

MODIFICATION OF RECOMBINANT ADENOVIRUS WITH IMMUNOGENIC PLASMODIUM CIRCUMSPOROZOITE PROTEIN EPITOPES

PRIORITY CLAIM

[0001] This application claims priority to and is a continuation-in-part of International Application No. PCT/US09/054212, filed on August 18, 2009, which is incorporated by reference in its entirety, as if fully set forth herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

[0002] This invention was made with government support under Grant No. 1R01AI081510-01A1 awarded by the National Institute of Allergy and Infectious Diseases (NIAID), an institute that is part of the National Institutes of Health. The government has certain rights in the invention.

FIELD OF THE INVENTION

[0003] The invention relates to the field of medicine and biotechnology. More particularly, the invention relates to the use of capsid-modified adenoviral vectors to induce a potent immune response to a malaria parasite antigen such as *Plasmodium* circumsporozone protein, which are suitable for vaccines against malaria.

BACKGROUND

[0004] Malaria is a severe disease that ranks among the most prevalent infections in tropical areas throughout the world. Approximately 300-500 million people become infected yearly, with relatively high rates of morbidity and mortality. Severe morbidity and mortality occur particularly in young children and in adults migrating to a malaria endemic area without having undergone prior malaria exposure. The World Health Organization (WHO) estimates that 2 - 3 million children die of malaria in Africa alone, every year. The widespread occurrence and the increasing incidence of malaria in many countries, caused by drug-resistant parasites (*Plasmodium falciparum*, recently also *Plasmodium vivax*) and insecticide-resistant vectors (*Anopheles* mosquitoes), underscore the need

for developing new methods for the control of this disease (Nussenzweig and Long 1994).

[0005] Malaria parasites have a complicated life cycle consisting of pre-erythrocytic, erythrocytic and sexual parasitic forms, representing a potential target for the development of a malaria vaccine. The pre-erythrocytic and erythrocytic forms are found in the host, while the sexual forms occur in the vector. Immunization with live-attenuated irradiated sporozoites (IrSp) has been shown to induce sterile protection (i.e., complete resistance against parasite challenge) in mice (Nussenzweig et al. 1967), non-human primates (Gwadz et al. 1979) and human (Clyde et al. 1973, Edelman et al. 1993). Protection conferred by IrSp is mediated by sporozoite neutralization by both humoral (B cell) and cellular (T cell) immune responses (Tsuji et al. 2001). Although an IrSp vaccination is an attractive solution, the only way to obtain sporozoites is by dissecting mosquito salivary glands, and there is currently no known technology to grow large numbers of sporozoites *in vitro*. Therefore, an alternate vaccine vector that can elicit an equally strong protective immunity against malaria is needed.

[0006] One promising target for such a vaccine vector is the circumsporozoite (CS) protein, which is expressed on the surface of the sporozoite. Effective neutralizing antibodies are directed against the immunodominant, species specific, repeat domains of the circumsporozoite (CS) protein. In *Plasmodium falciparum* (human malaria parasite), the repeats (NANP)_n are conserved among isolates from all areas of the world. This central repeat contains multiple repeat of B cell epitopes, and, therefore, the CS protein can induce a strong humoral immune response by triggering B cells (Tsuji et al. 2001). At the C-terminal region of the CS protein, there are several T cell epitopes, which can induce a significant cellular immune response (Tsuji et al. 2001). The humoral (antibody) response can eliminate parasites by interacting and neutralizing the infectivity of sporozoites (extra-cellular parasite) prior to entering hepatocyte, whereas the cellular (T cell) response can attack EEF (an intra-cellular parasite) by secreting interferon-gamma. These immune responses prevent the EEFs from maturing and dividing rapidly to form thousands of

merozoites that reenter the blood and infect erythrocytes causing the disease we recognize as malaria.

[0007] One CS-based malarial vaccine that is currently undergoing human trials is GlaxoSmithKline's RTS, S, fusion protein of the Hepatitis B surface antigen and a portion of *Plasmodium falciparum* circumsporozoite protein (PfCSP) in a form of virus-like particle (International Patent Application No. PCT/EP1992/002591 to SmithKline Beecham Biologicals S.A., filed November 11, 1992), has been shown to decrease malaria infection in clinical trials (Alonso et al. 2004, Alonso et al. 2005, Bejon et al. 2008). RTS, S induces an anti-PfCSP humoral immune response, but a relatively weak PfCSP-specific cellular (CD8+) response (Kester et al. 2008), which might be the reason for the relatively weak protection by RTS, S. In contrast, adenovirus-based malaria vaccines can induce a protective cellular immune response (International Patent Application No. PCT/EP2003/051019, filed December 16, 2003, Rodrigues et al. 1997). However, there are currently two obstacles that limit the use of an adenovirus-based platform as a malaria vaccine: (1) lack of a capability of inducing a potent humoral response against a transgene product, and (2) pre-existing immunity to adenovirus, especially adenovirus serotype 5, which hampers the immunogenicity of adenovirus-based vaccine.

[0008] One approach that has recently been taken in an attempt to augment adenovirus-induced humoral response is to insert a B cell antigenic epitope (e.g., a bacterial or viral epitope) in adenovirus capsid proteins such as Hexon, Fiber, Penton and pIX (Worgall et al. 2005, McConnell et al. 2006, Krause et al. 2006, Worgall et al. 2007).

[0009] In addition, to circumvent pre-existing immunity to adenovirus serotype 5 (Ad5), other adenovirus serotypes with lower seroprevalence, such as adenovirus serotype 11, 35, 26, 48, 49 and 50, have been evaluated as a vaccine platform and shown to induce immune response to a transgene in spite of the presence of anti-Ad5 immunity (International Patent Application No. PCT/EP2005/055183 to Crucell Holland B.V., filed October 12, 2005, Abbink et al. 2007). Substitution of Ad5 Hexon, which is the target capsid protein of

neutralizing antibody, with that of other serotypes has also been constructed in order to escape pre-existing anti-Ad5 immunity (Wu et al. 2002, Roberts et al. 2006).

[0010] There is, however, no improved adenoviral vector reported to have overcome the two obstacles at the same time in applying an adenoviral vector to a malaria vaccine mentioned above. Given that seroprevalence to Ad5 is high in malaria endemic areas (Ophorst et al. 2006.), there is a need for an adenovirus-based malaria vaccine that induces both protective humoral and cellular immune responses even in the presence of pre-existing immunity to adenovirus.

SUMMARY

[0011] The present disclosure relates to various adenovirus protein modifications to augment immune response to a transgene of a recombinant adenoviral vaccine and to circumvent pre-existing anti-adenovirus immunity.

[0012] More specifically, one embodiment is directed to a recombinant adenovirus derived from a recombinant adenovirus plasmid vector, wherein the recombinant adenovirus plasmid vector comprises a nucleotide sequence encoding (i) a *Plasmodium* circumsporozoite protein, or antigenic portion thereof, operably linked to a heterologous promoter; and (ii) a modified capsid or core protein, wherein an immunogenic epitope of *Plasmodium* circumsporozoite has been inserted into or replaces at least part of a capsid or core protein.

[0013] In some embodiments, the *Plasmodium* circumsporozoite protein further comprises a *Plasmodium falciparum* or *Plasmodium yoelii* circumsporozoite protein. The circumsporozoite protein may further comprise a codon-optimized *Plasmodium falciparum* or *Plasmodium yoelii* circumsporozoite protein, and in some aspects, may be encoded by the nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:1, respectively.

[0014] In other embodiments, the immunogenic epitope further comprises a B cell epitope of *Plasmodium* circumsporozoite protein. The B cell epitope may be incorporated in a modified capsid protein, and in some aspects, the capsid

protein may comprise a Hexon hypervariable region (HVR). The HVR may further comprise HVR1 or HVR5, wherein a portion of HVR1 or HVR5 is replaced with the B cell epitope. In other aspects, the capsid protein may further comprise a capsid Fiber protein wherein the B cell epitope is inserted into the Fiber protein. In some aspects, the B cell epitope is a *Plasmodium falciparum* circumsporozoite protein B cell epitope, wherein the B cell epitope is a repeat sequence, for example, (NANP)_n (SEQ ID NO:60), wherein the repeat sequence may be (NANP)₄, (NANP)₆, (NANP)₈, (NANP)₁₀, (NANP)₁₂, (NANP)₁₄, (NANP)₁₆, (NANP)₁₈, (NANP)₂₀, (NANP)₂₂ or (NANP)₂₈. In other aspects, the B cell epitope is a *Plasmodium yoelii* circumsporozoite protein B cell epitope, wherein the B cell epitope is a repeat sequence, for example, (QGPGAP)_n (SEQ ID NO:59), wherein the repeat sequence may be (QGPGAP)₃, (QGPGAP)₄, (QGPGAP)₅, (QGPGAP)₆, (QGPGAP)₇, (QGPGAP)₈, (QGPGAP)₉, (QGPGAP)₁₁, or (QGPGAP)₁₂.

[0015] In yet other embodiments, the immunogenic epitope further comprises a CD4+ or CD8+ T cell epitope of *Plasmodium* circumsporozoite protein. The CD4+ or CD8+ T cell epitope may be incorporated in a modified capsid or core protein. In some aspects, the capsid protein may comprise a Hexon hypervariable region (HVR). The HVR may further comprise HVR1 wherein a portion of HVR1 is replaced with the CD4+ or CD8+ T cell epitope. In other aspects, the core protein further comprises a pVII protein and a CD4+ T cell epitope is inserted into the pVII protein. In some aspects the CD4+ T cell epitope is a *Plasmodium falciparum* circumsporozoite CD4+ T cell epitope, wherein the CD4+ T cell epitope is EYLNKIQNSLSTEWSPCSVT (SEQ ID NO:62). In other aspects the CD4+ T cell epitope is a *Plasmodium yoelii* circumsporozoite CD4+ T cell epitope, wherein the CD4+ T cell epitope is YNRNIVNRLLGDALNGKPEEK (SEQ ID NO:61)

[0016] Other embodiments are directed to a pharmaceutical composition or malaria vaccine composition comprising a recombinant adenovirus according to the above embodiments. Further embodiments include a method of treating, preventing, or diagnosing malaria, comprising administering a therapeutic amount

of the pharmaceutical composition or malaria vaccine composition in accordance with the above embodiments.

[0017] In another embodiment, a method for treatment comprising administering a prime-boost vaccination, wherein a subject is given a series of increasing dosages or same dosages at a given time interval. The time interval may be any length sufficient to generate a humoral and/or cellular immune response. For example, as described below, the interval may be, but is not limited to, once every 3 weeks.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] Fig. 1 is a schematic diagram of a capsid-modified recombinant adenovirus in accordance with embodiments of the disclosure.

[0019] Fig. 2 is a schematic diagram illustrating the construction of the HVR1-Modified Adenovirus DNA of an HVR1-modified recombinant adenovirus plasmid vector.

