

(12) STANDARD PATENT
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. **AU 2017300965 B2**

(54) Title
Biofusion proteins as anti-malaria vaccines

(51) International Patent Classification(s)
A61K 39/015 (2006.01) **A61K 39/385** (2006.01)
A61K 39/00 (2006.01)

(21) Application No: **2017300965** (22) Date of Filing: **2017.07.21**

(87) WIPO No: **WO18/017020**

(30) Priority Data

(31)	Number	(32)	Date	(33)	Country
	16180544.5		2016.07.21		EP

(43) Publication Date: **2018.01.25**

(44) Accepted Journal Date: **2024.09.12**

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(51) International Patent Classification:

A61K 39/015 (2006.01) A61K 39/00 (2006.01)

A61K 39/385 (2006.01)

(21) International Application Number:

PCT/SG2017/050369

(22) International Filing Date:

21 July 2017 (21.07.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

16180544.5 21 July 2016 (21.07.2016) EP

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

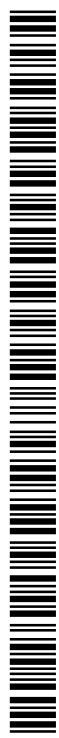
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

(54) Title: BIOFUSION PROTEINS AS ANTI-MALARIA VACCINES

(57) Abstract: 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.



Biofusion proteins as anti-malaria vaccines

The present invention relates to the protection against malaria, more particularly to a malaria vaccine which comprises a fusion protein.

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Background of the invention

The parasites responsible for malaria in human, including especially *Plasmodium falciparum*, exhibit different morphologies in the human host and express different antigens as a function of their localization in the organism of the infected host. The morphological and antigenic differences of these parasites during their life cycle in man enable at least four distinct stages of development. The very first stage of development of the parasite in human corresponds to the sporozoite form introduced into the blood of the host by bites of insect vectors of the parasite. The second stage corresponds to the passage of the parasite into the liver and to the infection of the hepatic cells in which the parasites develop to form the hepatic schizonts which, when they are mature (for example, in the case of *P. falciparum* on the 6th day after penetration of the sporozoites) release hepatic merozoites by bursting. The third stage is characterized by the infection of the blood erythrocytes by the asexual forms (blood stages schizonts) of the parasite releasing free merozoites when they mature; this erythrocytic stage of development corresponds to the pathogenic phase of the disease. The fourth stage corresponds to the formation of the forms with sexual potential (or gametocytes) which will become extracellular sexual forms or gametes in the mosquito.

There is no practical or effective vaccine that has been introduced into clinical practice.

Malaria sub-unit vaccines have so far shown a major deficiency in immunogenicity. The immune responses that are observed are at low titers and of short duration. A variety of approaches have been explored to address this deficiency, including a selection of adjuvants, expression in complex vectors such as virus-like particles (VLPs), adenovirus vectors, and setting up of complex prime-boost protocols. Even the RTS,S/AS01 vaccine (Mosquirix®), which was engineered using genes from the repeat and T-cell epitope in the pre-erythrocytic circumsporozoite protein (CSP) of the *Plasmodium falciparum* malaria parasite and a viral envelope protein of the hepatitis B virus (HBsAg), with sophisticated adjuvants such as AS01, suffers from very short duration of malaria-specific immune responses (whereas hepatitis B responses remain high for long).

Chemical conjugation of Plasmodium antigens to carrier proteins has also been disclosed. For instance a vaccine comprising Plasmodium protein Pfs25H conjugated to a detoxified form of Pseudomonas aeruginosa exoprotein A (repA) is under evaluation.

However chemical conjugation has several drawbacks. It is technically demanding, hardly reproducible, and quite expensive.

There is still a great need for vaccine products which show a good immunogenicity and protection against malaria, while being easy to reproduce and affordable.

Summary of the invention

The invention offers the advantage of an improved immunogenicity, thanks to novel constructs consisting of Plasmodium polypeptides fused with a carrier protein such as CRM197. Rather than coupling chemically the Plasmodium molecule to the carrier protein, the inventors developed a novel approach in which the parasite protein is encoded together with the carrier protein as a fusion protein, making a “bio-conjugated fusion product”, also designated further herein as “bio-fusion molecule”, which can be produced recombinantly, e.g. in E.coli.

The invention more particularly provides a fusion protein which comprises at least one antigenic amino acid sequence fused at the N-term and/or C-term of a carrier heterologous protein sequence, wherein the antigenic sequence comprises an epitope sequence of a Plasmodium protein and the carrier heterologous protein sequence is a sequence that is immunogenic in humans.

The antigenic sequence may be an antigenic protein which is expressed by Plasmodium at erythrocytic stage, or an epitopic fragment thereof.

Alternatively, the antigenic sequence may be an antigenic protein which is expressed by Plasmodium at pre-erythrocytic stage, or an epitopic fragment thereof.

A further aspect of the invention is a nucleic acid construct encoding the fusion protein as defined herein.

Also provided are a vector comprising the nucleic acid construct in an expression cassette as well as a host cell wherein the vector has been inserted.

It is further described an *in vitro* method for preparing a fusion protein, which method comprises allowing the host cell to reproduce under conditions which induce expression of the nucleic acid construct, and collecting the fusion protein which is so expressed.

According to the invention, a vaccine is provided, which comprises said fusion protein or a combination of at least two fusion proteins, which respectively comprise at least two different antigenic amino acid sequences, or a nucleic acid construct encoding said fusion protein(s), with a physiologically acceptable vehicle.

Such vaccine is useful in vaccinating a human subject against malaria.

Throughout the description and claims of the specification, the word “comprise” and variations of the word, such as “comprising” and “comprises”, is not intended to exclude other additives, components, integers or steps.

A reference herein to a patent document or other matter which is given as prior art is not to be taken as admission that the document or matter was known or that the information it contains was part of the common general knowledge as at the priority date of any of the claims.

Legends to the figures

Figure 1 is a diagrammatic representation of the coding sequences for PP21 (also named “Bio-fusion MSP3-1”). Scales in base pairs are shown below starting at the Nco I site.

Figure 2 shows pET26a-PP21 plasmid map (A), mini-preparation analysis by restriction enzyme digestion with Sma I (B) or Eco R I (C).

Figure 3: Recombinant protein PP21 purified by IMAC. (A) Analysis by electrophoresis under denaturing conditions and Coomassie blue staining. (B) Antigenicity assessed by Western blotting with murine anti-MSP3 immune sera at a 1:1000 dilution. The upper band observed is compatible with the theoretical molecular weight of the full length PP21 of 84 kDa. Another band at 37 kDa, less well recognized by the anti-MSP3 immune sera, could correspond to a degradation fragment of PP21.

Figure 4: Timescale of PP21 stability at different storage temperatures assessed by Western blotting with the anti-MSP3-1 mAb RAM1 at a 1:1000 dilution.

Figure 5: Determination of the Antigen Content of PP21 as compared to the positive control MSP3-LSP. The antigenicity of pre-clinical PP21 was determined by reactivity with a large panel of human and animal anti-MSP3 sera, including a human recombinant antibody. The antigen content provides a more precise measurement of the quantity of reactive epitopes. It is performed by serial dilutions of the antigen, used for coating in an Elisa assay and revealed by

a well-defined positive control (here a pool of rats immunized by the C-term region of MSP3). The reactivity of PP21 was identical to that of MSP3 synthetic and recombinant constructs

5 **Figure 6:** Significant improvement in specific antibody response induced in mice following 2 immunizations by the Bio-fusion MSP3-1 conjugate as compared to the current MSP3-1-LSP. Groups of 5 (BALB/c) or 4 (C57BL/6) mice were immunized using either only 1 µg of bio-fusion MSP3-1 or 10 µg of MSP3-1 LSP in Montanide ISA720 on days 0, 14 and 28. Blood samples were collected one week after the 2nd injection, on day 21 (A) and one week after the
10 3rd immunization, on day 35. Specific MSP3-1 LSP antibody titers were determined by ELISA. The results for each mouse (1 to 5) are shown separately (here after only two immunizations).

Figure 7: Comparison of antibody response induced in mice following 2 versus 3
15 immunizations by the Bio-fusion MSP3-1 as compared to the current MSP3-1-LSP. The third injection boosted the antibody response and confirmed the better immunogenicity of Bio-fusion MSP3-1 in C57Bl/6 mice and Balb/c mice . Mean titers of MSP3-1-LSP specific antibodies induced by 3 injections of 1 µg of Bio-fusion MSP3-1 reached 3×10^5 and 2×10^5 in C57Bl/6 and Balb/c respectively; whereas 3 injections of 10 µg of MSP3-1-LSP induced a
20 maximum of 10^5 and 2.5×10^4 mean titers in C57Bl/6 and Balb/c mice respectively.

Figure 8: Major improvement in duration of MSP3-1 specific antibodies induced in mice by the Bio-fusion MSP3-1 as compared to the current MSP3-1-LSP.
A and B : comparison of Bio-Fusion MSP3-CRM with MSP3-1-LSP: BALB/c (A-upper left
25 panel) and C57BL/6 (B-upper right panel) mice were immunized using either only 1 µg of Bio-fusion MSP3-1 or 10 µg of MSP3-1 LSP in Montanide ISA720 on days 0, 14 and 28. Blood samples were collected at different days over the follow-up. Specific MSP3-1 LSP antibody titers were determined by ELISA. The results shown correspond to the geometric mean of anti-MSP3-1 LSP antibody titers obtained in each group of mice at different days.
30 After 160 days of follow-up the mean antibody titer in the Bio-fusion-MSP3-1 conjugate immunized mice was 1.5×10^5 and 10^5 in C57bl/6 and Balb/c respectively, which is at least 10 fold higher than the mean titer of antibodies induced by MSP3-1-LSP and measured at day 160 after the first immunization.

C and D : Long-term persistence of immune responses elicited by MSP3-CRM: Groups of Balb/c and C57Bl6 mice (4 to 5 mice per group) were immunized by subcutaneous injection on days 0, 14 and 103 of 1µg of Bio-fusion MSP3-CRM adjuvanted in Montanide ISA 720 adjuvant (v/v). Blood samples were collected at different days. Specific MSP3 antibody titers were determined by ELISA. Results show that the titer increases remarkably after two immunizations and reaches at day 49 a maximum, whereas the third antigen injection, performed on day 103, did not induce any detectable increase in the magnitude of the antibody response. These specific antibodies decreased only slightly over time, and remained detectable at high titer even 540 days after immunization

E: Long-term persistence of immune responses elicited by MSP3-CRM after only 2 immunisations. In view of satisfactory responses observed after only two immunisations, this immunization scheme was analyzed in further seventeen Balb/c mice immunized by subcutaneous injection on days 0 and 14 only, using 2µg of Bio-fusion MSP3-CRM adjuvanted in Montanide ISA 720 (v/v). Blood samples were collected at different days. Specific MSP3-1-LSP antibody titers were determined by ELISA. Results show that the MSP3 antibody titer increased after two antigen injections and reaches a maximum between days 42 and 72 in all mice, and show that immune responses decreased only modestly over the 380 days follow-up of the experiment.

Figure 9: Improved recognition of MSP3-1 ADCI (Ab-dependent cellular inhibition) target epitopes by antibodies induced in mice immunized with Bio-fusion MSP3-1 as compared to MSP3-1-LSP. In the MSP3-1-LSP, The peptides “b”, “c” and “d” define distinct B-cell epitopes targeted by antibodies effective in the ADCI assay correlated to the protective effect of ant-MSP3-1 antibodies. To evaluate the ability of Bio-fusion MSP3-1 to induce antibodies to these epitopes we determined by ELISA the titers of antibodies to the peptides a, b, c and d in the sera. Hence the number of ADCI targets recognized by the novel formulation is considerably wider, and with higher titers. BALB/c and C57BL/6 mice were immunized using either only 1 µg of Bio-fusion MSP3-1 or 10 µg of MSP3-1 LSP in Montanide ISA720 on days 0, 14 and 28. Blood samples were collected one week after the 3rd immunization, on day 35. The mice sera were diluted at 1/400 and the titer of specific antibodies of different MSP3-1 peptides (a, b, c and d) was determined by ELISA. The results shown correspond to the optical density obtained with the sera of each mouse tested.

Figure 10: Human antibody responses in the HIMM model (Human Immunogenicity Mouse Model) immunized either with 1 µg of Bio-fusion MSP3-1, 10 µg of the current MSP3-1 LSP or 10 µg of the MSP3-1 C-term recombinant protein. NOD.Cg - Prkdc^{scid} - IL2rg^{tm1Wjl}/SzJ (NSG) mice were engrafted with human spleen cells stimulated or not in vitro with 1 µg/ml of antigen (4 mice per group). Each NSG mouse received an intraperitoneal injection (ip) of 30 x 10⁶ antigen-primed or unprimed spleen cells. At days 7 and 21, reconstituted mice were boosted with 1 µg of Bio-fusion MSP3-1, or 10 µg of MSP3-1-LSP or 10 µg of MSP3-1 C-term recombinant protein. All antigens were adjuvanted with Montanide ISA 720 (v/v) and injected intraperitoneally (ip). Mice reconstituted with unprimed spleen cells, received adjuvant alone. Blood samples were collected one week after each immunization. Specific antibodies were analyzed by total and specific IgG ELISA. The adjusted specific antibody titer was calculated using the following formula: (antigen specific antibody titer/total human IgG concentration) x 10 (10 mg/ml is considered as the mean human total IgG concentration). Geometric mean values (95 % CI) of ELISA titers are represented.

Figure 11: Human IFN-γ cellular responses in the HIMM model (Hu Lymph NSG mice) immunized either with 1 µg of Bio-fusion MSP3-1, 10 µg of the current MSP3-1 LSP or 10 µg of the MSP3-1 C-term recombinant protein. Same immunizing conditions as above. Cellular responses were evaluated by IFN-γ ELISPOT. At day 28, spleen cells of each group of mice were recovered, pooled and cultured in vitro with or without antigen stimulation. The results shown correspond to the specific Spot Forming Cells (SFC) obtained with each group of mice.

Figure 12: T-cell responses in HIMM: Marked improvement in CD4-Th1 responses in human lymphocytes grafted in mice immunized by either 1 µg of Bio-conjugate PP21 or 10 µg of MSP3-LSP.

Figure 13: Improved recognition of parasite native proteins by human antibodies elicited in the HIMM model immunized with Bio-fusion MSP3-1. NSG mice were engrafted with human spleen cells and immunized either with 1 µg of Bio-fusion MSP3-1, 10 µg of the current MSP3-1 LSP or 10 µg of the MSP3-1 C-term recombinant protein (as described in the figure 6). The reactivity of human antibodies in day 28 mice sera, with the parasite proteins, which is a critical feature to activate the ADCI defense mechanism during a malaria attack, was evaluated by Immunofluorescence Antibody Test (IFAT) on 3D7 *Plasmodium*

falciparum (Pf) infected red blood cells. The results shown correspond to the range of titers obtained with each group of mice.

Figure 14: The human antibody response elicited in the HIMM model immunized with 1 µg of Bio-fusion MSP3-1 does not depend on adjuvant used in the vaccine preparation. (A) NSG mice were engrafted with human spleen cells derived from two different donors and stimulated or not with 1 µg of Bio-fusion MSP3-1 adjuvanted with Montanide ISA720 (as described in the figure 6) (4 mice per group / donor). (B) NSG mice were engrafted with human spleen cells stimulated (9 mice) or not (8 mice) with 1 µg of Bio-fusion MSP3-1 adjuvanted with MF59 instead of Montanide ISA720 (as described in the figure 6 but with human lymphocytes from a distinct donor). In both cases, the specific MSP3-1 LSP antibody titers were determined by ELISA at day 28. The results shown correspond to the mean ± SD of the ELISA titers obtained with each group of mice.

Figure 15: Antibody Subclasses of human IgG antibodies elicited in human lymphocytes in the HIMM model immunized with Bio-fusion MSP3-1 adjuvanted with Montanide ISA720. NSG mice were engrafted with human spleen cells stimulated or not with 1 µg of MSP3 Bio-fusion (as described in the figure 10). The mice sera, collected at day 28, were diluted at 1/20. The specific MSP3-1 LSP antibody titers were determined by subclass IgG ELISA. The results shown correspond to the mean ± SD of optical density obtained with immunized and non immunized mice.

Figure 16: Subclasses of human IgG antibodies elicited in the HIMM model immunized with Bio-fusion MSP3-1 adjuvanted with MF59. NSG mice were engrafted with human spleen cells stimulated or not with 1 µg of Bio-fusion MSP3-1 adjuvanted with MF59 (as described in figure 14). The mice sera, collected at day 28, were diluted at 1/20. The specific MSP3-1 LSP antibody titers were determined by subclass IgG ELISA in the sera of responding mice. The results shown correspond to the mean ± SD of optical density obtained with immunized and non immunized mice. Both adjuvants led to obtain a dominance of the cytophilic subclass IgG1.

Figure 17 : Immunogenicity of 0.2 or 1 µg of PP21 in Balbc mice /PP21-montanide (upper left and right), or the same doses in C57bl mice (lower left and right panels) Evolution of anti-MSP3-1-LSP antibody titers determined as in Figures 6-8

Figure 18 : Cross-reactivity of anti-MSP3-1 Antibodies elicited by PP21 with other members of the MSP3 family of proteins (OD values by Elisa). C57Bl/6 (C) and Balb/c (B) mice received 2 injections (J0, J14) of 4µg PP21. Samples were collected on day 63.

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Figure 19: Immunogenicity of PP21 adjuvated by Alum Hydroxyde in C57BL(C) and Balb/C mice(B), at a 1 µg dose per immunisation. Antibody Titers determined by Elisa in C57BL (C) and Balb/C mice (B), are shown following 2 immunisations or 3 immunisations. Higher dilutions than 25:600 were not tested. Note that Alum OH which is a potent adjuvant in humans yielding high Th1 responses, is in contrast usually a poor adjuvant in rodents, still induced potent responses with PP21.

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Figure 20. High Immunogenicity of the Bio-fusion conjugate PP21 in South-American Saimiri sciureus monkeys. Saimiri sciureus South American monkeys born in captivity in the animal house of the Primate Center of Belem, Brasil, were immunized by 1µg of PP21 adjuvated by Montanide Isa 720, administered SC on days 0, 28 and 112 (dotted lines as compared to controls receiving Montanide alone, plain lines). Antibodies were determined by Elisa on the MSP3-LSP antigen, as well as by IFAT and WB (not shown). Even when using only 0.1µg antigen per immunisation, immune responses were about 5 fold lower, ie still very significant (not shown).

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Figure 21 : Antibody responses elicited by LSA3-CRM (PP25) versus LSA3-729 in Balb/C mice, receiving either 1µg of PP25 with Montanide ISA720 or 10µg of LSA3-729 in Montanide ISA720. Immunisations on day 0 ; 7 ; 28, serum collection on day 45.

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Figure 22 : IFN γ (ELISPOT) elicited in LSA3-CRM (PP25) versus LSA3-729 immunized Balb/C mice, challenged in vitro by DG 729.

Figure 23: Anti-LSA3-729 human antibody responses in HIMM and Reproducibility of the improvement of results: Anti-LSA3-729 human antibody responses in HIMM to the LSA3-CRM construct PP25 using lymphocytes from two human donors « A » and « B »

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Figure 24 : Improvement in the duration of immune responses elicited by PP25.

Figure 25 : A novel host cell for *P. falciparum* liver stage development in HuH7.5 was developed and compared to Human Primary Hepatocytes (HPH). The figure shows representative samples of liver schizonts at 4, 5 and 7 days after infection with sporozoites, immunostained with a mouse polyclonal anti PfHsp-70. Magnification 400X, scale bar 10 μ m. It was difficult to find satisfactory LS at day 7 in HPH. This hepatoma model was thereafter employed in a functional assay to measure antibodies able to inhibit the invasion of sporozoites into hepatocytes

Figure 26: Inhibition of sporozoite invasion in Hu7.5 hepatoma cells (ILSDA) by anti-Pf LSA3 antibodies. Shown is the correlation between anti-LSA3 reactivity on native proteins (by IFAT assays), with the functional inhibitory effect in the Inhibition of Liver Stages Development Assay (ILSDA). The smaller graph shows the same assays using the anti-Circumsporozoite mAb 2A10.

Figure 27: Strong B and T cell responses were elicited in Human Lymphocytes grafted in the HIMM model, by the construct PP23 (MSP3-2-CRMP97-MSP3-3). The upper panel (A) shows the antibody responses, the middle panel (B) the isotypes distribution, which is predominantly of the IgG1 class , the main cytophilic class able to act in cooperation with Monocytes in the ADCI mechanism. The lower panel (C) shows T-cells responses evaluated by secretion of IFN- γ restimulated in vitro by either MSP3-2 or MSP3-3.

Figure 28: Immunogenicity of 1 μ g compared to 10 μ g dose of Bio-fusion LSA5-CRM/Montanide ISA720 in BALb/c mice (n=5). Experimental conditions are similar to those described in Figure 8. Immunization by Bio-fusion LSA5-CRM /Montanide ISA720 was performed on days 0, 14 and 28 (arrows). Serum antibody detection was performed by ELISA titration on LSA5-LSP as antigen, using sera collected on days 0, 7, 21, 42.

Detailed description of the invention

Definitions

A "vaccine" is to be understood as meaning a composition for generating immunity for the prophylaxis and/or treatment of diseases. Accordingly, vaccines are medicaments which comprise antigens and are intended to be used in humans or animals for generating specific defense and protective substance by vaccination. A "vaccine," as used herein, means an

immunogenic composition capable of eliciting partial or complete protection against malaria. A vaccine can be prophylactic for infection and/or therapeutic in an infected individual.

The term “immunogenic” means that the composition or protein to which it refers is capable of inducing an immune response upon administration. "Immune response" in a subject refers to the development of an adaptative and/or innate immune response, including a humoral immune response, a cellular immune response, or a humoral and a cellular immune response to an antigen. A "humoral immune response" refers to one that is mediated by antibodies.

The term "protection" or “prevention" as used in this document refers to an absence of symptoms or to the presence of reduced symptoms of the disease after contact with the Plasmodium parasite. In particular, the term "prevention of malaria" refers to an absence of symptoms or to the presence of reduced symptoms in the treated subject after contact with a Plasmodium responsible for malaria.

The “patient” or “subject” is typically a mammal subject, preferably a human subject. The subject can be male or female, a child or an adult. A subject can be one who has been previously diagnosed or identified as having malaria. Alternatively, a subject can also be one who has not been previously diagnosed as having malaria, but who is at risk of developing such condition, e.g. due to infection or due to travel within a region in which malaria is prevalent. For example, a subject can be one who exhibits one or more symptoms for malaria. For instance the subject may be infected with Plasmodium falciparum or Plasmodium vivax.

A "homologous" or “substantially homologous” sequence to an original polypeptide is typically one which has at least about 80 percent identity to the sequence of the original polypeptide or an immunogenic or epitopic fragment of the original polypeptide, and which substantially retains the desired effect on the intended target of the original polypeptide (i.e., elicits an immunogenic response, or being recognized by an antibody). In increasingly preferred embodiments, the homologous sequence has at least about 85 percent, 90 percent, 95 percent, 97 percent or 99 percent identity to the sequence of the original polypeptide or an immunogenic or epitopic fragment thereof.

An "immunogenic fragment" generally has a length of at least five amino acids. With increasing preference, the length of the immunogenic fragment is at least 7, 9, 11, 13, 15, 17 and 19 amino acids. An “epitope” generally has a length of at least five amino acids, preferably at least 7 to 14 amino acids.. An “epitopic fragment” comprises such epitope and can thus be longer.

In the context of the present invention, the term “fusion or biofusion” means that, in the recombinant protein, the carrier protein is either directly linked to the antigenic Plasmodium

sequence, or is linked to the antigenic Plasmodium sequence by a peptide linker. The peptide linker may be a sequence of 1 to 35 amino acids, preferably 5 to 20 amino acids, still preferably 5 to 10 amino acids. In a preferred embodiment, the linker peptide is (Gly-Gly-Gly-Gly-Ser)_n, (Gly)_n or (EAAAK)_n, wherein n is 1 to 4, preferably 1 to 3. In either
 5 embodiment, a single polypeptide is formed.

The carrier protein

The carrier heterologous protein sequence may be advantageously selected from the group consisting of a cross-reacting material (CRM) of diphtheria toxoid, diphtheria toxoid (D), a
 10 non-toxic mutant recombinant of *Pseudomonas aeruginosa* exoprotein A (repA), meningococcal outer membrane protein complex (OMPC), tetanus toxoid (T), *H. influenza* protein D (hiD), and immunogenic fragments thereof.

In preferred embodiments, the carrier heterologous protein sequence may be CRM197 or an immunogenic fragment thereof, which fragment is preferably selected from the group
 15 consisting of Fragment A, Transmembrane Domain T, Receptor Binding domain R of CRM197, amino acid sequence 1-190 of CRM197, and amino acid sequence 1-389 of CRM197.

Fragment A of diphterin toxin extends from amino acid 1 to 201. CRM197 possesses an enzymatically inactive fragment A, showing a substitution of glycine 52 with glutamic acid.

20 Fragment B of diphterin toxin extends from amino acid 202 to 535.

Table 1 below shows additional information about particular carriers.

Carriers	Name	NCB:	SEQ ID NO
Diphtheria toxin	DIP_RS12515 toxin [<i>Corynebacterium diphtheriae</i> NCTC 13129]	NC_002935.2	SEQ ID NO : 81
CRM197			SEQ ID NO : 82
Tetanus toxoid	tetanus toxin [<i>Clostridium tetani</i>]	X04436.1	SEQ ID NO : 83
Hib protein D	<i>H.influenzae</i> (3639) gene for protein D	Z35656	SEQ ID NO : 84

Substantially homologous sequences may also be used.

The antigenic Plasmodium sequence

The fusion protein construct of the invention comprises at least one antigenic sequence comprising an epitope sequence of a Plasmodium protein.

