至少兩個不同抗原性胺基酸序列)之組合與生理上可接受之媒劑之疫苗。

在另一實施例中，提供包括編碼該(等)融合蛋白之核酸構築體之疫苗組合物。

在一些實施例中，疫苗可包括一或多種醫藥上可接受之媒劑或賦形劑。賦形劑包括本身不會誘導產生抗體且不會傷害接受組合物之個體之組分。適宜賦形劑通常係緩慢代謝之大分子，例如醣、聚乳酸、聚乙醇酸、聚合胺基酸、胺基酸共聚物、蔗糖、海藻糖、乳糖及脂質聚集體(例如油微滴或脂質體)。熟習此項技術者已熟知適宜醫藥媒劑，包括(但不限於)稀釋劑，例如水、生理鹽水及其他。適宜地，無菌無熱原磷酸鹽緩衝生理鹽水係醫藥媒劑。另外，可包含添加劑，例如潤濕劑或乳化劑、pH緩衝物質及諸如此類。

醫藥組合物、免疫原性組合物或疫苗可進一步包括佐劑。「佐劑」係用於增強組合物效能且包括(但不限於)氫氧化鋁(alum)、磷酸鋁、水包油或油包水性乳液、類鐸(Toll-like)受體激動劑、N-乙醯基-降胞壁醯基-L-丙胺醯基- D-異麩醯胺酸(-MDP)、N-乙醯基-胞壁醯基-L-蘇胺醯基-D-

異甾醯胺酸(nor-MDP)、PEI、AS01或AS02 (GlaxoSmithKline)、GLA-SE (IDRI)及類似調配物；與業內已知之類似佐劑。亦可使用基於純化角鯊烯及角鯊烷、經高度純化之二縮甘露醇單油酸酯乳化之Montanide®佐劑，包含ISA 51及720。MF59®係佐劑之另一實例，其係角鯊烯、聚氧乙稀山梨醇酐單油酸酯(Tween® 80)及山梨醇酐三油酸酯之水包油性乳液。

將疫苗調配成用於擬投與個體之適宜劑量。所投與劑量可隨個體之病狀、性別、體重及年齡、投與途徑及所用佐劑而變化。可使用諸如懸浮液或液體溶液等劑型之疫苗。可將疫苗與如上文所闡述之醫藥上可接受之媒劑一起調配。適宜劑量包括(但不限於)約0.1微克至約100微克，較佳為約1微克至約50微克、仍較佳地1微克至20微克、1微克至15微克或甚至1微克至10微克之本文所闡述之融合蛋白。

接種疫苗

免疫原性組合物或疫苗可為對組分/多抗原免疫原性組合物或疫苗。

在免疫原性組合物或疫苗預期用於多投與方案(例如初免-加強方案)之情形下，初免組合物可與加強組合物包括相同或不同組合物。然而，初免-加強方案在本發明背景中並非強制性。

可藉由任一便利途徑，較佳為非經腸、經肌內、經真皮內、經皮下、經黏膜或經靜脈內投與免疫原性組合物或疫苗。

可利用各種技術來進行DNA接種疫苗，例如電穿孔、無針方式(例如顆粒轟擊及高壓遞送)、真皮貼劑、呈微粒或脂質體形式之DNA疫苗調配物。

本發明闡述在個體中產生免疫反應之方法，其包括投與有效量之本發明疫苗之步驟。疫苗可預防性投與(亦即預防感染)或用以提供保護且較

佳地涉及誘導抗體及/或T細胞免疫性。該方法可產生一級免疫反應、二級免疫反應、加強反應或免疫反應之組合。

疫苗意欲在任一階段(包含紅血球前階段(例如肝階段)及/或有性或無性血液階段)對抗瘧疾來保護個體。

根據本發明來增加針對瘧原蟲屬抗原之免疫反應之量值及/或記憶。

尤其地，本發明之MSP3融合構築體觸發產生抗MSP3嗜細胞抗體，例如IgG1及IgG3抗體。可藉由量測該等抗體之效價來測定保護程度。

圖及實例闡釋本發明，而不限其範圍。

實例：

先前研究已展示，頻繁瘧疾暴露使得在成人中產生免疫性，此會預防或緩解疾病。此免疫性可藉由投與免疫球蛋白(IgG)自瘧疾免疫成人被動轉移。

鑑別出寄生蟲殺死機制，稱為抗體依賴性細胞調介之抑制(ADCI)。藉由ADCI篩選寬基因體DNA庫使得可鑑別裂殖子-表面蛋白3 (MSP3)且隨後鑑別若干其他抗原(包含PEBS)。

將嗜細胞抗體鑑別為保護代用品：發現調介ADCI之嗜細胞(結合白血球)抗MSP3抗體 IgG1及IgG3始終與在流行病學研究中於許多不同環境中瘧疾風險之減小有關。該等抗體亦調介針對感染動物中之惡性瘧原蟲之保護。

該等研究指示有效免疫反應所具有之特性且指導研發改良之疫苗調配物。

基於此，發明者現已展示，與MSP3-LSP (涵蓋MSP3-1之186-271區域之長合成肽)相比，在B細胞及T細胞層面上，融合蛋白CRM97-MSP3將

免疫原性增加20-100倍。參見**實例1**。使用10倍低之免疫化劑量，可由此達成對來自人類、小鼠及松鼠猴之淋巴球之免疫原性之重大改良及抗體持續時間之主要改良。

在紅血球前階段，先前研究已另外展示，可在黑猩猩中藉由LSA3來誘發針對大規模孢子攻擊之保護效能，該效能取決於很可能抑制LS產生之IFN- γ 及預防孢子侵襲之抗體。

在**實例2**中，發明者已展示，生物融合體CRM-LSA3構築體強烈增加T細胞及B細胞反應。

實例1及2中所獲得之結果已證實可使用來自紅血球階段之其他抗原(例如MSP3-2及MSP3-3與CRM之構築體)再現(參見**實例3**)。

實例4提供使用LSA5-CRM構築體之結果。

材料及方法

表現構築體之生成及大腸桿菌中之生物融合蛋白之產生

以化學方式合成(GenScript)編碼由去毒白喉毒素CRM197 (在N-末端及C-末端共價連接至瘧疾肽抗原)構成之嵌合免疫原之基因序列(圖1)且密碼子最佳化以在大腸桿菌中產生。分別在5'及3'末端添加用於Nco I及Xho I之限制位點以選殖於表現質體pET-26a (Novagen)中。藉由測序檢查插入穿梭質體pUC57中之序列且加速凍乾(4 μ g)。

PP21中之MSP3-1肽(plasmodB acc. Nbr PF3D7_1035400)對應於MSP3-1中之胺基酸(AA) 155至249。

已針對CRM197設計其他混合免疫原(表3)。在PP22中，MSP3-1肽藉由MSP3-2肽(MSP3-2之AA 178至257，PlasmodB acc. Nbr PF3D7_1035500)代替。在PP23中，C-末端之MSP3-2肽由MSP3-3肽

(MSP3-3 中之 AA 246 至 307，PlasmodB acc. Nbr PF3D7_1035600) 代替。PP25 在兩個 CRM197 末端含有相同 LSA3 肽 (AA 176 至 325，PlasmodB acc. Nbr PF3D7_0220000)。

表3：免疫原PP21、PP22、PP23、PP25及LSA5-CRM之物理化學特性

嵌合重組免疫原(大腸桿菌)		胺基酸 Nbr.	分子 量 (kDa)	pHi
PP21	MSP3-1 lsp*_CRM197_MSP3-1 lsp_6His	757	84	5,4
PP22	MSP3-2 lsp_CRM197_MSP3-2 lsp_6His	727	80	4,6
PP23	MSP3-2 lsp_CRM197_MSP3-3 lsp_6His	709	78	4,9
PP25	LSA3 lsp_CRM197_LSA3 lsp_6His	845	93	4,3
LSA5-CRM 蛋 白質	PEBS-CRM197-PEBS_6His	807	90	4.07

*lsp：長合成肽

將大腸桿菌轉移菌株Top 10 (Invitrogen) [F– *mcrA* Δ(*mrr-hsdRMS-mcrBC*) Φ80*lacZ*Δ*M15* Δ*lacX74* *recA1* *araD139* Δ(*ara leu*) 7697 *galU galK rpsL* (StrR) *endA1 nupG*]用於選殖分子程序及質體繁殖。

在菌株BL21 (DE3) [F – *ompT hsdSB (rB– mB) gal dcm* (DE3)] (NEB)中表現重組體。

使用Nco I及Xho I消解含有混合序列之穿梭質體pUC57 (Genscript) 及表現質體pET26a。藉由在電泳之後進行凝膠提取(QIAGEN)來回收插入體及線性化pET26a之帶。將凝膠純化插入體以3之插入體對質體比率接合

於pET26a內部。使用接合反應來轉變化學感受態大腸桿菌Top 10且平鋪於皮氏培養皿(Petri dish)中含有50 μ g/mL卡那黴素(kanamycin)之LB瓊脂培養基中。

在含有卡那黴素之液體培養基中挑選6個細菌菌落以用於二氧化矽管柱上之質體小量製備(QIAGEN)。藉由使用資訊性限制酶進行消解來檢查插入體在pET26a中之正確插入(圖2)。

選拔具有正確限制特徵之質體來轉變BL21 (DE3)細菌。

針對6個藉由上述限制酶消解分析之BL21 (DE3)純系來證實使用正確質體之轉變。

小體積細菌培養物中之重組蛋白產生之最佳化

在愛倫美氏器皿(Erlenmeyer vessel)中以小培養規模(1 L)分析諸如重組蛋白產生持續時間、誘導劑(IPTG)濃度及溫度等參數。將5 mL穩態過夜培養物稀釋至1 L (1:200)且進一步在30 $^{\circ}$ C下培養至600nm下之光學密度為0,7-0,8。使用兩種IPTG誘導劑濃度：0.1 mM及1 mM在三個溫度：22 $^{\circ}$ C、30 $^{\circ}$ C及37 $^{\circ}$ C下分析重組蛋白表現之誘導。在22 $^{\circ}$ C下過夜培養且藉由0.1 mM IPTG誘導之後獲得最佳重組體產量。

在藉由固定金屬親和力層析(IMAC)純化之後獲得1 mg至2 mg重組產物/公升細菌培養物之產量。

PP21之產生及純化

實施研究實驗室規模(1至2公升)之產生以獲得足夠PP21重組蛋白來實施鼠類及靈長類動物模型中之臨床前免疫原性研究。

先前已在小規模培養物中確立用於細菌培養及重組蛋白產生之方案。

藉由親和力在Ni-NTA樹脂(QIAGEN)上來純化C-末端六組胺酸加標籤重組蛋白PP21。

探究在天然或變性條件下之兩種純化程序。

實際上，儘管在天然條件中於細菌裂解物不溶性部分中看不到重組蛋白，但亦分析變性條件下之純化以評價三維PP21結構之假定構象效應對組胺酸標籤針對Ni-NTA樹脂上固定Ni²⁺金屬之可用性的效應。

天然條件下之純化：

- 藉由離心(4000g, 30 min, 4°C)回收細菌細胞。
- 將細菌糰粒懸浮於5 mL裂解緩衝液(50 mM NaH₂PO₄、300 mM NaCl、10 mM咪唑，pH 8.0)/克生物質中。
- 將裂解物在冰上與1 mg/mL溶菌酶一起搖晃30 min。
- 藉由530 sec破裂在150 W下使用30 sec冷卻間隔來裂解細菌。
- 將裂解物在冰上與5μg/mL DNase I及10μg/mL RNase A以及完整組蛋白酶抑制劑(Roche)一起搖晃30 min。
- 藉由在10000g、30 min及4°C下離心來清洗裂解物。
- 經由0.22 μm篩過濾裂解物且在4°C下於擺盤上以20 mL體積與200 μL Ni NTA樹脂一起培育過夜。
- 將樹脂在40 mL體積之裂解緩衝液中深度洗滌5次。將第一步驟上清液(樹脂培育後之裂解物)之等分試樣保存用於分析。離心步驟在200g下不超過5 min。
- 藉由在500 μL含有250 mM咪唑之裂解緩衝液中培育樹脂5倍來回收重組蛋白。
- 彙集洗脫部分且針對pH 7.3 PBS藉由超濾經由30 kDa篩來進行透

析。

藉由分光光度法在280 nM下量測蛋白質濃度且進一步藉由如圖3中針對PP21所展示之電泳(SDS-PAGE 10%)及免疫印漬進行表徵。

變性條件下之純化：

藉由離心(4000g, 30 min, 4°C)回收細菌細胞。

將細菌糰粒懸浮於5 mL變性裂解緩衝液(100 mM NaH₂PO₄、10 mM Tris-Cl、8 M脲、pH 8.0 NaOH)/克生物質中。

將裂解物在冰上搖晃30 min。

藉由530 sec破裂在150 W下使用30 sec冷卻間隔來進一步裂解細菌。

藉由在10000g、30 min及4°C下離心來清洗裂解物。

經由0,22 μm篩過濾裂解物且在4°C下於擺盤上以20 mL體積與200 μL Ni NTA樹脂一起培育過夜。

將樹脂在40 mL體積之變性裂解緩衝液中深度洗滌5次。將第一步驟上清液(樹脂培育後之裂解物)之等分試樣保存用於分析。離心步驟在200g下不超過5 min。

藉由在500 μL含有250 mM咪唑之裂解緩衝液中培育樹脂5倍來回收重組蛋白。

彙集洗脫部分且針對pH 7.3 PBS藉由超濾經由30 kDa篩來進行透析。

藉由兩種方法所達成之純化產量類似，從而表明親和力組胺酸標籤在天然形式之PP21中具有功能性。

在愛倫美氏器皿中以1公升規模於10個以上產生/純化試驗中重複獲

得0,7 mg至1mg重組蛋白PP21/公升細菌培養物之產量。

圖3展示藉由IMAC純化之重組蛋白PP21。

PP21之溫度穩定性

藉由西方印漬評價之隨儲存溫度而變化之PP21穩定性展示於圖4中。在在6℃溫度下儲存於冰箱中21天時段之後觀察到並無降解跡象。在室溫下，PP21開始在相同時段下展示降解跡象，而其在37℃下於8天之後完全降解。然而，此不穩定性不能歸因於假定固有分子不穩定性，此乃因其並非GMP製造產物且其可含有痕量蛋白酶。

藉由pET26a表現於大腸桿菌中之重組蛋白之胺基酸序列展示於下文中。括號中之序列係來自表現質體，粗體係來自CRM197白喉毒素。

將C-末端用於藉由固定金屬親和力層析(IMAC)純化之六組胺酸加下劃線。

PP21；以斜體加下劃線之MSP3-1之序列(PlasmodB ID：PF3D7_1035400)，殘基155至249 (95 aa)

[MKYLLPTAAAGLLLLAAQPAMAMG]*KTKEYAEKAKNAYEKAKN*
AYQKANQAVLKAKEASSYDYILGWEFGGGVPEHKKEENMLSHLYVSSKD
*KENISKENDDVLDEKEEEEAEETEEEELE***GADDVVDSSKSFVMENFSSY**
HG**TKPGYVDSIQKGIQKPKSGTQGN****YDDDWKEFYSTDNKYDAAG**
YSVDNENPLSGKAGGVVKVTYPGLTKVLALKVDNAETIKKELGL
SLTEPLMEQVGTEEFIKRFGDGASRVVLSLPFAEGSSSVEYINNWE
QAKALSVELEINFETRGRGQDAMYEYMAQACAGNRVRRSVGSS
LSCINLDWDVIRDKTKTKIESLKEHGPIKNKMSESPNKTVSEEKA
KQYLEEFHQTALEHPELSELKTVTGTNPVFAGANYAAWAVNVAQ

VIDSETADNLEKTTAALSILPGIGSVMGIADGAVHHNTEEIIVAQSI
 ALSSLMVAQAIPLVGELVDIGFAAYNFVESIINLFQVVHNSYNRPA
 YSPGHKTQPFLHDGYAVSWNTVEDSIIRTGFQGESGHDIKITAEN
 TPLPIAGVLLPTIPGKLDVNKSKTHISVNGRKIRMRCRAIDGDVTF
 CRPKSPVYVGNGVHANLHVAFHRSSSEKIHSNEISSDSIGVLGYQK
 TVDHTKVNSKLSLFFFEIKSKTKEYAEKAKNAYEKAKNAYQKANQAVLK
AKEASSYDYILGWEFGGGVPEHKKEENMLSHLYVSSKDKENISKENDDV
LDEKEEEAEETEEEELE[LEHHHHHH] (SEQ ID NO: 85)。

PP22 ； 以 斜 體 加 下 劃 線 之 MSP3-2 之 序 列 (PlasmodB ID :
 PF3D7_1035500) ， 殘 基 178 至 257 (79 aa)

[MKYLLPTAAAGLLLLAAQPAMAMG]LNNNILGWEFGGGAPQN
GAAEDKKTEYLLEQIKIPSWDRNNIPDENEQVIEDPQEDNKDEDEDEET
ETENLETEDDNNEEGADDVVDSSKSFVMENFSSYHGTPKPGYVDSIQ
 KGIQKPKSGTQGNYYDDDWKEFYSTDNKYDAAGYSVDNENPLSGK
 AGGVVKVTYPGLTKVLALKVDNAETIKKELGLSLTEPLMEQVGT
 EEFIKRFGDGASRVVLSLPFAEGSSSVEYINNWEQAKALSVELEIN
 FETRGRGQDAMYEYMAQACAGNRVRRSVGSSLSCINLDWDVIR
 DKTKTKIESLKEHGPIKNKMSESPNKTVSEEKAKQYLEEFHQ TAL
 EHPELSELKTVTGTNPVFAGANYAAWAVNVAQVIDSETADNLEK
 TTAALSILPGIGSVMGIADGAVHHNTEEIIVAQSIALSSLMVAQAIP
 LVGELVDIGFAAYNFVESIINLFQVVHNSYNRPAYSPGHKTQPFLH
 DGYAVSWNTVEDSIIRTGFQGESGHDIKITAENTPLPIAGVLLPTIP
 GKLDVNKSKTHISVNGRKIRMRCRAIDGDVTF CRPKSPVYVGNG

VHANLHVAFHRSSSEKIHSNEISSDSIGVLGYQKTV DHTKVNSKLS
 LFFEIKSLNNNILGWEFGGGAPONGAAEDKKTEYLLEQIKIPSWDRN
NIPDENEQVIEDPQEDNKDEDEDEETETENLETEDDNNEE[LEHHH
HHH] (SEQ ID NO: 86)。

PP23；在CRM197之前以斜體加下劃線之MSP3-2之序列(PlasmodB
 ID：PF3D7_1035500)，殘基178至257 (79 aa)，及在CRM197之後之斜體
 之MSP3-3之序列(PlasmodB acc. Nbr PF3D7_1035600)，殘基246至307
 (61 aa)。

[MKYLLPTAAAGLLLLAAQPAMAMG]LNNNILGWEFGGGAPQN
GAAEDKKTEYLLEQIKIPSWDRNNIPDENEQVIEDPQEDNKDEDEDEE
TETENLETEDDNNEEGADDVVDSSKSFVMENFSSYHGTKPGYVDSIQ
 KGIQKPKSGTQGN YDDDWKEFYSTDNKYDAAGYSVDNENPLSGK
 AGGVVKVTYPGLTKVLALKVDNAETIKKELGLSLTEPLMEQVGT
 EEFIKRFGDGASRVVLSLPFAEGSSSVEYINNWEQAKALSVELEIN
 FETRGRGRGDAMY EYMAQACAGNRVRRSVGSSLSCINLDWDVIR
 DKTKTKIESLKEHGPIKNKMSESPNKTVSEEKAKQYLEEFHQ TAL
 EHPELSELKTVTGTNPVFAGANYAAWAVNVAQVIDSETADNLEK
 TTAALSILPGIGSVMGIADGAVHHNTEEIVAQSIALSSLMVAQAIP
 LVGELVDIGFAAYNFVESIINLFQVVHNSYNRPAYSPGHKTQPFLH
 DGYAVSWNTVEDSIIRTGFQGESGHDIKITAENTPLPIAGVLLPTIP
 GKLDVNKSKTHISVNGRKRIRMRCRAIDGDVTFCRPKSPVYVGNG
 VHANLHVAFHRSSSEKIHSNEISSDSIGVLGYQKTV DHTKVNSKLS
 LFFEIKSSNEKGRPPTYSPILDDGIEFSGGLYFNEKKSTEENKQKNVLES

VNLTSWDKEDIVKENEDVK[LEHHHHHH](SEQ ID NO: 87)。

PP25 ； 以 斜 體 加 下 劃 線 之 LSA-3 之 序 列 (PlasmodB ID : PF3D7_0220000)，殘基176至325 (150 aa)

[MKYLLPTAAAGLLLLAAQPAMAMG]SDELFNELLNSVDVNGEV
KENILEESQVNDDIFNSLVKSVQQEQQHNVEEKVEESVEENDEESVEENV
EENVEENDDESVASSVEESIASSVDESIDSSIEENVAPTVEEIVAPTVEEIVA
PSVVESVAPSVEESVEENVEESVAENVEEG**ADDVVDSSKSFVMENFSS**
YHG**TKPGYVDSIQKGIQKPKSGTQGN****YDDDWKEFYSTDNKYDAA**
GYSVDNENPLSGKAGGVVKVTYPGLTKVLALKVDNAETIKKELG
LSLTEPLMEQVGTEEFIKRFGDGASRVVLSLPFAEGSSSVEYINNW
EQAKALSVELEINFETRGRGQDAMYEYMAQACAGNRVRRSVG
SSLSCINLDWDVIRDKTKTKIESLKEHGPIKNKMSESPNKTVSEEK
AKQYLEEFHQTALEHPELSELKTVTGTNPVFAGANYAAWAVNVA
QVIDSETADNLEKTTAALSILPGIGSVMGIADGAVHHNTEEIVAQS
IALSSLMVAQAIPLVGELVDIGFAAYNFVESIINLFQVVHNSYNRP
AYSPGHKTQPFLHDGYAVSWNTVEDSIIRTGFQGESGHDIKITAE
NTPLPIAGVLLPTIPGKLDVNKSKTHISVNGRKIRMRCRAIDGDVT
FCRPKSPVYVGNGVHANLHVAFHRSSEKIHSNEISSDSIGVLGYQ
KTVDHTKVNSKLSLFFEIKSSDELFNELLNSVDVNGEVKENILEESQV
NDDIFNSLVKSVQQEQQHNVEEKVEESVEENDEESVEENVEENVEENDD
ESVASSVEESIASSVDESIDSSIEENVAPTVEEIVAPTVEEIVAPSVVESVAPS
VEESVEENVEESVAENVEE[LEHHHHHH](SEQ ID NO: 88)。

LSA5-CRM蛋白序列(SEQ ID NO: 89)

IPEEQIEEVIQEEIIEQVVPEELIEEVVPEEIIIEEVIPEEIVEEVIYEEVI
PEELVEEVIAEKLKLVKEIVPEQVREEVTLEEIVEEMIPEEFVVEEVAPEVEIEE
IIPEELIEEVIPEVLVEEAVPEELIEKVIPGADDVVDSSKSFVMENFSSYH
 GTKPGYVDSIQKGIQKPKSGTQGNVDDDWKEFYSTDNKKYDAAGYSV
 DNENPLSGKAGGVVKVTYPGLTKVLALKVDNAETIKKELGLSLTEPL
 MEQVGTEEFIKRFGDGASRVVLSLPFAEGSSSV EYINNWEQAKALSV
 ELEINFETRGRGQDAMYEYMAQACAGNRVRRSVGSSLSCINLDWD
 VIRDKTKTKIESLKEHGPIKNKMSESPNKTVSEEKAKQYLEEFHQ TAL
 EHPSELKTVTGTNPVFAGANYAAWAVNVAQVIDSETADNLEKTT
 AALSILPGIGSVMGIADGAVHHNTEEIVAQSIALSSLMVAQAIPLVGE
 LVDIGFAAYNFVESIINLFQVVHNSYNRPAYSPGHKTQPFLHDGYAV
 SWNTVEDSIIRTGFQGESGHDIKITAENTPLPIAGVLLPTIPGKLDVNK
 SKTHISVNGRKRIRMRCRAIDGDVTFCRPKSPVYVGNGVHANLHVAFH
 RSSSEKIHSNEISSDSIGVLGYQKTVDHTKVNSKLSLFFFEIKS IPEEQIE
EVIQEEIIEQVVPEELIEEVVPEEIIIEEVIPEEIVEEVIYEEVIPEELVEEVIA
EKLKLVKEIVPEQVREEVTLEEIVEEMIPEEFVVEEVAPEVEIEEIIPEELIEEVI
PEVLVEEAVPEELIEKVIPH HHHHHH

人類免疫原性小鼠模型(HIMM)：該模型係基於在免疫缺陷 NOD-SCID-IL-2r γ null (NSG)小鼠中植入人類脾淋巴球(Hu-SPL-NSG)，且補充使用常見實驗室小鼠(例如Balb/C及C57BL)所獲得之資訊。

Balb/c或C57Bl/6小鼠之免疫化及血液採樣

使4至5隻Balb/c或C57Bl/6小鼠之組接受2或3次注射之 10 μ g MSP3-

1-LSP或1 μg PP21 (稀釋於100 μl pH 7.2磷酸鹽緩衝鹽水(PBS)且乳化於100 μl 佐劑Montanide ISA 720中)。藉由皮下注射免疫化且重複一次或兩次(間隔15天)。藉由尾部采血自第二注射之後兩週開始來收集血液且以15天間隔重複直至第一抗原注射之後160天。分離血清且儲存於 -20°C 下直至使用。使同時平行處置之其他組接受1 μg 或0.2 μg PP21。

小鼠血清中之抗MSP3-LSP抗體效價之測定

在小鼠血清中藉由酶聯免疫吸附分析(ELISA)測定MSP3-LSP特異性抗體效價。使用2 $\mu\text{g}/\text{ml}$ 經PBS稀釋之MSP3-1-LSP或MSP3-1-LSP肽a、b、c或d中之一者在 4°C 下過夜塗覆平底微量滴定板(Nunc-Thermo Scientific, USA)。在洗滌(PBS, pH 7.2)及飽和(PBS, 3%非脂乳)之後, 添加測試血清之連續稀釋液(稀釋於PBS、3%非脂乳、0.05% Tween20中)且培育1小時。陰性對照係由免疫前小鼠血清組成。藉由隨後添加辣根過氧化物酶偶聯之山羊抗小鼠IgG (H+L) (Invitrogen, USA)一小時、隨後添加過氧化物酶受質四甲基聯苯胺(Amresco, USA)來揭示特異性抗體。特異性抗體效價對應於最後正稀釋度之倒數。

人類脾供予及倫理考慮

根據 National Organization for Organ & Tissues Donation & Transplantation (NOOTDT), Lebanon之倫理協議自死亡器官移植供體獲得人類脾。由患者自己在其生命期間或在死亡後由其父母簽署供予器官以用於移植或科學研究之知情同意。

人類脾細胞製備

如先前所闡述, 在手術切除之後24小時內處理人類脾(Brams P, 1998)。簡言之, 解剖脾組織且製備細胞懸浮液。使用格氏溶液(Gey's

solution)將紅血球在25℃下裂解5-10 min。在洗滌之後，將白血球再懸浮於由37%胎牛血清(FCS) (Sigma,USA)、10%二甲基亞砷(DMSO) (Sigma,USA)及53% RPMI 1640 (Sigma,USA)組成之培養基中，且然後冷藏保存於液氮中直至使用。自每一脾供體分離之細胞之平均數量為 100 ± 40 億。

NSG小鼠中之人類脾細胞之植入及免疫化

自Jackson實驗室(USA)獲得NOD.Cg-Prkdcscid-IL2rytm1WjI /SzJ (NSG)小鼠且飼養於無菌微型隔離器中。在使用之前將所有食物、水、籠及襯墊高壓滅菌。將6-至8週齡NSG小鼠包含於實驗中。

將人類脾細胞在第0天以 4×10^6 個細胞/ml與或不與1 μ g/ml抗原在補充有10%胎牛血清、1%非必需胺基酸(NEAA 100 $\times$)、2 mM麩醯胺酸、2 mM丙酮酸鈉及50 μ g/ml慶大黴素(gentamicin) (完全培養基)之RPMI1640培養基中一起培養。所有培養試劑皆係購自Sigma, USA。在第1天，添加25 IU/ml之重組人類IL-2 (Gibco Invitrogen)。在第3天，收穫脾細胞，洗滌且再懸浮於漢克氏平衡鹽溶液(Hank's Balanced Salt Solution, HBSS)中。使每一NSG小鼠接受 30×10^6 個經抗原引發或未引發之脾細胞之腹膜腔內注射(ip)。在第7天及第21天，使用10 μ g經腹膜腔內(ip)注射之於200 μ l HBSS-Montanide ISA 720或MF59佐劑(v/v)中之抗原加強重構小鼠(Hu-SPL-NSG)。使用未引發脾細胞重構之小鼠僅接受佐劑。在每一加強之後一週收集血樣。

Hu-SPL-NSG小鼠血清中之人類MSP3-1-LSP特異性抗體之測定

藉由ELISA實施該等測定。簡言之，為檢測小鼠血清中之總人類IgG，使用於0.1M pH 9.5碳酸鹽緩衝液中之2.5 μ g/ml經純化山羊抗人類

IgG (H + L) (Invitrogen, USA)在4℃下過夜塗覆平底微量滴定板(Nunc-Thermo Scientific, USA)。在洗滌(PBS, pH 7.2)及飽和(PBS, 3%非脂乳)之後，添加測試血清(稀釋於PBS、3%非脂乳、0.05% Tween20中)且培育1小時。陰性對照係由相同動物之免疫前小鼠血清組成。藉由隨後添加辣根過氧化物酶偶聯之山羊抗人類IgG (H+L) (Invitrogen, USA)一小時、隨後添加過氧化物酶受質四甲基聯苯胺(Amresco, USA)來揭示人類IgG。計算Hu-SPL-NSG小鼠血清中之總人類IgG濃度並與標準人類IgG溶液(Zymed, USA)進行比較。實施相同測試以檢測抗原特異性抗體，只是使用於PBS中之2.5μg/ml MSP3-1-LSP塗覆板。在此情形下，陰性對照係由從未感染瘧原蟲屬之個體之血清組成，而陽性對照係由來自超免疫非洲成人之血清池組成。在兩種情形下，測試每一血清之連續稀釋液以測定抗體效價。對於特異性抗體效價測定而言，在產生高於截止值(陰性對照OD × 2)之吸光度時，測試可視為陽性。使用人類IgG子類之特異性二級小鼠單株抗體(分別以最終稀釋度1/4,000、1/10,000、1/10,000及1/60,000使用純系NL16 [IgG1 ; Skybio, UK]、HP6002 [IgG2 ; Sigma-Aldrich, Germany]及Zg4及GB7B [分別係IgG3及IgG4 ; Skybio, UK])、隨後使用辣根過氧化物酶偶聯之山羊抗小鼠IgG (以1/4000稀釋於PBS中) (Invitrogen)來檢測IgG子類。

藉由實時逆轉錄PCR (RTqPCR)來量化不同細胞介素、趨化介素及轉錄因子之基因表現

將經免疫化及未免疫化小鼠之脾細胞以 2×10^6 個細胞/ml於完全RPMI1640培養基中在使用免疫化抗原刺激或不刺激下進行培養。在培養24h之後使用RNeasy Mini套組(Quiagen, Germany)提取細胞RNA。使用

RevertAid M-MuLV 酶 (RevertAid 套組第一鏈合成套組, Thermo Scientific Fermentas) 在 20 μ l 反應混合物中實施逆轉錄。簡言之, 將 1 μ l 寡dT18 引子添加至約 400 ng 總RNA 中, 混合且在 65°C 下培育 5 min。將管置於冰上保持數分鐘且短暫離心, 然後添加如由製造商所推薦之 5 $\times$ 反應緩衝液、Ribolock Rnase 抑制劑 (20 u/ μ l)、dNTP (10 mM) 及逆轉錄酶 (200 u/ μ l)。將反應混合物在 42°C 下培育 60 min。藉由在 70°C 下加熱 5 min 來使酶鈍化。使用定量PCR 量測可視為 Th1 或 Treg 細胞之特性之不同人類細胞介素、趨化介素及轉錄因子之相對表現。使用如由製造商所推薦之 LightCycler 480 SYBR Green Master, La Roche 來實施PCR 混合物分析。在 95°C 下於 LightCycler 480 機器 (La Roche) 中實施PCR 擴增 5 min (1個循環), 隨後進行 45 個循環之 95°C、10 sec 培育及 55-57°C、10 sec 培育。一式三份運行每一試樣。用作內部參考之管家基因係貝塔-肌動蛋白(β -肌動蛋白)及次黃嘌呤磷酸核糖基轉移酶 1 (HPRT1) (geNorm 分析)。基於所產生PCR 曲線來計算循環臨限值(Ct)值。藉由 $2\Delta\Delta C_t$ 方法計算相對表現程度。

免疫螢光分析。

使用來自主要含有惡性瘧原蟲(3D7)之成熟裂殖體之紅血球培養物之風乾、丙酮固定之薄塗片來免疫化螢光分析。將稀釋於 PBS-1% 牛血清白蛋白中之 Hu-SPL-NSG 血清在 37°C 下於濕潤室中培育 1 h。在使用 PBS 洗滌之後, 藉由使用在 PBS 中稀釋至 1/400 之 Alexa Fluor 偶聯山羊抗小鼠 IgG (Molecular Probes 及 Invitrogen) 利用伊文思藍色對比染色 (Evans blue counterstain) (1/200) 來檢測抗體。

結論

實例1：PP21 (CRMP97-MS3融合構築體)之免疫原性

在下列動物模型中評價由PP21誘導之免疫反應：

- BALB-C小鼠
- C57BL小鼠
- 松鼠猴

• 人類免疫原性小鼠模型(HIMM)，其中在活體內對來自免疫受損NSG小鼠中所移植之人類脾組織之細胞免疫化且使用來自免疫化動物之血清及細胞用於免疫分析。

所有實驗皆係以對比方式利用臨床實驗中所使用之基準抗原MSP3-LSP (涵蓋MSP3-1之186-271區域之長合成肽)且使用Montanide ISA 720來實施，此乃因實驗室小鼠通常難以對氫氧化鋁具有反應且HIMM中之注射途徑不容許使用氫氧化鋁，且主要係由於旨在比較構築體而非佐劑，從而知曉在人類中，呈MSP3 LSP形式之氫氧化鋁佐劑化CRM (以腦膜炎球菌或肺炎球菌疫苗形式)提供極良好反應。

然而，亦在實驗室小鼠中使用氫氧化鋁實施成功免疫化，其在Balb/C中產生> 25600之效價(即使在兩次免疫化之後)，且在C57bl中產生3200-25600之效價(圖19)。

與小鼠中之MSP3-LSP相比，使用本發明之PP21生物融合體MSP3-1構築體可觀察到免疫原性之重大改良。

PP21在所使用所有模型中誘導高於基準抗原MSP3-LSP之靶嗜細胞子類之血清學反應。

1. 低劑量極為有效：對於其他CRM偶聯疫苗而言，獲得免疫原性之巨大增加，從而指示融合程序產生與化學偶聯同等有效之產物。易於採用

顯著較低劑量，此使得可比較僅1 μg PP21與10 μg 參考MSP3-LSP (過去，發現10 μg 與臨床中所採用之15 μg 在實驗室小鼠中並不顯著不同)。藉由不同方式測定該等差異，參見圖6至9。使用4個不同批次之PP21在4組Balb/C及C57bl小鼠中可再現結果。使用PP21之其他劑量發現著眼於較低劑量，例如在小鼠及松鼠猴中探究0.2 μg 以及1 μg 。高免疫原性亦引導探究僅2次(與3次相比)免疫化。

2. ADCI靶之識別之較寬廣度：含於疫苗構築體內之肽「b」、「c」及「d」定義由在ADCI中有效之抗體靶向之不同B細胞表位。分別在1 μg 及10 μg 下，與當前的MSP3-1-LSP (左側圖)相比，在使用PP21接種疫苗之小鼠之血清中與該等肽之反應性較高，如圖9 (右側圖)中所展示，從而表明在使用PP21時ADCI靶識別之量值及廣度較高且較寬。與此發現一致，主要經由肽«b»及«c-d»展現交叉反應之MSP3家族之6個成員之識別模式在使用PP21時較寬。此亦意指，由PP21誘發之抗體將經由與裂殖子表面上之6種(且並非僅一種)蛋白質之抗體橋觸發來觸發ADCI。

3. 人類淋巴球中之極高B細胞反應：更重要的是，人類B細胞反應(如在HIMM模型中所評價)展示類似重大改良且免疫原性增加40-100倍。(圖10)。在平行實驗中，使用PP21以及96個胺基酸之當前MSP3-LSP，使用1 μg PP21之抗體效價高於使用10 μg MSP3-LSP20至100倍。在3組各5隻屬於3 HLA種類之動物可再現結果。

4. 在使用Montanide ISA720或MF59作為佐劑時，結果亦可再現(圖14)

5. 在活體外使用寄生蟲組分MSP3-LSP攻擊人類淋巴球時，獲得高IFN- γ 分泌 (圖11)。此重要結果指示，CRM Th表位並不優先於瘧原蟲屬

特異性MSR3 T細胞表位且由此在藉由寄生蟲攻擊時預計可自接種疫苗個體獲得T輔助細胞，從而有較大機會在需要時快速產生回憶性抗體。

細胞介素特徵之詳細分析指示，具反應細胞主要係T輔助細胞類型1 (圖12展示使用CXCL10及Tbet獲得之結果之實例)

6. 嗜細胞IgG1之主導性：同型研究揭示(如使用強Th1反應所預計)幾乎完全有IgG1 (其亦係MSP3-LSP免疫化個體中之主導同型)構成之嗜細胞同型之較大主導性。此可見於使用Montanide或MF59作為佐劑時(圖15及16)。儘管該等結果係在人類模型中所獲得，但其可重複預測可在志願者中誘發之將來反應。

7. 與天然寄生蟲蛋白之反應性：在IFAT(圖13)及西方印漬中使由PP21接種疫苗誘發之抗體與寄生蟲天然蛋白進行反應。抗體反應性(不僅與合成抗原，且主要與寄生蟲蛋白)係在瘧疾攻擊期間活化ADCI防禦機制及適當加強天然寄生蟲攻擊之抗體反應之關鍵特徵。

8. 極低免疫化劑量較為有效：評價0.2 µg及1 µg/免疫化且與10 µg MSP3-LSP 進行比較(圖17)。在1 µg劑量之PP21下，在第2免疫化之後達到平穩，而在0.2 µg劑量下，需要第三免疫化方達到大致相同之高抗體濃度，且一隻動物不具有反應。然而，1 µg特徵指示，2次免疫化可足夠，且由此可值得探究。

9. 在南美松鼠猴中觀察到類似高免疫原性(圖20)：使用1 µg及0.2 µg由Montanide 720佐劑化之PP21來對通常對免疫化之反應較差之南美靈長類動物免疫化。在1 µg下達到接近小鼠中所看到之效價之高反應(參見圖18)且在0.2 µg下效價低約5倍(未展示)。儘管同一實驗中之效價對比尚未由巴西同事實施，但MSP3 LSP在用於此模型中時具有極差免疫原性。

10. 免疫反應之持續時間得以顯著改良(圖8之上圖及下圖)：長期分析展示基本組分之顯著改良；抗體反應之持續時間：在免疫化後隨訪藉由PP21或LSP免疫化之小鼠6個月。效價之衰減係漸進性，但較為緩慢，從而在6個月時，剩餘效價高於使用 MSP3-LSP所獲得之最大值。使用PP21在6個月以上時剩餘之效價在1/200 000 – 1/300 000範圍內，與之相比，使用當前MSP3-LSP之範圍約為1/50 000。

實例2：PP25 (CRMP97-LSA3融合構築體)之免疫原性

LSA3係紅血球前階段抗原，其具有許多有吸引力之特徵，藉由經保護對未保護志願者之差異反應發現，其在菌株中較為保守，其在大量動物(包含高級靈長類動物及黑猩猩)中具有高度抗原性及免疫原性，且隨後誘導針對子孢子階段之人類寄生蟲惡性瘧原蟲之大規模攻擊之免疫反應保護。保護與抗原特異性干擾素 γ 反應有關。將PP25之免疫原性與使用LSA3但並無偶聯或任一融合之對照構築體(DG729)進行比較。免疫化及免疫分析之條件與上文使用PP21所闡述相同。

如針對PP21中之MSP3之情形，使用LSA3-CRM97生物融合體(甚至使用低劑量抗原)觀察到抗體反應之類似顯著增加。亦可看到IFN- γ 反應之增加，但顯著性較小，此乃因不含載體之LSA3 (DG729)已係IFN-g反應之極良好誘導劑。

在人類免疫原性模型中亦證實balb/C及C57bl小鼠中所記錄之增加。

另外，抗LSA3抗體效價與子孢子階段之惡性瘧原蟲寄生蟲之抑制之間展示極強關聯。

參見圖21-26中所展示之結果。

實例3：PP23 (MSP3-2-CRMP97-MSP3-3)融合構築體之免疫原性

已證實，使用PP21 (其依賴於MSP3-1與CRM及與LSA3之融合)所獲得之結果可使用來自紅血球階段之其他抗原(例如MSP3-2及MSP3-3與CRM之構築體，稱為PP23)來再現。實際上，藉由構築體PP23 (MSP3-2-CRMP97-MSP3-3)在HIMM模型中所移植之人類淋巴球中誘發強B細胞及T細胞反應(圖27)，效價平均高於藉由於Montanide中之單獨MSP3-2 CT免疫化之小鼠10倍。抗體子類主要係IgG1種類，其係能夠與單核球在ADCI機制中協同作用之主要嗜細胞種類。類似地，誘導強T細胞反應，如藉由在活體外由MSP3-2或MSP3-3再刺激之PP23免疫化人類淋巴球之IFN- γ 分泌所量測。

實例4：LSA5-CRM

肝階段抗原-5 (LSA5) (亦稱為PEBS (紅血球前及血液階段抗原)或SR 11.1 (11.1惡性瘧原蟲基因之子區))在單一分子中組合MSP3及LSA3之特徵。其含有使其不同於mega-gene Pf 11.1之其餘部分之獨特序列，且在菌株中完全保守。其由來自經輻射-減毒之子孢子免疫之志願者之血清識別且因其誘導針對紅血球前及無性血液階段之保護而較為獨特。其表現於紅血球前及血液階段中。藉由以下方式來證實LSA5針對紅血球前階段之保護作用：彙聚性活體外侵襲抑制研究，藉由被動轉移抗LSA5抗體所達成之活體內保護，及藉由使用重組LSA5接種疫苗來防止攻擊之靈長類動物中之概念證據研究。對於血液階段而言，天然人類及人工誘導之動物抗Pf LSA5抗體施加殺死寄生蟲之ADCI調介之效應。在來自病區之個體中之抗原性較高，其中IgG3抗體在具有傳染免疫(亦即暴露誘導之保護)之個體中佔主導地位。大量流行病學研究發現與針對臨床瘧疾攻擊之保護之密切關聯及經藥物治療之腦瘧疾之改良預後。最後，LSA5具有高度免疫

原性，從而達成小鼠中之顯著較高效價及大於來自MSP3免疫化小鼠之血清之ADCI活性。

將LSA5與CRM197之生物融合體(其原理類似於先前3個實例)表現於大腸桿菌中，證實其抗原性且實施初級免疫原性研究。在使用與CRM之融合體時，LSA5免疫原性極高(圖28)；在BALb/c小鼠(n=5)中比較1 µg與10 µg劑量之生物融合體LSA5-CRM/Montanide ISA720之免疫原性。實驗條件類似於在圖8中使用MSP3所闡述者。在第0、14及28天(箭頭)藉由生物融合體LSA5-CRM /Montanide ISA720免疫化。藉由ELISA滴定利用LSA5-LSP作為抗原使用在第0、7、21、42天收集之血清來實施血清抗體檢測。

【序列表】

<110> 新加坡商全民疫苗私人有限公司

<120> 作為抗瘧疾疫苗之生物融合蛋白

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<160> 89

<170> PatentIn version 3.5

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<212> PRT

<213> 惡性瘧原蟲

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35 40 45

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Lys	Glu	Leu	Lys	Asn	Thr	Tyr	Glu	Glu	Lys	Met	Lys	His	Ile	Asn	Asn					
		915					920					925								
Ile	Tyr	Lys	Lys	His	Asp	Asp	Phe	Val	Asn	Ile	Tyr	Leu	Asn	Leu	Phe					
		930					935					940								
Phe	Gln	Ala	Arg	Lys	Asn	Ala	Ile	Leu	Ser	Asp	Ser	Gln	Arg	Glu	Glu					
		945					950					955			960					
Gln	Met	Asn	Leu	Phe	Ile	Lys	Leu	Lys	Asp	Lys	Tyr	Asp	Ile	Ile	Phe					
			965					970					975							
Gln	Lys	Lys	Ile	Glu	Leu	Thr	Asp	Ile	Leu	Lys	Asn	Val	Tyr	Asp	Cys					
			980					985					990							
Asn	Lys	Lys	Leu	Ile	Gly	His	Cys	Gln	Asp	Leu	Glu	Lys	Glu	Asn	Ser					
		995					1000					1005								
Thr	Leu	Gln	Asn	Lys	Leu	Ser	Asn	Glu	Ile	Lys	Asn	Ser	Lys	Met						
		1010					1015					1020								

Leu Ser Lys Asn Leu Ser Lys Asn Ser Asp Asp His Leu Leu Ile
1025 1030 1035

Glu Glu Asn Asn Glu Leu Arg Arg Arg Leu Ile Cys Ser Val Cys
1040 1045 1050

Met Glu Asn Phe Arg Asn Tyr Ile Ile Ile Lys Cys Gly His Ile
1055 1060 1065

Tyr Cys Asn Asn Cys Ile Phe Asn Asn Leu Lys Thr Arg Asn Arg
1070 1075 1080

Lys Cys Pro Gln Cys Lys Val Pro Phe Asp Lys Lys Asp Leu Gln
1085 1090 1095

Lys Ile Phe Leu Asp
1100

<210> 2
<211> 104
<212> PRT
<213> 惡性瘡原蟲

<400> 2

His Asn Asn Asn Glu Lys Asn Ile Ser Tyr Asp Lys Asn Leu Val Lys
1 5 10 15

Gln Glu Asn Asp Asn Lys Asp Glu Ala Arg Gly Asn Asp Asn Met Cys
20 25 30

Gly Asn Tyr Asp Ile His Asn Glu Arg Gly Glu Met Leu Asp Lys Gly
35 40 45

Lys Ser Tyr Ser Gly Asp Glu Lys Ile Asn Thr Ser Asp Asn Ala Lys
50 55 60

Ser Cys Ser Gly Asp Glu Lys Val Ile Thr Ser Asp Asn Gly Lys Ser
65 70 75 80

Tyr Asp Tyr Val Lys Asn Glu Ser Glu Glu Gln Glu Glu Lys Glu Asn
85 90 95

Met Leu Asn Asn Lys Lys Arg Ser
100

<210> 3
<211> 27
<212> PRT
<213> 惡性瘡原蟲

<400> 3

Lys Lys Arg Asn Val Glu Glu Glu Leu His Ser Leu Arg Lys Asn Tyr
1 5 10 15

Asn Ile Ile Asn Glu Glu Ile Glu Glu Ile Thr
20 25

<210> 4
<211> 80
<212> PRT
<213> 惡性瘡原蟲

<400> 4

Asn Glu Glu Glu Ile Thr Thr Lys Gly Ala Ser Ala Gln Ser Gly Ala
1 5 10 15

Ser Ala Gln Ser Gly Ala Ser Ala Gln Ser Gly Ala Ser Ala Gln Ser
20 25 30

Gly Ala Ser Ala Gln Ser Gly Ala Ser Ala Gln Ser Gly Thr Ser Gly
35 40 45

Pro Ser Gly Pro Ser Gly Thr Ser Pro Ser Ser Arg Ser Asn Thr Leu
50 55 60

Pro Arg Ser Asn Thr Ser Ser Gly Ala Ser Pro Pro Ala Asp Ala Ser
65 70 75 80

<210> 5
<211> 390
<212> PRT
<213> 惡性瘡原蟲

<400> 5

Met Ala His His His His His His Pro Gly Gly Ser Gly Ser Gly Thr
1 5 10 15

Met Ala Ile Ser Val Thr Met Asp Asn Ile Leu Ser Gly Phe Glu Asn
20 25 30

Glu Tyr Asp Val Ile Tyr Leu Lys Pro Leu Ala Gly Val Tyr Arg Ser
35 40 45

Leu Lys Lys Gln Ile Glu Lys Asn Ile Phe Thr Phe Asn Leu Asn Leu
50 55 60

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

Val Leu Glu Ser Asp Leu Met Gln Phe Lys His Ile Ser Ser Asn Glu
85 90 95

Tyr Ile Ile Glu Asp Ser Phe Lys Leu Leu Asn Ser Glu Gln Lys Asn
100 105 110

Thr Leu Leu Lys Ser Tyr Lys Tyr Ile Lys Glu Ser Val Glu Asn Asp
115 120 125

Ile Lys Phe Ala Gln Glu Gly Ile Ser Tyr Tyr Glu Lys Val Leu Ala
130 135 140

Lys Tyr Lys Asp Asp Leu Glu Ser Ile Lys Lys Val Ile Lys Glu Glu
145 150 155 160

Lys Glu Lys Phe Pro Ser Ser Pro Pro Thr Thr Pro Pro Ser Pro Ala
165 170 175

Lys Thr Asp Glu Gln Lys Lys Glu Ser Lys Phe Leu Pro Phe Leu Thr
180 185 190

Asn Ile Glu Thr Leu Tyr Asn Asn Leu Val Asn Lys Ile Asp Asp Tyr
195 200 205

Leu Ile Asn Leu Lys Ala Lys Ile Asn Asp Cys Asn Val Glu Lys Asp
210 215 220

Glu Ala His Val Lys Ile Thr Lys Leu Ser Asp Leu Lys Ala Ile Asp

[illegible]

<210>	6
<211>	272
<212>	PRT
<213>	惡性瘧原蟲

<400> 6

Met Lys Val Ile Lys Thr Leu Ser Ile Ile Asn Phe Phe Ile Phe Val
1 5 10 15

Thr Phe Asn Ile Lys Asn Glu Ser Lys Tyr Ser Asn Thr Phe Ile Asn

[illegible]