[0020] Fig. 3 is a schematic diagram illustrating the construction of the HVR5-Modified Adenovirus DNA of an HVR5-modified recombinant adenovirus plasmid vector.

[0021] Fig. 4 is a schematic diagram illustrating the construction of the Fiber-Modified Adenovirus DNA of a Fiber-modified recombinant adenovirus plasmid vector.

[0022] Fig. 5 is a schematic diagram illustrating the construction of the HVR1 and Fiber-Modified Adenovirus DNA of an HVR1 and Fiber-modified recombinant adenovirus plasmid vector.

[0023] Fig. 6 is a schematic diagram illustrating the construction of the Fiber and pVII-Modified Adenovirus DNA of a Fiber and pVII-modified recombinant adenovirus plasmid vector.

[0024] Fig. 7 is a schematic diagram illustrating the construction of the HVR1 and pVII-Modified Adenovirus DNA of an HVR1 and pVII-modified recombinant adenovirus plasmid vector.

[0025] Fig. 8 is a schematic diagram illustrating the construction of the HVR1, Fiber and pVII-Modified Adenovirus DNA of an HVR1, Fiber and pVII-modified recombinant adenovirus plasmid vector.

[0026] Fig. 9 is the nucleic acid sequence of codon-optimized *Plasmodium yoelii* circumsporozoite protein (PyCS, SEQ ID NO:1) and the corresponding amino acid sequence (SEQ ID NO:30)

[0027] Fig. 10 is the nucleic acid sequence of codon-optimized *Plasmodium falciparum* circumsporozoite protein (PfCSP, SEQ ID NO:2) and the corresponding amino acid sequence (SEQ ID NO:43)

[0028] Fig. 11 is the nucleic acid and amino acid sequences of a modified Hexon having three repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=3) in HVR1(SEQ ID NO:3, nucleic acid; SEQ ID NO:31, amino acid). The inserted (QGPGAP)₃ sequence is underlined.

[0029] Fig. 12 is the nucleic acid and amino acid sequences of a modified Hexon having four repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=4) in HVR1 (SEQ ID NO:4, nucleic acid; SEQ ID NO: 32, amino acid). The inserted (QGPGAP)₄ sequence is underlined.

[0030] Fig. 13 is the nucleic acid and amino acid sequences of modified Hexon having five repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=5) in HVR1 (SEQ ID NO:5, nucleic acid; SEQ ID NO: 33, amino acid). The inserted (QGPGAP)₅ sequence is underlined.

[0031] Fig. 14 is the nucleic acid and amino acid sequences of modified Hexon having six repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=6) in HVR1 (SEQ ID NO:6, nucleic acid; SEQ ID NO: 34, amino acid). The inserted (QGPGAP)₆ sequence is underlined.

[0032] Fig. 15 is the nucleic acid and amino acid sequences of modified Hexon having seven repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=7) in HVR1 (SEQ ID NO:7, nucleic acid; SEQ ID NO: 35, amino acid). The inserted (QGPGAP)₇ sequence is underlined.

[0033] Fig. 16 is the nucleic acid and amino acid sequences of modified Hexon having eight repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=8) in HVR1 (SEQ ID NO:8, nucleic acid; SEQ ID NO: 36, amino acid). The inserted (QGPGAP)₈ sequence is underlined.

[0034] Fig. 17 is the nucleic acid and amino acid sequences of modified Hexon having nine repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=9) in HVR1 (SEQ ID NO:9, nucleic acid; SEQ ID NO: 37, amino acid). The inserted (QGPGAP)₉ sequence is underlined.

[0035] Fig. 18 is the nucleic acid and amino acid sequences of modified Hexon having eleven repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=11) in HVR1 (SEQ ID NO:10, nucleic acid; SEQ ID NO: 38, amino acid). The inserted (QGPGAP)₁₁ sequence is underlined.

[0036] Fig. 19 is the nucleic acid and amino acid sequences of modified Hexon having twelve repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=12) in HVR1 (SEQ ID NO:11, nucleic acid; SEQ ID NO: 39, amino acid). The inserted (QGPGAP)₁₂ sequence is underlined.

[0037] Fig. 20 is the nucleic acid and amino acid sequences of modified Hexon having four repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=4) in HVR1 (SEQ ID NO:12, nucleic acid; SEQ ID NO: 44, amino acid). The inserted (NANP)₄ sequence is underlined.

[0038] Fig. 21 is the nucleic acid and amino acid sequences of modified Hexon having six repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=6) in HVR1 (SEQ ID NO:13, nucleic acid; SEQ ID NO: 45, amino acid). The inserted (NANP)₆ sequence is underlined.

[0039] Fig. 22 is the nucleic acid and amino acid sequences of modified Hexon having eight repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=8) in HVR1 (SEQ ID NO:14, nucleic acid; SEQ ID NO: 46, amino acid). The inserted (NANP)₈ sequence is underlined.

[0040] Fig. 23 is the nucleic acid and amino acid sequences of modified Hexon having ten repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=10) in HVR1 (SEQ ID NO:15, nucleic acid; SEQ ID NO: 47, amino acid). The inserted (NANP)₁₀ sequence is underlined.

[0041] Fig. 24 is the nucleic acid and amino acid sequences of modified Hexon having twelve repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=12) in HVR1 (SEQ ID NO:16, nucleic acid; SEQ ID NO: 48, amino acid). The inserted (NANP)₁₂ sequence is underlined.

[0042] Fig. 25 is the nucleic acid and amino acid sequences of modified Hexon having fourteen repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=14) in HVR1 (SEQ ID NO:17, nucleic acid; SEQ ID NO: 49, amino acid). The inserted (NANP)₁₄ sequence is underlined.

[0043] Fig. 26 is the nucleic acid and amino acid sequences of modified Hexon having sixteen repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=16) in HVR1 (SEQ ID NO:18, nucleic acid; SEQ ID NO: 50, amino acid). The inserted (NANP)₁₆ sequence is underlined.

[0044] Fig. 27 is the nucleic acid and amino acid sequences of modified Hexon having eighteen repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=18) in HVR1 (SEQ ID NO:19, nucleic acid; SEQ ID NO: 51, amino acid). The inserted (NANP)₁₈ sequence is underlined.

[0045] Fig. 28 is the nucleic acid and amino acid sequences of modified Hexon having twenty repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=20) in HVR1 (SEQ ID NO:20, nucleic acid; SEQ ID NO: 52, amino acid). The inserted (NANP)₂₀ sequence is underlined.

[0046] Fig. 29 is the nucleic acid and amino acid sequences of modified Hexon having twenty-two repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=22) in HVR1 (SEQ ID NO:21, nucleic acid; SEQ ID NO: 53, amino acid). The inserted (NANP)₂₂ sequence is underlined.

[0047] Fig. 30 is the nucleic acid and amino acid sequences of modified Hexon having twenty-eight repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=28) in HVR1 (SEQ ID NO:22, nucleic acid; SEQ ID NO: 54, amino acid). The inserted (NANP)₂₈ sequence is underlined.

[0048] Fig. 31 is the nucleic acid and amino acid sequences of modified Hexon having three repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=3) in HVR5 (SEQ ID NO:23, nucleic acid; SEQ ID NO:40, amino acid). The inserted (QGPGAP)₃ sequence is underlined.

[0049] Fig. 32 is the nucleic acid and amino acid sequences of modified Fiber having three repeats of the PyCS B cell epitope sequence (QGPGAP)_n, (SEQ ID NO:59; n=3) in Fiber (SEQ ID NO:24, nucleic acid; SEQ ID NO:41, amino acid). The inserted (QGPGAP)₃ sequence is underlined.

[0050] Fig. 33 is the nucleic acid and amino acid sequences of modified Fiber having four repeats of the PfCSP B cell epitope sequence (NANP)_n, (SEQ ID NO:60; n=4) in Fiber (SEQ ID NO:25, nucleic acid; SEQ ID NO:55, amino acid). The inserted (NANP)₄ sequence is underlined.

[0051] Fig. 34 is the nucleic acid and amino acid sequences of the modified pVII having the PyCS CD4+ epitope sequence YNRNIVNRLLGDALNGKPEEK, (SEQ ID NO:61) at the N-terminus of pVII (SEQ ID NO:26, nucleic acid; SEQ ID NO:42, amino acid). The inserted YNRNIVNRLLGDALNGKPEEK sequence is underlined.

[0052] Fig. 35 is the nucleic acid and amino acid sequences of the modified pVII having the PfCSP CD4+ epitope sequence EYLNKIQNSLSTEWSPCSVT, (SEQ ID NO:62) at the C-terminus of pVII (pVII-1; SEQ ID NO:27, nucleic acid;

SEQ ID NO:56, amino acid). The inserted EYLNKIQNSLSTEWSPCSVT sequence is underlined.

[0053] Fig. 36 is the nucleic acid and amino acid sequences of the modified pVII having the PfCSP CD4+ epitope sequence EYLNKIQNSLSTEWSPCSVT , (SEQ ID NO:62) before the first Nuclear Localization Signal (NLS) of pVII (pVII-2; SEQ ID NO:28, nucleic acid; SEQ ID NO:57, amino acid). The inserted EYLNKIQNSLSTEWSPCSVT sequence is underlined.

[0054] Fig. 37 is the nucleic acid and amino acid sequences of the modified pVII having the PfCSP CD4+ epitope sequence EYLNKIQNSLSTEWSPCSVT, (SEQ ID NO:62) between the two NLSs of pVII (pVII-3; SEQ ID NO:29, nucleic acid; SEQ ID NO:58, amino acid). The inserted EYLNKIQNSLSTEWSPCSVT sequence is underlined.

[0055] Fig. 38 shows PyCS protein expression in AD293 cells after transient transfection with PyCS-GFP/pShuttle-CMV. PyCS protein was detected by western blotting using mouse monoclonal anti-PyCS antibody (9D3).

[0056] Fig. 39 shows the results of silver staining and western blotting (A) and ELISA assay (B) of the purified capsid-modified recombinant PyCS-GFP adenoviruses to confirm the (QGPGAP)₃ epitope (SEQ ID NO:59; n=3) insertion into adenovirus capsid proteins. In the ELISA assay, ELISA plates were coated directly with purified adenoviruses and the inserted epitope in adenovirus particles was detected with anti-PyCS antibody.

[0057] Fig. 40 shows the results of silver staining and western blotting (A) and ELISA assay (B) of the purified capsid-modified recombinant PyCS adenoviruses to confirm the (QGPGAP)_n epitope (SEQ ID NO:59) insertion into adenovirus capsid proteins. In the ELISA assay, ELISA plates were coated directly with purified adenoviruses and the inserted epitope in adenovirus particles was detected with anti-PyCS antibody.