Said antigenic sequence may be of any Plasmodium antigen, from any Plasmodium species.

The "Plasmodium" genus of parasites infecting humans include, without limitation, *P. falciparum*, *P. vivax*, *P. knowles*, *P. ovale* and *P. malariae*. The antigens listed below are mostly antigens from *P. falciparum*. However orthologs in other Plasmodium species are encompassed as well. In particular *P. vivax* antigens have shown the same low immunogenicity as *P. falciparum* antigens.

Said antigen may be expressed in erythrocyte stage (also designated "blood stage") or pre-erythrocytic stage (sporozoites and liver stages).

Examples of antigenic sequences which may be used are listed in **Table 2** below. Substantially homologous sequences may also be used.

Antigens expressed in erythrocyte stage, which are target of Ab-dependent cellular inhibition (ADCI) defense mechanism include:

MSP3 (e.g. MSP3-1, MSP3-2, MSP3-3, MSP3-4, MSP3-7, MSP3-8), PEBS sub-region of 11-1 (also named LSA5), Glurp R0 and R2, SERP, P27 and P27A, P45, P90 and P77, P14, P181 (which is a combination of P77), MSP1-Block 2, MSP2 (two 3D7 and FC27 alleles, both dimorphic and constant regions), GBP 130 (especially both N and C moieties), protein 332, protein 11-1, MSP4, or any epitopic fragment thereof.

Preferably the antigenic sequence in the fusion protein is MSP3 or an epitopic fragment thereof.

In another preferred embodiment, the antigenic sequence in the fusion protein is LSA5 or an epitopic fragment thereof.

Plasmodium falciparum merozoite surface protein 3 (MSP-3) is a known asexual blood-stage malaria vaccine candidate antigen (Sirima et al, N Engl J Med 2011, 365(11):1062-1064; Demanga et al, Infect Immun 2010, 78(1):486-494; Daher et al, Infect Immun 2010, 78(1):477-485; Rousillon et al, Roussilhon, et al, PLoS Medicine, November 2007, 4, Issue 11, e320).

In particular any of the six MSP3 proteins may be used, preferably MSP3-1, as well as peptides a,b,c,d, e,f,, the recombinants C-term, but also full length and N-term of the protein. In a preferred embodiment, the antigenic sequence is MSP3 or an epitopic fragment thereof, which fragment encompasses motifs a, b, c, d, e and/or f of the C-terminal region of a Plasmodium MSP3 protein chosen among MSP3-1, MSP3-2, MSP3-3, MSP3-4, MSP3-7, MSP3-8.

Other antigens from the merozoite surface, particularly those loosely attached or cleaved and therefore which can be released from the merozoite surface, are encompassed.

Antigens expressed in the pre-erythrocytic stage include LSA3, PEBS, CS, Trap, and Salsa, and any epitopic fragment thereof. In *P. falciparum*, liver stage antigen-3 (LSA-3) is an antigen expressed at the pre-erythrocytic stage (Toure-Balde et al: Infect Immun 2009, 77(3):1189-1196; Daubersies et al: Nat Med 2000, 6(11):1258-1263).

Antigens involved in other stages or other mechanisms are also encompassed. Those include antigens involved in the sexual stages, e.g. Pf25 or Pf45/48, and antigens of blood stage involved in GIA mechanism of inhibition of merozoite invasion in red blood cells, such as Rh5, AMA1, MSP1-19, MSP1-42, MSP2 or MSP4-5, or involved in cyto-adherence, such as Var CSA.

Table 2: Antigenic sequences (*P falciparum*)

Antigen	Name	PlasmodB		Aminoacid sequence
Ag27	trophozoite exported protein 1 (TEX1)	PFF0165C	PF3D7_0603400	SEQ ID NO : 1
Ag27 (P27A)	# peptide 27A	#	#	SEQ ID NO : 2
Ag27 (P27)	# peptide 27	#	#	SEQ ID NO : 3
MSP1	merozoite surface protein 1 (MSP1) peptide block II	PFI1475w	PFI1475w	SEQ ID NO : 4
MSP1-42	merozoite surface protein-1 42kDa fragment [synthetic construct]	#		SEQ ID NO : 5
MSP2	merozoite surface protein 2 (MSP2)	PFB0300c	PF3D7_0206800	SEQ ID NO : 6
MSP3-1	merozoite surface protein 3-1	PF10_0345	PF3D7_1035400	SEQ ID NO : 7
MSP3-1CT	C-term	#	#	SEQ ID NO : 8
MSP3-1a	# peptide a	#	#	SEQ ID NO : 9
MSP3-1b	# peptide b	#	#	SEQ ID NO : 10

MSP3-1c	# peptide c	#	#	SEQ ID NO : 11
MSP3-1d	# peptide d	#	#	SEQ ID NO : 12
MSP3-1e	# peptide e	#	#	SEQ ID NO : 13
MSP3-1f	# peptide f	#	#	SEQ ID NO : 14
MSP3-2	merozoite surface protein 3-2	PF10_0346	PF3D7_1035500	SEQ ID NO : 15
MSP3-2CT	C-term	#	#	SEQ ID NO : 16
MSP3-2a	# peptide a	#	#	SEQ ID NO : 17
MSP3-2b	# peptide b	#	#	SEQ ID NO : 18
MSP3-2c	# peptide c	#	#	SEQ ID NO : 19
MSP3-2d	# peptide d	#	#	SEQ ID NO : 20
MSP3-2e	# peptide e	#	#	SEQ ID NO : 21
MSP3-2f	# peptide f	#	#	SEQ ID NO : 22
MSP3-3	merozoite surface protein 3-3	PF10_0347	PF3D7_1035600	SEQ ID NO : 23
MSP3-3CT	C-term	#	#	SEQ ID NO : 24
MSP3-3a	# peptide a	#	#	SEQ ID NO : 25
MSP3-3b	# peptide b	#	#	SEQ ID NO : 26
MSP3-3c	# peptide c	#	#	SEQ ID NO : 27
MSP3-3d	# peptide d	#	#	SEQ ID NO : 28
MSP3-3e	# peptide e	#	#	SEQ ID NO : 29
MSP3-3f	# peptide f	#	#	SEQ ID NO : 30
MSP3-4	merozoite surface protein 3-4	PF10_0348	PF3D7_1035700	SEQ ID NO : 31
MSP3-4CT	C-term	#	#	SEQ ID NO : 32
MSP3-4a	# peptide a	#	#	SEQ ID NO : 33
MSP3-4b	# peptide b	#	#	SEQ ID NO : 34
MSP3-4c	# peptide c	#	#	SEQ ID NO : 35
MSP3-4d	# peptide d	#	#	SEQ ID NO : 36
MSP3-4e	# peptide e	#	#	SEQ ID NO : 37
MSP3-4f	# peptide f	#	#	SEQ ID NO : 38
MSP3-7	merozoite surface protein 3-7	PF10_0352	PF3D7_1036000	SEQ ID NO : 39
MSP3-7CT	C-term	#	#	SEQ ID NO : 40
MSP3-7a	# peptide a	#	#	SEQ ID NO : 41
MSP3-7b	# peptide b	#	#	SEQ ID NO : 42
MSP3-7c	# peptide c	#	#	SEQ ID NO : 43
MSP3-7d	# peptide d	#	#	SEQ ID NO : 44
MSP3-7e	# peptide e	#	#	SEQ ID NO : 45
MSP3-7f	# peptide f	#	#	SEQ ID NO : 46
MSP3-8	merozoite surface protein 3-8	PF10_0355	PF3D7_1036300	SEQ ID NO : 47
MSP3-8CT	C-term	#	#	SEQ ID NO : 48
MSP3-8a	# peptide a	#	#	SEQ ID NO : 49
MSP3-8b	# peptide b	#	#	SEQ ID NO : 50
MSP3-8c	# peptide c	#	#	SEQ ID NO : 51
MSP3-8d	# peptide d	#	#	SEQ ID NO : 52
MSP3-8e	# peptide e	#	#	SEQ ID NO : 53

MSP3-8f	# peptide f	#	#	SEQ ID NO : 54
MSP4 (SALSA)	merozoite surface protein 4 (MSP4)	PFB0310c	PF3D7_0207000	SEQ ID NO : 55
Pf11.1	gametocyte-specific protein (Pf11-1)	PF10_0374	PF3D7_1038400	SEQ ID NO : 56
Pf11.1 (PEBS)	Subregion of Pf11.1 (also named LSA5)	#	#	SEQ ID NO : 57
Ag332	antigen 332, DBL-like protein (Pf332)	PF11_0356	PF3D7_1149000	SEQ ID NO : 58
SERP	serine repeat antigen 1 (SERA1)	PFB0360c	PF3D7_0208000	SEQ ID NO : 59
	serine repeat antigen 2 (SERA2)	PFB0355c	PF3D7_0207900	SEQ ID NO : 60
#	serine repeat antigen 3 (SERA3)	PFB0350c	PF3D7_0207800	SEQ ID NO : 61
#	serine repeat antigen 4 (SERA4)	PFB0345c	PF3D7_0207700	SEQ ID NO : 62
#	serine repeat antigen 5 (SERA5)	PFB0340c	PF3D7_0207600	SEQ ID NO : 63
GLURP	glutamate-rich protein (GLURP)	PF10_0344	PF3D7_1035300	SEQ ID NO : 64
GLURP-R0	peptide R0	#	#	SEQ ID NO : 65
GLURP-R2	peptide R2	#	#	SEQ ID NO : 66
Gbp130	glycophorin binding protein (GBP)	PF10_0159	PF3D7_1016300	SEQ ID NO : 67
P14	conserved Plasmodium protein, unknown function peptide 14	PFC0245c	PF3D7_0305500	SEQ ID NO : 68
P45	conserved Plasmodium protein, unknown function peptide 45	PF11_0207	PF3D7_1120000	SEQ ID NO : 69
P77	Snf2-related CBP activator, putative (SRCAP) peptide 77	PF08_0048	PF3D7_0820000	SEQ ID NO : 70
P90	conserved Plasmodium protein, unknown function peptide 90	PFD0520c	PF3D7_0410500	SEQ ID NO : 71
RH5	reticulocyte binding protein homologue 5 (RH5)	PFD1145c	PF3D7_0424100	SEQ ID NO : 72
AMA1	apical membrane antigen 1 (AMA1)	PF11_0344	PF3D7_1133400	SEQ ID NO : 73
Pfs25	25 kDa ookinete surface antigen precursor (Pfs25)	PF10_0303	PF3D7_1031000	SEQ ID NO : 74
VAR	erythrocyte membrane protein 1, PfEMP1 (VAR)	PFA0005w	PF3D7_0100100	SEQ ID NO : 75
LSA3	liver stage antigen 3	PFB0915w	PF3D7_0220000	SEQ ID NO : 76
LSA3 (DG729)	peptide DG729	#	#	SEQ ID NO : 77
CS	circumsporozoite (CS) protein	PFC0210c	PF3D7_0304600	SEQ ID NO : 78
TRAP	thrombospondin-related anonymous protein (TRAP)	PF13_0201	PF3D7_1335900	SEQ ID NO : 79
SALSA	merozoite surface protein 4 (MSP4)	PFB0310c	PF3D7_0207000	SEQ ID NO : 80

refers to the same reference as the line above

The fusion construct

In a particular embodiment, the fusion protein comprises or consists of MSP3 (preferably MSP3-1), LSA3, LSA5 (also named PEBS) or an epitopic fragment thereof, as the antigenic
5 sequence, fused to CRM197 or an immunogenic fragment thereof, as the carrier sequence.

In a preferred aspect, the fusion protein comprises two antigenic sequences which are either each located in C-term and N-term of the carrier protein sequence, or both located at the same terminus, wherein the two antigenic sequences are the same or different from each other.

10 In a preferred embodiment, the fusion between the antigenic sequence and the carrier sequence is a direct fusion.

In another embodiment, the at least one amino acid sequence may be linked at the N-term and/or C-term of the carrier heterologous protein sequence by a peptide linker, wherein the
15 peptide linker preferably is a sequence of 1 to 35 amino acids, preferably 5 to 20 amino acids.

In a preferred aspect, the peptide linker is (Gly-Gly-Gly-Gly-Ser)_n, (Gly)_n or (EAAAK)_n, wherein n is 1 to 4, preferably 1 to 3.

Acid nucleic, vectors and host cells

20 The fusion protein of the present invention can be made by any recombinant technique. Accordingly, another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding said fusion protein.

The expression vectors used in the present invention can provide for expression in vitro and/or in vivo (e.g. in a suitable host cell, host organism and/or expression system). They
25 typically comprise a polynucleotide sequence as defined above, and regulatory sequences (such as a suitable promoter(s), enhancer(s), terminator(s), etc.) allowing the expression (e.g. transcription and translation) of the protein product in the host cell or host organism.

The vectors according to the invention may be in the form of a vector, such as for example a plasmid, cosmid, YAC, a viral vector or transposon.

30 In a preferred but non-limiting aspect, a vector of the invention comprises i) at least one nucleic acid as described above; operably connected to ii) one or more regulatory elements, such as a promoter and optionally a suitable terminator; and optionally also iii) one or more further elements of genetic constructs such as 3'- or 5'-UTR sequences, leader sequences,

selection markers, expression markers/reporter genes, and/or elements that may facilitate or increase (the efficiency of) transformation or integration.

A preferred host cell is E.coli. However any prokaryotic or eukaryotic expression systems may be used, such as bacteria, yeast, filamentous fungi, insect, plant cells and mammalian cells.

Preferred vectors, promoters, and host cells, are all vectors, promoters and host cells able to express the recombinant protein, glycosylated or not-glycosylated, such as: the pET26a (with T7 promoter), or the pTrcHis2 (with trp lac promoter) plasmids for procaryotic expression, the pUC19 , pUC 57, or pCR4 TOPO plasmids for transfer, and the E. coli BL21 (DE3), or E coli NiCo21 host cells for protein expression, or E coli Top 10 only for plasmids amplification.

Vaccine formulation

The fusion protein is formulated in a pharmaceutical composition, in association with a physiologically acceptable vehicle, optionally combined with an adjuvant.

It is therefore provided a vaccine comprising the fusion protein, or a combination of at least two fusion proteins, which respectively comprise at least two different antigenic amino acid sequences, with a physiologically acceptable vehicle.

In another embodiment, it is provided a vaccine composition comprising a nucleic acid construct encoding said fusion protein(s).

In some embodiments, the vaccines may comprise one or more pharmaceutically acceptable vehicles or excipients. Excipients include any component that does not itself induce the production of antibodies and is not harmful to the subject receiving the composition. Suitable excipients are typically large, slowly metabolized macromolecules such as saccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, sucrose, trehalose, lactose and lipid aggregates (such as oil droplets or liposomes). Suitable pharmaceutical vehicles are well known to those of ordinary skill in the art, including, but not limited to, diluents, such as water, saline, and others. Suitably, sterile pyrogen-free, phosphate buffered physiologic saline is a pharmaceutical vehicle. Additionally, additives, such as wetting or emulsifying agents, pH buffering substances, and the like, may be present.

The pharmaceutical composition, immunogenic composition or vaccine may further comprise an adjuvant. "Adjuvants" are used to enhance efficacy of the composition and include, but are not limited to, aluminum hydroxide (alum), aluminum phosphate, oil-in-water or water-in-oil emulsions, agonists of Toll-like receptors, N-acetyl-normuramyl-L-alanyl- D-isoglutamine

(the-MDP), N-acetyl-muramyl-L-threonyl-D-isoglutamine (nor-MDP), PEI; AS01 or AS02 (GlaxoSmithKline), GLA-SE (IDRI) and similar formulations, ; and the like adjuvants known in the art. The Montanide® adjuvants which are based on purified squalene and squalane, emulsified with highly purified mannide mono-oleate, may be used as well, including ISA 51 and 720. MF59® is another example of an adjuvant, which is an oil-in-water emulsion of a squalene, polyoxyethylene sorbitan monooleate (Tween® 80) and sorbitan trioleate.

Vaccines are formulated into suitable dosage for the subject to which it is to be administered. The dosage administered may vary with the condition, sex, weight and age of the individual; the route of administration; and the adjuvant used. The vaccine may be used in dosage forms such as suspensions or liquid solutions. The vaccine may be formulated with a pharmaceutically acceptable vehicle as described above. Suitable dosages include, but are not limited to, about 0.1 to about 100 micrograms, preferably about 1 to about 50 micrograms, still preferably 1 to 20, 1 to 15, or even 1 to 10 micrograms, of the fusion protein described herein.

Vaccination

The immunogenic composition or vaccine may be a multi-component/multi- antigen immunogenic composition or vaccine.

Where the immunogenic composition or vaccine is intended for a multiple administration regime, such as a prime-boost regime, the prime composition may comprise the same or different composition as the boost composition. However a prime-boost regime is not compulsory at all in the context of the present invention.

The immunogenic composition or vaccine may be administered by any convenient route, preferably parenterally, intramuscularly, intradermally, subcutaneously, mucosally, or intravenously.

A variety of techniques are available for DNA vaccination, such as electroporation, needle-free approaches, such as particle bombardment and high-pressure delivery, dermal patches, formulation of DNA vaccine in microparticles or liposomes.

It is described a method for raising an immune response in a subject, comprising the step of administering an effective amount of a vaccine of the invention. The vaccines can be

administered prophylactically (i.e. to prevent infection) or to provide protective and preferably involves induction of antibodies and/or T cell immunity. The method may raise a primary immune response, a secondary immune response, a booster response or a combination of immune responses.

5

The vaccine is meant to protect the subject against malaria at any stage, including pre-erythrocytic-stages, such as liver-stage, and/or sexual or asexual blood-stage.

10 The magnitude and/or memory of the immune response against the Plasmodium antigens is increased according to the invention.

Especially, the MSP3 fusion constructs of the invention trigger production of anti-MSP3 cytophilic antibodies such as IgG1 and IgG3 antibodies. The level of protection may be determined by measuring the titer of said antibodies.

15 The Figures and Examples illustrate the invention without limiting its scope.

EXAMPLES:

Previous studies have shown that frequent malaria exposure leads to the development of immunity in adults, which prevents or alleviates disease. This immunity can be passively
20 transferred by administering immunoglobulin (IgG) from malaria-immune adults.

A parasite-killing mechanism, called antibody-dependent cell-mediated inhibition (ADCI), was identified. The screening of a genome-wide DNA library by ADCI led to the identification of merozoite-surface-protein 3 (MSP3) and later to several other antigens, including PEBS.

25 Cytophilic antibodies were identified as surrogates of protection: Cytophilic (leucocyte-binding) anti-MSP3 antibodies IgG1 and IgG3, which mediate ADCI were found to be consistently associated with a reduction in the risk of malaria in epidemiological studies in many different settings. These antibodies also mediate protection against *P.falciparum* in infected animals.

30 These studies indicate the characteristics which an efficient immune response bears and guide the development of improved vaccine formulations.

On this basis, the inventors have now shown that a fusion protein CRM97-MSP3 increases immunogenicity by 20-100 fold, at B and T-cell levels, as compared to MSP3-LSP (long synthetic peptide covering the 186-271 region of MSP3-1). See **Example 1**. Using 10 fold

lower immunizing doses, it translated into a major improvement in immunogenicity to lymphocytes from : humans, mice and saimiri monkeys, and a major improvement in duration of antibodies.

- 5 At pre-erythrocytic stage, previous studies have further shown that protective efficacy against massive sporozoites challenges can be elicited by LSA3 in Chimpanzees, which efficacy depends on IFN- γ likely inhibiting LS development, and on antibodies preventing sporozoite invasion.

In **Example 2**, the inventors have shown that a bio-fusion CRM-LSA3 construct strongly
10 increases T and B cell responses.

The results obtained in Examples 1 and 2 proved to be reproducible using other antigens from the erythrocytic stages such as MSP3-2 and MSP3-3 in a construct with CRM (See **Example 3**).

15 **Example 4** provides results with a LSA5-CRM construct.

Materials and methods

Generation of expression constructs and production of the Bio-fusion proteins in 20 *Escherichia coli*

The genetic sequences coding for the chimeric immunogens composed of the detoxified diphtheria toxin CRM197 covalently linked at both its N- and C-terminal end to malaria peptide antigens (Figure 1) were chemically synthesized (GenScript) and codon-optimized for the production in *E. coli*. Restriction sites for Nco I and Xho I were respectively added at the
25 5' and 3' extremities for cloning in the expression plasmid pET-26a (Novagen). The sequences inserted in the shuttle plasmid pUC57 were checked by sequencing and expedited lyophilized (4 μ g).

The MSP3-1 peptide in PP21 (plasmodB acc. Nbr PF3D7_1035400) corresponds to amino acids (AA) 155 to 249 in MSP3-1.

30 Other hybrid immunogens (Table 3) have been designed around CRM197. In PP22, the MSP3-1 peptide was replaced by a MSP3-2 peptide (AA 178 to 257 of MSP3-2, PlasmodB acc. Nbr PF3D7_1035500). In PP23, the MSP3-2 peptide at the C-extremity was replaced by an MSP3-3 peptide (AA 246 to 307 in MSP3-3, PlasmodB acc. Nbr PF3D7_1035600). PP25

contains the same LSA3 peptide on both CRM197 extremities (AA 176 to 325, PlasmodB acc. Nbr PF3D7_0220000).

Table 3: Physico-chemical characteristics of immunogens PP21, PP22, PP23, PP25 and LSA5-CRM

Chimeric Recombinant Immunogens (<i>E. coli</i>)			Aminoacids Nbr.	Mol.Wt. (kDa)	pHi
PP21	MSP3-1 p_6His	lsp*_CRM197_MSP3-1	757	84	5,4
PP22	MSP3-2 lsp_6His	lsp_CRM197_MSP3-2	727	80	4,6
PP23	MSP3-2 lsp_6His	lsp_CRM197_MSP3-3	709	78	4,9
PP25	LSA3 lsp_CRM197_LSA3	lsp_6His	845	93	4,3
LSA5-CRM protein	PEBS-CRM197_PEBs_6His		807	90	4.07

*lsp: long synthetic peptide

The *E. coli* transfer strain Top 10 (Invitrogen) [F– *mcrA* Δ (*mrr-hsdRMS-mcrBC*) Φ 80*lacZ* Δ M15 Δ *lacX74* *recA1* *araD139* Δ (*ara leu*) 7697 *galU* *galK* *rpsL* (StrR) *endA1* *mupG*] was used as a for the cloning molecular procedures and plasmid propagation.

Expression of recombinants was performed in strain BL21 (DE3) [F – *ompT* *hsdSB* (*rB– mB*) *gal dcm* (DE3)] (NEB).

The shuttle plasmid pUC57 containing the hybrid sequences (Genscript) and the expression plasmid pET26a were digested with Nco I and Xho I. The bands for the inserts and the linearized pET26a were recovered by gel extraction (QIAGEN) after electrophoresis. The gel-purified inserts were ligated inside pET26a with a ratio insert on plasmid of 3. The ligation reaction was used to transform chemically competent *E. coli* Top 10 and plated on LB agar media with 50µg/mL kanamycin in Petri dishes.

Six bacteria colonies were picked in liquid media with kanamycin for plasmid mini-preparations on silica column (QIAGEN). The correct insertion of inserts in pET26a was checked by digestion with informative restriction enzymes (**Figure 2**).

Plasmids with the correct restriction profile were selected to transform BL21 (DE3) bacteria.

Transformation with the correct plasmid was confirmed on six BL21 (DE3) clones that were analyzed by restriction enzyme digestion as above.

Optimization of the recombinant protein production in small volume bacteria cultures

Parameters such as the duration of recombinant protein production, the concentration of the inducer (IPTG) and temperature were analyzed on a small culture scale (1 L) in Erlenmeyer vessels. Five mL of a steady state overnight culture was diluted in 1 L (1:200) and further cultured at 30 °C to an optical density of 0,7-0,8 at 600nm. The induction of the recombinant protein expression was assayed with two IPTG inducer concentrations; 0.1 and 1 mM at three temperatures; 22, 30 and 37°C. The best recombinant yields were obtained after on overnight culture at 22°C and induction by 0.1 mM IPTG.

A yield of 1 to 2 mg of recombinant product per liter of bacteria culture was obtained after purification by immobilized metal affinity chromatography (IMAC).

Production and purification of PP21

Productions at a research laboratory scale (1 to 2 liters) were conducted to obtain sufficient PP21 recombinant protein to conduct pre-clinical immunogenicity studies in murine and primate models.

The protocol for the bacteria culture and recombinant protein production has been established formerly in small scale cultures.

The C-terminally hexa-histidine tagged recombinant protein PP21 was purified by affinity on Ni-NTA resin (QIAGEN).

Two purification procedures, under native or denaturing conditions, were investigated.

Indeed, although in native conditions, no recombinant protein was seen in the bacteria lysate insoluble fraction, purification under denaturing conditions was also assayed to assess the effect of a putative conformational effect of the tri-dimensional structure of PP21 on the availability of the histidine tag for the immobilized Ni²⁺ metal on the Ni-NTA resin.

Purification under native conditions:

- The bacteria cells were recovered by centrifugation (4000g, 30 mins, 4°C).
- The bacteria pellet was suspended in 5 mL of lysis buffer (50 mM NaH₂PO₄, 300 mM NaCl, 10 mM imidazole, pH 8.0) per gram of biomass.
- The lysate was rocked on ice 30 mins with 1 mg/mL of lysozyme.
- The bacteria were lysed by 5 30 sec bursts at 150 W with a 30 sec cooling intervals.
- The lysate was rocked on ice 30 min with 5µg/mL of DNase I and 10µg/mL of RNase A with a complete set of proteases inhibitors (Roche).
- The lysate was cleared by centrifugation at 10000g, 30 mins at 4°C.