Thr Ser Leu Leu Asn Asn Ser Ser Asn Ile Ala Ser Ile Asn Lys Phe
245 250 255

Val Val Leu Ile Ser Ala Thr Leu Val Leu Ser Phe Ala Ile Phe Ile
260 265 270

<210> 7
<211> 354
<212> PRT
<213> 惡性瘡原蟲

<400> 7

Met Lys Ser Phe Ile Asn Ile Thr Leu Ser Leu Phe Leu Leu His Leu
1 5 10 15

Tyr Ile Tyr Ile Asn Asn Val Ala Ser Lys Glu Ile Val Lys Lys Tyr
20 25 30

Asn Leu Asn Leu Arg Asn Ala Ile Leu Asn Asn Asn Ser Gln Ile Glu
35 40 45

Asn Glu Glu Asn Val Asn Thr Thr Ile Thr Gly Asn Asp Phe Ser Gly
50 55 60

Gly Glu Phe Leu Trp Pro Gly Tyr Thr Glu Glu Leu Lys Ala Lys Lys
65 70 75 80

Ala Ser Glu Asp Ala Glu Lys Ala Ala Asn Asp Ala Glu Asn Ala Ser
85 90 95

Lys Glu Ala Glu Glu Ala Ala Lys Glu Ala Val Asn Leu Lys Glu Ser
100 105 110

Asp Lys Ser Tyr Thr Lys Ala Lys Glu Ala Cys Thr Ala Ala Ser Lys
115 120 125

Ala Lys Lys Ala Val Glu Thr Ala Leu Lys Ala Lys Asp Asp Ala Glu
130 135 140

Lys Ser Ser Lys Ala Asp Ser Ile Ser Thr Lys Thr Lys Glu Tyr Ala
145 150 155 160

Glu Lys Ala Lys Asn Ala Tyr Glu Lys Ala Lys Asn Ala Tyr Gln Lys
165 170 175

Ala Asn Gln Ala Val Leu Lys Ala Lys Glu Ala Ser Ser Tyr Asp Tyr
180 185 190

Ile Leu Gly Trp Glu Phe Gly Gly Gly Val Pro Glu His Lys Lys Glu
195 200 205

Glu Asn Met Leu Ser His Leu Tyr Val Ser Ser Lys Asp Lys Glu Asn
210 215 220

Ile Ser Lys Glu Asn Asp Asp Val Leu Asp Glu Lys Glu Glu Glu Ala
225 230 235 240

Glu Glu Thr Glu Glu Glu Glu Leu Glu Glu Lys Asn Glu Glu Glu Thr
245 250 255

Glu Ser Glu Ile Ser Glu Asp Glu Glu Glu Glu Glu Glu Glu Glu
260 265 270

Lys Glu Glu Glu Asn Asp Lys Lys Lys Glu Gln Glu Lys Glu Gln Ser
275 280 285

Asn Glu Asn Asn Asp Gln Lys Lys Asp Met Glu Ala Gln Asn Leu Ile
290 295 300

Ser Lys Asn Gln Asn Asn Asn Glu Lys Asn Val Lys Glu Ala Ala Glu
305 310 315 320

Ser Ile Met Lys Thr Leu Ala Gly Leu Ile Lys Gly Asn Asn Gln Ile
325 330 335

Asp Ser Thr Leu Lys Asp Leu Val Glu Glu Leu Ser Lys Tyr Phe Lys
340 345 350

Asn His

<210> 8
<211> 188
<212> PRT

<213> 惡性瘡原蟲

<400> 8

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

<210> 9
<211> 25
<212> PRT

<213> 惡性瘡原蟲

<400> 9

Tyr Glu Lys Ala Lys Asn Ala Tyr Gln Lys Ala Asn Gln Ala Val Leu
1 5 10 15

Lys Ala Lys Glu Ala Ser Ser Tyr Asp
20 25

<210> 10
<211> 27
<212> PRT
<213> 惡性瘡原蟲

<400> 10

Ala Lys Glu Ala Ser Ser Tyr Asp Tyr Ile Leu Gly Trp Glu Phe Gly
1 5 10 15

Gly Gly Val Pro Glu His Lys Lys Glu Glu Asn
20 25

<210> 11
<211> 28
<212> PRT
<213> 惡性瘡原蟲

<400> 11

Pro Glu His Lys Lys Glu Glu Asn Met Leu Ser His Leu Tyr Val Ser
1 5 10 15

Ser Lys Asp Lys Glu Asn Ile Ser Lys Glu Asn Asp
20 25

<210> 12
<211> 41
<212> PRT
<213> 惡性瘡原蟲

<400> 12

Met Leu Ser His Leu Tyr Val Ser Ser Lys Asp Lys Glu Asn Ile Ser
1 5 10 15

Lys Glu Asn Asp Asp Val Leu Asp Glu Lys Glu Glu Glu Ala Glu Glu
20 25 30

Thr Glu Glu Glu Glu Leu Glu Glu Lys
35 40

- <210> 13
- <211> 34
- <212> PRT
- <213> 惡性瘧原蟲

<400> 13

Glu Glu Glu Asn Asp Lys Lys Lys Glu Gln Glu Lys Glu Gln Ser Asn
1 5 10 15

Glu Asn Asn Asp Gln Lys Lys Asp Met Glu Ala Gln Asn Leu Ile Ser
20 25 30

Lys Asn

- <210> 14
- <211> 53
- <212> PRT
- <213> 惡性瘧原蟲

<400> 14

Asn Leu Ile Ser Lys Asn Gln Asn Asn Asn Glu Lys Asn Val Lys Glu
1 5 10 15

Ala Ala Glu Ser Ile Met Lys Thr Leu Ala Gly Leu Ile Lys Gly Asn
20 25 30

Asn Gln Ile Asp Ser Thr Leu Lys Asp Leu Val Glu Glu Leu Ser Lys
35 40 45

Tyr Phe Lys Asn His
50

- <210> 15
- <211> 371
- <212> PRT
- <213> 惡性瘧原蟲

<400> 15

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

Gln Val Ile Glu Asp Pro Gln Glu Asp Asn Lys Asp Glu Asp Glu Asp
225 230 235 240

Glu Glu Thr Glu Thr Glu Asn Leu Glu Thr Glu Asp Asp Asn Asn Glu
245 250 255

Glu Ile Glu Glu Asn Glu Glu Asp Asp Ile Asp Glu Glu Ser Val Glu
260 265 270

Glu Lys Glu Glu Glu Glu Glu Lys Lys Glu Glu Glu Glu Lys Lys Glu
275 280 285

Glu Lys Lys Glu Glu Lys Lys Pro Asp Asn Glu Ile Thr Asn Glu Val
290 295 300

Lys Glu Glu Gln Lys Tyr Ser Ser Pro Ser Asp Ile Asn Ala Gln Asn
305 310 315 320

Leu Ile Ser Asn Lys Asn Lys Lys Asn Asp Glu Thr Lys Lys Thr Ala
325 330 335

Glu Asn Ile Val Lys Thr Leu Val Gly Leu Phe Asn Glu Lys Asn Glu
340 345 350

Ile Asp Ser Thr Ile Asn Asn Leu Val Gln Glu Met Ile His Leu Phe
355 360 365

Ser Asn Asn
370

<210> 16
<211> 211
<212> PRT
<213> 惡性瘧原蟲

<400> 16

Ser Glu Thr Asn Lys Asn Pro Thr Ser His Ser Asn Ser Thr Thr Thr
1 5 10 15

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

Gln Asn Gly Ala Ala Glu Asp Lys Lys Thr Glu Tyr Leu Leu Glu Gln
35 40 45

Ile Lys Ile Pro Ser Trp Asp Arg Asn Asn Ile Pro Asp Glu Asn Glu
50 55 60

Gln Val Ile Glu Asp Pro Gln Glu Asp Asn Lys Asp Glu Asp Glu Asp
65 70 75 80

Glu Glu Thr Glu Thr Glu Asn Leu Glu Thr Glu Asp Asp Asn Asn Glu
85 90 95

Glu Ile Glu Glu Asn Glu Glu Asp Asp Ile Asp Glu Glu Ser Val Glu
100 105 110

Glu Lys Glu Glu Glu Glu Lys Lys Glu Glu Glu Glu Lys Lys Glu
115 120 125

Glu Lys Lys Glu Glu Lys Lys Pro Asp Asn Glu Ile Thr Asn Glu Val
130 135 140

Lys Glu Glu Gln Lys Tyr Ser Ser Pro Ser Asp Ile Asn Ala Gln Asn
145 150 155 160

Leu Ile Ser Asn Lys Asn Lys Lys Asn Asp Glu Thr Lys Lys Thr Ala
165 170 175

Glu Asn Ile Val Lys Thr Leu Val Gly Leu Phe Asn Glu Lys Asn Glu
180 185 190

Ile Asp Ser Thr Ile Asn Asn Leu Val Gln Glu Met Ile His Leu Phe
195 200 205

Ser Asn Asn
210

- <210> 17
- <211> 21
- <212> PRT
- <213> 惡性瘡原蟲
- <400> 17

Ser Glu Thr Asn Lys Asn Pro Thr Ser His Ser Asn Ser Thr Thr Thr
1 5 10 15

Ser Leu Asn Asn Asn
20

<210> 18
<211> 27
<212> PRT
<213> 惡性瘡原蟲

<400> 18

Leu Asn Asn Asn Ile Leu Gly Trp Glu Phe Gly Gly Gly Ala Pro Gln
1 5 10 15

Asn Gly Ala Ala Glu Asp Lys Lys Thr Glu Tyr
20 25

<210> 19
<211> 33
<212> PRT
<213> 惡性瘡原蟲

<400> 19

Pro Gln Asn Gly Ala Ala Glu Asp Lys Lys Thr Glu Tyr Leu Leu Glu
1 5 10 15

Gln Ile Lys Ile Pro Ser Trp Asp Arg Asn Asn Ile Pro Asp Glu Asn
20 25 30

Glu

<210> 20
<211> 53
<212> PRT
<213> 惡性瘡原蟲

<400> 20

Leu Leu Glu Gln Ile Lys Ile Pro Ser Trp Asp Arg Asn Asn Ile Pro
1 5 10 15

Asp Glu Asn Glu Gln Val Ile Glu Asp Pro Gln Glu Asp Asn Lys Asp

20

25

30

Glu Asp Glu Asp Glu Glu Thr Glu Thr Glu Asn Leu Glu Thr Glu Asp

354045

Asp Asn Asn Glu Glu

50

<210> 21

<211> 42

<212> PRT

<213> 惡性瘡原蟲

<400> 21

Glu Glu Glu Lys Lys Glu Glu Lys Lys Glu Glu Lys Lys Pro Asp Asn

151015

Glu Ile Thr Asn Glu Val Lys Glu Glu Gln Lys Tyr Ser Ser Pro Ser

202530

Asp Ile Asn Ala Gln Asn Leu Ile Ser Asn

3540

<210> 22

<211> 52

<212> PRT

<213> 惡性瘡原蟲

<400> 22

Asn Leu Ile Ser Asn Lys Asn Lys Lys Asn Asp Glu Thr Lys Lys Thr

151015

Ala Glu Asn Ile Val Lys Thr Leu Val Gly Leu Phe Asn Glu Lys Asn

202530

Glu Ile Asp Ser Thr Ile Asn Asn Leu Val Gln Glu Met Ile His Leu

354045

Phe Ser Asn Asn

50

<210> 23

<211> 424

<212> PRT
<213> 惡性瘧原蟲

<400> 23

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

Ile Gly Ser Thr Leu Leu Asp Phe Phe Leu Pro Leu Pro Thr Lys Asn
210 215 220

Thr Asn Thr Tyr Glu Lys Lys Asn Glu Asn Lys Asn Val Ser Asn Val
225 230 235 240

Asp Ser Lys Thr Lys Ser Asn Glu Lys Gly Arg Pro Pro Thr Tyr Ser
245 250 255

Pro Ile Leu Asp Asp Gly Ile Glu Phe Ser Gly Gly Leu Tyr Phe Asn
260 265 270

Glu Lys Lys Ser Thr Glu Glu Asn Lys Gln Lys Asn Val Leu Glu Ser
275 280 285

Val Asn Leu Thr Ser Trp Asp Lys Glu Asp Ile Val Lys Glu Asn Glu
290 295 300

Asp Val Lys Asp Glu Lys Asp Glu Asp Asp Glu Glu Glu Glu Glu Lys
305 310 315 320

Tyr Glu Asn Glu Ile Ile Lys Gln Pro Glu Asp Ile Leu Asp Glu Glu
325 330 335

Glu Val Leu Glu Glu Glu Ile Leu Glu Glu Asn Lys Asn Asp Thr Val
340 345 350

Asp Thr Ser Asp Leu Glu Lys Lys Asn Ile Pro Asp Leu Ser Asn Asp
355 360 365

Asn Asn Tyr Tyr Ser Leu Ile Tyr Lys Asn Tyr Lys Asp Asn Asp Lys
370 375 380

Ser Glu Lys Thr Ala Gln Thr Leu Ile Thr Ala Leu Ile Ser Leu Leu
385 390 395 400

Asn Gly Lys Asn Glu Leu Asp Ala Thr Ile Arg Arg Leu Lys His Arg
405 410 415

Phe Met Glu Phe Phe Thr Tyr Asn

420

<210> 24
<211> 197
<212> PRT
<213> 惡性瘡原蟲

<400> 24

Tyr Glu Lys Lys Asn Glu Asn Lys Asn Val Ser Asn Val Asp Ser Lys
1 5 10 15

Thr Lys Ser Asn Glu Lys Gly Arg Pro Pro Thr Tyr Ser Pro Ile Leu
20 25 30

Asp Asp Gly Ile Glu Phe Ser Gly Gly Leu Tyr Phe Asn Glu Lys Lys
35 40 45

Ser Thr Glu Glu Asn Lys Gln Lys Asn Val Leu Glu Ser Val Asn Leu
50 55 60

Thr Ser Trp Asp Lys Glu Asp Ile Val Lys Glu Asn Glu Asp Val Lys
65 70 75 80

Asp Glu Lys Asp Glu Asp Asp Glu Glu Glu Glu Lys Tyr Glu Asn
85 90 95

Glu Ile Ile Lys Gln Pro Glu Asp Ile Leu Asp Glu Glu Glu Val Leu
100 105 110

Glu Glu Glu Ile Leu Glu Glu Asn Lys Asn Asp Thr Val Asp Thr Ser
115 120 125

Asp Leu Glu Lys Lys Asn Ile Pro Asp Leu Ser Asn Asp Asn Asn Tyr
130 135 140

Tyr Ser Leu Ile Tyr Lys Asn Tyr Lys Asp Asn Asp Lys Ser Glu Lys
145 150 155 160

Thr Ala Gln Thr Leu Ile Thr Ala Leu Ile Ser Leu Leu Asn Gly Lys
165 170 175

Asn Glu Leu Asp Ala Thr Ile Arg Arg Leu Lys His Arg Phe Met Glu

180

185

190

Phe Phe Thr Tyr Asn

195

<210> 25

<211> 24

<212> PRT

<213> 惡性瘡原蟲

<400> 25

Tyr Glu Lys Lys Asn Glu Asn Lys Asn Val Ser Asn Val Asp Ser Lys

1 5 10 15

Thr Lys Ser Asn Glu Lys Gly Arg

20

<210> 26

<211> 26

<212> PRT

<213> 惡性瘡原蟲

<400> 26

Ser Asn Glu Lys Gly Arg Pro Pro Thr Tyr Ser Pro Ile Leu Asp Asp

1 5 10 15

Gly Ile Glu Phe Ser Gly Gly Leu Tyr Phe

20 25

<210> 27

<211> 29

<212> PRT

<213> 惡性瘡原蟲

<400> 27

Gly Ile Glu Phe Ser Gly Gly Leu Tyr Phe Asn Glu Lys Lys Ser Thr

1 5 10 15

Glu Glu Asn Lys Gln Lys Asn Val Leu Glu Ser Val Asn

20 25

<210> 28

<211> 32

<212> PRT

<213> 惡性瘡原蟲

<400> 28

Ser Thr Glu Glu Asn Lys Gln Lys Asn Val Leu Glu Ser Val Asn Leu
1 5 10 15

Thr Ser Trp Asp Lys Glu Asp Ile Val Lys Glu Asn Glu Asp Val Lys
20 25 30

<210> 29

<211> 33

<212> PRT

<213> 惡性瘡原蟲

<400> 29

Asp Thr Ser Asp Leu Glu Lys Lys Asn Ile Pro Asp Leu Ser Asn Asp
1 5 10 15

Asn Asn Tyr Tyr Ser Leu Ile Tyr Lys Asn Tyr Lys Asp Asn Asp Lys
20 25 30

Ser

<210> 30

<211> 52

<212> PRT

<213> 惡性瘡原蟲

<400> 30

Ser Leu Ile Tyr Lys Asn Tyr Lys Asp Asn Asp Lys Ser Glu Lys Thr
1 5 10 15

Ala Gln Thr Leu Ile Thr Ala Leu Ile Ser Leu Leu Asn Gly Lys Asn
20 25 30

Glu Leu Asp Ala Thr Ile Arg Arg Leu Lys His Arg Phe Met Glu Phe
35 40 45

Phe Thr Tyr Asn
50

<210> 31

<211> 697
<212> PRT
<213> 惡性瘡原蟲

<400> 31

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

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

Glu Lys Tyr Leu Lys Glu Ile Cys Ser Glu Cys Asp Cys Lys Tyr Lys
420 425 430

Asp Leu Asp Asn Thr Phe Lys Glu Phe Lys Asp Asn Val Thr Leu Leu
435 440 445

Lys Ala Val Ile Asp Asn Lys Lys Asn Gln Asp Ser Leu Thr Thr Thr
450 455 460

Ser Leu Ser Thr Ser Ile Asn Ser Val Arg Asp Ser Ser Asn Leu Asp
465 470 475 480

Gln Arg Gly Asn Ile Thr Thr Ser Gln Gly Asn Ser His Arg Ala Thr
485 490 495

Val Val Gln Gln Val Asp Gln Thr Asn Arg Leu Asp Asn Val Asn Ser
500 505 510

Val Thr Gln Arg Gly Asn Asn Asn Tyr Asn Asn Asn Leu Glu Arg Gly
515 520 525

Leu Gly Ser Gly Ala Leu Pro Gly Thr Asn Ile Ile Thr Glu Glu Lys
530 535 540

Tyr Ser Leu Glu Leu Ile Lys Leu Thr Ser Lys Asp Glu Glu Asp Ile
545 550 555 560

Ile Lys His Asn Glu Asp Val Arg Glu Glu Ile Glu Glu Gln Gln Glu
565 570 575

Asp Ile Glu Glu Asp Glu Glu Glu Leu Glu Asn Glu Gly Glu Glu Thr
580 585 590

Lys Glu Glu Asp Asp Glu Glu Lys Asn Glu Thr Asn Asp Thr Glu Asp
595 600 605

Thr Asp Asp Thr Glu Asp Thr Glu Asp Ile Glu Glu Glu Asn Lys Glu
610 615 620

Lys Glu Leu Ser Asn Gln Gln Gln Ser Glu Lys Lys Ser Ile Ser Lys
625 630 635 640

Val Asp Glu Asp Ser Tyr Arg Ile Leu Ser Val Ser Tyr Lys Asp Asn
645 650 655

Asn Glu Val Lys Asn Val Ala Glu Ser Ile Val Lys Lys Leu Phe Ser
660 665 670

Leu Phe Asn Asp Asn Asn Asn Leu Glu Thr Ile Phe Lys Gly Leu Thr
675 680 685

Glu Asp Met Thr Asp Leu Phe Gln Lys
690 695

<210> 32
<211> 190
<212> PRT
<213> 惡性瘡原蟲

<400> 32

Asp Asn Val Asn Ser Val Thr Gln Arg Gly Asn Asn Asn Tyr Asn Asn
1 5 10 15

Asn Leu Glu Arg Gly Leu Gly Ser Gly Ala Leu Pro Gly Thr Asn Ile
20 25 30

Ile Thr Glu Glu Lys Tyr Ser Leu Glu Leu Ile Lys Leu Thr Ser Lys
35 40 45

Asp Glu Glu Asp Ile Ile Lys His Asn Glu Asp Val Arg Glu Glu Ile
50 55 60

Glu Glu Gln Gln Glu Asp Ile Glu Glu Asp Glu Glu Glu Leu Glu Asn
65 70 75 80

Glu Gly Glu Glu Thr Lys Glu Glu Asp Asp Glu Glu Lys Asn Glu Thr
85 90 95

Asn Asp Thr Glu Asp Thr Asp Asp Thr Glu Asp Thr Glu Asp Ile Glu
100 105 110

Glu Glu Asn Lys Glu Lys Glu Leu Ser Asn Gln Gln Gln Ser Glu Lys
115 120 125

Lys Ser Ile Ser Lys Val Asp Glu Asp Ser Tyr Arg Ile Leu Ser Val
130 135 140

Ser Tyr Lys Asp Asn Asn Glu Val Lys Asn Val Ala Glu Ser Ile Val
145 150 155 160

Lys Lys Leu Phe Ser Leu Phe Asn Asp Asn Asn Asn Leu Glu Thr Ile
165 170 175

Phe Lys Gly Leu Thr Glu Asp Met Thr Asp Leu Phe Gln Lys
180 185 190

<210> 33
<211> 25
<212> PRT
<213> 惡性瘧原蟲

<400> 33

Asp Asn Val Asn Ser Val Thr Gln Arg Gly Asn Asn Asn Tyr Asn Asn
1 5 10 15

Asn Leu Glu Arg Gly Leu Gly Ser Gly
20 25

<210> 34
<211> 27
<212> PRT
<213> 惡性瘧原蟲

<400> 34

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

Thr Glu Glu Lys Tyr Ser Leu Glu Leu Ile Lys
20 25

<210> 35
<211> 28
<212> PRT
<213> 惡性瘧原蟲

<400> 35

Lys Tyr Ser Leu Glu Leu Ile Lys Leu Thr Ser Lys Asp Glu Glu Asp

1 5 10 15

Ile Ile Lys His Asn Glu Asp Val Arg Glu Glu Ile
20 25

<210> 36
<211> 28
<212> PRT
<213> 惡性瘡原蟲

<400> 36

Leu Thr Ser Lys Asp Glu Glu Asp Ile Ile Lys His Asn Glu Asp Val
1 5 10 15

Arg Glu Glu Ile Glu Glu Gln Gln Glu Asp Ile Glu
20 25

<210> 37
<211> 34
<212> PRT
<213> 惡性瘡原蟲

<400> 37

Glu Glu Asn Lys Glu Lys Glu Leu Ser Asn Gln Gln Gln Ser Glu Lys
1 5 10 15

Lys Ser Ile Ser Lys Val Asp Glu Asp Ser Tyr Arg Ile Leu Ser Val
20 25 30

Ser Tyr

<210> 38
<211> 51
<212> PRT
<213> 惡性瘡原蟲

<400> 38

Arg Ile Leu Ser Val Ser Tyr Lys Asp Asn Asn Glu Val Lys Asn Val
1 5 10 15

Ala Glu Ser Ile Val Lys Lys Leu Phe Ser Leu Phe Asn Asp Asn Asn
20 25 30

Asn Leu Glu Thr Ile Phe Lys Gly Leu Thr Glu Asp Met Thr Asp Leu
35 40 45

Phe Gln Lys
50

<210> 39
<211> 405
<212> PRT
<213> 惡性瘡原蟲

<400> 39

Met Asn Lys Phe Leu Asn Ile Ile Phe Tyr Ile Phe Leu Ile Leu Asn
1 5 10 15

Phe Ser Phe Phe Gln Ser Asn Ala Thr Ser Lys Glu Ile Gln Lys Asp
20 25 30

Glu Gln Lys Asn Leu Arg Asn Gly Ser Ser Ile Asn Asn Asn Lys Asn
35 40 45

Ile Glu Asn Lys Asn Asp Asn Ile Glu Thr Gln Tyr Glu Ala Ser Glu
50 55 60

Tyr Ile Glu Lys Gln Asn Asp Ile Leu Asn Met Tyr Asn Asp Glu Lys
65 70 75 80

Glu Lys Asn Asn Asn Asn Ser Leu Asp Thr Asn Val Thr Lys Asn Thr
85 90 95

Val Ile Asp Asn Ser Asn Lys Phe Gln Ser Ile Glu Asp Asn Asn Val
100 105 110

Tyr Asn Lys Gly Ile Phe Val Gly Thr Gly Ile Lys Leu Asn Asp Ser
115 120 125

Gln Thr Thr Ser Asp Asn Tyr Lys Asn Glu Arg Tyr Gln Ile Asp Asp
130 135 140

Glu Lys Leu Lys Tyr Gly Gly Ser Phe Asp Thr Ile Phe Ser Gly Phe
145 150 155 160

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

Asn Gln Leu Asp Pro Ser Leu Lys Asp Leu Glu Asn Glu Leu Thr Phe
385 390 395 400

Phe Leu Asn Asn Tyr
405

<210> 40
<211> 192
<212> PRT
<213> 惡性瘡原蟲

<400> 40

Pro Glu Gly Pro Arg Ala Asn Asn Arg Asn Glu Asn Asn Gln Asn Thr
1 5 10 15

Asp Pro Tyr Asn His Tyr Phe Ala Trp Glu Ile Gly Gly Gly Ala Pro
20 25 30

Thr Tyr Lys Pro Glu Asn Asn Lys Asn Asp Asn Ile Leu Leu Glu His
35 40 45

Val Lys Ile Thr Ser Trp Asp Lys Glu Asp Ile Ile Lys Glu Asn Glu
50 55 60

Asp Thr Lys Arg Glu Val Gln Glu Thr Glu Asp Thr Asp Glu Thr Glu
65 70 75 80

Asp Thr Asp Glu Thr Glu Glu Thr Glu Asp Met Glu Asp Glu Asn Glu
85 90 95

Ile Val Glu Asp Gln Leu Gln Glu Asn Glu Asp Asp Glu Asp Asn Val
100 105 110

Asn Leu Glu Asp Ile Asn Lys Asn Thr Arg Asn Asp Ile Phe Glu Glu
115 120 125

Gln Ile Lys Leu Asp Ser Thr Gln Asp Asp Lys Ala Gln Lys Leu Ile
130 135 140

Ser Asn Glu Tyr Lys Lys Thr Glu Glu Lys Lys Ser Leu Glu Asp His
145 150 155 160

Val Asn Leu Leu Phe Asn Phe Leu Gln Thr Asn Asn Gln Leu Asp Pro
165 170 175

Ser Leu Lys Asp Leu Glu Asn Glu Leu Thr Phe Phe Leu Asn Asn Tyr
180 185 190

<210> 41
<211> 26
<212> PRT
<213> 惡性瘧原蟲

<400> 41

Pro Glu Gly Pro Arg Ala Asn Asn Arg Asn Glu Asn Asn Gln Asn Thr
1 5 10 15

Asp Pro Tyr Asn His Tyr Phe Ala Trp Glu
20 25

<210> 42
<211> 22
<212> PRT
<213> 惡性瘧原蟲

<400> 42

Tyr Asn His Tyr Phe Ala Trp Glu Ile Gly Gly Gly Ala Pro Thr Tyr
1 5 10 15

Lys Pro Glu Asn Asn Lys
20

<210> 43
<211> 27
<212> PRT
<213> 惡性瘧原蟲

<400> 43

Pro Thr Tyr Lys Pro Glu Asn Asn Lys Asn Asp Asn Ile Leu Leu Glu
1 5 10 15

His Val Lys Ile Thr Ser Trp Asp Lys Glu Asp
20 25

<210> 44
<211> 29
<212> PRT
<213> 惡性瘡原蟲

<400> 44

Ile Leu Leu Glu His Val Lys Ile Thr Ser Trp Asp Lys Glu Asp Ile
1 5 10 15

Ile Lys Glu Asn Glu Asp Thr Lys Arg Glu Val Gln Glu
20 25

<210> 45
<211> 35
<212> PRT
<213> 惡性瘡原蟲

<400> 45

Val Asn Leu Glu Asp Ile Asn Lys Asn Thr Arg Asn Asp Ile Phe Glu
1 5 10 15

Glu Gln Ile Lys Leu Asp Ser Thr Gln Asp Asp Lys Ala Gln Lys Leu
20 25 30

Ile Ser Asn
35

<210> 46
<211> 52
<212> PRT
<213> 惡性瘡原蟲

<400> 46

Gln Lys Leu Ile Ser Asn Glu Tyr Lys Lys Thr Glu Glu Lys Lys Ser
1 5 10 15

Leu Glu Asp His Val Asn Leu Leu Phe Asn Phe Leu Gln Thr Asn Asn
20 25 30

Gln Leu Asp Pro Ser Leu Lys Asp Leu Glu Asn Glu Leu Thr Phe Phe
35 40 45

Leu Asn Asn Tyr
50

<210> 47
 <211> 762
 <212> PRT
 <213> 惡性瘡原蟲

<400> 47

Met Ile Tyr Ile Leu Ser Ile Val Phe Tyr Ile Phe Phe Leu His Ile
 1 5 10 15

Asp Ile Tyr Val Asn Ile Tyr Ser Thr Cys Phe Val Val Asn Glu Gly
 20 25 30

Asn Pro Asn Leu Arg Asn Asn Ile Ile Asn Asp Asp Glu Leu Lys Gly
 35 40 45

Lys Ala Tyr Asn Asn Thr Ile Asp Ala Asn Asn Gln Asn Ile Glu Tyr
 50 55 60

Asn Lys Asn Leu Lys His Asn Val Asn Ser Ser His Ile Ser Lys Phe
 65 70 75 80

Ser Asp Ile Met Asp Gln Glu Asp Lys Gly Asp Asn Glu Asn Ser His
 85 90 95

Asp Ile Lys Phe Glu Glu Lys Lys Asn Ile Asn Lys Ser Leu Asp Ala
 100 105 110

Glu Ser Asn Tyr Gly Ile Asn Glu Ile Ser Ile Thr Gly Asn Asp Ser
 115 120 125

Asn Ser Asp Asn Ser Asn Gln Asn Ile Phe Pro Asp Gly Ser Glu Leu
 130 135 140

Ala Gly Gly Ile Pro Arg Ser Ile Tyr Thr Ile Asn Leu Gly Phe Asn
 145 150 155 160

Lys Cys Pro Thr Glu Glu Ile Cys Lys Asp Phe Ser Asn Leu Pro Gln
 165 170 175

Cys Arg Lys Asn Val His Glu Arg Asn Asn Trp Leu Gly Ser Ser Val
 180 185 190

Lys Asn Phe Ser Ser Asp Asn Lys Gly Val Leu Val Pro Pro Arg Arg
195 200 205

Gln Ser Leu Cys Leu Arg Ile Thr Leu Gln Asp Phe Arg Thr Lys Lys
210 215 220

Lys Lys Glu Gly Asp Phe Glu Lys Phe Ile Tyr Ser Tyr Ala Ser Ser
225 230 235 240

Glu Ala Arg Lys Leu Arg Thr Ile His Asn Asn Asn Leu Glu Lys Ala
245 250 255

His Gln Ala Ile Arg Tyr Ser Phe Ala Asp Ile Gly Asn Ile Ile Arg
260 265 270

Gly Asp Asp Met Met Asp Thr Pro Thr Ser Lys Glu Thr Ile Thr Tyr
275 280 285

Leu Glu Lys Val Leu Lys Ile Tyr Asn Glu Asn Asn Asp Lys Pro Lys
290 295 300

Asp Ala Lys Lys Trp Trp Thr Glu Asn Arg His His Val Trp Glu Ala
305 310 315 320

Met Met Cys Gly Tyr Gln Ser Ala Gln Lys Asp Asn Gln Cys Thr Gly
325 330 335

Tyr Gly Asn Ile Asp Asp Ile Pro Gln Phe Leu Arg Trp Phe Arg Glu
340 345 350

Trp Gly Thr Tyr Val Cys Glu Glu Ser Glu Lys Asn Met Asn Thr Leu
355 360 365

Lys Ala Val Cys Phe Pro Lys Gln Pro Arg Thr Glu Ala Asn Pro Ala
370 375 380

Leu Thr Val His Glu Asn Glu Met Cys Ser Ser Thr Leu Lys Lys Tyr
385 390 395 400

Glu Glu Trp Tyr Asn Lys Arg Lys Thr Glu Trp Thr Glu Gln Ser Ile

				405					410					415	
Lys	Tyr	Asn	Asn	Asp	Lys	Ile	Asn	Tyr	Thr	Asp	Ile	Lys	Thr	Leu	Ser
			420					425					430		
Pro	Ser	Glu	Tyr	Leu	Ile	Glu	Lys	Cys	Pro	Glu	Cys	Lys	Cys	Thr	Lys
		435					440					445			
Lys	Asn	Leu	Gln	Asp	Val	Phe	Glu	Leu	Thr	Phe	Asp	Gly	Lys	Ala	Leu
	450					455					460				
Leu	Glu	Lys	Leu	Lys	Lys	Glu	Glu	Ser	Pro	Val	Ser	Asn	Ser	Val	Asn
465					470					475					480
Ala	Leu	Pro	Glu	Pro	Gly	Gln	Ile	Thr	Leu	Pro	Asp	Pro	Ser	Leu	Lys
				485					490					495	
Gln	Thr	Thr	Gln	Gln	Glu	Asn	Gln	Pro	Val	Val	Glu	Thr	Pro	Val	Thr
			500					505					510		
Thr	Ala	Val	Ile	Asn	Glu	His	Gln	Gly	Gln	Thr	Glu	Pro	Asn	Lys	Gly
		515					520					525			
Asp	Asn	Asn	Asn	Glu	Arg	Glu	Asn	His	Glu	Ser	Asn	Val	Gly	Ser	Ile
	530					535					540				
Gln	Glu	Val	Asn	Gln	Gly	Ser	Val	Ser	Glu	Glu	Ser	His	Ser	Lys	Thr
545					550					555					560
Ile	Asp	Pro	Ser	Lys	Ile	Asp	Asp	Arg	Leu	Glu	Leu	Ser	Ser	Gly	Ser
				565					570					575	
Ser	Ser	Leu	Glu	Gln	His	Ser	Lys	Glu	Asp	Val	Lys	Lys	Gly	Cys	Ala
			580					585					590		
Leu	Glu	Leu	Val	Pro	Leu	Ser	Leu	Ser	Asp	Ile	Glu	Gln	Ile	Ala	Asn
		595					600					605			
Glu	Ser	Glu	Asp	Val	Leu	Glu	Glu	Ile	Glu	Glu	Glu	Ile	Asn	Thr	Asp
	610					615					620				

Gly Glu Ile Glu Tyr Ile Thr Glu Glu Glu Ile Lys Glu Asp Ile Glu
625 630 635 640

Glu Glu Thr Glu Glu Asp Ile Glu Glu Glu Thr Glu Glu Glu Thr Glu
645 650 655

Glu Glu Thr Glu Glu Glu Ala Asp Glu Glu Thr Val Lys Glu Ile Glu
660 665 670

Asp Lys Pro Glu Gln Glu Ile Lys Asn Lys Ser Leu Glu Glu Lys Gln
675 680 685

Ile Asp Lys Asn Thr Asp Thr Ser Glu Lys Lys Gly Phe Asn Asn Ser
690 695 700

Glu Lys Asp Glu Lys Ala Arg Asn Leu Ile Ser Lys Asn Tyr Lys Asn
705 710 715 720

Tyr Asn Glu Leu Asp Lys Asn Val His Thr Leu Val Asn Ser Ile Ile
725 730 735

Ser Leu Leu Glu Glu Gly Asn Gly Ser Asp Ser Thr Leu Asn Ser Leu
740 745 750

Ser Lys Asp Ile Thr Asn Leu Phe Lys Asn
755 760

<210> 48
<211> 226
<212> PRT
<213> 惡性瘧原蟲

<400> 48

His Glu Ser Asn Val Gly Ser Ile Gln Glu Val Asn Gln Gly Ser Val
1 5 10 15

Ser Glu Glu Ser His Ser Lys Thr Ile Asp Pro Ser Lys Ile Asp Asp
20 25 30

Arg Leu Glu Leu Ser Ser Gly Ser Ser Ser Leu Glu Gln His Ser Lys
35 40 45

Glu Asp Val Lys Lys Gly Cys Ala Leu Glu Leu Val Pro Leu Ser Leu
50 55 60

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

Ile Glu Glu Glu Ile Asn Thr Asp Gly Glu Ile Glu Tyr Ile Thr Glu
85 90 95

Glu Glu Ile Lys Glu Asp Ile Glu Glu Glu Thr Glu Glu Asp Ile Glu
100 105 110

Glu Glu Thr Glu Glu Glu Thr Glu Glu Glu Thr Glu Glu Glu Ala Asp
115 120 125

Glu Glu Thr Val Lys Glu Ile Glu Asp Lys Pro Glu Gln Glu Ile Lys
130 135 140

Asn Lys Ser Leu Glu Glu Lys Gln Ile Asp Lys Asn Thr Asp Thr Ser
145 150 155 160

Glu Lys Lys Gly Phe Asn Asn Ser Glu Lys Asp Glu Lys Ala Arg Asn
165 170 175

Leu Ile Ser Lys Asn Tyr Lys Asn Tyr Asn Glu Leu Asp Lys Asn Val
180 185 190

His Thr Leu Val Asn Ser Ile Ile Ser Leu Leu Glu Glu Gly Asn Gly
195 200 205

Ser Asp Ser Thr Leu Asn Ser Leu Ser Lys Asp Ile Thr Asn Leu Phe
210 215 220

Lys Asn
225

<210> 49
<211> 33
<212> PRT
<213> 惡性瘡原蟲

<400> 49

His Glu Ser Asn Val Gly Ser Ile Gln Glu Val Asn Gln Gly Ser Val
1 5 10 15

Ser Glu Glu Ser His Ser Lys Thr Ile Asp Pro Ser Lys Ile Asp Asp
20 25 30

Arg

<210> 50
<211> 29
<212> PRT
<213> 惡性瘡原蟲

<400> 50

Ser Lys Thr Ile Asp Pro Ser Lys Ile Asp Asp Arg Leu Glu Leu Ser
1 5 10 15

Ser Gly Ser Ser Ser Leu Glu Gln His Ser Lys Glu Asp
20 25

<210> 51
<211> 29
<212> PRT
<213> 惡性瘡原蟲

<400> 51

Glu Gln His Ser Lys Glu Asp Val Lys Lys Gly Cys Ala Leu Glu Leu
1 5 10 15

Val Pro Leu Ser Leu Ser Asp Ile Glu Gln Ile Ala Asn
20 25

<210> 52
<211> 33
<212> PRT
<213> 惡性瘡原蟲

<400> 52

Ala Leu Glu Leu Val Pro Leu Ser Leu Ser Asp Ile Glu Gln Ile Ala
1 5 10 15

Asn Glu Ser Glu Asp Val Leu Glu Glu Ile Glu Glu Glu Ile Asn Thr
20 25 30

Asp

<210> 53
<211> 41
<212> PRT
<213> 惡性瘡原蟲

<400> 53

Glu Ile Glu Asp Lys Pro Glu Gln Glu Ile Lys Asn Lys Ser Leu Glu
1 5 10 15

Glu Lys Gln Ile Asp Lys Asn Thr Asp Thr Ser Glu Lys Lys Gly Phe
20 25 30

Asn Asn Ser Glu Lys Asp Glu Lys Ala
35 40

<210> 54
<211> 61
<212> PRT
<213> 惡性瘡原蟲

<400> 54

Asn Asn Ser Glu Lys Asp Glu Lys Ala Arg Asn Leu Ile Ser Lys Asn
1 5 10 15

Tyr Lys Asn Tyr Asn Glu Leu Asp Lys Asn Val His Thr Leu Val Asn
20 25 30

Ser Ile Ile Ser Leu Leu Glu Glu Gly Asn Gly Ser Asp Ser Thr Leu
35 40 45

Asn Ser Leu Ser Lys Asp Ile Thr Asn Leu Phe Lys Asn
50 55 60

<210> 55
<211> 272
<212> PRT
<213> 惡性瘡原蟲

<400> 55

Met Trp Ile Val Lys Phe Leu Ile Val Val His Phe Phe Ile Ile Cys
1 5 10 15

Thr Ile Asn Phe Asp Lys Leu Tyr Ile Ser Tyr Ser Tyr Asn Ile Val
20 25 30

Pro Glu Asn Gly Arg Met Leu Asn Met Arg Ile Leu Gly Glu Glu Lys
35 40 45

Pro Asn Val Asp Gly Val Ser Thr Ser Asn Thr Pro Gly Gly Asn Glu
50 55 60

Ser Ser Ser Ala Ser Pro Asn Leu Ser Asp Ala Ala Glu Lys Lys Asp
65 70 75 80

Glu Lys Glu Ala Ser Glu Gln Gly Glu Glu Ser His Lys Lys Glu Asn
85 90 95

Ser Gln Glu Ser Ala Asn Gly Lys Asp Asp Val Lys Glu Glu Lys Lys
100 105 110

Thr Asn Glu Lys Lys Asp Asp Gly Lys Thr Asp Lys Val Gln Glu Lys
115 120 125

Val Leu Glu Lys Ser Pro Lys Glu Ser Gln Met Val Asp Asp Lys Lys
130 135 140

Lys Thr Glu Ala Ile Pro Lys Lys Val Val Gln Pro Ser Ser Ser Asn
145 150 155 160

Ser Gly Gly His Val Gly Glu Glu Glu Asp His Asn Glu Gly Glu Gly
165 170 175

Glu His Glu Glu Glu Glu Glu His Glu Glu Asp Asp Asp Asp Glu Asp
180 185 190

Asp Asp Thr Tyr Asn Lys Asp Asp Leu Glu Asp Glu Asp Leu Cys Lys
195 200 205

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

Asn Arg Arg Val Lys Cys Lys Cys Lys Glu Gly Tyr Lys Leu Glu Gly
225 230 235 240

Ile Glu Cys Val Glu Leu Leu Ser Leu Ala Ser Ser Ser Leu Asn Leu
245 250 255

Ile Phe Asn Ser Phe Ile Thr Ile Phe Val Val Ile Leu Leu Ile Asn
260 265 270

<210> 56
<211> 9563
<212> PRT
<213> 惡性瘡原蟲

<400> 56

Met Lys Lys Glu Ser Tyr Arg Phe Leu Asn Ile Ser Ile Asn Asn Gly
1 5 10 15

Ser Asp Lys Lys Lys Lys Ser Asn Phe Phe Val Lys Ile Lys Asn Gly
20 25 30

Thr Asp Leu Lys Asp Thr Lys Lys Asp Arg Ile Arg Phe His Phe Tyr
35 40 45

Phe Tyr Phe Phe Ile Val Lys Ile Ile Leu Leu Ser Leu Leu Ile Trp
50 55 60

Thr Val Ile Tyr Ser Asn Asn Cys Ser Asn Gly Lys Tyr Lys Ser Thr
65 70 75 80

Leu Tyr Ile Val Gly Asn His Leu Arg Phe Arg Gly Phe Arg Ile Leu
85 90 95

Ala Glu Asn Glu Tyr Glu Met Lys Thr Lys Tyr Lys Thr Leu Met Val
100 105 110

Asn Ile Asp Asp Asn Asp Leu Gly Lys Arg Gly Asn Lys Ile Lys Pro
115 120 125

Lys His Lys Lys Val Glu Ile Asn Leu Asn Asp Asn Asn Leu Ser Asn
130 135 140

Asn Glu Ser Lys Arg Lys Ser Arg Arg Lys Lys Val Lys Val Asn Leu
145 150 155 160

Lys Asp Asn Leu Ala Lys Arg Glu Gly Lys Met Lys Arg Arg Asn Lys
165 170 175

Lys Glu Lys Arg Arg Lys Glu Lys Asp Asn Lys Lys Met Asn Glu Leu
180 185 190

Lys Leu Lys Arg Glu Tyr Lys Glu Ser Tyr Leu Leu Asp Asn Lys Ser
195 200 205

Asp Met Asp Val Ile Arg Asn Asp Lys Phe Ser Tyr Phe Thr Leu Tyr
210 215 220

Lys Asn Asn Leu Phe Pro Asn Ser Asn Asn Tyr Phe Leu His Met Leu
225 230 235 240

Lys Thr Tyr Asp Glu Glu Asn Lys Gly Ile Asp Glu Asn Thr Asp Ile
245 250 255

Asn Glu Asn Val Glu Glu Asn Glu Tyr Val Asp Lys Asn Thr Glu Gly
260 265 270

Asp Lys Asp Gly Asp Glu Asp Lys Gly Gly Gly Glu Ser Glu Gly Gly
275 280 285

Asp Gly His Gly Ser Ala Gly Asp Ser Ala Gly Gly Asp Arg Gly Gly
290 295 300

Asp Glu Asn Lys Asp Lys Asp Asn Glu Glu Asn Lys Asp Lys Lys Gly
305 310 315 320

Asn Lys Asp Asp Asp Asp Glu Glu Glu Glu Glu Glu Glu Glu Asp Asp
325 330 335

Glu Glu Lys Glu Glu Lys Asp Glu Lys Asp Glu Lys Asp Glu Lys Asp
340 345 350

Glu Lys Asp Glu Lys Asp Glu Lys Asp Glu Lys Asp Glu Lys Asp Glu
355 360 365

Lys Asp Glu Lys Asp Glu Lys Asp Glu Lys Asp Glu Lys Gly Glu Lys
370 375 380

Asp Glu Ser Lys Gly Glu Glu Lys Phe Leu Lys Glu Glu Lys Met Pro
385 390 395 400

Lys Lys Glu Glu Asn Met Gln Asp Lys Ile Glu Arg Asp Lys Glu Phe
405 410 415

Glu Gly Phe Lys Asp Glu Tyr Phe Thr Gln Met Glu Gly Gly Ala Tyr
420 425 430

Gly Ile Thr Val Glu His Glu Gly Gln Lys Leu Arg Glu Thr Leu Thr
435 440 445

Glu Gly Val Glu Gly Tyr Glu Lys Val Ile Glu Glu Met Glu Gln Thr
450 455 460

Lys Leu Asp Glu Phe Leu Leu Pro Thr Asn Glu Gly Lys Ser Asp Asp
465 470 475 480

Phe Val Ser Glu Met Glu Glu Glu Arg Leu Phe Asn Phe Val Ser Tyr
485 490 495

Met Glu Glu Glu Val Lys Asp Lys Met Phe Ile Glu Arg Glu Gln Gly
500 505 510

Thr Glu Glu Glu Val Ile His Glu Asp Leu Ser Asp Glu Lys Ile Gly
515 520 525

Ile Glu Lys Lys Glu Leu Glu Thr Phe Val Gln Asp Val Ser Asp Glu
530 535 540

Val Leu Gln Asp Glu Gln Leu Ile Glu Glu Glu Lys Leu Thr Glu Glu
545 550 555 560

Glu Lys Leu Thr Glu Glu Glu Lys Leu Thr Glu Glu Glu Lys Leu Thr
565 570 575

Glu Asp Glu Gln Leu Ile Glu Glu Glu Lys Leu Thr Glu Glu Glu Lys

580	585	590
Leu Thr Glu Glu Glu Lys Leu Thr Glu Glu Glu Lys Leu Thr Glu Glu 595 600 605		
Glu Lys Leu Thr Glu Glu Glu Lys Leu Thr Glu Glu Glu Lys Leu Thr 610 615 620		
Glu Glu Glu Lys Leu Thr Glu Glu Glu Lys Leu Thr Glu Glu Glu Ile 625 630 635 640		
Phe Ile Glu Glu Asp Lys Ile Ser Pro Lys Glu Val Glu Glu Pro Leu 645 650 655		
Glu Asp Val Leu Met Glu Lys Met Glu Lys Glu Tyr Lys Glu Ile Leu 660 665 670		
His Glu Gly Lys Ser Val Val Thr Gln Asp Met Asp Glu Lys Leu Leu 675 680 685		
Ser Glu Asn Leu Glu Asp Asp Leu Ile Pro Glu Glu Ile Ile Glu Glu 690 695 700		
Leu Val Asp Glu Glu Leu Val Glu Glu Val Thr Ala Glu Glu Ile Val 705 710 715 720		
Glu Glu Phe Val Ala Glu Val Glu Ile Glu Glu Lys Ile Pro Lys Glu 725 730 735		
Leu Val Glu Glu Val Met Pro Glu Glu Asp Val Asp Glu Val Val Pro 740 745 750		
Glu Glu Leu Val Glu Glu Val Val Pro Glu Glu Leu Ile Glu Gly Val 755 760 765		
Ile Pro Glu Glu Leu Val Glu Asp Val Ile Pro Glu Lys Val Leu Glu 770 775 780		
Lys Val Ile Pro Glu Glu Ile Ile Glu Glu Leu Val Leu Glu Glu Val 785 790 795 800		

Val Glu Glu Ile Lys His Glu Glu Leu Val Glu Glu Glu Ile Pro Glu
805 810 815

Glu Val Thr Glu Glu Val Ile Pro Asp Glu Val Val Glu Glu Val Ile
820 825 830

Pro Glu Glu Leu Ile Glu Lys Val Val Lys Glu Glu Leu Val Glu Lys
835 840 845

Val Val Ala Glu Glu Ile Val Glu Glu Val Val Pro Glu Glu Leu Val
850 855 860

Glu Lys Val Val Ala Glu Glu Ile Val Glu Glu Val Ile Pro Glu Glu
865 870 875 880

Leu Ile Glu Glu Val Ile Thr Glu Lys Pro Ala Glu Glu Val Ile Pro
885 890 895

Glu Glu Leu Val Glu Glu Val Ile Pro Lys Glu Ile Val Glu Glu Val
900 905 910

Leu Pro Glu Glu Val Val Lys Glu Val Ile Pro Glu Glu Val Val Glu
915 920 925

Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile Pro Glu Glu Ile
930 935 940

Val Glu Glu Val Val Pro Glu Glu Leu Val Glu Glu Met Lys Pro Glu
945 950 955 960

Glu Val Val Glu Glu Val Ile Ser Glu Glu Leu Val Glu Glu Met Lys
965 970 975

Pro Glu Glu Val Val Glu Glu Met Lys Pro Glu Glu Val Val Glu Glu
980 985 990

Val Thr Pro Glu Lys Val Val Glu Glu Val Val Pro Glu Glu Leu Val
995 1000 1005

Glu Glu Met Lys Pro Glu Glu Val Val Glu Glu Val Ile Ser Glu
1010 1015 1020

Glu	Leu	Val	Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
1025						1030					1035			
Thr	Pro	Glu	Lys	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val
1040						1045					1050			
Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Ser	Glu
1055						1060					1065			
Glu	Leu	Val	Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
1070						1075					1080			
Ile	Ser	Glu	Glu	Leu	Val	Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val
1085						1090					1095			
Glu	Glu	Val	Thr	Pro	Glu	Lys	Val	Val	Glu	Glu	Val	Val	Pro	Glu
1100						1105					1110			
Glu	Leu	Val	Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
1115						1120					1125			
Ile	Ser	Glu	Glu	Leu	Val	Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val
1130						1135					1140			
Glu	Glu	Val	Thr	Pro	Glu	Lys	Val	Val	Glu	Glu	Val	Val	Pro	Glu
1145						1150					1155			
Glu	Leu	Val	Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
1160						1165					1170			
Ile	Ser	Glu	Glu	Leu	Val	Glu	Glu	Met	Lys	Pro	Glu	Glu	Val	Val
1175						1180					1185			
Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu
1190						1195					1200			
Glu	Val	Val	Glu	Glu	Ile	Ile	Pro	Glu	Glu	Val	Val	His	Glu	Ala
1205						1210					1215			
Lys	His	Glu	Glu	Leu	Phe	Glu	Lys	Thr	Val	Pro	Glu	Val	Glu	Val
1220						1225					1230			

Gln	Glu	Ile	Ile	Pro	Lys	Glu	Leu	Val	Glu	Val	Ile	Pro	Glu	Glu
	1235					1240					1245			
Val	Leu	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Glu	Ile
	1250					1255					1260			
Ile	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro
	1265					1270					1275			
Glu	Glu	Ile	Val	Gln	Glu	Val	Ile	Pro	Glu	Asp	Leu	Met	Glu	Glu
	1280					1285					1290			
Val	Val	Pro	Glu	Glu	Ile	Ile	Glu	Glu	Lys	Ile	Leu	Glu	Glu	Ile
	1295					1300					1305			
Val	Glu	Glu	Glu	Ile	His	Glu	Glu	Ile	Val	Glu	Glu	Ile	Ile	Ser
	1310					1315					1320			
Glu	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Ala	Glu	Val	Val	Glu	Glu
	1325					1330					1335			
Met	Ile	Pro	Glu	Lys	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu
	1340					1345					1350			
Val	Glu	Glu	Val	Ile	Ser	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro
	1355					1360					1365			
Val	Glu	Val	Leu	Glu	Glu	Val	Val	Pro	Val	Glu	Val	Leu	Glu	Glu
	1370					1375					1380			
Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Phe
	1385					1390					1395			
Ile	Glu	Glu	Met	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Val	Pro
	1400					1405					1410			
Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
	1415					1420					1425			
Val	Pro	Val	Glu	Leu	Leu	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Leu

1430	1435	1440
Glu Glu Val Ile Pro Glu	Glu Leu Val Glu Glu Val	Val Pro Glu
1445	1450	1455
Glu Leu Val Glu Asp Val	Ile Pro Glu Glu Leu Ile	Ala Glu Val
1460	1465	1470
Val Ser Glu Glu Leu Val	Glu Glu Ile Pro Glu	Glu Val Leu
1475	1480	1485
Glu Glu Val Ile Pro Glu	Glu Leu Val Glu Glu Val	Ile Pro Glu
1490	1495	1500
Glu Leu Val Glu Glu Val	Ile Pro Glu Val Leu Val	Glu Glu Val
1505	1510	1515
Ile Pro Glu Glu Leu Val	Glu Glu Val Ile Pro Glu	Val Leu Val
1520	1525	1530
Glu Glu Glu Val Pro Glu	Glu Leu Val Glu Glu Val	Ile Pro Glu
1535	1540	1545
Leu Leu Val Ala Glu Val	Ile Pro Glu Glu Leu Val	Ala Glu Val
1550	1555	1560
Ile Pro Glu Glu Phe Val	Glu Glu Val Ile Pro Glu	Glu Val Val
1565	1570	1575
Glu Glu Leu Val Pro Glu	Glu Leu Val Glu Glu Val	Ile Pro Glu
1580	1585	1590
Glu Ile Val Glu Glu Val	Val Glu Glu Val Val Glu	Glu Ile Ile
1595	1600	1605
Pro Glu Glu Val Ile Glu	Glu Val Ile Pro Glu Glu	Ile Val Lys
1610	1615	1620
Glu Val Val Pro Glu Val	Leu Val Glu Glu Val Val	Pro Glu Glu
1625	1630	1635

Ile Val 1640	Glu Glu Val Val 1645	Pro Glu Glu Ile Val 1650	Glu Glu Val Val
Pro Glu 1655	Glu Leu Val Glu 1660	Val Val Pro Glu 1665	Glu Leu Ile Glu
Glu Val 1670	Ile Pro Glu Glu 1675	Leu Val Glu Glu Val 1680	Ile Pro Glu Val
Leu Val 1685	Glu Glu Val Ile 1690	Pro Glu Val Leu Val 1695	Glu Glu Met Val
Leu Glu 1700	Glu Leu Val Glu 1705	Val Ile Pro Glu 1710	Val Leu Val Glu
Glu Met 1715	Val Pro Glu Glu 1720	Val Glu Lys Met 1725	Val Leu Glu Glu
Val Val 1730	Glu Glu Val Ile 1735	Pro Glu Glu Val Val 1740	Glu Glu Val Ile
Pro Glu 1745	Glu Asp Val Glu 1750	Gln Val Ile Pro Glu 1755	Glu Leu Ile Glu
Glu Val 1760	Val Pro Glu Glu 1765	Val Ile Glu Glu Val 1770	Ile Thr Glu Glu
Val Val 1775	Glu Glu Val Leu 1780	Pro Glu Glu Leu Val 1785	Glu Lys Val Val
Glu Glu 1790	Glu Ile Leu Glu 1795	Glu Val Ile Pro Glu 1800	Glu Leu Val Glu
Glu Val 1805	Val Arg Glu Glu 1810	Leu Ile Glu Glu Val 1815	Val Thr Glu Glu
Leu Val 1820	Glu Lys Val Val 1825	Glu Glu Ile Val 1830	Glu Glu Val Val
Leu Ala 1835	Glu Val Val Glu 1840	Glu Val Ile Pro Gln 1845	Glu Ile Val Glu

Glu Val 1850	Ile Pro Glu Glu Val 1855	Val Glu Glu Val 1860	Ile Pro Lys Glu
Ile Val 1865	Glu Glu Val Ile Pro 1870	Glu Glu Leu Val 1875	Glu Glu Val Val
Pro Glu 1880	Glu Leu Val Ala Glu 1885	Val Ile Pro Glu Glu 1890	Leu Val Ala
Glu Val 1895	Ile Pro Glu Glu Leu 1900	Ile Glu Glu Val 1905	Val Thr Glu Glu
Leu Val 1910	Glu Glu Val Ile Pro 1915	Glu Glu Val Val 1920	Glu Glu Val Ile
Pro Glu 1925	Glu Val Val Glu Glu 1930	Val Val Pro Glu Glu 1935	Leu Val Glu
Glu Val 1940	Val Pro Glu Glu Leu 1945	Val Glu Glu Val 1950	Val Pro Glu Glu
Ile Val 1955	Glu Glu Leu Leu Pro 1960	Lys Glu Val Val 1965	Glu Glu Val Ile
Tyr Glu 1970	Glu Gln Val Glu Glu 1975	Val Ile Pro Glu Glu 1980	Leu Val Ala
Glu Val 1985	Ile Pro Glu Lys Leu 1990	Val Glu Glu Val 1995	Ile Pro Glu Glu
Leu Val 2000	Glu Glu Val Ile Pro 2005	Glu Glu Leu Val 2010	Glu Glu Val Val
Pro Glu 2015	Val Val Glu Glu Val 2020	Val Pro Glu Glu 2025	Leu Val Glu Glu
Val Ile 2030	Pro Glu Glu Leu Val 2035	Glu Glu Val Ile 2040	Pro Glu Val Leu
Val Glu 2045	Glu Glu Val Pro Glu 2050	Glu Leu Val Glu 2055	Glu Val Ile Pro

Glu	Glu	Leu	Val	Glu	Glu	Met	Leu	Pro	Glu	Glu	Leu	Ile	Glu	Val
2060						2065					2070			
Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu
2075						2080					2085			
Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro
2090						2095					2100			
Glu	Glu	Leu	Ile	Glu	Glu	Leu	Val	Pro	Glu	Val	Glu	Ile	Glu	Glu
2105						2110					2115			
Ile	Leu	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Leu	Val	Pro	Glu	Glu	Ile
2120						2125					2130			
Ile	Glu	Glu	Val	Ile	Pro	Lys	Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro
2135						2140					2145			
Glu	Val	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val
2150						2155					2160			
Val	Pro	Glu	Ile	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu
2165						2170					2175			
Val	Val	Pro	Glu	Glu	Ile	Ile	Glu	Glu	Lys	Ile	Ser	Glu	Glu	Val
2180						2185					2190			
Val	Glu	Glu	Val	Leu	Pro	Lys	Glu	Ile	Val	Glu	Glu	Val	Ile	Pro
2195						2200					2205			
Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Ala	Glu
2210						2215					2220			
Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu
2225						2230					2235			
Phe	Glu	Glu	Glu	Ile	Pro	Glu	Val	Val	Val	Glu	Glu	Val	Val	Pro
2240						2245					2250			
Glu	Val	Val	Glu	Glu	Glu	Ile	Pro	Glu	Val	Val	Val	Glu	Glu	Val