[0058] Fig. 41 illustrates a single immunization regimen with capsid-modified PyCS adenoviruses having (QGPGAP)_n repeats (SEQ ID NO:59, n=3, 4,

5, 6, 9, 12) (A) and PyCS-specific CD8⁺ response two weeks after immunization (B).

[0059] Fig. 42 illustrates a prime and boost immunization regimen with capsid-modified PyCS adenoviruses having (QGPGAP)_n repeats (SEQ ID NO:59, n=3) (A), PyCS-specific humoral responses at week 10 (B), and malaria parasite burden in liver 42 hours after sporozoite challenge (C).

[0060] Fig. 43 illustrates anti-sporozoite antibody titer determined by indirect immunofluorescence assay (IFA) (A) and *in vitro* sporozoite neutralizing activity (B) of pooled serum samples prepared from mice given the regimen in Fig. 42.

[0061] Fig. 44 illustrates a prime and boost immunization regimen with capsid-modified PyCS adenoviruses having (QGPGAP)_n repeats (SEQ ID NO:59, n=4, 6) in HVR1(A), PyCS-specific humoral responses at week 9 (B), malaria parasite burden in liver 42 hours after sporozoite challenge (C), and *in vitro* sporozoite neutralizing activity of pooled serum samples (D). Mice were immunized with or without adjuvant.

[0062] Fig. 45 illustrates a prime and boost immunization regimen with capsid-modified PyCS adenoviruses having (QGPGAP)_n repeats (SEQ ID NO:59, n=6, 9, 12) in HVR1(A), PyCS-specific humoral responses at week 9 (B), PyCS-specific CD8⁺ T cell responses at week 9 (C), and malaria parasite burden in liver 42 hours after sporozoite challenge (D). Mice were immunized with or without adjuvant.

[0063] Fig. 46 shows PfCSP protein expression in AD293 cells after transient transfection with PfCSP/pShuttle-CMV. PfCSP was detected by western blotting using mouse monoclonal anti-NANP antibody (2A10).

[0064] Fig. 47 illustrates the results of silver staining and western blotting (A), and ELISA assay (B) of the purified capsid-modified recombinant PfCSP adenoviruses to confirm the (NANP)₄ epitope (SEQ ID NO:60; n=4) insertion into adenovirus capsid proteins. The inserted (NANP)₄ epitope (SEQ ID NO:60; n=4)

was detected with mouse monoclonal anti-NANP antibody (2A10). In the ELISA assay, ELISA plates were coated directly with purified adenoviruses.

[0065] Fig. 48 shows the results of silver staining and western blotting (A) and ELISA assay (B) of the purified capsid-modified recombinant PfCSP adenoviruses to confirm the (NANP)_n epitope (SEQ ID NO:60; n=4, 6, 8, 10, 12, 14, 16, 18, 20, 22) insertion into adenovirus capsid proteins. In the ELISA assay, ELISA plates were coated directly with purified adenoviruses and the inserted epitope in adenovirus particles was detected with anti-PfCSP antibody (2A10).

[0066] Fig. 49 illustrates the prime and boost immunization regimen with capsid-modified recombinant PfCSP adenoviruses having (NANP)₄ (SEQ ID NO:60; n=4) (A) and PfCSP-specific humoral responses at week 9 (B).

[0067] Fig. 50 illustrates the prime and boost immunization regimen with capsid-modified recombinant PfCSP adenoviruses having (NANP)_n (SEQ ID NO:60; n=4, 6, 8, 10) in HVR1 (A) and PfCSP-specific humoral responses at week 9 (B).

[0068] Fig. 51 illustrates the prime and boost immunization regimen with capsid-modified recombinant PfCSP adenoviruses having (NANP)_n (SEQ ID NO:60; n=10, 16, 22) in HVR1 (A) and PfCSP-specific humoral responses at week 9 (B). Mice were immunized with or without adjuvant.

[0069] Fig. 52 illustrates the result of silver staining analysis of purified (QGPGAP)₃-modified Fiber and pVII-1 ((QGPGAP)₃-Fib/CD4-pVII-1/PyCS-GFP) adenovirus (A) and anti-QGPGAP antibody titer at week 10 in mice immunized with (QGPGAP)₃-Fib/PyCS-GFP or (QGPGAP)₃-Fib/CD4-pVII-1/PyCS-GFP as described in Fig. 49 (B). The results of two independent experiments were plotted in the figure after normalization with the median antibody titers in B-Fib/PyCS-GFP-immunized group.

[0070] Fig. 53 shows schematic diagrams of the structure of the adenovirus pVII proteins with the PfCSP CD4⁺ epitope sequence EYLNKIQNLSLSTEWSPCSVT (SEQ ID NO:62) inserted at the before the first

Nuclear Localization Signal (NLS) of pVII (PfCD4-pVII-2; SEQ ID NO:28, nucleic acid; SEQ ID NO:57, amino acid) and between the two NLSs of pVII (PfCD4-pVII-3; SEQ ID NO:29, nucleic acid; SEQ ID NO:58, amino acid) (A) and the results of silver staining to confirm the epitope insertion into pVII (B).

[0071] Fig. 54 illustrates the prime and boost immunization regimen with HVR1 and pVII-modified recombinant PfCSP adenoviruses (A), PfCSP-specific humoral responses at week 6 (B), and PfCSP-specific CD4+ (EYLNKIQNSLSTEWSPCSVT ; SEQ ID NO:62) response at week 9 (C).

[0072] Fig. 55 illustrates *in vitro* neutralization of recombinant adenovirus by human serum samples. AD293 cells were infected with recombinant adenoviruses in the presence of diluted human serum for overnight and GFP expression was measured as a marker of infection.

[0073] Fig. 56 illustrates the effect of anti-adenovirus immunity on the induction of PyCS-specific T cell response by capsid-modified PyCS-GFP adenoviruses *in vivo*. (A) is the brief description of the study design. (B) shows PyCS-specific CD8+ T cell response in mice immunized with wild-type (wt)/empty adenovirus twice followed by priming with capsid-modified PyCS-GFP adenoviruses.

[0074] Fig. 57 illustrates the effect of anti-adenovirus immunity on the induction of PyCS-specific humoral immune response by capsid-modified PyCS-GFP adenoviruses *in vivo*. (A) is the brief description of the study design. (B) shows PyCS-specific humoral immune response in mice immunized with wild-type (wt)/empty adenovirus twice followed by two doses of capsid-modified PyCS-GFP adenoviruses.

MEANS FOR SOLVING THE PROBLEMS

[0075] The present inventors have found a novel recombinant adenovirus having a novel, capsid-modified structure that is derived from a recombinant adenovirus plasmid vector. The recombinant adenovirus is capable of infecting mammalian cells, causing the cells to express a *Plasmodium* circumsporozoite

protein. The recombinant adenovirus also has one or more capsid proteins that have been modified by having a desired immunogenic antigen, such as B cell epitope, T cell epitope of *Plasmodium* circumsporozoite protein. The recombinant adenovirus is obtained by the method of transfecting cells with the linearized recombinant adenovirus plasmid vector. Using the obtained recombinant adenovirus, the present inventors carried out extensive research on pharmaceuticals containing as an active ingredient a recombinant adenovirus having malaria infection preventive and therapeutic effects. As a result, the inventors found that the obtained recombinant adenovirus has the desired pharmaceutical effects.

DETAILED DESCRIPTION

[0076] The following description provides specific details for a thorough understanding of, and enabling description for, embodiments of the disclosure. However, one skilled in the art will understand that the disclosure may be practiced without these details. In other instances, well-known structures and functions have not been shown or described in detail to avoid unnecessarily obscuring the description of the embodiments of the disclosure.

[0077] The abbreviations used for the amino acids, peptides, base sequences, and nucleic acids in the present disclosure are based on the abbreviations specified in the IUPAC-IUB Communication on Biochemical Nomenclature, Eur. J. Biochem., 138: 9 (1984), "Guideline for Preparing Specifications Including Base Sequences and Amino Acid Sequences" (United States Patent and Trademark Office), and those commonly used in this technical field.

[0078] A "nucleotide sequence," "polynucleotide" or "DNA molecule" as contemplated by the current disclosure, may include double strand DNA or single strand DNA (i.e., a sense chain and an antisense chain constituting the double strand DNA), and is not limited to a full length thereof. Nucleotide sequences encoding an immunogenic foreign gene, such as those disclosed herein below, encompass double strand DNA containing genomic DNA, single strand DNA (sense chain) containing cDNA, single strand DNA (antisense chain) having a

sequence complementary to the sense chain, synthetic DNA, and fragments thereof, unless otherwise mentioned.

[0079] Nucleotide sequences, polynucleotides or DNA molecules as used herein are not limited to the functional region, and may include at least one of an expression suppression region, a coding region, a leader sequence, an exon, and an intron. Further, examples of nucleotide sequences or polynucleotides may include RNA or DNA. A polypeptide containing a specific amino acid sequence and a polynucleotide containing a specific DNA sequence may include fragments, homologs, derivatives, and mutants of the polynucleotide. Examples of mutants of a nucleotide sequence or polynucleotide (such as mutant DNA), include naturally occurring allelic mutants; artificial mutants; and mutants having deletion, substitution, addition, and/or insertion. It should be understood that such mutants encode polypeptides having substantially the same function as the polypeptide encoded by the original non-mutated polynucleotide.

[0080] The present disclosure relates to a recombinant adenovirus that can express an antigenic determinant of a *Plasmodium* parasite, and comprises one or more modified capsid and/or core proteins. The recombinant adenovirus is derived from a recombinant adenovirus plasmid vector, the generation of which is described in the Examples below. The use of adenovirus as a vector is discussed further below. The recombinant adenovirus plasmid vectors described herein may be used as a malaria vaccine or pharmaceutical composition, wherein both humoral and cellular immune responses against the *Plasmodium* parasite are induced.

[0081] The *Plasmodium* parasite may be selected from any of the known *Plasmodium* (*P.*) species, for example, *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax*, *P. knowlesi*, *P. berghei*, *P. chabaudi* and *P. yoelii*. In some embodiments, the antigenic determinant is derived from the rodent-specific *Plasmodium yoelii* or the human-specific *Plasmodium falciparum*

[0082] In one embodiment, a recombinant adenovirus capsid-modified plasmid vector (also described as a recombinant adenovirus plasmid vector

herein) is a plasmid that encodes and produces a capsid and/or core-modified recombinant adenovirus (also described as a recombinant adenovirus herein) that has a structure comprising one or more modified capsid and/or core proteins. In accordance with the embodiments of the disclosure, the modification of the capsid and/or core proteins may be accomplished by insertion of at least one immunogenic epitope of a *Plasmodium* circumsporozoite protein. Alternatively, at least part of the capsid and/or core protein may be deleted and replaced by at least one immunogenic epitope of a *Plasmodium* circumsporozoite protein. In some embodiments, the immunogenic epitope is a B-cell and/or T-cell epitope of a *Plasmodium* circumsporozoite protein. The addition of a B cell or T cell epitope may serve to enhance the efficacy of an adenoviral vector used as a malaria vaccine by establishing or enhancing the humoral immune response to the CS protein. The modified capsid and core proteins and their significance with respect to their use in the recombinant adenovirus described herein are discussed further below.