- The lysate was filtered through a 0,22 µm sieve and incubated overnight on a rocking tray at 4°C with 200 µL of Ni NTA resin in a 20 mL volume.
 - The resin was extensively washed in a 40 mL volume of lysis buffer five times. An aliquot of the first step supernatant (lysate post-resin incubation) was conserved for analysis.
- 5 Centrifugation steps did not exceed 5 mins at 200g.
- The recombinant proteins were recovered by incubating the resin in 500 µL lysis buffer containing 250 mM imidazole 5-fold
 - The eluted fractions were pooled and dialyzed against PBS pH 7.3 by ultrafiltration through a 30 kDa sieve.
- 10 The protein concentration was measured by spectrophotometry at 280 nM and further characterized by electrophoresis (SDS-PAGE 10%) and immunoblotting as shown in Figure 3 for PP21.

Purification under denaturing conditions:

The bacteria cells were recovered by centrifugation (4000g, 30 mins, 4°C).

- 15 The bacteria pellet was suspended in 5 mL of denaturing lysis buffer (100 mM NaH₂PO₄, 10 mM Tris-Cl, 8 M urea, NaOH pH 8.0) per gram of biomass.

The lysate was rocked on ice 30 mins.

The bacteria were further lysed by 5 30 sec bursts at 150 W with a 30 sec cooling intervals.

The lysate was cleared by centrifugation at 10000g, 30 min at 4°C.

- 20 The lysate was filtered through a 0,22 µm sieve and incubated overnight on a rocking tray at 4°C with 200 µL of Ni NTA resin in a 20 mL volume.

The resin was extensively washed in a 40 mL volume of denaturing lysis buffer five times. An aliquot of the first step supernatant (lysate post-resin incubation) was conserved for analysis. Centrifugation steps did not exceed 5 min at 200g.

- 25 The recombinant proteins were recovered by incubating the resin in 500 µL lysis buffer containing 250 mM imidazole 5-fold.

The eluted fractions were pooled and dialyzed against PBS pH 7.3 by ultrafiltration through a 30 kDa sieve.

- 30 The purification yield was similar by the two methods, suggesting that the affinity histidine tag is functional in the native form of PP21.

Production yields of 0,7 to 1mg of the recombinant protein PP21 per liter of bacteria culture have been reproducibly obtained in more than 10 production / purification trials at the 1 liter scale in Erlenmeyer vessels.

Figure 3 shows recombinant protein PP21 purified by IMAC.

Temperature stability of PP21

The stability of PP21 in function of the storage temperature assessed by *Western blotting* is shown in **Figure 4**. No signs of degradations were observed after a period of 21 days storage in a fridge at a temperature of 6°C. At room temperature, PP21 started to show signs of degradation at the same period whereas it was completely degraded at 37°C after 8 days. However, this instability cannot be attributed to putative intrinsic molecule instability as it is not a GMP manufactured product and it might contain traces of proteases.

Amino acid sequences of recombinant proteins expressed in *E.coli* by pET26a are shown below. Sequences in brackets come from the expression plasmid, bold from the CRM197 diphtheria toxin.

The hexa-histidine tag at the C-terminal used for purification by immobilized metal affinity chromatography (IMAC) is underlined.

PP21 sequence of MSP3-1 in italics-underlined (PlasmodB ID : PF3D7_1035400), residues 155 to 249 (95 aa)

[MKYLLPTAAAGLLLLAAQPAMAMG]**KTKEYAEKAKNAYEKAKNAYOKANOAVLKAKE**
ASSYDYILGWEFGGGVPEHKKEENMLSHLYVSSKDKENISKENDDVLDEKEEEEAEETEEEE
LEGADDVVDSSKSFVMENFSSYHGTPGYVDSIQKGIQKPKSGTQGNYYDDDWKE
FYSTDNKYDAAGYSVDNENPLSGKAGGVVKVTPGLTKVLALKVDNAETIKKE
LGLSLTEPLMEQVGTEEFIKRFGDGASRVVLSLPFAEGSSSVEYINNWEQAKALS
VELEINFETRGRGQDAMYEYMAQACAGNRVRRSVGSSLSCINLDWDVIRDKT
KTKIESLKEHGPIKNKMSESPNKTVSEEKAKQYLEEFHQTALEHPELSELKTVTG
TNPVFAGANYAAWAVNVAQVIDSETADNLEKTTAALSILPGIGSVMGIADGAVH
HNTTEEIVAQSIALSSLMVAQAIPLVGELVDIGFAAYNFVESIINLFQVVHNSYNRP
AYSPGHKTQPFLHDGYAVSWNTVEDSIIRTGFQGESGHDIKITAENTPLPIAGVLL
PTIPGKLDVNKSKTHISVNGRKIRMRCRAIDGDVTFRCRPSVPYVGNGVHANLH
VAFHRSSSEKIHSNEISSDSIGVLGYQKTVDHDKVNSKLSLFFEIKSK**KTKEYAEKAKN**
AYEKAKNAYOKANOAVLKAKEASSYDYILGWEFGGGVPEHKKEENMLSHLYVSSKDKENI
SKENDDVLDEKEEEEAEETEEEELE**[LEHHHHHHHH]** (SEQ ID NO: 85).

PP22 ; sequence of MSP3-2 in italics-underlined (PlasmodB ID : PF3D7_1035500), residues 178 to 257 (79 aa)

[MKYLLPTAAAGLLLLAAQPAMAMG]**LNNNILGWEFGGGAPONGAAEDKKTEYLLEOI**
KIPSWDRNNIPDENEQVIEDPOEDNKDEDEDEETETENLETEDDNNEEGADDVVDSSKS

FVMENFSSYHGTPGYVDSIQKGIQKPKSGTQGNYYYYDDWKEFYSTDNKKYDAAG
 YSVDNENPLSGKAGGVVKVTYPGLTKVLALKVDNAETIKKELGLSLTEPLMEQV
 GTEEFIKRFGDGASRVVLSLPFAEGSSSVEYINNWEQAKALSVELEINFETRGRK
 GQDAMYEYMAQACAGNRVRRSVGSSLSCINLDWDVIRDKTKTKIESLKEHGPIK
 5 NKMSSEPNKTVSEEKAKQYLEEFHQTALEHPELSELKTVTGTPNFAGANYAAW
 AVNVAQVIDSETADNLEKTTAALSILPGIGSVMGIADGAVHHNTEEIVAQSIALSSL
 MVAQAIPLVGELVDIGFAAYNFVESIINLFQVVHNSYNRPAYSPGHKTQPFLHDGY
 AVSWNTVEDSIIRTGFQGESGHDIKITAENTPLPIAGVLLPTIPGKLDVNKSKTHIS
 VNGRKIRMRCRAIDGDVTFCRPKSPVYVGNGVHANLHVAFHRSSEKIHSNEISS
 10 DSIGVLGYQKTV DHTKVNSKLSLFFEIKSLNNNILGWEFGGGAPONGAAEDKKTEY
LLEQIKIPSWDRNNIPDENEQVIEDPOEDNKDEDEDEETETENLETEDDNNEELEH
HHHHH (SEQ ID NO: 86).

PP23 ; sequence of MSP3-2 in italics-underlined before CRM197 (PlasmodB ID :
 15 PF3D7_1035500), residues 178 to 257 (79 aa) and MSP3-3 in italics after CRM197
 (PlasmodB acc. Nbr PF3D7_1035600), residues 246 to 307 (61 aa).

[MKYLLPTAAAGLLLLAAQPAMAMG]LNNNILGWEFGGGAPONGAAEDKKTEYLLEQI
KIPSWDRNNIPDENEQVIEDPOEDNKDEDEDEETETENLETEDDNNEEGADDVVDDSSKS
 20 FVMENFSSYHGTPGYVDSIQKGIQKPKSGTQGNYYYYDDWKEFYSTDNKKYDAAG
 YSVDNENPLSGKAGGVVKVTYPGLTKVLALKVDNAETIKKELGLSLTEPLMEQV
 GTEEFIKRFGDGASRVVLSLPFAEGSSSVEYINNWEQAKALSVELEINFETRGRK
 GQDAMYEYMAQACAGNRVRRSVGSSLSCINLDWDVIRDKTKTKIESLKEHGPIK
 NKMSSEPNKTVSEEKAKQYLEEFHQTALEHPELSELKTVTGTPNFAGANYAAW
 25 AVNVAQVIDSETADNLEKTTAALSILPGIGSVMGIADGAVHHNTEEIVAQSIALSSL
 MVAQAIPLVGELVDIGFAAYNFVESIINLFQVVHNSYNRPAYSPGHKTQPFLHDGY
 AVSWNTVEDSIIRTGFQGESGHDIKITAENTPLPIAGVLLPTIPGKLDVNKSKTHIS
 VNGRKIRMRCRAIDGDVTFCRPKSPVYVGNGVHANLHVAFHRSSEKIHSNEISS
DSIGVLGYQKTV DHTKVNSKLSLFFEIKSSNEKGRPPTYSPILDDGIEFSGGLYFNEKK
 30 STEENKQKNVLESVNLTSWDKEDIVKENEDVKLEHHHHHHH (SEQ ID NO: 87).

PP25 ; sequence of LSA-3 in italics-underlined (PlasmodB ID : PF3D7_0220000), residues
 176 to 325 (150 aa)

[MKYLLPTAAAGLLLLAAQPAMAMG]SDELFNELLNSVDVNGEVKENILEESQVNDDIF
NSLVKSVQOEQOHNVEEKVEESVEENDEESVEENVEENVEENDDES
IDSSIEENVAPTVEEIVAPTVEEIVAPSVVESVAPSVESVEENVEESVAENVEE
 GADDVVDS
 SKSFVMENFSSYHGTPGYVDSIQKGIQKPKSGTQGNYYYYWKEFYSTDNKYDA
 5 AGYSVDNENPLSGKAGGVVKVTPGLTKVLALKVDNAETIKKELGLSLTEPLME
 QVGTEEFIKRFGDGASRVVLSLPAEGSSSV EYINNWEQAKALSVELEINFETR
 KRGQDAMY EYMAQACAGNRVRRSVGSSSLSCINLDWDVIRDKTKTKIESLKEHG
 PIKNKMSESPNKT VSEEKAKQYLEEFHQTALEHPELSELKTVTGTNPVFAGANY
 AAWAVNVAQVIDSETADNLEKTTAALSILPGIGSVMGIADGAVHHNTEEIVAQSI
 10 ALSSLMVAQAIPLVGELVDIGFAAYNFVESIINLFQVVHNSYNRPAYSPGHKTQPF
 LHDGYAVSWNTVEDSIIRTFQGESGHDIKITAENTPLPIAGVLLPTIPGKLDV NK
 SKTHISVNGR KIRMRCRAIDGDVTF CRPKSPVYVGNGVHANLHVAFHRSSEKIH
 SNEISSDSIGVLGYQKTV DHTKVN SKLSLFFEIKSSDELFNELLNSVDVNGEVKENILE
ESQVNDDIFNSLVKSVQOEQOHNVEEKVEESVEENDEESVEENVEENVEENDDES
 15 ASSVEES
SIASSVDESIDSSIEENVAPTVEEIVAPTVEEIVAPSVVESVAPSVESVEENVEESVAENVEE
LEHHHHHHH (SEQ ID NO: 88).

LSA5-CRM Protein Sequence (SEQ ID NO: 89)

IPEEQIEEVIQEEHIEQVVP EELIEEVVPEEHIEEVIPEEIVEEVIYEEVIPEELV EEVIAEKL VKE
 20 IVPEQVREEVTLEEIVEEMIPEEFV EEVVAPEVEIEEHPEELIEEVIPEVLVEEAVPEELIEKVTP
 GADDVVDS SKSFVMENFSSYHGTPGYVDSIQKGIQKPKSGTQGNYYYYWKEFYST
 DNKYDAAGYSVDNENPLSGKAGGVVKVTPGLTKVLALKVDNAETIKKELGLSLTE
 PLMEQVGTEEFIKRFGDGASRVVLSLPAEGSSSV EYINNWEQAKALSVELEINFETR
 GKRQDAMY EYMAQACAGNRVRRSVGSSSLSCINLDWDVIRDKTKTKIESLKEHGPI
 25 KNKMSESPNKT VSEEKAKQYLEEFHQTALEHPELSELKTVTGTNPVFAGANYA AWA
 VNVAQVIDSETADNLEKTTAALSILPGIGSVMGIADGAVHHNTEEIVAQSIALSSLMV
 AQAIPLVGELVDIGFAAYNFVESIINLFQVVHNSYNRPAYSPGHKTQPF LHDGYAVSW
 NTVEDSIIRTFQGESGHDIKITAENTPLPIAGVLLPTIPGKLDV NK SKTHISVNGR KIR
 MRCRAIDGDVTF CRPKSPVYVGNGVHANLHVAFHRSSEKIH SNEISSDSIGVLGYQK
 30 TVDHTKVN SKLSLFFEIKSIPEEQIEEVIQEEHIEQVVP EELIEEVVPEEHIEEVIPEEIVEEVI
YEEVIPEELV EEVIAEKL VKEIVPEQVREEVTLEEIVEEMIPEEFV EEVVAPEVEIEEHPEELIE
EVIPEVLVEEAVPEELIEKVTPHHHHHH

The Human Immunogenicity Mouse Model (HIMM): the model is based upon the engraftment of immunodeficient NOD-SCID-IL-2 γ null (NSG) mice with human spleen lymphocytes (Hu-SPL-NSG), and complements the information obtained using ordinary laboratory mice such as Balb/C and C57BL.

5 **Immunization of Balb/c or C57Bl/6 mice and blood sampling**

Groups of 4 to 5 Balb/c or C57Bl/6 mice received 2 or 3 injections of 10 μ g of MSP3-1-LSP or 1 μ g of PP21 diluted in 100 μ l of Phosphate Buffer Saline pH 7.2 (PBS) and emulsified in 100 μ l of adjuvant Montanide ISA 720. Immunizations were performed by subcutaneous injection and repeated once or twice fifteen days apart. Blood collection was performed by tail
10 bleeding starting two weeks after the second injection and repeated at fifteen days interval up to 160 days after the first antigen injection. Sera were separated and stored at -20°C until used. Other groups handled simultaneously in parallel, received either 1 μ g or 0.2 μ g of PP21.

Determination of anti-MSP3-LSP antibody titers in mice sera

MSP3-LSP specific antibody titers were determined in mice sera by Enzyme Linked
15 Immunosorbent Assay (ELISA). Flat-bottomed microtitration plates (Nunc-Thermo Scientific, USA) were coated overnight at 4°C with 2 μ g/ml of PBS diluted MSP3-1-LSP or one of the MSP3-1-LSP peptides a, b, c or d. After washing (PBS, pH 7.2) and saturation (PBS, 3% non-fat milk), serial dilutions of test sera (diluted in PBS, 3% non-fat milk, 0.05% Tween20) were added and incubated for 1 hour. Negative control consists of a preimmune
20 mouse serum. Specific antibodies were revealed by subsequent addition of horseradish peroxidase-conjugated goat anti-mouse IgG (H+L) (Invitrogen, USA) for one hour, followed by the peroxidase substrate Tetramethylbenzidine (Amresco, USA). Specific antibody titer corresponds to the reverse of the last positive dilution.

25

Human spleen donation and ethical considerations

The human spleens were obtained from deceased organ transplant donors according to an ethical agreement with the National Organization for Organ & Tissues Donation & Transplantation (NOOTDT) in Lebanon. The informed consent to donate organs for
30 transplantation or scientific research was signed by the patients themselves during their lifetime or by their parents following the death.

Human spleen cell preparation

Human spleens were processed within 24 hours after surgical excision as previously described (Brams P, 1998). Briefly, splenic tissue was dissected and a cell suspension was prepared.

Red blood cells were lysed using Gey's solution for 5-10 min at 25°C. After washing, leucocytes were resuspended in medium consisting of 37% fetal calf serum (FCS) (Sigma,USA), 10% dimethyl sulfoxide (DMSO) (Sigma,USA) and 53% RPMI 1640 (Sigma,USA), and then cryopreserved in liquid nitrogen until used. The mean number of cells isolated from each spleen donor was 10 ± 4 billion.

Engraftment and immunization of human spleen cells in NSG mice

NOD.Cg-Prkdcscid-IL2rytm1WjI /SzJ (NSG) mice were obtained from The Jackson Laboratories (USA) and housed in sterile microisolators. All food, water, caging and bedding was autoclaved before use. Six- to 8-week old NSG mice were included in the experiments.

Human spleen cells were cultured on day 0 at 4×10^6 cells/ml with or without 1 µg/ml of antigen in RPMI1640 medium supplemented with 10% Fetal Calf Serum, 1% non-essential amino acids (NEAA 100x), 2 mM glutamine, 2 mM sodium pyruvate and 50 µg/ml gentamicin (complete medium). All culture reagents were purchased from Sigma, USA. On day 1, recombinant human IL-2 (Gibco Invitrogen) was added at 25 IU/ml. On day 3, the spleen cells were harvested, washed and resuspended in Hank's Balanced Salt Solution (HBSS). Each NSG mouse received an intraperitoneal injection (ip) of 30×10^6 antigen-primed or unprimed spleen cells. At day 7, and day 21, reconstituted mice (Hu-SPL-NSG) were boosted with 10 µg of antigen injected intraperitoneally (ip) in 200 µl of HBSS-Montanide ISA 720 or MF59 adjuvant (v/v). Mice reconstituted with unprimed spleen cells, received only adjuvant. Blood samples were collected one week after each booster.

Determination of human MSP3-1-LSP specific antibodies in Hu-SPL-NSG mice sera

These determinations were performed by ELISA. Briefly, for the detection of total human IgG in mouse serum, flat-bottomed microtitration plates (Nunc-Thermo Scientific, USA) were coated overnight at 4°C with 2.5µg/ml purified goat anti-human IgG (H + L) (Invitrogen, USA) in 0.1M carbonate buffer, pH 9.5. After washing (PBS, pH 7.2) and saturation (PBS, 3% non-fat milk), test sera (diluted in PBS, 3% non-fat milk, 0.05% Tween 20) were added and incubated for 1 hour. Negative controls consisted of preimmune mouse serum of the same animals. Human IgG were revealed by subsequent addition of horseradish peroxidase-conjugated goat anti-human IgG (H+L) (Invitrogen, USA) for one hour, followed by the peroxidase substrate Tetramethylbenzidine (Amresco, USA). Total human IgG concentration in the Hu-SPL-NSG mouse serum was calculated in comparison with a standard human IgG solution (Zymed, USA). The same test was performed for the detection of antigen specific antibodies, except that plates were coated with MSP3-1-LSP at 2.5µg/ml in PBS. In this case, negative controls consisted of sera of individuals that have never been infected with

Plasmodium, while positive controls consisted of a pool of sera from hyperimmune African adults. In both cases, serial dilutions of each serum were tested in order to determine antibody titer. For specific antibody titer determination, a test was considered positive when it yielded an absorbance above cut-off (negative control OD x 2). The detection of IgG subclasses was performed using secondary mouse monoclonal antibodies specific for human IgG subclasses (clones NL16 [IgG1; Skybio, UK], HP6002 [IgG2; Sigma-Aldrich, Germany], and Zg4 and GB7B [IgG3 and IgG4, respectively; Skybio, UK] were used at final dilutions of 1/4,000, 1/10,000, 1/10,000, and 1/60,000, respectively), followed by horseradish peroxidase conjugated goat anti-mouse IgG diluted 1/4000 in PBS (Invitrogen).

Quantification of gene expression of different cytokines, chemokines and transcription factors by Real-Time Reverse Transcription PCR (RTqPCR)

Spleen cells of immunized and non immunized mice were cultured at 2×10^6 cells/ml in complete RPMI1640 medium, with or without stimulation with the immunizing antigen. Total cellular RNA was extracted after a 24h culture using RNeasy Mini Kit (Quiagen, Germany).

Reverse transcription was carried out using RevertAid M-MuLV enzyme (RevertAid kit First Strand Synthesis kit, Thermo Scientific Fermentas) in a 20 μ l reaction mixture. Briefly, 1 μ l of oligo dT18 primer was added to about 400 ng of total RNA, mixed and incubated at 65°C for 5 min. The tube was placed on ice for a few minutes and centrifuged briefly before the addition of 5x reaction buffer, Ribolock Rnase inhibitor (20 u/ μ l), dNTPs (10 mM) and reverse transcriptase (200 u/ μ l) as recommended by the manufacturer. The reaction mixture was incubated at 42°C for 60 min. The enzyme was inactivated by heating at 70°C for 5 min. Quantitative PCR was used to measure the relative expression of different human cytokines, chemokines and transcription factors considered as characteristic for Th1 or Treg cells. The PCR mixture was performed using LightCycler 480 SYBR Green Master, La Roche as recommended by the manufacturer. PCR amplifications were performed at 95°C for 5 min (1 cycle), followed by 45 cycles of incubation at 95°C for 10 sec and 55-57°C for 10 sec in the LightCycler 480 machine (La Roche). Each sample was run in triplicate. The housekeeping genes used as internal references were beta-actin (β -actin) and hypoxanthine phosphoribosyltransferase 1 (HPRT1) (geNorm analysis). The cycle threshold (Ct) value was calculated based on the produced PCR curve. The relative expression levels were calculated by the $2^{-\Delta\Delta C_t}$ method.

Immunofluorescence assays.

Immunofluorescence assays were performed using air-dried, acetone-fixed, thin smears from red blood cell cultures containing predominantly mature schizonts of *P. falciparum* (3D7).

Hu-SPL-NSG Sera diluted in PBS–1% bovine serum albumin were incubated at 37°C in a humid chamber for 1 h. After being washed with PBS, antibodies were detected by using an Alexa Fluor-conjugated goat anti-mouse IgG (Molecular Probes and Invitrogen) diluted to 1/400 in PBS with Evans blue counterstain (1/200).

5

Results

Example 1: Immunogenicity of PP21, a CRMP97-MS3 fusion construct

The immune responses induced by PP21 were assessed in the following animal models:

10

- BALB-C mice
- C57BL mice
- *Saimiri sciureus* monkeys
- The human immunogenicity mouse model (HIMM), where cells from human spleen tissue grafted in immunocompromised NSG mice are immunized in vivo and sera and cells from the immunized animals are used for immuno-assays.

15

All experiments were performed in comparative manner with the benchmark antigen MSP3-LSP (long synthetic peptide covering the 186-271 region of MSP3-1) used in clinical experiments, and using Montanide ISA 720 because laboratory mice respond usually poorly to alum, because the route of injection in HIMM does not allow to use alum, and above all because we were aiming at comparing constructs and not adjuvants, knowing that in humans alum adjuvated CRM (in meningococcal or pneumococcal vaccines) as MSP3 LSP provide very good responses.

20

Yet a succesful immunization with alum was also performed in lab mice, yielding titers of > 25 600 in Balb/C,even after two immunisarions, and 3200-25600 in C57bl (Figure 19).

25

A major improvement of immunogenicity was observed using the PP21 Bio-fusion MSP3-1 construct of the invention, as compared to MSP3-LSP in mice.

PP21 induces higher serological responses of the target cytophilic subclasses than the benchmark antigen MSP3-LSP in all models used.

30

1. Low doses are very efficient: As with other CRM conjugated vaccines a major increase in immunogenicity was obtained, indicating that the fusion procedure produced as efficient products as chemical conjugation. We readily employed markedly lower dosages, which led to compare only 1 µg of PP21 with 10 µg of the reference MSP3-LSP (10 µG was found in the past not significantly different in lab mice from the 15 µG employed in the clinic). These differences were determined by different means see Figures 6 to 9. Results were reproducible with 4 distinct batches of PP21 in 4 groups of Balb/C and C57bl mice. Further dose-finding with PP21 focussed

on lower dosage, eg 0.2 µg compared to 1 µg investigated in mice and in Saimiri monkeys. The high immunogenicity led us also to investigate only 2 as compared to 3 immunisations.

2. Wider breadth of recognition of ADCI targets : The peptides “b”, “c” and “d” contained within the vaccine construct define distinct B-cell epitopes targeted by antibodies effective in ADCI.

5 Reactivity with these peptides were higher in sera of mice vaccinated with PP21 as shown in Figure 9 (right-hand panel) as compared to the current MSP3-1-LSP (left-hand panel), at 1 and 10 µg respectively, suggesting that the magnitude and breadth of recognition of ADCI targets are higher and wider with PP21. In agreement with this finding the pattern of recognition of the 6 members of the MSP3 family, which exhibit cross-reactions through peptide « b » and « c-d »
10 mainly, was wider with PP21. This also means that antibodies elicited by PP21 will trigger ADCI through triggering by antibody bridges to 6 proteins on the merozoite surface and not only one.

3. Very high B cell responses in Human lymphocytes : More importantly, human B-cell responses as assessed in the HIMM model showed similar major improvements with
15 immunogenicity increased by 40-100 times. (Figure 10). In parallel experiments, using PP21 head to head with the present MSP3-LSP of 96 amino-acid, antibody titers were 20 to 100 fold higher with 1 µg of PP21 than with 10 µg of MSP3-LSP. Results were reproducible in 3 groups of 5 animals belonging to 3 HLA-classes.

4. Results are also reproducible when using either Montanide ISA720 or MF59 as adjuvants
20 (Figure 14)

5. High IFN-γ secretion was obtained when Human lymphocytes were in vitro challenged with the parasite component MSP3-LSP (Figure 11). This important result indicates that CRM Th epitopes did not override the plasmodium-specific MSR3 T-cell epitopes and therefore that a Tcell help can be expected from vaccinated individuals when challenged by the parasite, yielding
25 great chances for a fast anamnestic antibody rise when it is needed.

Detailed analysis of cytokine profiles indicate that the responding cells are predominantly of a Thelper type 1 type (Figure 12 showing examples of results obtained with CXCL10 and Tbet)

6. Dominance of cytophilic IgG1: Isotype studies revealed as expected with strong Th1 responses a large dominance of the cytophilic isotypes, almost entirely made of IgG1 which is
30 also the dominant isotype in MSP3-LSP immunized individuals. This was true when using either Montanide or MF59 as adjuvants (Figures 15 and 16). Although these result were obtained in a human model they bode very well of future responses which could be elicited in volunteers.