2255	2260	2265
Val Pro Glu Val Val Glu Glu	Val Ile Pro Glu Glu	Leu Val Glu
2270	2275	2280
Glu Val Ile Pro Glu Glu Leu	Ile Glu Glu Val Ile	Pro Glu Glu
2285	2290	2295
Val Ala Glu Glu Val Leu Pro	Glu Glu Leu Ile Glu	Glu Val Ile
2300	2305	2310
Pro Glu Glu Leu Val Glu Glu	Val Val Pro Glu Glu	Leu Val Ala
2315	2320	2325
Glu Val Ile Pro Glu Glu Ile	Val Glu Glu Val Val	Arg Glu Glu
2330	2335	2340
Leu Val Glu Glu Val Val Pro	Glu Glu Val Val Glu	Glu Val Ile
2345	2350	2355
Pro Lys Glu Ile Val Glu Glu	Val Val Ser Glu Glu	Val Val Glu
2360	2365	2370
Glu Val Ile Pro Lys Glu Ile	Val Glu Glu Glu Val	Pro Glu Glu
2375	2380	2385
Leu Val Glu Val Val Pro Glu	Glu Leu Val Glu Glu	Val Val Pro
2390	2395	2400
Glu Glu Leu Val Glu Glu Val	Val Pro Glu Glu Leu	Val Glu Glu
2405	2410	2415
Val Val Pro Glu Glu Leu Val	Glu Glu Val Val Pro	Glu Glu Leu
2420	2425	2430
Val Glu Glu Val Val Pro Glu	Val Val Glu Glu Val	Gln Glu Gln
2435	2440	2445
Leu Val Glu Glu Phe Ile Pro	Glu Glu Val Val Glu	Glu Leu Val
2450	2455	2460

Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu
	2465					2470					2475			
Glu	Val	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Leu	Pro	Glu	Glu
	2480					2485					2490			
Val	Val	Lys	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile
	2495					2500					2505			
Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Ile	Val	Glu
	2510					2515					2520			
Glu	Val	Leu	Pro	Glu	Glu	Val	Val	Lys	Glu	Val	Ile	Pro	Glu	Glu
	2525					2530					2535			
Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile
	2540					2545					2550			
Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu
	2555					2560					2565			
Glu	Val	Val	Ser	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu
	2570					2575					2580			
Ile	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Leu	Glu	Glu	Val	Val
	2585					2590					2595			
Glu	Glu	Val	Val	Pro	Glu	Ile	Val	Glu	Glu	Val	Val	Pro	Glu	Val
	2600					2605					2610			
Val	Glu	Glu	Val	Ile	Thr	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Ile
	2615					2620					2625			
Lys	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu
	2630					2635					2640			
Glu	Ile	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val
	2645					2650					2655			
Ile	Ser	Glu	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Val
	2660					2665					2670			

Glu	Glu	Val	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Leu	Pro	Lys
2675						2680					2685			
Glu	Ile	Val	Glu	Glu	Val	Ile	Ser	Glu	Lys	Val	Val	Glu	Glu	Met
2690						2695					2700			
Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val
2705						2710					2715			
Glu	Glu	Val	Ile	Pro	Glu	Val	Glu	Ile	Glu	Glu	Ile	Leu	Pro	Glu
2720						2725					2730			
Glu	Leu	Ile	Glu	Glu	Leu	Val	Ala	Glu	Glu	Val	Ile	Glu	Glu	Val
2735						2740					2745			
Ile	Pro	Lys	Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Lys	Leu	Ile
2750						2755					2760			
Glu	Asp	Val	Val	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Leu	Pro	Glu
2765						2770					2775			
Glu	Val	Val	Lys	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
2780						2785					2790			
Leu	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Val	Glu
2795						2800					2805			
Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Leu	Pro	Lys	Glu
2810						2815					2820			
Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Glu	Ile	Glu	Glu	Ile	Leu
2825						2830					2835			
Pro	Glu	Glu	Ile	Ile	Glu	Glu	Leu	Val	Ala	Lys	Glu	Val	Ile	Glu
2840						2845					2850			
Glu	Val	Ile	Pro	Lys	Glu	Leu	Ile	Glu	Glu	Ala	Ile	Thr	Glu	Glu
2855						2860					2865			
Val	Val	Glu	Glu	Met	Ile	Pro	Glu	Glu	Ile	Ile	Glu	Glu	Val	Val
2870						2875					2880			

Pro	Glu	Glu	Val	Ile	Glu	Glu	Val	Ile	Thr	Glu	Glu	Val	Val	Glu
	2885					2890					2895			
Glu	Val	Val	Pro	Glu	Glu	Val	Ile	Glu	Glu	Val	Ile	Thr	Glu	Glu
	2900					2905					2910			
Val	Val	Glu	Glu	Ala	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile
	2915					2920					2925			
Pro	Glu	Val	Glu	Ile	Glu	Glu	Val	Leu	Pro	Glu	Glu	Leu	Ile	Glu
	2930					2935					2940			
Glu	Leu	Val	Pro	Glu	Glu	Val	Thr	Glu	Glu	Val	Ile	Thr	Glu	Glu
	2945					2950					2955			
Val	Val	Glu	Glu	Ala	Ile	Ser	Glu	Val	Val	Glu	Glu	Val	Ile	Pro
	2960					2965					2970			
Glu	Glu	Ile	Val	Lys	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu
	2975					2980					2985			
Ile	Ile	Thr	Glu	Glu	Ile	Ala	Glu	Glu	Ile	Ile	Pro	Lys	Glu	Leu
	2990					2995					3000			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Val	Glu	Ile	Ile	Pro
	3005					3010					3015			
Glu	Lys	Leu	Val	Glu	Glu	Phe	Val	Ser	Glu	Glu	Leu	Val	Glu	Glu
	3020					3025					3030			
Leu	Val	Pro	Glu	Glu	Ile	Val	Glu	Lys	Val	Val	Pro	Glu	Glu	Leu
	3035					3040					3045			
Val	Glu	Glu	Ile	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro
	3050					3055					3060			
Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu
	3065					3070					3075			
Phe	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Leu	Pro	Glu	Gln	Leu

3080	3085	3090
Val Glu Glu Val Ile Ser Glu	Val Val Glu Glu Val	Val Pro Glu
3095	3100	3105
Glu Leu Val Glu Glu Val Ile	Pro Glu Glu Val Val	Glu Glu Leu
3110	3115	3120
Val Ala Glu Glu Val Ile Glu	Glu Val Ile Pro Lys	Glu Leu Ile
3125	3130	3135
Glu Glu Ala Ile Thr Glu Glu	Val Glu Glu Val Ile	Pro Glu Glu
3140	3145	3150
Ile Val Glu Glu Val Ile Pro	Glu Glu Val Val Lys	Glu Val Ile
3155	3160	3165
Pro Glu Val Glu Ile Glu Glu	Ile Leu Pro Glu Glu	Leu Ile Glu
3170	3175	3180
Glu Leu Val Ala Lys Glu Val	Ile Glu Glu Val Ile	Thr Glu Glu
3185	3190	3195
Val Ala Glu Glu Val Ile Pro	Glu Glu Ile Val Gln	Glu Val Ile
3200	3205	3210
Pro Glu Glu Val Val Glu Glu	Ile Ile Thr Glu Val	Glu Ile Glu
3215	3220	3225
Glu Val Leu Pro Glu Glu Leu	Ile Asp Glu Val Val	Pro Glu Glu
3230	3235	3240
Val Thr Glu Glu Val Ile Thr	Glu Glu Val Met Pro	Glu Glu Val
3245	3250	3255
Val Lys Glu Val Ile Pro Glu	Glu Ile Ala Glu Glu	Val Ile Pro
3260	3265	3270
Lys Glu Leu Val Glu Glu Val	Ile Pro Glu Glu Val	Val Glu Glu
3275	3280	3285

Ile	Ile	Pro	Glu	Val	Glu	Ile	Glu	Glu	Val	Leu	Pro	Glu	Glu	Val
3290						3295					3300			
Ile	Glu	Glu	Val	Val	Pro	Glu	Val	Glu	Ile	Glu	Glu	Leu	Ile	Pro
3305						3310					3315			
Asp	Glu	Val	Val	Glu	Glu	Val	Leu	Pro	Glu	Glu	Leu	Val	Glu	Glu
3320						3325					3330			
Val	Ile	Pro	Glu	Glu	Val	Ala	Val	Glu	Val	Val	Pro	Glu	Glu	Val
3335						3340					3345			
Ile	Glu	Glu	Ala	Val	Pro	Glu	Glu	Ile	Val	Glu	Glu	Phe	Ile	Pro
3350						3355					3360			
Glu	Glu	Gln	Ile	Glu	Glu	Val	Ile	Gln	Glu	Glu	Ile	Ile	Glu	Gln
3365						3370					3375			
Val	Val	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Val	Val	Pro	Glu	Glu	Ile
3380						3385					3390			
Ile	Glu	Glu	Val	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Ile	Tyr
3395						3400					3405			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Ala	Glu
3410						3415					3420			
Lys	Leu	Val	Lys	Glu	Ile	Val	Pro	Glu	Gln	Val	Arg	Glu	Glu	Val
3425						3430					3435			
Thr	Leu	Glu	Glu	Ile	Val	Glu	Glu	Met	Ile	Pro	Glu	Glu	Phe	Val
3440						3445					3450			
Glu	Glu	Val	Ala	Pro	Glu	Val	Glu	Ile	Glu	Glu	Ile	Ile	Pro	Glu
3455						3460					3465			
Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Val	Glu	Glu	Ala
3470						3475					3480			
Val	Pro	Glu	Glu	Leu	Ile	Glu	Lys	Val	Ile	Pro	Glu	Val	Leu	Val
3485						3490					3495			

Glu	Glu	Ile	Ile	Tyr	Lys	Glu	Gly	Ile	Pro	Glu	Val	Leu	Ile	Glu
	3500					3505					3510			
Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Gln	Glu	Val	Ile	Pro	Glu	Glu
	3515					3520					3525			
Ile	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Phe	Ile	Glu	Glu	Met	Ile
	3530					3535					3540			
Pro	Gln	Glu	Val	Val	Lys	Glu	Val	Ile	Thr	Glu	Lys	Phe	Ile	Glu
	3545					3550					3555			
Glu	Met	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu
	3560					3565					3570			
Phe	Ile	Glu	Glu	Met	Ile	Pro	Glu	Val	Val	Val	Glu	Glu	Val	Val
	3575					3580					3585			
Pro	Glu	Glu	Leu	Val	Glu	Glu	Met	Leu	Pro	Glu	Glu	Leu	Ile	Glu
	3590					3595					3600			
Val	Val	Val	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Glu
	3605					3610					3615			
Leu	Val	Glu	Glu	Val	Val	Ala	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile
	3620					3625					3630			
Pro	Glu	Glu	Leu	Val	Glu	Lys	Val	Val	Pro	Glu	Val	Val	Glu	Glu
	3635					3640					3645			
Phe	Ile	His	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu
	3650					3655					3660			
Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val
	3665					3670					3675			
Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val
	3680					3685					3690			
Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu
	3695					3700					3705			

Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro
	3710					3715					3720			
Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
	3725					3730					3735			
Ile	Pro	Glu	Val	Leu	Phe	Glu	Glu	Glu	Ile	Pro	Glu	Glu	Leu	Val
	3740					3745					3750			
Glu	Val	Val	Pro	Val	Glu	Leu	Leu	Glu	Glu	Ala	Ile	Pro	Glu	Glu
	3755					3760					3765			
Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile
	3770					3775					3780			
Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu
	3785					3790					3795			
Glu	Val	Ile	Leu	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu
	3800					3805					3810			
Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile
	3815					3820					3825			
Pro	Glu	Val	Leu	Val	Glu	Glu	Glu	Ile	Pro	Glu	Lys	Leu	Val	Glu
	3830					3835					3840			
Glu	Asp	Ile	Pro	Glu	Lys	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu
	3845					3850					3855			
Leu	Val	Glu	Val	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile
	3860					3865					3870			
Pro	Glu	Glu	Leu	Val	Lys	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Lys
	3875					3880					3885			
Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Glu	Ile	Pro	Lys	Val
	3890					3895					3900			
Val	Glu	Glu	Val	Leu	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Met	Leu

3905	3910	3915
Glu Glu Val Val Glu Glu Val Val Pro Glu Ile Val Glu Glu Val		
3920	3925	3930
Val Pro Glu Glu Leu Val Glu Glu Val Val Pro Glu Val Val Glu		
3935	3940	3945
Glu Val Val Pro Glu Glu Ile Val Glu Glu Val Ile Pro Glu Glu		
3950	3955	3960
Leu Val Glu Glu Val Val Lys Glu Glu Leu Val Glu Glu Val Val		
3965	3970	3975
Lys Glu Glu Leu Val Glu Glu Val Val Lys Glu Glu Leu Val Glu		
3980	3985	3990
Glu Val Ile Pro Glu Val Leu Val Glu Glu Val Val Pro Glu Glu		
3995	4000	4005
Leu Leu Glu Glu Val Ile Pro Lys Val Leu Val Glu Glu Val Ile		
4010	4015	4020
Pro Glu Leu Leu Val Glu Glu Val Val Pro Glu Val Ile Glu Glu		
4025	4030	4035
Val Val Pro Glu Val Val Glu Glu Val Val Pro Glu Glu Leu Leu		
4040	4045	4050
Glu Glu Val Ile Pro Glu Val Leu Val Glu Glu Glu Ile Pro Glu		
4055	4060	4065
Lys Leu Val Glu Glu Val Val Pro Glu Glu Leu Val Glu Glu Val		
4070	4075	4080
Ile Pro Glu Val Leu Val Glu Glu Val Val Pro Glu Glu Leu Val		
4085	4090	4095
Glu Glu Val Ile Ser Glu Glu Leu Val Glu Glu Val Ile Pro Glu		
4100	4105	4110

Glu 4115	Leu	Val	Glu	Glu	Val	Ile 4120	Pro	Glu	Glu	Val	Val 4125	Glu	Glu	Val
Val 4130	Pro	Glu	Val	Val	Glu	Glu 4135	Val	Val	Pro	Glu	Val 4140	Val	Glu	Glu
Val 4145	Val	Pro	Glu	Val	Val	Glu 4150	Glu	Val	Val	Pro	Glu 4155	Val	Val	Glu
Glu 4160	Val	Val	Pro	Glu	Val	Val 4165	Glu	Glu	Val	Val	Pro 4170	Glu	Val	Val
Glu 4175	Glu	Val	Val	Pro	Glu	Val 4180	Val	Glu	Glu	Val	Val 4185	Pro	Glu	Val
Val 4190	Glu	Glu	Val	Val	Pro	Glu 4195	Val	Val	Glu	Glu	Val 4200	Val	Pro	Glu
Glu 4205	Leu	Ile	Glu	Glu	Val	Ile 4210	Pro	Glu	Glu	Ile	Val 4215	Glu	Glu	Val
Ile 4220	Pro	Glu	Glu	Leu	Val	Ala 4225	Glu	Val	Ile	Pro	Glu 4230	Lys	Leu	Val
Glu 4235	Glu	Val	Ile	Pro	Glu	Glu 4240	Leu	Val	Glu	Glu	Val 4245	Ile	Pro	Glu
Glu 4250	Leu	Val	Glu	Glu	Val	Ile 4255	Pro	Glu	Glu	Leu	Val 4260	Glu	Glu	Val
Leu 4265	Pro	Glu	Glu	Val	Val	Glu 4270	Glu	Ala	Val	Pro	Glu 4275	Val	Val	Glu
Glu 4280	Ile	Val	Pro	Glu	Glu	Leu 4285	Ile	Glu	Glu	Val	Ile 4290	Pro	Glu	Glu
Leu 4295	Ile	Lys	Glu	Val	Val	Pro 4300	Glu	Glu	Val	Ile	Glu 4305	Glu	Val	Ile
Thr 4310	Glu	Glu	Val	Val	Glu	Glu 4315	Val	Leu	Pro	Glu	Glu 4320	Ile	Val	Glu

Glu Val 4325	Leu Pro Glu Glu Val 4330	Ile Glu Glu Val Val 4335	Pro Glu Glu
Leu Val 4340	Glu Glu Val Leu Pro 4345	Glu Glu Val Val Glu 4350	Glu Val Val
Pro Glu 4355	Glu Leu Val Glu Glu 4360	Val Val Pro Glu Glu 4365	Leu Val Glu
Glu Val 4370	Ile Pro Glu Glu Leu 4375	Val Glu Glu Val Leu 4380	Pro Glu Glu
Val Val 4385	Glu Glu Val Val Pro 4390	Lys Glu Leu Val Glu 4395	Glu Leu Ile
Pro Glu 4400	Glu Leu Val Glu Glu 4405	Val Ile Pro Glu Glu 4410	Leu Val Glu
Glu Val 4415	Val Pro Glu Glu Leu 4420	Val Ala Glu Val Ile 4425	Pro Glu Glu
Leu Val 4430	Glu Glu Val Ile Pro 4435	Glu Glu Leu Val Glu 4440	Glu Val Ile
Pro Glu 4445	Glu Leu Val Glu Glu 4450	Glu Ile Pro Glu Glu 4455	Leu Val Glu
Glu Val 4460	Ile Leu Glu Glu Leu 4465	Val Glu Glu Val Val 4470	Pro Glu Glu
Leu Ile 4475	Glu Glu Val Val Pro 4480	Glu Glu Leu Ile Glu 4485	Glu Val Val
Pro Glu 4490	Glu Leu Ile Glu Glu 4495	Val Val Glu Lys Val 4500	Ile Pro Glu
Glu Ile 4505	Ile Glu Glu Val Val 4510	Pro Glu Glu Val Ile 4515	Glu Glu Val
Ile Thr 4520	Glu Glu Val Val Glu 4525	Glu Val Val Pro Glu 4530	Lys Val Ile

Glu Glu Val Ile Thr Glu Glu Val Val Glu Glu Val Val Pro Glu
4535 4540 4545

Glu Val Ile Asp Glu Val Ile Thr Glu Glu Val Val Glu Glu Val
4550 4555 4560

Val Pro Glu Glu Val Ile Glu Glu Val Ile Ile Glu Glu Val Val
4565 4570 4575

Glu Glu Val Val Pro Glu Glu Val Ile Glu Glu Val Ile Thr Glu
4580 4585 4590

Glu Val Val Glu Glu Ala Ile Pro Glu Glu Leu Val Glu Glu Val
4595 4600 4605

Ile Pro Glu Val Leu Val Glu Glu Glu Ile Pro Glu Glu Leu Val
4610 4615 4620

Glu Glu Val Ile Leu Glu Glu Leu Val Glu Glu Val Val Ala Glu
4625 4630 4635

Glu Leu Ile Glu Glu Val Val Glu Glu Val Ile Pro Glu Lys Leu
4640 4645 4650

Val Glu Glu Val Ile Pro Glu Glu Ile Val Glu Glu Val Ile Pro
4655 4660 4665

Glu Glu Leu Val Glu Val Val Val Pro Glu Glu Leu Val Glu Glu
4670 4675 4680

Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile His Glu Glu Leu
4685 4690 4695

Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile His
4700 4705 4710

Glu Glu Ile Val Glu Glu Val Ile Pro Glu Glu Val Val Glu Glu
4715 4720 4725

Val Ile Pro Glu Glu Ile Val Glu Glu Val Val Pro Glu Glu Leu

4730	4735	4740
Leu Glu Glu Val Ile Pro Glu	Leu Leu Val Glu Glu	Val Val Pro
4745	4750	4755
Glu Val Val Glu Glu Val Val	Pro Val Glu Leu Leu	Glu Glu Val
4760	4765	4770
Val Glu Glu Val Ile Thr Glu	Glu Val Ile Pro Glu	Glu Leu Ile
4775	4780	4785
Lys Glu Val Ile Ser Glu Glu	Leu Val Glu Glu Leu	Ile Pro Glu
4790	4795	4800
Glu Val Val Gln Glu Val Ile	Thr Glu Glu Val Leu	Glu Glu Val
4805	4810	4815
Ile Pro Glu Glu Ile Val Glu	Glu Leu Ile Pro Glu	Lys Leu Ile
4820	4825	4830
Gly Glu Val Val Pro Glu Lys	Val Val Glu Glu Val	Val Leu Glu
4835	4840	4845
Glu Val Val Glu Glu Val Ile	Pro Glu Glu Ile Val	Glu Glu Val
4850	4855	4860
Ile Thr Glu Glu Val Leu Ala	Glu Glu Ile Val Glu	Glu Phe Val
4865	4870	4875
Pro Glu Glu Leu Val Glu Glu	Met Leu Pro Glu Glu	Val Val Glu
4880	4885	4890
Glu Arg Val Arg Glu Val Glu	Ile Glu Glu Met Val	Pro Glu Val
4895	4900	4905
Leu Val Glu Glu Val Leu Pro	Glu Val Val Glu Glu	Val Ile Thr
4910	4915	4920
Glu Glu Val Val Glu Glu Met	Val Pro Glu Glu Val	Val Glu Glu
4925	4930	4935

Met	Val	Pro	Lys	Glu	Ile	Val	Glu	Glu	Val	Leu	Pro	Glu	Glu	Val
	4940					4945					4950			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Met	Val	Pro
	4955					4960					4965			
Glu	Val	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Ile	Val	Glu	Lys
	4970					4975					4980			
Val	Val	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Val	Ala	Glu	Glu	Ile
	4985					4990					4995			
Ile	Glu	Glu	Val	Ile	Thr	Glu	Glu	Val	Val	Glu	Glu	Ile	Val	Pro
	5000					5005					5010			
Gly	Glu	Val	Val	Glu	Glu	Met	Val	Pro	Glu	Glu	Ile	Ile	Glu	Glu
	5015					5020					5025			
Val	Val	Pro	Glu	Glu	Val	Ile	Glu	Glu	Val	Ile	Thr	Glu	Glu	Val
	5030					5035					5040			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro
	5045					5050					5055			
Glu	Ile	Ser	Val	Glu	Val	Glu	Ile	Pro	Glu	Val	Leu	Val	Glu	Glu
	5060					5065					5070			
Val	Ile	Pro	Glu	Lys	Leu	Val	Lys	Val	Val	Pro	Glu	Glu	Leu	Val
	5075					5080					5085			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Thr	Glu
	5090					5095					5100			
Ala	Leu	Val	Glu	Glu	Val	Val	Asp	Val	Val	Val	Pro	Glu	Glu	Ile
	5105					5110					5115			
Phe	Glu	Glu	Val	Leu	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro
	5120					5125					5130			
Glu	Glu	Val	Val	Glu	Glu	Met	Val	Pro	Glu	Glu	Val	Val	Glu	Glu
	5135					5140					5145			

Val Val Pro Glu Glu Leu Val Glu Glu Val Ile Pro Glu Glu Val
5150 5155 5160

Val Glu Lys Val Val Pro Glu Gln Leu Val Glu Lys Val Val Pro
5165 5170 5175

Glu Glu Leu Val Glu Lys Val Leu Pro Glu Glu Leu Val Glu Glu
5180 5185 5190

Val Val Pro Glu Glu Leu Ile Glu Glu Val Val Thr Glu Glu Val
5195 5200 5205

Ile Glu Glu Ile Ile Pro Glu Glu Ile Ile Glu Glu Ile Ile Pro
5210 5215 5220

Glu Glu Val Val Glu Glu Arg Val Ser Ile Glu Val Val Glu Glu
5225 5230 5235

Leu Val Pro Glu Glu Leu Ile Glu Glu Val Val Ala Glu Glu Ile
5240 5245 5250

Phe Glu Glu Val Val Pro Glu Lys Leu Ile Glu Glu Val Val Ala
5255 5260 5265

Glu Glu Leu Ile Glu Glu Met Val Pro Glu Val Val Glu Glu Val
5270 5275 5280

Val Glu Glu Ile Ile Pro Glu Glu Val Ile Glu Glu Val Ile Pro
5285 5290 5295

Glu Glu Ile Arg Glu Glu Ile Ile Pro Glu Glu Val Val Glu Glu
5300 5305 5310

Val Ile Glu Glu Val Ile Pro Glu Glu Leu Ile Glu Glu Glu Ile
5315 5320 5325

Ser Arg Glu Ile Val Glu Glu Val Ile Pro Glu Glu Val Val Glu
5330 5335 5340

Glu Met Met Pro Glu Glu Val Ile Glu Glu Val Ile Pro Glu Glu
5345 5350 5355

Ile Arg Glu Glu Met Ile Pro Glu Glu Val Val Glu Glu Met Ile
5360 5365 5370

Pro Glu Ile Glu Ile Glu Gln Val Leu Pro Glu Glu Leu Ile Glu
5375 5380 5385

Glu Leu Val Pro Glu Val Glu Ile Glu Glu Ile Leu Pro Glu Glu
5390 5395 5400

Leu Ile Glu Glu Leu Val Pro Glu Gly Val Ile Glu Glu Val Ile
5405 5410 5415

Pro Lys Glu Leu Ile Glu Glu Val Ile Pro Glu Glu Leu Ile Lys
5420 5425 5430

Glu Val Val Pro Glu Glu Val Val Glu Glu Val Ile Pro Lys Glu
5435 5440 5445

Ile Val Glu Glu Val Val Pro Glu Glu Leu Ile Glu Glu Val Ile
5450 5455 5460

Pro Glu Glu Leu Ile Glu Glu Val Val Pro Glu Glu Met Ile Glu
5465 5470 5475

Glu Val Ile Pro Glu Glu Leu Ile Glu Glu Val Val Pro Glu Glu
5480 5485 5490

Met Ile Glu Glu Val Ile Pro Glu Glu Leu Ile Glu Glu Val Val
5495 5500 5505

Pro Glu Glu Val Lys Glu Glu Val Ile Pro Val Glu Leu Ile Glu
5510 5515 5520

Glu Val Val Pro Glu Glu Met Ile Glu Glu Val Ile Ser Glu Glu
5525 5530 5535

Val Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Leu
5540 5545 5550

Pro Glu Val Phe Val Glu Glu Ile Val Pro Lys Glu Leu Val Glu

5555	5560	5565
Glu Val Ile Pro Glu Glu Ile Val Glu Glu Val Ile Pro Glu Glu 5570 5575 5580		
Leu Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile 5585 5590 5595		
Ser Glu Glu Leu Leu Glu Glu Val Ile Pro Glu Leu Leu Val Glu 5600 5605 5610		
Glu Val Val Pro Glu Val Ile Glu Glu Val Val Pro Glu Val Val 5615 5620 5625		
Glu Glu Val Ile Pro Glu Val Val Glu Glu Val Val Thr Glu Glu 5630 5635 5640		
Leu Val Glu Glu Val Ile Pro Glu Glu Val Val Glu Glu Met Ile 5645 5650 5655		
Pro Gly Val Glu Ile Glu Glu Val Leu Pro Glu Glu Leu Val Glu 5660 5665 5670		
Glu Val Ile Pro Glu Glu Ile Val Glu Glu Val Ile Ser Glu Glu 5675 5680 5685		
Asp Phe Glu Glu Val Ile Pro Glu Ala Leu Val Glu Glu Val Ile 5690 5695 5700		
Pro Glu Leu Leu Val Glu Glu Val Val Leu Glu Glu Leu Ile Glu 5705 5710 5715		
Glu Val Ile Pro Glu Val Val Glu Glu Val Ile Pro Glu Glu Val 5720 5725 5730		
Val Glu Glu Val Ile Pro Glu Glu Val Val Glu Lys Val Val Pro 5735 5740 5745		
Glu Glu Leu Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu 5750 5755 5760		

Val Ile Pro Glu Glu Val Pro Glu Glu Val Val Pro Glu Glu Leu
5765 5770 5775

Val Glu Glu Val Ile Ser Glu Glu Leu Val Glu Glu Val Ile Pro
5780 5785 5790

Glu Glu Ile Val Glu Glu Val Ile Pro Glu Glu Ile Val Glu Glu
5795 5800 5805

Val Met Pro Glu Glu Val Ala Glu Glu Val Val Pro Glu Glu Leu
5810 5815 5820

Val Glu Glu Glu Val Pro Glu Glu Leu Val Glu Glu Val Ile Pro
5825 5830 5835

Glu Val Leu Val Glu Glu Val Ile Pro Glu Glu Ile Val Glu Glu
5840 5845 5850

Val Val Pro Glu Glu Val Val Glu Val Val Ile Pro Glu Glu Phe
5855 5860 5865

Ile Glu Glu Ile Ile Pro Glu Glu Val Val Val Glu Val Thr Pro
5870 5875 5880

Glu Glu Leu Ile Glu Glu Met Lys Pro Glu Glu Leu Phe Glu Glu
5885 5890 5895

Val Ile Pro Lys Glu Leu Ile Glu Glu Ile Ile Pro Glu Glu Leu
5900 5905 5910

Ile Lys Glu Val Ile Pro Glu Glu Ile Ile Glu Glu Val Ile Ser
5915 5920 5925

Lys Glu Ile Val Glu Glu Val Val Glu Glu Glu Ile Ile Glu Glu
5930 5935 5940

Val Ile Pro Glu Glu Ile Val Glu Glu Val Val Pro Glu Glu Leu
5945 5950 5955

Val Glu Lys Lys Val Pro Glu Glu Ile Val Glu Glu Val Ile Tyr
5960 5965 5970

Glu	Glu	Phe	Leu	Glu	Glu	Ile	Met	Pro	Glu	Glu	Leu	Ile	Glu	Glu
5975						5980					5985			
Met	Lys	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Ile	Ile	Pro	Arg	Glu	Ile
5990						5995					6000			
Val	Glu	Glu	Ile	Ile	Thr	Glu	Glu	Val	Val	Glu	Glu	Met	Lys	Pro
6005						6010					6015			
Glu	Glu	Leu	Val	Glu	Glu	Met	Val	Pro	Glu	Glu	Val	Val	Glu	Glu
6020						6025					6030			
Met	Val	Pro	Glu	Glu	Val	Val	Glu	Glu	Met	Val	Pro	Glu	Glu	Val
6035						6040					6045			
Val	Glu	Glu	Val	Ile	Thr	Glu	Lys	Leu	Ile	Glu	Glu	Val	Val	Pro
6050						6055					6060			
Glu	Glu	Ile	Ile	Glu	Glu	Leu	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu
6065						6070					6075			
Val	Ile	Pro	Glu	Lys	Leu	Ile	Glu	Glu	Met	Ile	Pro	Glu	Glu	Val
6080						6085					6090			
Val	Glu	Glu	Met	Leu	Leu	Glu	Glu	Val	Val	Glu	Glu	Val	Val	Pro
6095						6100					6105			
Glu	Val	Glu	Ile	Glu	Glu	Met	Ile	Pro	Glu	Gln	Leu	Val	Glu	Glu
6110						6115					6120			
Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Lys	Glu	Ile	Pro	Glu	Val	Val
6125						6130					6135			
Glu	Glu	Ile	Ile	Thr	Glu	Glu	Val	Val	Glu	Glu	Met	Val	Pro	Glu
6140						6145					6150			
Glu	Val	Val	Glu	Glu	Met	Val	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
6155						6160					6165			
Ile	Leu	Glu	Lys	Leu	Ile	Glu	Glu	Val	Val	Pro	Val	Glu	Val	Ile
6170						6175					6180			

Glu	Glu	Val	Val	Pro	Glu	Glu	Val	Ile	Glu	Glu	Val	Ile	Pro	Glu
6185						6190					6195			
Lys	Leu	Ile	Glu	Glu	Ile	Ile	Pro	Glu	Val	Leu	Val	Glu	Glu	Val
6200						6205					6210			
Val	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Phe
6215						6220					6225			
Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu
6230						6235					6240			
Leu	Val	Glu	Lys	Val	Val	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Ile
6245						6250					6255			
Pro	Glu	Phe	Val	Glu	Glu	Val	Ile	Ser	Glu	Glu	Ile	Val	Glu	Glu
6260						6265					6270			
Val	Val	Thr	Glu	Glu	Leu	Ile	Glu	Glu	Met	Ile	Pro	Glu	Glu	Val
6275						6280					6285			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro
6290						6295					6300			
Val	Glu	Leu	Ile	Glu	Glu	Val	Val	Pro	Val	Glu	Leu	Leu	Glu	Glu
6305						6310					6315			
Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Val	Glu	Leu
6320						6325					6330			
Ile	Glu	Glu	Val	Val	Pro	Val	Glu	Leu	Leu	Glu	Glu	Val	Ile	Pro
6335						6340					6345			
Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Val	Lys	Glu	Val
6350						6355					6360			
Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu
6365						6370					6375			
Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu

6380	6385	6390
Glu Val Val Pro Glu Glu Leu Ile Glu Glu Val Ile Pro Glu Glu 6395 6400 6405		
Leu Ile Lys Glu Val Leu Pro Glu Glu Val Ile Glu Glu Leu Lys 6410 6415 6420		
Pro Glu Glu Leu Ile Glu Glu Ile Ile Pro Glu Glu Val Val Glu 6425 6430 6435		
Glu Val Ile Pro Glu Glu Leu Ile Glu Glu Met Ile Pro Glu Leu 6440 6445 6450		
Leu Val Glu Glu Glu Val Pro Glu Glu Leu Val Glu Glu Val Ile 6455 6460 6465		
Pro Glu Val Leu Val Glu Glu Met Val Pro Glu Glu Ile Val Glu 6470 6475 6480		
Glu Val Ile Pro Glu Glu Leu Ile Ala Glu Phe Ala Pro Glu Glu 6485 6490 6495		
Leu Phe Glu Lys Val Ile Pro Glu Glu Val Val Glu Glu Leu Val 6500 6505 6510		
Ser Glu Glu Leu Val Glu Glu Val Leu Pro Glu Val Val Glu Glu 6515 6520 6525		
Val Leu Pro Glu Val Phe Glu Glu Val Ile Pro Glu Glu Val Ile 6530 6535 6540		
Glu Glu Ile Val Pro Glu Glu Val Met Glu Glu Val Val Pro Lys 6545 6550 6555		
Glu Leu Ile Glu Glu Val Ile Pro Glu Glu Leu Ile Glu Glu Val 6560 6565 6570		
Ile Pro Glu Glu Val Ala Glu Glu Val Val Pro Glu Lys Leu Ile 6575 6580 6585		

Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Ile	Lys	Glu	Val	Val	Pro	Glu
6590						6595					6600			
Glu	Leu	Ile	Glu	Glu	Val	Ile	Thr	Glu	Glu	Val	Val	Glu	Glu	Ala
6605						6610					6615			
Ile	Ser	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Val	Val
6620						6625					6630			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Val	Val	Pro	Glu
6635						6640					6645			
Glu	Leu	Ile	Glu	Glu	Ile	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
6650						6655					6660			
Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val
6665						6670					6675			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu
6680						6685					6690			
Glu	Leu	Val	Glu	Lys	Leu	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
6695						6700					6705			
Ile	Pro	Glu	Leu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Val	Val
6710						6715					6720			
Glu	Glu	Leu	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu
6725						6730					6735			
Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Pro	Glu	Glu	Val
6740						6745					6750			
Ile	Arg	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val
6755						6760					6765			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Pro	Glu	Glu	Val	Val	Pro	Glu
6770						6775					6780			
Glu	Leu	Val	Gln	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
6785						6790					6795			

Val	His	Glu	Glu	Val	Pro	Glu	Glu	Val	Val	Pro	Glu	Lys	Leu	Val
6800						6805					6810			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Phe	Glu	Glu	Val	Val	Pro	Glu
6815					6820						6825			
Glu	Val	Pro	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
6830					6835						6840			
Ile	Ser	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val
6845					6850						6855			
Glu	Glu	Phe	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu
6860					6865						6870			
Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Phe
6875					6880						6885			
Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val
6890					6895						6900			
Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Val	Glu	Glu	Glu	Ile	Pro	Glu
6905					6910						6915			
Lys	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
6920					6925						6930			
Ile	Pro	Glu	Val	Leu	Val	Glu	Glu	Val	Val	Thr	Glu	Glu	Val	Pro
6935					6940						6945			
Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Ala	Glu	Val	Val	Pro	Glu
6950					6955						6960			
Glu	Leu	Val	Lys	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
6965					6970						6975			
Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val
6980					6985						6990			
Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu
6995					7000						7005			

Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
7010						7015					7020			
Val	Pro	Val	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val
7025						7030					7035			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu
7040						7045					7050			
Glu	Ile	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
7055						7060					7065			
Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Ile	Ser	Glu	Glu	Leu	Ile
7070						7075					7080			
Glu	Glu	Val	Val	Pro	Val	Glu	Leu	Leu	Glu	Glu	Val	Val	Pro	Val
7085						7090					7095			
Glu	Val	Leu	Glu	Asp	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val
7100						7105					7110			
Ile	Pro	Glu	Glu	Phe	Ile	Glu	Glu	Met	Ile	Pro	Glu	Glu	Ile	Ile
7115						7120					7125			
Glu	Glu	Ala	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Ile	Pro	Glu
7130						7135					7140			
Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile
7145						7150					7155			
Pro	Glu	Glu	Val	Val	Glu	Lys	Val	Val	Pro	Glu	Glu	Leu	Val	Glu
7160						7165					7170			
Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu
7175						7180					7185			
Val	Pro	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile
7190						7195					7200			
Ser	Glu	Glu	Leu	Val	Glu	Glu	Ile	Ile	Pro	Glu	Glu	Leu	Val	Glu

7205	7210	7215
Glu Val Ile Pro Glu Glu Val	Val Glu Glu Val Val	Pro Glu Glu
7220	7225	7230
Leu Val Glu Glu Val Ile Pro	Glu Glu Leu Val Glu	Glu Val Ile
7235	7240	7245
Pro Glu Glu Leu Val Glu Glu	Val Ile Pro Glu Val	Val Glu Glu
7250	7255	7260
Val Ile Pro Glu Lys Leu Val	Glu Glu Val Val Pro	Glu Glu Leu
7265	7270	7275
Ile Glu Glu Met Ile Pro Glu	Glu Ile Val Glu Glu	Val Val Pro
7280	7285	7290
Glu Val Val Glu Glu Val Ile	Pro Glu Glu Leu Ile	Glu Glu Val
7295	7300	7305
Ile Pro Glu Glu Leu Val Glu	Glu Val Ile Pro Glu	Lys Leu Ile
7310	7315	7320
Glu Glu Met Ile Pro Glu Glu	Leu Val Glu Glu Val	Ile Leu Glu
7325	7330	7335
Glu Val Val Glu Glu Val Ile	Pro Glu Glu Val Val	Glu Glu Val
7340	7345	7350
Leu Pro Glu Glu Leu Val Glu	Glu Val Val Pro Glu	Glu Leu Val
7355	7360	7365
Glu Glu Val Ala Pro Val Glu	Leu Leu Glu Glu Val	Ile Pro Glu
7370	7375	7380
Glu Leu Leu Glu Glu Val Ile	Pro Glu Glu Leu Val	Glu Glu Val
7385	7390	7395
Ile Pro Glu Glu Leu Val Glu	Asp Val Ile Pro Glu	Glu Leu Val
7400	7405	7410

Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Ile	Ile	Pro	Glu
7415						7420					7425			
Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Val	Glu	Glu	Glu
7430						7435					7440			
Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val
7445						7450					7455			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Leu	Ile	Pro	Glu
7460						7465					7470			
Val	Leu	Glu	Glu	Val	Ile	Pro	Glu	Lys	Leu	Val	Glu	Glu	Val	Val
7475						7480					7485			
Pro	Val	Glu	Leu	Leu	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Ile	Glu
7490						7495					7500			
Glu	Val	Val	Pro	Glu	Val	Leu	Val	Glu	Val	Ile	Pro	Glu	Lys	Val
7505						7510					7515			
Val	Glu	Glu	Val	Ile	His	Glu	Glu	Ile	Val	Lys	Glu	Val	Val	Pro
7520						7525					7530			
Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Ile	Val	Glu	Glu
7535						7540					7545			
Val	Val	Pro	Glu	Glu	Val	Leu	Glu	Glu	Val	Ile	Pro	Lys	Val	Leu
7550						7555					7560			
Leu	Glu	Glu	Glu	Ile	Pro	Glu	Lys	Leu	Val	Glu	Glu	Val	Ile	Pro
7565						7570					7575			
Glu	Glu	Leu	Ile	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu
7580						7585					7590			
Val	Met	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu
7595						7600					7605			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro
7610						7615					7620			

Glu Glu Leu Val Glu Glu Val Val Pro Val Glu Leu Leu Glu Glu
7625 7630 7635

Ile Val Pro Val Glu Leu Leu Glu Glu Val Ile Pro Glu Glu Leu
7640 7645 7650

Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Val Pro
7655 7660 7665

Glu Glu Leu Val Ala Glu Val Ile Pro Glu Lys Leu Val Glu Glu
7670 7675 7680

Val Ile Pro Glu Lys Leu Val Glu Glu Val Ile Pro Glu Glu Leu
7685 7690 7695

Val Glu Glu Val Val Pro Glu Glu Leu Val Ala Glu Val Ile Pro
7700 7705 7710

Glu Lys Leu Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu
7715 7720 7725

Ile Ile Pro Glu Glu Leu Val Glu Glu Val Val Pro Glu Glu Leu
7730 7735 7740

Val Glu Glu Val Val Pro Glu Glu Leu Val Glu Glu Val Ile Pro
7745 7750 7755

Glu Glu Leu Val Glu Glu Val Ile Pro Glu Val Leu Val Glu Glu
7760 7765 7770

Glu Val Pro Glu Glu Leu Val Glu Glu Val Ile Pro Glu Glu Leu
7775 7780 7785

Val Glu Glu Met Leu Pro Glu Glu Leu Ile Glu Val Val Val Pro
7790 7795 7800

Glu Glu Leu Val Glu Glu Val Val Pro Glu Glu Leu Val Glu Glu
7805 7810 7815

Val Val Pro Glu Glu Val Val Glu Glu Val Ile Pro Glu Glu Leu
7820 7825 7830

Ile	Glu	Glu	Leu	Val	Pro	Glu	Val	Glu	Ile	Glu	Glu	Ile	Leu	Pro
7835						7840					7845			
Glu	Glu	Leu	Ile	Glu	Glu	Leu	Val	Pro	Glu	Glu	Ile	Ile	Glu	Glu
7850						7855					7860			
Val	Ile	Pro	Lys	Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Val	Val
7865						7870					7875			
Val	Glu	Glu	Val	Val	Pro	Glu	Val	Leu	Val	Glu	Glu	Val	Val	Pro
7880						7885					7890			
Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Val	Glu	Glu
7895						7900					7905			
Glu	Val	Pro	Glu	Glu	Leu	Val	Glu	Asp	Val	Ile	Pro	Glu	Glu	Leu
7910						7915					7920			
Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro
7925						7930					7935			
Glu	Glu	Val	Val	Glu	Glu	Val	Leu	Pro	Glu	Glu	Leu	Val	Glu	Glu
7940						7945					7950			
Val	Val	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu
7955						7960					7965			
Val	Glu	Glu	Glu	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro
7970						7975					7980			
Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Pro	Glu	Lys
7985						7990					7995			
Val	Ile	Pro	Glu	Lys	Leu	Val	Glu	Glu	Leu	Ile	Pro	Glu	Glu	Val
8000						8005					8010			
Val	Glu	Glu	Leu	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Met	Val	Pro
8015						8020					8025			
Ile	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Thr	Glu	Val	Leu	Glu	Glu

8030	8035	8040
Val Ile Pro Glu Ile Val 8045	Val Glu Glu Val Val 8050	Pro Glu Glu Leu 8055
Val Glu Glu Val Ile Pro 8060	Glu Glu Leu Val Glu 8065	Glu Glu Val Ile Pro 8070
Glu Ile Val Val Glu Glu 8075	Val Val Pro Glu Glu 8080	Leu Val Glu Glu 8085
Val Ile Pro Glu Glu Leu 8090	Val Glu Glu Val Val 8095	Pro Glu Glu Leu 8100
Val Glu Glu Val Val Pro 8105	Glu Glu Ile Val Glu 8110	Glu Glu Leu Leu Pro 8115
Lys Glu Ile Val Glu Glu 8120	Val Ile Tyr Glu Glu 8125	Gln Val Glu Glu 8130
Val Ile His Glu Glu Leu 8135	Val Ala Glu Val Ile 8140	Pro Glu Glu Val 8145
Val Glu Glu Val Val Pro 8150	Glu Val Val Glu Glu 8155	Val Val Pro Glu 8160
Ile Val Ala Glu Val Ile 8165	Pro Glu Glu Val Val 8170	Glu Glu Val Val 8175
Pro Glu Val Val Glu Glu 8180	Val Val Pro Glu Val 8185	Val Glu Glu Val 8190
Ile Pro Glu Glu Val Val 8195	Glu Glu Val Ile Pro 8200	Glu Glu Phe Ile 8205
Glu Glu Met Ile Pro Glu 8210	Glu Ile Val Glu Glu 8215	Val Val Pro Glu 8220
Val Val Glu Glu Val Ile 8225	Pro Glu Glu Leu Val 8230	Ala Glu Val Ile 8235

Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Phe	Glu
8240						8245					8250			
Glu	Glu	Ile	Pro	Glu	Val	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val
8255						8260					8265			
Val	Glu	Glu	Glu	Ile	Pro	Glu	Val	Val	Val	Glu	Glu	Val	Val	Pro
8270						8275					8280			
Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Leu
8285						8290					8295			
Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Met	Val	Pro	Ile	Glu	Ile	Val
8300						8305					8310			
Glu	Glu	Val	Val	Pro	Thr	Glu	Val	Leu	Glu	Glu	Val	Ile	Pro	Glu
8315						8320					8325			
Ile	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
8330						8335					8340			
Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val
8345						8350					8355			
Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val
8360						8365					8370			
Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro
8375						8380					8385			
Glu	Val	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu
8390						8395					8400			
Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Ile	Ile	Pro	Glu	Glu	Ile
8405						8410					8415			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Val	Val	Pro
8420						8425					8430			
Glu	Val	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu
8435						8440					8445			

Val Ile Pro Glu Glu Leu Phe Glu Glu Val Val Pro Glu Glu Leu
8450 8455 8460

Val Ala Glu Val Ile Pro Glu Glu Ile Val Glu Glu Val Ile Pro
8465 8470 8475

Glu Glu Leu Ile Glu Glu Phe Val Pro Glu Glu Leu Val Glu Glu
8480 8485 8490

Glu Val Pro Glu Glu Leu Val Glu Glu Val Ile Pro Glu Val Leu
8495 8500 8505

Val Glu Glu Val Ile Pro Glu Glu Phe Val Glu Glu Val Ile Pro
8510 8515 8520

Glu Glu Ile Val Glu Glu Val Ile Pro Glu Glu Ile Val Glu Glu
8525 8530 8535

Val Ile Pro Glu Glu Val Val Glu Glu Val Val Pro Glu Ile Val
8540 8545 8550

Ala Glu Val Ile Pro Glu Glu Val Val Glu Glu Val Val Pro Glu
8555 8560 8565

Val Val Glu Glu Val Val Pro Glu Val Ile Glu Glu Val Val Pro
8570 8575 8580

Glu Val Ile Glu Glu Val Val Pro Glu Val Val Glu Glu Val Val
8585 8590 8595

Pro Glu Val Val Glu Glu Val Val Pro Glu Val Val Glu Glu Val
8600 8605 8610

Val Pro Val Glu Val Leu Glu Glu Val Ile Pro Glu Glu Val Val
8615 8620 8625

Glu Glu Val Ile Pro Glu Glu Phe Ile Glu Glu Met Ile Pro Glu
8630 8635 8640

Glu Ile Val Glu Glu Val Val Pro Glu Val Val Glu Asp Val Ile
8645 8650 8655

Pro	Glu	Glu	Leu	Ile	Ala	Glu	Val	Val	Ser	Glu	Glu	Leu	Phe	Glu
8660						8665					8670			
Glu	Glu	Ile	Pro	Glu	Glu	Leu	Val	Glu	Val	Val	Pro	Val	Glu	Leu
8675						8680					8685			
Leu	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro
8690						8695					8700			
Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu
8705						8710					8715			
Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu
8720						8725					8730			
Phe	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro
8735						8740					8745			
Glu	Glu	Ile	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Ile	Glu	Glu
8750						8755					8760			
Phe	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu	Glu	Val	Pro	Glu	Glu	Leu
8765						8770					8775			
Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Val	Glu	Glu	Val	Ile	Pro
8780						8785					8790			
Glu	Glu	Phe	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu
8795						8800					8805			
Val	Ile	Pro	Glu	Glu	Leu	Phe	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu
8810						8815					8820			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Ile	Pro
8825						8830					8835			
Glu	Glu	Leu	Ile	Glu	Glu	Val	Val	Pro	Glu	Val	Leu	Val	Glu	Glu
8840						8845					8850			
Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu

8855	8860	8865
Phe Glu Glu Val Val Pro	Glu Glu Leu Val Ala	Glu Val Ile Pro
8870	8875	8880
Glu Glu Ile Val Glu Glu	Val Ile Pro Glu Glu	Leu Ile Glu Glu
8885	8890	8895
Phe Val Pro Glu Glu Leu	Val Glu Glu Glu Val	Pro Glu Glu Leu
8900	8905	8910
Val Glu Glu Val Ile Pro	Glu Val Leu Val Glu	Glu Glu Val Pro
8915	8920	8925
Glu Glu Leu Val Glu Glu	Val Ile Pro Glu Glu	Leu Val Glu Glu
8930	8935	8940
Met Leu Pro Glu Glu Leu	Ile Glu Val Val Val	Pro Glu Glu Leu
8945	8950	8955
Val Glu Glu Val Val Pro	Glu Ile Val Glu Glu	Val Val Pro Glu
8960	8965	8970
Glu Leu Val Glu Glu Val	Ile Pro Glu Glu Val	Val Glu Glu Val
8975	8980	8985
Leu Pro Glu Lys Leu Val	Glu Glu Val Val Pro	Glu Ile Val Glu
8990	8995	9000
Glu Val Ala Pro Glu Val	Val Glu Glu Val Ile	Pro Glu Glu Leu
9005	9010	9015
Val Glu Glu Ile Ile Pro	Glu Ile Leu Val Glu	Glu Val Val Pro
9020	9025	9030
Ile Glu Val Val Glu Glu	Ala Val Pro Glu Val	Val Val Glu Glu
9035	9040	9045
Val Val Pro Glu Lys Ile	Val Glu Glu Val Val	Pro Glu Lys Val
9050	9055	9060

Leu	Glu	Glu	Val	Ile	Pro	Glu	Leu	Leu	Val	Glu	Glu	Ile	Val	Pro
9065						9070					9075			
Ile	Glu	Val	Val	Gly	Glu	Ile	Val	Pro	Glu	Glu	Val	Val	Glu	Lys
9080						9085					9090			
Ile	Val	Pro	Met	Glu	Val	Val	Glu	Glu	Leu	Leu	Pro	Glu	Val	Val
9095						9100					9105			
Glu	Glu	Val	Pro	His	Glu	Ile	Val	Glu	Glu	Glu	Val	Val	Lys	Glu
9110						9115					9120			
Val	Ile	Pro	Glu	Asp	Glu	Lys	Lys	Val	Glu	Ile	Val	Glu	Ile	Ile
9125						9130					9135			
Ile	Glu	Glu	Lys	Val	Glu	Lys	Ile	Pro	Lys	Lys	Lys	Val	Ile	Glu
9140						9145					9150			
Lys	Lys	Lys	Glu	Lys	Glu	Lys	Ile	Arg	Lys	Pro	Lys	Lys	Lys	Val
9155						9160					9165			
Glu	Lys	Glu	Ile	Lys	Pro	Lys	Glu	Val	Lys	Gly	Val	Lys	Gly	Lys
9170						9175					9180			
Leu	Lys	Lys	Asp	Val	Lys	Ala	Lys	His	Leu	Lys	Gly	Ser	Lys	Val
9185						9190					9195			
Lys	Ile	Thr	Glu	Asp	Ile	Gln	Lys	Lys	Met	Glu	Asp	Asp	Ile	Lys
9200						9205					9210			
Glu	Lys	Ile	Met	Glu	Lys	Glu	Leu	Lys	Glu	Glu	Ile	Lys	Asp	Lys
9215						9220					9225			
Glu	Tyr	Leu	Arg	Lys	Val	Ile	Pro	Lys	Glu	Glu	Lys	Lys	Glu	Pro
9230						9235					9240			
Ile	Pro	Lys	Lys	Gly	Lys	Ser	Val	Glu	Pro	Lys	Lys	Glu	Lys	Gln
9245						9250					9255			
Ala	Gly	Val	Lys	Lys	Glu	Lys	Val	Pro	Glu	Thr	Lys	Lys	Glu	Lys
9260						9265					9270			

Ala	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Val	Gln	Ala	Pro	Lys	Lys	Glu
9275						9280					9285			
Lys	Val	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Pro	Ala	Val	Pro	Lys	Lys
9290						9295					9300			
Glu	Lys	Val	Pro	Glu	Pro	Lys	Lys	Glu	Lys	Val	Pro	Glu	Pro	Lys
9305						9310					9315			
Lys	Glu	Lys	Ala	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Val	Gln	Ala	Pro
9320						9325					9330			
Lys	Lys	Glu	Lys	Ala	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Ala	Pro	Ala
9335						9340					9345			
Pro	Lys	Lys	Glu	Lys	Ala	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Ala	Pro
9350						9355					9360			
Ala	Pro	Lys	Lys	Glu	Lys	Pro	Ala	Val	Pro	Lys	Lys	Glu	Lys	Pro
9365						9370					9375			
Ala	Val	Pro	Lys	Lys	Glu	Lys	Val	Pro	Glu	Thr	Lys	Lys	Glu	Lys
9380						9385					9390			
Val	Pro	Glu	Thr	Lys	Lys	Glu	Lys	Val	Pro	Glu	Thr	Lys	Lys	Glu
9395						9400					9405			
Lys	Val	Pro	Val	Pro	Lys	Lys	Glu	Lys	Val	Pro	Ala	Pro	Lys	Lys
9410						9415					9420			
Glu	Lys	Val	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Val	Pro	Ala	Pro	Lys
9425						9430					9435			
Lys	Glu	Lys	Pro	Ala	Val	Pro	Lys	Lys	Glu	Lys	Val	Pro	Glu	Thr
9440						9445					9450			
Lys	Lys	Glu	Lys	Ala	Pro	Glu	Pro	Lys	Lys	Glu	Lys	Ala	Pro	Glu
9455						9460					9465			
Pro	Lys	Lys	Glu	Lys	Ala	Pro	Glu	Pro	Lys	Lys	Glu	Lys	Ala	Pro
9470						9475					9480			

Glu Pro Lys Lys Glu Lys Ala Pro Ala Pro Lys Lys Glu Lys Val
9485 9490 9495

Pro Val Pro Lys Lys Glu Lys Val Pro Ala Pro Lys Lys Glu Lys
9500 9505 9510

Val Pro Ala Pro Lys Lys Glu Lys Pro Ala Val Pro Lys Lys Glu
9515 9520 9525

Lys Val Pro Glu Thr Lys Lys Glu Lys Glu Lys Asp Ser Gln Pro
9530 9535 9540

Lys Lys Glu Lys Ala Lys Glu Thr Ser Arg Pro Pro Lys Lys Glu
9545 9550 9555

Lys Glu Lys Gly Lys
9560

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<211> 133
<212> PRT
<213> 惡性瘡原蟲

<400> 57

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Gln Val Val Pro Glu Glu Leu Ile Glu Glu Val Val Pro Glu Glu Ile
20 25 30

Ile Glu Glu Val Ile Pro Glu Glu Ile Val Glu Glu Val Ile Tyr Glu
35 40 45

Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile Ala Glu Lys Leu
50 55 60