[0083] The one or more modified capsid and/or core proteins may be a modified Hexon protein, a modified Fiber protein, a modified pVII protein or a combination thereof. In one embodiment, a portion of a Hexon hypervariable region (HVR) and/or a portion of Fiber protein is replaced by at least one B-cell and/or T-cell epitope of a *Plasmodium* circumsporozoite protein. Alternatively, one or more B-cell and/or T cell epitope of a *Plasmodium* circumsporozoite protein may be inserted in the Fiber protein or Hexon HVR. In some aspects, the modified HVR may be HVR1, HVR2, HVR3, HVR4, HVR5, HVR6 or HVR7. In other aspects, the modified HVR may be HVR1 or HVR5. In some embodiments, the HVR-modified Hexon may have a nucleic acid sequence of SEQ ID NO:3 (Fig. 11), SEQ ID NO:4 (Fig. 12), SEQ ID NO:5 (Fig. 13), SEQ ID NO:6 (Fig. 14), SEQ ID NO:7 (Fig. 15), SEQ ID NO:8 (Fig. 16), SEQ ID NO:9 (Fig. 17), SEQ ID NO:10 (Fig. 18), SEQ ID NO:11 (Fig. 19), SEQ ID NO:12 (Fig. 20), SEQ ID NO:13 (Fig. 21), SEQ ID NO:14 (Fig. 22), SEQ ID NO:15 (Fig. 23), SEQ ID NO:16 (Fig. 24), SEQ ID NO:17 (Fig. 25), SEQ ID NO:18 (Fig. 26), SEQ ID NO:19 (Fig. 27), SEQ ID NO:20 (Fig. 28), SEQ ID NO:21 (Fig. 29), SEQ ID NO:22 (Fig. 30), or SEQ ID

NO:23 (Fig. 31). In other embodiments, the modified Fiber protein may have a nucleic acid sequence of SEQ ID NO:24 (Fig. 32) or SEQ ID NO:25 (Fig. 33).

[0084] In another embodiment, a T-cell epitope of a *Plasmodium* circumsporozoite protein may be inserted into an adenovirus core pVII protein at any of the following sites: the C-terminus, before the first Nuclear Localization Signal (NLS) or between the two NLS. Alternatively, a T-cell epitope of a *Plasmodium* circumsporozoite protein may replace a portion of the pVII protein. In some embodiments, the modified pVII protein may have a nucleic acid sequence of SEQ ID NO:26 (Fig.34), SEQ ID NO:27 (Fig.35), SEQ ID NO:28 (Fig.36) or SEQ ID NO:29 (Fig.37).

[0085] In the recombinant adenovirus may express a transgenic protein or recombinant transgenic protein. In some embodiments, the transgenic protein or recombinant transgenic protein is a *Plasmodium* circumsporozoite protein or an antigenic determinant that is encoded by a recombinant adenovirus plasmid vector as described herein, and is expressed by a recombinant adenovirus produced by said recombinant adenovirus plasmid vector after infection of one or more host cells,

[0086] Thus, in some embodiments, the recombinant adenovirus plasmid vectors comprise a nucleotide sequence encoding a recombinant transgenic protein. In one embodiment, the recombinant transgenic protein may comprise an antigenic determinant of *P. yoelii*, a rodent-specific parasite, wherein the antigenic determinant comprises a *P. yoelii* circumsporozoite (CS) protein gene or an antigenic portion thereof. In another embodiment, the recombinant transgenic protein may comprise an antigenic determinant of *P. falciparum*, a human-specific parasite, wherein the antigenic determinant comprises a *P. falciparum* circumsporozoite gene (CS) protein or an antigenic portion thereof. The *P. falciparum* CS protein has demonstrated prevention of malaria when used as the basis of active immunization in humans against mosquito-borne infection. The antigenic determinant may further comprise an immunogenic epitope, such as a B cell and/or T cell epitope.

[0087] In some embodiments, the CS protein is codon-optimized for enhanced expression in a subject. Codon-optimization is based on the required amino acid content, the general optimal codon usage in the subject of interest as well as any aspects that should be avoided to ensure proper expression. Such aspects may be splice donor or acceptor sites, stop codons, polyadenylation (pA) signals, GC- and AT-rich sequences, internal TATA boxes, or any other aspects known in the art. In some embodiments, the DNA sequence of the codon-optimized CS transgene is shown in Fig. 9 (SEQ ID NO:1, *P. yoelii*) and Fig. 10 (SEQ ID NO: 2, *P. falciparum*).

[0088] In some embodiments, the recombinant adenovirus plasmid vector may be one of the following modified *P. falciparum* recombinant adenovirus plasmid vectors: HVR1-modified adenovirus vector (NANP-HVR1/PfCSP) constructed as shown in Fig. 2, using a B cell epitope coding sequence of (NANP)_n (SEQ ID NO:60); Fiber-modified adenovirus vector (NANP-Fib/PfCSP) constructed as shown in Fig. 4, using a B cell epitope coding sequence of (NANP)_n (SEQ ID NO:60); HVR1 and Fiber-modified adenovirus vector (NANP-HVR1/B-Fib/PfCSP) constructed as shown in Fig. 5, using a B cell epitope coding sequence of (NANP)_n (SEQ ID NO:60); HVR1 and pVII-modified adenovirus vector (NANP-HVR1/CD4-pVII/PfCSP) constructed as shown in Fig.7, using a B cell epitope of (NANP)_n (SEQ ID NO:60) and a CD4 epitope coding sequence of EYLNKIQNSLSTEWSPCSVT (SEQ ID NO:62); Fiber and pVII-modified adenovirus vector (NANP-Fib/CD4-pVII/PfCSP) constructed as shown in Fig. 6, using a B cell epitope of (NANP)_n (SEQ ID NO:60) and a CD4 epitope coding sequence of EYLNKIQNSLSTEWSPCSVT (SEQ ID NO:62); and HVR1, Fiber and pVII-modified adenovirus vector (NANP-HVR1/Fib/CD4-pVII/PfCSP) constructed as shown in Fig. 8, using a B cell epitope of (NANP)_n (SEQ ID NO:60) and a CD4 epitope coding sequence of EYLNKIQNSLSTEWSPCSVT (SEQ ID NO:62).

[0089] In other embodiments, the recombinant adenovirus plasmid vector may be one of the following modified *P. yoelii* recombinant adenovirus plasmid vectors: HVR1-modified adenovirus vector (QGPGAP-HVR1/PyCS) constructed

as shown in Fig. 2, using a B cell epitope coding sequence of (QGPGAP)_n (SEQ ID NO:59); Fiber-modified adenovirus vector (QGPGAP-Fib/PyCS) constructed as shown in Fig. 4, using a B cell epitope coding sequence of (QGPGAP)_n (SEQ ID NO:59); HVR1 and Fiber-modified adenovirus vector (QGPGAP-HVR1/B-Fib/PyCS) constructed as shown in Fig. 5, using a B cell epitope coding sequence of (QGPGAP)_n (SEQ ID NO:59); HVR1 and pVII-modified adenovirus vector (QGPGAP-HVR1/CD4-pVII/PyCS) constructed as shown in Fig.7, using a B cell epitope of (QGPGAP)_n (SEQ ID NO:59) and a CD4 epitope coding sequence of YNRNIVNRLLGDALNGKPEEK, (SEQ ID NO:61); Fiber and pVII-modified adenovirus vector (QGPGAP-Fib/CD4-pVII/PyCS) constructed as shown in Fig. 6, using a B cell epitope of (QGPGAP)_n (SEQ ID NO:59) and a CD4 epitope coding sequence of YNRNIVNRLLGDALNGKPEEK, (SEQ ID NO:61); and HVR1, Fiber and pVII-modified adenovirus vector (QGPGAP-HVR1/Fib/CD4-pVII/PyCS) constructed as shown in Fig. 8, using a B cell epitope of (QGPGAP)_n (SEQ ID NO:59) and a CD4 epitope coding sequence of YNRNIVNRLLGDALNGKPEEK, (SEQ ID NO:61).

[0090] In other embodiments, a recombinant adenovirus may be produced by one of the following modified *P. falciparum* or *P. yoelii* recombinant adenovirus plasmid vectors: NANP-HVR1/PfCSP or QGPGAP-HVR1/PyCS (Fig. 2), NANP-Fib/PfCSP or QGPGAP-Fib/PyCS (Fig. 4), NANP-HVR1/B-Fib/PfCSP or QGPGAP-HVR1/B-Fib/PyCS (Fig. 5), NANP-HVR1/CD4-pVII/PfCSP or QGPGAP-HVR1/CD4-pVII/PyCS (Fig.7), NANP-Fib/CD4-pVII/PfCSP or QGPGAP-Fib/CD4-pVII/PyCS (Fig. 6), NANP-HVR1/Fib/CD4-pVII/PfCSP or QGPGAP-HVR1/Fib/CD4-pVII/PyCS (Fig. 8). The recombinant adenovirus may be produced in accordance with the methods described herein for producing a recombinant adenovirus plasmid vector with the ability to express a recombinant transgenic protein (e.g., *Plasmodium* CS protein) in mammalian host cells.

[0091] Purification of a recombinant adenovirus may be performed by using known virus purification methods. For example, purification of 0.5 to 1.0 mL of a stock virus obtained by the method of producing a recombinant adenovirus protein by inoculating insect cells (1×10^7 cells/10 cm dish), such as AD293 cells. The

culture supernatant is then collected several days after the infection, and a virus pellet obtained by centrifugation is suspended in a buffer, such as PBS (Phosphate Buffered Saline). The resulting suspension is subjected to a sucrose gradient of 10 to 60% and then centrifuged (25,000 rpm for 60 minutes at 4°C) to collect a virus band. The collected virus is further suspended in PBS, subsequently centrifuged under the same conditions as above, and the resulting purified recombinant virus pellet is stored at 4°C in a buffer, such as PBS.

[0092] Another embodiment is directed to a pharmaceutical composition essentially comprising at least one active ingredient. In one embodiment, an active ingredient of the pharmaceutical composition may comprise a recombinant adenovirus, which may be obtained by the genetic engineering techniques described herein. More specifically, the active ingredient may be a recombinant adenovirus comprising modified capsid and/or core proteins, wherein a portion of a Hexon hypervariable region (HVR), a portion of Fiber protein, a portion of pVII protein or a combination thereof is replaced by at least one immunogenic epitope of *Plasmodium* circumsporozoite protein. Alternatively, one or more B-cell and/or T cell epitope of a *Plasmodium* circumsporozoite protein may be inserted in the Fiber protein, Hexon HVR or pVII protein. The recombinant adenovirus plasmid vector further comprises a transgenic protein or recombinant transgenic protein that is expressed by the recombinant adenovirus after infecting one or more host cells. The transgenic protein or recombinant transgenic protein may be a *Plasmodium* circumsporozoite protein or a malaria antigen of a *Plasmodium* circumsporozoite protein, wherein the malaria antigen comprises at least one immunogenic epitope (e.g., a B cell or T cell epitope) of *Plasmodium* circumsporozoite protein.