7. Reactivity with native parasite proteins: Antibodies elicited by PP21 vaccination reacted with the parasite native proteins in IFAT (Figure 13) and Western Blots The reactivity of antibodies,

not only with the synthetic antigens, but above all with the parasite proteins is a critical feature to activate the ADCI defence mechanism during a malaria attack, and for the proper boosting of antibody responses by natural parasite challenges.

8. Very low immunizing doses are efficient: 0.2 µg and 1 µg per immunisation were assessed compared to 10 µg for MSP3-LSP (Figures 17) . At the one µg dose of PP21 a plateau was reached after the 2nd immunisation, whereas at a 0.2 µg dose a third immunisation was required to reach about the same high levels of antibodies, and one animal did not respond. Yet the one microG profile indicates that 2 immunisations might be sufficient, and hence may deserve being explored.

9. Similar high immunogenicity is observed in South American Saimiri sciureus monkeys (Figure 20): 1 µg and 0.2 µg PP21 adjuvanted by Montanide 720 were used to immunize South American primates that respond usually poorly to immunisation. High responses close to titers seen in mice were reached at 1 µg, (see Figure 18) and about 5 fold lower titers at 0.2 µg (not shown). Though the comparison of titers in the same experiment has not yet be performed by our Brazilian colleagues, MSP3 LSP was very poorly immunogenic when it was employed in this model.

10. The duration of immune responses is markedly improved (Figure 8 upper and lower panels): Long term analysis showed a marked improvement of an essential component; the duration of antibody responses: Mice immunized by PP21 or LSP were followed up for 6 months post immunisation. The decay of titers is progressive but slow, so that at 6 months the titers remaining are higher than the peak obtained using MSP3-LSP. Titers remained with PP21 in the range 1/200 000 – 1/300 000 for more than 6 months, compared to a range of ca 1/50 000 for the current MSP3-LSP.

Example 2: Immunogenicity of PP25, a CRMP97-LSA3 fusion construct

LSA3 is a pre-erythrocytic stage antigen, which has many attractive features, it was discovered by the differential responses of protected versus non-protected volunteers, it is conserved across strains, it is highly antigenic and immunogenic in a large range of animals including higher primates and chimpanzees, and induces in the latter immune responses protective against massive challenges by the human parasite Plasmodium falciparum at sporozoite stage. Protection is associated with antigen-specific Interferon gamma responses. The immunogenicity of PP25 was compared to control construction using LSA3 without conjugate nor any fusion (DG729). Conditions of immunization and immune-analysis are identical to those described above with PP21.

A similar major increase in antibody responses with LSA3-CRM97 biofusion, even using the antigen at low doses, was observed as was the case for MSP3 in PP21. The increase in IFN- γ responses was also seen but was less marked as LSA3 (DG729) without carrier is already a very good inducer of IFN-g responses.

- 5 The increase recorded in balb/C and C57bl mice, was also confirmed in the Human Immunogenicity model.

We further showed a very strong correlation between anti-LSA3 antibody titers with inhibition of *P.falciparum* parasites at sporozoite stage.

See results shown in **Figures 21-26**.

10

Example 3: Immunogenicity of PP23, a MSP3-2-CRMP97-MSP3-3 fusion constructs

The results obtained with PP21 relying on the fusion of MSP3-1 with CRM, and with LSA3, proved to be reproducible using other antigens from the erythrocytic stages such as MSP3-2 and MSP3-3 in a construct with CRM, named PP23. Indeed, strong B and T cell responses were
15 elicited in Human Lymphocytes grafted in the HIMM model, by the construct PP23 (MSP3-2-CRMP97-MSP3-3) (**Figure 27**), the titers being on average 10 fold higher than in mice immunized by MSP3-2 CT alone in Montanide. Antibody sub-classes were predominantly of the IgG1 class, which is the main cytophilic class able to act in cooperation with monocytes in the ADCI mechanism. Similarly strong T-cells responses were induced as measured by secretion of
20 IFN- γ by PP23-immunized human lymphocytes restimulated in vitro by either MSP3-2 or MSP3-3.

Example 4 : LSA5-CRM

Liver-stage antigen-5 (LSA5), also known as PEBS (pre-erythrocytic and blood stages antigen),
25 or SR 11.1 (sub-region of 11.1 *P.falciparum* gene) combines in a single molecule the features of both MSP3 and LSA3. It contains a unique sequence that differentiates it from the remaining of the mega-gene Pf 11.1, and is fully conserved across strains. It was recognized by sera from volunteers immunized with radiation- attenuated sporozoites and is unique as it induces protection against both pre-erythrocytic and asexual blood stages. It is expressed in both pre-
30 erythrocytic and blood stages. The protective role of LSA5 against pre-erythrocytic stages is supported by convergent in vitro invasion inhibition studies, in vivo protection by passive transfer of anti-LSA5 antibodies, and by proof-of-concept studies in primates protected from challenge by vaccination with recombinant LSA5. Against the blood-stages, both naturally-occurring human and artificially-induced animal anti-Pf LSA5 antibodies exert a parasite-killing

ADCI-mediated effect. Antigenicity is high in individuals from endemic areas with IgG3 antibodies predominating in individuals with premunition ie. exposure induced protection. A large number of epidemiological studies found strong association with protection against clinical malaria attacks and improved prognosis of drug-treated cerebral malaria. Finally LSA5 is highly immunogenic, achieving remarkably high titers in mice and greater ADCI activity than sera from MSP3-immunized mice.

A Bio-fusion of LSA5 with CRM197 similar in its principles to the previous 3 examples, was expressed in *E.coli*, its antigenicity ascertained and preliminary immunogenicity studies conducted. LSA5 immunogenicity was very high using the fusion with CRM (Figure 28); immunogenicity of 1 µg was compared to 10 µg dose of Bio-fusion LSA5-CRM/Montanide ISA720 in BALb/c mice (n=5). Experimental conditions were similar to those described in Figure 8 with MSP3. Immunization by Bio-fusion LSA5-CRM /Montanide ISA720 was performed on days 0,14 and 28 (arrows). Serum antibody detection was performed by ELISA titration on LSA5-LSP as antigen, using sera collected on days 0, 7, 21, 42.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS :

1. A fusion protein which comprises at least one antigenic amino acid sequence fused at the N-term and/or C-term to a carrier heterologous protein sequence, wherein the antigenic sequence comprises an epitope sequence of a Plasmodium protein and the carrier heterologous protein sequence is a sequence that is immunogenic in humans, wherein the antigenic sequence is MSP3, LSA3, or LSA5, or an epitopic fragment of MSP3 that encompasses motifs a, b, c, d, e, and/or f of the C-terminal region of a Plasmodium MSP3 protein chosen among MSP3-1, MSP3-2, MSP3-3, MSP3-4, MSP3-7, MSP3-8, preferably selected from SEQ ID NO: 7 to SEQ ID NO: 54, or an epitopic fragment of LSA3 that is peptide DG729 of SEQ ID NO: 771.
2. The fusion protein of claim 1, wherein the carrier heterologous protein sequence is selected from the group consisting of a cross-reacting material (CRM) of diphtheria toxoid, diphtheria toxoid (D), a non-toxic mutant recombinant *Pseudomonas aeruginosa* exoprotein A (repA), meningococcal outer membrane protein complex (OMPC), tetanus toxoid (T), *H. influenza* protein D (hiD), and immunogenic fragments thereof, wherein the carrier heterologous protein sequence preferably is CRM197 or an immunogenic fragment thereof, which fragment is preferably selected from the group consisting of Fragment A, Transmembrane Domain T, Receptor Binding domain R of CRM197, amino acid sequence 1-190 of CRM197, and amino acid sequence 1-389 of CRM197.
3. The fusion protein according to claim 1 or claim 2, wherein the carrier heterologous protein sequence is CRM197 or an immunogenic fragment thereof; which immunogenic fragment is selected from the group consisting of Fragment A, Transmembrane Domain T, Receptor Binding domain R of CRM197, amino acid sequence 1-190 of CRM197, and amino acid sequence 1-389 of CRM197.
4. The fusion protein according to any of claims 1-3, comprising two antigenic sequences which are either each located in C-term and N-term of the carrier protein sequence, or both located at the same terminus.
5. The fusion protein according to any of claims 1-3, wherein the at least one amino acid sequence is linked at the N-term and/or C-term of the carrier heterologous protein

sequence by a peptide linker, wherein the peptide linker preferably is a sequence of 1 to 35 amino acids, preferably 5 to 20 amino acids.

6. The fusion protein according to claim 5, wherein the peptide linker is (Gly-Gly-Gly-Gly-Ser)_n, (Gly)_n or (EAAAK)_n, wherein n is 1 to 4, preferably 1 to 3.
7. A nucleic acid construct encoding the fusion protein as defined in any of claims 1 to 6.
8. A vector comprising the nucleic acid construct of claim 7 in an expression cassette.
9. A host cell wherein the vector of claim 8 has been inserted.
10. An *in vitro* method for preparing a fusion protein as defined in any of claims 1 to 6, which method comprises allowing the host cell of claim 9 to reproduce under conditions which induce expression of the nucleic acid construct as defined in claim 7, and collecting the fusion protein which is so expressed.
11. A vaccine comprising the fusion protein as defined in any of claims 1 to 6, or a combination of at least two fusion proteins as defined in any of claims 1 to 6, which respectively comprise at least two different antigenic amino acid sequences, or a nucleic acid construct encoding said fusion protein(s), as defined in claim 7, with a physiologically acceptable vehicle.
12. The vaccine of claim 11, for use in vaccinating a human subject against malaria.
13. A method of preventing malaria, comprising administering the fusion protein as defined in any of claims 1 to 6, or a combination of at least two fusion proteins as defined in any of claims 1 to 6, which respectively comprise at least two different antigenic amino acid sequences, or a nucleic acid construct encoding said fusion protein(s), as defined in claim 7, to a subject in need thereof.
14. Use of the fusion protein as defined in any of claims 1 to 6, or a combination of at least two fusion proteins as defined in any of claims 1 to 6, which respectively comprise at least two different antigenic amino acid sequences, or a nucleic acid construct encoding

said fusion protein(s), as defined in claim 7, in the manufacture of a medicament for the prophylactic treatment of malaria.

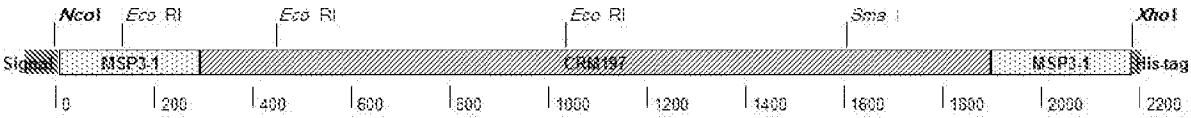


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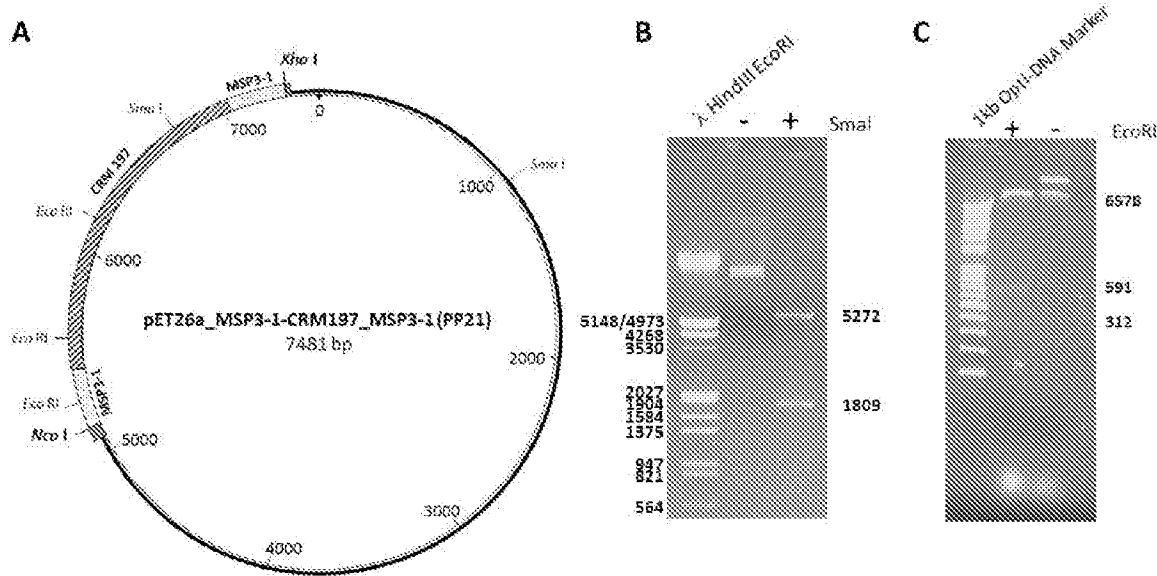


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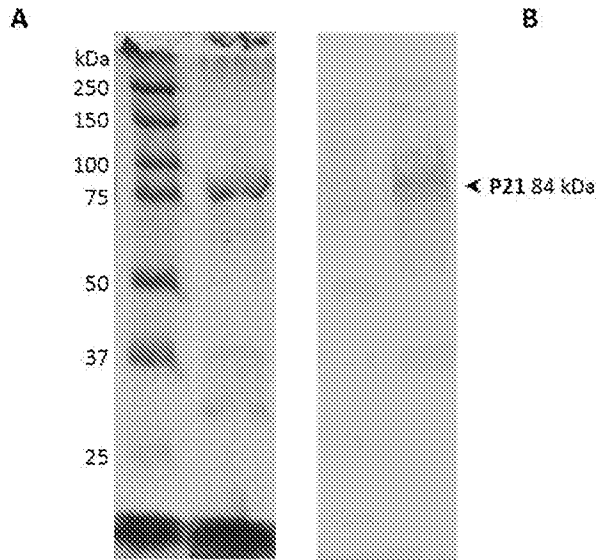


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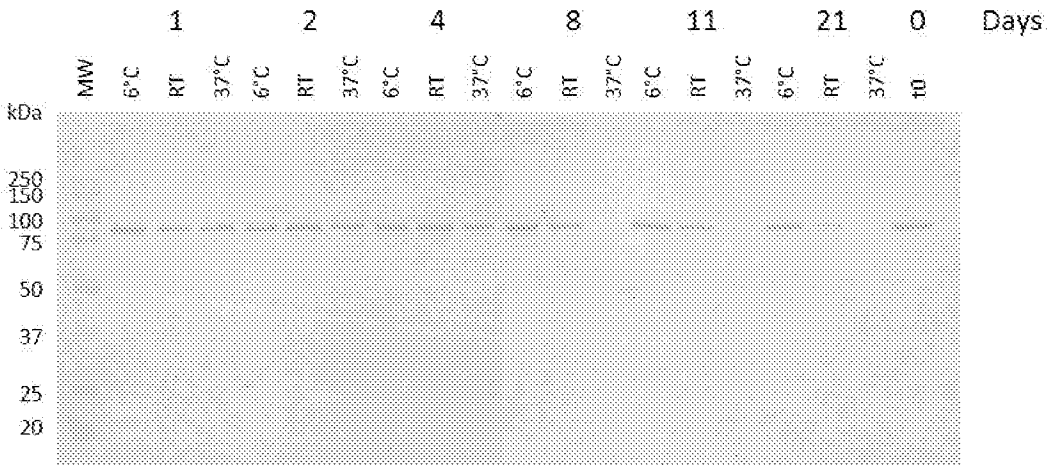


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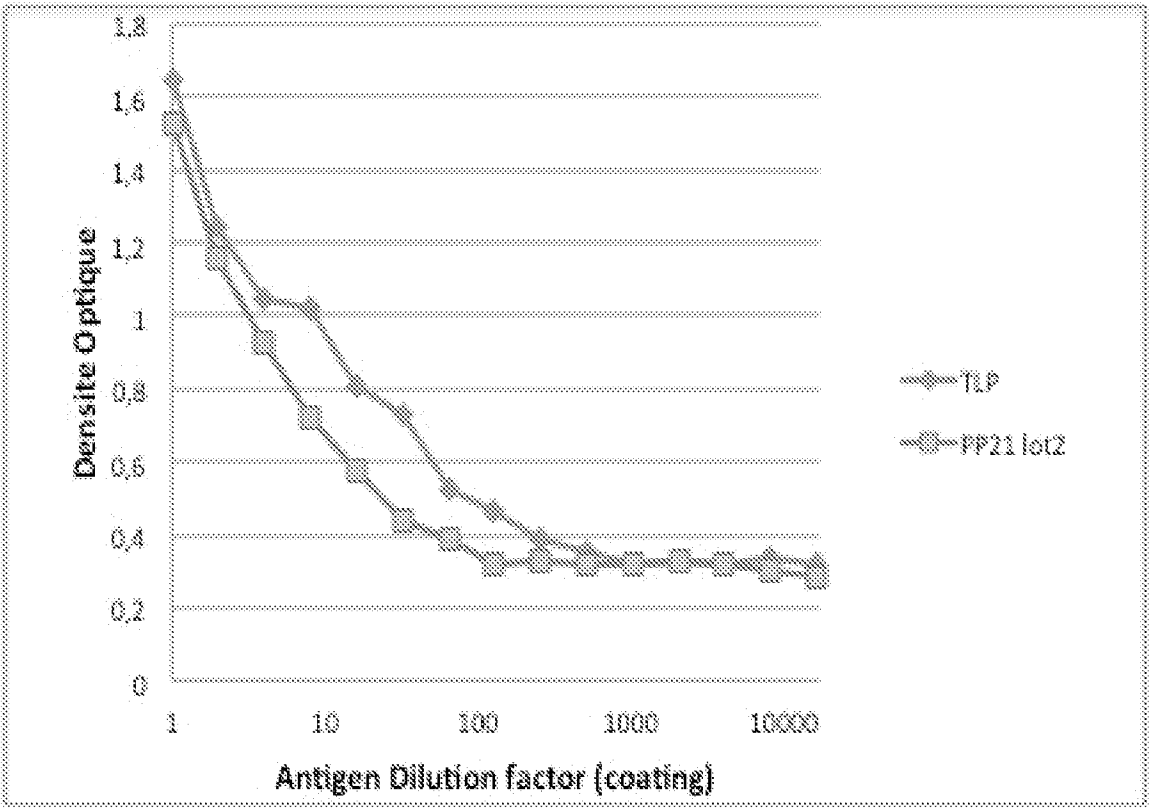


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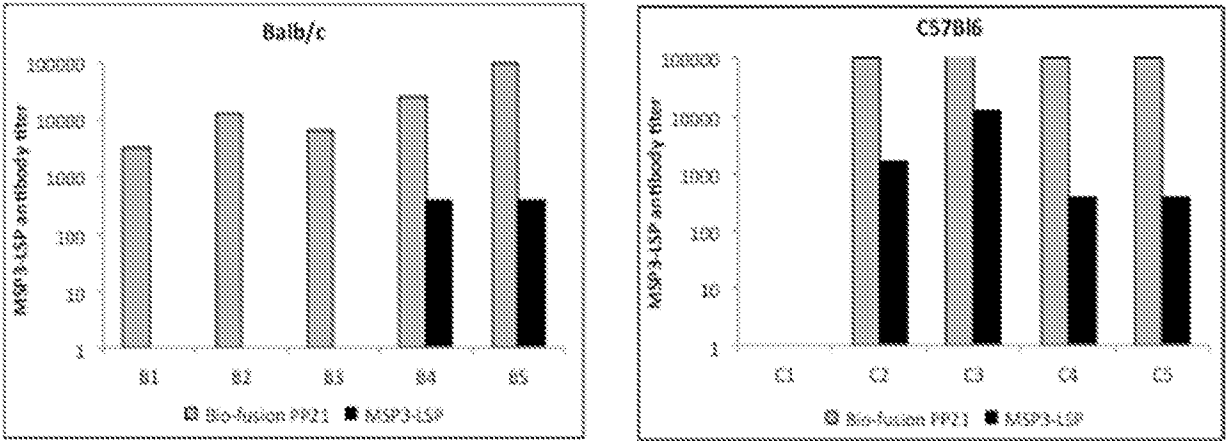


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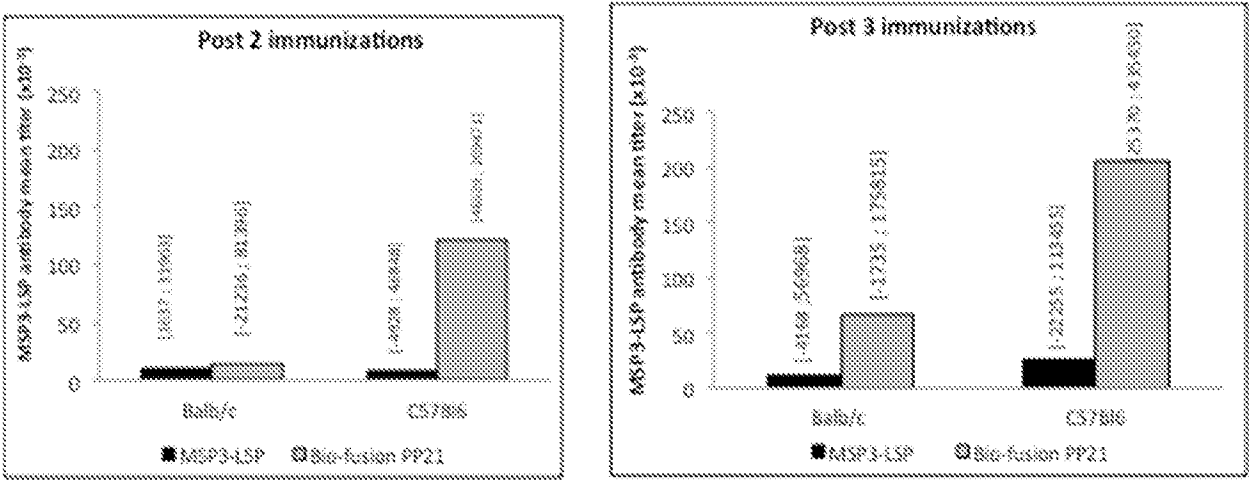


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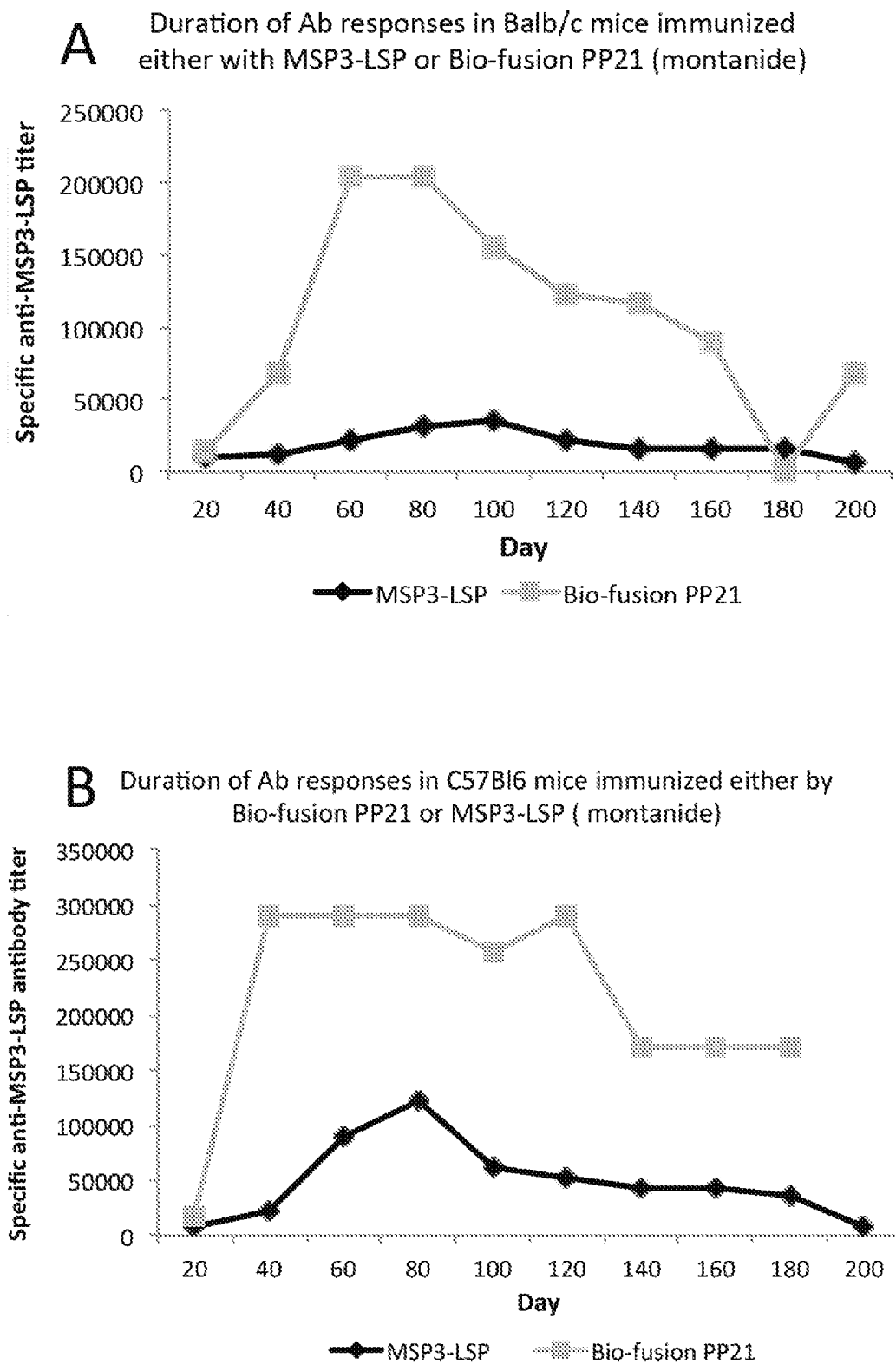