Val Lys Glu Ile Val Pro Glu Gln Val Arg Glu Glu Val Thr Leu Glu
65 70 75 80

Glu Ile Val Glu Glu Met Ile Pro Glu Glu Phe Val Glu Glu Val Ala
85 90 95

Pro Glu Val Glu Ile Glu Glu Ile Ile Pro Glu Glu Leu Ile Glu Glu
100 105 110

Val Ile Pro Glu Val Leu Val Glu Glu Ala Val Pro Glu Glu Leu Ile
115 120 125

Glu Lys Val Ile Pro
130

<210> 58
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<212> PRT
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<400> 58

Met Ser Asn Ile Asn Asn Lys Asp Ser Ser Thr Glu Trp Asn Cys Lys
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Glu Asp Val Gly Cys Val Pro Pro Arg Arg Gln Asn Leu Asn Met Glu
20 25 30

Arg Leu Asp Asn Glu Asn Glu Asp Ser Val Pro Asp Phe Met Lys Lys
35 40 45

Thr Phe Tyr Leu Ala Ala Ala Gly Glu Gly Lys Lys Leu Arg Glu Lys
50 55 60

His Asp Glu Ser Cys Asp Glu Phe Cys Asp Ala Trp Asn Arg Ser Leu
65 70 75 80

Ala Asp Tyr Lys Asp Ile Phe Gln Gly Lys Asp Met Trp Asn Asp Gly
85 90 95

Lys Tyr Gly Glu Ala Lys Asn His Ile Lys Asn Ala Phe Gly Asp Met
100 105 110

Asn Asn Arg Lys Thr Met Leu Asn Glu Ile Glu Lys Gly Ile Lys Asp
115 120 125

Glu Thr Phe Ser Arg Glu Asn Gly Leu Asp Val Cys Lys Ser Gln Cys
130 135 140

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

355	360	365
Lys Ile Pro Glu Pro Ile Ile Arg Glu Ala Pro Lys Tyr Val Pro Lys		
370	375	380
Lys Pro Val Pro Pro Gln His Ile Pro Arg Gly Asp Asn Val Pro Arg		
385	390	400
Asn Ile Asp Val Asn Gly Ser Lys Asp Glu Tyr Ser Pro Glu Thr Glu		
	405	410
Ser Ala Asn Ser Lys Ile Lys Pro Thr Tyr Glu Glu Asn Asp Glu Asp		
	420	425
Lys Ser Lys Ile Ser Ile Glu Thr Ser Glu Ile Asp Arg Asp Lys Glu		
	435	440
Pro Phe Arg Ile Ser Glu Glu Lys Lys Val Val Lys Glu Asp Val Gln		
	450	455
Glu Leu Glu Asn Ile Glu Tyr Glu Phe Asp Glu Thr Phe Asp Phe Phe		
465	470	475
Asp Glu Asp Ala Lys Arg Asn Ile Asp Asp Ile Arg Lys Asp Ile Gln		
	485	490
Ser Gln Ile Met Lys Ser Val Glu Asn Tyr Asn Ser Glu Lys Glu Glu		
	500	505
Phe Lys Arg Asn Ile Glu Thr Gln Leu Ile Glu Ser Gly Asp Gly Met		
	515	520
Asn Ala Gly Asn Tyr Ser Ser Ala Leu Gln Asp Asn Ser Thr Glu Ile		
	530	535
Pro Thr Met Val Leu Val Pro Gly Val Leu Thr Val Phe Leu Leu Thr		
545	550	555
Ile Ile Trp Val Leu Val Tyr Lys His Ser Leu Ile Asp Arg Val His		
	565	570
		575

Gly Thr Gly Lys Thr Lys Lys Glu Glu Lys Met Lys Glu Leu Glu Ser
580 585 590

Glu Glu Phe Pro Lys Glu Lys Tyr Asn Ile Glu Asp Met Glu Glu Thr
595 600 605

Glu Lys Glu Asn Glu Ile Glu Lys Ile Met Asp Glu Asn Lys Glu Thr
610 615 620

Glu Gln Thr Glu Glu Gly Asn Thr Glu Glu Phe Val Gln Glu Lys Glu
625 630 635 640

Leu Asn Gln Glu Thr Leu Glu Asn Glu Ile Ile Val Asp His Ile Lys
645 650 655

Glu Glu Glu Asp Thr Arg Asn Val Lys Glu Gln Glu Ser Val Leu Glu
660 665 670

Glu Ser Pro Ile Glu Glu Leu Pro Val Glu Asn Asn Ile Gly Lys Ile
675 680 685

Asn Glu Glu Val Glu Glu Phe Ile Leu Asn Glu Ile Pro Leu Glu Glu
690 695 700

Gln Val Pro Lys Glu Leu Pro Gln Glu Glu Ile Glu Glu Ile Val Val
705 710 715 720

Glu Glu Leu Pro Ile Asp Glu His Leu Ser Ser Glu Glu Thr Thr Val
725 730 735

Thr Glu Glu Asp Thr Phe Lys Gly Gln Leu Ile Asn Glu Glu Lys Pro
740 745 750

Val Glu Glu Lys Ser Val Ser Glu Glu Ile Pro Val Glu Glu Lys Ser
755 760 765

Val Ser Glu Glu Ile Pro Val Glu Glu Lys Ser Val Ser Glu Glu Ile
770 775 780

Pro Val Glu Glu Lys Ser Val Ser Glu Glu Ile Pro Val Glu Glu Lys
785 790 795 800

Asn Val Ser Glu Glu Ile Pro Val Glu Glu Lys Asn Val Ser Glu Glu
805 810 815

Ile Pro Val Glu Glu Lys Asn Val Ser Glu Glu Ile Pro Val Glu Glu
820 825 830

Glu Asn Val Ser Glu Glu Ile Pro Glu Gly Gly Ile Ala Ile Glu Asp
835 840 845

Val Pro Val Asp Glu Glu Thr Val Thr Glu Glu Ile Thr Val Asp Glu
850 855 860

Lys Ile Tyr Asp Lys Leu Pro Asn Glu Ile Glu Thr Val Asn Glu Glu
865 870 875 880

Met Pro Val Glu Asp Glu Thr Leu Thr Glu Gln Ile Ser Ser Glu His
885 890 895

Glu Arg Val Pro Glu Glu Ile Ile Glu Glu Lys Pro Phe Thr Glu Gly
900 905 910

Glu Glu Thr Glu Ser Leu Thr Asp Glu Ile Val Glu Glu Gly Val Val
915 920 925

Thr Asp Asp Ile Pro Glu Glu Gln Ile Ile Thr Glu Lys Val Gln Glu
930 935 940

Glu Glu Glu Phe Val Thr Gly Glu Leu Ser Glu Glu Asp Ile Ile Asn
945 950 955 960

Glu Lys Val Gln Glu Glu Asp Glu Ser Val Thr Glu Glu Leu Pro Glu
965 970 975

Glu Asp Ile Ile Asn Glu Lys Val Gln Glu Glu Glu Glu Ser Ala Tyr
980 985 990

Gln Glu Ile Val Gln Asp Gly Ser Val Thr Lys Asp Val Glu Tyr Lys
995 1000 1005

Glu Leu Val Asn Asp Asp Val Arg Asp Lys Glu Asn Phe Val Ile
1010 1015 1020

Glu	Glu	Asp	Pro	Phe	Lys	Gly	Gln	Leu	Ile	Asn	Glu	Gly	Leu	Pro
	1025					1030					1035			
Val	Glu	Glu	Glu	Phe	Val	Thr	Lys	Glu	Leu	Pro	Val	Lys	Glu	Glu
	1040					1045					1050			
Ser	Val	Phe	Glu	Glu	Leu	Thr	Glu	Glu	Asp	Gln	Ser	Val	Thr	Lys
	1055					1060					1065			
Glu	Ile	Pro	Val	Glu	Glu	His	Ser	Val	Phe	Lys	Glu	Val	Asp	Glu
	1070					1075					1080			
Ile	Glu	Ser	Val	Thr	Asp	Glu	Ile	Val	Glu	Glu	Glu	Gly	Ser	Val
	1085					1090					1095			
Asn	Glu	Glu	Val	Glu	Glu	Glu	Val	Ser	Val	Ser	Gly	Glu	Val	Asp
	1100					1105					1110			
Glu	Thr	Glu	Tyr	Val	Thr	Glu	Glu	Val	Glu	Glu	Thr	Glu	Leu	Val
	1115					1120					1125			
Asn	Glu	Glu	Val	Leu	Lys	Glu	Glu	Gly	Ser	Ala	Ser	Glu	Lys	Val
	1130					1135					1140			
Val	Lys	Glu	Glu	Gly	Ser	Ala	Ser	Glu	Lys	Ile	Val	Glu	Glu	Glu
	1145					1150					1155			
Gly	Ser	Val	Thr	Glu	Glu	Thr	Ala	Ser	Glu	Glu	Ile	Val	Glu	Glu
	1160					1165					1170			
Glu	Gly	Ser	Val	Thr	Glu	Glu	Ser	Ser	Ser	Glu	Glu	Ile	Val	Glu
	1175					1180					1185			
Asp	Glu	Gly	Ser	Val	Thr	Glu	Glu	Ser	Ser	Ser	Glu	Glu	Ile	Val
	1190					1195					1200			
Glu	Glu	Glu	Gly	Ser	Val	Ile	Glu	Glu	Ser	Ala	Ser	Glu	Val	Ile
	1205					1210					1215			
Val	Glu	Asp	Glu	Val	Ser	Ala	Ser	Lys	Glu	Ile	Val	Glu	Asp	Glu

1220	1225	1230
Ala Ser Val Thr Glu Glu	Val Val Glu Glu Glu	Gly Ala Val Ser
1235	1240	1245
Asp Glu Val Gln Val Thr	Glu Ser Val Glu Asp	Glu Ile Ile Asn
1250	1255	1260
Gln Gly Ile Val Asp Glu	Val Ile Val Glu Gln	Glu Ala Ser Val
1265	1270	1275
Thr Asp Glu Ile Val Lys	Glu Asp Glu Ser Val	Ile Glu Glu Ile
1280	1285	1290
Ala Val Glu Glu Thr Val	Thr Glu Val Val Glu	Glu Thr Lys Pro
1295	1300	1305
Met Asp Glu Glu Ile Val	Asp Gln Gly Ser Val	Val Glu Asn Val
1310	1315	1320
Glu Glu Lys Lys Thr Met	Asp Glu Glu Ile Val	Asp Gln Gly Ser
1325	1330	1335
Val Val Glu Asn Val Glu	Glu Lys Lys Thr Met	Asp Glu Glu Ile
1340	1345	1350
Gly Asp Gln Gly Ser Val	Ala Glu Lys Val Glu	Glu Glu Leu
1355	1360	1365
Val Thr Glu Glu Val Ile	Glu Arg Glu Gly Ser	Ile Asn Glu Asp
1370	1375	1380
Ile Val Lys Glu Ala Ser	Ile Thr Glu Glu Val	Glu Gln Ile Glu
1385	1390	1395
Pro Val Thr Gly Lys Val	Glu Lys Ile Glu Ser	Ile Thr Asp Glu
1400	1405	1410
Ile Lys Glu Gln Leu Val	Pro Glu Asp Ile Lys	Glu Glu Gln Leu
1415	1420	1425

Asp	Phe	Glu	Glu	Ile	Val	Ala	Gln	Arg	Ala	Ser	Val	Asn	Asp	Glu
1430						1435					1440			
Lys	Val	Glu	Val	Ala	Ser	Ile	Thr	Glu	Glu	Val	Glu	Glu	Glu	Glu
1445						1450					1455			
Lys	Ser	Val	Ser	Glu	Glu	Val	Leu	Glu	Glu	Glu	Gly	Ser	Thr	Thr
1460						1465					1470			
Glu	Lys	Val	Val	Lys	Gly	Ser	Ser	Thr	Glu	Val	Val	Val	Glu	Glu
1475						1480					1485			
Gln	Gly	Ser	Val	Thr	Glu	Asn	Leu	Leu	Glu	Glu	Glu	Ser	Ala	Ser
1490						1495					1500			
Gln	Gly	Ile	Val	Glu	Lys	Glu	Glu	Phe	Val	Asp	Glu	Glu	Asp	Ser
1505						1510					1515			
Val	Lys	Asp	Gln	Asn	Val	Phe	Glu	Lys	Glu	Gly	Ser	Val	Thr	Glu
1520						1525					1530			
Gln	Leu	Val	Glu	Glu	Glu	Lys	Gly	Leu	Ile	Asn	Glu	Asp	Asn	Glu
1535						1540					1545			
Lys	Glu	Glu	Leu	Ile	Thr	Glu	Met	Ser	Glu	Glu	Ile	Lys	Ser	Val
1550						1555					1560			
Asn	Glu	Glu	Ile	Glu	Glu	Thr	Asp	Leu	Ser	Thr	Glu	Glu	Ile	Ile
1565						1570					1575			
Lys	Gln	Gln	Gly	Leu	Ala	Thr	Tyr	Glu	Phe	Val	Glu	Glu	Glu	Lys
1580						1585					1590			
Ser	Leu	Thr	Asp	Lys	Leu	Leu	Glu	Glu	Glu	Ser	Val	Thr	Lys	Glu
1595						1600					1605			
Val	Gly	Glu	Thr	Glu	Leu	Ser	Thr	Gln	Glu	Val	Val	Asp	Glu	Lys
1610						1615					1620			
Val	Ser	Val	Thr	Glu	Glu	Val	Ile	Glu	Glu	Glu	Lys	Ser	Val	Ser
1625						1630					1635			

Glu	Glu	Val	Leu	Glu	Glu	Gly	Ser	Ala	Thr	Glu	Glu	Val	Val	Glu
1640						1645					1650			
Glu	Gly	Ser	Cys	Thr	Glu	Val	Val	Val	Glu	Glu	Gly	Ser	Cys	Thr
1655						1660					1665			
Glu	Val	Val	Val	Glu	Glu	Gly	Ser	Cys	Thr	Glu	Ile	Val	Val	Glu
1670						1675					1680			
Lys	Gly	Ser	Asp	Thr	Glu	Ile	Val	Val	Glu	Glu	Gly	Ser	Ala	Thr
1685						1690					1695			
Glu	Ile	Val	Val	Glu	Glu	Gly	Ser	Ala	Thr	Glu	Val	Val	Val	Glu
1700						1705					1710			
Glu	Gly	Ser	Ala	Thr	Glu	Glu	Val	Val	Glu	Glu	Gly	Ser	Val	Ser
1715						1720					1725			
Glu	Glu	Met	Leu	Glu	Glu	Glu	Gly	Ser	Ala	Thr	Glu	Glu	Val	Val
1730						1735					1740			
Glu	Glu	Gly	Leu	Ser	Ser	Asp	Asn	Val	Gln	Lys	Ser	Lys	Gly	Val
1745						1750					1755			
Ile	Glu	Asn	Val	Gly	Glu	Ile	Tyr	Ser	Val	Lys	Thr	Ala	Lys	Asp
1760						1765					1770			
Glu	Ser	Met	Asn	Glu	Lys	Ile	Pro	Leu	Glu	Lys	Ser	Ser	Phe	Val
1775						1780					1785			
Asp	Asp	Glu	Ser	Phe	Lys	Gly	Gln	Gly	Pro	Thr	Asp	Asn	Val	Ser
1790						1795					1800			
Val	Glu	Asp	Val	Asn	Ser	Glu	Asp	Ile	Ile	Asn	Glu	His	Thr	Pro
1805						1810					1815			
Leu	Glu	Glu	Thr	Lys	Ile	Glu	Glu	Leu	Pro	Thr	Glu	Tyr	Ile	Thr
1820						1825					1830			
Thr	Ala	Asp	Ile	His	Thr	Lys	Gly	Glu	Thr	Glu	Thr	Lys	Tyr	Asn
1835						1840					1845			

Leu 1850	Ile	Tyr	Glu	Lys	Ile	Asn 1855	Glu	Glu	Val	Glu	Lys 1860	Ala	Lys	Phe
Gln 1865	Glu	Glu	Lys	Ile	Thr	Glu 1870	Asn	Ile	Pro	Val	Glu 1875	Arg	Glu	Ser
Val 1880	Thr	Glu	Asp	Ile	Val	Gln 1885	Glu	Pro	Ser	Leu	Ala 1890	Gln	Glu	Val
Glu 1895	Gln	Lys	Glu	Ser	Asp	Thr 1900	Asn	Glu	Ile	Glu	Glu 1905	Thr	Lys	Leu
Ala 1910	Asn	Glu	Lys	Ile	Ile	Pro 1915	Glu	Val	Ser	Val	Thr 1920	Glu	Asn	Val
Val 1925	Glu	Lys	Glu	Gly	Leu	Asp 1930	Thr	Glu	Glu	Val	Leu 1935	Glu	Glu	Asp
Glu 1940	Ser	Ile	Thr	Glu	Glu	Ile 1945	Val	Glu	Glu	Glu	Val 1950	Ser	Ser	Ser
Glu 1955	Glu	Ile	Val	Glu	Glu	Glu 1960	Glu	Ser	Ser	Ser	Glu 1965	Glu	Ile	Val
Glu 1970	Glu	Glu	Glu	Ser	Ser	Ser 1975	Glu	Glu	Ile	Val	Glu 1980	Glu	Glu	Glu
Ser 1985	Ser	Ser	Glu	Glu	Ile	Val 1990	Glu	Glu	Glu	Glu	Ser 1995	Ser	Ser	Glu
Glu 2000	Ile	Val	Glu	Glu	Glu	Glu 2005	Ser	Ser	Ser	Glu	Glu 2010	Ile	Ile	Glu
Glu 2015	Val	Ser	Ser	Thr	Glu	Glu 2020	Val	Leu	Glu	Glu	Glu 2025	Gly	Ser	Val
Thr 2030	Glu	Glu	Ile	Val	Glu	Glu 2035	Glu	Val	Ser	Thr	Thr 2040	Glu	Glu	Val
Lys	Asp	Ile	Gly	Ser	Val	Ser	Glu	Glu	Val	Leu	Glu	Glu	Glu	Gly

2045	2050	2055
Phe Gly Thr Glu Glu Phe Val Gly Gln Gln Gly Ser Val Ile Glu 2060 2065 2070		
Glu Ile Val Glu Thr Glu Ser Ser Thr Glu Lys Val Leu Glu Asp 2075 2080 2085		
Val Gly Ser Asn Val Glu Glu Ile Val Gln Glu Glu Gly Pro Val 2090 2095 2100		
Ala Gln Glu Ile Val His Glu Glu Val Ser Thr Thr Glu Lys His 2105 2110 2115		
Asp Glu Val Asp Arg Ser Thr Thr Glu Glu Ile Val Glu Lys Val 2120 2125 2130		
Gly Ser Val Ser Glu Glu Ile Ile Val Glu Glu Val Ser Ala Ser 2135 2140 2145		
Glu Glu Ile Val Glu Glu Gly Ser Val Thr Glu Glu Val Val Glu 2150 2155 2160		
Glu Glu Lys Leu Ile Asn Glu Val Gly Glu Thr Glu Ser Val Thr 2165 2170 2175		
Glu Glu Ile Val Gln Lys Glu Val Ser Asp Ala Glu Glu Val Leu 2180 2185 2190		
Gly Gln Glu Gly Ser Met Asn Glu Glu Ile Leu Glu Lys Glu Ser 2195 2200 2205		
Ile Val Glu Glu Ile Val Gly Pro Glu Gly Ser Val Thr Glu Glu 2210 2215 2220		
Ile Val Asp His Gly Ser Phe Ala Glu Glu Val Lys Glu Glu Glu 2225 2230 2235		
Leu Val Thr Glu Glu Ala Val Gln Tyr Glu Gly Ser Val Thr Glu 2240 2245 2250		

Glu	Ile	Lys	Glu	Glu	Glu	Ser	Ile	Thr	Glu	Asn	Glu	Ala	Ile	Glu
2255						2260					2265			
Glu	Ser	Ala	Phe	Ala	Glu	Ile	Ile	Glu	Glu	Lys	Gly	Pro	Asn	Thr
2270						2275					2280			
Asp	Glu	Ile	Val	Lys	Glu	Glu	Gly	Leu	Asp	Thr	Glu	Glu	Ile	Val
2285						2290					2295			
Asn	Glu	Val	Ser	Val	Thr	Asp	Glu	Val	Ile	Glu	Glu	Glu	Lys	Leu
2300						2305					2310			
Val	Asn	Glu	Gln	Ile	Val	Gly	Glu	Glu	Arg	Ser	Val	Thr	Glu	Lys
2315						2320					2325			
Pro	Val	Glu	Val	Glu	Arg	Ser	Ala	Thr	Glu	Asp	Leu	Val	Glu	Glu
2330						2335					2340			
Glu	Ala	Ser	Val	Thr	Glu	Lys	Val	Ser	Val	His	Glu	Gly	Ser	Thr
2345						2350					2355			
Thr	Glu	Gln	Ile	Leu	Asp	Glu	Ser	Val	Ala	Glu	Glu	Ile	Val	Glu
2360						2365					2370			
Glu	Glu	Val	Ser	Val	Asp	Asp	Lys	Ile	Ile	Glu	Glu	Glu	Val	Ser
2375						2380					2385			
Val	Asp	Glu	Val	Val	Glu	Glu	Glu	Gly	Ser	Val	Ile	Glu	Glu	Ile
2390						2395					2400			
Val	Glu	Glu	Glu	Glu	Ser	Val	Pro	Glu	Glu	Ile	Leu	Glu	Glu	Glu
2405						2410					2415			
Leu	Ser	Gly	Ser	Glu	Glu	Val	Leu	Glu	Asp	Glu	Trp	Val	Thr	Asp
2420						2425					2430			
Ala	Phe	Met	Gly	Gln	Glu	Gly	Ser	Val	Ile	Glu	Glu	Ile	Glu	Glu
2435						2440					2445			
Ile	Val	Asp	Gly	Glu	Gly	Ser	Ile	Thr	Glu	Glu	Ile	Val	Glu	Asp
2450						2455					2460			

Gly	Ser	Ala	Asn	Glu	Lys	Ile	Val	Glu	Glu	Glu	Pro	Ser	Arg	Val
	2465					2470					2475			
Glu	Glu	Val	Leu	Gly	Lys	Glu	Gly	Phe	Val	Ile	Glu	Glu	Ile	Ile
	2480					2485					2490			
Glu	Glu	Gly	Ser	Val	Ile	Glu	Gln	Val	Glu	Asp	Thr	Lys	Thr	Val
	2495					2500					2505			
Ser	Glu	Lys	Ser	Glu	Glu	Ser	Ser	Ala	Ile	Glu	Glu	Val	Lys	Glu
	2510					2515					2520			
Val	Lys	Glu	Glu	Glu	Ser	Ile	Ser	Glu	Lys	Ile	Val	Glu	Lys	Glu
	2525					2530					2535			
Glu	Ser	Val	Thr	Glu	Glu	Ile	Val	Arg	Gln	Glu	Glu	Ser	Thr	Thr
	2540					2545					2550			
Glu	Lys	Ile	Val	Lys	Asp	Val	Ser	Pro	Thr	Glu	Asp	Phe	Val	Glu
	2555					2560					2565			
Gln	Thr	Asp	Ser	Val	Thr	Glu	Lys	Val	Ile	Glu	Gln	Glu	Gly	Ser
	2570					2575					2580			
Asn	Thr	Glu	Val	Ala	Glu	Asp	Val	Glu	Glu	Lys	Glu	Ser	Ala	Ser
	2585					2590					2595			
Asp	Glu	His	Glu	Gln	Glu	Asp	Val	Ser	Val	Asn	Ala	Gln	Val	Thr
	2600					2605					2610			
Tyr	Glu	Lys	Lys	Ser	Val	Thr	Lys	Glu	Ile	Val	Asp	Glu	Val	Ser
	2615					2620					2625			
Arg	Thr	Glu	Glu	Ile	Val	Glu	Glu	Asn	Gly	Ser	Val	Thr	Glu	Gly
	2630					2635					2640			
Val	Asp	Glu	Thr	Gly	Ser	Val	Thr	Glu	Glu	Ile	Ile	Glu	Glu	Ala
	2645					2650					2655			
Thr	Val	Thr	Glu	Glu	Val	Val	Glu	Asp	Gly	Ser	Val	Thr	Glu	Glu
	2660					2665					2670			

Val	Val	Glu	Asp	Gly	Ser	Val	Ile	Gln	Glu	Val	Val	Glu	Asp	Gly
	2675					2680					2685			
Ser	Val	Thr	Glu	Glu	Ile	Val	Gln	Glu	Asn	Gly	Ser	Val	Thr	Glu
	2690					2695					2700			
Glu	Ile	Val	Glu	Glu	Glu	Gly	Ser	Val	Asn	Glu	Glu	Val	Glu	Glu
	2705					2710					2715			
Glu	Val	Ser	Val	Ser	Gly	Glu	Val	Asp	Glu	Thr	Glu	Tyr	Val	Thr
	2720					2725					2730			
Glu	Glu	Val	Glu	Glu	Glu	Gly	Ser	Val	Val	Glu	Glu	Ile	Val	Glu
	2735					2740					2745			
Glu	Glu	Gly	Ser	Val	Ser	Gly	Glu	Val	Asp	Glu	Thr	Glu	Tyr	Val
	2750					2755					2760			
Thr	Glu	Glu	Val	Glu	Glu	Glu	Gly	Ser	Val	Val	Glu	Glu	Ile	Val
	2765					2770					2775			
Glu	Glu	Glu	Gly	Ser	Val	Ser	Gly	Glu	Val	Asp	Glu	Thr	Glu	Tyr
	2780					2785					2790			
Val	Thr	Glu	Glu	Val	Glu	Glu	Glu	Gly	Ser	Val	Val	Glu	Glu	Ile
	2795					2800					2805			
Val	Glu	Glu	Glu	Gly	Ser	Val	Ser	Gly	Glu	Val	Asp	Glu	Thr	Glu
	2810					2815					2820			
Tyr	Val	Thr	Glu	Glu	Val	Glu	Glu	Glu	Gly	Ser	Val	Val	Glu	Glu
	2825					2830					2835			
Ile	Val	Glu	Glu	Glu	Gly	Ser	Val	Val	Glu	Glu	Ile	Val	Glu	Glu
	2840					2845					2850			
Glu	Gly	Ser	Val	Ser	Glu	Val	Val	Asp	Glu	Thr	Glu	Leu	Val	Asn
	2855					2860					2865			
Asp	Glu	Ile	Val	Glu	Gln	Ala	Pro	Phe	Thr	Glu	Glu	Val	Glu	Glu

2870	2875	2880
Gln Val Ser Val Asn Asp	Glu Ile Ile Glu Asp	Ala Ser Val Ala
2885	2890	2895
Glu Ala Val Glu Glu Ser	Glu Ser Ile Thr Glu	Ser Val Ser Gln
2900	2905	2910
Glu Glu Glu Thr Glu Lys	Gly Phe Val Ile Glu	Lys Val Glu Glu
2915	2920	2925
Thr Gly Ala Val Thr Glu	Glu Ile Val Gln Asp	Gly Leu Ile Thr
2930	2935	2940
Glu Glu Ile Leu Glu Glu	Ser Glu Ser Val Asn	Gly Glu Ile Ile
2945	2950	2955
Asn Lys Glu Ser Asp Ala	Glu Glu Ile Leu Glu	Thr Glu Phe Leu
2960	2965	2970
Thr Glu Glu Val Val Gly	Gln Ala Gly Ser Thr	Ser Glu Glu Ile
2975	2980	2985
Val Glu Glu Glu Gly Ser	Val Thr Lys Glu Val	Glu Glu Lys Glu
2990	2995	3000
Ser Val Thr Glu Glu Leu	Val Asp Glu Gly Ser	Val Thr Glu Glu
3005	3010	3015
Leu Val Asp Glu Gly Ser	Val Thr Glu Glu Val	Val Glu Gln Gly
3020	3025	3030
Gly Ser Ile Ala Gln Glu	Ile Val Glu Glu Glu	Ser Ala Thr Glu
3035	3040	3045
Glu Ile Ile Arg Asp Glu	Thr Asn Val Glu Glu	Val Leu Glu Lys
3050	3055	3060
Glu Gly Ser Ala Thr Glu	Glu Ile Val Gln Asp	Gly Ser Gly Thr
3065	3070	3075

Asn	Asp	Phe	Val	Gly	Lys	Gln	Gly	Ser	Val	Ile	Glu	Glu	Val	Val
	3080					3085					3090			
Glu	Glu	Glu	Ile	Ser	Thr	Thr	Glu	Glu	Lys	Leu	Lys	Glu	Glu	Ala
	3095					3100					3105			
Ser	Ala	Ile	Glu	Glu	Phe	Val	Glu	Glu	Glu	Ser	Ile	Arg	Glu	Asp
	3110					3115					3120			
Val	Leu	Glu	Glu	Ser	Leu	Val	Thr	Glu	Asn	Val	Val	Gly	Gln	Gln
	3125					3130					3135			
Glu	Ser	Val	Thr	Glu	Glu	Ile	Val	Asp	Gly	Glu	Gly	Ser	Phe	Thr
	3140					3145					3150			
Glu	Asp	Ile	Val	Glu	Glu	Glu	Glu	Ser	Val	Thr	Glu	Glu	Ile	Val
	3155					3160					3165			
Val	Asp	Glu	Glu	Ser	Val	Thr	Lys	Glu	Ile	Val	Glu	Asp	Glu	Glu
	3170					3175					3180			
Leu	Val	Thr	Glu	Glu	Ile	Val	Glu	Asp	Glu	Gly	Ser	Phe	Thr	Glu
	3185					3190					3195			
Glu	Ile	Val	Glu	Asp	Glu	Gly	Ser	Phe	Thr	Glu	Glu	Val	Ile	Glu
	3200					3205					3210			
Glu	Arg	Ser	Leu	Ile	Glu	Glu	Val	Glu	Asp	Thr	Glu	Thr	Val	Ala
	3215					3220					3225			
Glu	Lys	Glu	Glu	Gly	Ser	Val	Ile	Lys	Glu	Ile	Ile	Asp	Glu	Lys
	3230					3235					3240			
Ser	Leu	Thr	Glu	Lys	Ile	Val	Glu	Glu	Glu	Lys	Ser	Val	Thr	Glu
	3245					3250					3255			
Glu	Val	Glu	Glu	Lys	Glu	Ser	Val	Lys	Glu	Glu	Val	Glu	Glu	Gln
	3260					3265					3270			
Arg	Leu	Val	Val	Glu	Glu	Glu	Gly	Ser	Ala	Thr	Glu	Gly	Ile	Val
	3275					3280					3285			

Glu	Asp	Arg	Leu	Ala	Thr	Glu	Gly	Ile	Val	Asp	Asp	Ile	Leu	Val
	3290					3295					3300			
Thr	Glu	Glu	Ile	Val	Glu	Asp	Gly	Leu	Ala	Thr	Asp	Glu	Phe	Val
	3305					3310					3315			
Glu	Gln	Gln	Gly	Ser	Ile	Ile	Glu	Glu	Val	Leu	Asp	Asp	Glu	Gly
	3320					3325					3330			
Ser	Val	Thr	Glu	Glu	Ile	Val	Glu	Glu	Glu	Gly	Ser	Pro	Asn	Glu
	3335					3340					3345			
Glu	Ile	Val	Glu	Gly	Val	Ser	Val	Ile	Glu	Glu	Asp	Asp	Asn	Ile
	3350					3355					3360			
Glu	Pro	Val	Ser	Glu	Glu	Ile	Val	Glu	Gly	Ser	Val	Thr	Glu	Glu
	3365					3370					3375			
Met	Ile	Lys	Glu	Gly	Leu	Glu	Asn	Glu	Val	Ile	Leu	Asp	Glu	Asp
	3380					3385					3390			
Ser	Ile	Thr	Glu	Glu	Ala	Leu	Glu	Lys	Glu	Gly	Ser	Val	Ser	Glu
	3395					3400					3405			
Glu	Ile	Val	Glu	Glu	Met	Gly	Ser	Leu	Thr	Glu	Glu	Ile	Val	Asp
	3410					3415					3420			
Glu	Glu	Arg	Ser	Thr	Ser	Glu	Asp	Met	Ile	Glu	Glu	Gly	Ser	Ala
	3425					3430					3435			
Ser	Glu	Glu	Ile	Ile	Gln	Glu	Glu	Ser	Gln	Val	Glu	Glu	Val	Val
	3440					3445					3450			
Glu	Glu	Val	Ser	Val	Ile	Asp	Glu	Ile	Val	Glu	Glu	Asp	Glu	Leu
	3455					3460					3465			
Asp	Thr	Lys	Glu	Val	Val	Glu	Glu	Ile	Glu	Phe	Asn	Thr	Glu	Glu
	3470					3475					3480			
Val	Val	Glu	His	Lys	Glu	Glu	Glu	Gly	Ser	Val	Ala	Glu	Glu	Ile
	3485					3490					3495			

Val	Gln	Glu	Glu	Lys	Glu	Gly	Ser	Val	Asn	Glu	Glu	Ile	Ile	Glu
3500						3505					3510			
Glu	Val	Gly	Ser	Ile	Thr	Glu	Glu	Met	Val	Glu	Gln	Asp	Val	Ser
3515						3520					3525			
Asp	Asn	Glu	Glu	Ile	Val	Glu	Glu	Arg	Ser	Val	Ile	Glu	Glu	Ala
3530						3535					3540			
Glu	Glu	Asn	Val	Trp	Ile	Glu	Lys	Glu	Val	Glu	Glu	Glu	Gly	Leu
3545						3550					3555			
Asp	Asn	Glu	Glu	Val	Ile	Asp	Glu	Glu	Asp	Ser	Val	Ser	Glu	Gln
3560						3565					3570			
Ala	Glu	Glu	Glu	Val	Tyr	Ile	Asn	Glu	Glu	Ile	Leu	Lys	Glu	Ser
3575						3580					3585			
Ser	Asp	Val	Glu	Asp	Val	Lys	Val	Glu	Asn	Glu	Leu	Met	Asn	Glu
3590						3595					3600			
Glu	Val	Asn	Glu	Glu	Thr	Gln	Ser	Val	Ala	Glu	Asn	Asn	Glu	Glu
3605						3610					3615			
Asp	Lys	Glu	Leu	Asp	Asn	Tyr	Val	Val	Glu	Glu	Thr	Glu	Ser	Val
3620						3625					3630			
Thr	Glu	Glu	Val	Val	Val	Asp	Glu	Val	Pro	Asn	Ser	Lys	Glu	Val
3635						3640					3645			
Gln	Glu	Ile	Glu	Ser	Ile	Ile	Glu	Glu	Ile	Val	Glu	Asp	Gly	Leu
3650						3655					3660			
Thr	Thr	Asp	Asp	Leu	Val	Gly	Gln	Gln	Gly	Ser	Val	Ile	Glu	Glu
3665						3670					3675			
Val	Val	Glu	Glu	Val	Gly	Ser	Asp	Ser	Glu	Glu	Ile	Val	Glu	Glu
3680						3685					3690			
Ala	Ser	Ile	Thr	Glu	Glu	Val	Glu	Lys	Lys	Glu	Ser	Val	Thr	Glu

3695	3700	3705
Asp Ile Leu Val Glu Glu Ser 3710 3715	Val Thr Gly Asp Ile Leu Val Glu 3720	
Gly Ser Val Thr Glu Glu Val 3725 3730	Val Gly Glu Glu Lys Leu Val Ser 3735	
Glu Glu Ile Val Thr Glu Glu 3740 3745	Gly Ser Val Ala Gln Glu Ile Val 3750	
Glu Glu Asp Ala Pro Ala Thr 3755 3760	Glu Glu Ile Asp Glu Ile Glu Ser 3765	
Val Thr Glu Glu Val Val Glu 3770 3775	Glu Glu Gly Pro Val Asp Glu Glu 3780	
Ile Val Gln Glu Glu Gly Ser 3785 3790	Val Thr Glu Glu Ile Ile Gln Gly 3795	
Glu Ser Lys Val Glu Glu Val 3800 3805	Val Glu Glu Gln Gly Ser Glu Asn 3810	
Glu Glu Ile Phe Val Glu Glu 3815 3820	Val Ser Ala Ser Gln Glu Ile Val 3825	
Gln Asn Glu Ser Gly Thr Glu 3830 3835	Glu Ile Leu Glu Lys Val Ser Ala 3840	
Ser Gln Glu Ile Val Gln Asp 3845 3850	Gly Ser Val Thr Glu Gln Ile Ile 3855	
Glu Glu Gln Lys Pro Val Thr 3860 3865	Glu Glu Val Val Asn Glu Glu Glu 3870	
Ser Ile Thr His Glu Ile Ile 3875 3880	Gln Glu Glu Ser His Val Glu Lys 3885	
Val Val Gln Gln Gly Ser Val 3890 3895	Ala Glu Glu Val Val Glu Asn Pro 3900	

Val	Ser	Val	Thr	Glu	Glu	Ile	Val	Glu	Lys	Glu	Gly	Ser	Val	Thr
	3905					3910					3915			
Glu	Asp	Ile	Gly	Gln	Glu	Gly	Tyr	Val	Ala	Glu	Glu	Ile	Val	Glu
	3920					3925					3930			
Glu	Glu	Glu	Phe	Asp	Asn	Glu	Glu	Ile	Leu	Glu	Glu	Glu	Ser	Val
	3935					3940					3945			
Ala	Glu	Glu	Phe	Val	Glu	Glu	Gly	Phe	Asp	Asn	Glu	Glu	Ile	Phe
	3950					3955					3960			
Val	Glu	Gln	Ile	Ser	Asp	Ser	Glu	Ile	Val	Lys	Glu	Glu	Asn	Ser
	3965					3970					3975			
Val	Asn	Glu	Glu	Val	Leu	Glu	Glu	Glu	Gly	Ser	Tyr	Thr	Glu	Glu
	3980					3985					3990			
Ile	Leu	Glu	Glu	Glu	Gly	Ser	Tyr	Thr	Glu	Glu	Ile	Leu	Glu	Glu
	3995					4000					4005			
Glu	Gly	Ser	Phe	Thr	Glu	Glu	Ile	Leu	Glu	Glu	Glu	Gly	Ser	Tyr
	4010					4015					4020			
Asn	Glu	Glu	Ile	Leu	Glu	Glu	Glu	Gly	Ser	Tyr	Asn	Glu	Glu	Ile
	4025					4030					4035			
Leu	Glu	Glu	Glu	Gly	Ser	Tyr	Asn	Glu	Glu	Ile	Leu	Glu	Glu	Glu
	4040					4045					4050			
Gly	Ser	Tyr	Asn	Glu	Glu	Ile	Leu	Glu	Glu	Glu	Gly	Ser	Ala	Thr
	4055					4060					4065			
Asp	Tyr	Phe	Val	Gly	Gln	Gly	Ser	Asp	Asn	Glu	Glu	Ile	Ile	Glu
	4070					4075					4080			
Glu	Gly	Ser	Ala	Thr	Asp	Tyr	Phe	Val	Gly	Gln	Gly	Ser	Asp	Asn
	4085					4090					4095			
Glu	Glu	Ile	Ile	Glu	Glu	Gly	Ser	Ala	Thr	Asp	Tyr	Phe	Val	Gly
	4100					4105					4110			

Gln Gly Ser Ile Ile Glu Glu Val Leu Glu Glu Glu Gly Leu Asp	4115	4120	4125
Thr Glu Lys Val Phe Glu Asn Glu Gly Ser Ala Thr Glu Phe Glu	4130	4135	4140
Glu Thr Glu Ser Phe Thr Glu Val Val Glu Glu Thr Glu Ser Val	4145	4150	4155
Asn Glu Asn Ile Leu Glu Glu Thr Ser Ile Asn Glu Val Gln Lys	4160	4165	4170
Ile Glu Ser Ile Thr Glu Asp Ile Lys Glu Gln Leu Val Pro Glu	4175	4180	4185
Glu Ile Lys Glu Glu Gln Leu Asp Ser Glu Glu Ile Lys Glu Glu	4190	4195	4200
Gln Leu Asp Ser Glu Glu Ile Lys Glu Glu Gln Leu Val Pro Glu	4205	4210	4215
Glu Ile Lys Glu Glu Gln Leu Asp Ser Glu Glu Ile Lys Glu Glu	4220	4225	4230
Gln Leu Asp Ser Glu Glu Ile Lys Glu Glu Gln Leu Asp Ser Glu	4235	4240	4245
Glu Ile Lys Glu Glu Gln Leu Asp Ser Glu Glu Ile Lys Glu Glu	4250	4255	4260
Gln Leu Val Pro Glu Glu Ile Lys Glu Glu Gln Leu Asp Ser Glu	4265	4270	4275
Glu Ile Lys Glu Glu Gln Leu Val Pro Glu Glu Ile Lys Glu Glu	4280	4285	4290
Gln Leu Asp Ser Glu Glu Ile Lys Glu Glu Gln Leu Asp Ser Glu	4295	4300	4305
Glu Ile Lys Glu Glu Gln Leu Asp Ser Glu Glu Ile Lys Glu Glu	4310	4315	4320

Gln	Leu	Asp	Ser	Glu	Glu	Ile	Lys	Glu	Gln	Lys	Gly	Ser	Val	Asn
4325						4330					4335			
Glu	Glu	Val	Val	Glu	Glu	Glu	Gly	Ser	Val	Thr	Glu	Glu	Ile	Lys
4340						4345					4350			
Glu	Gln	Glu	Glu	Ser	Val	Asn	Glu	Glu	Val	Leu	Glu	Glu	Val	Glu
4355						4360					4365			
Glu	Thr	Glu	Ser	Ile	Lys	Glu	Glu	Ile	Val	Glu	Gly	Gly	Ile	Ala
4370						4375					4380			
Thr	Gln	Glu	Ile	Ile	Glu	Glu	Glu	Ser	Asp	Thr	Lys	Glu	Val	Val
4385						4390					4395			
Glu	Glu	Glu	Val	Ile	Asp	Ser	Glu	Lys	Leu	Val	Asp	Ala	Gly	Ser
4400						4405					4410			
Val	Thr	Gly	Glu	Val	Met	Pro	Glu	Glu	Val	Ser	Val	Thr	Asp	Glu
4415						4420					4425			
Val	Val	Glu	Glu	Gly	Ser	Thr	Thr	Glu	Glu	Val	Leu	Glu	Glu	Gln
4430						4435					4440			
Lys	Ser	Val	Asn	Glu	Glu	Val	Val	Glu	Asp	Gly	Leu	Thr	Ile	Asp
4445						4450					4455			
Asp	Phe	Val	Gly	Leu	Gln	Gly	Ser	Thr	Thr	Glu	Glu	Val	Val	Glu
4460						4465					4470			
Glu	Asp	Gly	Ser	Ala	Ile	Glu	Lys	Ile	Leu	Glu	Glu	Glu	Thr	Ala
4475						4480					4485			
Thr	Glu	Glu	Ile	Val	Glu	Lys	Gln	Val	Ser	Val	Thr	Glu	Asp	Ile
4490						4495					4500			
Val	Glu	Lys	Glu	Gly	Ser	Val	Asn	Glu	Glu	Ile	Ile	Glu	Glu	Ala
4505						4510					4515			
Ser	Val	Ala	Glu	Glu	Ile	Ile	Gln	Gly	Gly	Ser	Phe	Thr	Glu	Glu

4520	4525	4530
Ile Val Gly Gln Glu Glu Ser	Ala Thr Glu Glu Val	Ile Asp Glu
4535	4540	4545
Glu Gly Leu Ile Ser Asn Glu	Ile Glu Glu Glu Glu	Glu Lys Ser
4550	4555	4560
Val Thr Glu Glu Met Ile Glu	Glu Val Glu Glu Val	Ser Val Asp
4565	4570	4575
Asp Glu Val Glu Glu Val Ser	Val Ala Glu Glu Ile	Val Glu Glu
4580	4585	4590
Glu Leu Val Asp Asp Glu Ile	Leu Pro Glu Glu Leu	Ser Ala Thr
4595	4600	4605
Glu Asp Val Ile Glu Glu Val	Arg Ser Val Thr Asp	Glu Ile Val
4610	4615	4620
Gln Glu Glu Ser Val Cys Glu	Glu Ile Leu Glu Gln	Glu Val Ser
4625	4630	4635
Ala Ser Glu Glu Tyr Val Asp	Asp Lys Ser Val Thr	Asp Asp Phe
4640	4645	4650
Val Gly His Glu Arg Ser Val	Ile Gln Asp Val Glu	Asn Thr Glu
4655	4660	4665
Ser Val Thr Glu Glu Ile Ala	Glu Val Asp Lys Ser	Val Ile Glu
4670	4675	4680
Glu Ala Val Glu Lys Gln Gly	Ser Val Thr Glu Glu	Lys Val Gln
4685	4690	4695
Glu Gly Val Ser Ala Ile Glu	Glu Ile Glu Glu Leu	Glu Ser Val
4700	4705	4710
Thr Glu Glu Ile Ala Glu Glu	Asp Lys Ser Val Ile	Glu Glu Ala
4715	4720	4725

Val 4730	Glu	Lys	Gln	Gly	Ser	Val 4735	Thr	Glu	Glu	Ile	Val 4740	Glu	Glu	Glu
Glu 4745	Leu	Asp	Thr	Glu	Glu	Val 4750	Leu	Glu	Asp	Lys	Ser 4755	Val	Thr	Gly
Asp 4760	Val	Val	Glu	Gln	Glu	Gly 4765	Ser	Gly	Lys	Asp	Glu 4770	Ser	Glu	Ala
Lys 4775	Glu	Ser	Phe	Thr	Glu	Glu 4780	Val	Asp	Glu	Leu	Lys 4785	Ser	Val	Lys
Glu 4790	Glu	Asp	Gln	Glu	Thr	Glu 4795	Tyr	Ile	Ser	Arg	Glu 4800	Ile	Glu	Glu
Glu 4805	Ser	Ala	Thr	Glu	Gln	His 4810	Ser	Glu	Gln	Glu	Leu 4815	Ser	Ile	Asn
Lys 4820	Glu	Val	Val	Glu	Thr	Glu 4825	Ser	Leu	Thr	Lys	Asp 4830	Ile	Glu	Glu
Glu 4835	Lys	Ser	Thr	Thr	Gln	Glu 4840	Ile	Leu	Glu	Glu	Thr 4845	Gln	Ser	Val
Asn 4850	Glu	Glu	Ile	Val	Glu	Glu 4855	Glu	Arg	Asp	Thr	Asp 4860	Glu	Val	Leu
Lys 4865	Glu	Lys	Val	Ser	Pro	Ser 4870	Glu	Glu	Val	Ile	Glu 4875	Glu	Gln	Ala
Ser 4880	Thr	Thr	Glu	Glu	Phe	Val 4885	Glu	Glu	Arg	Ser	Ser 4890	Thr	Asp	Glu
Ile 4895	Val	Glu	Val	Glu	Asp	Leu 4900	Phe	Thr	Glu	Glu	Val 4905	Lys	Glu	Arg
Glu 4910	Gly	Ser	Val	Thr	Glu	Glu 4915	Ile	Val	Glu	Glu	Gly 4920	Ser	Asp	Thr
Gly 4925	Glu	Ile	Val	Glu	Glu	Glu 4930	Gly	Ser	Asp	Thr	Glu 4935	Glu	Ile	Leu

Glu	Glu	Gly	Ser	Phe	Asn	Glu	Glu	Ile	Val	Glu	Glu	Glu	Gly	Ser
	4940					4945					4950			
Ile	Thr	Glu	Glu	Ile	Leu	Gln	Gly	Ser	Val	Thr	Glu	Glu	Ile	Leu
	4955					4960					4965			
Gln	Gly	Ser	Val	Thr	Glu	Glu	Phe	Val	Gly	Gln	Gln	Gly	Ser	Val
	4970					4975					4980			
Ile	Glu	Glu	Ile	Val	Glu	Thr	Glu	Ser	Ala	Ile	Glu	Glu	Arg	Val
	4985					4990					4995			
Glu	Glu	Glu	Ser	Ala	Thr	Glu	Glu	Val	Asp	Glu	Arg	Glu	Ser	Val
	5000					5005					5010			
Thr	Glu	Val	Val	Glu	Glu	Glu	Val	Ser	Ser	Ser	Asp	Glu	Val	Val
	5015					5020					5025			
Glu	Gly	Ser	Ile	Glu	Glu	Val	Ile	Glu	Asn	Glu	Gly	Ser	Val	Thr
	5030					5035					5040			
Glu	Glu	Ile	Leu	Glu	His	Glu	Val	Ser	Ala	Asp	Glu	Asn	Phe	Val
	5045					5050					5055			
Gly	Gln	Ala	Val	Ser	Val	Ile	Glu	Glu	Val	Glu	Gly	Thr	Glu	Ser
	5060					5065					5070			
Val	Thr	Glu	Glu	Val	Val	Glu	Glu	Thr	Glu	Ser	Val	Ser	Glu	Glu
	5075					5080					5085			
Ile	Val	Glu	Val	Ser	Pro	Thr	Glu	Asn	Val	Val	Gln	Gln	Thr	Asp
	5090					5095					5100			
Ser	Val	Ile	Glu	Glu	Val	Val	Glu	Gln	Lys	Glu	Gly	Ser	Phe	Asn
	5105					5110					5115			
Glu	Glu	Ile	Asp	Ile	Arg	Glu	Leu	Gly	Asp	Asp	Gly	Val	Glu	Glu
	5120					5125					5130			
Arg	Glu	Lys	Ile	Ser	Thr	Glu	Glu	Val	Val	Gly	Gln	Asp	Lys	Ser
	5135					5140					5145			

Ala	Thr	Gly	Asp	Val	Glu	Glu	Val	Ser	Ser	Thr	Glu	Asp	Glu	Glu
5150						5155					5160			
Glu	Val	Ser	Ser	Thr	Glu	Gly	Leu	Glu	Glu	Val	Ser	Ser	Thr	Glu
5165						5170					5175			
Gly	Leu	Glu	Glu	Val	Ser	Asn	Thr	Glu	Asp	Val	Glu	Glu	Val	Ser
5180						5185					5190			
Ser	Thr	Glu	Asp	Val	Glu	Glu	Gly	Ser	Val	Ala	Glu	Asn	Val	Lys
5195						5200					5205			
Glu	Thr	Lys	Ser	Ile	Thr	Glu	Glu	Val	Ser	Val	Glu	Glu	Asp	Ile
5210						5215					5220			
Ile	Thr	Asp	Lys	Val	Ser	Val	Glu	Gln	Glu	Val	Met	Ala	Glu	Ala
5225						5230					5235			
Ser	Val	Glu	Glu	Asn	Ile	Leu	Thr	Glu	Val	Pro	Val	Glu	Glu	Glu
5240						5245					5250			
Ile	Met	Thr	Glu	Lys	Leu	Ser	Val	Glu	Asp	Lys	Ala	Leu	Asn	Glu
5255						5260					5265			
Lys	Ile	Met	Ser	Glu	Glu	Glu	Ile	Val	Ile	Glu	Asp	Gly	Asn	Val
5270						5275					5280			
His	Glu	Val	Val	Pro	Ala	Glu	Val	Ser	Val	Thr	Glu	Glu	Ile	Pro
5285						5290					5295			
Gly	Val	Glu	Glu	Thr	Thr	Asn	Asn	Glu	Ser	His	Val	Lys	Gly	Glu
5300						5305					5310			
Asn	Val	Val	Asn	Glu	Val	Val	Val	Asp	Asp	Asn	Ser	Val	Asn	Asp
5315						5320					5325			
Glu	Ile	Gln	Phe	Asp	Asp	Asp	Ser	Ser	Ile	Glu	Ile	Tyr	Thr	Val
5330						5335					5340			
Asp	Ser	Lys	Asp	Val	Phe	His	Lys	Glu	Glu	Asn	Tyr	Asp	Ser	Phe

5345	5350	5355
Arg Glu 5360	Glu Val Arg Ser Asp 5365	Glu Asn Ile His Ile Phe Arg Lys 5370
Lys Asn 5375	Glu Asn Phe Val Lys 5380	Lys Ile Glu Asn Glu Lys Ser Ser 5385
Val Gly 5390	His Val Pro Thr Glu 5395	Tyr Thr Ser Lys Glu Asn Ile Ala 5400
Glu Glu 5405	Val Pro Ser His Ile 5410	Met Phe Lys Glu Asn Val Thr Glu 5415
Glu Val 5420	Pro Lys Glu Val Lys 5425	Tyr Glu Glu Asn Thr Val Glu Glu 5430
Val Phe 5435	Glu Glu Val Thr Ser 5440	Lys Glu Asn Ile Ile Glu Glu Ala 5445
Pro Gly 5450	Asp Ile Asn Ser Glu 5455	Glu Asn Ile Ile Glu Glu Val Pro 5460
Glu Val 5465	Val Thr Ser Glu Glu 5470	Ile Val Val Gln Asn Asp Val Asn 5475
Asn Ile 5480	Asn Thr Asn Ile Asp 5485	His Met Phe Asp Phe Asp Leu Asp 5490
Asp Ile 5495	Leu Lys Ile Pro Glu 5500	Ala Gln Arg Lys Leu Asn Lys Leu 5505
Arg Thr 5510	Leu Val Asp Val His 5515	Leu Asp Val Ile Glu Lys Met Gln 5520
Arg Asp 5525	Glu Trp Lys Lys Asn 5530	Lys Arg Asp Phe Leu Tyr Ile Cys 5535
Leu Lys 5540	Glu Ile Asn Lys Leu 5545	Ser Glu Asp Thr Leu Met Lys Phe 5550

Tyr	Gly	Ser	Asp	Ser	Asn	Lys	Ser	Ala	Asn	Asp	Asn	Asp	Thr	Val
	5555					5560					5565			
Met	Val	Ile	Lys	Ile	Leu	Lys	Asp	Lys	Trp	Gly	Thr	Gly	Arg	Ile
	5570					5575					5580			
Val	Asp	Thr	Ile	Ala	Asn	Ser	Leu	Asn	Lys	Ser	Tyr	Asn	Ser	Leu
	5585					5590					5595			
Tyr	His	Asn	Leu	Tyr	Ile	Glu	Met	Glu	Lys	Asp	Leu	Leu	Ile	Asn
	5600					5605					5610			
Lys	Thr	Glu	Thr	Phe	Asn	Lys	Trp	Ser	Lys	Gln	His	Trp	Asn	Lys
	5615					5620					5625			
Leu	Asp	Asn	Trp	Lys	Glu	Glu	Lys	Trp	Phe	Lys	Leu	Phe	Lys	Arg
	5630					5635					5640			
Asp	Leu	Lys	Ile	Asp	Met	Arg	Asn	Thr	Tyr	Glu	Ser	Asp	Gln	Asn
	5645					5650					5655			
Asp	Glu	Glu	Asn	Asn	Glu	Glu	Ser	Met	Asn	Glu	Leu	Ser	Asp	Glu
	5660					5665					5670			
Leu	Ile	Lys	Asn	Asn	Thr	Ser	Asp	Asn	Met	Arg	Asn	Glu	Gln	Lys
	5675					5680					5685			
Thr	Leu	Glu	Lys	Asn	Lys	Glu	Tyr	Ser	Asn	Leu	Ser	Lys	Asp	Leu
	5690					5695					5700			
Gly	Leu	Ile	Glu	Lys	Gln	Lys	Ile	Ile	Trp	Lys	Ser	Trp	Ile	Val
	5705					5710					5715			
Lys	Asn	Val	Asn	Asn	Ile	Glu	Asn	Trp	Phe	Asp	Glu	Met	Trp	Phe
	5720					5725					5730			
Lys	Asn	Val	Val	Asn	Glu	Leu	Lys	Glu	Lys	Asn	Asp	Val	Ser	Asn
	5735					5740					5745			
Val	Leu	Gln	Glu	Asn	Ala	Ser	Glu	Ala	Ser	Val	Glu	Asn	Tyr	Ile
	5750					5755					5760			