[0093] In some embodiments, the active ingredient of the pharmaceutical composition is a recombinant adenovirus derived from a recombinant adenovirus plasmid vector, wherein the recombinant adenovirus plasmid vector is one of the following modified *P. falciparum* or *P. yoelii* recombinant adenovirus plasmid vectors: NANP-HVR1/PfCSP or QGPGAP-HVR1/PyCS (Fig. 2), NANP-Fib/PfCSP or QGPGAP-Fib/PyCS (Fig. 4), NANP-HVR1/B-Fib/PfCSP or QGPGAP-HVR1/B-

Fib/PyCS (Fig. 5), NANP-HVR1/CD4-pVII/PfCSP or QGPGAP-HVR1/CD4-pVII/PyCS (Fig.7), NANP-Fib/CD4-pVII/PfCSP or QGPGAP-Fib/CD4-pVII/PyCS (Fig. 6), NANP-HVR1/Fib/CD4-pVII/PfCSP or QGPGAP-HVR1/Fib/CD4-pVII/PyCS (Fig. 8). These recombinant adenovirus plasmid vectors are capable of producing recombinant adenoviruses when transfected into cells (e.g., AD293 cells) and wherein the recombinant transgenic protein may be expressed in mammalian cells, including human cells.

[0094] . When given to a subject, a pharmaceutical composition having an active ingredient is a recombinant adenovirus as described herein enhances malaria infection-preventing effects against a malaria infectious antigen and reduces the infectivity titer, as described further in the Examples below. Thus, the recombinant adenovirus may be used for the treatment of malaria infections associated with infection of target cells and tissues. Examples of target cells affected by such malaria infection include blood cells, hepatic cells, renal cells, brain cells, lung cells, epithelial cells, and muscular cells. Examples of tissues comprising such cells include the lung, liver, kidney, brain, arteries and veins, the stomach, intestines, urethra, skin, and muscle.

[0095] In some aspects, the pharmaceutical composition may enhance malaria infection- preventing effects against infectious antigens, for example, malaria antigens such as sporozoite surface antigens (Circumsporozoite Protein (CSP) and Thrombospondin Related Adhesive Protein (TRAP)) of malaria parasites, merozoite surface membrane protein (MSPI), malaria S antigen secreted from erythrocytes infected with malaria, and *P. falciparum* Erythrocyte Membrane Protein-1 (PfEMPI) protein present in the knobs of erythrocytes infected with malaria. The pharmaceutical composition may enhance malaria infection-preventing effects against a *Plasmodium* parasite, selected from any known *Plasmodium* (*P*) species, for example, *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax*, *P. knowlesi*, *P. berghei*, *P. chabaudi* and *P. yoelii*, by reducing the infectivity titer. When administered to a subject, a reduction of the infectivity titer by the pharmaceutical composition may result in an increased survival, disease-free survival, or infection-free survival period and survival, disease-free survival,

or infection-free survival rate when compared to subjects not administered the pharmaceutical composition. Thus, in some aspects, the pharmaceutical composition is useful as a preventive or therapeutic agent for malaria infections caused by pathogens such as *Plasmodium*. In further aspects, the pharmaceutical composition is useful as a preventive or therapeutic agent for complications resulting from a malaria infection caused by pathogens such as *Plasmodium*.

[0096] The infection-preventing effect of the recombinant adenovirus of the present invention in a subject can be provided, for example, by administering the pharmaceutical composition containing the capsid-modified recombinant adenovirus of the present invention and additives for pharmaceutical administration to vertebrates, particularly mammals, including humans, by intramuscular (i.m.), subcutaneous (s.c.), intracutaneous (i.c.), intradermal (i.d.), intraperitoneal (i.p.), nasal, or respiratory route, and then immunizing the vertebrates with the pharmaceutical composition containing the recombinant adenovirus described herein as an active ingredient several times. To evaluate the infection-preventing effect, the survival rate, disease-free survival, or infection-free survival of subjects immunized with the pharmaceutical composition several times followed by infection by a target pathogen (such as a selected *Plasmodium* species) may be compared with the survival rate, disease-free survival, or infection-free survival of subjects not given the pharmaceutical composition.

[0097] In some embodiments, the pharmaceutical composition may additionally comprise a pharmaceutically effective amount of capsid and/or core-modified recombinant adenovirus as described herein and a pharmaceutically acceptable carrier, which is described further below.

[0098] Another embodiment is directed to a vaccine composition essentially comprising at least one active ingredient. In one embodiment, an active ingredient of the vaccine composition may comprise a recombinant adenovirus, derived from a recombinant adenovirus plasmid vector as described herein. More specifically, the active ingredient may be a recombinant adenovirus comprising modified capsid or core proteins, wherein a portion of a Hexon hypervariable

region (HVR), a portion of Fiber protein, a portion of pVII protein or a combination thereof are replaced by at least one immunogenic epitope of *Plasmodium* circumsporozoite protein. Alternatively, at least one immunogenic epitope of a *Plasmodium* circumsporozoite protein may be inserted in the pVII protein, Fiber protein or Hexon HVR, or a combination thereof. In some embodiments, the active ingredient of the vaccine composition may be derived from a recombinant adenovirus plasmid vector illustrated in Figs. 2-8, for example, NANP-HVR1/PfCSP or QGPGAP-HVR1/PyCS (Fig. 2), NANP-Fib/PfCSP or QGPGAP-Fib/PyCS (Fig. 4), NANP-HVR1/B-Fib/PfCSP or QGPGAP-HVR1/B-Fib/PyCS (Fig. 5), NANP-HVR1/CD4-pVII/PfCSP or QGPGAP-HVR1/CD4-pVII/PyCS (Fig. 7), NANP-Fib/CD4-pVII/PfCSP or QGPGAP-Fib/CD4-pVII/PyCS (Fig. 6), NANP-HVR1/Fib/CD4-pVII/PfCSP or QGPGAP-HVR1/Fib/CD4-pVII/PyCS (Fig. 8).

[0099] In some aspects, the vaccine composition, when administered to a subject, first comprises a recombinant adenovirus having one or more antigenic portions of a *Plasmodium* CS protein (i.e., a B cell epitope, T cell epitope or both) inserted into or replacing at least a part of a capsid or core protein. The vaccine composition may then express a recombinant transgenic protein, wherein the recombinant transgenic protein is a *Plasmodium* CS protein comprising a B cell epitope, T cell epitope or both. The antigenic portions of the *Plasmodium* CS protein are found in the recombinant transgenic protein and the modified capsid or core proteins promote or enhance acquired humoral immunity, cellular immunity, or both as described in the Examples below. Thus, in some aspects, the recombinant adenovirus as described herein is useful as a vaccine to promote or enhance humoral immunity, cellular immunity, or both.

[00100] In further embodiments, the vaccine composition may enhance infection-preventing effects against infectious antigens, for example, malaria antigens such as sporozoite surface antigens (CSP and TRAP) of malaria parasites, merozoite surface membrane protein MSP1, malaria S antigen secreted from erythrocytes infected with malaria, PfEMPI protein present in the knobs of erythrocytes infected with malaria, Serine-Rich Antigen (SERA) protein, Tyrosine-

Rich Acidic Matrix Protein (TRAMP), and Apical Membrane Antigen-1 (AMA1) protein. Further, a reduced infectivity titer (e.g., the viral infectivity titer) resulting from administration of a vaccine composition described herein may result in an increased survival, disease-free survival or infection-free survival period and survival, disease-free survival or infection-free survival rate when compared to subjects not administered the vaccine composition. Thus, in some aspects, the vaccine composition is also useful as a preventive or therapeutic agent for malaria infections caused by pathogens such as *Plasmodium*. In further aspects, the vaccine composition is also useful as a preventive or therapeutic agent for complications resulting from a malaria infection by pathogens such as *Plasmodium*.

[00101] A vaccine composition as described herein may comprise a therapeutically effective amount of a recombinant adenovirus as described herein, and further comprising a pharmaceutically acceptable carrier according to a standard method. Examples of acceptable carriers include physiologically acceptable solutions, such as sterile saline and sterile buffered saline.

[00102] In some embodiments, the vaccine or pharmaceutical composition may be used in combination with a pharmaceutically effective amount of an adjuvant to enhance the anti-malaria effects. Any immunologic adjuvant that may stimulate the immune system and increase the response to a vaccine, without having any specific antigenic effect itself may be used as the adjuvant. Many immunologic adjuvants mimic evolutionarily conserved molecules known as pathogen-associated molecular patterns (PAMPs) and are recognized by a set of immune receptors known as Toll-like Receptors (TLRs). Examples of adjuvants that may be used in accordance with the embodiments described herein include Freund's complete adjuvant, Freund's incomplete adjuvant, double stranded RNA (a TLR3 ligand), LPS, LPS analogs such as monophosphoryl lipid A (MPL) (a TLR4 ligand), flagellin (a TLR5 ligand), lipoproteins, lipopeptides, single stranded RNA, single stranded DNA, imidazoquinolin analogs (TLR7 and TLR8 ligands), CpG DNA (a TLR9 ligand), Ribi's adjuvant (monophosphoryl-lipid A/trehalose dicorynocolate), glycolipids (α -GalCer analogs), unmethylated CpG islands, oil

emulsion, liposomes, virosomes, saponins (active fractions of saponin such as QS21), muramyl dipeptide, alum, aluminum hydroxide, squalene, BCG, cytokines such as GM-CSF and IL-12, chemokines such as MIP 1- α and RANTES, N-acetylmuramine-L-alanyl-D-isoglutamine (MDP), thymosin α 1 and MF59. The amount of adjuvant used can be suitably selected according to the degree of symptoms, such as softening of the skin, pain, erythema, fever, headache, and muscular pain, which might be expressed as part of the immune response in humans or animals after the administration of this type of vaccine.

[00103] In some embodiments, the vaccine or pharmaceutical composition described herein may be used in combination with other known pharmaceutical products, such as immune response-promoting peptides and antibacterial agents (synthetic antibacterial agents). The vaccine or pharmaceutical composition may further comprise other drugs and additives. Examples of drugs or additives that may be used in conjunction with a vaccine or pharmaceutical composition described herein include drugs that aid intracellular uptake of the recombinant adenovirus or recombinant transgenic protein of the present invention, liposome and other drugs and/or additives that facilitate transfection, (e.g., fluorocarbon emulsifiers, cochleates, tubules, golden particles, biodegradable microspheres, and cationic polymers).