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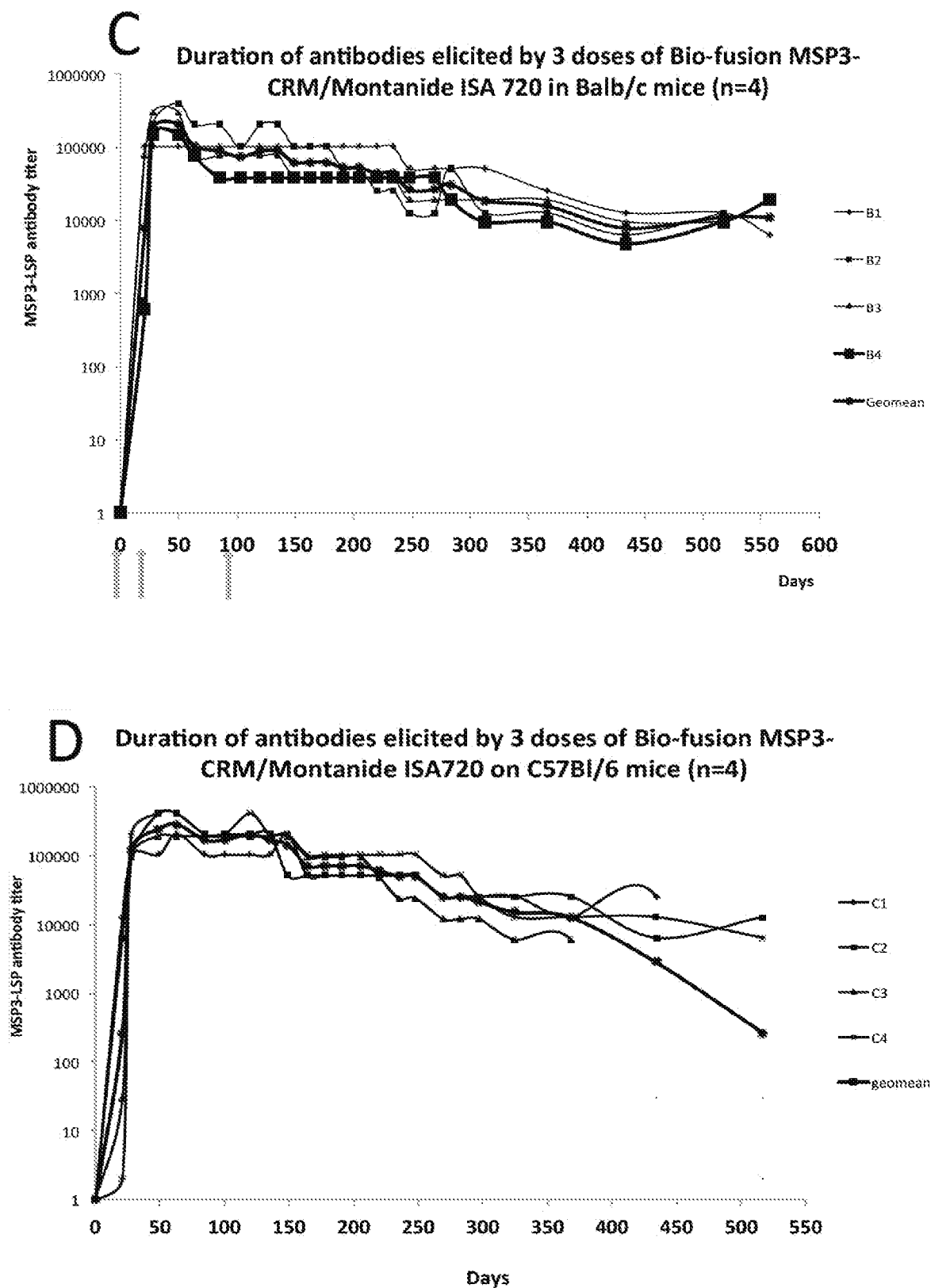


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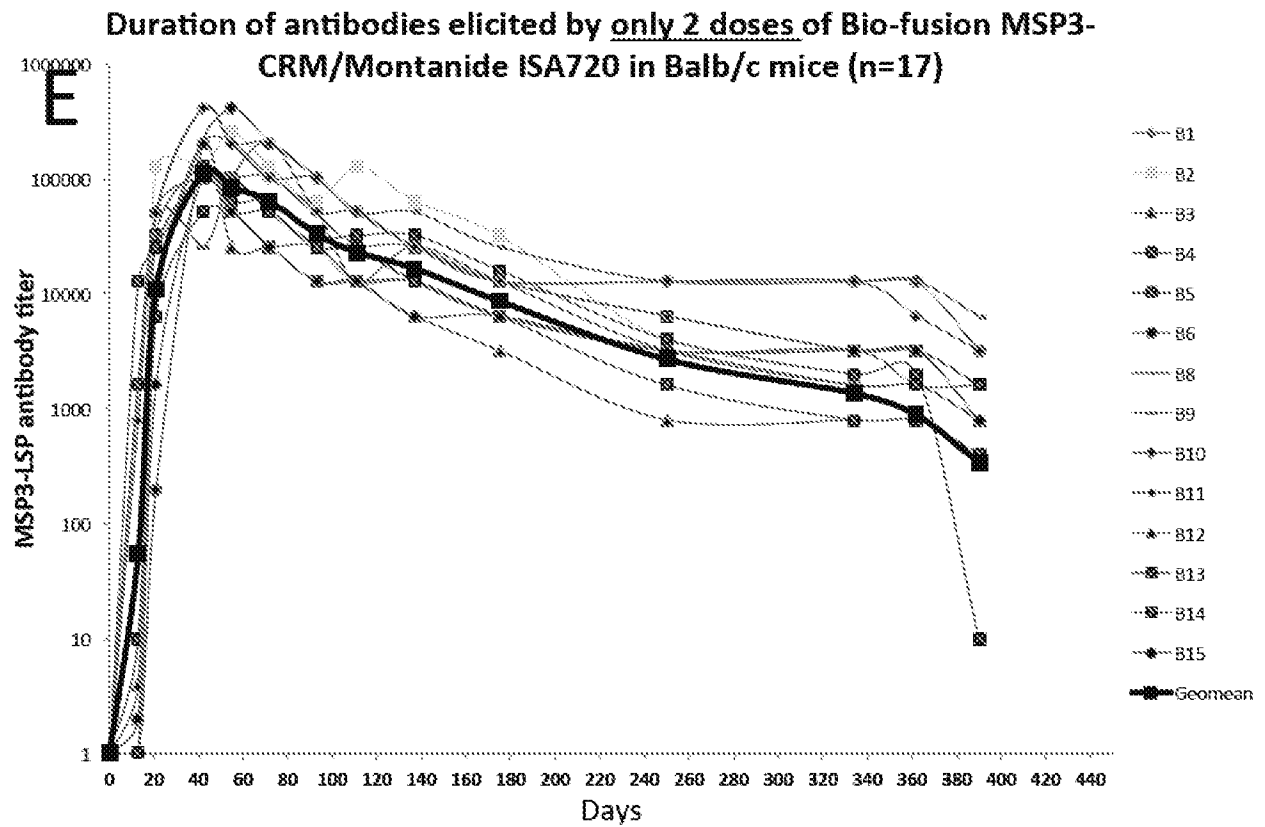


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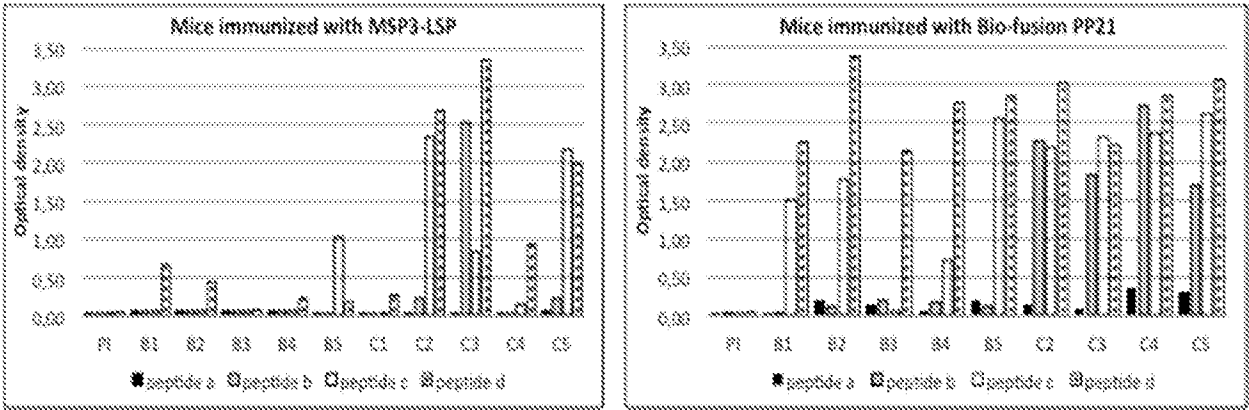


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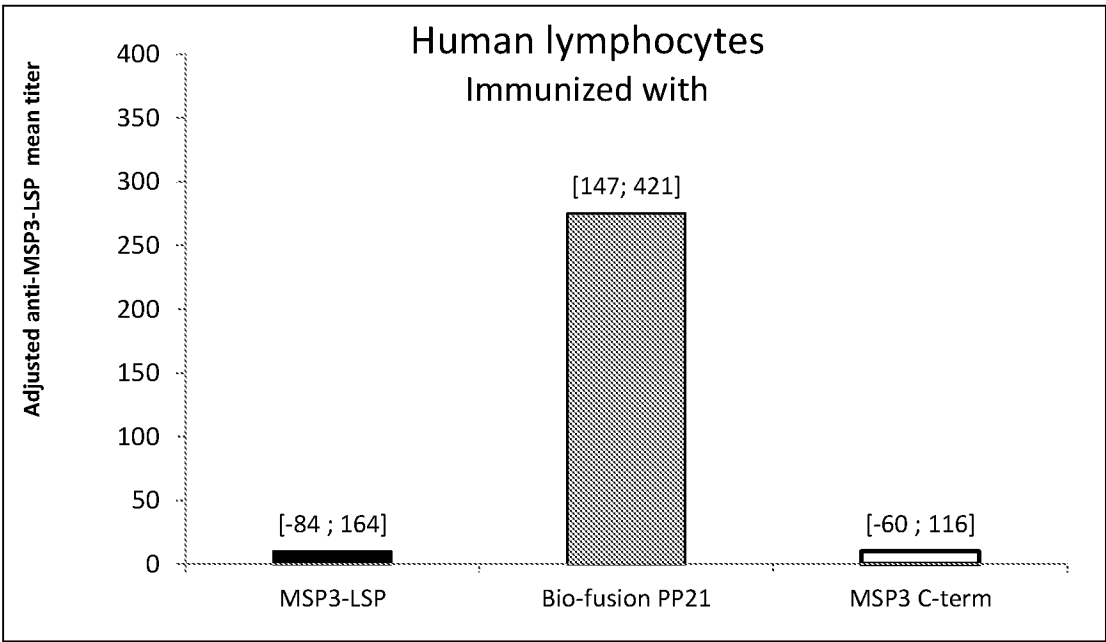


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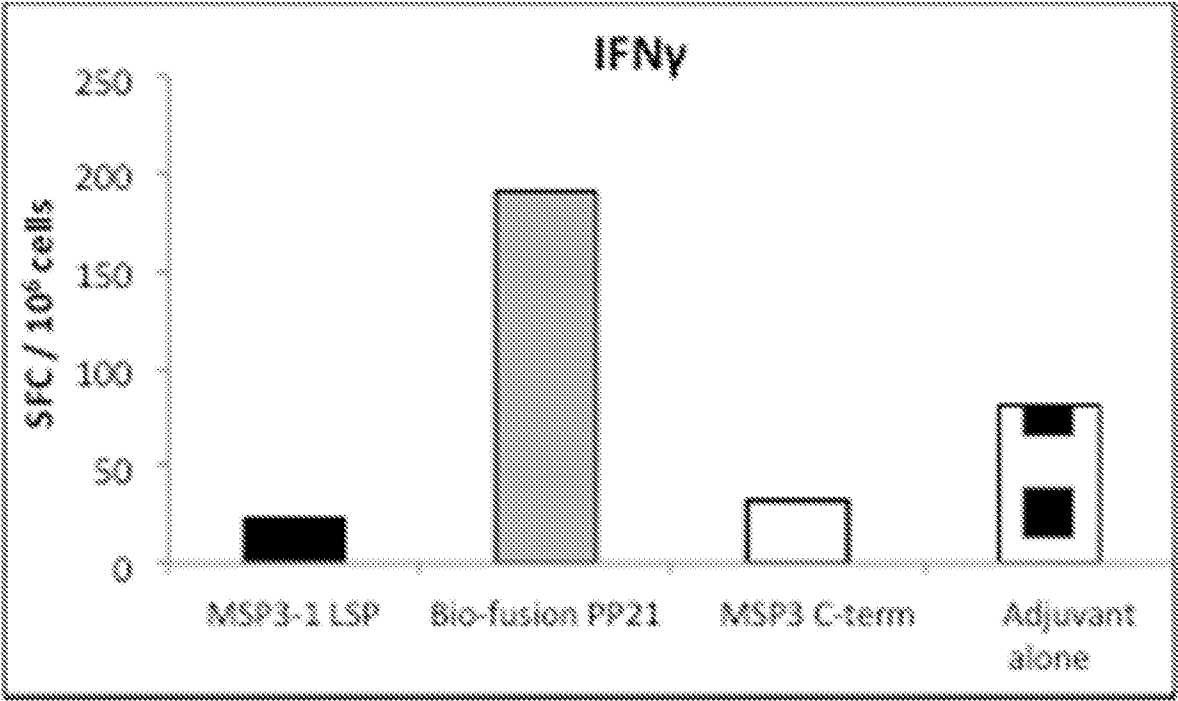


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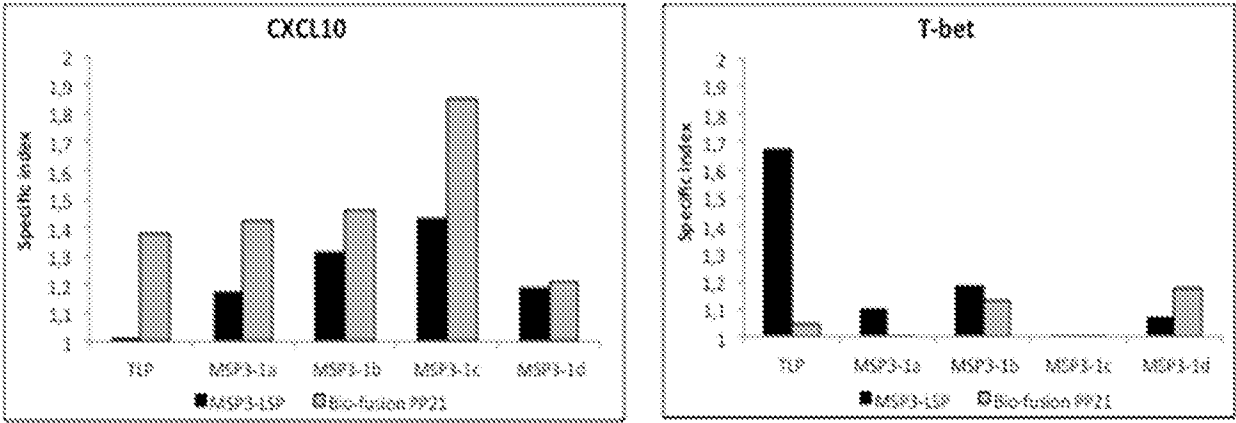


Figure 12

Immunizing antigen	IFAT titers on Pf 3D7 mature schizonts
MSP3-C term	negative
Bio-fusion MSP3-1	160 - 320
MSP3-1 LSP	0 - 20
Adjuvant alone	negative

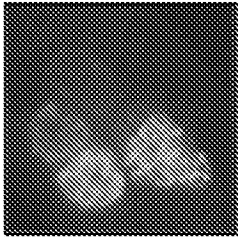


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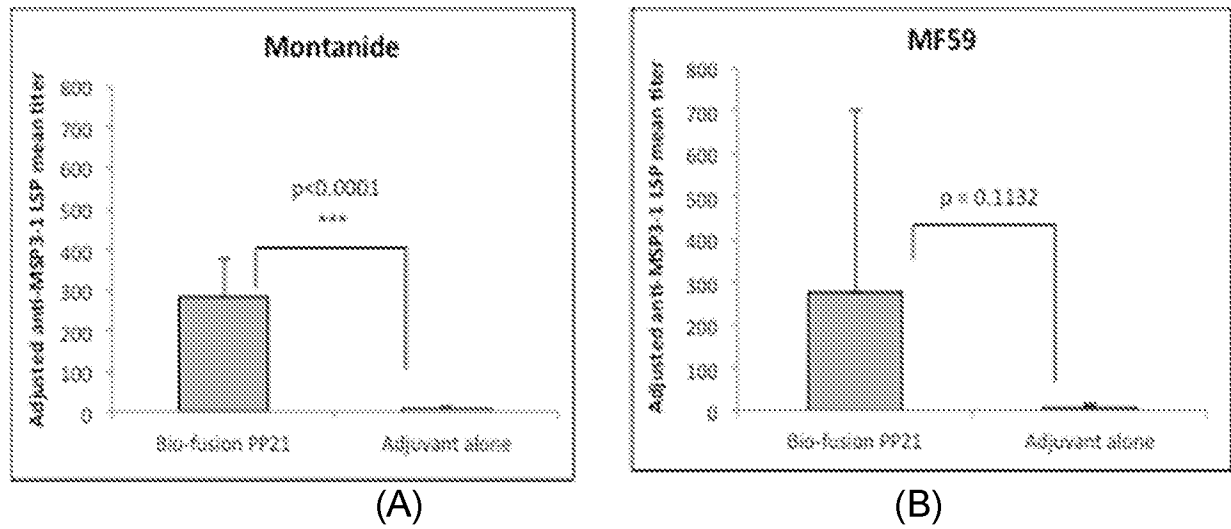


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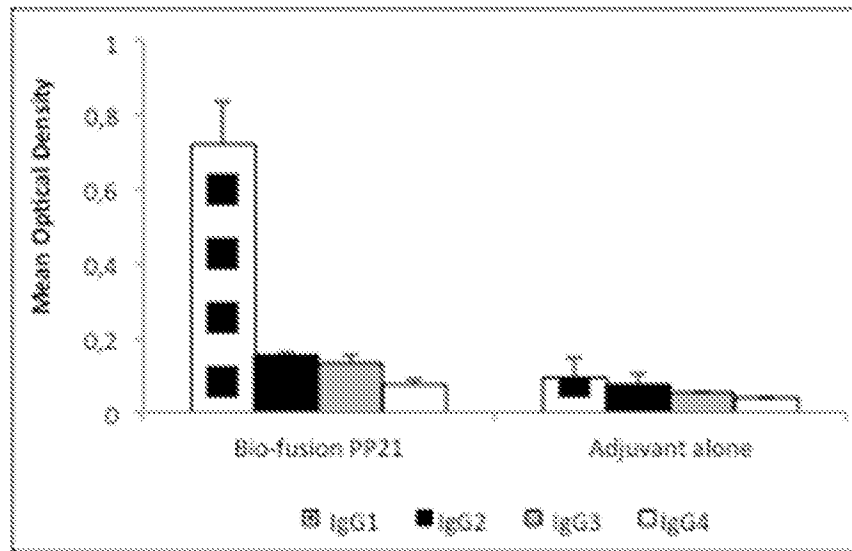


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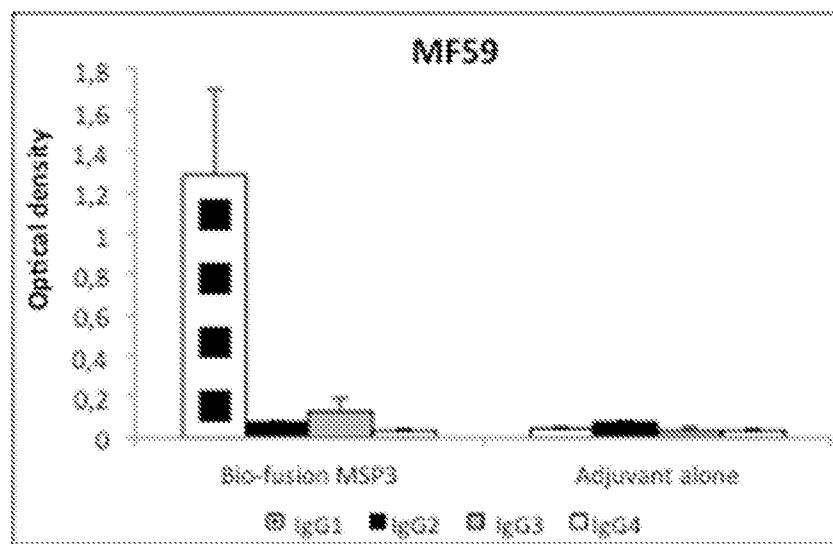


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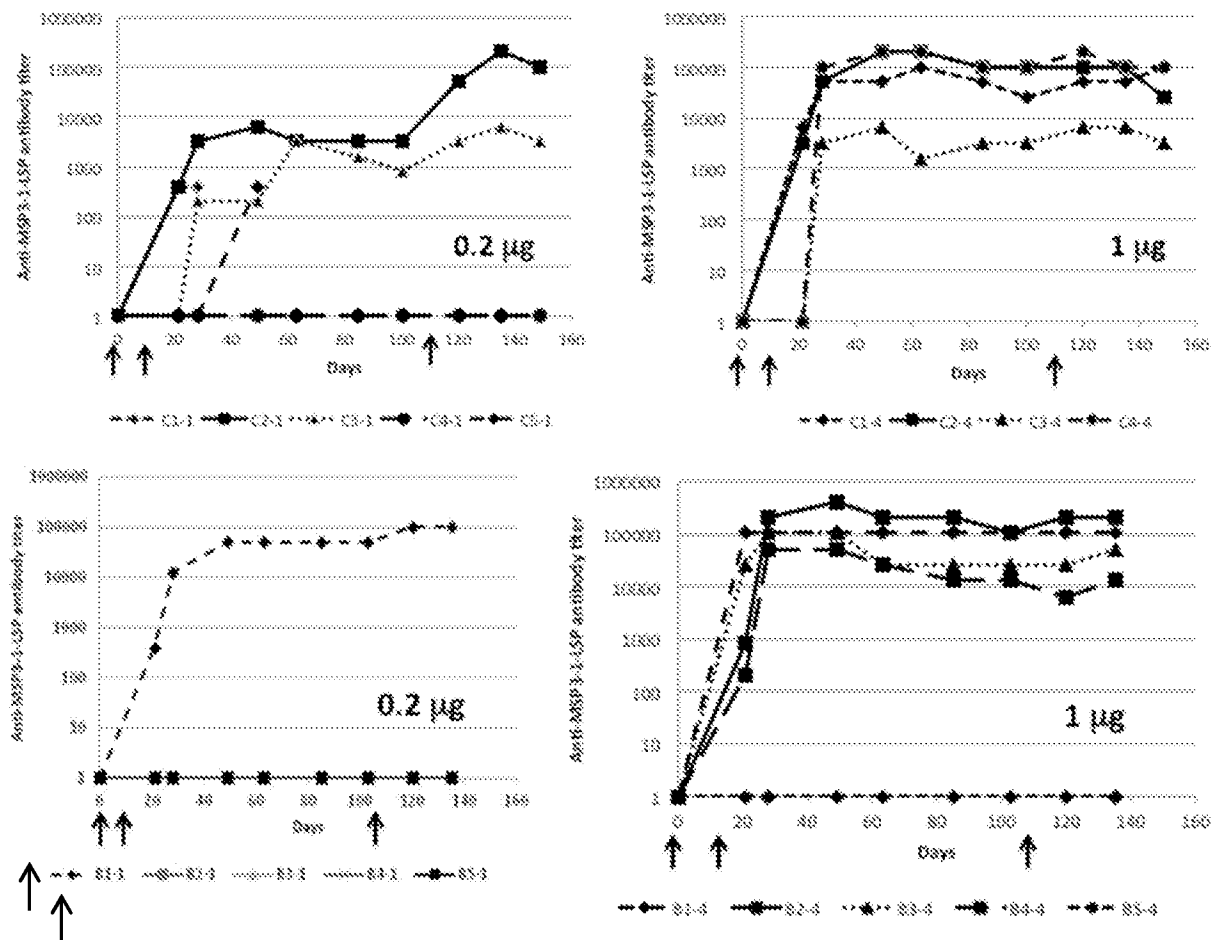