Ser	Asp	Val	Glu	Asp	Ser	Lys	Asp	Met	Thr	Asn	Ser	Ile	Asn	Asp
5765						5770					5775			
Ser	Glu	Lys	Ser	Lys	Ile	Val	Ala	Ser	Ser	Ser	Lys	Thr	Thr	Asn
5780						5785					5790			
Glu	Glu	Tyr	Ile	Ile	Leu	Ser	Arg	Lys	Asp	Leu	Ile	Tyr	Asn	Ile
5795						5800					5805			
Ile	Val	Met	Val	His	Met	Met	Val	Leu	Asp	Gln	Phe	Lys	Tyr	Asp
5810						5815					5820			
Glu	Leu	Lys	Tyr	Ala	Lys	Lys	Arg	Phe	Leu	Asn	Arg	Ser	Ile	Asp
5825						5830					5835			
Lys	Phe	Ile	Lys	Glu	Lys	Lys	Ile	Lys	Asp	Lys	Glu	Thr	Val	Leu
5840						5845					5850			
Asp	Tyr	Tyr	Ile	Asp	Asp	Ile	Ile	Lys	Arg	Ile	Val	Glu	Asp	Thr
5855						5860					5865			
Ser	His	Val	Asn	Asn	Ile	Lys	Glu	Lys	Ala	Ile	Asp	His	Tyr	Thr
5870						5875					5880			
Ser	His	Asp	Trp	Phe	Arg	Leu	Leu	Arg	Gln	Gly	Asn	Lys	Ala	Gln
5885						5890					5895			
Asn	Ser	Ile	Ser	Gln	Glu	Val	Asp	Ile	Leu	Thr	Glu	Lys	Tyr	Lys
5900						5905					5910			
Lys	Leu	Ile	Ser	Glu	Glu	Asp	Asn	Lys	Lys	Glu	Asn	Asn	Asn	Asn
5915						5920					5925			
Asn	Asp	Asp	Glu	Val	Lys	Pro	Glu	Leu	Lys	Asp	Asn	Ile	Lys	Cys
5930						5935					5940			
Glu	Glu	Asn	Val	Ser	Phe	Asn	Ile	Leu	Arg	Arg	Ser	Asn	Lys	Lys
5945						5950					5955			
Asp	Gln	Leu	Pro	Leu	Glu	Glu	Lys	Lys	Asn	Lys	Asn	Gly	Asp	Leu
5960						5965					5970			

Asn Asn Thr Leu Thr Glu Ser Asp Gly Lys Lys Ile Asn Ile Asn
5975 5980 5985

Glu Ala Ile Glu Glu Ser Lys Asn Gly Asn Glu Asp Lys Asn Ser
5990 5995 6000

Gly Asn Met Glu Lys Ser Arg Lys Pro Arg Asp Arg Arg Thr Glu
6005 6010 6015

Arg Lys Glu Lys Asp Gln Asp Leu Arg Val Gln Leu Leu Gln Asp
6020 6025 6030

Tyr Glu Asn Ile Phe Glu Gln Ile Gln Asn Met Glu Asn Gln Asn
6035 6040 6045

Lys Asp Lys Asn Lys Lys Glu Thr Lys Asn Ile Leu Lys Thr Ser
6050 6055 6060

Ile Asp Leu Asp Lys Asn Leu Leu Arg Glu Tyr Lys Lys Glu Lys
6065 6070 6075

Asn Ile Ile Asn Gln Ser Glu Lys Glu Phe Ser Val Asn Glu Asn
6080 6085 6090

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<213> 惡性瘡原蟲

<400> 59

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1 5 10 15

Ile Asn Val Ile Arg Thr Arg Gly Glu Glu Asp Asp Asp Asn Asn Asn
20 25 30

Ile Ser Gly Lys Ser Ile Leu Gly Thr Ser His Asn Asn Ile Ser Asn
35 40 45

Ile Asp Leu Ser Ser Ile Pro Asn Leu Asp Ser Asn Ile His Ala Ser
50 55 60

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

275	280	285
Thr Asn Cys Phe Leu Ser Gly Asn Ile Asn Ile Glu Lys Cys Leu Glu		
290	295	300
Cys Thr Leu Leu Val Gln Asn Asn Asp Thr Ser Ser Glu Cys Phe Thr		
305	310	315
Tyr Val Ser Asn Asp Val Arg Glu Asn Phe Asn Gln Ile Lys Ala Glu		
	325	330
Ala Glu Asp Asp Glu Asn Phe Arg Asn Tyr His Leu Thr Asp Thr Ile		
	340	345
Asn Asn Ile Leu Lys Arg Ile Tyr Lys Ile Asn Lys Asn Glu Gly Lys		
	355	360
Lys Glu Leu Ile Thr Leu Glu Glu Leu Asp Asn Phe Leu Lys Glu Ser		
	370	375
Ile Thr Asp Tyr Cys Lys Ile Leu Arg Glu Ile Asp Thr Asn Gly Thr		
385	390	395
Leu Val Asn His Glu Leu Gly Asn Asn Val Asp Val Phe Asn Asn Leu		
	405	410
Ile Arg Leu Leu Lys Leu His Lys Asn Glu Ser Ile Ser Thr Leu His		
	420	425
Asn Lys Leu Arg Asn Ser Ala Ile Cys Met Lys Tyr Pro Asp Lys Trp		
	435	440
Ile Glu Lys Lys Thr Gly Leu Ile Leu Pro Asn Val Val Asn Asn Asn		
	450	455
Ile Ile Tyr Asn Asn Lys Tyr Glu Lys Leu Asn Glu Glu Lys Lys Arg		
465	470	475
Lys Ile Tyr Asp Asn Lys Asp Asp Ser Lys Ile Ser Asp Ile Ile Asn		
	485	490
		495

Ile Lys Lys Tyr Ile Phe Thr Asn Asn Thr Leu Lys Tyr Phe Asn Asn
500 505 510

Asp Lys Gln Phe Cys Asn Ser Ser Phe Cys Asn Arg Leu Lys Asp Glu
515 520 525

Asn Asn Cys Ile Ser Lys Ile Gln Ile Glu Asp Gln Gly Asn Cys Ala
530 535 540

Ile Ser Trp Ile Phe Ala Ser Lys Tyr Tyr Leu Glu Thr Leu Lys Cys
545 550 555 560

Met Lys Gly Tyr Glu Pro His Ala Ile Ser Ala Leu Tyr Ile Ala Asn
565 570 575

Cys Ser Lys Arg Lys His Lys Asn Arg Cys Asn Val Gly Ser Asn Pro
580 585 590

Leu Glu Phe Leu Gln Ile Ile Glu Glu Asn Gln Phe Leu Pro Met Asp
595 600 605

Thr Asn Tyr Leu Tyr Ser Tyr Thr Lys Val Gly Asn Asp Cys Pro Asp
610 615 620

Glu Glu Lys Asn Trp Val Asn Leu Leu Lys His Thr Arg Met Leu Asn
625 630 635 640

Tyr Asn Asn Lys His Arg Ser Thr Leu Ser Thr Lys Ala Tyr Arg Ala
645 650 655

Tyr Glu Ser Glu His Phe Lys Asp Lys Met Asp Thr Phe Ile Lys Leu
660 665 670

Ile Lys Asp Glu Ile Met Asn Asn Gly Ser Val Ile Ala Tyr Val Lys
675 680 685

Ala Glu Asn Val Leu Gly Tyr Glu Leu Asn Gly Lys Asn Val Gln Asn
690 695 700

Leu Cys Gly Asp Lys Thr Pro Asp His Ala Val Asn Ile Val Gly Tyr
705 710 715 720

Gly	Asn	Tyr	Ile	Asn	Asp	Glu	Asp	Glu	Lys	Lys	Ser	Tyr	Trp	Ile	Val	
				725					730					735		
Arg	Asn	Ser	Trp	Gly	Lys	Tyr	Trp	Gly	Asp	Glu	Gly	Tyr	Phe	Lys	Val	
			740					745					750			
Asp	Met	Tyr	Gly	Pro	Ser	Thr	Cys	Glu	Asp	Asn	Phe	Ile	His	Thr	Val	
		755					760					765				
Val	Val	Phe	Asn	Ile	Asn	Met	Pro	Lys	Ser	Lys	Lys	Ser	Pro	Val	Lys	
	770					775					780					
Ile	Thr	Phe	Pro	Leu	Tyr	Asn	Tyr	Tyr	Leu	Lys	Tyr	Ser	Pro	Asp	Phe	
785					790					795					800	
Tyr	His	Asn	Leu	Tyr	Tyr	Lys	Asn	Phe	Asn	Ser	Lys	Lys	Ser	Met	Lys	
			805						810					815		
Leu	Val	Asn	Ala	Ser	Asp	Glu	His	Lys	Asn	Ile	Tyr	Ser	Gln	Glu	Asp	
			820					825					830			
Lys	Val	Asn	His	Lys	Lys	Gly	Ser	Lys	Ile	Leu	Asn	Ser	Glu	Val	Thr	
		835					840					845				
Thr	Ser	Leu	Leu	Ser	Gln	Glu	Ile	Ser	Gln	Arg	Arg	Gly	Glu	Asp	Asp	
	850					855					860					
Asp	Ile	Asp	Thr	Leu	Ile	Gly	Asp	Ser	Pro	Asp	Ile	Asn	Glu	Gln	Glu	
865					870					875					880	
Lys	Asn	Ile	Lys	Asp	Glu	Phe	Asn	Lys	Ser	Ser	Ile	Thr	His	Asn	Ser	
				885					890					895		
Val	Ser	Ser	Ser	Asn	Ile	Thr	Lys	Ser	Asn	Lys	Asn	Thr	Asn	Lys	Val	
			900					905					910			
Lys	Ile	Tyr	His	Ile	Ile	Lys	His	Val	Lys	Asn	Thr	Lys	Ile	Lys	Ile	
		915					920					925				
Gly	Phe	Val	Lys	Tyr	Asp	Asn	Tyr	Asn	Thr	Ile	Gly	Thr	Asn	His	Thr	
	930					935					940					

Cys Ser Arg Ser Tyr Ser Glu Asp Gln Glu Lys His Glu Gly Cys Ile
945 950 955 960

Lys Phe Cys Glu Leu His Trp Asn Glu Cys Lys Asp Lys Thr Ser Pro
965 970 975

Gly Tyr Cys Leu Thr Lys Leu Lys Gly Ser Asn Glu Cys Phe Phe Cys
980 985 990

Tyr Val

<210> 60
<211> 1105
<212> PRT
<213> 惡性瘧原蟲

<400> 60

Met Lys Phe His Ile Ser Phe Phe Leu Ile Leu Tyr Ile Val Phe Phe
1 5 10 15

Lys Asn Thr Ile Lys Ser Glu Thr Thr Thr Asp Glu Ser Ala Thr Gly
20 25 30

Ser Leu Ser Ser Asp Gly Ser Arg Val Thr Thr Gln Ala Arg Ile Glu
35 40 45

Lys Pro Lys Gln Gln Pro Thr Leu Pro Thr Leu Ala Gln Glu Thr Gln
50 55 60

Pro Gln Gln Gln Gln Gln Gln Lys Glu Val Gly Ser Gly Ile Gly Ala
65 70 75 80

Glu Gln Lys Val Glu Ser Ala Arg Pro Gly Ala Glu Val Ser Gln Ser
85 90 95

Asp Val Glu Arg Ala Gly Arg Ser Ser Gly Thr Gly Gly Ser Val Gly
100 105 110

Thr Lys Ile Ser Pro Gly Ser Gln Gly Gln Gly Lys Val Ala Gly Pro
115 120 125

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

340	345	350
Asp Cys Phe Leu Ser Gly Asn Val Asp Ile Glu Lys Cys Leu Gln Cys		
355	360	365
Thr Leu Leu Val Ile Lys Ala Asp Lys Asn Asp Glu Cys Leu Lys Tyr		
370	375	380
Val Ser Lys Asn Val Lys Asp Arg Phe Glu Glu Ile Leu Thr Lys Gly		
385	390	395
Glu Asp Asp Ala Asp Ser Asp Glu Tyr Asp Phe Ile Ala Pro Ala Asn		
405	410	415
Tyr Ile Leu Lys Asn Ile Tyr Lys Lys Asn Asp Thr Asn Gly Lys Lys		
420	425	430
Glu Leu Leu His Phe Lys Asp Ile Asn Asn Asn Leu Lys Leu Glu Leu		
435	440	445
Ile Asn Tyr Cys Asn Leu Leu Lys Asp Asn Asp Val Ser Gly Ile Leu		
450	455	460
Thr Tyr Glu Lys Leu Gly Asn Val Gln Asp Ile Phe Asn Asn Leu Thr		
465	470	475
Lys Leu Leu Glu Glu His Lys Glu Glu Asn Asn Tyr Val Leu Tyr His		
485	490	495
Lys Met Lys Asn Glu Val Leu Cys Leu Lys Asn Ala Asn Asp Trp Met		
500	505	510
Lys Asn Lys Thr Gly Leu Val Leu Pro Gln Leu Lys Tyr Ser Leu Asn		
515	520	525
Lys Phe Asn Lys Asn Lys Glu Asn Tyr Ile Lys Glu Asn Ile Phe Glu		
530	535	540
Glu Asp Glu Asn Gly Ile Val Asp Leu Thr Lys Phe Pro Val Asp Thr		
545	550	555
		560

Ser Tyr Ser Ser Tyr Asn Tyr Ala Asp Ser Leu Tyr Cys Asn Arg Glu
565 570 575

Tyr Cys Asn Arg Leu Lys Asp His Asn Asn Cys Ile Ser Lys Ile Asn
580 585 590

Val Glu Asp Gln Lys Asn Cys Ala Leu Ser Trp Ala Phe Ala Ser Ile
595 600 605

Tyr His Leu Glu Thr Ile Lys Cys Met Lys Gly Tyr Glu Pro Leu Asn
610 615 620

Ala Ser Val Leu Tyr Val Thr Asn Cys Leu Lys Asn Lys Asn Asn Asp
625 630 635 640

Val Cys Thr Glu Gly Ser Asn Pro Leu Val Phe Leu Glu Thr Ile Glu
645 650 655

Glu Lys Gly Phe Leu Pro Thr Glu Ser Asn Tyr Pro Tyr Asp Gln Ser
660 665 670

Lys Val Gly Asp Val Cys Pro Gln Val Gln Asn Asp Trp Asp Asn Val
675 680 685

Phe Glu Asn Thr Lys Val Leu Glu Tyr Asn Asn Ala Pro Phe Ser Val
690 695 700

Gly Thr Lys Gly Tyr Ile Ala Tyr Glu Ser Glu Val Phe Gln Lys Asp
705 710 715 720

Ile Asp Ser Phe Val Lys Leu Ile Lys Asp Glu Ile Met Asn Lys Gly
725 730 735

Ser Val Ile Ala Tyr Val Lys Ala Lys Asn Val Leu Gly Tyr Glu Leu
740 745 750

Asn Gly Lys Lys Val Gln Asn Leu Cys Gly Asp Lys Lys Pro Asp His
755 760 765

Ala Val Asn Ile Val Gly Tyr Gly Asn Tyr Ile Asn Asn Lys Gly Glu
770 775 780

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

Pro Ser Ile Val Ser Pro Thr Ala Ala Glu Lys Ser Arg Lys Ala
1010 1015 1020

Gln Ile Phe His Val Leu Lys His Ile Lys Asn Ser Arg Ile Lys
1025 1030 1035

Met Gly Leu Val Lys Tyr Asp Asn Ser Asp Asn Ile Gly Gly Asp
1040 1045 1050

His Val Cys Ser Arg Thr Tyr Ala Val Asn Pro Glu Lys Gln Glu
1055 1060 1065

Glu Cys Val Lys Phe Cys Glu Glu Asn Trp Glu Asn Cys Lys Asn
1070 1075 1080

Lys Pro Ser Pro Gly Tyr Cys Leu Ala Lys Leu Lys Asn Thr Asn
1085 1090 1095

Glu Cys Phe Phe Cys Tyr Val
1100 1105

<210> 61
<211> 930
<212> PRT
<213> 惡性瘧原蟲

<400> 61

Met Lys Phe Ser Ile Ser Leu Phe Leu Ile Leu Cys Val Leu Phe Cys
1 5 10 15

Lys Asn Asp Ile Lys Cys Thr Thr Val Asp Glu Ser Thr Lys Glu Gly
20 25 30

Ser Gln Asn Pro Lys Asn Ser Ser Ser Thr Thr Pro Ala Ser Gly Ser
35 40 45

Gln Lys Gly Ser Ser Ser Glu Ser Pro Gly Ser Ser Val Glu Lys Gln
50 55 60

Ser Gln Glu Ser Asn Lys Glu Ser Thr Asn Gly Gly Asn Val Val Ser
65 70 75 80

Gln Gly Thr Pro Ala Asn Thr Phe Gly Gln Asn Ser Asn Asn Pro Ser
85 90 95

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

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

Gly Ser Cys Asn Ala Asn Phe Gln Leu Phe Leu Val Pro His Ile Phe
130 135 140

Ile Asn Val Glu Thr Lys Glu Asn Asn Ile Gln Leu Asp Val Lys Phe
145 150 155 160

Leu Lys Leu Thr Lys Arg Ile Asp Phe Ala Lys Asp Lys Ser Met Leu
165 170 175

Lys Asn Lys Cys Glu Ser Gly Lys Asn Gln Thr Phe Lys Phe Val Leu
180 185 190

Tyr Phe Lys Asp Asp Ile Leu Thr Ile Lys Trp Lys Val Tyr Glu Glu
195 200 205

Lys Ser Ala Thr Pro Gln Lys Ser Glu Glu Asn Thr Val Asp Ile Lys
210 215 220

Leu Tyr Lys Leu Pro Lys Leu Asp Gln Thr Ile Thr Ser Ile Gln Val
225 230 235 240

His Thr Leu Ser Ile Glu Gly Thr Ser Tyr Leu Met Glu Ser Lys Asp
245 250 255

Tyr Ser Leu Gly Asn Asn Leu Pro Glu Lys Cys Asp Ala Ile Ala Ser
260 265 270

Asp Cys Phe Leu Ser Gly Asn Ile Asn Val Glu Lys Cys Leu Lys Cys
275 280 285

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

290	295	300
Val Ser Lys Asp Lys Pro Lys Glu Thr Lys Leu Ala Val Ser Gly Ser		
305	310	315 320
Glu Val Lys Glu Val Lys Ala Ala Ser Val Asp His Ser Asn Asp Lys		
	325	330 335
Glu Tyr Glu Leu Ser Gln Ser Ile Asn Asn Ile Leu Asn Lys Met Tyr		
	340	345 350
Lys Lys Glu Ser Asn Asp Glu Lys Asn Asn Lys Lys Glu Leu Ile Lys		
	355	360 365
Leu Glu Asp Ala Asp Asp Ser Leu Gln Lys Glu Leu Asn Lys Tyr Cys		
	370	375 380
Asn Ser Leu Lys Glu Val Asp Leu Asn Gly Val Leu Ser Lys Asn Glu		
385	390	395 400
Val Gly Asn Glu Lys Asp Val Phe Asn Asn Leu Thr Thr Leu Leu Lys		
	405	410 415
Glu His Met Leu Glu Ser His His Val Val Phe Glu Lys Leu Lys Asn		
	420	425 430
Ser Ala Leu Cys Leu Lys Asn Ile Asp Asp Trp Leu Lys Asn Lys Asn		
	435	440 445
Gly Leu Ile Val Pro Pro Ser Lys Tyr Lys Leu Lys Asp Thr Asn Glu		
	450	455 460
Lys Lys Glu Leu Asn Asn Asn Val Glu Val Ile Glu Asp Met Phe Lys		
465	470	475 480
Ala Asn Glu His Gly Ile Val Asp Leu Thr Lys Phe Pro Ile Asp Thr		
	485	490 495
Asn Tyr Ser Ser Tyr Lys His Ile Asp His Thr Tyr Cys Asn Asn Asp		
	500	505 510

Tyr Cys Asn Trp Ser Lys Asp Lys Asn Ser Cys Ile Ser Lys Ile Asn
 515 520 525
 Val Glu Asp Gln Lys Asn Cys Ala Leu Ser Trp Ala Phe Ala Ser Lys
 530 535 540
 Tyr His Leu Glu Thr Ile Lys Cys Met Lys Gly Tyr Glu His Ile Pro
 545 550 555 560
 Ile Ser Ser Leu Tyr Ile Ala Asn Cys Ser Lys Asn Glu Lys Lys Asp
 565 570 575
 Val Cys Thr Glu Gly Ser Asn Pro Leu Lys Val Leu Gln Met Ile Val
 580 585 590
 Glu Lys Gly Phe Leu Pro Thr Glu Gly Asp Tyr Ser Tyr Glu Gln Ser
 595 600 605
 Lys Val Gly Glu Thr Cys Pro Glu Val Gln Asn Gly Trp Val Asn Leu
 610 615 620
 Trp Ala Asn Ala Lys Leu Leu Glu Gln Asn Asn Asp Glu His Asn Ser
 625 630 635 640
 Leu Ser Thr Lys Gly Tyr Thr Ala Tyr Glu Ser Glu Ala Phe Gln Lys
 645 650 655
 Asp Met His Ser Phe Val Lys Leu Ile Lys Asp Glu Ile Met Asn Lys
 660 665 670
 Gly Ser Val Ile Ala Tyr Val Lys Ala Asp Lys Ile Met Ala Tyr Glu
 675 680 685
 Phe Asn Gly Lys Lys Val Gln Asn Leu Cys Gly Asp Lys Thr Pro Asp
 690 695 700
 His Ala Val Asn Ile Ile Gly Tyr Gly Asn Tyr Ile Asn Asp Glu His
 705 710 715 720
 Gln Lys Lys Ser Tyr Trp Ile Val Arg Asn Ser Trp Gly Lys His Trp
 725 730 735

Gly Asp Lys Gly His Phe Lys Val Asp Met Tyr Gly Pro Ser Asp Cys
740 745 750

Glu Asp Asn Phe Ile His Ser Val Val Ile Phe Asn Val Asp Leu Pro
755 760 765

Ile Asn Gln Glu Ser Val Lys Lys Glu Pro Lys Ile Tyr Asn Tyr Tyr
770 775 780

Leu Lys Ala Ser Pro Asp Phe Tyr His Asn Leu Tyr Tyr Lys Asn Phe
785 790 795 800

Asp Ser Gln Lys Gly Lys Ala Asp Gln Ala Glu Asn Lys Lys Ser Tyr
805 810 815

Leu Tyr Gly Gln Glu Glu Ser Thr Ser Glu Gln Leu Pro Ser Ser Leu
820 825 830

Ser Ser Pro Gln Asn Asn Lys Gln Ser Glu Arg Ser Lys Glu Lys Val
835 840 845

Asp Ile Phe His Val Leu Lys His Ile Lys Asp Ser Lys Ile Lys Met
850 855 860

Gly Ile Val Lys Tyr Asp His Ser Asp Ala Leu Gly Glu Asp Asn Val
865 870 875 880

Cys Ser Arg Ser Tyr Ser Ser Asn Pro Glu Lys Gln Glu Gly Cys Val
885 890 895

Lys Phe Cys Asn Glu Asn Trp Gly Lys Cys Lys Asp Ala Ala Ser Pro
900 905 910

Gly Phe Cys Leu Ser Glu Leu Glu Lys Thr Asn Asp Cys Phe Phe Cys
915 920 925

Tyr Ile
930

<210> 62
<211> 962

<212> PRT

<213> 惡性瘡原蟲

<400> 62

Met Lys Ile His Ile Phe Leu Ile Ala Thr Ile Tyr Val Leu Phe Ser
1 5 10 15

Glu Lys Leu Ile Lys Trp Thr Thr Ala Ser Thr Thr Gln Gly Gly Asp
20 25 30

Thr Asp Thr His Pro Gly Thr Pro Pro Gly Glu Gly Ser Asp Val Ser
35 40 45

Gln Gly Ala Gly Gln Asp Ala Ser Gln Gly Ala Gly Gln Asp Ala Asn
50 55 60

Pro Asp Pro Thr Leu Pro Lys Pro Pro Ser Pro Pro Ala Asp Asp Thr
65 70 75 80

Lys Asp Thr Gly Ser Gln Gly Asp Ala Asp Ser Ser Ser Ser Lys Ile
85 90 95

Glu Ile Pro Pro Leu Val Lys Pro Glu Asn His Lys Thr Ile Val Ser
100 105 110

Ala Met Leu Lys Asn Tyr Lys Gly Val Lys Val Thr Gly Thr Cys Gly
115 120 125

Ala Asp Phe Gly Leu Phe Leu Val Pro His Ile Tyr Val His Val Lys
130 135 140

Ser Glu Asp Thr Glu Ile Glu Leu Ser Ser Glu Leu Ala Pro Pro Glu
145 150 155 160

Met Gln Thr Lys Phe Asp Lys Thr Gln Leu Lys Lys Phe Cys Val Lys
165 170 175

Asp Asp Thr Lys Lys Phe Asp Phe Ile Ala Tyr Ile Tyr Lys Asp Ile
180 185 190

Leu Val Phe Lys Trp Lys Val Tyr Glu Glu Gly Leu Ser Lys Glu Gln
195 200 205

Asp Val Asp Glu Met Lys Tyr Leu Leu Pro Asn Leu Lys Gln Pro Ile
210 215 220

Thr Ser Ile Gln Val His Ser Trp Thr Gly Thr Lys Glu Ser Tyr Ile
225 230 235 240

Leu Glu Ser Lys Asp Tyr Val Leu Gly Glu Gly Met Pro Glu Lys Cys
245 250 255

Asp Ala Ile Ala Thr Asp Cys Phe Leu Ser Gly Phe Thr Asp Ile Gly
260 265 270

Lys Cys Phe Gln Cys Lys Leu Leu Met Gln Glu Lys Asn Ile Asn Asp
275 280 285

Ser Cys Phe Lys Tyr Val Ser Ser Asn Gln Lys Glu Leu Ile Lys Lys
290 295 300

Gln Leu Lys Ile Thr Ala Gln Asp Asp Glu Glu Ser Ser Glu Tyr His
305 310 315 320

Leu Ser Glu Ser Ile Lys Asn Leu Leu Lys Asn Ile Tyr Lys Lys Asn
325 330 335

Asn Asp Asp Asn Lys Lys Lys Glu Leu Leu His Phe Glu Asn Val Asn
340 345 350

Ser Ala Leu Lys Ser Glu Leu Leu Asn Tyr Cys Asn Leu Leu Lys Glu
355 360 365

Val Asn Met Asn Gly Val Leu Lys Asp His Gln Leu Gly Asn Val Gln
370 375 380

Asp Val Phe Asn Asn Leu Thr Lys Leu Leu Glu Glu His Lys Glu Glu
385 390 395 400

Asn Asp Asn Val Leu Tyr His Lys Met Lys Asn Glu Ala Leu Cys Leu
405 410 415

Lys Asn Val Asn Asp Trp Met Lys Asn Lys Thr Gly Leu Leu Leu Pro

420										425					430						
Gln	Leu	Ser	Tyr	Asp	Leu	Thr	Tyr	Lys	Asn	Asn	Asn	Phe	Thr	Glu	Phe						
		435					440					445									
Thr	Gln	Asn	Lys	Ser	Tyr	Thr	Ser	Gln	Asn	Ile	Val	Asp	Lys	Leu	Tyr						
	450					455					460										
Cys	Asn	His	Glu	Tyr	Cys	Asn	Arg	Leu	Lys	Asp	His	Asn	Asn	Cys	Ile						
465					470					475					480						
Ser	Lys	Ile	Asn	Val	Glu	Asp	Gln	Lys	Asn	Cys	Ala	Leu	Ser	Trp	Ala						
				485					490					495							
Phe	Ala	Ser	Lys	Tyr	His	Leu	Glu	Thr	Ile	Lys	Cys	Met	Lys	Gly	Tyr						
			500					505					510								
Glu	Pro	Leu	Asn	Ala	Ser	Val	Leu	Tyr	Val	Thr	Asn	Cys	Leu	Lys	Asn						
		515					520					525									
Lys	Asn	Lys	Asp	Val	Cys	Thr	Glu	Gly	Ser	Asn	Pro	Leu	Val	Phe	Leu						
	530					535					540										
Glu	Thr	Ile	Glu	Glu	Lys	Gly	Phe	Leu	Pro	Thr	Glu	Ser	Asn	Tyr	Pro						
					550					555					560						
Tyr	Asp	Gln	Ser	Lys	Val	Gly	Asp	Ile	Cys	Pro	Gln	Leu	Gln	Asn	Asp						
				565					570					575							
Trp	Asp	Asn	Val	Phe	Glu	Asn	Thr	Lys	Val	Leu	Asp	Tyr	Asn	Asn	Gly						
			580					585					590								
Pro	Phe	Ser	Val	Gly	Thr	Lys	Gly	Tyr	Ile	Ala	Tyr	Glu	Ser	Glu	Ala						
		595					600					605									
Phe	Gln	Lys	Asp	Met	His	Ser	Phe	Val	Lys	Leu	Val	Lys	Asp	Glu	Ile						
	610					615					620										
Met	Asn	Lys	Gly	Ser	Val	Ile	Ala	Tyr	Val	Lys	Ala	Glu	Asn	Val	Leu						
625					630					635					640						

Gly Tyr Glu Leu Asn Gly Lys Lys Val Gln Asn Leu Cys Gly Asp Lys
645 650 655

Thr Pro Asp His Val Val Asn Ile Val Gly Tyr Gly Asn Tyr Ile Asn
660 665 670

Asn Lys Gly Glu Lys Lys Ser Tyr Trp Ile Val Arg Asn Ser Trp Gly
675 680 685

Lys Tyr Trp Gly Asp Asp Gly Tyr Phe Lys Val Asp Met Tyr Gly Pro
690 695 700

Ser Thr Cys Glu Asp Asn Phe Ile His Thr Val Val Val Phe Asn Val
705 710 715 720

Gln Val Pro Ile Asn Glu Lys Phe Asp Lys Lys Glu His Asp Ile Tyr
725 730 735

Asn Tyr Tyr Leu Lys Thr Ser Pro Glu Phe Tyr His Asn Leu Tyr Tyr
740 745 750

Lys Thr Phe Asn Ser Asn Lys Glu Glu Lys Ser Met Asn Lys Asn Ser
755 760 765

Tyr Val Tyr Gly Gln Asp Thr Thr Pro Val Glu Asn Glu Ala Pro Arg
770 775 780

Ser Gly Val Gln Lys Pro Thr Glu Leu Ser Ser Thr Glu Ser Gln Thr
785 790 795 800

Val Ser Pro Pro Asn Glu Ser Gln Thr Glu Ser Leu Leu Ser Gly Gly
805 810 815

Ser Gln Val Thr Asn Pro Thr Leu Thr Gln Ser Thr Ser Ser Ser Ser
820 825 830

Gly Gln Gln Glu Thr Gly Pro Leu Ser Thr Gln Gly Leu Ser Pro Ala
835 840 845

Thr Gly Asp Pro Lys Gly Lys Glu Gln Glu Ala Ser Pro Ala Glu Gly
850 855 860

Leu Ser Gly Val Leu Asn Pro Thr Lys Glu Val Thr Ser Glu Glu Lys
865 870 875 880

Ile Gln Ile Ile His Leu Leu Lys His Ile Lys Asn Ser Lys Ile Arg
885 890 895

Arg Gly Leu Val Lys Tyr Asn His Glu Phe Glu Val Gly Asp Asn Ser
900 905 910

Cys Ser Arg Ser Thr Ser Lys Asn Ala Glu Met His Asp Glu Cys Val
915 920 925

Asn Ile Cys Glu Lys Tyr Trp Pro Glu Cys Arg Gly Thr Ala Val Pro
930 935 940

Gly Tyr Cys Leu Ser Thr His Asp Asp Lys Asn Glu Cys Asp Phe Cys
945 950 955 960

Tyr Val

<210> 63
<211> 997
<212> PRT
<213> 惡性瘡原蟲

<400> 63

Met Lys Ser Tyr Ile Ser Leu Phe Phe Ile Leu Cys Val Ile Phe Asn
1 5 10 15

Lys Asn Val Ile Lys Cys Thr Gly Glu Ser Gln Thr Gly Asn Thr Gly
20 25 30

Gly Gly Gln Ala Gly Asn Thr Gly Gly Asp Gln Ala Gly Ser Thr Gly
35 40 45

Gly Ser Pro Gln Gly Ser Thr Gly Ala Ser Pro Gln Gly Ser Thr Gly
50 55 60

Ala Ser Pro Gln Gly Ser Thr Gly Ala Ser Gln Pro Gly Ser Ser Glu
65 70 75 80

Pro Ser Asn Pro Val Ser Ser Gly His Ser Val Ser Thr Val Ser Val
85 90 95

Ser Gln Thr Ser Thr Ser Ser Glu Lys Gln Asp Thr Ile Gln Val Lys
100 105 110

Ser Ala Leu Leu Lys Asp Tyr Met Gly Leu Lys Val Thr Gly Pro Cys
115 120 125

Asn Glu Asn Phe Ile Met Phe Leu Val Pro His Ile Tyr Ile Asp Val
130 135 140

Asp Thr Glu Asp Thr Asn Ile Glu Leu Arg Thr Thr Leu Lys Lys Thr
145 150 155 160

Asn Asn Ala Ile Ser Phe Glu Ser Asn Ser Gly Ser Leu Glu Lys Lys
165 170 175

Lys Tyr Val Lys Leu Pro Ser Asn Gly Thr Thr Gly Glu Gln Gly Ser
180 185 190

Ser Thr Gly Thr Val Arg Gly Asp Thr Glu Pro Ile Ser Asp Ser Ser
195 200 205

Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
210 215 220

Ser Ser Ser Ser Ser Ser Ser Ser Ser Glu Ser Leu Pro Ala Asn Gly
225 230 235 240

Pro Asp Ser Pro Thr Val Lys Pro Pro Arg Asn Leu Gln Asn Ile Cys
245 250 255

Glu Thr Gly Lys Asn Phe Lys Leu Val Val Tyr Ile Lys Glu Asn Thr
260 265 270

Leu Ile Leu Lys Trp Lys Val Tyr Gly Glu Thr Lys Asp Thr Thr Glu
275 280 285

Asn Asn Lys Val Asp Val Arg Lys Tyr Leu Ile Asn Glu Lys Glu Thr
290 295 300

Pro Phe Thr Asn Ile Leu Ile His Ala Tyr Lys Glu His Asn Gly Thr
305 310 315 320

Asn Leu Ile Glu Ser Lys Asn Tyr Ala Ile Gly Ser Asp Ile Pro Glu
325 330 335

Lys Cys Asp Thr Leu Ala Ser Asn Cys Phe Leu Ser Gly Asn Phe Asn
340 345 350

Ile Glu Lys Cys Phe Gln Cys Ala Leu Leu Val Glu Lys Glu Asn Lys
355 360 365

Asn Asp Val Cys Tyr Lys Tyr Leu Ser Glu Asp Ile Val Ser Lys Phe
370 375 380

Lys Glu Ile Lys Ala Glu Thr Glu Asp Asp Asp Glu Asp Asp Tyr Thr
385 390 395 400

Glu Tyr Lys Leu Thr Glu Ser Ile Asp Asn Ile Leu Val Lys Met Phe
405 410 415

Lys Thr Asn Glu Asn Asn Asp Lys Ser Glu Leu Ile Lys Leu Glu Glu
420 425 430

Val Asp Asp Ser Leu Lys Leu Glu Leu Met Asn Tyr Cys Ser Leu Leu
435 440 445

Lys Asp Val Asp Thr Thr Gly Thr Leu Asp Asn Tyr Gly Met Gly Asn
450 455 460

Glu Met Asp Ile Phe Asn Asn Leu Lys Arg Leu Leu Ile Tyr His Ser
465 470 475 480

Glu Glu Asn Ile Asn Thr Leu Lys Asn Lys Phe Arg Asn Ala Ala Val
485 490 495

Cys Leu Lys Asn Val Asp Asp Trp Ile Val Asn Lys Arg Gly Leu Val
500 505 510

Leu Pro Glu Leu Asn Tyr Asp Leu Glu Tyr Phe Asn Glu His Leu Tyr

515	520	525
Asn Asp Lys Asn Ser Pro Glu Asp Lys Asp Asn Lys Gly Lys Gly Val		
530	535	540
Val His Val Asp Thr Thr Leu Glu Lys Glu Asp Thr Leu Ser Tyr Asp		
545	550	555
Asn Ser Asp Asn Met Phe Cys Asn Lys Glu Tyr Cys Asn Arg Leu Lys		
	565	570
Asp Glu Asn Asn Cys Ile Ser Asn Leu Gln Val Glu Asp Gln Gly Asn		
	580	585
Cys Asp Thr Ser Trp Ile Phe Ala Ser Lys Tyr His Leu Glu Thr Ile		
	595	600
Arg Cys Met Lys Gly Tyr Glu Pro Thr Lys Ile Ser Ala Leu Tyr Val		
	610	620
Ala Asn Cys Tyr Lys Gly Glu His Lys Asp Arg Cys Asp Glu Gly Ser		
625	630	635
Ser Pro Met Glu Phe Leu Gln Ile Ile Glu Asp Tyr Gly Phe Leu Pro		
	645	650
Ala Glu Ser Asn Tyr Pro Tyr Asn Tyr Val Lys Val Gly Glu Gln Cys		
	660	665
Pro Lys Val Glu Asp His Trp Met Asn Leu Trp Asp Asn Gly Lys Ile		
	675	680
Leu His Asn Lys Asn Glu Pro Asn Ser Leu Asp Gly Lys Gly Tyr Thr		
	690	700
Ala Tyr Glu Ser Glu Arg Phe His Asp Asn Met Asp Ala Phe Val Lys		
705	710	715
Ile Ile Lys Thr Glu Val Met Asn Lys Gly Ser Val Ile Ala Tyr Ile		
	725	730
		735

Lys Ala Glu Asn Val Met Gly Tyr Glu Phe Ser Gly Lys Lys Val Gln
 740 745 750
 Asn Leu Cys Gly Asp Asp Thr Ala Asp His Ala Val Asn Ile Val Gly
 755 760 765
 Tyr Gly Asn Tyr Val Asn Ser Glu Gly Glu Lys Lys Ser Tyr Trp Ile
 770 775 780
 Val Arg Asn Ser Trp Gly Pro Tyr Trp Gly Asp Glu Gly Tyr Phe Lys
 785 790 795 800
 Val Asp Met Tyr Gly Pro Thr His Cys His Phe Asn Phe Ile His Ser
 805 810 815
 Val Val Ile Phe Asn Val Asp Leu Pro Met Asn Asn Lys Thr Thr Lys
 820 825 830
 Lys Glu Ser Lys Ile Tyr Asp Tyr Tyr Leu Lys Ala Ser Pro Glu Phe
 835 840 845
 Tyr His Asn Leu Tyr Phe Lys Asn Phe Asn Val Gly Lys Lys Asn Leu
 850 855 860
 Phe Ser Glu Lys Glu Asp Asn Glu Asn Asn Lys Lys Leu Gly Asn Asn
 865 870 875 880
 Tyr Ile Ile Phe Gly Gln Asp Thr Ala Gly Ser Gly Gln Ser Gly Lys
 885 890 895
 Glu Ser Asn Thr Ala Leu Glu Ser Ala Gly Thr Ser Asn Glu Val Ser
 900 905 910
 Glu Arg Val His Val Tyr His Ile Leu Lys His Ile Lys Asp Gly Lys
 915 920 925
 Ile Arg Met Gly Met Arg Lys Tyr Ile Asp Thr Gln Asp Val Asn Lys
 930 935 940
 Lys His Ser Cys Thr Arg Ser Tyr Ala Phe Asn Pro Glu Asn Tyr Glu
 945 950 955 960

Lys Cys Val Asn Leu Cys Asn Val Asn Trp Lys Thr Cys Glu Glu Lys
965 970 975

Thr Ser Pro Gly Leu Cys Leu Ser Lys Leu Asp Thr Asn Asn Glu Cys
980 985 990

Tyr Phe Cys Tyr Val
995

<210> 64
<211> 1233
<212> PRT
<213> 惡性瘡原蟲

<400> 64

Met Arg Asn Leu Phe His Ile Thr Ile Cys Leu Val Thr Leu Asn Leu
1 5 10 15

Phe Ile Leu Glu Ile Asn Ala Lys Thr Asn Thr Ser Glu Asn Arg Asn
20 25 30

Lys Arg Ile Gly Gly Pro Lys Leu Arg Gly Asn Val Thr Ser Asn Ile
35 40 45

Lys Phe Pro Ser Asp Asn Lys Gly Lys Ile Ile Arg Gly Ser Asn Asp
50 55 60

Lys Leu Asn Lys Asn Ser Glu Asp Val Leu Glu Gln Ser Glu Lys Ser
65 70 75 80

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

Lys Glu Ser Ile Phe Ile Gln Glu Asp Gln Glu Gly Gln Thr His Ser
100 105 110

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

Asp Ser Lys Asn Glu Ser Ser Asp Ile Ile Ser Val Asn Asn Lys Ser
130 135 140

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

Asp Gln Ser Gln His Asn Ile Asn Val Leu Gln Glu Asn Asn Ile Asn
370 375 380

Asn His Gln Leu Glu Pro Gln Glu Lys Pro Asn Ile Glu Ser Phe Glu
385 390 395 400

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

Glu Glu Ile Ile Asp Asp Val Pro Ser Pro Lys His Ser Asn His Glu
420 425 430

Thr Phe Glu Glu Glu Thr Ser Glu Ser Glu His Glu Glu Ala Val Ser
435 440 445

Glu Lys Asn Ala His Glu Thr Val Glu His Glu Glu Thr Val Ser Gln
450 455 460

Glu Ser Asn Pro Glu Lys Ala Asp Asn Asp Gly Asn Val Ser Gln Asn
465 470 475 480

Ser Asn Asn Glu Leu Asn Glu Asn Glu Phe Val Glu Ser Glu Lys Ser
485 490 495

Glu His Glu Pro Ala Glu Asn Glu Glu Ser Ser Leu Glu Glu Gly His
500 505 510

His Glu Glu Ile Val Pro Glu Gln Asn Asn Glu Glu Ser Gly Glu Ser
515 520 525

Lys Leu Val Asp Asn Asp Glu Gly Gly Phe Glu Glu Ala His His Glu
530 535 540

Asn Phe Ser Ser Glu Val Ser Asn Ser Glu Leu Asn Glu Asn Glu Phe
545 550 555 560

Val Glu Ser Asp Lys Ser Val Thr Glu Pro Ala Glu His Glu Glu Val
565 570 575

Val Ser Glu Glu Ser Asn Pro Glu Pro Ala Glu Asn Glu Glu Ser Ser

580	585	590
Ile Glu Glu Ala His Gln Glu Glu Ile Val Pro Glu Gln Asn Asp Glu		
595	600	605
Glu Ser Gly Glu Ser Gly Leu Val Asp Asn Glu Glu Gly Asp Phe Glu		
610	615	620
Glu Pro Asn His Glu Glu Phe Glu Pro Asp Gln Asn Asp Ser Glu Leu		
625	630	635
Ser Glu Asn Glu Leu Val Glu Ser Glu Lys Ser Val Ser Glu Pro Ala		
645	650	655
Glu His Val Glu Ile Val Ser Glu Lys Ser Val Ser Glu Pro Ala Glu		
660	665	670
His Val Glu Ile Val Ser Glu Lys Ser Thr Ser Glu Pro Ala Glu His		
675	680	685
Val Glu Ser Val Ser Glu Gln Ser Asn Asn Glu Pro Ser Glu Lys Lys		
690	695	700
Asp Gly Pro Val Pro Ser Lys Pro Phe Glu Glu Ile Glu Lys Val Asp		
705	710	715
Val Gln Pro Lys Ile Val Asp Leu Gln Ile Ile Glu Pro Asn Phe Val		
725	730	735
Asp Ser Gln Pro Asn Pro Gln Glu Pro Val Glu Pro Ser Phe Val Lys		
740	745	750
Ile Glu Lys Val Pro Ser Glu Glu Asn Lys His Ala Ser Val Asp Pro		
755	760	765
Glu Val Lys Glu Lys Glu Asn Val Ser Glu Val Val Glu Glu Lys Gln		
770	775	780
Asn Ser Gln Glu Ser Val Glu Glu Ile Pro Val Asn Glu Asp Glu Phe		
785	790	795
		800

Glu Asp Val His Thr Glu Gln Leu Asp Leu Asp His Lys Thr Val Asp
805 810 815

Pro Glu Ile Val Glu Val Glu Glu Ile Pro Ser Glu Leu His Glu Asn
820 825 830

Glu Val Ala His Pro Glu Ile Val Glu Ile Glu Glu Val Phe Pro Glu
835 840 845

Pro Asn Gln Asn Asn Glu Phe Gln Glu Ile Asn Glu Asp Asp Lys Ser
850 855 860

Ala His Ile Gln His Glu Ile Val Glu Val Glu Glu Ile Leu Pro Glu
865 870 875 880

Asp Asp Lys Asn Glu Lys Val Glu His Glu Ile Val Glu Val Glu Glu
885 890 895

Ile Leu Pro Glu Asp Lys Asn Glu Lys Val Gln His Glu Ile Val Glu
900 905 910

Val Glu Glu Ile Leu Pro Glu Asp Lys Asn Glu Lys Val Glu His Glu
915 920 925

Ile Val Glu Val Glu Glu Ile Leu Pro Glu Asp Lys Asn Glu Lys Gly
930 935 940

Gln His Glu Ile Val Glu Val Glu Glu Ile Leu Pro Glu Asp Lys Asn
945 950 955 960

Glu Lys Val Gln His Glu Ile Val Glu Val Glu Glu Ile Leu Pro Glu
965 970 975

Asp Lys Asn Glu Lys Gly Gln His Glu Ile Val Glu Val Glu Glu Ile
980 985 990

Leu Pro Glu Asp Lys Asn Glu Lys Val Glu His Glu Ile Val Glu Val
995 1000 1005

Glu Glu Ile Leu Pro Glu Asp Lys Asn Glu Lys Gly Gln His Glu
1010 1015 1020

Ile	Val	Glu	Val	Glu	Glu	Ile	Leu	Pro	Glu	Asp	Asp	Lys	Asn	Glu
1025						1030					1035			
Lys	Gly	Gln	His	Glu	Ile	Val	Glu	Val	Glu	Glu	Ile	Leu	Pro	Glu
1040						1045					1050			
Ile	Val	Glu	Ile	Glu	Glu	Val	Pro	Ser	Gln	Thr	Asn	Asn	Asn	Glu
1055						1060					1065			
Asn	Ile	Glu	Thr	Ile	Lys	Pro	Glu	Glu	Lys	Lys	Asn	Glu	Phe	Ser
1070						1075					1080			
Val	Val	Glu	Glu	Lys	Ala	Ile	Pro	Gln	Glu	Pro	Val	Val	Pro	Thr
1085						1090					1095			
Leu	Asn	Glu	Asn	Glu	Asn	Val	Thr	Pro	Lys	Pro	Ser	Glu	Gly	Glu
1100						1105					1110			
Ser	Thr	Lys	Pro	Asp	Ile	Val	Gln	Ile	Lys	Ile	Val	Gln	Glu	Asn
1115						1120					1125			
Lys	Pro	Asn	Lys	Lys	Glu	Thr	Pro	Val	Val	Asp	Gly	Pro	Lys	His
1130						1135					1140			
Val	Glu	Gln	Asn	Ile	Gln	Glu	Asp	Asp	Asn	Asp	Glu	Glu	Asp	Asp
1145						1150					1155			
Asp	Asp	Ile	Asp	Phe	Glu	Gly	Leu	Ser	Arg	Lys	Asp	Asp	Glu	Lys
1160						1165					1170			
Asp	Ser	Ser	Asn	Lys	Asn	Lys	Lys	Lys	Ser	Ser	Phe	Ile	Thr	Tyr
1175						1180					1185			
Ile	Ser	Thr	Lys	Lys	Phe	Lys	Lys	Val	Ser	Gln	Thr	Ile	Val	Ser
1190						1195					1200			
Val	Met	Ile	Asn	Ala	Tyr	Asp	Gly	Val	Ile	Gln	Val	Val	Ser	Thr
1205						1210					1215			
Ile	Lys	Gly	Ile	Ala	Lys	Asp	Ile	Val	Ile	Phe	Phe	Gln	Asn	Ile
1220						1225					1230			

<210> 65
<211> 396
<212> PRT
<213> 惡性瘧原蟲

<400> 65

Asp Ile Pro Lys Glu Ser Ile Phe Ile Gln Glu Asp Gln Glu Gly Gln
1 5 10 15

Thr His Ser Glu Leu Asn Pro Glu Thr Ser Glu His Ser Lys Asp Leu
20 25 30

Asn Asn Asn Asp Ser Lys Asn Glu Ser Ser Asp Ile Ile Ser Val Asn
35 40 45

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

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

Ser Thr Glu Pro Phe Pro Asn Gln Lys His Lys Asp Leu Gln Gln Asp
85 90 95

Leu Asn Asp Glu Pro Leu Glu Pro Phe Pro Thr Gln Ile His Lys Asp
100 105 110

Tyr Lys Glu Lys Asn Leu Ile Asn Glu Glu Asp Ser Glu Pro Phe Pro
115 120 125

Arg Gln Lys His Lys Lys Val Asp Asn His Asn Glu Glu Lys Asn Val
130 135 140

Phe His Glu Asn Gly Ser Ala Asn Gly Asn Gln Gly Ser Leu Lys Leu
145 150 155 160

Lys Ser Phe Asp Glu His Leu Lys Asp Glu Lys Ile Glu Asn Glu Pro
165 170 175

Leu Val His Glu Asn Leu Ser Ile Pro Asn Asp Pro Ile Glu Gln Ile
180 185 190

Leu Asn Gln Pro Glu Gln Glu Thr Asn Ile Gln Glu Gln Leu Tyr Asn
195 200 205

Glu Lys Gln Asn Val Glu Glu Lys Gln Asn Ser Gln Ile Pro Ser Leu
210 215 220

Asp Leu Lys Glu Pro Thr Asn Glu Asp Ile Leu Pro Asn His Asn Pro
225 230 235 240

Leu Glu Asn Ile Lys Gln Ser Glu Ser Glu Ile Asn His Val Gln Asp
245 250 255

His Ala Leu Pro Lys Glu Asn Ile Ile Asp Lys Leu Asp Asn Gln Lys
260 265 270

Glu His Ile Asp Gln Ser Gln His Asn Ile Asn Val Leu Gln Glu Asn
275 280 285

Asn Ile Asn Asn His Gln Leu Glu Pro Gln Glu Lys Pro Asn Ile Glu
290 295 300

Ser Phe Glu Pro Lys Asn Ile Asp Ser Glu Ile Ile Leu Pro Glu Asn
305 310 315 320

Val Glu Thr Glu Glu Ile Ile Asp Asp Val Pro Ser Pro Lys His Ser
325 330 335

Asn His Glu Thr Phe Glu Glu Glu Thr Ser Glu Ser Glu His Glu Glu
340 345 350

Ala Val Ser Glu Lys Asn Ala His Glu Thr Val Glu His Glu Glu Thr
355 360 365

Val Ser Gln Glu Ser Asn Pro Glu Lys Ala Asp Asn Asp Gly Asn Val
370 375 380

Ser Gln Asn Ser Asn Asn Glu Leu Asn Glu Asn Glu
385 390 395

<210> 66

<211> 436
<212> PRT
<213> 惡性瘡原蟲

<400> 66

Asp Gly Pro Val Pro Ser Lys Pro Phe Glu Glu Ile Glu Lys Val Asp
1 5 10 15

Val Gln Pro Lys Ile Val Asp Leu Gln Ile Ile Glu Pro Asn Phe Val
20 25 30

Asp Ser Gln Pro Asn Pro Gln Glu Pro Val Glu Pro Ser Phe Val Lys
35 40 45

Ile Glu Lys Val Pro Ser Glu Glu Asn Lys His Ala Ser Val Asp Pro
50 55 60

Glu Val Lys Glu Lys Glu Asn Val Ser Glu Val Val Glu Glu Lys Gln
65 70 75 80

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

Glu Asp Val His Thr Glu Gln Leu Asp Leu Asp His Lys Thr Val Asp
100 105 110

Pro Glu Ile Val Glu Val Glu Glu Ile Pro Ser Glu Leu His Glu Asn
115 120 125

Glu Val Ala His Pro Glu Ile Val Glu Ile Glu Glu Val Phe Pro Glu
130 135 140

Pro Asn Gln Asn Asn Glu Phe Gln Glu Ile Asn Glu Asp Asp Lys Ser
145 150 155 160

Ala His Ile Gln His Glu Ile Val Glu Val Glu Glu Ile Leu Pro Glu
165 170 175

Asp Asp Lys Asn Glu Lys Val Glu His Glu Ile Val Glu Val Glu Glu
180 185 190

Ile Leu Pro Glu Asp Lys Asn Glu Lys Val Gln His Glu Ile Val Glu

195	200	205
Val Glu Glu Ile Leu Pro Glu Asp Lys Asn Glu Lys Val Glu His Glu		
210	215	220
Ile Val Glu Val Glu Glu Ile Leu Pro Glu Asp Lys Asn Glu Lys Gly		
225	230	235
Gln His Glu Ile Val Glu Val Glu Glu Ile Leu Pro Glu Asp Lys Asn		
245	250	255
Glu Lys Val Gln His Glu Ile Val Glu Val Glu Glu Ile Leu Pro Glu		
260	265	270
Asp Lys Asn Glu Lys Gly Gln His Glu Ile Val Glu Val Glu Glu Ile		
275	280	285
Leu Pro Glu Asp Lys Asn Glu Lys Val Glu His Glu Ile Val Glu Val		
290	295	300
Glu Glu Ile Leu Pro Glu Asp Lys Asn Glu Lys Gly Gln His Glu Ile		
305	310	315
Val Glu Val Glu Glu Ile Leu Pro Glu Asp Asp Lys Asn Glu Lys Gly		
325	330	335
Gln His Glu Ile Val Glu Val Glu Glu Ile Leu Pro Glu Ile Val Glu		
340	345	350
Ile Glu Glu Val Pro Ser Gln Thr Asn Asn Asn Glu Asn Ile Glu Thr		
355	360	365
Ile Lys Pro Glu Glu Lys Lys Asn Glu Phe Ser Val Val Glu Glu Lys		
370	375	380
Ala Ile Pro Gln Glu Pro Val Val Pro Thr Leu Asn Glu Asn Glu Asn		
385	390	395
Val Thr Pro Lys Pro Ser Glu Gly Glu Ser Thr Lys Pro Asp Ile Val		
405	410	415