[00104] In some embodiments, the amount of the active ingredient contained in the vaccine or pharmaceutical composition described herein may be selected from a wide range of concentrations, Virus Particle Unit (VPU), Plaque Forming Unit (PFU), weight to volume percent (w/v %) or other quantitative measure of active ingredient amount, as long as it is a therapeutically or pharmaceutically effective amount. The dosage of the vaccine or pharmaceutical composition may be appropriately selected from a wide range according to the desired therapeutic effect, the administration method (administration route), the therapeutic period, the patient's age, gender, and other conditions, etc.

[00105] In some aspects, when a recombinant adenovirus is administered to a human subject as an active ingredient of the vaccine or pharmaceutical composition, the dosage of the recombinant adenovirus may be administered in

an amount approximately corresponding to 10^2 to 10^{14} PFU, preferably 10^5 to 10^{12} PFU, and more preferably 10^6 to 10^{10} PFU per patient, calculated as the PFU of the recombinant virus.

[00106] In further aspects, when a recombinant adenovirus is administered to a subject as an active ingredient of the vaccine or pharmaceutical composition, the dosage may be selected from a wide range in terms of the amount of expressible DNA introduced into the vaccine host or the amount of transcribed RNA. The dosage also depends on the strength of the transcription and translation promoters used in any transfer vectors used.

[00107] In some embodiments, the vaccine composition or pharmaceutical composition described herein may be administered by directly injecting a recombinant adenovirus suspension prepared by suspending the recombinant adenovirus in PBS (phosphate buffered saline) or saline into a local site (e.g., into the lung tissue, liver, muscle or brain), by nasal or respiratory inhalation, or by intravascular (i.v.) (e.g., intra-arterial, intravenous, and portal venous), subcutaneous (s.c.), intracutaneous (i.c.), intradermal (i.d.), or intraperitoneal (i.p.) administration. The vaccine or pharmaceutical composition of the present invention may be administered more than once. More specifically, after the initial administration, one or more additional vaccinations may be given as a booster. One or more booster administrations can enhance the desired effect. After the administration of the vaccine or pharmaceutical composition, booster immunization with a pharmaceutical composition containing the recombinant adenovirus as described herein may be performed.

[00108] In further embodiments, use of various other adjuvants, drugs or additives with the vaccine of the invention, as discussed above, may enhance the therapeutic effect achieved by the administration of the vaccine or pharmaceutical composition. The pharmaceutically acceptable carrier may contain a trace amount of additives, such as substances that enhance the isotonicity and chemical stability. Such additives should be non-toxic to a human or other mammalian subject in the dosage and concentration used, and examples thereof include buffers such as phosphoric acid, citric acid, succinic acid, acetic acid, and

other organic acids, and salts thereof; antioxidants such as ascorbic acid; low molecular weight (e.g., less than about 10 residues) polypeptides (e.g., polyarginine and tripeptide) proteins (e.g., serum albumin, gelatin, and immunoglobulin); amino acids (e.g., glycine, glutamic acid, aspartic acid, and arginine) ; monosaccharides, disaccharides, and other carbohydrates (e.g., cellulose and derivatives thereof, glucose, mannose, and dextrin) , chelating agents (e.g., EDTA); sugar alcohols (e.g., mannitol and sorbitol); counterions (e.g., sodium); nonionic surfactants (e.g., polysorbate and poloxamer) ; and PEG.

[00109] The vaccine or pharmaceutical composition containing a recombinant adenovirus described herein may be stored as an aqueous solution or a lyophilized product in a unit or multiple dose container such as a sealed ampoule or a vial.

[00110] Another embodiment further provides a method of preventing malaria infection, or a method of treating malaria comprising administering an effective amount of the recombinant adenoviral vaccine, formulation, or pharmaceutical composition. The present invention further provides a method of immunostimulation comprising administering an effective amount of a recombinant adenoviral vaccine composition, formulation, pharmaceutical composition or a combination thereof to a subject. Subjects may include humans, animals (such as mammals, birds, reptiles, fish, and amphibians), or any other subjects that may become infected with a malaria parasite. Malaria parasites may include a *Plasmodium* parasite, selected from any of known *Plasmodium* (*P*) species, for example, *P. falciparum*, *P. malariae*, *P. ovale*, *P. vivax*, *P. knowlesi*, *P. berghei*, *P. chabaudi* and *P. yoelii*.

[00111] In some embodiments, a recombinant adenovirus as described herein may be formed alone or may be together with a pharmaceutically acceptable carrier into a vaccine composition, formulation, or pharmaceutical composition, and administered to the subject. The administration route may be, for example, any administration route mentioned above. The pharmaceutically acceptable carrier for use in the present invention can be suitably selected from carriers commonly used in this technical field, according to the form of the

pharmaceutical composition to be produced. For example, when the pharmacological composition is formed into an aqueous solution, purified water (sterile water) or a physiological buffer solution can be used as the carrier. When the pharmaceutical composition is formed into other appropriate solutions, organic esters capable of being injected, such as glycol, glycerol and olive oil may be used as the carrier. The composition may contain stabilizers, excipients and other commonly used substances in this technical field, and particularly in the field of vaccine formulations.

[00112] In further embodiments, the amount of recombinant adenovirus used in a vaccine composition, formulation, or pharmaceutical composition may be suitably selected from a wide range of concentrations, VPU, PFU, weight to volume percent (w/v %) or other quantitative measure of active ingredient amount. In some aspects, a suitable range of recombinant adenovirus in the composition is preferably about 0.0002 to about 0.2 (w/v %), and more preferably 0.001 to 0.1 (w/v %). The method of administration of a recombinant adenovirus vaccine composition, formulation, or pharmaceutical composition according to some embodiments may be suitably selected according to the dosage form, the patient's age, gender and other conditions such as the severity of the disease. A suitable dosage form is a form for parenteral administration, such as injections, drops, nasal drops, and inhalants. When the composition is formed into an injection or drops, the injection can be intravenously administered and mixed with a replacement fluid such as a glucose solution or an amino acid solution as appropriate, or can be administered intramuscularly (i.m.), intracutaneously (i.c.), subcutaneously (s.c.) intradermally (i.d.), or intraperitoneally (i.p.).

[00113] In other embodiments, the daily dosage of a recombinant adenovirus vaccine composition, formulation, or pharmaceutical composition may vary depending on the subject's condition, body weight, age, gender, etc. In some aspects, the dosage of a recombinant adenovirus is administered in an amount of approximately 0.001 to 100 mg per kg of body weight per day. The vaccine, formulation, or composition of the invention may be administered in one or more administrations per day.

[00114] In further embodiments, when a recombinant adenovirus is administered to a human subject as an active ingredient of the vaccine composition, formulation or pharmaceutical composition, the dosage of the recombinant adenovirus is administered in an amount approximately corresponding to 10^2 to 10^{14} PFU, preferably 10^5 to 10^{12} PFU, and more preferably 10^6 to 10^{10} PFU per patient, calculated as the PFU of the recombinant adenovirus particle. The vaccine composition of the present invention should be administered according to Good Medical Practice, considering the clinical condition (for example, the condition to be prevented or treated) of each patient, the delivery site of the vaccine composition containing the recombinant adenovirus, the target tissue, the administration method, the dosage regimen, and other factors known to those skilled in the art. Therefore, the proper dosage of the vaccine composition herein is determined in consideration of the above.

[00115] Yet another embodiment of the disclosure relates to a method of treating or preventing a malaria infection in a subject, the method comprising administering an immunologic or therapeutic amount of a malaria vaccine composition comprising a recombinant adenovirus. The recombinant adenovirus of the malaria vaccine may comprise an antigenic determinant of a *Plasmodium* parasite, and may further comprise one or more modified capsid or core proteins. An immunologic, pharmacologic or therapeutic amount may be any suitable amount wherein a potent immune response is generated against one or more antigenic portions of the (CS) protein (i.e., the transgene, B cell epitope, or CD4+ T cell epitope) such that malarial infection is prevented or reduced in severity.

[00116] When a subject is first exposed or "primed" to an adenovirus vector, the immune system produces neutralizing antibodies against that specific vector. The immune response to the adenovirus is generally directed against the capsid proteins. Therefore, subsequent exposure to the same adenovirus vector, or "boosts," can reduce the efficacy of transgene expression. Therefore, in some embodiments, the method of treating or preventing a malaria infection described above may comprise a priming step using a first recombinant adenovirus vector followed by one or more boosting steps using one or more different recombinant

adenovirus vectors. This method may be used in subjects that have not yet been exposed to a wild-type adenovirus, or in a subject that has been previously exposed to a wild-type adenovirus vector, wherein the priming step recombinant adenovirus vector is used to circumvent existing adenovirus immunity. Further embodiments and examples are described below.

Adenovirus as a vector

[00117] Adenoviruses are non-enveloped DNA viruses comprising a set of viral capsid proteins (described below) and a viral genome, that have been widely used to deliver one or more therapeutic or antigenic transgene to a variety of cells *in vitro* and *in vivo*. Many adenovirus serotypes exist. Of the known adenovirus serotypes, serotype 5 (Ad5) is preferably used as a vector for foreign gene transduction because of its strong infectivity *in vivo* (Abbink et al. 2007).

Expression of the antigenic transgene may be controlled by any promoter or enhancer element known in the art. Promoters which may be used to control gene expression include, but are not limited to, cytomegalovirus immediate early promoter (CMV), simian virus 40 (SV40) early promoter, cellular polypeptide chain elongation factor 1 alpha (EF1) promoter, Rous sarcoma virus (RSV) promoter, and tetracycline-regulated (TR) promoter. A polyadenylation (pA) signal after the coding sequence may also be used for efficient transcription and translation. The recombinant adenovirus vector described herein may be replication-defective, having a deletion at least in the E1 region of the adenoviral genome, since the E1 region is required for replication, transcription, translation and packaging processes. In some aspects, the E2, E3 and/or E4 regions may also be deleted. In further aspects, a Kozak consensus sequence may be used for a more efficient translation (Kozak 1987).

[00118] The adenovirus (Ad) system is an attractive vector for the development of recombinant vaccines for a number of reasons. One reason is that recombinant adenoviral vectors infect most mammalian cell types (both replicative and non-replicative), including, but not limited to, mouse and human cell types. Thus, the same vector may be used successfully in mouse models and human clinical trials alike. Another reason is that any transferred genetic

information remains epichromosomal, avoiding insertional mutagenesis and alteration of the cellular genotype (Crystal 1995). Yet another reason is that the transgene remains unaltered after successive rounds of viral replication. Other advantages of using adenovirus include that recombinant adenovirus: 1) has a high virion stability, 2) is well tolerated, 3) may be grown at high titer, 4) can accommodate large transgenes, 5) has a genome that has been extensively studied for many years such that the complete DNA sequence of several serotypes is known, facilitating the manipulation of the Ad genome by recombinant DNA techniques (Graham and Prevec 1992).