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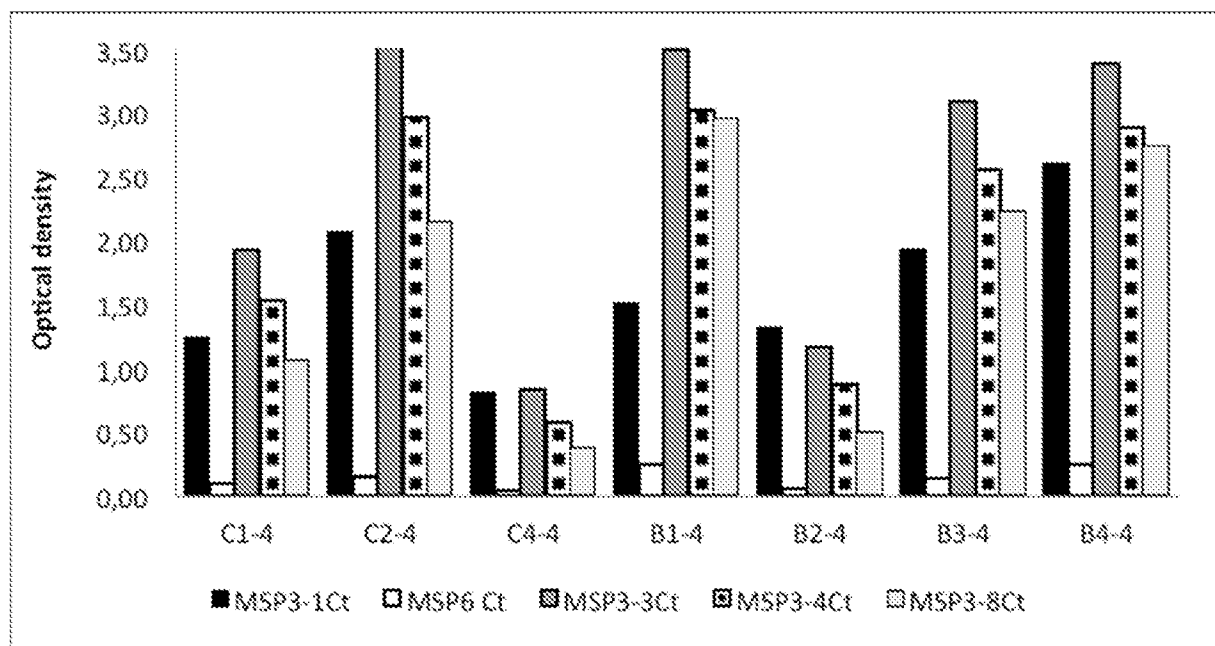


Figure 18

	C1 PP21	C2 PP21	C3 PP21	C4 PP21	B1 PP21	B2 PP21	B3 PP21	B4 PP21	B5 PP21
J21 (post 2 injections)	400	200	0	1600	>> 25600	>>> 25600	>> 25600	>> 25600	>>> 25600
J35 (post 3 injections)	6400	25600	3200	6400	>> 25600	>>> 25600	>>> 25600	>>> 25600	>>> 25600

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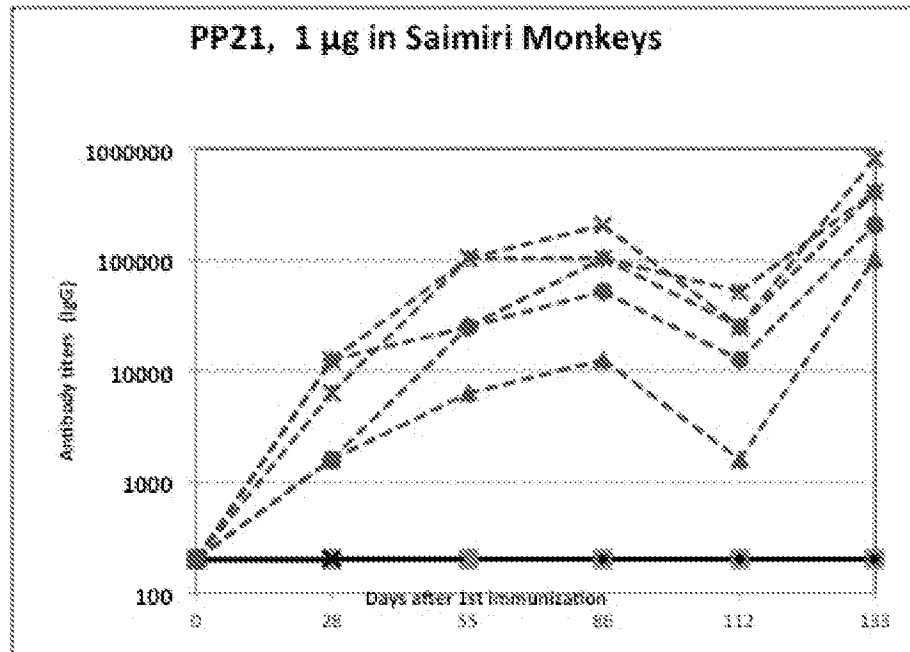


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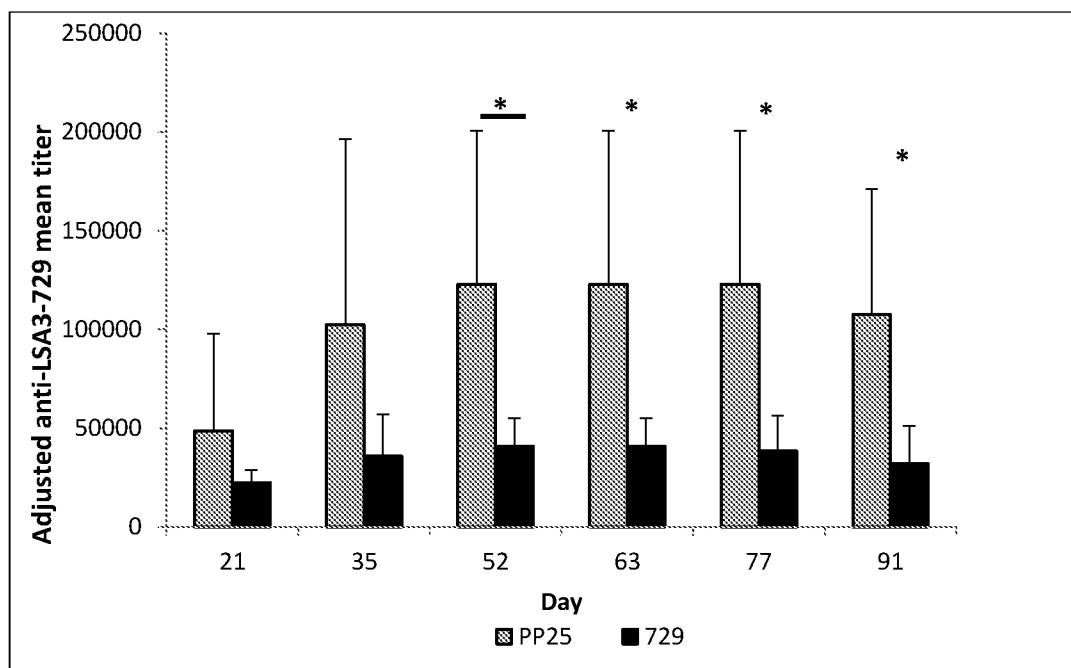


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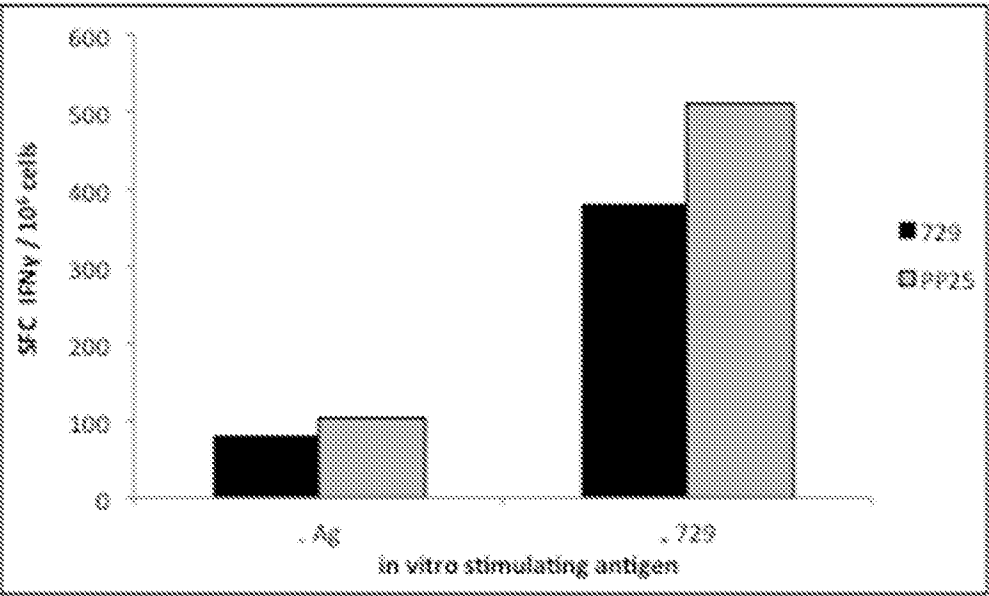


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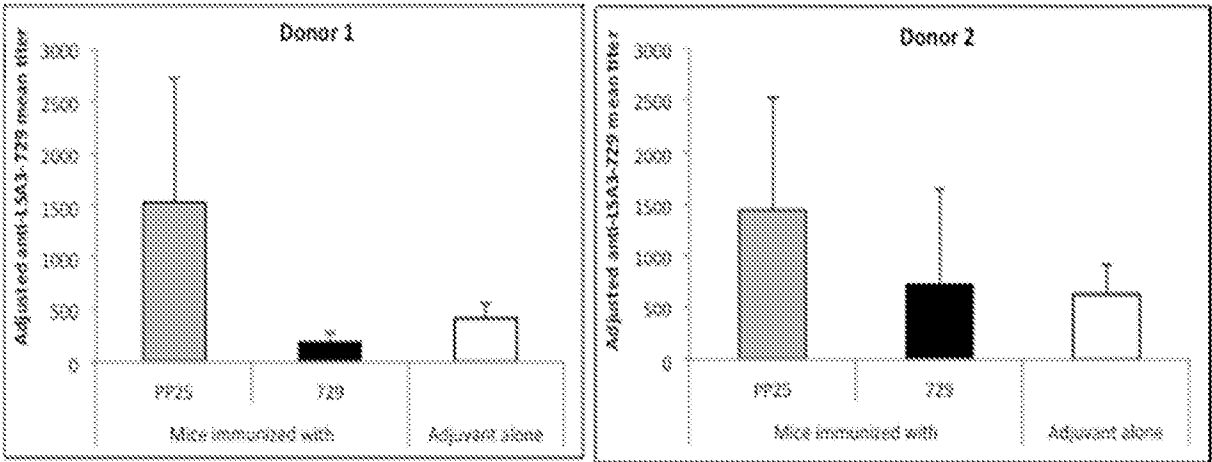


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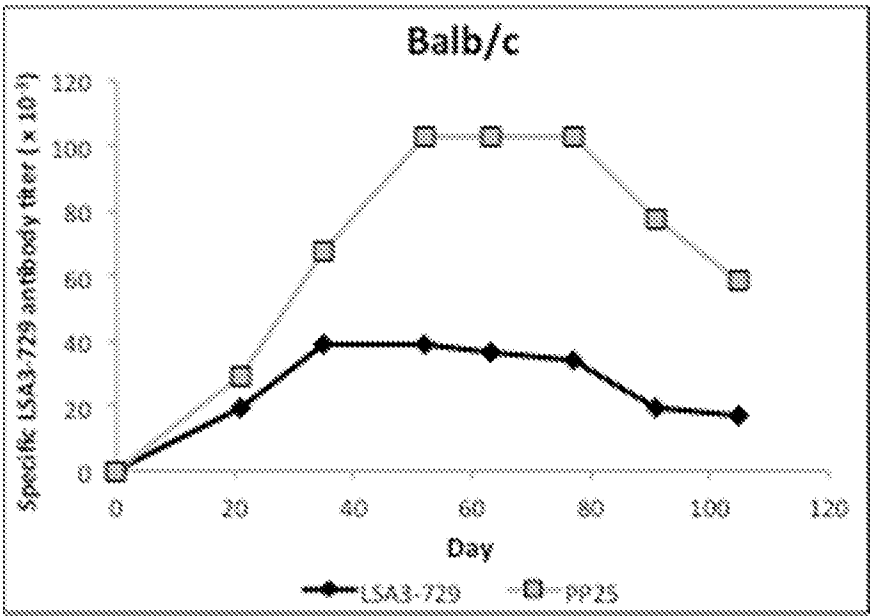


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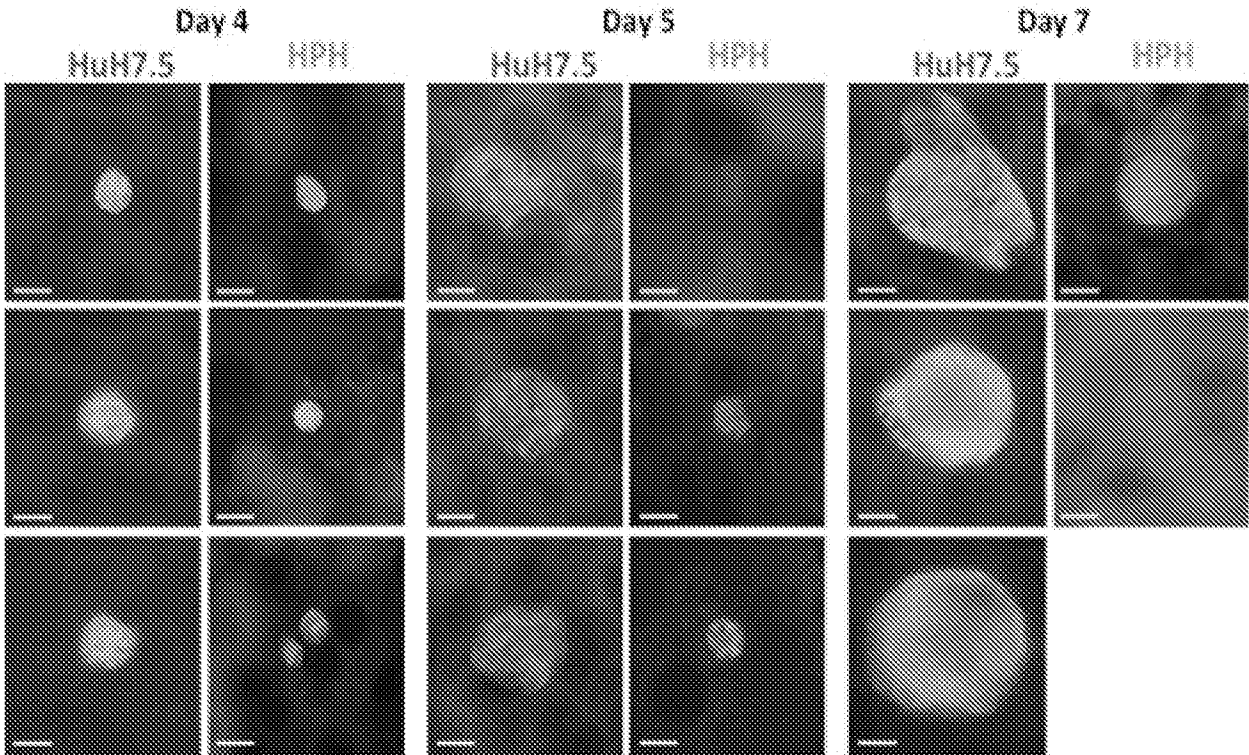


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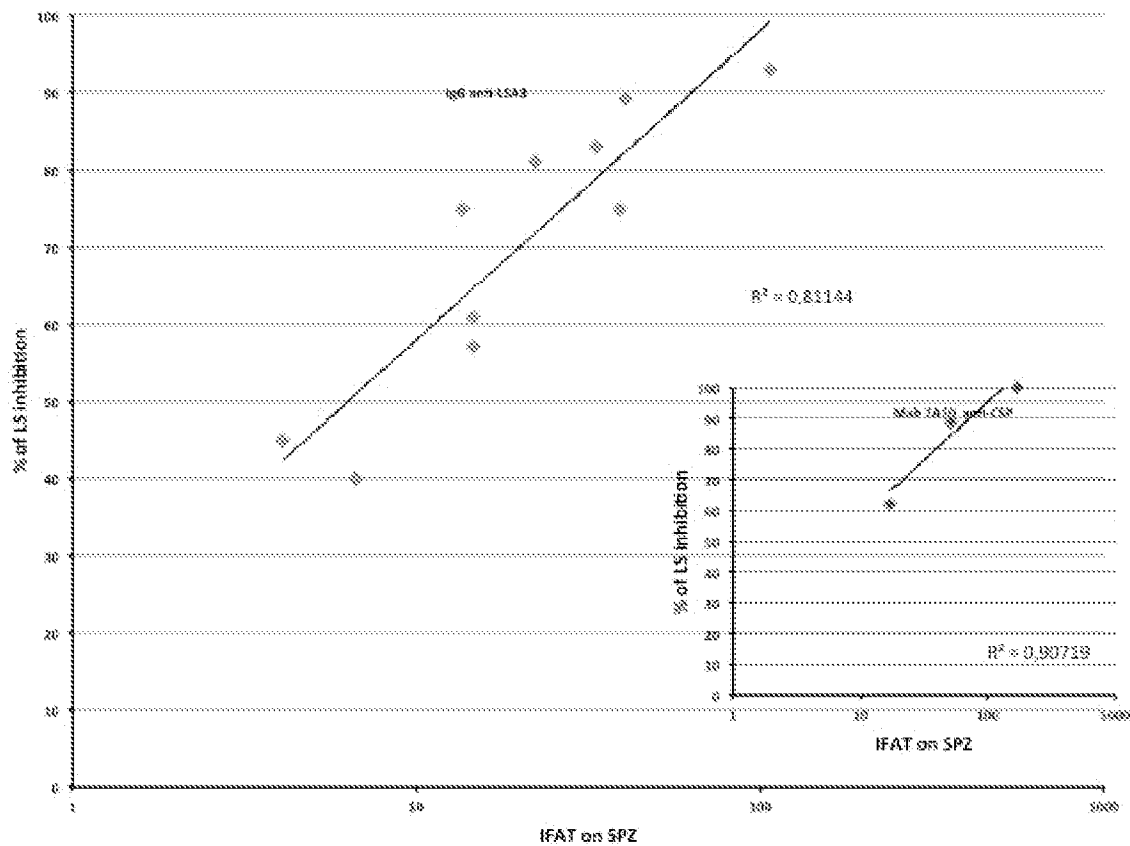


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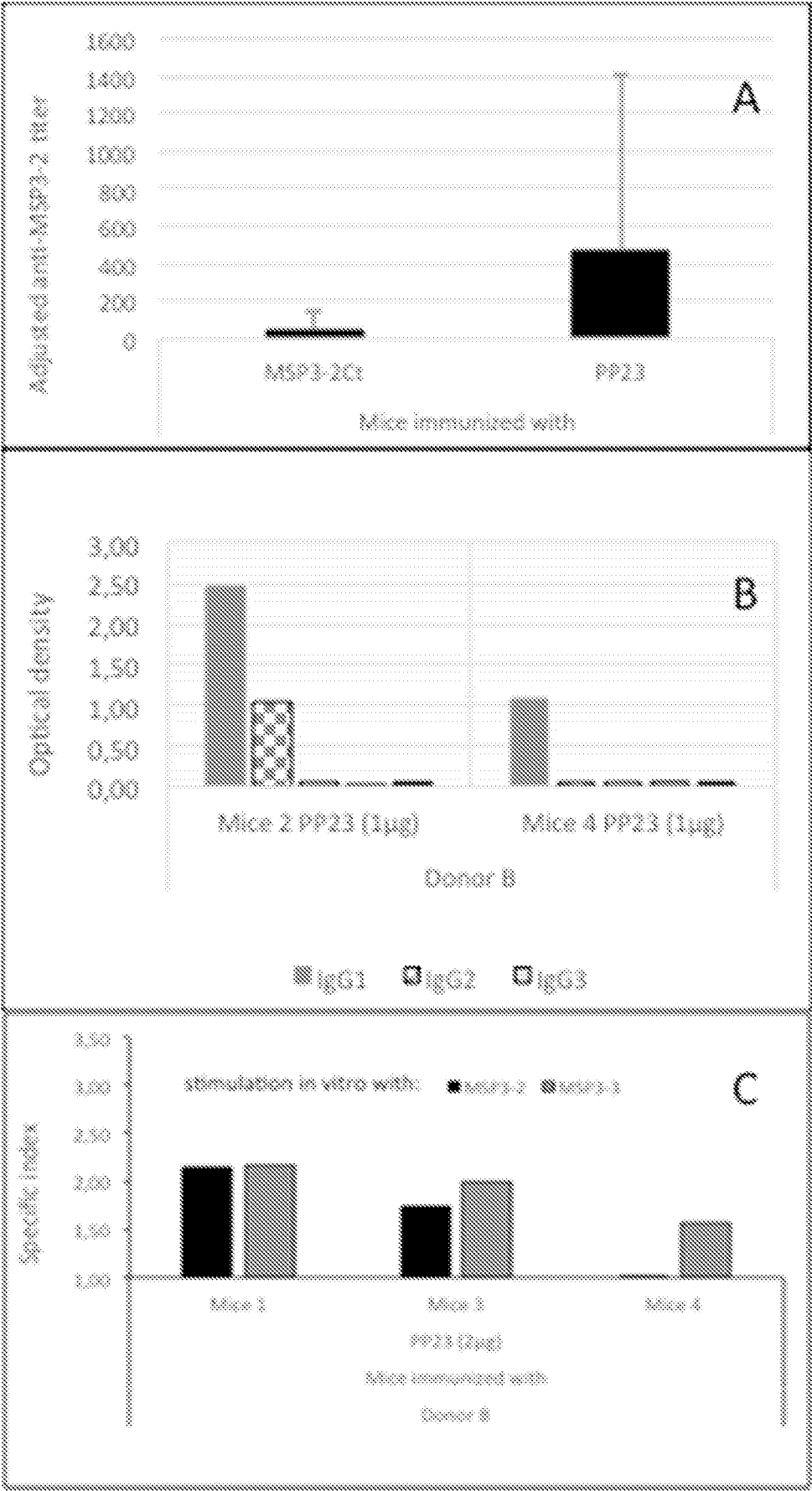


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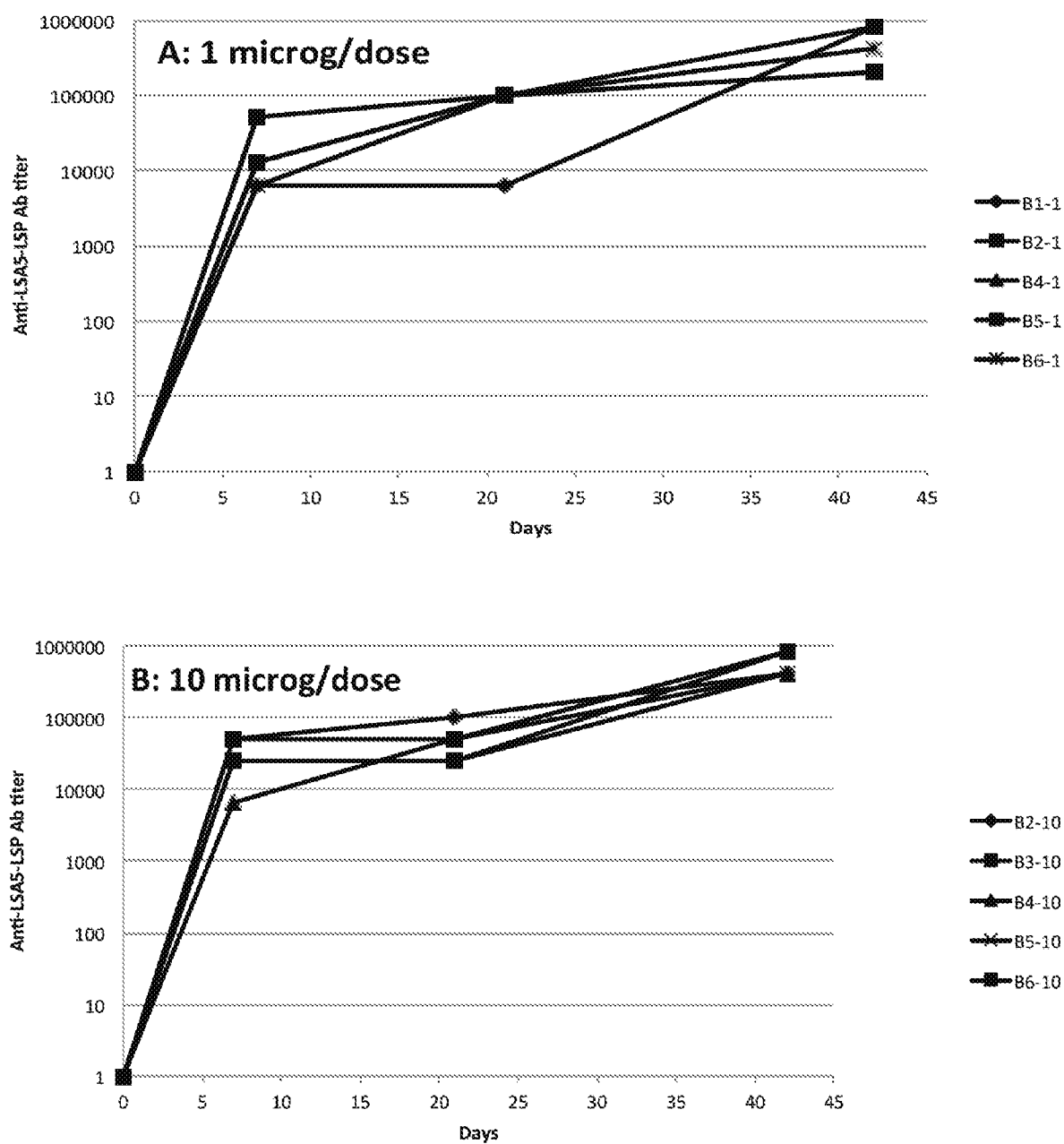


Figure 28

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<210> 13
<211> 34
<212> PRT
<213> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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

FP9025-seql-000001.txt

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> Plasmodium falciparum

<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

FP9025-seq1-000001.txt

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 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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<400> 19

FP9025-seq1-000001.txt

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> Plasmodium falciparum
<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
35 40 45