Gln Ile Lys Ile Val Gln Glu Asn Lys Pro Asn Lys Lys Glu Thr Pro
420 425 430

Val Val Asp Gly
435

<210> 67
<211> 824
<212> PRT
<213> 惡性瘡原蟲

<400> 67

Met Arg Leu Ser Lys Val Ser Asp Ile Lys Ser Thr Gly Val Ser Asn
1 5 10 15

Tyr Lys Asn Phe Asn Ser Lys Asn Ser Ser Lys Tyr Ser Leu Met Glu
20 25 30

Val Ser Lys Lys Asn Glu Lys Lys Asn Ser Leu Gly Ala Phe His Ser
35 40 45

Lys Lys Ile Leu Leu Ile Phe Gly Ile Ile Tyr Val Val Leu Leu Asn
50 55 60

Ala Tyr Ile Cys Gly Asp Lys Tyr Glu Lys Ala Val Asp Tyr Gly Phe
65 70 75 80

Arg Glu Ser Arg Ile Leu Ala Glu Gly Glu Asp Thr Cys Ala Arg Lys
85 90 95

Glu Lys Thr Thr Leu Arg Lys Ser Lys Gln Lys Thr Ser Thr Arg Thr
100 105 110

Val Ala Thr Gln Thr Lys Lys Asp Glu Glu Asn Lys Ser Val Val Thr
115 120 125

Glu Glu Gln Lys Val Glu Ser Asp Ser Glu Lys Gln Lys Arg Thr Lys
130 135 140

Lys Val Val Lys Lys Gln Ile Asn Ile Gly Asp Thr Glu Asn Gln Lys
145 150 155 160

Glu Gly Lys Asn Val Lys Lys Val Ile Lys Lys Glu Lys Lys Lys Glu
165 170 175

Glu Ser Gly Lys Pro Glu Glu Asn Lys His Ala Asn Glu Ala Ser Lys
180 185 190

Lys Gln Glu Pro Lys Ala Ser Lys Val Ser Gln Lys Pro Ser Thr Ser
195 200 205

Thr Arg Ser Asn Asn Glu Val Lys Ile Arg Ala Ala Ser Asn Gln Glu
210 215 220

Thr Leu Thr Ser Ala Asp Pro Glu Gly Gln Ile Met Arg Glu Tyr Ala
225 230 235 240

Ala Asp Pro Glu Tyr Arg Lys His Leu Glu Ile Phe Tyr Lys Ile Leu
245 250 255

Thr Asn Thr Asp Pro Asn Asp Glu Val Glu Arg Arg Asn Ala Asp Asn
260 265 270

Lys Glu Asp Leu Thr Ser Ala Asp Pro Glu Gly Gln Ile Met Arg Glu
275 280 285

Tyr Ala Ser Asp Pro Glu Tyr Arg Lys His Leu Glu Ile Phe Tyr Lys
290 295 300

Ile Leu Thr Asn Thr Asp Pro Asn Asp Asp Val Glu Arg Arg Asn Ala
305 310 315 320

Asp Asn Lys Glu Asp Leu Thr Ser Ala Asp Pro Glu Gly Gln Ile Met
325 330 335

Arg Glu Tyr Ala Ala Asp Pro Glu Tyr Arg Lys His Leu Glu Val Phe
340 345 350

His Lys Ile Leu Thr Asn Thr Asp Pro Asn Asp Glu Val Glu Arg Arg
355 360 365

Asn Ala Asp Asn Lys Glu Asp Leu Thr Ser Ala Asp Pro Glu Gly Gln
370 375 380

Ile	Met	Arg	Glu	Tyr	Ala	Ala	Asp	Pro	Glu	Tyr	Arg	Lys	His	Leu	Glu
385					390					395					400
Val	Phe	His	Lys	Ile	Leu	Thr	Asn	Thr	Asp	Pro	Asn	Asp	Glu	Val	Glu
				405					410					415	
Arg	Arg	Asn	Ala	Asp	Asn	Lys	Glu	Leu	Thr	Ser	Ser	Asp	Pro	Glu	Gly
			420					425					430		
Gln	Ile	Met	Arg	Glu	Tyr	Ala	Ala	Asp	Pro	Glu	Tyr	Arg	Lys	His	Leu
		435					440					445			
Glu	Val	Phe	His	Lys	Ile	Leu	Thr	Asn	Thr	Asp	Pro	Asn	Asp	Glu	Val
	450					455					460				
Glu	Arg	Arg	Asn	Ala	Asp	Asn	Lys	Glu	Asp	Leu	Thr	Ser	Ala	Asp	Pro
465					470					475					480
Glu	Gly	Gln	Ile	Met	Arg	Glu	Tyr	Ala	Ala	Asp	Pro	Glu	Tyr	Arg	Lys
				485					490					495	
His	Leu	Glu	Val	Phe	His	Lys	Ile	Leu	Thr	Asn	Thr	Asp	Pro	Asn	Asp
			500					505					510		
Glu	Val	Glu	Arg	Arg	Asn	Ala	Asp	Asn	Lys	Glu	Asp	Leu	Thr	Ser	Ala
		515					520					525			
Asp	Pro	Glu	Gly	Gln	Ile	Met	Arg	Glu	Tyr	Ala	Ala	Asp	Pro	Glu	Tyr
	530					535					540				
Arg	Lys	His	Leu	Glu	Ile	Phe	His	Lys	Ile	Leu	Thr	Asn	Thr	Asp	Pro
545					550					555					560
Asn	Asp	Glu	Val	Glu	Arg	Arg	Asn	Ala	Asp	Asn	Lys	Glu	Asp	Leu	Thr
				565					570					575	
Ser	Ala	Asp	Pro	Glu	Gly	Gln	Ile	Met	Arg	Glu	Tyr	Ala	Ala	Asp	Pro
			580					585					590		
Glu	Tyr	Arg	Lys	His	Leu	Glu	Ile	Phe	Tyr	Lys	Ile	Leu	Thr	Asn	Thr
		595					600					605			

Asp	Pro	Asn	Asp	Glu	Val	Glu	Arg	Arg	Asn	Ala	Asp	Asn	Lys	Glu	Glu
	610					615					620				
Leu	Thr	Ser	Ser	Asp	Pro	Glu	Gly	Gln	Ile	Met	Arg	Glu	Tyr	Ala	Ala
625					630					635					640
Asp	Pro	Glu	Tyr	Arg	Lys	His	Leu	Glu	Ile	Phe	His	Lys	Ile	Leu	Thr
				645					650					655	
Asn	Thr	Asp	Pro	Asn	Asp	Glu	Val	Glu	Arg	Arg	Asn	Ala	Asp	Asn	Lys
			660					665					670		
Glu	Asp	Leu	Thr	Ser	Ala	Asp	Pro	Glu	Gly	Gln	Ile	Met	Arg	Glu	Tyr
		675					680					685			
Ala	Ala	Asp	Pro	Glu	Tyr	Arg	Lys	His	Leu	Glu	Ile	Phe	Tyr	Lys	Ile
	690					695					700				
Leu	Thr	Asn	Thr	Asp	Pro	Asn	Asp	Glu	Val	Glu	Arg	Arg	Asn	Ala	Asp
705					710					715					720
Asn	Lys	Glu	Asp	Leu	Thr	Ser	Ala	Asp	Pro	Glu	Gly	Gln	Ile	Met	Arg
				725					730					735	
Glu	Tyr	Ala	Ser	Asp	Pro	Glu	Tyr	Arg	Lys	His	Leu	Glu	Ile	Phe	Tyr
			740					745					750		
Lys	Ile	Leu	Thr	Asn	Thr	Asp	Pro	Asn	Asp	Asp	Val	Glu	Arg	Arg	Asn
		755					760					765			
Ala	Asp	Asn	Lys	Glu	Asp	Leu	Thr	Ser	Ala	Asp	Pro	Glu	Gly	Gln	Ile
	770					775					780				
Met	Arg	Glu	Tyr	Ala	Ala	Asp	Pro	Glu	Tyr	Arg	Lys	His	Leu	Glu	Val
785					790					795					800
Phe	His	Lys	Ile	Leu	Thr	Asn	Thr	Asp	Pro	Asn	Asp	Glu	Val	Glu	Arg
				805					810					815	
Gln	Asn	Ala	Asp	Asn	Asn	Glu	Ala								

820

<210> 68
<211> 41
<212> PRT
<213> 惡性瘡原蟲

<400> 68

Gly Met Asn Asn Met Asn Gly Asp Ile Asn Asn Ile Asn Gly Asp Ile
1 5 10 15

Asn Asn Met Asn Gly Asp Ile Asn Asn Met Asn Gly Asp Ile Asn Asn
20 25 30

Met Asn Gly Asp Ile Asn Asn Met Asn
35 40

<210> 69
<211> 37
<212> PRT
<213> 惡性瘡原蟲

<400> 69

Glu Glu Ile Lys Glu Glu Ile Lys Glu Val Lys Glu Glu Ile Lys Glu
1 5 10 15

Val Lys Glu Glu Ile Lys Glu Val Lys Glu Glu Ile Lys Glu Val Lys
20 25 30

Glu Glu Ile Lys Glu
35

<210> 70
<211> 28
<212> PRT
<213> 惡性瘡原蟲

<400> 70

Glu Lys Leu Lys Lys Tyr Asn Asn Glu Ile Ser Ser Leu Lys Lys Glu
1 5 10 15

Leu Asp Ile Leu Asn Glu Lys Met Gly Lys Cys Thr
20 25

<210> 71
<211> 38
<212> PRT
<213> 惡性瘡原蟲

<400> 71

Thr Lys Lys Leu Asn Lys Glu Leu Ser Glu Gly Asn Lys Glu Leu Glu
1 5 10 15

Lys Leu Glu Lys Asn Ile Lys Glu Leu Glu Glu Thr Asn Asn Thr Leu
20 25 30

Glu Asn Asp Ile Lys Val
35

<210> 72
<211> 526
<212> PRT
<213> 惡性瘡原蟲

<400> 72

Met Ile Arg Ile Lys Lys Lys Leu Ile Leu Thr Ile Ile Tyr Ile His
1 5 10 15

Leu Phe Ile Leu Asn Arg Leu Ser Phe Glu Asn Ala Ile Lys Lys Thr
20 25 30

Lys Asn Gln Glu Asn Asn Leu Thr Leu Leu Pro Ile Lys Ser Thr Glu
35 40 45

Glu Glu Lys Asp Asp Ile Lys Asn Gly Lys Asp Ile Lys Lys Glu Ile
50 55 60

Asp Asn Asp Lys Glu Asn Ile Lys Thr Asn Asn Ala Lys Asp His Ser
65 70 75 80

Thr Tyr Ile Lys Ser Tyr Leu Asn Thr Asn Val Asn Asp Gly Leu Lys
85 90 95

Tyr Leu Phe Ile Pro Ser His Asn Ser Phe Ile Lys Lys Tyr Ser Val
100 105 110

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

Thr Asn Leu Phe Glu Gln Leu Ser Cys Tyr Asn Asn Asn Phe Cys Asn
340 345 350

Thr Asn Gly Ile Arg Tyr His Tyr Asp Glu Tyr Ile His Lys Leu Ile
355 360 365

Leu Ser Val Lys Ser Lys Asn Leu Asn Lys Asp Leu Ser Asp Met Thr
370 375 380

Asn Ile Leu Gln Gln Ser Glu Leu Leu Leu Thr Asn Leu Asn Lys Lys
385 390 395 400

Met Gly Ser Tyr Ile Tyr Ile Asp Thr Ile Lys Phe Ile His Lys Glu
405 410 415

Met Lys His Ile Phe Asn Arg Ile Glu Tyr His Thr Lys Ile Ile Asn
420 425 430

Asp Lys Thr Lys Ile Ile Gln Asp Lys Ile Lys Leu Asn Ile Trp Arg
435 440 445

Thr Phe Gln Lys Asp Glu Leu Leu Lys Arg Ile Leu Asp Met Ser Asn
450 455 460

Glu Tyr Ser Leu Phe Ile Thr Ser Asp His Leu Arg Gln Met Leu Tyr
465 470 475 480

Asn Thr Phe Tyr Ser Lys Glu Lys His Leu Asn Asn Ile Phe His His
485 490 495

Leu Ile Tyr Val Leu Gln Met Lys Phe Asn Asp Val Pro Ile Lys Met
500 505 510

Glu Tyr Phe Gln Thr Tyr Lys Lys Asn Lys Pro Leu Thr Gln
515 520 525

<210> 73
<211> 622
<212> PRT
<213> 惡性瘧原蟲

<400> 73

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

Ile Pro Asp Asn Asp Lys Asn Ser Asn Tyr Lys Tyr Pro Ala Val Tyr
 225 230 235 240
 Asp Asp Lys Asp Lys Lys Cys His Ile Leu Tyr Ile Ala Ala Gln Glu
 245 250 255
 Asn Asn Gly Pro Arg Tyr Cys Asn Lys Asp Glu Ser Lys Arg Asn Ser
 260 265 270
 Met Phe Cys Phe Arg Pro Ala Lys Asp Ile Ser Phe Gln Asn Tyr Thr
 275 280 285
 Tyr Leu Ser Lys Asn Val Val Asp Asn Trp Glu Lys Val Cys Pro Arg
 290 295 300
 Lys Asn Leu Gln Asn Ala Lys Phe Gly Leu Trp Val Asp Gly Asn Cys
 305 310 315 320
 Glu Asp Ile Pro His Val Asn Glu Phe Pro Ala Ile Asp Leu Phe Glu
 325 330 335
 Cys Asn Lys Leu Val Phe Glu Leu Ser Ala Ser Asp Gln Pro Lys Gln
 340 345 350
 Tyr Glu Gln His Leu Thr Asp Tyr Glu Lys Ile Lys Glu Gly Phe Lys
 355 360 365
 Asn Lys Asn Ala Ser Met Ile Lys Ser Ala Phe Leu Pro Thr Gly Ala
 370 375 380
 Phe Lys Ala Asp Arg Tyr Lys Ser His Gly Lys Gly Tyr Asn Trp Gly
 385 390 395 400
 Asn Tyr Asn Thr Glu Thr Gln Lys Cys Glu Ile Phe Asn Val Lys Pro
 405 410 415
 Thr Cys Leu Ile Asn Asn Ser Ser Tyr Ile Ala Thr Thr Ala Leu Ser
 420 425 430
 His Pro Ile Glu Val Glu Asn Asn Phe Pro Cys Ser Leu Tyr Lys Asp

435					440					445					
Glu	Ile	Met	Lys	Glu	Ile	Glu	Arg	Glu	Ser	Lys	Arg	Ile	Lys	Leu	Asn
450						455					460				
Asp	Asn	Asp	Asp	Glu	Gly	Asn	Lys	Lys	Ile	Ile	Ala	Pro	Arg	Ile	Phe
465					470					475					480
Ile	Ser	Asp	Asp	Lys	Asp	Ser	Leu	Lys	Cys	Pro	Cys	Asp	Pro	Glu	Met
				485					490					495	
Val	Ser	Asn	Ser	Thr	Cys	Arg	Phe	Phe	Val	Cys	Lys	Cys	Val	Glu	Arg
			500					505					510		
Arg	Ala	Glu	Val	Thr	Ser	Asn	Asn	Glu	Val	Val	Val	Lys	Glu	Glu	Tyr
		515					520					525			
Lys	Asp	Glu	Tyr	Ala	Asp	Ile	Pro	Glu	His	Lys	Pro	Thr	Tyr	Asp	Lys
	530					535					540				
Met	Lys	Ile	Ile	Ile	Ala	Ser	Ser	Ala	Ala	Val	Ala	Val	Leu	Ala	Thr
545					550					555					560
Ile	Leu	Met	Val	Tyr	Leu	Tyr	Lys	Arg	Lys	Gly	Asn	Ala	Glu	Lys	Tyr
				565					570					575	
Asp	Lys	Met	Asp	Glu	Pro	Gln	Asp	Tyr	Gly	Lys	Ser	Asn	Ser	Arg	Asn
			580					585					590		
Asp	Glu	Met	Leu	Asp	Pro	Glu	Ala	Ser	Phe	Trp	Gly	Glu	Glu	Lys	Arg
		595					600					605			
Ala	Ser	His	Thr	Thr	Pro	Val	Leu	Met	Glu	Lys	Pro	Tyr	Tyr		
	610					615					620				
<210> 74															
<211> 217															
<212> PRT															
<213> 惡性瘧原蟲															
<400> 74															
Met	Asn	Lys	Leu	Tyr	Ser	Leu	Phe	Leu	Phe	Leu	Phe	Ile	Gln	Leu	Ser

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

<210> 75
 <211> 2163
 <212> PRT
 <213> 惡性瘧原蟲

<400> 75

Met Val Thr Gln Ser Ser Gly Gly Gly Ala Ala Gly Ser Ser Gly Glu
 1 5 10 15

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

Glu Lys Val Glu Lys Tyr Ala Asn Ser Lys Ile Tyr Lys Glu Ala Leu
 35 40 45

Lys Gly Asp Leu Ser Gln Ala Ser Ile Leu Ser Glu Leu Ala Gly Thr
 50 55 60

Tyr Lys Pro Cys Ala Leu Glu Tyr Glu Tyr Tyr Lys His Thr Asn Gly
 65 70 75 80

Gly Gly Lys Gly Lys Arg Tyr Pro Cys Thr Glu Leu Gly Glu Lys Val
 85 90 95

Glu Pro Arg Phe Ser Asp Thr Leu Gly Gly Gln Cys Thr Asn Lys Lys
 100 105 110

Ile Glu Gly Asn Lys Tyr Ile Lys Gly Lys Asp Val Gly Ala Cys Ala
 115 120 125

Pro Tyr Arg Arg Leu His Leu Cys Ser His Asn Leu Glu Ser Ile Gln
 130 135 140

Thr Asn Asn Tyr Asn Ser Gly Asn Ala Lys His Asn Leu Leu Val Asp
 145 150 155 160

Val Cys Met Ala Ala Lys Tyr Glu Gly Asp Ser Ile Lys Asn Tyr Tyr
 165 170 175

Pro Lys Tyr Gln Arg Thr Tyr Pro Asp Thr Asn Ser Gln Leu Cys Thr
 180 185 190

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

Pro Thr Thr Ile Ile Ile Lys Thr Ala Asn Arg Lys Thr Thr Ile Asn
420 425 430

Asn Leu Tyr Val Lys Glu Phe Tyr Lys Lys Leu Gln Glu Lys Tyr Gly
435 440 445

Asp Val Glu Asn Phe Leu Gln Lys Leu Asn Glu Glu Gln Ile Cys Lys
450 455 460

Asn Gln Pro Tyr Asn Asp Glu Ser Ser Ile Asp Ile Asn Phe Lys Ser
465 470 475 480

Ile Lys Asp Ile Asp Ile Phe Ser His Thr Glu Tyr Cys Gln Ala Cys
485 490 495

Pro Trp Cys Gly Ala Lys Arg Lys Gly Lys Gly Trp Glu Pro Lys Glu
500 505 510

Lys Thr Cys Gly Lys Thr Lys Thr Tyr Asp Pro Lys Lys Thr Thr Asn
515 520 525

Ile Pro Ile Leu Thr Pro Tyr Ile Ser Gln Gln Ser Ile Leu Lys Lys
530 535 540

Tyr Asn Lys Phe Cys Asn Gly Asn Gly Gly Asn Gly Ala Pro Ala Thr
545 550 555 560

Ala Thr Gly Gly Gly Gln Ile Lys Asn Trp Gln Cys His Tyr Glu Gly
565 570 575

Asp Asn Asn Asp Asn Cys Val Glu Gly Glu Trp Lys Glu Phe Lys Glu
580 585 590

Gly Lys Asn Val Met Ser Tyr Asn Ala Phe Phe Trp Lys Trp Val His
595 600 605

Asp Met Leu Ile Asp Ser Met Gln Trp Arg Asn Glu His Gly Asn Cys
610 615 620

Ile Asn Lys Asp Asn Asp Asn Thr Cys Lys Asn Ser Cys Lys Arg Pro
625 630 635 640

Cys Glu Cys Phe Lys Arg Trp Val Asp Gln Lys Lys Lys Asn Glu Trp
 645 650 655
 Glu Ala Ile Lys Asp His Phe Lys Lys Gln Asn Ile Ala Ala Glu Thr
 660 665 670
 Gln Cys Asp Pro Gly Val Thr Leu Gln Trp Val Leu Ile Leu Asp Phe
 675 680 685
 Leu Lys Asp Glu Ser Thr Glu Asp Lys Glu Asn Lys Val Ser Ala Glu
 690 695 700
 Glu Ala Lys Glu Ile Lys His Leu Arg Gln Met Leu Gln Gln Ala Gly
 705 710 715 720
 Val Asp Asp Pro Ala Ala Phe Ala Arg Pro Cys Thr Glu Asp Gly Val
 725 730 735
 Ala Glu Gln Asp Thr Ile Met Asp Lys Leu Leu Asn Arg Glu Glu Asn
 740 745 750
 Asp Ala Thr Glu Cys Lys Lys Cys Asp Lys Pro Pro Pro Ala Pro Thr
 755 760 765
 Ala Gly Asp Arg Gly Pro Gly Ala Arg Ala Asp Pro His Asp Val Gln
 770 775 780
 Gln Pro Arg Pro Pro Gly Ser Gly Pro Gly Thr Asp Ala Asn Asp Glu
 785 790 795 800
 Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp Glu Glu Asp Gly Glu Ala
 805 810 815
 Lys Glu Glu Glu Glu Asp Glu Glu Lys Gln Glu Asp Val His Gln Glu
 820 825 830
 Glu Lys Ala Lys Lys Glu Glu Pro Gln Lys Glu Glu Val Ala Arg Thr
 835 840 845
 Pro Lys Asp Asp Val Asn Val Cys Asn Ile Val Asn Asn Val Phe Thr

850	855	860
Asp Gly Ser Ser Leu Gln Ala Ala Cys Ser Leu Lys Tyr Gly Lys Asn 865 870 875 880		
Ala Pro Thr Ser Trp Lys Cys Val Thr Pro Ser Gly Asn Thr Ser Asp 885 890 895		
Thr Thr Val Lys Ser Gly Asp Thr Thr Gly Gly Ser Ile Cys Val Pro 900 905 910		
Pro Arg Arg Arg Arg Leu Tyr Val Thr Pro Leu Thr Arg Leu Thr Gly 915 920 925		
Gly Asp Ser Thr Thr Gln Ala Ser Gln Ala Ser Glu Val Gln Thr Gln 930 935 940		
Ala Arg Gly Ser Asn Thr Asp Lys Ser Pro Gly Ser Ser Glu Ala Ala 945 950 955 960		
Gln Gly Asp Gly Val Ser Lys Asp Pro Gln Lys Ala Leu Leu Lys Ala 965 970 975		
Phe Val Glu Ser Ala Ala Val Glu Thr Phe Phe Leu Trp Asp Arg Tyr 980 985 990		
Lys Lys Ile Lys Glu Lys Glu Lys Lys Glu Lys Lys Lys Thr Tyr Glu 995 1000 1005		
Gln Ile Tyr Glu Ser Thr Asp Tyr Asp Asp Glu Glu Lys Asp Pro 1010 1015 1020		
Gln Glu Glu Leu Lys Lys Gly Ile Ile Pro Asp Glu Phe Lys Arg 1025 1030 1035		
Gln Met Phe Tyr Thr Leu Gly Asp Tyr Lys Asp Ile Leu Tyr Ser 1040 1045 1050		
Gly Asp Thr Val Asn Gly Gly Asn Glu Asp Lys Ile Lys Lys Ala 1055 1060 1065		

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

Glu	Phe	Thr	Lys	Gln	Ser	Asn	Val	Tyr	Glu	Glu	Gln	Lys	Thr	Lys
	1280					1285					1290			
Cys	Gln	Lys	Glu	Ser	Lys	Ser	Ala	Lys	Gly	Asn	Asn	His	Gly	Asn
	1295					1300					1305			
Glu	Phe	Cys	Gly	Thr	Gln	Gly	Thr	Cys	Asp	Thr	Ala	Gly	Asp	Phe
	1310					1315					1320			
Leu	Asn	Arg	Leu	Lys	Ser	Gly	Pro	Cys	Lys	Lys	Glu	Asn	Gly	Lys
	1325					1330					1335			
Asp	Asn	Gln	Glu	Asp	Glu	Ile	Asn	Phe	Lys	Asp	Glu	Asp	Lys	Thr
	1340					1345					1350			
Phe	Gly	His	Glu	Asn	Tyr	Cys	Ala	Pro	Cys	Pro	Val	Phe	Lys	Asp
	1355					1360					1365			
Ile	Cys	Lys	Lys	Lys	Asp	Cys	Arg	Asn	Ala	Ser	Asn	Asn	Met	Cys
	1370					1375					1380			
Asn	Gly	Lys	Asp	Phe	Ile	Thr	Ala	Glu	Asp	Ile	Lys	Ile	Met	Asp
	1385					1390					1395			
Ser	Ser	Ser	Glu	Glu	Val	Asn	Met	Leu	Val	Ser	Asp	Asn	Asp	Thr
	1400					1405					1410			
Asn	Lys	Phe	Asp	Gly	Gly	Leu	Asp	Ala	Cys	Lys	Asp	Ala	His	Ile
	1415					1420					1425			
Phe	Lys	Gly	Ile	Lys	Glu	Asn	Lys	Trp	Ser	Cys	Gly	Asn	Val	Cys
	1430					1435					1440			
Gly	Tyr	Asn	Val	Cys	Lys	Pro	Lys	Lys	Val	Asn	Gly	Glu	Lys	Gly
	1445					1450					1455			
Ser	Gly	Glu	Asn	Asn	Asp	Gln	Ile	Ile	Thr	Ile	Arg	Gly	Leu	Val
	1460					1465					1470			
Thr	His	Trp	Val	Gln	Asn	Phe	Leu	Asp	Asp	Tyr	Asn	Lys	Ile	Arg
	1475					1480					1485			

Thr	Lys	Leu	Lys	Pro	Cys	Arg	Asn	Asn	Gly	Glu	Val	Ser	Lys	Cys
	1490					1495					1500			
Ile	Lys	Asp	Cys	Val	Lys	Lys	Trp	Val	Glu	Lys	Lys	Thr	Glu	Glu
	1505					1510					1515			
Trp	Pro	Lys	Ile	Arg	Asp	Arg	Tyr	Leu	Glu	Pro	Tyr	Lys	Ser	Asp
	1520					1525					1530			
Asp	Gly	Tyr	Asn	Lys	Lys	Ser	Leu	Val	Arg	Ser	Phe	Met	Glu	Thr
	1535					1540					1545			
Leu	Ile	Pro	Leu	Met	Asp	Leu	Thr	Asn	Gly	Lys	Glu	Lys	Ile	Gln
	1550					1555					1560			
Glu	Leu	Asn	Lys	Phe	Leu	Arg	Ser	Tyr	Glu	Cys	Asn	Cys	Ala	Asp
	1565					1570					1575			
Asn	Ser	Gln	Gln	Lys	Gly	Asp	Thr	Pro	Lys	Asp	Ile	Val	Glu	Cys
	1580					1585					1590			
Leu	Leu	Glu	Lys	Leu	Glu	Asp	Lys	Ala	Asn	Lys	Cys	Lys	Thr	Gln
	1595					1600					1605			
Thr	Ser	Gly	Thr	Asp	Cys	His	Pro	Ser	Thr	Pro	Leu	Glu	Asp	Asp
	1610					1615					1620			
Asp	Glu	Pro	Leu	Glu	Glu	Thr	Glu	Glu	Asn	Thr	Val	Glu	Gln	Pro
	1625					1630					1635			
Asn	Ile	Cys	Pro	Thr	Lys	Gln	Pro	Gln	Pro	Glu	Lys	Glu	Asp	Gly
	1640					1645					1650			
Cys	Glu	Ala	Ala	Pro	Thr	Thr	Ala	Glu	Glu	Thr	Ser	Pro	Thr	Ala
	1655					1660					1665			
Thr	Ser	Glu	Gly	Thr	Glu	Asn	Gln	Ser	Pro	Pro	Pro	Pro	Pro	Pro
	1670					1675					1680			
Ala	Pro	Ala	Pro	Ala	Pro	Ala	Pro	Ala	Pro	Glu	Lys	Ser	Gln	Pro

1685					1690					1695				
Lys	Glu 1700	Asp	Lys	Lys	Val	Glu 1705	Pro	Gln	Pro	Lys	Pro 1710	Gln	Pro	Thr
Asn	Pro 1715	Pro	Pro	Asn	Leu	Phe 1720	Asn	Asn	Pro	Ala	Val 1725	Ile	Pro	Ala
Leu	Met 1730	Ser	Ser	Thr	Ile	Met 1735	Trp	Ser	Ile	Gly	Ile 1740	Gly	Phe	Ala
Ala	Phe 1745	Thr	Tyr	Phe	Leu	Leu 1750	Lys	Lys	Lys	Thr	Lys 1755	Ser	Ser	Val
Gly	Asn 1760	Leu	Phe	Gln	Ile	Leu 1765	Gln	Ile	Pro	Gln	Asn 1770	Asp	Tyr	Gly
Ile	Pro 1775	Thr	Leu	Lys	Ser	Lys 1780	Asn	Arg	Tyr	Ile	Pro 1785	Tyr	Arg	Ser
Gly	Thr 1790	Tyr	Lys	Gly	Lys	Thr 1795	Tyr	Ile	Tyr	Met	Glu 1800	Gly	Asp	Ser
Ser	Gly 1805	Asp	Glu	Lys	Tyr	Ala 1810	Phe	Met	Ser	Asp	Thr 1815	Thr	Asp	Val
Thr	Ser 1820	Ser	Glu	Ser	Glu	Tyr 1825	Glu	Glu	Leu	Asp	Ile 1830	Asn	Asp	Ile
Tyr	Val 1835	Pro	His	Ala	Pro	Lys 1840	Tyr	Lys	Thr	Leu	Ile 1845	Glu	Val	Val
Leu	Glu 1850	Pro	Ser	Gly	Asn	Asn 1855	Thr	Thr	Ala	Ser	Gly 1860	Lys	Asn	Thr
Pro	Ser 1865	Asp	Thr	Gln	Asn	Asp 1870	Ile	Pro	Thr	Ser	Asp 1875	Thr	Pro	Pro
Pro	Ile 1880	Thr	Asp	Asn	Glu	Trp 1885	Asn	Thr	Leu	Lys	Asp 1890	Glu	Phe	Ile

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

Lys Thr Tyr Asn Glu Pro Tyr Tyr Asp Val Gln Asp Asp Ile Tyr
2105 2110 2115

Tyr Asp Val Asn Asp His Asp Ala Ser Thr Val Asp Ser Asn Asn
2120 2125 2130

Met Asp Val Pro Ser Arg Val Gln Ile Glu Met Asp Val Asn Thr
2135 2140 2145

Lys Leu Val Lys Glu Lys Tyr Pro Ile Ala Asp Val Trp Asp Ile
2150 2155 2160

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<400> 76

Met Thr Asn Ser Asn Tyr Lys Ser Asn Asn Lys Thr Tyr Asn Glu Asn
1 5 10 15

Asn Asn Glu Gln Ile Thr Thr Ile Phe Asn Arg Thr Asn Met Asn Pro
20 25 30

Ile Lys Lys Cys His Met Arg Glu Lys Ile Asn Lys Tyr Phe Phe Leu
35 40 45

Ile Lys Ile Leu Thr Cys Thr Ile Leu Ile Trp Ala Val Gln Tyr Ala
50 55 60

Asn Asn Ser Asp Ile Asn Lys Ser Trp Lys Lys Asn Thr Tyr Val Asp
65 70 75 80

Lys Lys Leu Asn Lys Leu Phe Asn Arg Ser Leu Gly Glu Ser Gln Val
85 90 95

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

Leu Glu Glu Gly Asn Thr Leu Thr Glu Ser Val Asp Asp Asn Lys Asn
115 120 125

Leu Glu Glu Ala Glu Asp Ile Lys Glu Asn Ile Leu Leu Ser Asn Ile
130 135 140

Glu Glu Pro Lys Glu Asn Ile Ile Asp Asn Leu Leu Asn Asn Ile Gly
145 150 155 160

Gln Asn Ser Glu Lys Gln Glu Ser Val Ser Glu Asn Val Gln Val Ser
165 170 175

Asp Glu Leu Phe Asn Glu Leu Leu Asn Ser Val Asp Val Asn Gly Glu
180 185 190

Val Lys Glu Asn Ile Leu Glu Glu Ser Gln Val Asn Asp Asp Ile Phe
195 200 205

Asn Ser Leu Val Lys Ser Val Gln Gln Glu Gln Gln His Asn Val Glu
210 215 220

Glu Lys Val Glu Glu Ser Val Glu Glu Asn Asp Glu Glu Ser Val Glu
225 230 235 240

Glu Asn Val Glu Glu Asn Val Glu Glu Asn Asp Asp Glu Ser Val Ala
245 250 255

Ser Ser Val Glu Glu Ser Ile Ala Ser Ser Val Asp Glu Ser Ile Asp
260 265 270

Ser Ser Ile Glu Glu Asn Val Ala Pro Thr Val Glu Glu Ile Val Ala
275 280 285

Pro Thr Val Glu Glu Ile Val Ala Pro Ser Val Val Glu Ser Val Ala
290 295 300

Pro Ser Val Glu Glu Ser Val Glu Glu Asn Val Glu Glu Ser Val Ala
305 310 315 320

Glu Asn Val Glu Glu Ser Val Ala Glu Asn Val Glu Glu Ser Val Ala
325 330 335

Glu Asn Val Glu Glu Ser Val Ala Glu Asn Val Glu Glu Ser Val Ala
340 345 350

Glu Asn Val Glu Glu Ser Val Ala Glu Asn Val Glu Glu Ile Val Ala
355 360 365

Pro Thr Val Glu Glu Ser Val Ala Pro Thr Val Glu Glu Ile Val Ala
370 375 380

Pro Ser Val Glu Glu Ser Val Ala Pro Ser Val Glu Glu Ile Val Val
385 390 395 400

Pro Thr Val Glu Glu Ser Val Ala Glu Asn Val Glu Glu Ile Val Ala
405 410 415

Pro Ser Val Glu Glu Ile Val Ala Pro Ser Val Glu Glu Ile Val Ala
420 425 430

Pro Thr Val Glu Glu Ser Val Ala Pro Thr Val Glu Glu Ile Val Ala
435 440 445

Pro Ser Val Glu Glu Ser Val Ala Pro Ser Val Glu Glu Ile Val Val
450 455 460

Pro Thr Val Glu Glu Ser Val Ala Glu Asn Val Glu Glu Ser Val Ala
465 470 475 480

Glu Asn Val Glu Glu Ile Val Ala Pro Ser Val Glu Glu Ile Val Ala
485 490 495

Pro Ser Val Glu Glu Ile Val Ala Pro Ser Val Glu Glu Ile Val Ala
500 505 510

Pro Ser Val Glu Glu Ile Val Ala Pro Ser Val Glu Glu Ile Val Ala
515 520 525

Pro Ser Val Glu Glu Ile Val Ala Pro Ser Val Glu Glu Ile Val Ala
530 535 540

Pro Ser Val Glu Glu Ile Val Ala Pro Thr Val Glu Glu Ile Val Ala
545 550 555 560

Pro Thr Val Glu Glu Ile Val Ala Pro Ser Val Glu Glu Ile Val Ala

	565		570		575
Pro Thr Val	Glu Glu Ser Val	Ala Glu Asn Val	Ala Thr Asn Leu Ser		
	580	585	590		
Asp Asn Leu	Leu Ser Asn Leu	Leu Gly Gly Ile Glu	Thr Glu Glu Ile		
	595	600	605		
Lys Asp Ser	Ile Leu Asn Glu	Ile Glu Glu Val	Lys Glu Asn Val Val		
	610	615	620		
Thr Thr Ile	Leu Glu Asn Val	Glu Glu Thr Thr	Ala Glu Ser Val Thr		
	625	630	635	640	
Thr Phe Ser	Asn Ile Leu Glu	Glu Ile Gln Glu	Asn Thr Ile Thr	Asn	
	645	650	655		
Asp Thr Ile	Glu Glu Lys Leu	Glu Glu Leu His	Glu Asn Val Leu Ser		
	660	665	670		
Ala Ala Leu	Glu Asn Thr Gln	Ser Glu Glu Glu	Lys Lys Glu Val Ile		
	675	680	685		
Asp Val Ile	Glu Glu Val Lys	Glu Glu Val Ala	Thr Thr Leu Ile Glu		
	690	695	700		
Thr Val Glu	Gln Ala Glu	Glu Glu Ser Ala	Ser Thr Ile Thr	Glu Ile	
	705	710	715	720	
Phe Glu Asn	Leu Glu Glu	Asn Ala Val Glu	Ser Asn Glu Asn	Val Ala	
	725	730	735		
Glu Asn Leu	Glu Lys Leu	Asn Glu Thr	Val Phe Asn Thr	Val Leu Asp	
	740	745	750		
Lys Val Glu	Glu Thr Val	Glu Ile Ser Gly	Glu Ser Leu Glu	Asn Asn	
	755	760	765		
Glu Met Asp	Lys Ala Phe	Phe Ser Glu	Ile Phe Asp	Asn Val Lys Gly	
	770	775	780		

Ile Gln Glu Asn Leu Leu Thr Gly Met Phe Arg Ser Ile Glu Thr Ser
785 790 795 800

Ile Val Ile Gln Ser Glu Glu Lys Val Asp Leu Asn Glu Asn Val Val
805 810 815

Ser Ser Ile Leu Asp Asn Ile Glu Asn Met Lys Glu Gly Leu Leu Asn
820 825 830

Lys Leu Glu Asn Ile Ser Ser Thr Glu Gly Val Gln Glu Thr Val Thr
835 840 845

Glu His Val Glu Gln Asn Val Tyr Val Asp Val Asp Val Pro Ala Met
850 855 860

Lys Asp Gln Phe Leu Gly Ile Leu Asn Glu Ala Gly Gly Leu Lys Glu
865 870 875 880

Met Phe Phe Asn Leu Glu Asp Val Phe Lys Ser Glu Ser Asp Val Ile
885 890 895

Thr Val Glu Glu Ile Lys Asp Glu Pro Val Gln Lys Glu Val Glu Lys
900 905 910

Glu Thr Val Ser Ile Ile Glu Glu Met Glu Glu Asn Ile Val Asp Val
915 920 925

Leu Glu Glu Glu Lys Glu Asp Leu Thr Asp Lys Met Ile Asp Ala Val
930 935 940

Glu Glu Ser Ile Glu Ile Ser Ser Asp Ser Lys Glu Glu Thr Glu Ser
945 950 955 960

Ile Lys Asp Lys Glu Lys Asp Val Ser Leu Val Val Glu Glu Val Gln
965 970 975

Asp Asn Asp Met Asp Glu Ser Val Glu Lys Val Leu Glu Leu Lys Asn
980 985 990

Met Glu Glu Glu Leu Met Lys Asp Ala Val Glu Ile Asn Asp Ile Thr
995 1000 1005

Ser	Lys	Leu	Ile	Glu	Glu	Thr	Gln	Glu	Leu	Asn	Glu	Val	Glu	Ala
1010						1015					1020			
Asp	Leu	Ile	Lys	Asp	Met	Glu	Lys	Leu	Lys	Glu	Leu	Glu	Lys	Ala
1025						1030					1035			
Leu	Ser	Glu	Asp	Ser	Lys	Glu	Ile	Ile	Asp	Ala	Lys	Asp	Asp	Thr
1040						1045					1050			
Leu	Glu	Lys	Val	Ile	Glu	Glu	Glu	His	Asp	Ile	Thr	Thr	Thr	Leu
1055						1060					1065			
Asp	Glu	Val	Val	Glu	Leu	Lys	Asp	Val	Glu	Glu	Asp	Lys	Ile	Glu
1070						1075					1080			
Lys	Val	Ser	Asp	Leu	Lys	Asp	Leu	Glu	Glu	Asp	Ile	Leu	Lys	Glu
1085						1090					1095			
Val	Lys	Glu	Ile	Lys	Glu	Leu	Glu	Ser	Glu	Ile	Leu	Glu	Asp	Tyr
1100						1105					1110			
Lys	Glu	Leu	Lys	Thr	Ile	Glu	Thr	Asp	Ile	Leu	Glu	Glu	Lys	Lys
1115						1120					1125			
Glu	Ile	Glu	Lys	Asp	His	Phe	Glu	Lys	Phe	Glu	Glu	Glu	Ala	Glu
1130						1135					1140			
Glu	Ile	Lys	Asp	Leu	Glu	Ala	Asp	Ile	Leu	Lys	Glu	Val	Ser	Ser
1145						1150					1155			
Leu	Glu	Val	Glu	Glu	Glu	Lys	Lys	Leu	Glu	Glu	Val	His	Glu	Leu
1160						1165					1170			
Lys	Glu	Glu	Val	Glu	His	Ile	Ile	Ser	Gly	Asp	Ala	His	Ile	Lys
1175						1180					1185			
Gly	Leu	Glu	Glu	Asp	Asp	Leu	Glu	Glu	Val	Asp	Asp	Leu	Lys	Gly
1190						1195					1200			
Ser	Ile	Leu	Asp	Met	Leu	Lys	Gly	Asp	Met	Glu	Leu	Gly	Asp	Met
1205						1210					1215			

Asp	Lys	Glu	Ser	Leu	Glu	Asp	Val	Thr	Ala	Lys	Leu	Gly	Glu	Arg
	1220					1225					1230			
Val	Glu	Ser	Leu	Lys	Asp	Val	Leu	Ser	Ser	Ala	Leu	Gly	Met	Asp
	1235					1240					1245			
Glu	Glu	Gln	Met	Lys	Thr	Arg	Lys	Lys	Ala	Gln	Arg	Pro	Lys	Leu
	1250					1255					1260			
Glu	Glu	Val	Leu	Leu	Lys	Glu	Glu	Val	Lys	Glu	Glu	Pro	Lys	Lys
	1265					1270					1275			
Lys	Ile	Thr	Lys	Lys	Lys	Val	Arg	Phe	Asp	Ile	Lys	Asp	Lys	Glu
	1280					1285					1290			
Pro	Lys	Asp	Glu	Ile	Val	Glu	Val	Glu	Met	Lys	Asp	Glu	Asp	Ile
	1295					1300					1305			
Asp	Glu	Asp	Ile	Glu	Glu	Asp	Val	Glu	Glu	Asp	Ile	Glu	Glu	Asp
	1310					1315					1320			
Lys	Val	Glu	Asp	Ile	Asp	Glu	Asp	Ile	Asp	Glu	Asp	Ile	Asp	Glu
	1325					1330					1335			
Asp	Ile	Gly	Glu	Asp	Lys	Asp	Glu	Val	Ile	Asp	Leu	Ile	Val	Gln
	1340					1345					1350			
Lys	Glu	Lys	Arg	Ile	Glu	Lys	Val	Lys	Glu	Lys	Lys	Lys	Lys	Leu
	1355					1360					1365			
Glu	Lys	Lys	Val	Glu	Glu	Gly	Val	Ser	Gly	Leu	Lys	Lys	His	Val
	1370					1375					1380			
Asp	Glu	Val	Met	Lys	Tyr	Val	Gln	Lys	Ile	Asp	Lys	Glu	Val	Asp
	1385					1390					1395			
Lys	Glu	Val	Ser	Lys	Ala	Leu	Glu	Ser	Lys	Asn	Asp	Val	Thr	Asn
	1400					1405					1410			
Val	Leu	Lys	Gln	Asn	Gln	Asp	Phe	Phe	Ser	Lys	Val	Lys	Asn	Phe

1415

1420

1425

Val Lys Lys Tyr Lys Val Phe Ala Ala Pro Phe Ile Ser Ala Val

143014351440

Ala Ala Phe Ala Ser Tyr Val Val Gly Phe Phe Thr Phe Ser Leu

144514501455

Phe Ser Ser Cys Val Thr Ile Ala Ser Ser Thr Tyr Leu Leu Ser

146014651470

Lys Val Asp Lys Thr Ile Asn Lys Asn Lys Glu Arg Pro Phe Tyr

147514801485

Ser Phe Val Phe Asp Ile Phe Lys Asn Leu Lys His Tyr Leu Gln

149014951500

Gln Met Lys Glu Lys Phe Ser Lys Glu Lys Asn Asn Asn Val Ile

150515101515

Glu Val Thr Asn Lys Ala Glu Lys Lys Gly Asn Val Gln Val Thr

152015251530

Asn Lys Thr Glu Lys Thr Thr Lys Val Asp Lys Asn Asn Lys Val

153515401545

Pro Lys Lys Ser Arg Thr Gln Lys Ser Lys

15501555

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<213> 惡性瘧原蟲

<400> 77

Ser Asp Glu Leu Phe Asn Glu Leu Leu Asn Ser Val Asp Val Asn Gly

151015

Glu Val Lys Glu Asn Ile Leu Glu Glu Ser Gln Val Asn Asp Asp Ile

202530

Phe Asn Ser Leu Val Lys Ser Val Gln Gln Glu Gln Gln His Asn Val

35

40

45

Glu

Glu

Lys

Val

Glu

Glu

Ser

Val

Glu

Glu

Asn

Asp

Glu

Glu

Ser

Val

50

55

60

Glu

Glu

Asn

Val

Glu

Glu

Asn

Val

Glu

Glu

Asn

Asp

Asp

Glu

Ser

Val

65

70

75

80

Ala

Ser

Ser

Val

Glu

Glu

Ser

Ile

Ala

Ser

Ser

Val

Asp

Glu

Ser

Ile

85

90

95

Asp

Ser

Ser

Ile

Glu

Glu

Asn

Val

Ala

Pro

Thr

Val

Glu

Glu

Ile

Val

100

105

110

Ala

Pro

Thr

Val

Glu

Glu

Ile

Val

Ala

Pro

Ser

Val

Val

Glu

Ser

Val

120

125

Ala

Pro

Ser

Val

Glu

Glu

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Glu

Asn

Val

Glu

Glu

Ser

Val

135

140

Ala

Glu

Asn

Val

Glu

Glu

145

150

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<212> PRT
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<400> 78

Met

Met

Arg

Lys

Leu

Ala

Ile

Leu

Ser

Val

Ser

Ser

Phe

Leu

Phe

Val

1

5

10

15

Glu

Ala

Leu

Phe

Gln

Glu

Tyr

Gln

Cys

Tyr

Gly

Ser

Ser

Ser

Asn

Thr

20

25

30

Arg

Val

Leu

Asn

Glu

Leu

Asn

Tyr

Asp

Asn

Ala

Gly

Thr

Asn

Leu

Tyr

35

40

45

Asn

Glu

Leu

Glu

Met

Asn

Tyr

Tyr

Gly

Lys

Gln

Glu

Asn

Trp

Tyr

Ser

50

55

60

Leu

Lys

Lys

Asn

Ser

Arg

Ser

Leu

Gly

Glu

Asn

Asp

Asp

Gly

Asn

Asn

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

Pro Asn Arg Asn Val Asp Glu Asn Ala Asn Ala Asn Ser Ala Val Lys
290 295 300

Asn Asn Asn Asn Glu Glu Pro Ser Asp Lys His Ile Lys Glu Tyr Leu
305 310 315 320

Asn Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro Cys Ser Val
325 330 335

Thr Cys Gly Asn Gly Ile Gln Val Arg Ile Lys Pro Gly Ser Ala Asn
340 345 350

Lys Pro Lys Asp Glu Leu Asp Tyr Ala Asn Asp Ile Glu Lys Lys Ile
355 360 365

Cys Lys Met Glu Lys Cys Ser Ser Val Phe Asn Val Val Asn Ser Ser
370 375 380

Ile Gly Leu Ile Met Val Leu Ser Phe Leu Phe Leu Asn
385 390 395

<210> 79
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<400> 79

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

Phe Phe Asp Leu Phe Leu Val Asn Gly Arg Asp Val Gln Asn Asn Ile
20 25 30

Val Asp Glu Ile Lys Tyr Arg Glu Glu Val Cys Asn Asp Glu Val Asp
35 40 45

Leu Tyr Leu Leu Met Asp Cys Ser Gly Ser Ile Arg Arg His Asn Trp
50 55 60

Val Asn His Ala Val Pro Leu Ala Met Lys Leu Ile Gln Gln Leu Asn
65 70 75 80

Leu Asn Asp Asn Ala Ile His Leu Tyr Ala Ser Val Phe Ser Asn Asn
85 90 95

Ala Arg Glu Ile Ile Arg Leu His Ser Asp Ala Ser Lys Asn Lys Glu
100 105 110

Lys Ala Leu Ile Ile Ile Lys Ser Leu Leu Ser Thr Asn Leu Pro Tyr
115 120 125

Gly Lys Thr Asn Leu Thr Asp Ala Leu Leu Gln Val Arg Lys His Leu
130 135 140

Asn Asp Arg Ile Asn Arg Glu Asn Ala Asn Gln Leu Val Val Ile Leu
145 150 155 160

Thr Asp Gly Ile Pro Asp Ser Ile Gln Asp Ser Leu Lys Glu Ser Arg
165 170 175

Lys Leu Ser Asp Arg Gly Val Lys Ile Ala Val Phe Gly Ile Gly Gln
180 185 190

Gly Ile Asn Val Ala Phe Asn Arg Phe Leu Val Gly Cys His Pro Ser
195 200 205

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

Asn Val Ile Gly Pro Phe Met Lys Ala Val Cys Val Glu Val Glu Lys
225 230 235 240

Thr Ala Ser Cys Gly Val Trp Asp Glu Trp Ser Pro Cys Ser Val Thr
245 250 255

Cys Gly Lys Gly Thr Arg Ser Arg Lys Arg Glu Ile Leu His Glu Gly
260 265 270

Cys Thr Ser Glu Leu Gln Glu Gln Cys Glu Glu Glu Arg Cys Leu Pro
275 280 285

Lys Arg Glu Pro Leu Asp Val Pro Asp Glu Pro Glu Asp Asp Gln Pro
290 295 300

Arg Pro Arg Gly Asp Asn Phe Ala Val Glu Lys Pro Asn Glu Asn Ile
305 310 315 320

Ile Asp Asn Asn Pro Gln Glu Pro Ser Pro Asn Pro Glu Glu Gly Lys
325 330 335

Gly Glu Asn Pro Asn Gly Phe Asp Leu Asp Glu Asn Pro Glu Asn Pro
340 345 350

Pro Asn Pro Pro Asn Pro Pro Asn Pro Pro Asn Pro Pro Asn Pro Pro
355 360 365

Asn Pro Asp Ile Pro Glu Gln Glu Pro Asn Ile Pro Glu Asp Ser Glu
370 375 380

Lys Glu Val Pro Ser Asp Val Pro Lys Asn Pro Glu Asp Asp Arg Glu
385 390 395 400

Glu Asn Phe Asp Ile Pro Lys Lys Pro Glu Asn Lys His Asp Asn Gln
405 410 415

Asn Asn Leu Pro Asn Asp Lys Ser Asp Arg Tyr Ile Pro Tyr Ser Pro
420 425 430

Leu Ser Pro Lys Val Leu Asp Asn Glu Arg Lys Gln Ser Asp Pro Gln
435 440 445

Ser Gln Asp Asn Asn Gly Asn Arg His Val Pro Asn Ser Glu Asp Arg
450 455 460

Glu Thr Arg Pro His Gly Arg Asn Asn Glu Asn Arg Ser Tyr Asn Arg
465 470 475 480

Lys His Asn Asn Thr Pro Lys His Pro Glu Arg Glu Glu His Glu Lys
485 490 495

Pro Asp Asn Asn Lys Lys Lys Ala Gly Ser Asp Asn Lys Tyr Lys Ile
500 505 510

Ala Gly Gly Ile Ala Gly Gly Leu Ala Leu Leu Ala Cys Ala Gly Leu
515 520 525

Ala Tyr Lys Phe Val Val Pro Gly Ala Ala Thr Pro Tyr Ala Gly Glu
530 535 540

Pro Ala Pro Phe Asp Glu Thr Leu Gly Glu Glu Asp Lys Asp Leu Asp
545 550 555 560

Glu Pro Glu Gln Phe Arg Leu Pro Glu Glu Asn Glu Trp Asn
565 570

<210> 80
<211> 272
<212> PRT
<213> 惡性瘡原蟲

<400> 80

Met Trp Ile Val Lys Phe Leu Ile Val Val His Phe Phe Ile Ile Cys
1 5 10 15

Thr Ile Asn Phe Asp Lys Leu Tyr Ile Ser Tyr Ser Tyr Asn Ile Val
20 25 30

Pro Glu Asn Gly Arg Met Leu Asn Met Arg Ile Leu Gly Glu Glu Lys
35 40 45

Pro Asn Val Asp Gly Val Ser Thr Ser Asn Thr Pro Gly Gly Asn Glu
50 55 60

Ser Ser Ser Ala Ser Pro Asn Leu Ser Asp Ala Ala Glu Lys Lys Asp
65 70 75 80

Glu Lys Glu Ala Ser Glu Gln Gly Glu Glu Ser His Lys Lys Glu Asn
85 90 95

Ser Gln Glu Ser Ala Asn Gly Lys Asp Asp Val Lys Glu Glu Lys Lys
100 105 110

Thr Asn Glu Lys Lys Asp Asp Gly Lys Thr Asp Lys Val Gln Glu Lys
115 120 125

Val Leu Glu Lys Ser Pro Lys Glu Ser Gln Met Val Asp Asp Lys Lys
130 135 140

Lys Thr Glu Ala Ile Pro Lys Lys Val Val Gln Pro Ser Ser Ser Asn
145 150 155 160

Ser Gly Gly His Val Gly Glu Glu Glu Asp His Asn Glu Gly Glu Gly
165 170 175

Glu His Glu Glu Glu Glu Glu His Glu Glu Asp Asp Asp Asp Glu Asp
180 185 190

Asp Asp Thr Tyr Asn Lys Asp Asp Leu Glu Asp Glu Asp Leu Cys Lys
195 200 205

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

Asn Arg Arg Val Lys Cys Lys Cys Lys Glu Gly Tyr Lys Leu Glu Gly
225 230 235 240

Ile Glu Cys Val Glu Leu Leu Ser Leu Ala Ser Ser Ser Leu Asn Leu
245 250 255

Ile Phe Asn Ser Phe Ile Thr Ile Phe Val Val Ile Leu Leu Ile Asn
260 265 270

<210> 81
<211> 560
<212> PRT
<213> 惡性瘧原蟲

<400> 81

Met Ser Arg Lys Leu Phe Ala Ser Ile Leu Ile Gly Ala Leu Leu Gly
1 5 10 15

Ile Gly Ala Pro Pro Ser Ala His Ala Gly Ala Asp Asp Val Val Asp
20 25 30

Ser Ser Lys Ser Phe Val Met Glu Asn Phe Ser Ser Tyr His Gly Thr
35 40 45

Lys Pro Gly Tyr Val Asp Ser Ile Gln Lys Gly Ile Gln Lys Pro Lys
50 55 60

Ser Gly Thr Gln Gly Asn Tyr Asp Asp Asp Trp Lys Gly Phe Tyr Ser
65 70 75 80

Thr Asp Asn Lys Tyr Asp Ala Ala Gly Tyr Ser Val Asp Asn Glu Asn
85 90 95

Pro Leu Ser Gly Lys Ala Gly Gly Val Val Lys Val Thr Tyr Pro Gly
100 105 110

Leu Thr Lys Val Leu Ala Leu Lys Val Asp Asn Ala Glu Thr Ile Lys
115 120 125

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

Thr Glu Glu Phe Ile Lys Arg Phe Gly Asp Gly Ala Ser Arg Val Val
145 150 155 160

Leu Ser Leu Pro Phe Ala Glu Gly Ser Ser Ser Val Glu Tyr Ile Asn
165 170 175

Asn Trp Glu Gln Ala Lys Ala Leu Ser Val Glu Leu Glu Ile Asn Phe
180 185 190

Glu Thr Arg Gly Lys Arg Gly Gln Asp Ala Met Tyr Glu Tyr Met Ala
195 200 205

Gln Ala Cys Ala Gly Asn Arg Val Arg Arg Ser Val Gly Ser Ser Leu
210 215 220

Ser Cys Ile Asn Leu Asp Trp Asp Val Ile Arg Asp Lys Thr Lys Thr
225 230 235 240

Lys Ile Glu Ser Leu Lys Glu His Gly Pro Ile Lys Asn Lys Met Ser
245 250 255

Glu Ser Pro Asn Lys Thr Val Ser Glu Glu Lys Ala Lys Gln Tyr Leu
260 265 270

Glu Glu Phe His Gln Thr Ala Leu Glu His Pro Glu Leu Ser Glu Leu

275	280	285
Lys Thr Val Thr Gly Thr Asn Pro Val Phe Ala Gly Ala Asn Tyr Ala		
290	295	300
Ala Trp Ala Val Asn Val Ala Gln Val Ile Asp Ser Glu Thr Ala Asp		
305	310	315
Asn Leu Glu Lys Thr Thr Ala Ala Leu Ser Ile Leu Pro Gly Ile Gly		
	325	330
Ser Val Met Gly Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu		
	340	345
Ile Val Ala Gln Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala		
	355	360
Ile Pro Leu Val Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn		
	370	375
Phe Val Glu Ser Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr		
385	390	395
Asn Arg Pro Ala Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu His		
	405	410
Asp Gly Tyr Ala Val Ser Trp Asn Thr Val Glu Asp Ser Ile Ile Arg		
	420	425
Thr Gly Phe Gln Gly Glu Ser Gly His Asp Ile Lys Ile Thr Ala Glu		
	435	440
Asn Thr Pro Leu Pro Ile Ala Gly Val Leu Leu Pro Thr Ile Pro Gly		
	450	455
Lys Leu Asp Val Asn Lys Ser Lys Thr His Ile Ser Val Asn Gly Arg		
465	470	475
Lys Ile Arg Met Arg Cys Arg Ala Ile Asp Gly Asp Val Thr Phe Cys		
	485	490
		495