[00119] In one embodiment, the adenovirus vaccine platform is used as a viral vector for development of a vaccine that targets a pre-erythrocytic malaria parasite, and provides protection from malaria infection. Among known recombinant viral vectors (Rodrigues et al. 1997, Bruña-Romero et al. 2001, Anderson et al. 2004, Tao et al. 2005), adenovirus has been shown to be a suitable viral vector for a malaria vaccine because it can induce a strong protective cellular immune response to pre-erythrocytic malaria parasites (Rodrigues et al. 1997). The malaria parasite may be any one of the *Plasmodium* family. In some embodiments, the targeted parasite may be *P. yoelii* or *P. falciparum*.

Adenovirus vectors expressing PyCS as a transgene elicits a malaria-specific CD8+ T cell response

[00120] Adenovirus is an attractive vector for inducing a significant CD8+ T cell-mediated protective immunity against malaria (Rodrigues et al. 1997, Rodrigues et al. 1998). The immunogenicity of a recombinant adenovirus expressing the *P. yoelii* (a rodent malaria parasite) CS protein, AdPyCS, was determined using a rodent malaria model. The inoculation of mice with AdPyCS induces complete immunity in a significant proportion of mice, preventing the occurrence of parasitemia (Rodrigues et al. 1997). This protective effect is primarily mediated by CD8+ T cells, as evidenced by depletion of the T cell population and is corroborated by the fact that AdPyCS was unable to induce high titers of antibody response against malaria parasites.

[00121] To quantitatively measure the infectivity of capsid-modified adenovirus, the shuttle vector may contain a GFP expression cassette and cloning sites for a transgene. The resulting shuttle vector (GFP/pShuttle-CMV) has dual pCMV promoters and SV40pAs for a transgene and GFP from pmaxGFP (Amara, Germany). The optimized PyCS fragment was inserted into KpnI and HindIII sites of GFP/pShuttle-CMV.

[00122] The immunogenicity of Ad(PyCS+GFP) was determined by measuring the magnitude of the CS-specific CD8⁺ T cell response and the level of protective immunity against the plasmodial liver stages. Administration of Ad(PyCS+GFP) via different routes, at an optimal dose, 10¹⁰ viral particle (v.p.) elicited the same pattern of anti-malarial protective responses that AdPyCS was shown to elicit, with the s.c. and i.m. routes inducing the strongest response resulted in the highest degree of liver stage inhibition in mice challenged with live *P. yoelii* sporozoites. This illustrates that as a vaccine, Ad(PyCS+GFP) behaves equivalently to AdPyCS (Rodrigues et al 1997), and is a potentially useful tool in determining the *in vivo* tropism of AdPyCS.

Adenovirus capsid and core proteins

[00123] The studies above confirm that recombinant adenoviral vectors expressing a CS protein elicit a strong cellular immune response by CD8⁺ T cells, but no appreciable humoral response. Therefore, because the humoral response to wild-type adenovirus can often be attributed to capsid proteins, recombinant adenoviral vectors with modified capsid and core proteins were constructed to 1) enhance humoral immunity via B cell activation, 2) enhance humoral immunity via T helper cell activation, and 3) circumvent existing adenoviral immunity.

[00124] Adenovirus is a non-enveloped naked double stranded DNA virus with an icosahedral shape, having 20 faces of equilateral triangles. The adenovirus capsid consists of 252 capsomers, of which 240 are Hexon trimers and 12 are penton pentamers. A Fiber protein, which projects from each penton base, mediates attachment to host cells by interaction with the cellular receptor. A secondary interaction occurs between the RGD (Asp-Arg-Gly) motif in the penton base with $\alpha\beta 3$, $\alpha\beta 5$ and similar integrins, facilitating subsequent

internalization of adenovirus into the cell (Mathias et al. 1994, Wickham et al. 1993). Most of the adenovirus use the coxsackie-adenovirus receptor, CAR, as a cellular receptor (Bergelson et al. 1997). In addition, MHC class I molecules, VCAM, and heparan sulfate, are shown to mediate attachment and entry of Ad5 (Chu et al. 2001, Hong et al. 1997). Following entry via endocytosis, the Ad5 rapidly escapes from endocytic compartments into the cytosol (Meier and Greber 2003, Leopold and Crystal 2007). The virion then translocates to the nucleus using microtubules. The Fiber protein is shed as the earliest capsid protein in the process (Nakano et al. 2000, Hong et al 2003). Adenoviruses of different serotypes demonstrate different trafficking patterns (Miyazawa et al. 1999, Miyazawa et al. 2001). Changing or modifying the Fiber protein can impact trafficking, which may be particularly important with regard to antigen processing and presentation, following infection of antigen presenting cells (APC).

[00125] The adenovirus Fiber is a trimer divided into Fiber tail, shaft and knob domains (Henry et al. 1994, Rux and Burnett 2004, Chroboczek et al. 1995). The three dimensional structure of the knob domain is known, and together with mutagenesis studies, these studies allow the areas involved in CAR interaction and trimerization to be visualized (Kirby et al. 1999, Xia et al. 1995). The Fiber shaft projects from the virion and the Fiber knob contains the Coxsackie and Adenovirus Receptor (CAR) interaction domain (Roelvink et al. 1999, Bewley et al. 1999). The CAR-binding site of the Fiber knob consists primarily of residues from the AB loop and CD loop and extends secondarily to the FG and HI loop and the B, E and F β sheets (Roelvink et al. 1999, Bewley et al. 1999). The HI loop has been the best studied insertion site on the Fiber knob (Worgall et al. 2004, Mizuguchi and Hayakawa 2004, Koizumi et al. 2003, Belousova et al. 2002, Nouredдини and Curiel 2005, Nicklin et al. 2001), and incorporation of an epitope into the HI loop (residue 543 and 544) resulted in potent anti-epitope immunity (Krause et al. 2006). Therefore, an immunodominant CS-derived B cell epitope was initially inserted into the HI loop of the Fiber protein.

[00126] Hexon is the most abundant protein of the adenovirus capsid with 720 copies per virion. In the mature virus, Hexon exists as homotrimeric

capsomeres which make up the facets of the icosahedral virion (Rux and Burnett 2004). The crystal structures of adenovirus serotypes 2 and 5 (Ad2 and Ad5) Hexons have been solved, revealing a complex molecular architecture (Athapilly et al. 1994, Roberts et al. 1986, Rux and Burnett 2000). The base of each monomeric subunit consists of two beta-barrel motifs that are present in the capsid proteins of many icosahedral viruses. Three long loops (DE1, FG1, and FG2) extend out from the base structure to form the tower region of each molecule (Rux and Burnett 2004). Sequences within these loop domains protrude to the surface of the capsid to form the exterior of the virion. Alignments from different adenovirus serotypes show that the sequences located on the capsid exterior are poorly conserved in both length and amino acid sequence (Crawford-Miksza and Schnurr 1996). Furthermore, it has been shown that the sequences located in these poorly conserved domains, termed hypervariable regions (HVRs), contain the determinants against which serotype-specific antibodies are produced (Top 1975, Rux and Burnett 2000, Top et al. 1971).

[00127] Based on early sequence alignments, seven HVRs were identified throughout the Hexon molecule (Crawford-Miksza and Schnurr 1996, Roberts et al 2006). Because the HVRs are poorly conserved between serotypes and do not appear to be involved in maintaining the structural integrity of Hexon, small changes could be made to these domains without affecting the viability of the virus (Rux and Burnett 2000). For example a hexahistidine tag can be inserted into HVR2, HVR3, HVR5, HVR6, and HVR7 without compromising virus viability (Wu et al. 2005). Thus, Hexon HVRs are often used as targets to efficiently induce an antibody response against peptides located in Hexon HVRs (Worgall et al. 2005, Crompton et al. 1994). Due to its poor conservation in length between serotypes and its position on the outermost surface of the adenovirus capsid (Rux and Burnett 2000, Crawford-Miksza and Schnurr 1996), Hexon HVR5 was initially chosen as a site for epitope insertion. Further, the crystal structure of Hexon indicates that HVR5 is a flexible loop on the capsid surface, suggesting that HVR5 can accommodate relatively large peptides without compromising the structural integrity of the capsid (Roberts et al. 1986). Hexon-specific CD4⁺ and CD8⁺ epitopes have recently been identified (Leen et al. 2008), and the CD4⁺ T cell

response to adenovirus is focused against conserved residues within the Hexon protein in humans (Onion et al. 2007, Heemskerk et al. 2006).

[00128] The adenovirus core is composed of the viral genome and four core proteins. The terminal protein (TP) is covalently linked to the 5' end of each linear viral DNA strand at two copies per virion. Noncovalently and nonspecifically bound to the viral DNA through arginine-rich portions are three other core proteins μ (μ), V (pV) and VII (pVII). pVII is the major core protein contributing roughly 700-800 copies per virion, and serves as a histone-like center around which viral DNA is wrapped to form nucleosome structures.

Modification of adenovirus capsid proteins to enhance humoral immunity

[00129] In some embodiments, circumsporozoite (CS) adenoviral vectors that have an immunodominant CS protein B epitope in an adenovirus capsid protein (inserted in the Hexon or Fiber) are described. The transgene may be under a promoter such as CMV to augment cell-mediated and humoral immune responses to CS protein.

[00130] A central repeat region is the conserved structure of CS protein among *Plasmodium* species, and antibody against this repeat sequence has been shown to have sporozoite neutralizing activity. Examples of a repeat sequence in *Plasmodium* CS protein are (NANP)_n repeat (*P. falciparum*; SEQ ID NO:60), ANGAGNQPG repeat (*P. vivax*; SEQ ID NO:63) and NAAG repeat (*P. malariae*; SEQ ID NO:64), which can be inserted into adenovirus capsid proteins. In some embodiments, four or more (NANP)_n repeats (SEQ ID NO:60) of PfCSP may be inserted into HVR1 of adenovirus serotype 5 Hexon. In some embodiments, two, four, six, eight, ten, fourteen, sixteen, eighteen, twenty, twenty-two, twenty-four, twenty-six, or twenty-eight (NANP)_n repeats (SEQ ID NO:60; n=2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28) of PfCSP are inserted into HVR1 of adenovirus serotype 5 Hexon. The (NANP)_n repeat sequence may be additionally inserted in the in the HI loop of Fiber.