Asp Asn Asn Glu Glu
50

<210> 21
<211> 42
<212> PRT
<213> Plasmodium falciparum
<400> 21

Glu Glu Glu Lys Lys Glu Glu Lys Lys Glu Glu Lys Lys Pro Asp Asn
1 5 10 15

Glu Ile Thr Asn Glu Val Lys Glu Glu Gln Lys Tyr Ser Ser Pro Ser
20 25 30

Asp Ile Asn Ala Gln Asn Leu Ile Ser Asn
35 40

<210> 22
<211> 52
<212> PRT
<213> Plasmodium falciparum
<400> 22

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

Ala Glu Asn Ile Val Lys Thr Leu Val Gly Leu Phe Asn Glu Lys Asn
20 25 30

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

Phe Ser Asn Asn
50

<210> 23
<211> 424
<212> PRT
<213> Plasmodium falciparum
<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

FP9025-seql-000001.txt

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> Plasmodium falciparum

<400> 24

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

FP9025-seq1-000001.txt

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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<400> 30

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

FP9025-seql-000001.txt

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> Plasmodium falciparum
<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

FP9025-seql-000001.txt

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

FP9025-seql-000001.txt

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> Plasmodium falciparum

<400> 32

FP9025-seq1-000001.txt

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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<400> 38

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

FP9025-seq1-000001.txt

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> Plasmodium falciparum

<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

FP9025-seql-000001.txt

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> Plasmodium falciparum

<400> 40

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

FP9025-seq1-000001.txt

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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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

FP9025-seq1-000001.txt

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> Plasmodium falciparum
<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

FP9025-seql-000001.txt

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

FP9025-seql-000001.txt

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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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> Plasmodium falciparum

<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

FP9025-seql-000001.txt

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 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> Plasmodium falciparum

<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

FP9025-seq1-000001.txt

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 Asp Asp
 325 330 335
 Glu Glu Lys Glu 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
 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

FP9025-seq1-000001.txt

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

FP9025-seq1-000001.txt

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
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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			
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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			
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1355						1360					1365			

Val	Glu	Val	Leu	Glu	Glu	Val	Val	Pro	Val	Glu	Val	Leu	Glu	Glu
1370						1375					1380			
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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			
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1430						1435					1440			
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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	Glu	Ile	Pro	Glu	Glu	Val	Leu
1475						1480					1485			
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1490						1495					1500			
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1505						1510					1515			
Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Val	Leu	Val
1520						1525					1530			
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1535						1540					1545			
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1550						1555					1560			
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1565						1570					1575			
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1580						1585					1590			
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1595						1600					1605			
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1610						1615					1620			

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1625						1630					1635			
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1640						1645					1650			
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1655						1660					1665			
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1670						1675					1680			
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1685						1690					1695			
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1700						1705					1710			
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1715						1720					1725			
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1730						1735					1740			
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1745						1750					1755			
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1760						1765					1770			
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1775						1780					1785			
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1790						1795					1800			
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1805						1810					1815			
Leu	Val	Glu	Lys	Val	Val	Glu	Glu	Glu	Ile	Val	Glu	Glu	Val	Val
1820						1825					1830			
Leu	Ala	Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Gln	Glu	Ile	Val	Glu
1835						1840					1845			
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1850						1855					1860			
Ile	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val
1865						1870					1875			

Pro Glu Glu Leu Val Ala Glu Val Ile Pro Glu Glu Leu Val Ala
 1880 1885 1890

 Glu Val Ile Pro Glu Glu Leu Ile Glu Glu Val Val Thr Glu Glu
 1895 1900 1905

 Leu Val Glu Glu Val Ile Pro Glu Glu Val Val Glu Glu Val Ile
 1910 1915 1920

 Pro Glu Glu Val Val Glu Glu Val Val Pro Glu Glu Leu Val Glu
 1925 1930 1935

 Glu Val Val Pro Glu Glu Leu Val Glu Glu Val Val Pro Glu Glu
 1940 1945 1950

 Ile Val Glu Glu Leu Leu Pro Lys Glu Val Val Glu Glu Val Ile
 1955 1960 1965

 Tyr Glu Glu Gln Val Glu Glu Val Ile Pro Glu Glu Leu Val Ala
 1970 1975 1980

 Glu Val Ile Pro Glu Lys Leu Val Glu Glu Val Ile Pro Glu Glu
 1985 1990 1995

 Leu Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Val
 2000 2005 2010

 Pro Glu Val Val Glu Glu Val Val Pro Glu Glu Leu Val Glu Glu
 2015 2020 2025

 Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile Pro Glu Val Leu
 2030 2035 2040

 Val Glu Glu Glu Val Pro Glu Glu Leu Val Glu Glu Val Ile Pro
 2045 2050 2055

 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
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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			

FP9025-seq1-000001.txt

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 Leu Val Glu Glu Val Ile Pro Glu Glu Val Val Glu Glu Val
 4115 4120 4125
 Val Pro Glu Val Val Glu Glu Val Val Pro Glu Val Val Glu Glu
 4130 4135 4140
 Val Val Pro Glu Val Val Glu Glu Val Val Pro Glu Val Val Glu
 4145 4150 4155
 Glu Val Val Pro Glu Val Val Glu Glu Val Val Pro Glu Val Val
 4160 4165 4170

Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val
4175						4180					4185			
Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu
4190						4195					4200			
Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val
4205						4210					4215			
Ile	Pro	Glu	Glu	Leu	Val	Ala	Glu	Val	Ile	Pro	Glu	Lys	Leu	Val
4220						4225					4230			
Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu
4235						4240					4245			
Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val
4250						4255					4260			
Leu	Pro	Glu	Glu	Val	Val	Glu	Glu	Ala	Val	Pro	Glu	Val	Val	Glu
4265						4270					4275			
Glu	Ile	Val	Pro	Glu	Glu	Leu	Ile	Glu	Glu	Val	Ile	Pro	Glu	Glu
4280						4285					4290			
Leu	Ile	Lys	Glu	Val	Val	Pro	Glu	Glu	Val	Ile	Glu	Glu	Val	Ile
4295						4300					4305			
Thr	Glu	Glu	Val	Val	Glu	Glu	Val	Leu	Pro	Glu	Glu	Ile	Val	Glu
4310						4315					4320			
Glu	Val	Leu	Pro	Glu	Glu	Val	Ile	Glu	Glu	Val	Val	Pro	Glu	Glu
4325						4330					4335			
Leu	Val	Glu	Glu	Val	Leu	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Val
4340						4345					4350			
Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu
4355						4360					4365			
Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Leu	Pro	Glu	Glu
4370						4375					4380			
Val	Val	Glu	Glu	Val	Val	Pro	Lys	Glu	Leu	Val	Glu	Glu	Leu	Ile
4385						4390					4395			
Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu
4400						4405					4410			
Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Ala	Glu	Val	Ile	Pro	Glu	Glu
4415						4420					4425			

Leu Val Glu Glu Val Ile Pro Glu Glu Leu Val Glu Glu Val Ile
 4430 4435 4440
 Pro Glu Glu Leu Val Glu Glu Glu Ile Pro Glu Glu Leu Val Glu
 4445 4450 4455
 Glu Val Ile Leu Glu Glu Leu Val Glu Glu Val Val Pro Glu Glu
 4460 4465 4470
 Leu Ile Glu Glu Val Val Pro Glu Glu Leu Ile Glu Glu Val Val
 4475 4480 4485
 Pro Glu Glu Leu Ile Glu Glu Val Val Glu Lys Val Ile Pro Glu
 4490 4495 4500
 Glu Ile Ile Glu Glu Val Val Pro Glu Glu Val Ile Glu Glu Val
 4505 4510 4515
 Ile Thr Glu Glu Val Val Glu Glu Val Val Pro Glu Lys Val Ile
 4520 4525 4530
 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 Ile 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	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu
8045						8050					8055			
Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Ile	Pro
8060						8065					8070			
Glu	Ile	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu	Val	Glu	Glu
8075						8080					8085			
Val	Ile	Pro	Glu	Glu	Leu	Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Leu
8090						8095					8100			
Val	Glu	Glu	Val	Val	Pro	Glu	Glu	Ile	Val	Glu	Glu	Leu	Leu	Pro
8105						8110					8115			
Lys	Glu	Ile	Val	Glu	Glu	Val	Ile	Tyr	Glu	Glu	Gln	Val	Glu	Glu
8120						8125					8130			
Val	Ile	His	Glu	Glu	Leu	Val	Ala	Glu	Val	Ile	Pro	Glu	Glu	Val
8135						8140					8145			
Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu
8150						8155					8160			
Ile	Val	Ala	Glu	Val	Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Val
8165						8170					8175			
Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val
8180						8185					8190			
Ile	Pro	Glu	Glu	Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Phe	Ile
8195						8200					8205			
Glu	Glu	Met	Ile	Pro	Glu	Glu	Ile	Val	Glu	Glu	Val	Val	Pro	Glu
8210						8215					8220			
Val	Val	Glu	Glu	Val	Ile	Pro	Glu	Glu	Leu	Val	Ala	Glu	Val	Ile
8225						8230					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
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Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Ile	Glu	Glu	Val	Val	Pro
8570						8575					8580			
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8585						8590					8595			
Pro	Glu	Val	Val	Glu	Glu	Val	Val	Pro	Glu	Val	Val	Glu	Glu	Val
8600						8605					8610			
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8615						8620					8625			
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8675						8680					8685			
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8690						8695					8700			
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8705						8710					8715			
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8720						8725					8730			
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8750						8755					8760			

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8975						8980					8985			
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Val	Glu	Glu	Ile	Ile	Pro	Glu	Ile	Leu	Val	Glu	Glu	Val	Val	Pro
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Leu	Glu	Glu	Val	Ile	Pro	Glu	Leu	Leu	Val	Glu	Glu	Ile	Val	Pro
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Ile	Glu	Val	Val	Gly	Glu	Ile	Val	Pro	Glu	Glu	Val	Val	Glu	Lys
9080						9085					9090			
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9095						9100					9105			
Glu	Glu	Val	Pro	His	Glu	Ile	Val	Glu	Glu	Glu	Val	Val	Lys	Glu
9110						9115					9120			
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9125						9130					9135			
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9170						9175					9180			
Leu	Lys	Lys	Asp	Val	Lys	Ala	Lys	His	Leu	Lys	Gly	Ser	Lys	Val
9185						9190					9195			
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Ala	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Val	Gln	Ala	Pro	Lys	Lys	Glu
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9380						9385					9390			
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9425						9430					9435			
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9440						9445					9450			
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9455						9460					9465			
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9470						9475					9480			
Glu	Pro	Lys	Lys	Glu	Lys	Ala	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Val
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Val	Pro	Ala	Pro	Lys	Lys	Glu	Lys	Pro	Ala	Val	Pro	Lys	Lys	Glu
9515						9520					9525			

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Val Lys Glu Ile Val Pro Glu Gln Val Arg Glu Glu Val Thr Leu Glu
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FP9025-seq1-000001.txt

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 Thr Phe Tyr Leu Ala Ala Ala Gly Glu Gly Lys Lys Leu Arg Glu Lys
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 His Asp Glu Ser Cys Asp Glu Phe Cys Asp Ala Trp Asn Arg Ser Leu
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 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
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 Glu Thr Phe Ser Arg Glu Asn Gly Leu Asp Val Cys Lys Ser Gln Cys
 130 135 140
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 Ala Glu Trp Glu Glu Glu Phe Cys Asp Gly Leu Asn Lys His Glu Glu
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 Gln Leu Lys Ser Cys Thr Lys Asp Ile Asn Cys Asp Ile Lys Cys Ser
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 Asn Phe Lys Asp Trp Leu Glu Thr Lys Lys Asp Glu Tyr Asp Ile Gln
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 Ser Arg Val Phe Glu Lys Lys Tyr Ala Asn Asp Asn Lys Ser Lys His
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 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
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 Ala Thr Lys Lys Asn Gly Glu Ser Ile Met Asp Arg Ile Pro Lys Ser
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FP9025-seql-000001.txt

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 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
 385 390 395 400
 Asn Ile Asp Val Asn Gly Ser Lys Asp Glu Tyr Ser Pro Glu Thr Glu
 405 410 415
 Ser Ala Asn Ser Lys Ile Lys Pro Thr Tyr Glu Glu Asn Asp Glu Asp
 420 425 430
 Lys Ser Lys Ile Ser Ile Glu Thr Ser Glu Ile Asp Arg Asp Lys Glu
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 Pro Phe Arg Ile Ser Glu Glu Lys Lys Val Val Lys Glu Asp Val Gln
 450 455 460
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 465 470 475 480
 Asp Glu Asp Ala Lys Arg Asn Ile Asp Asp Ile Arg Lys Asp Ile Gln
 485 490 495
 Ser Gln Ile Met Lys Ser Val Glu Asn Tyr Asn Ser Glu Lys Glu Glu
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 515 520 525
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 Pro Thr Met Val Leu Val Pro Gly Val Leu Thr Val Phe Leu Leu Thr
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 Ile Ile Trp Val Leu Val Tyr Lys His Ser Leu Ile Asp Arg Val His
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Gly Thr Gly Lys Thr Lys Lys Glu Glu Lys Met Lys Glu Leu Glu Ser
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 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
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 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
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 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
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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

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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
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Gln Glu Ile Val Gln Asp Gly Ser Val Thr Lys Asp Val Glu Tyr Lys
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Glu Glu Asp Pro Phe Lys Gly Gln Leu Ile Asn Glu Gly Leu Pro
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Asn Glu Glu Val Glu Glu Glu Val Ser Val Ser Gly Glu Val Asp
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FP9025-seql-000001.txt

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Val Lys 1145	Glu Glu Gly Ser	Ala 1150	Ser Glu Lys Ile Val 1155	Glu Glu Glu
Gly Ser 1160	Val Thr Glu Glu	Thr 1165	Ala Ser Glu Glu Ile 1170	Val Glu Glu
Glu Gly 1175	Ser Val Thr Glu	Glu 1180	Ser Ser Ser Glu Glu 1185	Ile Val Glu
Asp Glu 1190	Gly Ser Val Thr	Glu 1195	Glu Ser Ser Ser Glu 1200	Glu Ile Val
Glu Glu 1205	Glu Gly Ser Val	Ile 1210	Glu Glu Ser Ala Ser 1215	Glu Val Ile
Val Glu 1220	Asp Glu Val Ser	Ala 1225	Ser Lys Glu Ile Val 1230	Glu Asp Glu
Ala Ser 1235	Val Thr Glu Glu	Val 1240	Val Glu Glu Glu Gly 1245	Ala Val Ser
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Thr Asp 1280	Glu Ile Val Lys	Glu 1285	Asp Glu Ser Val Ile 1290	Glu Glu Ile
Ala Val 1295	Glu Glu Thr Val	Thr 1300	Glu Val Val Glu Glu 1305	Thr Lys Pro
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Glu Glu 1325	Lys Lys Thr Met	Asp 1330	Glu Glu Ile Val Asp 1335	Gln Gly Ser
Val Val 1340	Glu Asn Val Glu	Glu 1345	Lys Lys Thr Met Asp 1350	Glu Glu Ile
Gly Asp 1355	Gln Gly Ser Val	Ala 1360	Glu Lys Val Glu Glu 1365	Glu Glu Leu

FP9025-seq1-000001.txt

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	1490					1495					1500			
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	1505					1510					1515			
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	1535					1540					1545			
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	1565					1570					1575			
Lys	Gln	Gln	Gly	Leu	Ala	Thr	Tyr	Glu	Phe	Val	Glu	Glu	Glu	Lys
	1580					1585					1590			
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FP9025-seq1-000001.txt

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	1820					1825					1830			
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	1835					1840					1845			
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Glu	Ile	Val	Glu	Glu	Glu	Glu	Ser	Ser	Ser	Glu	Glu	Ile	Ile	Glu
2000						2005					2010			
Glu	Val	Ser	Ser	Thr	Glu	Glu	Val	Leu	Glu	Glu	Glu	Gly	Ser	Val
2015						2020					2025			
Thr	Glu	Glu	Ile	Val	Glu	Glu	Glu	Val	Ser	Thr	Thr	Glu	Glu	Val
2030						2035					2040			
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			

FP9025-seql-000001.txt

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			

FP9025-seq1-000001.txt

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			

FP9025-seq1-000001.txt

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			

FP9025-seq1-000001.txt

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

FP9025-seq1-000001.txt

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	Val	Thr	Gly	Asp	Ile	Leu	Val	Glu
	3710					3715					3720			
Gly	Ser	Val	Thr	Glu	Glu	Val	Val	Gly	Glu	Glu	Lys	Leu	Val	Ser
	3725					3730					3735			
Glu	Glu	Ile	Val	Thr	Glu	Glu	Gly	Ser	Val	Ala	Gln	Glu	Ile	Val
	3740					3745					3750			
Glu	Glu	Asp	Ala	Pro	Ala	Thr	Glu	Glu	Ile	Asp	Glu	Ile	Glu	Ser
	3755					3760					3765			
Val	Thr	Glu	Glu	Val	Val	Glu	Glu	Glu	Gly	Pro	Val	Asp	Glu	Glu
	3770					3775					3780			
Ile	Val	Gln	Glu	Glu	Gly	Ser	Val	Thr	Glu	Glu	Ile	Ile	Gln	Gly
	3785					3790					3795			
Glu	Ser	Lys	Val	Glu	Glu	Val	Val	Glu	Glu	Gln	Gly	Ser	Glu	Asn
	3800					3805					3810			
Glu	Glu	Ile	Phe	Val	Glu	Glu	Val	Ser	Ala	Ser	Gln	Glu	Ile	Val
	3815					3820					3825			
Gln	Asn	Glu	Ser	Gly	Thr	Glu	Glu	Ile	Leu	Glu	Lys	Val	Ser	Ala
	3830					3835					3840			
Ser	Gln	Glu	Ile	Val	Gln	Asp	Gly	Ser	Val	Thr	Glu	Gln	Ile	Ile
	3845					3850					3855			
Glu	Glu	Gln	Lys	Pro	Val	Thr	Glu	Glu	Val	Val	Asn	Glu	Glu	Glu
	3860					3865					3870			
Ser	Ile	Thr	His	Glu	Ile	Ile	Gln	Glu	Glu	Ser	His	Val	Glu	Lys
	3875					3880					3885			
Val	Val	Gln	Gln	Gly	Ser	Val	Ala	Glu	Glu	Val	Val	Glu	Asn	Pro
	3890					3895					3900			
Val	Ser	Val	Thr	Glu	Glu	Ile	Val	Glu	Lys	Glu	Gly	Ser	Val	Thr
	3905					3910					3915			

FP9025-seql-000001.txt

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			

FP9025-seql-000001.txt

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			

FP9025-seql-000001.txt

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

FP9025-seql-000001.txt

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	Glu	Val	Arg	Ser	Asp	Glu	Asn	Ile	His	Ile	Phe	Arg	Lys
5360						5365					5370			
Lys	Asn	Glu	Asn	Phe	Val	Lys	Lys	Ile	Glu	Asn	Glu	Lys	Ser	Ser
5375						5380					5385			
Val	Gly	His	Val	Pro	Thr	Glu	Tyr	Thr	Ser	Lys	Glu	Asn	Ile	Ala
5390						5395					5400			
Glu	Glu	Val	Pro	Ser	His	Ile	Met	Phe	Lys	Glu	Asn	Val	Thr	Glu
5405						5410					5415			
Glu	Val	Pro	Lys	Glu	Val	Lys	Tyr	Glu	Glu	Asn	Thr	Val	Glu	Glu
5420						5425					5430			
Val	Phe	Glu	Glu	Val	Thr	Ser	Lys	Glu	Asn	Ile	Ile	Glu	Glu	Ala
5435						5440					5445			

FP9025-seq1-000001.txt

Pro	Gly	Asp	Ile	Asn	Ser	Glu	Glu	Asn	Ile	Ile	Glu	Glu	Val	Pro
	5450					5455					5460			
Glu	Val	Val	Thr	Ser	Glu	Glu	Ile	Val	Val	Gln	Asn	Asp	Val	Asn
	5465					5470					5475			
Asn	Ile	Asn	Thr	Asn	Ile	Asp	His	Met	Phe	Asp	Phe	Asp	Leu	Asp
	5480					5485					5490			
Asp	Ile	Leu	Lys	Ile	Pro	Glu	Ala	Gln	Arg	Lys	Leu	Asn	Lys	Leu
	5495					5500					5505			
Arg	Thr	Leu	Val	Asp	Val	His	Leu	Asp	Val	Ile	Glu	Lys	Met	Gln
	5510					5515					5520			
Arg	Asp	Glu	Trp	Lys	Lys	Asn	Lys	Arg	Asp	Phe	Leu	Tyr	Ile	Cys
	5525					5530					5535			
Leu	Lys	Glu	Ile	Asn	Lys	Leu	Ser	Glu	Asp	Thr	Leu	Met	Lys	Phe
	5540					5545					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			

FP9025-seq1-000001.txt

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			

FP9025-seq1-000001.txt

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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 <211> 994
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 <400> 59
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 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 Ser Ser Asp Thr Lys Glu Trp Ser Pro Asn Asn Leu Thr Ser Lys
 65 70 75 80
 Lys Lys Lys Lys Lys Lys Glu Ile Arg Pro Lys Asp Ile Met Ser Asn
 85 90 95

FP9025-seq1-000001.txt

Ser Asp Ser Ser Asn Thr Ser Ser Ile Asn Lys Gln Asn Asn Asn Gln
100 105 110

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

Pro Cys Asn Val Asn Leu Ser Ile Phe Leu Val Pro His Ile Tyr Ile
130 135 140

Asp Val Glu Thr Lys Tyr Asn Asn Ile Glu Leu Lys Tyr Glu Leu Asp
145 150 155 160

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

Thr Ser Asp Asp Thr Leu Met Asn Thr Asn Phe Asn Val Gly Val Ser
180 185 190

Arg Asp Thr Leu Asp Lys Asp Arg Leu Tyr Asn Ile Cys Ala Glu Asn
195 200 205

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

Lys Trp Lys Val Tyr Glu Thr Gly Val Thr Asn Asn Lys Val Asp Ile
225 230 235 240

Arg Gln Tyr Lys Met Lys Glu Leu Thr Arg Pro Ile Thr Thr Ile Gln
245 250 255

Ile His Ser Val Ser Glu Asn Lys Asp Thr His Leu Leu Glu Ser Lys
260 265 270

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
305 310 315 320

Tyr Val Ser Asn Asp Val Arg Glu Asn Phe Asn Gln Ile Lys Ala Glu
325 330 335

Ala Glu Asp Asp Glu Asn Phe Arg Asn Tyr His Leu Thr Asp Thr Ile
340 345 350

Asn Asn Ile Leu Lys Arg Ile Tyr Lys Ile Asn Lys Asn Glu Gly Lys
355 360 365

FP9025-seql-000001.txt

Lys Glu Leu Ile Thr Leu Glu Glu Leu Asp Asn Phe Leu Lys Glu Ser
 370 375 380
 Ile Thr Asp Tyr Cys Lys Ile Leu Arg Glu Ile Asp Thr Asn Gly Thr
 385 390 395 400
 Leu Val Asn His Glu Leu Gly Asn Asn Val Asp Val Phe Asn Asn Leu
 405 410 415
 Ile Arg Leu Leu Lys Leu His Lys Asn Glu Ser Ile Ser Thr Leu His
 420 425 430
 Asn Lys Leu Arg Asn Ser Ala Ile Cys Met Lys Tyr Pro Asp Lys Trp
 435 440 445
 Ile Glu Lys Lys Thr Gly Leu Ile Leu Pro Asn Val Val Asn Asn Asn
 450 455 460
 Ile Ile Tyr Asn Asn Lys Tyr Glu Lys Leu Asn Glu Glu Lys Lys Arg
 465 470 475 480
 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

FP9025-seq1-000001.txt

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

FP9025-seql-000001.txt

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

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<211> 1105
<212> PRT
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<400> 60

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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

FP9025-seq1-000001.txt

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
 385 390 395 400
 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
 465 470 475 480
 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
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 Lys Val Gly Asp Val Cys Pro Gln Val Gln Asn Asp Trp Asp Asn Val
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FP9025-seq1-000001.txt

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Gly	Thr	Lys	Gly	Tyr	Ile	Ala	Tyr	Glu	Ser	Glu	Val	Phe	Gln	Lys	Asp
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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	Lys	Ser	Tyr	Trp	Ile	Val	Arg	Asn	Ser	Trp	Gly	Lys	Tyr	Trp	Gly
785					790					795					800
Asp	Asp	Gly	Tyr	Phe	Lys	Val	Asp	Met	Tyr	Gly	Pro	Pro	Thr	Cys	Glu
				805					810					815	
Asp	Asn	Phe	Ile	His	Ser	Val	Val	Val	Phe	Asn	Val	Glu	Val	Pro	Val
			820					825					830		
Asn	Glu	Asn	Phe	Asp	Lys	Lys	Glu	His	Asp	Ile	Tyr	Lys	Ser	Tyr	Leu
		835					840					845			
Lys	Asn	Ser	Pro	Asp	Phe	Tyr	His	Asn	Ile	Tyr	Tyr	Lys	Asn	Tyr	Asn
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Phe	Glu	Asn	Tyr	Val	Ser	Pro	Ile	Ser	Thr	Trp	Ser	Glu	Val	Leu	His
865					870					875					880
Asn	Thr	Leu	Tyr	Asn	Asn	Asn	Leu	Ile	Trp	Gly	Gln	Glu	Thr	Thr	Asp
				885					890					895	
Pro	Ile	Gly	Glu	Gly	Lys	Leu	Pro	Ala	Ser	Glu	Ala	Gly	His	Leu	Arg
			900					905					910		
Gly	Glu	Gly	Lys	Gly	Asn	Ser	Glu	Glu	Asn	Gln	Gly	Gln	Arg	Ser	Asn
		915					920					925			
Ala	Asn	Gly	Ala	Ile	Ser	Ser	Asn	Gln	Ser	Thr	Gly	Gly	Lys	Ile	Thr
	930					935					940				
Lys	Gln	Gly	Glu	Ser	Lys	Asp	Asp	Gly	Val	Ala	Leu	Pro	Val	Ser	Thr
945					950					955					960