Arg Pro Lys Ser Pro Val Tyr Val Gly Asn Gly Val His Ala Asn Leu
500 505 510

His Val Ala Phe His Arg Ser Ser Ser Glu Lys Ile His Ser Asn Glu
515 520 525

Ile Ser Ser Asp Ser Ile Gly Val Leu Gly Tyr Gln Lys Thr Val Asp
530 535 540

His Thr Lys Val Asn Ser Lys Leu Ser Leu Phe Phe Glu Ile Lys Ser
545 550 555 560

<210> 82
<211> 535
<212> PRT
<213> 惡性瘡原蟲

<400> 82

Gly Ala Asp Asp Val Val Asp Ser Ser Lys Ser Phe Val Met Glu Asn
1 5 10 15

Phe Ser Ser Tyr His Gly Thr Lys Pro Gly Tyr Val Asp Ser Ile Gln
20 25 30

Lys Gly Ile Gln Lys Pro Lys Ser Gly Thr Gln Gly Asn Tyr Asp Asp
35 40 45

Asp Trp Lys Glu Phe Tyr Ser Thr Asp Asn Lys Tyr Asp Ala Ala Gly
50 55 60

Tyr Ser Val Asp Asn Glu Asn Pro Leu Ser Gly Lys Ala Gly Gly Val
65 70 75 80

Val Lys Val Thr Tyr Pro Gly Leu Thr Lys Val Leu Ala Leu Lys Val
85 90 95

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

Pro Leu Met Glu Gln Val Gly Thr Glu Glu Phe Ile Lys Arg Phe Gly
115 120 125

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

Ile Gly Phe Ala Ala Tyr Asn Phe Val Glu Ser Ile Ile Asn Leu Phe
355 360 365

Gln Val Val His Asn Ser Tyr Asn Arg Pro Ala Tyr Ser Pro Gly His
370 375 380

Lys Thr Gln Pro Phe Leu His Asp Gly Tyr Ala Val Ser Trp Asn Thr
385 390 395 400

Val Glu Asp Ser Ile Ile Arg Thr Gly Phe Gln Gly Glu Ser Gly His
405 410 415

Asp Ile Lys Ile Thr Ala Glu Asn Thr Pro Leu Pro Ile Ala Gly Val
420 425 430

Leu Leu Pro Thr Ile Pro Gly Lys Leu Asp Val Asn Lys Ser Lys Thr
435 440 445

His Ile Ser Val Asn Gly Arg Lys Ile Arg Met Arg Cys Arg Ala Ile
450 455 460

Asp Gly Asp Val Thr Phe Cys Arg Pro Lys Ser Pro Val Tyr Val Gly
465 470 475 480

Asn Gly Val His Ala Asn Leu His Val Ala Phe His Arg Ser Ser Ser
485 490 495

Glu Lys Ile His Ser Asn Glu Ile Ser Ser Asp Ser Ile Gly Val Leu
500 505 510

Gly Tyr Gln Lys Thr Val Asp His Thr Lys Val Asn Ser Lys Leu Ser
515 520 525

Leu Phe Phe Glu Ile Lys Ser
530 535

<210> 83
<211> 1315
<212> PRT
<213> 惡性瘧原蟲

<400> 83

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

Gln Asp Pro Ala Leu Leu Leu Met His Glu Leu Ile His Val Leu His
225 230 235 240

Gly Leu Tyr Gly Met Gln Val Ser Ser His Glu Ile Ile Pro Ser Lys
245 250 255

Gln Glu Ile Tyr Met Gln His Thr Tyr Pro Ile Ser Ala Glu Glu Leu
260 265 270

Phe Thr Phe Gly Gly Gln Asp Ala Asn Leu Ile Ser Ile Asp Ile Lys
275 280 285

Asn Asp Leu Tyr Glu Lys Thr Leu Asn Asp Tyr Lys Ala Ile Ala Asn
290 295 300

Lys Leu Ser Gln Val Thr Ser Cys Asn Asp Pro Asn Ile Asp Ile Asp
305 310 315 320

Ser Tyr Lys Gln Ile Tyr Gln Gln Lys Tyr Gln Phe Asp Lys Asp Ser
325 330 335

Asn Gly Gln Tyr Ile Val Asn Glu Asp Lys Phe Gln Ile Leu Tyr Asn
340 345 350

Ser Ile Met Tyr Gly Phe Thr Glu Ile Glu Leu Gly Lys Lys Phe Asn
355 360 365

Ile Lys Thr Arg Leu Ser Tyr Phe Ser Met Asn His Asp Pro Val Lys
370 375 380

Ile Pro Asn Leu Leu Asp Asp Thr Ile Tyr Asn Asp Thr Glu Gly Phe
385 390 395 400

Asn Ile Glu Ser Lys Asp Leu Lys Ser Glu Tyr Lys Gly Gln Asn Met
405 410 415

Arg Val Asn Thr Asn Ala Phe Arg Asn Val Asp Gly Ser Gly Leu Val
420 425 430

Ser Lys Leu Ile Gly Leu Cys Lys Lys Ile Ile Pro Pro Thr Asn Ile

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

Tyr Glu Gly Asn Phe Ile Gly Ala Leu Glu Thr Thr Gly Val Val Leu
660 665 670

Leu Leu Glu Tyr Ile Pro Glu Ile Thr Leu Pro Val Ile Ala Ala Leu
675 680 685

Ser Ile Ala Glu Ser Ser Thr Gln Lys Glu Lys Ile Ile Lys Thr Ile
690 695 700

Asp Asn Phe Leu Glu Lys Arg Tyr Glu Lys Trp Ile Glu Val Tyr Lys
705 710 715 720

Leu Val Lys Ala Lys Trp Leu Gly Thr Val Asn Thr Gln Phe Gln Lys
725 730 735

Arg Ser Tyr Gln Met Tyr Arg Ser Leu Glu Tyr Gln Val Asp Ala Ile
740 745 750

Lys Lys Ile Ile Asp Tyr Glu Tyr Lys Ile Tyr Ser Gly Pro Asp Lys
755 760 765

Glu Gln Ile Ala Asp Glu Ile Asn Asn Leu Lys Asn Lys Leu Glu Glu
770 775 780

Lys Ala Asn Lys Ala Met Ile Asn Ile Asn Ile Phe Met Arg Glu Ser
785 790 795 800

Ser Arg Ser Phe Leu Val Asn Gln Met Ile Asn Glu Ala Lys Lys Gln
805 810 815

Leu Leu Glu Phe Asp Thr Gln Ser Lys Asn Ile Leu Met Gln Tyr Ile
820 825 830

Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Lys Lys Leu Glu
835 840 845

Ser Lys Ile Asn Lys Val Phe Ser Thr Pro Ile Pro Phe Ser Tyr Ser
850 855 860

Lys Asn Leu Asp Cys Trp Val Asp Asn Glu Glu Asp Ile Asp Val Ile
865 870 875 880

Leu	Lys	Lys	Ser	Thr	Ile	Leu	Asn	Leu	Asp	Ile	Asn	Asn	Asp	Ile	Ile	885	890	895	
Ser	Asp	Ile	Ser	Gly	Phe	Asn	Ser	Ser	Val	Ile	Thr	Tyr	Pro	Asp	Ala	900	905	910	
Gln	Leu	Val	Pro	Gly	Ile	Asn	Gly	Lys	Ala	Ile	His	Leu	Val	Asn	Asn	915	920	925	
Glu	Ser	Ser	Glu	Val	Ile	Val	His	Lys	Ala	Met	Asp	Ile	Glu	Tyr	Asn	930	935	940	
Asp	Met	Phe	Asn	Asn	Phe	Thr	Val	Ser	Phe	Trp	Leu	Arg	Val	Pro	Lys	945	950	955	960
Val	Ser	Ala	Ser	His	Leu	Glu	Gln	Tyr	Gly	Thr	Asn	Glu	Tyr	Ser	Ile	965	970	975	
Ile	Ser	Ser	Met	Lys	Lys	His	Ser	Leu	Ser	Ile	Gly	Ser	Gly	Trp	Ser	980	985	990	
Val	Ser	Leu	Lys	Gly	Asn	Asn	Leu	Ile	Trp	Thr	Leu	Lys	Asp	Ser	Ala	995	1000	1005	
Gly	Glu	Val	Arg	Gln	Ile	Thr	Phe	Arg	Asp	Leu	Pro	Asp	Lys	Phe		1010	1015	1020	
Asn	Ala	Tyr	Leu	Ala	Asn	Lys	Trp	Val	Phe	Ile	Thr	Ile	Thr	Asn		1025	1030	1035	
Asp	Arg	Leu	Ser	Ser	Ala	Asn	Leu	Tyr	Ile	Asn	Gly	Val	Leu	Met		1040	1045	1050	
Gly	Ser	Ala	Glu	Ile	Thr	Gly	Leu	Gly	Ala	Ile	Arg	Glu	Asp	Asn		1055	1060	1065	
Asn	Ile	Thr	Leu	Lys	Leu	Asp	Arg	Cys	Asn	Asn	Asn	Asn	Gln	Tyr		1070	1075	1080	
Val	Ser	Ile	Asp	Lys	Phe	Arg	Ile	Phe	Cys	Lys	Ala	Leu	Asn	Pro		1085	1090	1095	

Lys	Glu	Ile	Glu	Lys	Leu	Tyr	Thr	Ser	Tyr	Leu	Ser	Ile	Thr	Phe
1100						1105					1110			
Leu	Arg	Asp	Phe	Trp	Gly	Asn	Pro	Leu	Arg	Tyr	Asp	Thr	Glu	Tyr
1115						1120					1125			
Tyr	Leu	Ile	Pro	Val	Ala	Ser	Ser	Ser	Lys	Asp	Val	Gln	Leu	Lys
1130						1135					1140			
Asn	Ile	Thr	Asp	Tyr	Met	Tyr	Leu	Thr	Asn	Ala	Pro	Ser	Tyr	Thr
1145						1150					1155			
Asn	Gly	Lys	Leu	Asn	Ile	Tyr	Tyr	Arg	Arg	Leu	Tyr	Asn	Gly	Leu
1160						1165					1170			
Lys	Phe	Ile	Ile	Lys	Arg	Tyr	Thr	Pro	Asn	Asn	Glu	Ile	Asp	Ser
1175						1180					1185			
Phe	Val	Lys	Ser	Gly	Asp	Phe	Ile	Lys	Leu	Tyr	Val	Ser	Tyr	Asn
1190						1195					1200			
Asn	Asn	Glu	His	Ile	Val	Gly	Tyr	Pro	Lys	Asp	Gly	Asn	Ala	Phe
1205						1210					1215			
Asn	Asn	Leu	Asp	Arg	Ile	Leu	Arg	Val	Gly	Tyr	Asn	Ala	Pro	Gly
1220						1225					1230			
Ile	Pro	Leu	Tyr	Lys	Lys	Met	Glu	Ala	Val	Lys	Leu	Arg	Asp	Leu
1235						1240					1245			
Lys	Thr	Tyr	Ser	Val	Gln	Leu	Lys	Leu	Tyr	Asp	Asp	Lys	Asn	Ala
1250						1255					1260			
Ser	Leu	Gly	Leu	Val	Gly	Thr	His	Asn	Gly	Gln	Ile	Gly	Asn	Asp
1265						1270					1275			
Pro	Asn	Arg	Asp	Ile	Leu	Ile	Ala	Ser	Asn	Trp	Tyr	Phe	Asn	His
1280						1285					1290			
Leu	Lys	Asp	Lys	Ile	Leu	Gly	Cys	Asp	Trp	Tyr	Phe	Val	Pro	Thr

129513001305

Asp Glu Gly Trp Thr Asn Asp13101315

<210> 84<211> 364<212> PRT<213> 惡性瘡原蟲<400> 84

Met Lys Leu Lys Thr Leu Ala Leu Ser Leu Leu Ala Ala Gly Val Leu15

Ala Gly Cys Ser Ser His Ser Ser Asn Met Ala Asn Thr Gln Met Lys202530

Ser Asp Lys Ile Ile Ile Ala His Arg Gly Ala Ser Gly Tyr Leu Pro354045

Glu His Thr Leu Glu Ser Lys Ala Leu Ala Phe Ala Gln Gln Ala Asp505560

Tyr Leu Glu Gln Asp Leu Ala Met Thr Lys Asp Gly Arg Leu Val Val65707580

Ile His Asp His Phe Leu Asp Gly Leu Thr Asp Val Ala Lys Lys Phe859095

Pro His Arg His Arg Lys Asp Gly Arg Tyr Tyr Val Ile Asp Phe Thr100105110

Leu Lys Glu Ile Gln Ser Leu Glu Met Thr Glu Asn Phe Glu Thr Lys115120125

Asp Gly Lys Gln Ala Gln Val Tyr Pro Asn Arg Phe Pro Leu Trp Lys130135140

Ser His Phe Arg Ile His Thr Phe Glu Asp Glu Ile Glu Phe Ile Gln145150155160

Gly Leu Glu Lys Ser Thr Gly Lys Lys Val Gly Ile Tyr Pro Glu Ile

165170175

Lys Ala Pro Trp Phe His His Gln Asn Gly Lys Asp Ile Ala Ala Glu
180185190

Thr Leu Lys Val Leu Lys Lys Tyr Gly Tyr Asp Lys Lys Thr Asp Met
195200205

Val Tyr Leu Gln Thr Phe Asp Phe Asn Glu Leu Lys Arg Ile Lys Thr
210215220

Glu Leu Leu Pro Gln Met Gly Met Asp Leu Lys Leu Val Gln Leu Ile
225230235240

Ala Tyr Thr Asp Trp Lys Glu Thr Gln Glu Lys Asp Pro Lys Gly Tyr
245250255

Trp Val Asn Tyr Asn Tyr Asp Trp Met Phe Lys Pro Gly Ala Met Ala
260265270

Glu Val Val Lys Tyr Ala Asp Gly Val Gly Pro Gly Trp Tyr Met Leu
275280285

Val Asn Lys Glu Glu Ser Lys Pro Asp Asn Ile Val Tyr Thr Pro Leu
290295300

Val Lys Glu Leu Ala Gln Tyr Asn Val Glu Val His Pro Tyr Thr Val
305310315320

Arg Lys Asp Ala Leu Pro Ala Phe Phe Thr Asp Val Asn Gln Met Tyr
325330335

Asp Ala Leu Leu Asn Lys Ser Gly Ala Thr Gly Val Phe Thr Asp Phe
340345350

Pro Asp Thr Gly Val Glu Phe Leu Lys Gly Ile Lys
355360

- <210> 85
- <211> 757
- <212> PRT
- <213> 人工序列

<220>

<223> PP21 生物融合蛋白

<400> 85

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala
1 5 10 15

Ala Gln Pro Ala Met Ala Met Gly Lys Thr Lys Glu Tyr Ala Glu Lys
20 25 30

Ala Lys Asn Ala Tyr Glu Lys Ala Lys Asn Ala Tyr Gln Lys Ala Asn
35 40 45

Gln Ala Val Leu Lys Ala Lys Glu Ala Ser Ser Tyr Asp Tyr Ile Leu
50 55 60

Gly Trp Glu Phe Gly Gly Gly Val Pro Glu His Lys Lys Glu Glu Asn
65 70 75 80

Met Leu Ser His Leu Tyr Val Ser Ser Lys Asp Lys Glu Asn Ile Ser
85 90 95

Lys Glu Asn Asp Asp Val Leu Asp Glu Lys Glu Glu Glu Ala Glu Glu
100 105 110

Thr Glu Glu Glu Glu Leu Glu Gly Ala Asp Asp Val Val Asp Ser Ser
115 120 125

Lys Ser Phe Val Met Glu Asn Phe Ser Ser Tyr His Gly Thr Lys Pro
130 135 140

Gly Tyr Val Asp Ser Ile Gln Lys Gly Ile Gln Lys Pro Lys Ser Gly
145 150 155 160

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

Asn Lys Tyr Asp Ala Ala Gly Tyr Ser Val Asp Asn Glu Asn Pro Leu
180 185 190

Ser Gly Lys Ala Gly Gly Val Val Lys Val Thr Tyr Pro Gly Leu Thr

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

Glu Lys Thr Thr Ala Ala Leu Ser Ile Leu Pro Gly Ile Gly Ser Val
 420 425 430

Met Gly Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu Ile Val
 435 440 445

Ala Gln Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala Ile Pro
 450 455 460

Leu Val Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn Phe Val
 465 470 475 480

Glu Ser Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr Asn Arg
 485 490 495

Pro Ala Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu His Asp Gly
 500 505 510

Tyr Ala Val Ser Trp Asn Thr Val Glu Asp Ser Ile Ile Arg Thr Gly
 515 520 525

Phe Gln Gly Glu Ser Gly His Asp Ile Lys Ile Thr Ala Glu Asn Thr
 530 535 540

Pro Leu Pro Ile Ala Gly Val Leu Leu Pro Thr Ile Pro Gly Lys Leu
 545 550 555 560

Asp Val Asn Lys Ser Lys Thr His Ile Ser Val Asn Gly Arg Lys Ile
 565 570 575

Arg Met Arg Cys Arg Ala Ile Asp Gly Asp Val Thr Phe Cys Arg Pro
 580 585 590

Lys Ser Pro Val Tyr Val Gly Asn Gly Val His Ala Asn Leu His Val
 595 600 605

Ala Phe His Arg Ser Ser Ser Glu Lys Ile His Ser Asn Glu Ile Ser
 610 615 620

Ser Asp Ser Ile Gly Val Leu Gly Tyr Gln Lys Thr Val Asp His Thr
 625 630 635 640

Lys Val Asn Ser Lys Leu Ser Leu Phe Phe Glu Ile Lys Ser Lys Thr
645 650 655

Lys Glu Tyr Ala Glu Lys Ala Lys Asn Ala Tyr Glu Lys Ala Lys Asn
660 665 670

Ala Tyr Gln Lys Ala Asn Gln Ala Val Leu Lys Ala Lys Glu Ala Ser
675 680 685

Ser Tyr Asp Tyr Ile Leu Gly Trp Glu Phe Gly Gly Gly Val Pro Glu
690 695 700

His Lys Lys Glu Glu Asn Met Leu Ser His Leu Tyr Val Ser Ser Lys
705 710 715 720

Asp Lys Glu Asn Ile Ser Lys Glu Asn Asp Asp Val Leu Asp Glu Lys
725 730 735

Glu Glu Glu Ala Glu Glu Thr Glu Glu Glu Glu Leu Glu Leu Glu His
740 745 750

His His His His His
755

<210> 86
<211> 727
<212> PRT
<213> 人工序列

<220>
<223> PP22 生物融合蛋白

<400> 86

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala
1 5 10 15

Ala Gln Pro Ala Met Ala Met Gly Leu Asn Asn Asn Ile Leu Gly Trp
20 25 30

Glu Phe Gly Gly Gly Ala Pro Gln Asn Gly Ala Ala Glu Asp Lys Lys
35 40 45

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

Thr Arg Gly Lys Arg Gly Gln Asp Ala Met Tyr Glu Tyr Met Ala Gln
275 280 285

Ala Cys Ala Gly Asn Arg Val Arg Arg Ser Val Gly Ser Ser Leu Ser
290 295 300

Cys Ile Asn Leu Asp Trp Asp Val Ile Arg Asp Lys Thr Lys Thr Lys
305 310 315 320

Ile Glu Ser Leu Lys Glu His Gly Pro Ile Lys Asn Lys Met Ser Glu
325 330 335

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

Glu Phe His Gln Thr Ala Leu Glu His Pro Glu Leu Ser Glu Leu Lys
355 360 365

Thr Val Thr Gly Thr Asn Pro Val Phe Ala Gly Ala Asn Tyr Ala Ala
370 375 380

Trp Ala Val Asn Val Ala Gln Val Ile Asp Ser Glu Thr Ala Asp Asn
385 390 395 400

Leu Glu Lys Thr Thr Ala Ala Leu Ser Ile Leu Pro Gly Ile Gly Ser
405 410 415

Val Met Gly Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu Ile
420 425 430

Val Ala Gln Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala Ile
435 440 445

Pro Leu Val Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn Phe
450 455 460

Val Glu Ser Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr Asn
465 470 475 480

Arg Pro Ala Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu His Asp
485 490 495

Gly Tyr Ala Val Ser Trp Asn Thr Val Glu Asp Ser Ile Ile Arg Thr
500 505 510

Gly Phe Gln Gly Glu Ser Gly His Asp Ile Lys Ile Thr Ala Glu Asn
515 520 525

Thr Pro Leu Pro Ile Ala Gly Val Leu Leu Pro Thr Ile Pro Gly Lys
530 535 540

Leu Asp Val Asn Lys Ser Lys Thr His Ile Ser Val Asn Gly Arg Lys
545 550 555 560

Ile Arg Met Arg Cys Arg Ala Ile Asp Gly Asp Val Thr Phe Cys Arg
565 570 575

Pro Lys Ser Pro Val Tyr Val Gly Asn Gly Val His Ala Asn Leu His
580 585 590

Val Ala Phe His Arg Ser Ser Ser Glu Lys Ile His Ser Asn Glu Ile
595 600 605

Ser Ser Asp Ser Ile Gly Val Leu Gly Tyr Gln Lys Thr Val Asp His
610 615 620

Thr Lys Val Asn Ser Lys Leu Ser Leu Phe Phe Glu Ile Lys Ser Leu
625 630 635 640

Asn Asn Asn Ile Leu Gly Trp Glu Phe Gly Gly Gly Ala Pro Gln Asn
645 650 655

Gly Ala Ala Glu Asp Lys Lys Thr Glu Tyr Leu Leu Glu Gln Ile Lys
660 665 670

Ile Pro Ser Trp Asp Arg Asn Asn Ile Pro Asp Glu Asn Glu Gln Val
675 680 685

Ile Glu Asp Pro Gln Glu Asp Asn Lys Asp Glu Asp Glu Asp Glu Glu
690 695 700

Thr Glu Thr Glu Asn Leu Glu Thr Glu Asp Asp Asn Asn Glu Glu Leu

705 710 715 720

Glu His His His His His His
725

<210> 87
<211> 709
<212> PRT
<213> 人工序列

<220>
<223> PP23生物融合蛋白

<400> 87

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala
1 5 10 15

Ala Gln Pro Ala Met Ala Met Gly Leu Asn Asn Asn Ile Leu Gly Trp
20 25 30

Glu Phe Gly Gly Gly Ala Pro Gln Asn Gly Ala Ala Glu Asp Lys Lys
35 40 45

Thr Glu Tyr Leu Leu Glu Gln Ile Lys Ile Pro Ser Trp Asp Arg Asn
50 55 60

Asn Ile Pro Asp Glu Asn Glu Gln Val Ile Glu Asp Pro Gln Glu Asp
65 70 75 80

Asn Lys Asp Glu Asp Glu Asp Glu Glu Thr Glu Thr Glu Asn Leu Glu
85 90 95

Thr Glu Asp Asp Asn Asn Glu Glu Gly Ala Asp Asp Val Val Asp Ser
100 105 110

Ser Lys Ser Phe Val Met Glu Asn Phe Ser Ser Tyr His Gly Thr Lys
115 120 125

Pro Gly Tyr Val Asp Ser Ile Gln Lys Gly Ile Gln Lys Pro Lys Ser
130 135 140

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

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

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

Val Ala Phe His Arg Ser Ser Ser Glu Lys Ile His Ser Asn Glu Ile
595 600 605

Ser Ser Asp Ser Ile Gly Val Leu Gly Tyr Gln Lys Thr Val Asp His
610 615 620

Thr Lys Val Asn Ser Lys Leu Ser Leu Phe Phe Glu Ile Lys Ser Ser
625 630 635 640

Asn Glu Lys Gly Arg Pro Pro Thr Tyr Ser Pro Ile Leu Asp Asp Gly
645 650 655

Ile Glu Phe Ser Gly Gly Leu Tyr Phe Asn Glu Lys Lys Ser Thr Glu
660 665 670

Glu Asn Lys Gln Lys Asn Val Leu Glu Ser Val Asn Leu Thr Ser Trp
675 680 685

Asp Lys Glu Asp Ile Val Lys Glu Asn Glu Asp Val Lys Leu Glu His
690 695 700

His His His His His
705

<210> 88
<211> 867
<212> PRT
<213> 人工序列

<220>
<223> PP25 生物融合蛋白

<400> 88

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala
1 5 10 15

Ala Gln Pro Ala Met Ala Met Gly Ser Asp Glu Leu Phe Asn Glu Leu
20 25 30

Leu Asn Ser Val Asp Val Asn Gly Glu Val Lys Glu Asn Ile Leu Glu
35 40 45

Glu Ser Gln Val Asn Asp Asp Ile Phe Asn Ser Leu Val Lys Ser Val

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

Ala Glu Thr Ile Lys Lys Glu Leu Gly Leu Ser Leu Thr Glu Pro Leu
275 280 285

Met Glu Gln Val Gly Thr Glu Glu Phe Ile Lys Arg Phe Gly Asp Gly
290 295 300

Ala Ser Arg Val Val Leu Ser Leu Pro Phe Ala Glu Gly Ser Ser Ser
305 310 315 320

Val Glu Tyr Ile Asn Asn Trp Glu Gln Ala Lys Ala Leu Ser Val Glu
325 330 335

Leu Glu Ile Asn Phe Glu Thr Arg Gly Lys Arg Gly Gln Asp Ala Met
340 345 350

Tyr Glu Tyr Met Ala Gln Ala Cys Ala Gly Asn Arg Val Arg Arg Ser
355 360 365

Val Gly Ser Ser Leu Ser Cys Ile Asn Leu Asp Trp Asp Val Ile Arg
370 375 380

Asp Lys Thr Lys Thr Lys Ile Glu Ser Leu Lys Glu His Gly Pro Ile
385 390 395 400

Lys Asn Lys Met Ser Glu Ser Pro Asn Lys Thr Val Ser Glu Glu Lys
405 410 415

Ala Lys Gln Tyr Leu Glu Glu Phe His Gln Thr Ala Leu Glu His Pro
420 425 430

Glu Leu Ser Glu Leu Lys Thr Val Thr Gly Thr Asn Pro Val Phe Ala
435 440 445

Gly Ala Asn Tyr Ala Ala Trp Ala Val Asn Val Ala Gln Val Ile Asp
450 455 460

Ser Glu Thr Ala Asp Asn Leu Glu Lys Thr Thr Ala Ala Leu Ser Ile
465 470 475 480

Leu Pro Gly Ile Gly Ser Val Met Gly Ile Ala Asp Gly Ala Val His
485 490 495

His Asn Thr Glu Glu Ile Val Ala Gln Ser Ile Ala Leu Ser Ser Leu
500 505 510

Met Val Ala Gln Ala Ile Pro Leu Val Gly Glu Leu Val Asp Ile Gly
515 520 525

Phe Ala Ala Tyr Asn Phe Val Glu Ser Ile Ile Asn Leu Phe Gln Val
530 535 540

Val His Asn Ser Tyr Asn Arg Pro Ala Tyr Ser Pro Gly His Lys Thr
545 550 555 560

Gln Pro Phe Leu His Asp Gly Tyr Ala Val Ser Trp Asn Thr Val Glu
565 570 575

Asp Ser Ile Ile Arg Thr Gly Phe Gln Gly Glu Ser Gly His Asp Ile
580 585 590

Lys Ile Thr Ala Glu Asn Thr Pro Leu Pro Ile Ala Gly Val Leu Leu
595 600 605

Pro Thr Ile Pro Gly Lys Leu Asp Val Asn Lys Ser Lys Thr His Ile
610 615 620

Ser Val Asn Gly Arg Lys Ile Arg Met Arg Cys Arg Ala Ile Asp Gly
625 630 635 640

Asp Val Thr Phe Cys Arg Pro Lys Ser Pro Val Tyr Val Gly Asn Gly
645 650 655

Val His Ala Asn Leu His Val Ala Phe His Arg Ser Ser Ser Glu Lys
660 665 670

Ile His Ser Asn Glu Ile Ser Ser Asp Ser Ile Gly Val Leu Gly Tyr
675 680 685

Gln Lys Thr Val Asp His Thr Lys Val Asn Ser Lys Leu Ser Leu Phe
690 695 700

Phe Glu Ile Lys Ser Ser Asp Glu Leu Phe Asn Glu Leu Leu Asn Ser
705 710 715 720

Val Asp Val Asn Gly Glu Val Lys Glu Asn Ile Leu Glu Glu Ser Gln
725 730 735

Val Asn Asp Asp Ile Phe Asn Ser Leu Val Lys Ser Val Gln Gln Glu
740 745 750

Gln Gln His Asn Val Glu Glu Lys Val Glu Glu Ser Val Glu Glu Asn
755 760 765

Asp Glu Glu Ser Val Glu Glu Asn Val Glu Glu Asn Val Glu Glu Asn
770 775 780

Asp Asp Glu Ser Val Ala Ser Ser Val Glu Glu Ser Ile Ala Ser Ser
785 790 795 800

Val Asp Glu Ser Ile Asp Ser Ser Ile Glu Glu Asn Val Ala Pro Thr
805 810 815

Val Glu Glu Ile Val Ala Pro Thr Val Glu Glu Ile Val Ala Pro Ser
820 825 830

Val Val Glu Ser Val Ala Pro Ser Val Glu Glu Ser Val Glu Glu Asn
835 840 845

Val Glu Glu Ser Val Ala Glu Asn Val Glu Glu Leu Glu His His His
850 855 860

His His His
865

<210> 89
<211> 807
<212> PRT
<213> 惡性瘧原蟲

<400> 89

Ile Pro Glu Glu Gln Ile Glu Glu Val Ile Gln Glu Glu Ile Ile Glu
1 5 10 15

Gln Val Val Pro Glu Glu Leu Ile Glu Glu Val Val Pro Glu Glu Ile
20 25 30

Ile Glu Glu Val Ile Pro Glu Glu Ile Val Glu Glu Val Ile Tyr Glu
35 40 45

Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile Ala Glu Lys Leu
50 55 60

Val Lys Glu Ile Val Pro Glu Gln Val Arg Glu Glu Val Thr Leu Glu
65 70 75 80

Glu Ile Val Glu Glu Met Ile Pro Glu Glu Phe Val Glu Glu Val Ala
85 90 95

Pro Glu Val Glu Ile Glu Glu Ile Ile Pro Glu Glu Leu Ile Glu Glu
100 105 110

Val Ile Pro Glu Val Leu Val Glu Glu Ala Val Pro Glu Glu Leu Ile
115 120 125

Glu Lys Val Ile Pro Gly Ala Asp Asp Val Val Asp Ser Ser Lys Ser
130 135 140

Phe Val Met Glu Asn Phe Ser Ser Tyr His Gly Thr Lys Pro Gly Tyr
145 150 155 160

Val Asp Ser Ile Gln Lys Gly Ile Gln Lys Pro Lys Ser Gly Thr Gln
165 170 175

Gly Asn Tyr Asp Asp Asp Trp Lys Glu Phe Tyr Ser Thr Asp Asn Lys
180 185 190

Tyr Asp Ala Ala Gly Tyr Ser Val Asp Asn Glu Asn Pro Leu Ser Gly
195 200 205

Lys Ala Gly Gly Val Val Lys Val Thr Tyr Pro Gly Leu Thr Lys Val
210 215 220

Leu Ala Leu Lys Val Asp Asn Ala Glu Thr Ile Lys Lys Glu Leu Gly
225 230 235 240

Leu Ser Leu Thr Glu Pro Leu Met Glu Gln Val Gly Thr Glu Glu Phe

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

Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala Ile Pro Leu Val
465 470 475 480

Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn Phe Val Glu Ser
485 490 495

Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr Asn Arg Pro Ala
500 505 510

Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu His Asp Gly Tyr Ala
515 520 525

Val Ser Trp Asn Thr Val Glu Asp Ser Ile Ile Arg Thr Gly Phe Gln
530 535 540

Gly Glu Ser Gly His Asp Ile Lys Ile Thr Ala Glu Asn Thr Pro Leu
545 550 555 560

Pro Ile Ala Gly Val Leu Leu Pro Thr Ile Pro Gly Lys Leu Asp Val
565 570 575

Asn Lys Ser Lys Thr His Ile Ser Val Asn Gly Arg Lys Ile Arg Met
580 585 590

Arg Cys Arg Ala Ile Asp Gly Asp Val Thr Phe Cys Arg Pro Lys Ser
595 600 605

Pro Val Tyr Val Gly Asn Gly Val His Ala Asn Leu His Val Ala Phe
610 615 620

His Arg Ser Ser Ser Glu Lys Ile His Ser Asn Glu Ile Ser Ser Asp
625 630 635 640

Ser Ile Gly Val Leu Gly Tyr Gln Lys Thr Val Asp His Thr Lys Val
645 650 655

Asn Ser Lys Leu Ser Leu Phe Phe Glu Ile Lys Ser Ile Pro Glu Glu
660 665 670

Gln Ile Glu Glu Val Ile Gln Glu Glu Ile Ile Glu Gln Val Val Pro
675 680 685

Glu Glu Leu Ile Glu Glu Val Val Pro Glu Glu Ile Ile Glu Glu Val
690 695 700

Ile Pro Glu Glu Ile Val Glu Glu Val Ile Tyr Glu Glu Val Ile Pro
705 710 715 720

Glu Glu Leu Val Glu Glu Val Ile Ala Glu Lys Leu Val Lys Glu Ile
725 730 735

Val Pro Glu Gln Val Arg Glu Glu Val Thr Leu Glu Glu Ile Val Glu
740 745 750

Glu Met Ile Pro Glu Glu Phe Val Glu Glu Val Ala Pro Glu Val Glu
755 760 765

Ile Glu Glu Ile Ile Pro Glu Glu Leu Ile Glu Glu Val Ile Pro Glu
770 775 780

Val Leu Val Glu Glu Ala Val Pro Glu Glu Leu Ile Glu Lys Val Ile
785 790 795 800

Pro His His His His His His
805

【發明申請專利範圍】

【第1項】

一種生物融合體經純化瘧疾疫苗，其包括由特定抗體及/或淋巴球辨識之瘧原蟲屬(*Plasmodium*)抗原性胺基酸序列，該序列與源自微生物毒素之非寄生免疫原性分子融合，該生物融合體經純化瘧疾疫苗於體內引起抗瘧原蟲屬感染之特定免疫反應及保護性免疫學反應。

【第2項】

如請求項1之疫苗，其中該非寄生免疫原性分子係選自由以下組成之群：白喉類毒素之交叉反應材料(CRM)、白喉類毒素(D)、無毒突變重組銅綠假單胞菌(*Pseudomonas aeruginosa*)胞外蛋白A (repA)、腦膜炎球菌外膜蛋白複合物(OMPC)、破傷風類毒素(T)、流行性感冒嗜血桿菌蛋白D (H. influenza protein D, hiD)及其免疫原性片段。

【第3項】

如請求項2之疫苗，其中該非寄生免疫原性分子係CRM197或其免疫原性片段。

【第4項】

如請求項3之疫苗，其中該片段係選自由以下組成之群：CRM197之片段A、跨膜結構域T、受體結合結構域R、CRM197之胺基酸序列1至190及CRM197之胺基酸序列1至389。

【第5項】

如請求項1至4中任一項之疫苗，其中該抗原性胺基酸序列係由紅血球階段之瘧原蟲屬表現之抗原性蛋白或其表位片段。

【第6項】

如請求項5之疫苗，其中該抗原性胺基酸序列係選自由以下組成之群：MSP3、LSA5（亦稱為PEBS或11-1之子區）、Glurp R0及R2、SERP、P27及P27A、P45、P90及P77、P14、P181、MSP1-區2、MSP2、GBP 130、蛋白質332、蛋白質11-1、MSP4或其任一表位片段。

【第7項】

如請求項6之疫苗，其中該抗原性胺基酸序列係MSP3或其表位片段。

【第8項】

如請求項7之疫苗，其中該片段涵蓋選自MSP3-1、MSP3-2、MSP3-3、MSP3-4、MSP3-7及MSP3-8之瘧原蟲屬MSP3蛋白之C-末端區域之基序a、b、c、d、e及/或f。

【第9項】

如請求項8之疫苗，其中該瘧原蟲屬MSP3蛋白係MSP3-1。

【第10項】

如請求項1至4中任一項之疫苗，其中該抗原性胺基酸序列係由紅血球前階段之瘧原蟲屬表現之抗原性蛋白或其表位片段。

【第11項】

如請求項10之疫苗，其中該抗原性胺基酸序列係選自由以下組成之群：LSA3、LSA5（亦稱為PEBS或11-1之子區）、CS、Trap及Salsa及其任一表位片段。

【第12項】

如請求項1至4中任一項之疫苗，其中該抗原性胺基酸序列係選自由以下組成之群：Pf25、Pf45/48、Rh5、AMA1、MSP1-19、MSP1-42、

MSP2、MSP4-5、Var CSA及其任一表位片段。

【第13項】

如請求項1至4中任一項之疫苗，其包括作為該抗原性胺基酸序列之MSP3、LSA3、LSA5或其表位片段，其融合至作為該非寄生免疫原性分子之CRM197或其免疫原性片段。

【第14項】

如請求項13之疫苗，其中該MSP3係MSP3-1。

【第15項】

如請求項1至4中任一項之疫苗，其中該抗原性胺基酸序列係選自SEQ ID NO:1至80。

【第16項】

如請求項1至4中任一項之疫苗，其包括兩個各自位於該非寄生免疫原性分子之C-末端及N-末端或皆位於相同末端之抗原性胺基酸序列。

【第17項】

如請求項1至4中任一項之疫苗，其中該抗原性胺基酸序列藉由肽連接體連接於該非寄生免疫原性分子之N-末端及/或C-末端。

【第18項】

如請求項17之疫苗，其中該肽連接體係1至35個胺基酸之序列。

【第19項】

如請求項18之疫苗，其中該肽連接體係5至20個胺基酸之序列。

【第20項】

如請求項17之疫苗，其中該肽連接體係(Gly-Gly-Gly-Gly-Ser)_n、(Gly)_n或(EAAAK)_n，其中n為1至4。

【第21項】

如請求項20之疫苗，其中n為1至3。

【第22項】

一種核酸構築體，其編碼如請求項1至21中任一項所定義之生物融合體。

【第23項】

一種載體，其在表現盒中包括如請求項22之核酸構築體。

【第24項】

一種宿主細胞，其中已插入如請求項23之載體。

【第25項】

一種製備如請求項1至21中任一項所定義之生物融合體之活體外方法，該方法包括容許如請求項24之宿主細胞在誘導表現如請求項22所定義之核酸構築體之條件下繁殖，及收集所表現之該生物融合體。

【第26項】

一種疫苗，其包括如請求項1至21中任一項所定義之生物融合體、或至少兩種分別包括至少兩個不同抗原性胺基酸序列之如請求項1至21中任一項所定義之生物融合體之組合、或如請求項22所定義之編碼該(等)生物融合體之核酸構築體，與生理上可接受之媒劑。

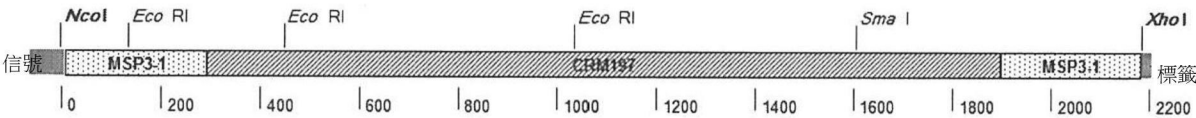
【第27項】

如請求項26之疫苗，其用於對人類個體接種疫苗來對抗瘧疾。

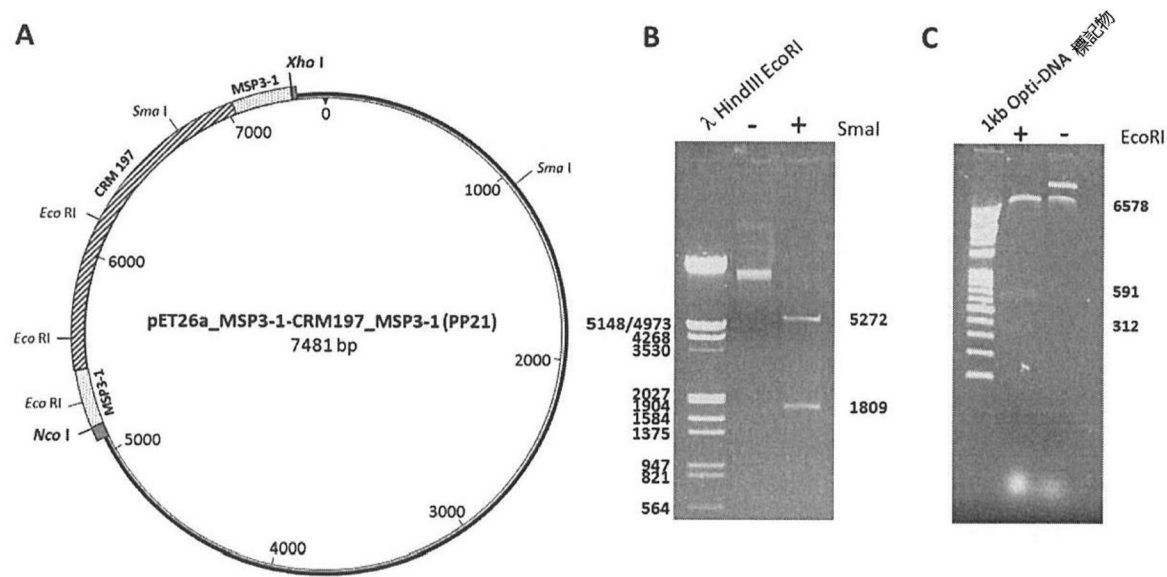
【第28項】

一種如請求項1至21及26中任一項之疫苗之用途，其用以製造用於對人類個體接種疫苗來對抗瘧疾之藥物。

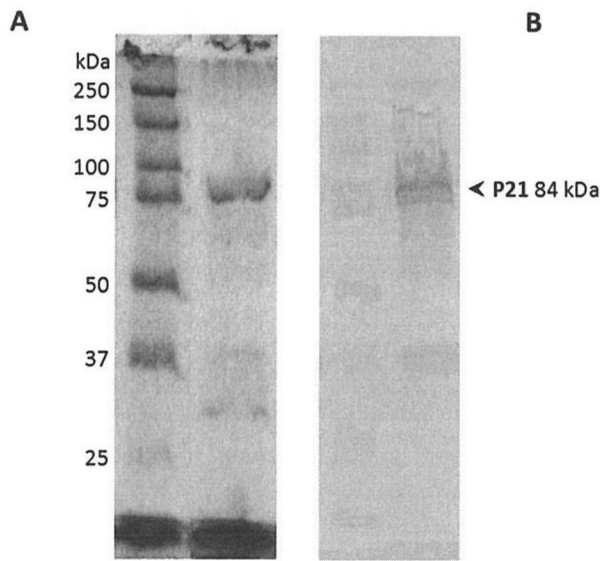
【發明圖式】



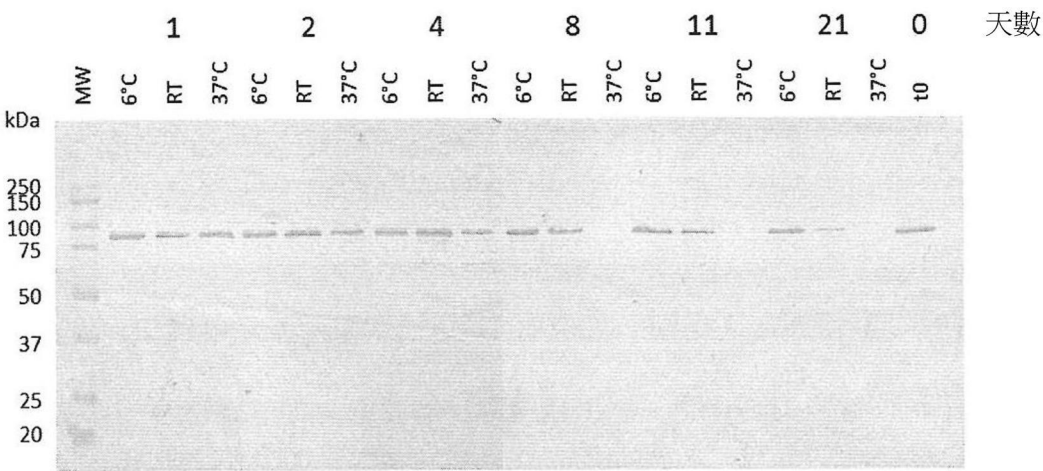
【圖 1】



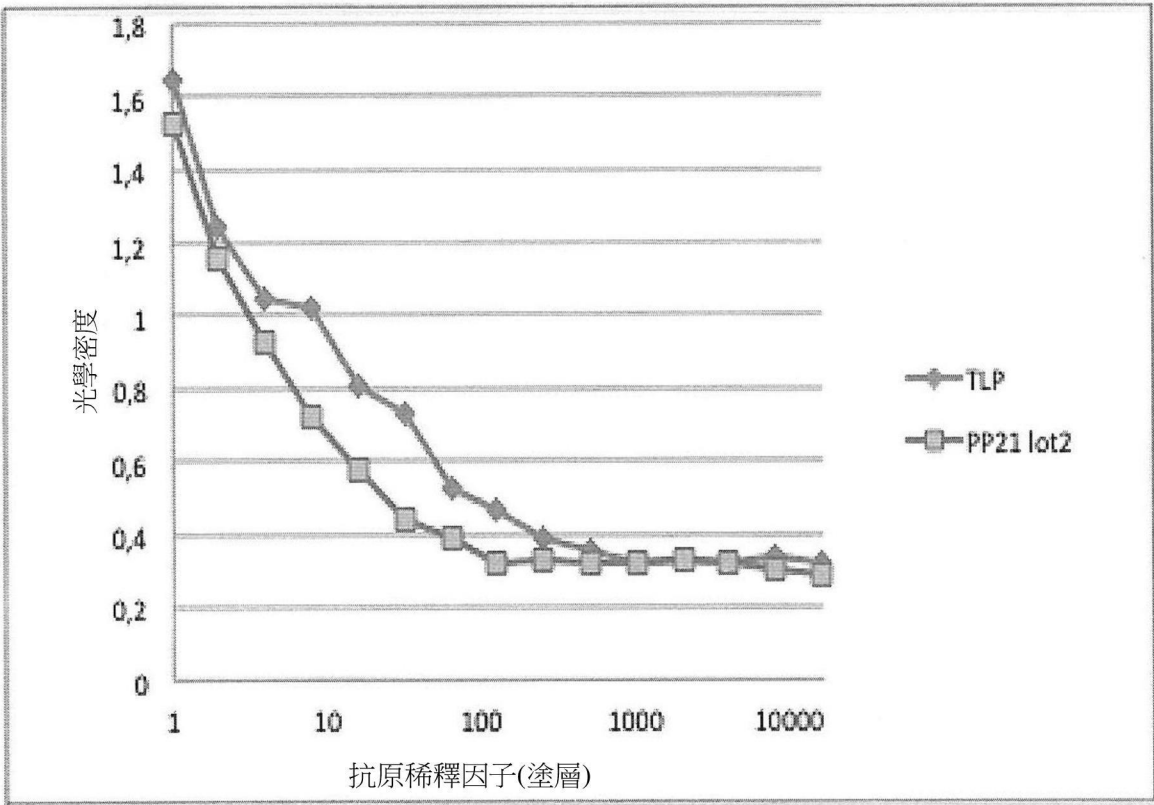
【圖 2】



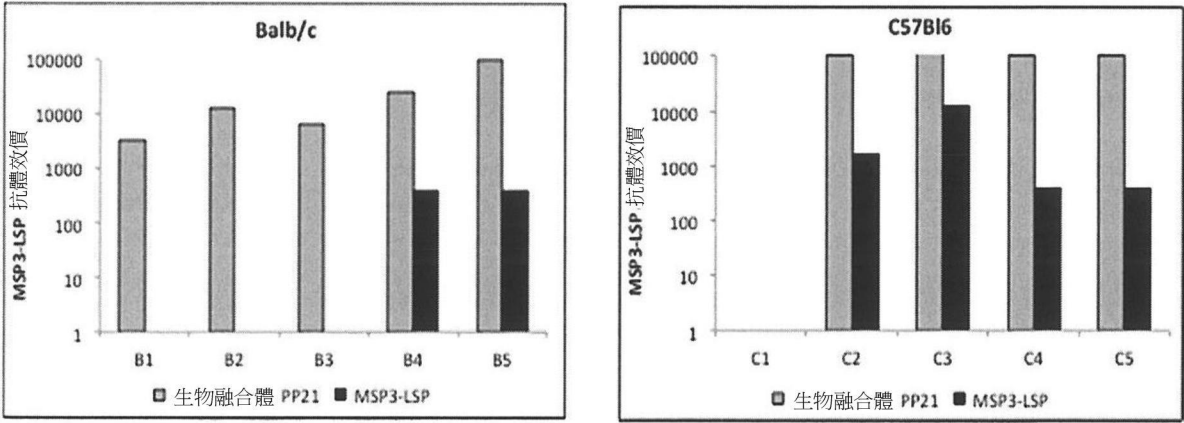
【圖 3】



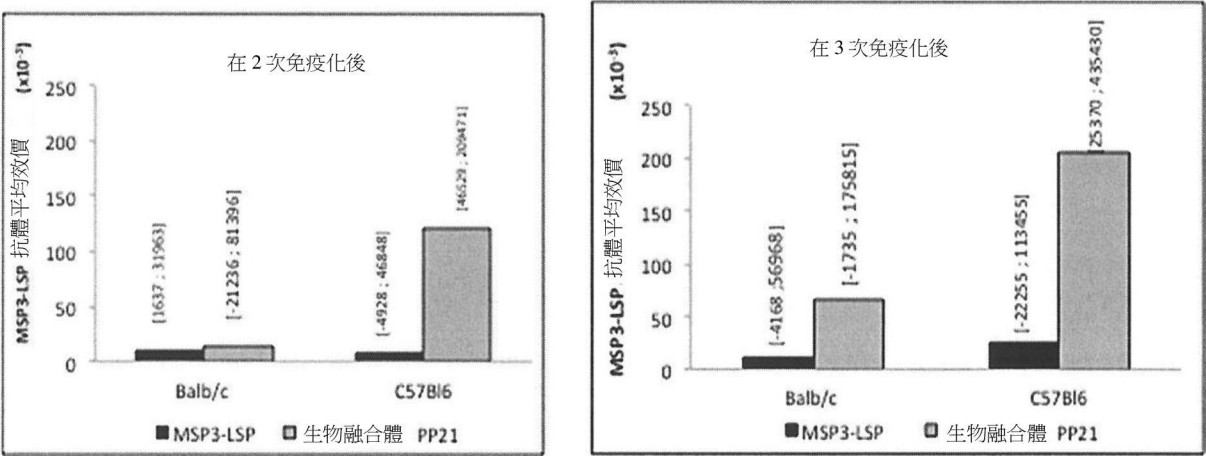
【圖 4】



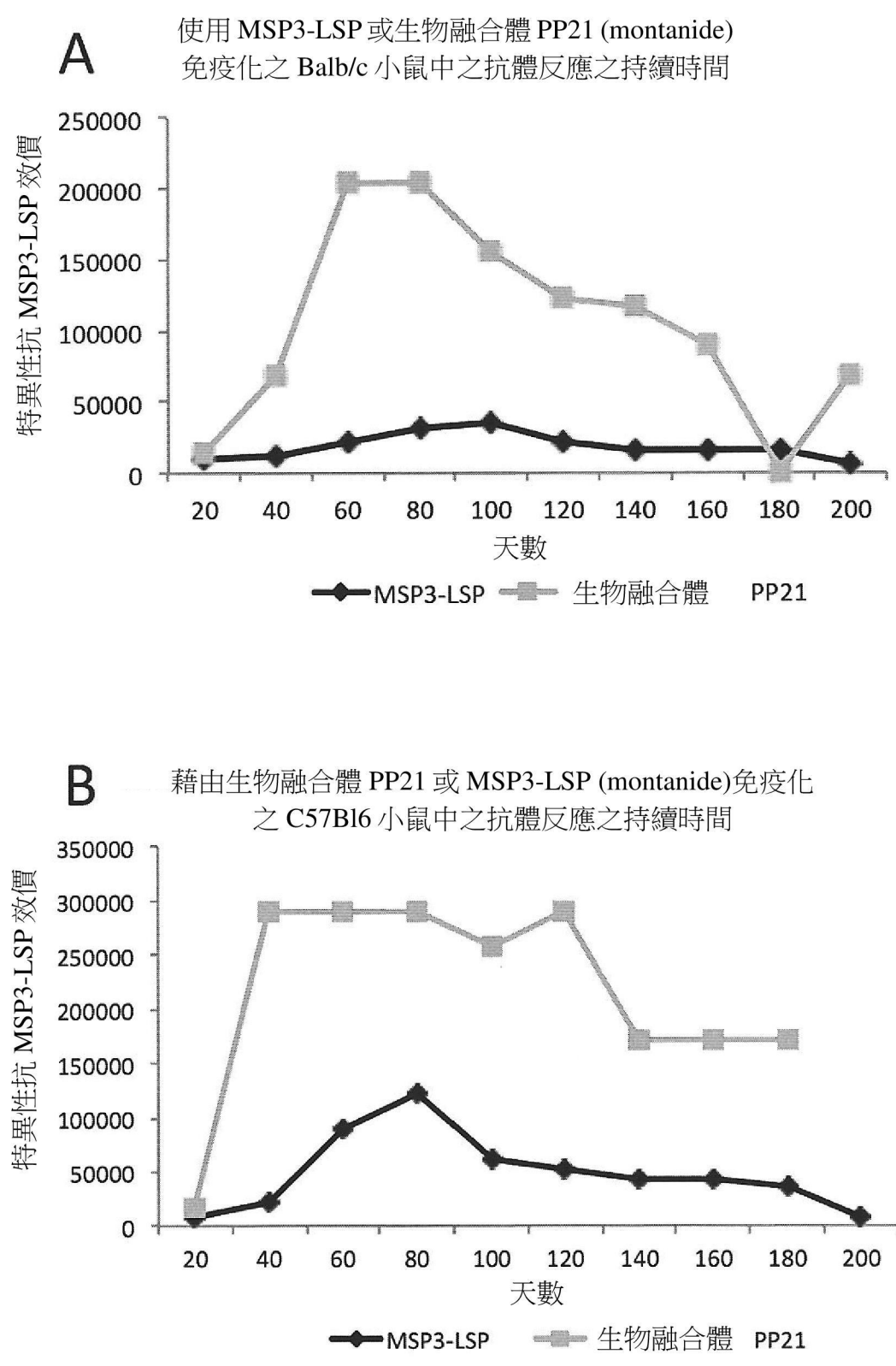
【圖 5】



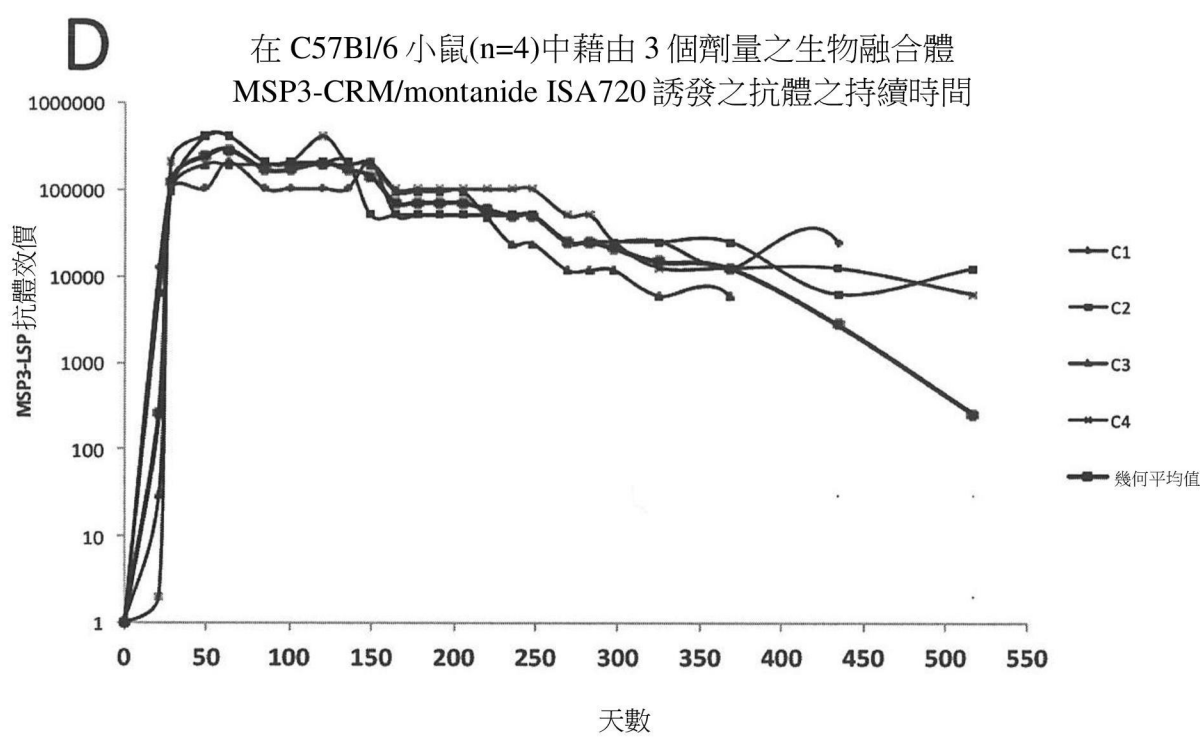
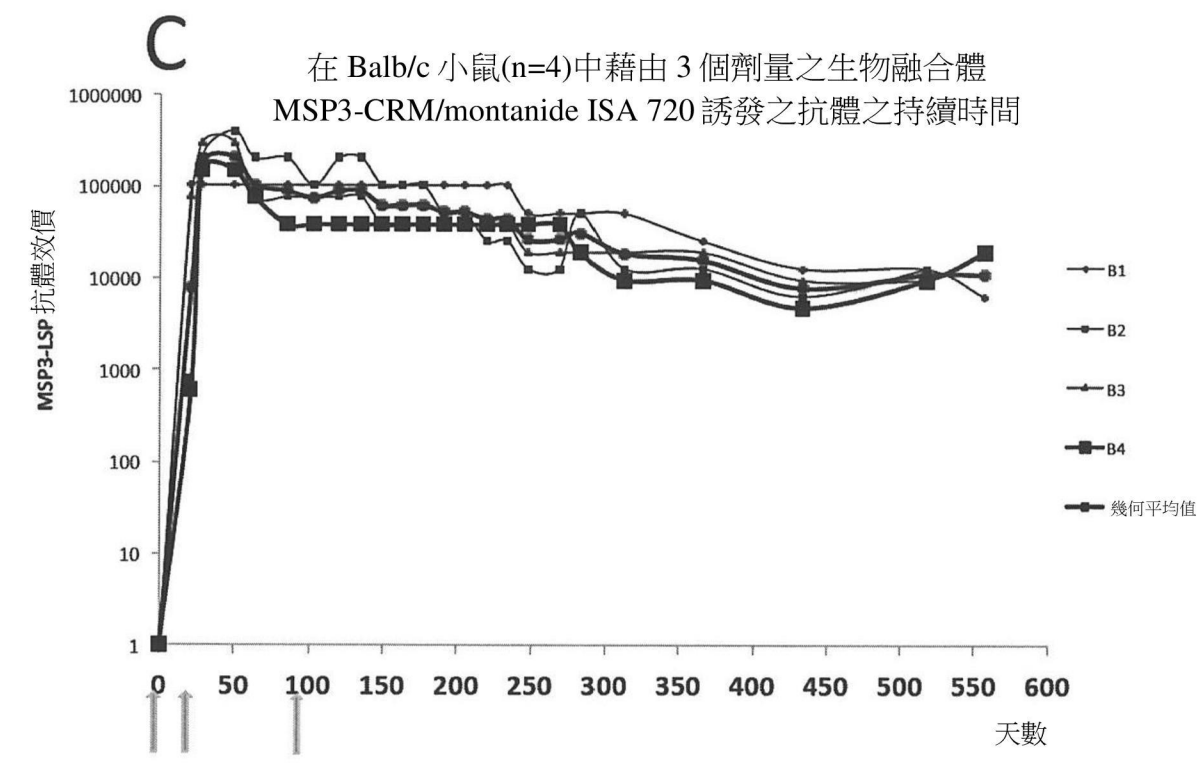
【圖 6】



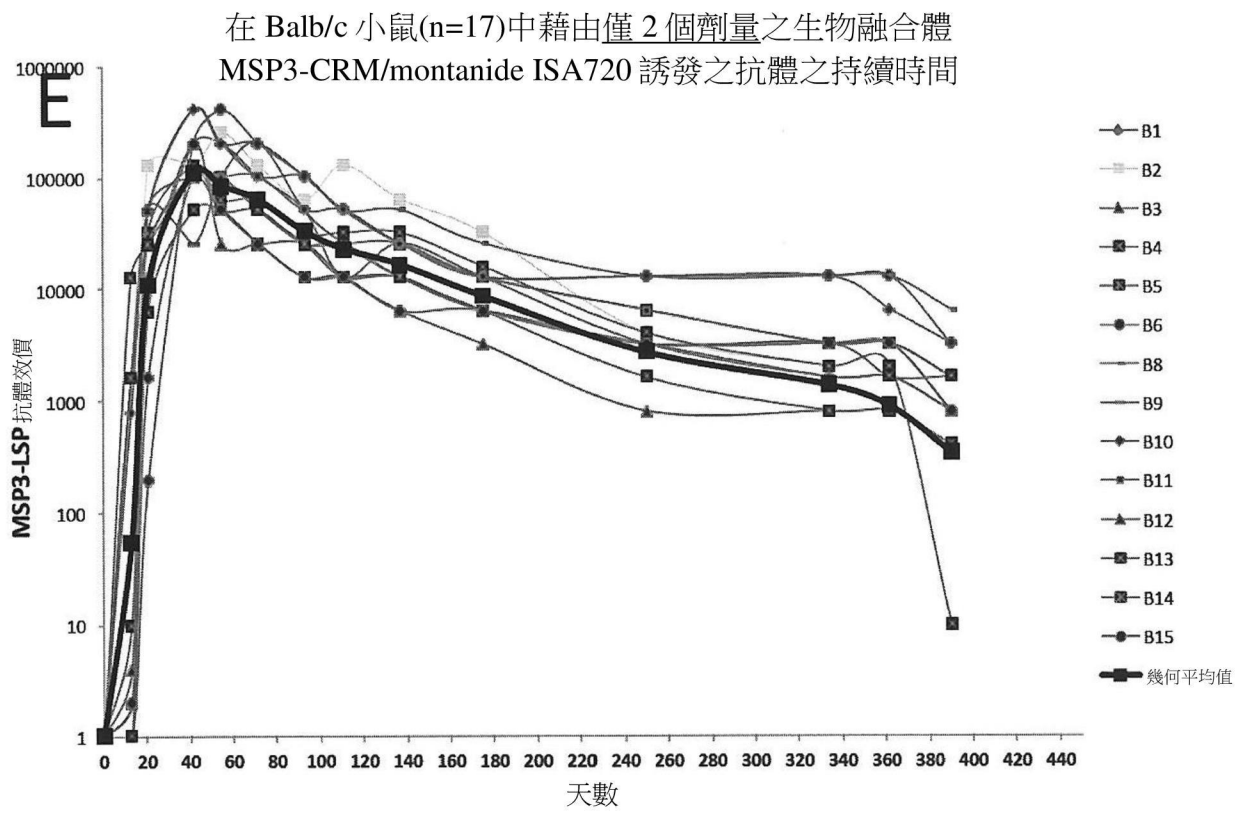
【圖 7】



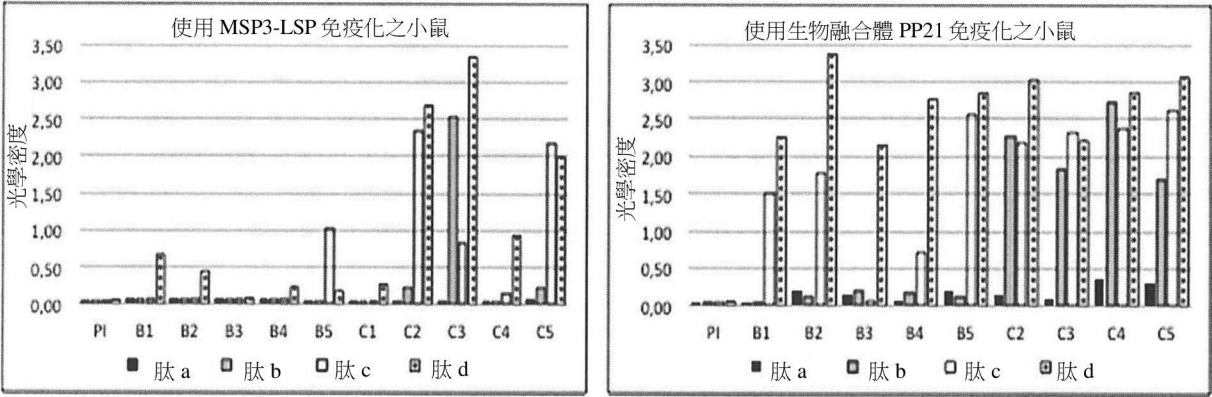
【圖 8】



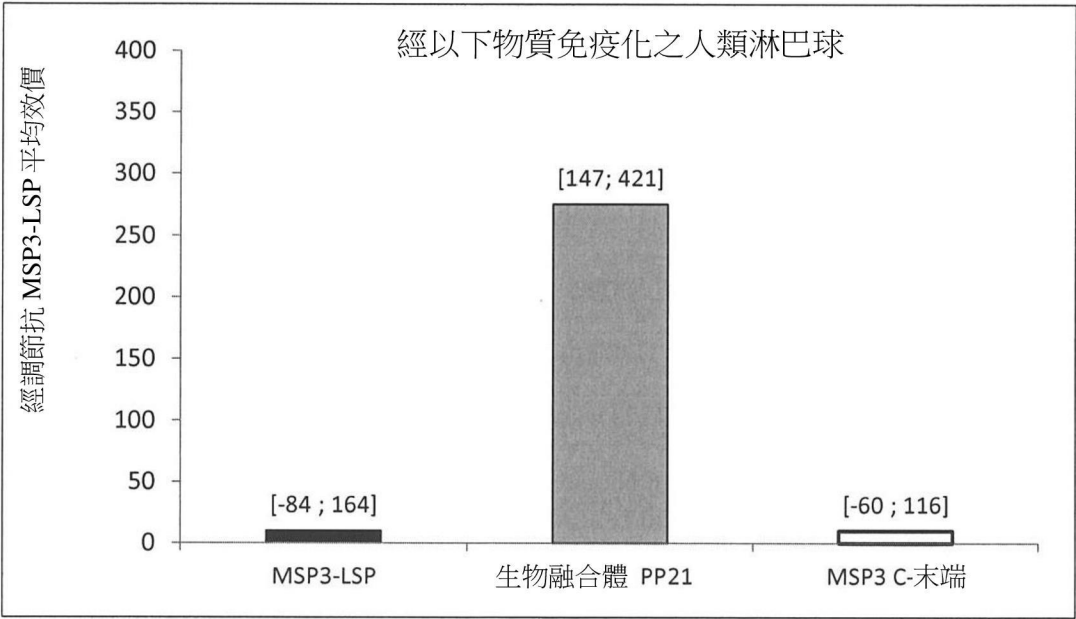
【圖 8】(續)



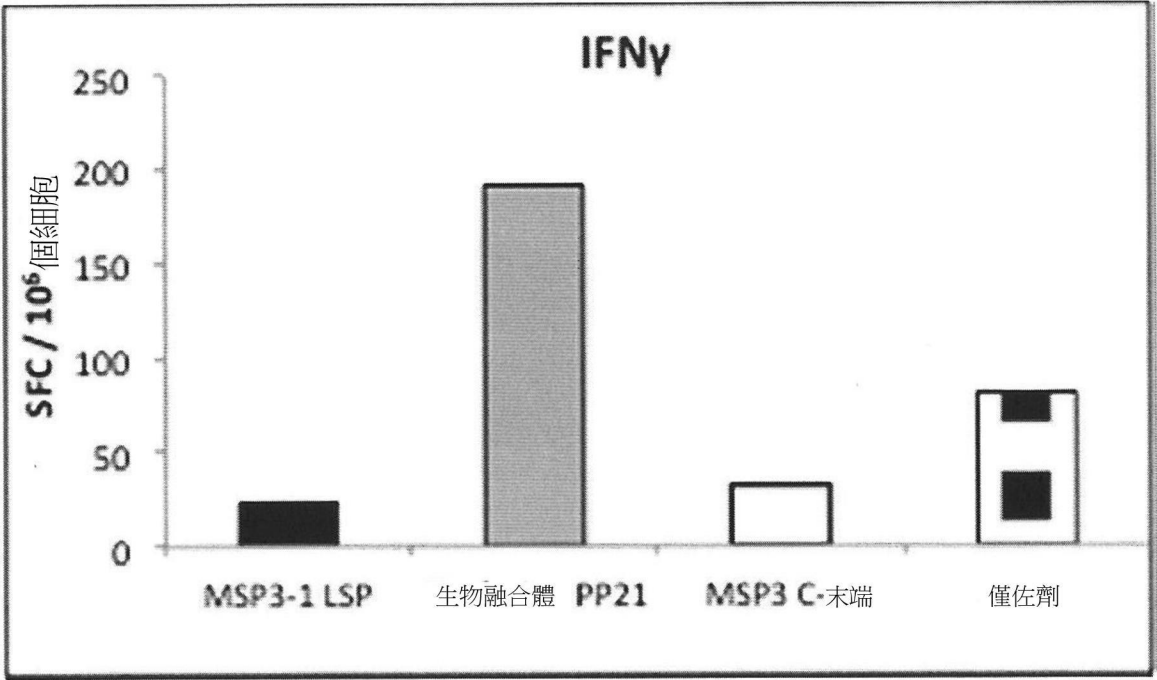
【圖 8】(續)



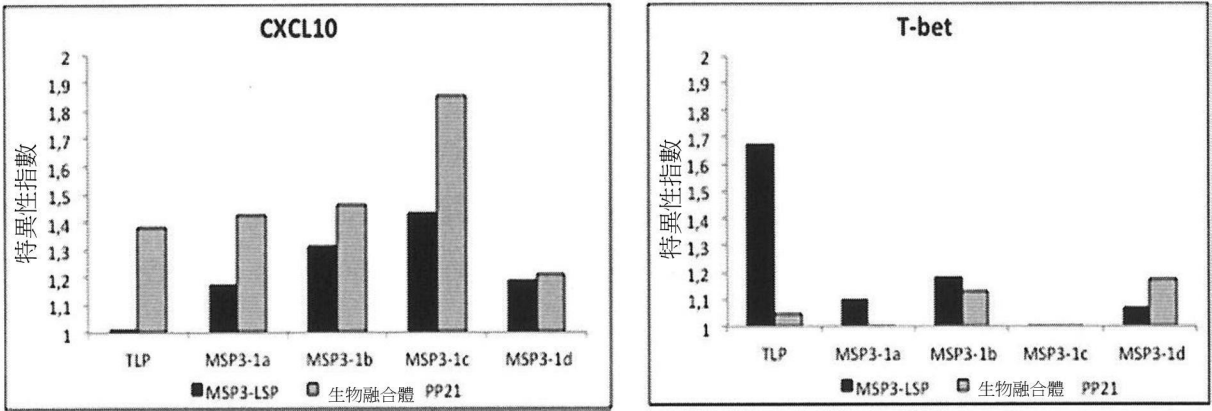
【圖 9】



【圖 10】

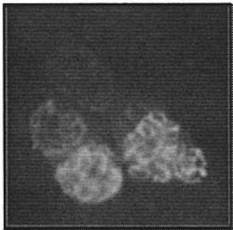


【圖 11】

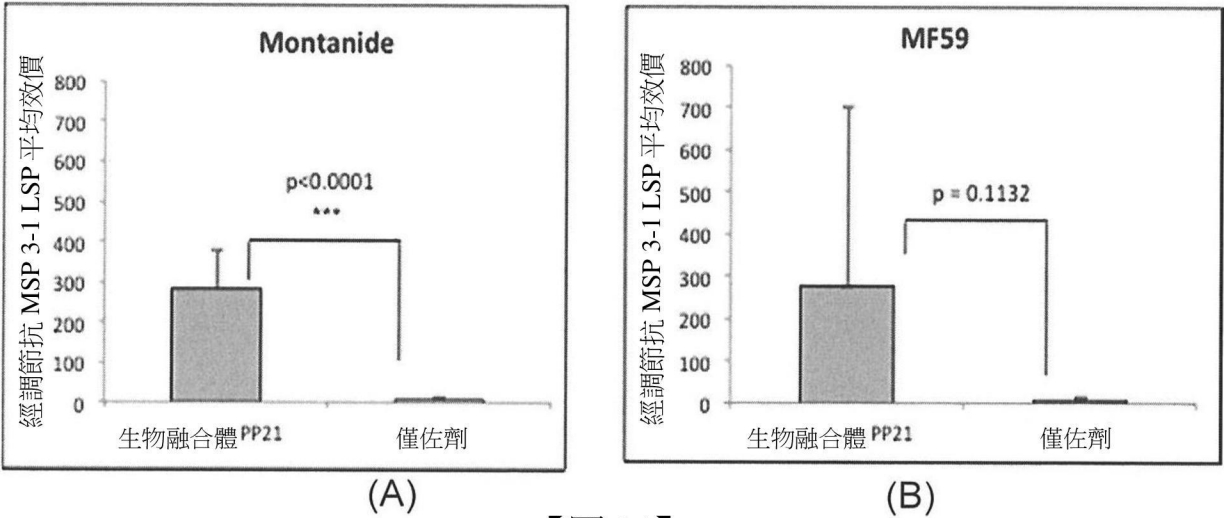


【圖 12】

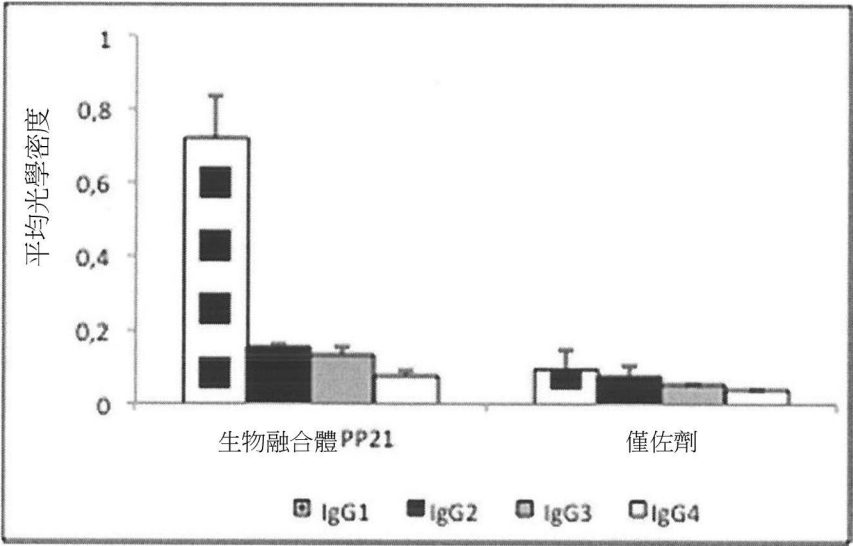
免疫化抗原	Pf 3D7 成熟裂殖體上之 IFAT 效價
MSP3-C 末端	陰性
生物融合體 MSP3-1	160 - 320
MSP3-1 LSP	0 - 20
僅佐劑	陰性



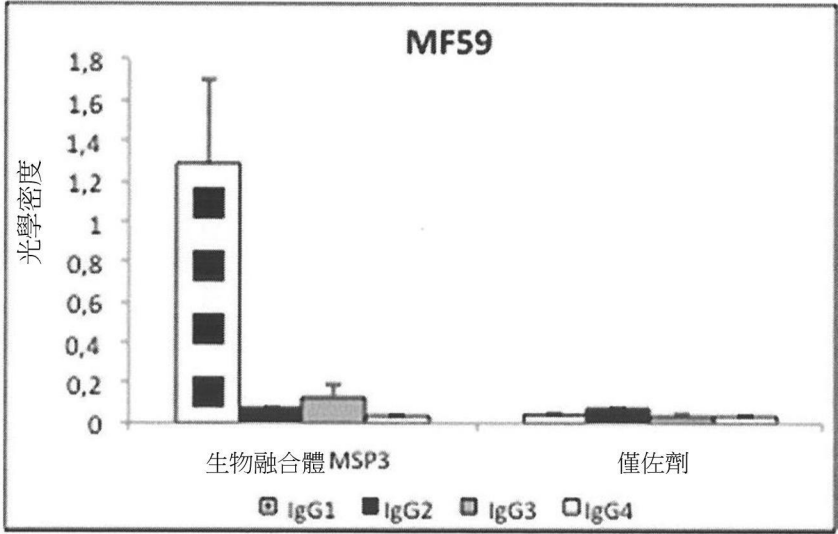
【圖 13】



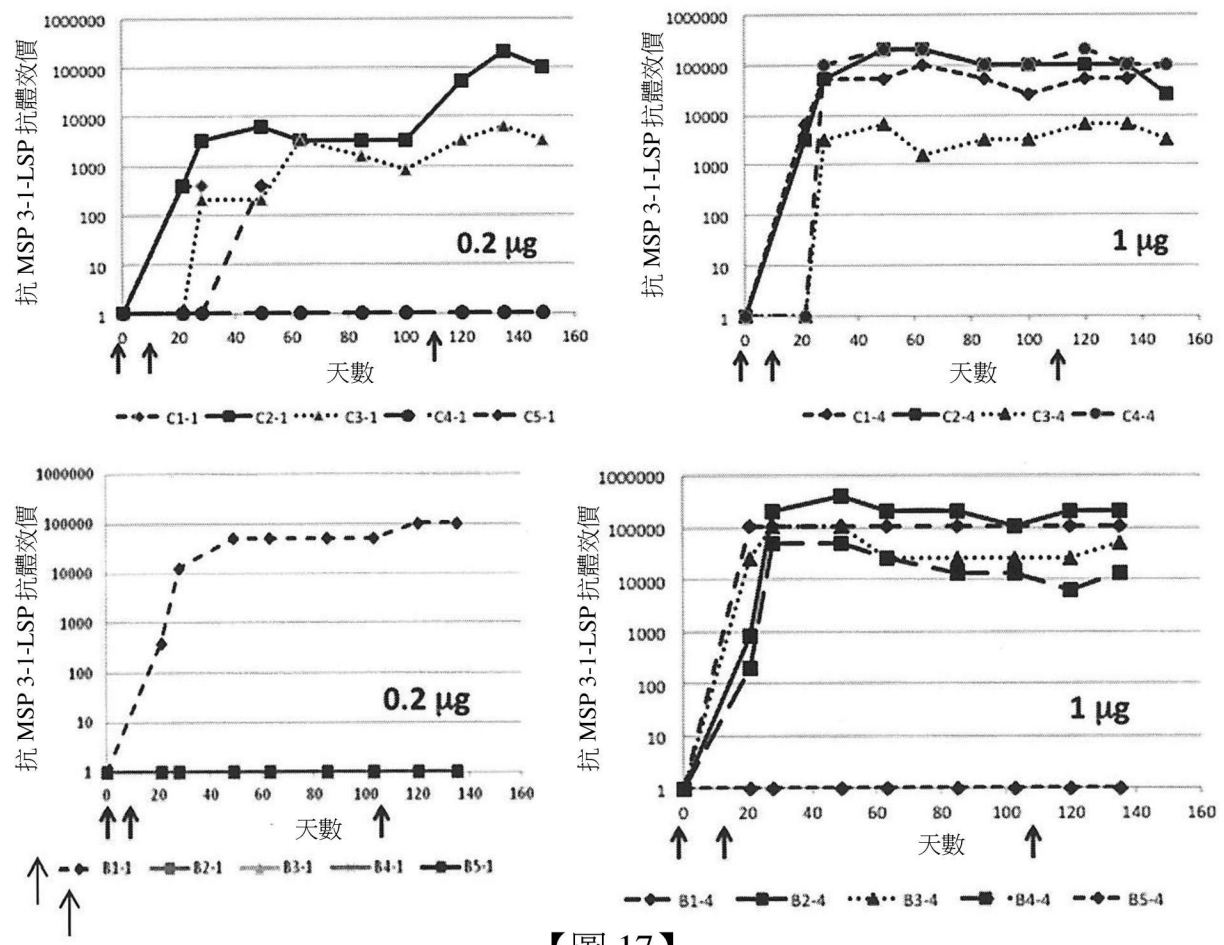
【圖 14】



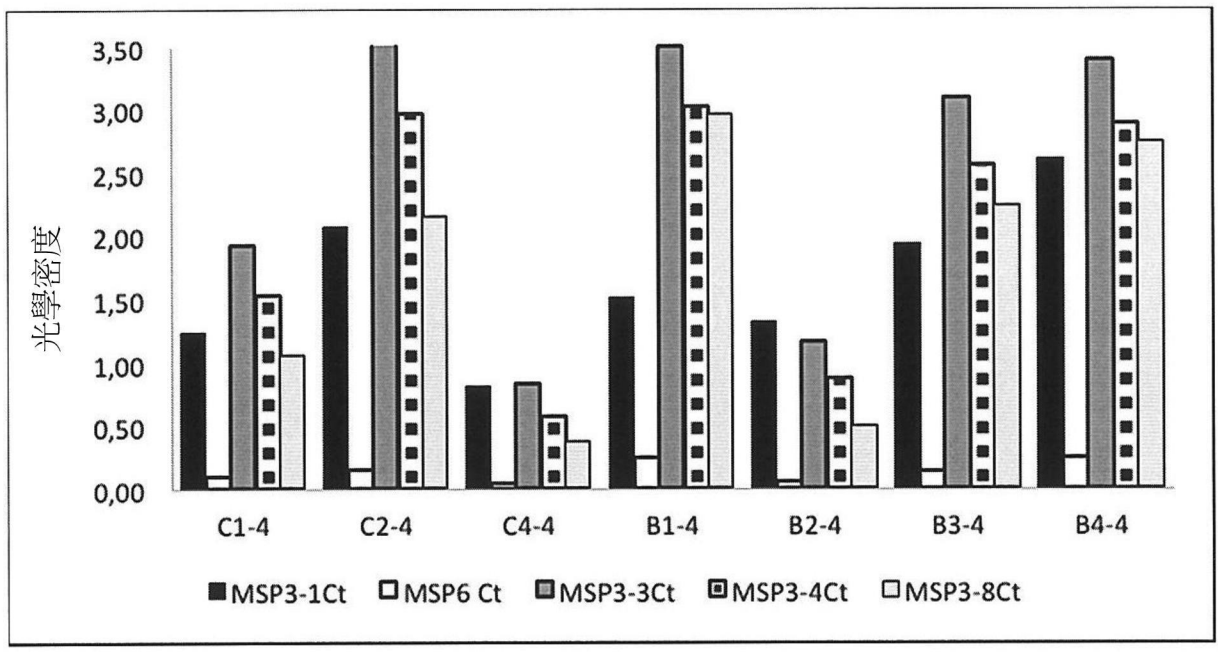
【圖 15】



【圖 16】



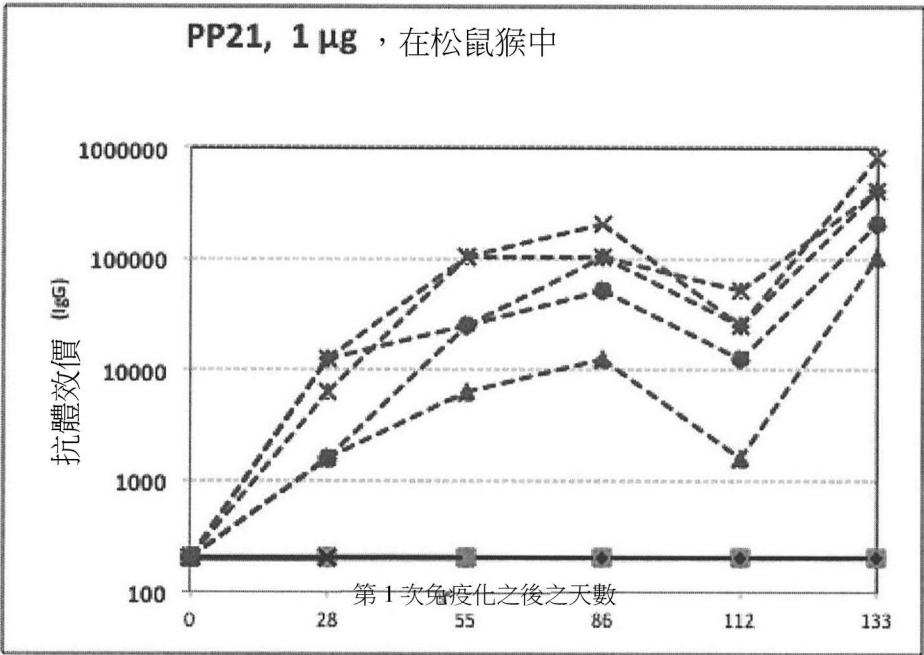
【圖 17】



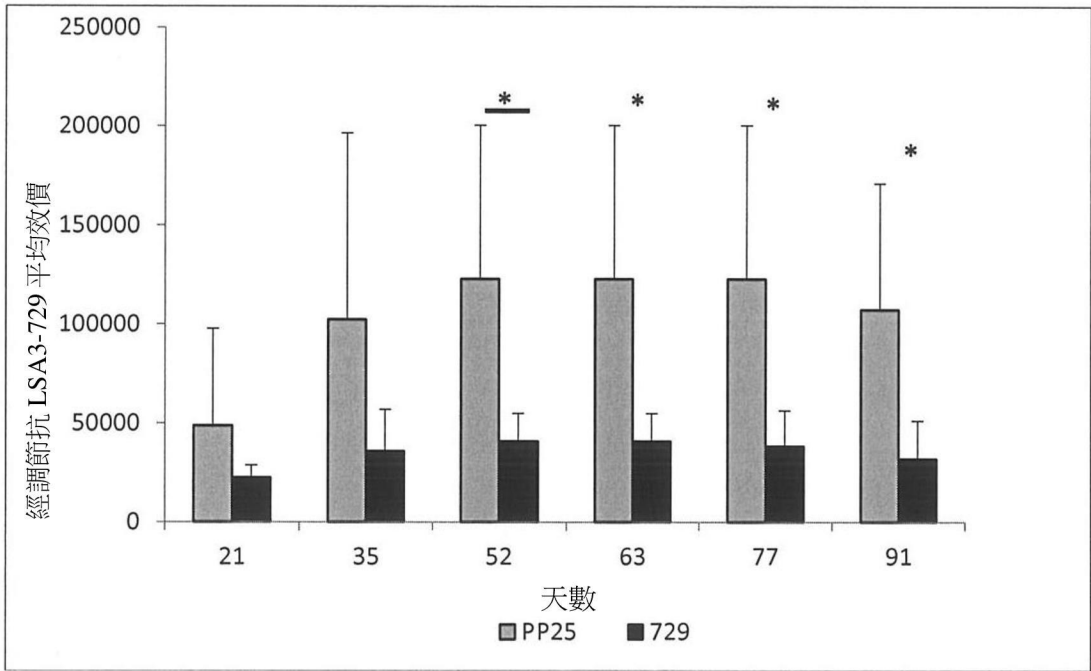
【圖 18】

	C1 PP21	C2 PP21	C3 PP21	C4 PP21	B1 PP21	B2 PP21	B3 PP21	B4 PP21	B5 PP21
J21 (2 次注射後)	400	200	0	1600	>> 25600	>>> 25600	>> 25600	>> 25600	>>> 25600
J35 (3 次注射後)	6400	25600	3200	6400	>> 25600	>>> 25600	>>> 25600	>>> 25600	>>> 25600

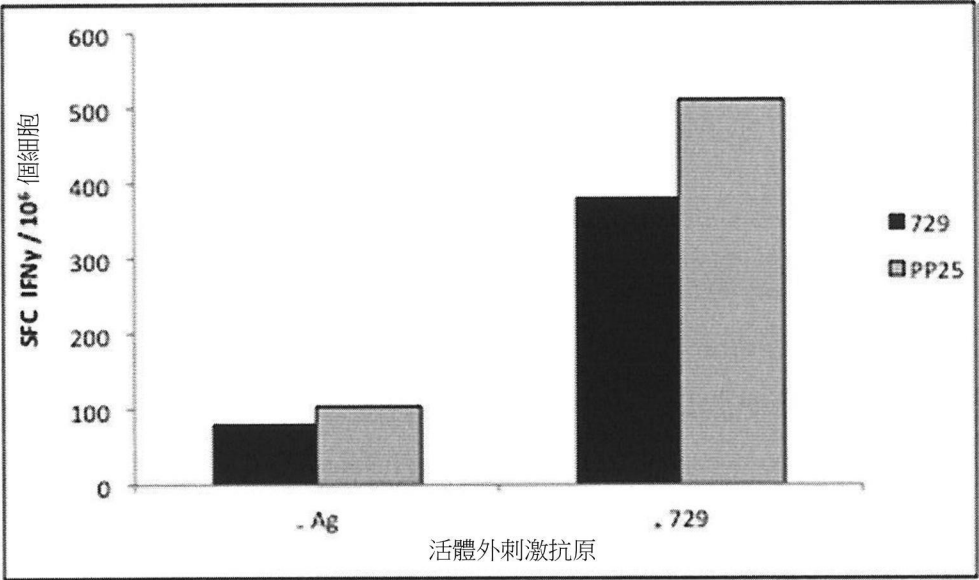
【圖 19】



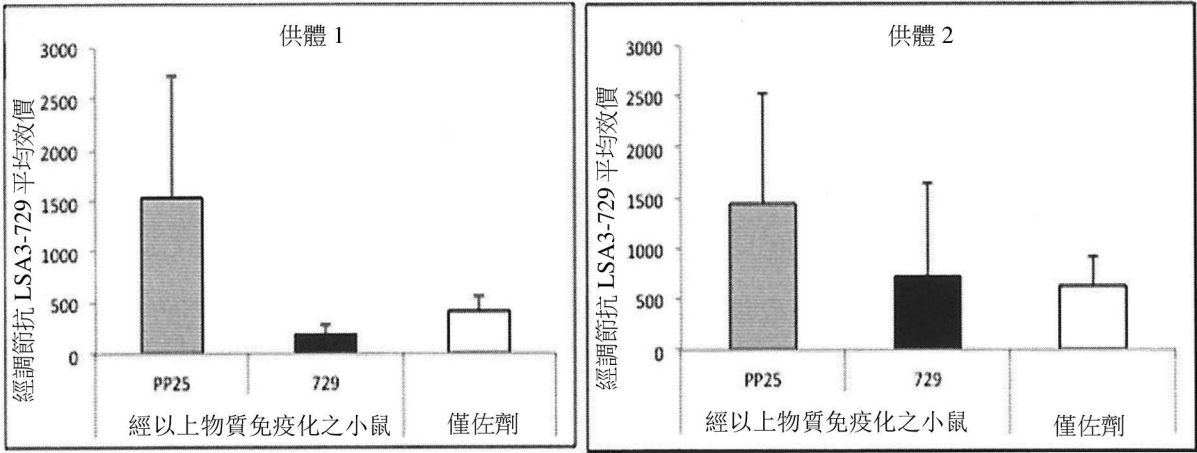
【圖 20】



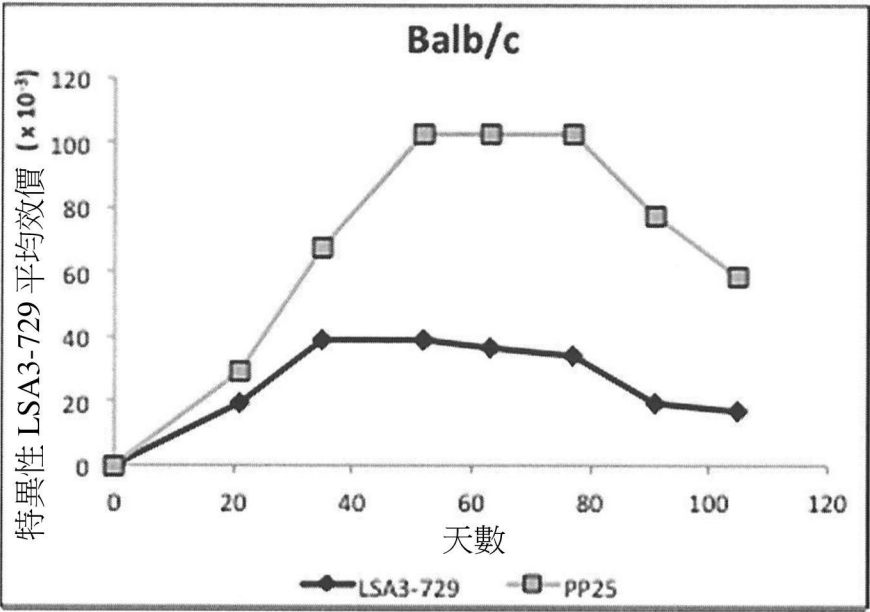
【圖 21】



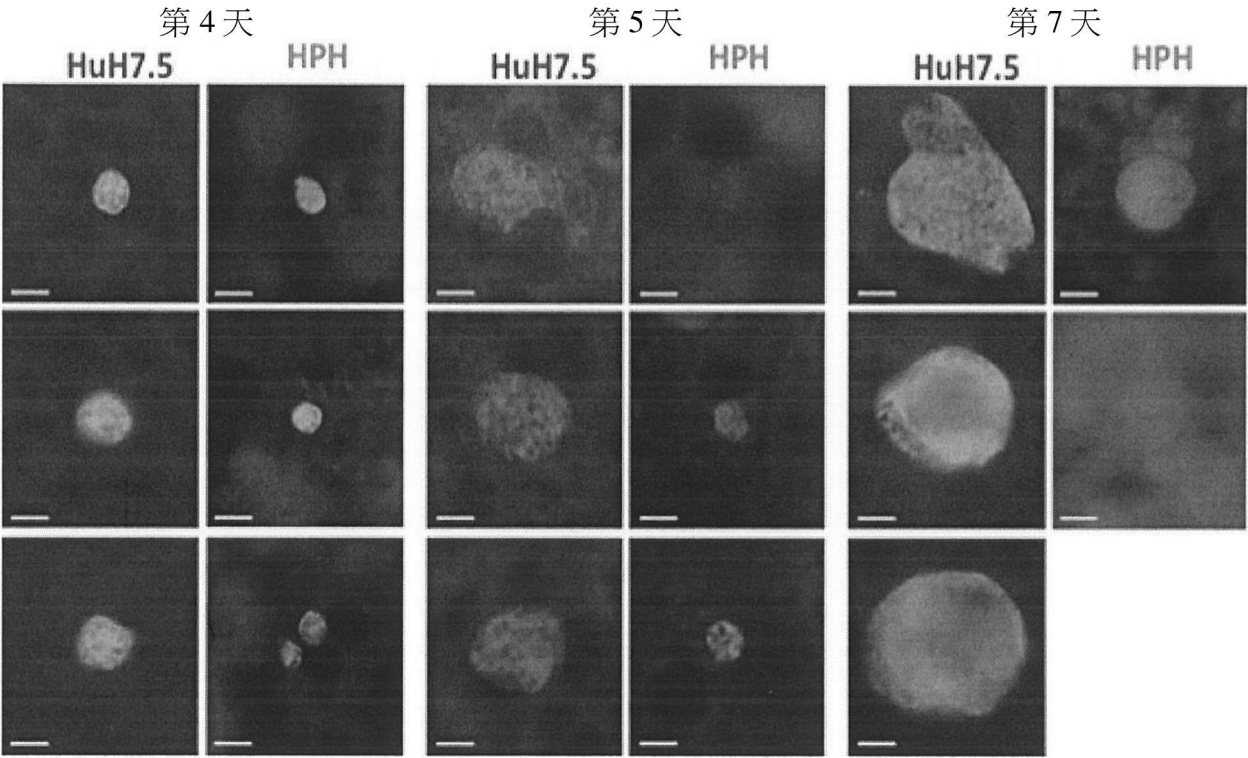
【圖 22】



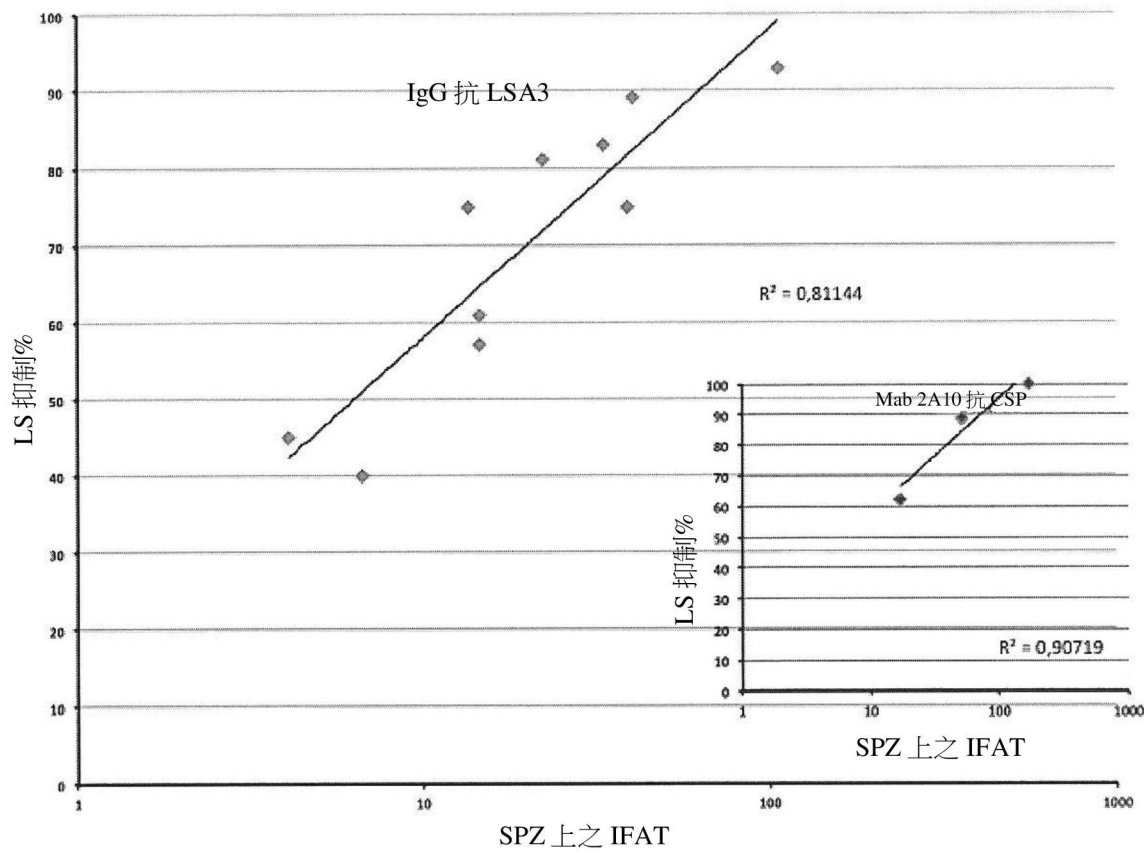
【圖 23】



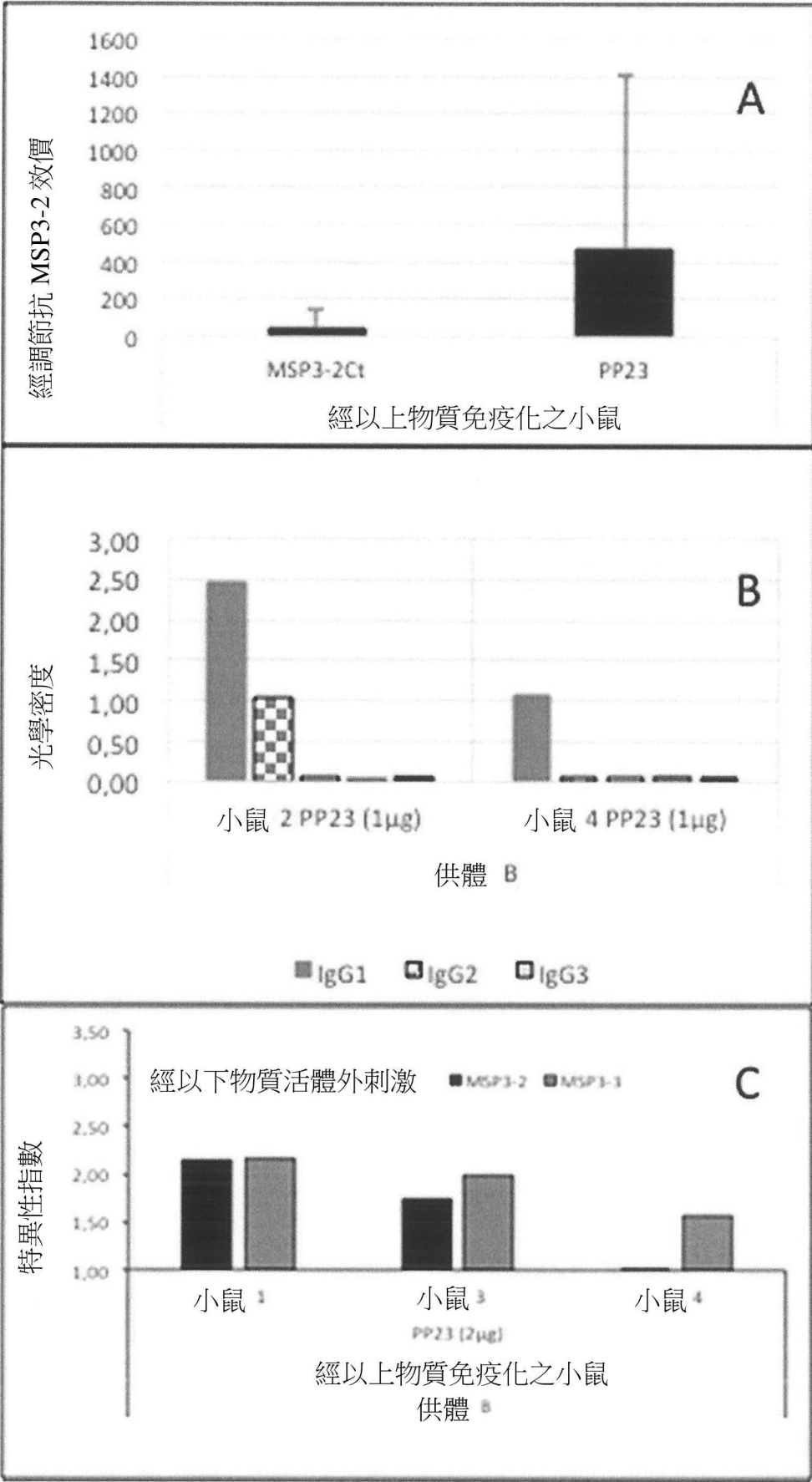
【圖 24】



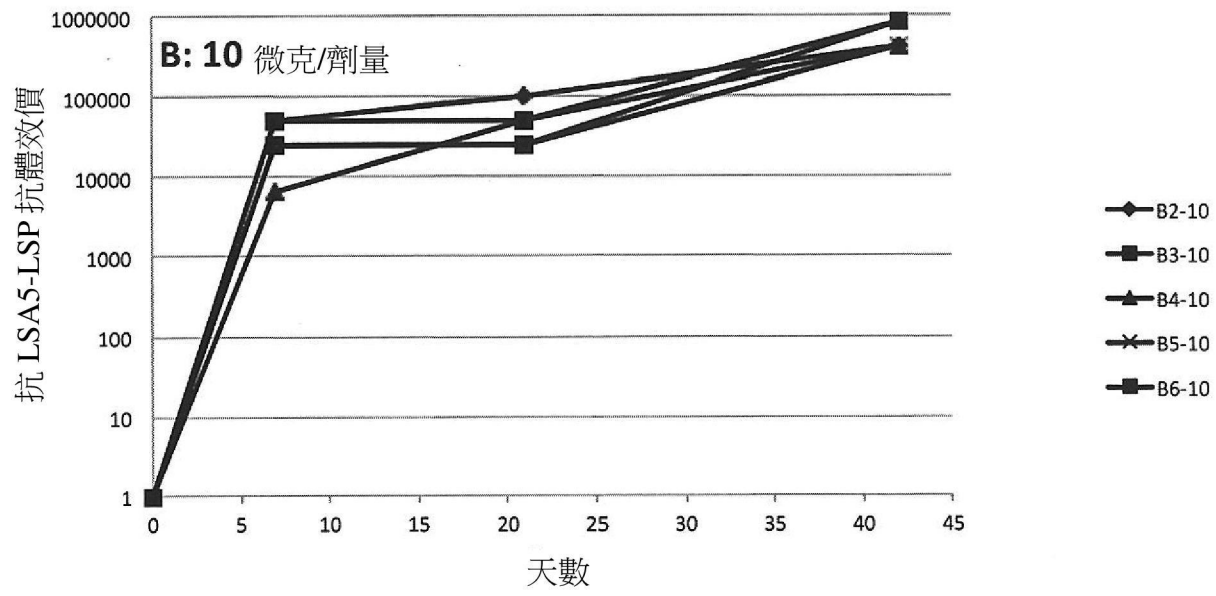
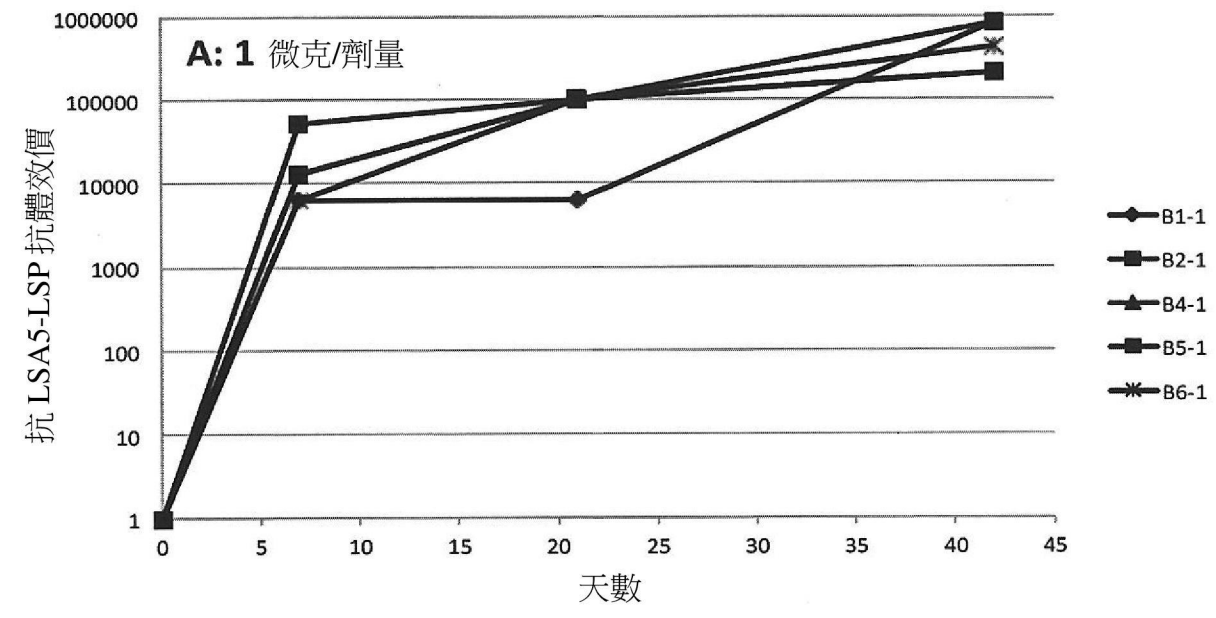
【圖 25】



【圖 26】



【圖 27】



【圖 28】