Asp Gly Lys Pro Asn Thr Ser Ser Ser Val Val Asp Thr Asn Asp Gln
965 970 975

Arg Ser Leu Pro Asn Pro Arg Ala Thr Ser Leu Gln Pro Pro Ser Val
980 985 990

Gln Ile Pro Asn His Glu Gly Thr Ser Ala Pro Gly Asn Ser Arg Thr
995 1000 1005

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> Plasmodium falciparum

<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
Page 106

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
Page 108

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> Plasmodium falciparum

<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

FP9025-seq1-000001.txt

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
545 550 555 560

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

FP9025-seql-000001.txt

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
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> Plasmodium falciparum

<400> 63

Met Lys Ser Tyr Ile Ser Leu Phe Phe Ile Leu Cys Val Ile Phe Asn
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FP9025-seql-000001.txt

Lys Asn Val Ile Lys Cys Thr Gly Glu Ser Gln Thr Gly Asn Thr Gly
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 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

FP9025-seq1-000001.txt

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
 545 550 555 560

FP9025-seql-000001.txt

Asn Ser Asp Asn Met Phe Cys Asn Lys Glu Tyr Cys Asn Arg Leu Lys
 565 570 575
 Asp Glu Asn Asn Cys Ile Ser Asn Leu Gln Val Glu Asp Gln Gly Asn
 580 585 590
 Cys Asp Thr Ser Trp Ile Phe Ala Ser Lys Tyr His Leu Glu Thr Ile
 595 600 605
 Arg Cys Met Lys Gly Tyr Glu Pro Thr Lys Ile Ser Ala Leu Tyr Val
 610 615 620
 Ala Asn Cys Tyr Lys Gly Glu His Lys Asp Arg Cys Asp Glu Gly Ser
 625 630 635 640
 Ser Pro Met Glu Phe Leu Gln Ile Ile Glu Asp Tyr Gly Phe Leu Pro
 645 650 655
 Ala Glu Ser Asn Tyr Pro Tyr Asn Tyr Val Lys Val Gly Glu Gln Cys
 660 665 670
 Pro Lys Val Glu Asp His Trp Met Asn Leu Trp Asp Asn Gly Lys Ile
 675 680 685
 Leu His Asn Lys Asn Glu Pro Asn Ser Leu Asp Gly Lys Gly Tyr Thr
 690 695 700
 Ala Tyr Glu Ser Glu Arg Phe His Asp Asn Met Asp Ala Phe Val Lys
 705 710 715 720
 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

FP9025-seq1-000001.txt

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
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<210> 64
<211> 1233
<212> PRT
<213> Plasmodium falciparum

<400> 64

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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

FP9025-seq1-000001.txt

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

Ile Lys Gln Ser Glu Ser Glu Ile Asn His Val Gln Asp His Ala Leu
 340 345 350
 Pro Lys Glu Asn Ile Ile Asp Lys Leu Asp Asn Gln Lys Glu His Ile
 355 360 365
 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

FP9025-seq1-000001.txt

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
625 630 635 640

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
705 710 715 720

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
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 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

FP9025-seq1-000001.txt

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
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Ile Lys Gly Ile Ala Lys Asp Ile Val Ile Phe Phe Gln Asn Ile
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<213> Plasmodium falciparum

<400> 65

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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

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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
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
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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
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<212> PRT
<213> Plasmodium falciparum

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<400> 66

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 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
 225 230 235 240
 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

FP9025-seql-000001.txt

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
305 310 315 320

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
385 390 395 400

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> Plasmodium falciparum

<400> 67

Met Arg Leu Ser Lys Val Ser Asp Ile Lys Ser Thr Gly Val Ser Asn
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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

FP9025-seq1-000001.txt

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

FP9025-seq1-000001.txt

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

FP9025-seql-000001.txt

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

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Gln Asn Ala Asp Asn Asn Glu Ala
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<210> 68
<211> 41
<212> PRT
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<400> 68

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Met Asn Gly Asp Ile Asn Asn Met Asn
 35 40

<210> 69
 <211> 37
 <212> PRT
 <213> Plasmodium falciparum

<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> Plasmodium falciparum

<400> 70

Glu Lys Leu Lys Lys Tyr Asn Asn Glu Ile Ser Ser Leu Lys Lys Glu
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Leu Asp Ile Leu Asn Glu Lys Met Gly Lys Cys Thr
 20 25

<210> 71
 <211> 38
 <212> PRT
 <213> Plasmodium falciparum

<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
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<210> 72
 <211> 526
 <212> PRT
 <213> Plasmodium falciparum

<400> 72

FP9025-seq1-000001.txt

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

FP9025-seq1-000001.txt

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
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Glu Tyr Phe Gln Thr Tyr Lys Lys Asn Lys Pro Leu Thr Gln
515 520 525

<210> 73
<211> 622
<212> PRT
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<400> 73

Met Arg Lys Leu Tyr Cys Val Leu Leu Leu Ser Ala Phe Glu Phe Thr
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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
 Page 132

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
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<210> 74
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 <212> PRT
 <213> Plasmodium falciparum

<400> 74

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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
 145 150 155 160

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> Plasmodium falciparum

<400> 75

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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

FP9025-seql-000001.txt

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

FP9025-seq1-000001.txt

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

FP9025-seq1-000001.txt

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

FP9025-seql-000001.txt

Lys Lys Ile Lys Glu Lys Glu Lys Lys Glu Lys Lys Lys Thr Tyr Glu
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 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

FP9025-seql-000001.txt

Asp	Asn 1250	Pro	Ser	Thr	Asp	Ala 1255	Asp	Leu	Lys	Cys	Pro 1260	Gly	Cys	Gly
Arg	Glu 1265	Cys	Arg	Lys	Tyr	Lys 1270	Lys	Trp	Ile	Glu	Lys 1275	Lys	Lys	Glu
Glu	Phe 1280	Thr	Lys	Gln	Ser	Asn 1285	Val	Tyr	Glu	Glu	Gln 1290	Lys	Thr	Lys
Cys	Gln 1295	Lys	Glu	Ser	Lys	Ser 1300	Ala	Lys	Gly	Asn	Asn 1305	His	Gly	Asn
Glu	Phe 1310	Cys	Gly	Thr	Gln	Gly 1315	Thr	Cys	Asp	Thr	Ala 1320	Gly	Asp	Phe
Leu	Asn 1325	Arg	Leu	Lys	Ser	Gly 1330	Pro	Cys	Lys	Lys	Glu 1335	Asn	Gly	Lys
Asp	Asn 1340	Gln	Glu	Asp	Glu	Ile 1345	Asn	Phe	Lys	Asp	Glu 1350	Asp	Lys	Thr
Phe	Gly 1355	His	Glu	Asn	Tyr	Cys 1360	Ala	Pro	Cys	Pro	Val 1365	Phe	Lys	Asp
Ile	Cys 1370	Lys	Lys	Lys	Asp	Cys 1375	Arg	Asn	Ala	Ser	Asn 1380	Asn	Met	Cys
Asn	Gly 1385	Lys	Asp	Phe	Ile	Thr 1390	Ala	Glu	Asp	Ile	Lys 1395	Ile	Met	Asp
Ser	Ser 1400	Ser	Glu	Glu	Val	Asn 1405	Met	Leu	Val	Ser	Asp 1410	Asn	Asp	Thr
Asn	Lys 1415	Phe	Asp	Gly	Gly	Leu 1420	Asp	Ala	Cys	Lys	Asp 1425	Ala	His	Ile
Phe	Lys 1430	Gly	Ile	Lys	Glu	Asn 1435	Lys	Trp	Ser	Cys	Gly 1440	Asn	Val	Cys
Gly	Tyr 1445	Asn	Val	Cys	Lys	Pro 1450	Lys	Lys	Val	Asn	Gly 1455	Glu	Lys	Gly
Ser	Gly 1460	Glu	Asn	Asn	Asp	Gln 1465	Ile	Ile	Thr	Ile	Arg 1470	Gly	Leu	Val
Thr	His 1475	Trp	Val	Gln	Asn	Phe 1480	Leu	Asp	Asp	Tyr	Asn 1485	Lys	Ile	Arg
Thr	Lys 1490	Leu	Lys	Pro	Cys	Arg 1495	Asn	Asn	Gly	Glu	Val 1500	Ser	Lys	Cys

FP9025-seql-000001.txt

Ile	Lys 1505	Asp	Cys	Val	Lys	Lys 1510	Trp	Val	Glu	Lys	Lys 1515	Thr	Glu	Glu
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Asp	Gly 1535	Tyr	Asn	Lys	Lys	Ser 1540	Leu	Val	Arg	Ser	Phe 1545	Met	Glu	Thr
Leu	Ile 1550	Pro	Leu	Met	Asp	Leu 1555	Thr	Asn	Gly	Lys	Glu 1560	Lys	Ile	Gln
Glu	Leu 1565	Asn	Lys	Phe	Leu	Arg 1570	Ser	Tyr	Glu	Cys	Asn 1575	Cys	Ala	Asp
Asn	Ser 1580	Gln	Gln	Lys	Gly	Asp 1585	Thr	Pro	Lys	Asp	Ile 1590	Val	Glu	Cys
Leu	Leu 1595	Glu	Lys	Leu	Glu	Asp 1600	Lys	Ala	Asn	Lys	Cys 1605	Lys	Thr	Gln
Thr	Ser 1610	Gly	Thr	Asp	Cys	His 1615	Pro	Ser	Thr	Pro	Leu 1620	Glu	Asp	Asp
Asp	Glu 1625	Pro	Leu	Glu	Glu	Thr 1630	Glu	Glu	Asn	Thr	Val 1635	Glu	Gln	Pro
Asn	Ile 1640	Cys	Pro	Thr	Lys	Gln 1645	Pro	Gln	Pro	Glu	Lys 1650	Glu	Asp	Gly
Cys	Glu 1655	Ala	Ala	Pro	Thr	Thr 1660	Ala	Glu	Glu	Thr	Ser 1665	Pro	Thr	Ala
Thr	Ser 1670	Glu	Gly	Thr	Glu	Asn 1675	Gln	Ser	Pro	Pro	Pro 1680	Pro	Pro	Pro
Ala	Pro 1685	Ala	Pro	Ala	Pro	Ala 1690	Pro	Ala	Pro	Glu	Lys 1695	Ser	Gln	Pro
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

FP9025-seql-000001.txt

Gly	Asn	Leu	Phe	Gln	Ile	Leu	Gln	Ile	Pro	Gln	Asn	Asp	Tyr	Gly
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Ile	Pro	Thr	Leu	Lys	Ser	Lys	Asn	Arg	Tyr	Ile	Pro	Tyr	Arg	Ser
	1775					1780					1785			
Gly	Thr	Tyr	Lys	Gly	Lys	Thr	Tyr	Ile	Tyr	Met	Glu	Gly	Asp	Ser
	1790					1795					1800			
Ser	Gly	Asp	Glu	Lys	Tyr	Ala	Phe	Met	Ser	Asp	Thr	Thr	Asp	Val
	1805					1810					1815			
Thr	Ser	Ser	Glu	Ser	Glu	Tyr	Glu	Glu	Leu	Asp	Ile	Asn	Asp	Ile
	1820					1825					1830			
Tyr	Val	Pro	His	Ala	Pro	Lys	Tyr	Lys	Thr	Leu	Ile	Glu	Val	Val
	1835					1840					1845			
Leu	Glu	Pro	Ser	Gly	Asn	Asn	Thr	Thr	Ala	Ser	Gly	Lys	Asn	Thr
	1850					1855					1860			
Pro	Ser	Asp	Thr	Gln	Asn	Asp	Ile	Pro	Thr	Ser	Asp	Thr	Pro	Pro
	1865					1870					1875			
Pro	Ile	Thr	Asp	Asn	Glu	Trp	Asn	Thr	Leu	Lys	Asp	Glu	Phe	Ile
	1880					1885					1890			
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			

FP9025-seql-000001.txt

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
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 2135 2140 2145
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 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
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 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

FP9025-seq1-000001.txt

Glu Asn Val Glu Glu Ser Val Ala Glu Asn Val Glu Glu Ile Val Ala
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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
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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
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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 625	Thr	Ile	Leu	Glu	Asn 630	Val	Glu	Glu	Thr	Thr 635	Ala	Glu	Ser	Val	Thr 640
Thr	Phe	Ser	Asn	Ile 645	Leu	Glu	Glu	Ile	Gln 650	Glu	Asn	Thr	Ile	Thr 655	Asn
Asp	Thr	Ile	Glu 660	Glu	Lys	Leu	Glu	Glu 665	Leu	His	Glu	Asn	Val 670	Leu	Ser
Ala	Ala	Leu 675	Glu	Asn	Thr	Gln	Ser 680	Glu	Glu	Glu	Lys	Lys 685	Glu	Val	Ile
Asp	Val 690	Ile	Glu	Glu	Val	Lys 695	Glu	Glu	Val	Ala	Thr 700	Thr	Leu	Ile	Glu
Thr 705	Val	Glu	Gln	Ala	Glu 710	Glu	Glu	Ser	Ala	Ser 715	Thr	Ile	Thr	Glu	Ile 720
Phe	Glu	Asn	Leu	Glu 725	Glu	Asn	Ala	Val	Glu 730	Ser	Asn	Glu	Asn	Val 735	Ala
Glu	Asn	Leu	Glu 740	Lys	Leu	Asn	Glu	Thr 745	Val	Phe	Asn	Thr	Val 750	Leu	Asp
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Glu 770	Met	Asp	Lys	Ala	Phe	Phe 775	Ser	Glu	Ile	Phe	Asp 780	Asn	Val	Lys	Gly
Ile 785	Gln	Glu	Asn	Leu	Leu 790	Thr	Gly	Met	Phe	Arg 795	Ser	Ile	Glu	Thr	Ser 800
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Ser	Ser	Ile	Leu 820	Asp	Asn	Ile	Glu	Asn 825	Met	Lys	Glu	Gly	Leu 830	Leu	Asn
Lys	Leu 835	Glu	Asn	Ile	Ser	Ser	Thr 840	Glu	Gly	Val	Gln	Glu 845	Thr	Val	Thr
Glu 850	His	Val	Glu	Gln	Asn	Val 855	Tyr	Val	Asp	Val	Asp 860	Val	Pro	Ala	Met
Lys 865	Asp	Gln	Phe	Leu	Gly 870	Ile	Leu	Asn	Glu	Ala 875	Gly	Gly	Leu	Lys	Glu 880
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 915 920 925
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 930 935 940
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 945 950 955 960
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 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
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 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
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 1130 1135 1140
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Gly	Leu	Glu	Glu	Asp	Asp	Leu	Glu	Glu	Val	Asp	Asp	Leu	Lys	Gly
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Ser	Ile	Leu	Asp	Met	Leu	Lys	Gly	Asp	Met	Glu	Leu	Gly	Asp	Met
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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			
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1310						1315					1320			
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1340						1345					1350			
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1355						1360					1365			
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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
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Val Lys Lys Tyr Lys Val Phe Ala Ala Pro Phe Ile Ser Ala Val
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Ala Ala Phe Ala Ser Tyr Val Val Gly Phe Phe Thr Phe Ser Leu
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Phe Ser Ser Cys Val Thr Ile Ala Ser Ser Thr Tyr Leu Leu Ser
 1460 1465 1470

Lys Val Asp Lys Thr Ile Asn Lys Asn Lys Glu Arg Pro Phe Tyr
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Ser Phe Val Phe Asp Ile Phe Lys Asn Leu Lys His Tyr Leu Gln
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Glu Val Thr Asn Lys Ala Glu Lys Lys Gly Asn Val Gln Val Thr
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Ala Ser Ser Val Glu Glu Ser Ile Ala Ser Ser Val Asp Glu Ser Ile
 Page 149

85

90

95

Asp Ser Ser Ile Glu Glu Asn Val Ala Pro Thr Val Glu Glu Ile Val
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Glu Asp Asn Glu Lys Leu Arg Lys Pro Lys His Lys Lys Leu Lys Gln
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FP9025-seq1-000001.txt

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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
<211> 574
<212> PRT
<213> Plasmodium falciparum

<400> 79

Met Asn His Leu Gly Asn Val Lys Tyr Leu Val Ile Val Phe Leu Ile
1 5 10 15

FP9025-seql-000001.txt

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

FP9025-seq1-000001.txt

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

FP9025-seq1-000001.txt

Glu Pro Glu Gln Phe Arg Leu Pro Glu Glu Asn Glu Trp Asn
565 570

<210> 80
<211> 272
<212> PRT
<213> Plasmodium falciparum

<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 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> Plasmodium falciparum

<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
 Page 155

195

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
305 310 315 320

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

Ser Val Met Gly Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu
340 345 350

Ile Val Ala Gln Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala
355 360 365

Ile Pro Leu Val Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn
370 375 380

Phe Val Glu Ser Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr
385 390 395 400

Asn Arg Pro Ala Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu His
405 410 415

Asp Gly Tyr Ala Val Ser Trp Asn Thr Val Glu Asp Ser Ile Ile Arg
420 425 430

Thr Gly Phe Gln Gly Glu Ser Gly His Asp Ile Lys Ile Thr Ala Glu
435 440 445

Asn Thr Pro Leu Pro Ile Ala Gly Val Leu Leu Pro Thr Ile Pro Gly
450 455 460

Lys Leu Asp Val Asn Lys Ser Lys Thr His Ile Ser Val Asn Gly Arg

465 470 475 480

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 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> Plasmodium falciparum

<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
145 150 155 160

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
 225 230 235 240
 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
 305 310 315 320
 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> Plasmodium falciparum
<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

FP9025-seql-000001.txt

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

FP9025-seq1-000001.txt

Asn Ile Glu Ser Lys₄₀₅ Asp Leu Lys Ser Glu₄₁₀ Tyr Lys Gly Gln Asn₄₁₅ Met
 Arg Val Asn Thr₄₂₀ Asn Ala Phe Arg Asn₄₂₅ Val Asp Gly Ser Gly₄₃₀ Leu Val
 Ser Lys Leu₄₃₅ Ile Gly Leu Cys Lys₄₄₀ Lys Ile Ile Pro Pro₄₄₅ Thr Asn Ile
 Arg Glu₄₅₀ Asn Leu Tyr Asn Arg₄₅₅ Thr Ala Ser Leu Thr₄₆₀ Asp Leu Gly Gly
 Glu₄₆₅ Leu Cys Ile Lys Ile₄₇₀ Lys Asn Glu Asp Leu₄₇₅ Thr Phe Ile Ala Glu₄₈₀
 Lys Asn Ser Phe Ser₄₈₅ Glu Glu Pro Phe Gln₄₉₀ Asp Glu Ile Val Ser₄₉₅ Tyr
 Asn Thr Lys Asn₅₀₀ Lys Pro Leu Asn Phe₅₀₅ Asn Tyr Ser Leu Asp₅₁₀ Lys Ile
 Ile Val Asp₅₁₅ Tyr Asn Leu Gln Ser₅₂₀ Lys Ile Thr Leu Pro₅₂₅ Asn Asp Arg
 Thr Thr₅₃₀ Pro Val Thr Lys Gly₅₃₅ Ile Pro Tyr Ala Pro₅₄₀ Glu Tyr Lys Ser
 Asn₅₄₅ Ala Ala Ser Thr Ile₅₅₀ Glu Ile His Asn Ile₅₅₅ Asp Asp Asn Thr Ile₅₆₀
 Tyr Gln Tyr Leu Tyr₅₆₅ Ala Gln Lys Ser Pro₅₇₀ Thr Thr Leu Gln Arg₅₇₅ Ile
 Thr Met Thr Asn₅₈₀ Ser Val Asp Asp Ala₅₈₅ Leu Ile Asn Ser Thr₅₉₀ Lys Ile
 Tyr Ser Tyr₅₉₅ Phe Pro Ser Val Ile₆₀₀ Ser Lys Val Asn Gln₆₀₅ Gly Ala Gln
 Gly Ile₆₁₀ Leu Phe Leu Gln Trp₆₁₅ Val Arg Asp Ile Ile₆₂₀ Asp Asp Phe Thr
 Asn₆₂₅ Glu Ser Ser Gln Lys₆₃₀ Thr Thr Ile Asp Lys₆₃₅ Ile Ser Asp Val Ser₆₄₀
 Thr Ile Val Pro Tyr₆₄₅ Ile Gly Pro Ala Leu₆₅₀ Asn Ile Val Lys Gln₆₅₅ Gly
 Tyr Glu Gly Asn₆₆₀ Phe Ile Gly Ala Leu₆₆₅ Glu Thr Thr Gly Val₆₇₀ Val Leu

FP9025-seql-000001.txt

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

FP9025-seql-000001.txt

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

FP9025-seql-000001.txt

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
1295 1300 1305

Asp Glu Gly Trp Thr Asn Asp
1310 1315

<210> 84
<211> 364
<212> PRT
<213> Plasmodium falciparum

<400> 84

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

Ala Gly Cys Ser Ser His Ser Ser Asn Met Ala Asn Thr Gln Met Lys
20 25 30

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

Glu His Thr Leu Glu Ser Lys Ala Leu Ala Phe Ala Gln Gln Ala Asp
50 55 60

Tyr Leu Glu Gln Asp Leu Ala Met Thr Lys Asp Gly Arg Leu Val Val
65 70 75 80

Ile His Asp His Phe Leu Asp Gly Leu Thr Asp Val Ala Lys Lys Phe
85 90 95

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

Leu Lys Glu Ile Gln Ser Leu Glu Met Thr Glu Asn Phe Glu Thr Lys
115 120 125

Asp Gly Lys Gln Ala Gln Val Tyr Pro Asn Arg Phe Pro Leu Trp Lys
130 135 140

Ser His Phe Arg Ile His Thr Phe Glu Asp Glu Ile Glu Phe Ile Gln
145 150 155 160

Gly Leu Glu Lys Ser Thr Gly Lys Lys Val Gly Ile Tyr Pro Glu Ile
165 170 175

Lys Ala Pro Trp Phe His His Gln Asn Gly Lys Asp Ile Ala Ala Glu
180 185 190

Thr Leu Lys Val Leu Lys Lys Tyr Gly Tyr Asp Lys Lys Thr Asp Met
195 200 205

Val Tyr Leu Gln Thr Phe Asp Phe Asn Glu Leu Lys Arg Ile Lys Thr
210 215 220

Glu Leu Leu Pro Gln Met Gly Met Asp Leu Lys Leu Val Gln Leu Ile
225 230 235 240

Ala Tyr Thr Asp Trp Lys Glu Thr Gln Glu Lys Asp Pro Lys Gly Tyr
245 250 255

Trp Val Asn Tyr Asn Tyr Asp Trp Met Phe Lys Pro Gly Ala Met Ala
260 265 270

Glu Val Val Lys Tyr Ala Asp Gly Val Gly Pro Gly Trp Tyr Met Leu
275 280 285

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

Val Lys Glu Leu Ala Gln Tyr Asn Val Glu Val His Pro Tyr Thr Val
305 310 315 320

Arg Lys Asp Ala Leu Pro Ala Phe Phe Thr Asp Val Asn Gln Met Tyr
325 330 335

Asp Ala Leu Leu Asn Lys Ser Gly Ala Thr Gly Val Phe Thr Asp Phe
340 345 350

Pro Asp Thr Gly Val Glu Phe Leu Lys Gly Ile Lys
355 360

<210> 85
<211> 757
<212> PRT
<213> Artificial Sequence

<220>

<223> PP21 biofusion protein

<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
 225 230 235 240

Glu Phe Ile Lys Arg Phe Gly Asp Gly Ala Ser Arg Val Val Leu Ser
 245 250 255

FP9025-seql-000001.txt

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
 305 310 315 320
 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
 385 390 395 400
 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

FP9025-seq1-000001.txt

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
755

<210> 86

<211> 727

<212> PRT

<213> Artificial Sequence

<220>

<223> PP22 biofusion protein

<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> Artificial Sequence

<220>
<223> PP23 biofusion protein

<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

FP9025-seql-000001.txt

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

FP9025-seql-000001.txt

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> Artificial Sequence

<220>
<223> PP25 biofusion protein

<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

FP9025-seq1-000001.txt

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

FP9025-seq1-000001.txt

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> Plasmodium falciparum

<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 Gly Asp Gly Ala Ser Arg Val Val Leu Ser Leu Pro
 Page 178

260

265

270

Phe Ala Glu Gly Ser Ser Ser Val Glu Tyr Ile Asn Asn Trp Glu Gln
 275 280 285

Ala Lys Ala Leu Ser Val Glu Leu Glu Ile Asn Phe Glu Thr Arg Gly
 290 295 300

Lys Arg Gly Gln Asp Ala Met Tyr Glu Tyr Met Ala Gln Ala Cys Ala
 305 310 315 320

Gly Asn Arg Val Arg Arg Ser Val Gly Ser Ser Leu Ser Cys Ile Asn
 325 330 335

Leu Asp Trp Asp Val Ile Arg Asp Lys Thr Lys Thr Lys Ile Glu Ser
 340 345 350

Leu Lys Glu His Gly Pro Ile Lys Asn Lys Met Ser Glu Ser Pro Asn
 355 360 365

Lys Thr Val Ser Glu Glu Lys Ala Lys Gln Tyr Leu Glu Glu Phe His
 370 375 380

Gln Thr Ala Leu Glu His Pro Glu Leu Ser Glu Leu Lys Thr Val Thr
 385 390 395 400

Gly Thr Asn Pro Val Phe Ala Gly Ala Asn Tyr Ala Ala Trp Ala Val
 405 410 415

Asn Val Ala Gln Val Ile Asp Ser Glu Thr Ala Asp Asn Leu Glu Lys
 420 425 430

Thr Thr Ala Ala Leu Ser Ile Leu Pro Gly Ile Gly Ser Val Met Gly
 435 440 445

Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu Ile Val Ala Gln
 450 455 460

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

FP9025-seq1-000001.txt