[00131] In some embodiments, immunodominant neutralizing B cell epitopes to CS were mapped to develop improved CS protein adenovirus vaccines. Mice immunized with recombinant *P. yoelii* CS protein (PyCS) generated high titers against the two major immunodominant B epitopes, QGPGAP (SEQ ID NO:59) and QQPP (SEQ ID NO:65), but the *in vitro* neutralization assay indicated that the humoral immune response to QGPGAP epitope (SEQ ID NO:59) itself may account for neutralizing activity because the neutralization could be reversed by adding (QGPGAP)₃ peptide (SEQ ID NO:59; n=3) to the medium. In some embodiments, three or more (QGPGAP)_n repeats (SEQ ID NO:59) of PyCS are inserted into HVR1 of adenovirus serotype 5 Hexon. In some embodiments, three, four, five, six, seven, eight, nine, ten, eleven, or twelve (QGPGAP)_n repeats (SEQ ID NO:59; n=3, 4, 5, 6, 7, 8, 9, 10, 11, 12) of PyCS may be inserted into HVR1 of adenovirus serotype 5 Hexon. The (QGPGAP)_n repeat sequence may be additionally inserted in the in the HI loop of Fiber.

[00132] The B cell epitope peptide should be presented on the surface of adenovirus virions so that immune system can recognize the epitope efficiently. Such insertion sites could be HVRs of Hexon and Loop structures in Fiber, and different insertion sites can be combined.

Modification of adenovirus capsid and core proteins to enhance T helper cell activation

[00133] In another embodiment, a CD4⁺ epitope specific to the transgene used in an adenoviral vector may be incorporated into adenovirus proteins such as pVII, pV and Hexon to augment immunogenicity of the adenoviral-based vaccine. Professional antigen presenting cells (APC) such as dendritic cells (DC) and B cells can uptake particulated pathogens like virus particles via endocytosis and present CD4⁺ epitopes in the pathogen to CD4⁺ T cells which acts as helper cells for humoral and/or cellular immune responses. pVII and Hexon may easily be used as adenovirus target proteins to insert antigenic CD4⁺ peptides because of high copy number of pVII (700-800 copies) and Hexon (720 copies) in one virion.

Modification of adenovirus capsid proteins to circumvent existing adenovirus immunity

[00134] In some embodiments, adenovirus Fiber and Hexon capsid proteins may be modified to insert a B cell or T helper cell epitope to overcome existing immunity to adenovirus and/or enhance the humoral response to an adenovirus vaccine. An estimated 80% of young adults in human population have circulating neutralizing antibodies to adenovirus (Douglas 2007), especially to serotype 5 (Ad5). In studies utilizing adenovirus as a gene therapy vector, it was found that the presence of neutralizing antibodies in animals limits the expression of transgenes delivered by adenovirus. In addition to neutralizing antibodies, CD8+ T cell responses also contributed to the limitation of recombinant gene expression (Yang et al. 1995, Yang et al 1996). Such pre-existing immunity to adenovirus has previously been reported to inhibit the efficacy of a recombinant adenovirus vaccine (Papp et al. 1999) and also reduces immunogenicity of adenovirus-based vaccines in a clinical trial (Priddy et al. 2008).

[00135] Hexon is a major target for anti-Ad capsid immune responses (Roy et al. 2005, Wohlfart 1988), and is likely responsible for the potent adjuvant effect of adenovirus, including the induction of CD4+ and CD8+ T cell responses. Therefore, one strategy that has been employed to circumvent pre-existing anti-adenovirus immunity is to replace all or part of the Hexon with a different protein, for example, rare serotypes such as adenovirus 11, 24, 26 and 35. Because Hexon is a major target of anti-adenovirus neutralizing antibody (Youil et al. 2002, Sumida et al. 2005), the entire Hexon or HVRs of Hexon may be swapped with the rare serotypes (Wu et al. 2002, Roberts et al. 2006).

[00136] In another strategy as described in one embodiment herein, an adenoviral Hexon may be modified by replacement of HVR1 or HVR5 with an antigenic peptide to circumvent pre-existing anti-adenovirus immunity or anti-adenovirus neutralizing antibody induced by previous vaccination with adenoviral vector. In some embodiments, an antigenic peptide may be an immunogenic epitope of *Plasmodium* CS protein, and in certain aspects, the epitope may

comprise a central repeat sequence, CD4+ epitope sequence or CD8+ epitope sequence.

[00137] Repeat administration with an Ad vector of the same serotype is prevented due to anti-Ad immunity following immunization. Therefore, many Ad vaccines impede boosting of the vaccine by preventing expression and presentation of the antigen encoded by the transgene (Yang 1995, Hackett et al. 2000, Harvey et al. 1999, Mastrangeli et al. 1996). The addition of a specific epitope to the Ad capsid, such as those described in the examples below, may reduce or eliminate this impediment according to some embodiments.

[00138] The following examples are provided to better illustrate the embodiments and are not to be interpreted as limiting the scope of any claimed embodiment. The extent that specific materials are mentioned, it is merely for purposes of illustration and is not intended to limit the invention. One skilled in the art may develop equivalent means or reactants without the exercise of inventive capacity and without departing from the scope of the invention. It will be understood that many variations can be made in the procedures herein described while still remaining within the bounds of the present invention. It is the intention of the inventors that such variations are included within the scope of the invention.

Example 1: Construction of capsid-modified Plasmodium circumsporozoite protein adenovirus plasmid vectors and recombinant adenovirus particles

Epitope Mapping

[00139] First, an immunodominant neutralizing B cell epitope in PyCS was chosen. Naïve Balb/c mice were immunized with recombinant PyCS-protein with incomplete Freund adjuvant three times and the pooled serum was used to determine the critical epitope of neutralizing antibody.

[00140] Briefly, in the neutralizing assay, human CD81 expressing HepG2 cells were used as target cells. CD81 is a molecule necessary for malaria parasites to form parasitophorous vacuoles in hepatocytes where they multiply and develop into schizonts (Silvie et al 2006), thus greatly increasing the *in vitro* infectivity of sporozoites.

[00141] In this assay, PyCS synthetic peptides were added to the wells to block peptide specific antibody. The results of epitope mapping indicated that the PyCS central repeat sequence, QGPGAP (SEQ ID NO:59), is a more potent neutralizing epitope in PyCS than QQPP (SEQ ID NO:65). Therefore, insertion of the (QGPGAP)_n epitope (SEQ ID NO:59) was used to modify adenovirus capsid proteins, Hexon and/or Fiber.

Construction of capsid-modified plasmid vectors

[00142] Adenovirus shuttle vector pShuttle-CMV (STRATAGENE) was modified by inserting a GFP-expression cassette under the cloning site. First, BsmBI-SacI fragment (pCMV+GFP) and SacI-BsmBI fragment (SV40 poly A signal) of pmaxGFP (Lonza, Cologne, Germany) were blunted and inserted into the blunted Sall and KpnI sites of pUC19 respectively. The BamHI-EcoRI fragment of the resulting pCMV-GFP/pUC19 was inserted into the same sites of SV40pA/ pUC19 to create SV40pA-pCMV-GFP fragment. The fragment was blunted and inserted into the EcoRV site of pShuttle-CMV. The resulting shuttle vector (GFP/pShuttle-CMV) has dual pCMV promoters and SV40pAs for a transgene and GFP.

[00143] Another modification of the Adenovirus shuttle vector pShuttle-CMV was done to replace the CMV promoter region with CMV5 promoter from pQBI-AdCMV5 (QBIogene). The SgrAI-KpnI fragment of pShuttle-CMV was replaced with the fragment containing the CMV5 promoter sequence and the upstream sequence from CMV promoter in pShuttle-CMV to construct pShuttle-CMV5 vector.

[00144] The *P. yoelii* CS (PyCS) gene was codon-optimized except for the (QGPGAP)_n repeats (SEQ ID NO:59) by overlapping PCR reaction based on JCat codon-optimization algorithm (<http://www.jcat.de/>).

[00145] The PfCSP amino acid sequence of *P. falciparum* 3D7 strain was used as a template sequence for codon-optimization. Codon-optimization for protein expression in humans was done by Integrated DNA Technologies' (Coralville, IA USA) optimization software. DNA fragments that encode whole

PfCSP except for the GPI-anchored motif at the C-terminus (Fig. 10; SEQ ID NO:2) were synthesized by Integrated DNA Technologies

[00146] Codon-optimized PyCS gene (Fig. 9; SEQ ID NO:1) or PfCSP gene (Fig. 10; SEQ ID NO:2) was inserted into KpnI and HindIII sites of pShuttle-CMV, pShuttle-CMV5, or GFP/pShuttle-CMV. The resulting Plasmodium circumsporozoite protein coding adenovirus shuttle vectors were used for homologous recombination with AdEasy-1 to construct adenovirus genome which has Plasmodium circumsporozoite antigenic gene and intact adenovirus protein coding sequences. Briefly, Plasmodium circumsporozoite protein coding adenovirus shuttle vectors were linearized by PmeI digestion, and E. coli BJ5183 cells were co-transformed with the linearized shuttle vector and pAdEasy-1 vector (Bruna-Romero et al 2003) for homologous recombination.

[00147] Modification of adenovirus capsid proteins is summarized and illustrated in Fig. 1. Modification of HVR1 sequence in the adenovirus genome DNA is illustrated in Fig. 2. Briefly, AdEasy-1 was digested with SfiI and the 6.4kbp fragment was subcloned into EcoRI and PstI sites of pUC19 using EcoRI-SfiI and PstI-SfiI linker oligomers. To replace HVR1 with a Plasmodium circumsporozoite protein B cell epitope, the region containing AgeI and NdeI sites was amplified by two-step PCR using primers which have the epitope sequence instead of HVR1 sequence. The PCR product was digested with AgeI and NdeI, and then used to replace the native AgeI-NdeI region of SfiI fragment in SfiI/pUC19 vector. After confirming the sequence, the SfiI fragment of adenovirus genome DNA was replaced with the SfiI fragment containing the circumsporozoite epitope sequence to produce an HVR1- modified Hexon. In some embodiments, an HVR-modified Hexon may have a nucleic acid sequence of SEQ ID NO:3 (Fig. 11), SEQ ID NO:4 (Fig. 12), SEQ ID NO:5 (Fig. 13), SEQ ID NO:6 (Fig. 14), SEQ ID NO:7 (Fig. 15), SEQ ID NO:8 (Fig. 16), SEQ ID NO:9 (Fig. 17), SEQ ID NO:10 (Fig. 18), SEQ ID NO:11 (Fig. 19), SEQ ID NO:12 (Fig. 20), SEQ ID NO:13 (Fig. 21), SEQ ID NO:14 (Fig. 22), SEQ ID NO:15 (Fig. 23), SEQ ID NO:16 (Fig. 24), SEQ ID NO:17 (Fig. 25), SEQ ID NO:18 (Fig. 26), SEQ ID NO:19 (Fig. 27), SEQ

ID NO:20 (Fig. 28), SEQ ID NO:21 (Fig. 29), SEQ ID NO:22 (Fig. 30), or SEQ ID NO:23 (Fig. 31).

[00148] To insert (NANP)₂₈ (SEQ ID NO:60; n=28) in HVR1, a part of the central repeat region of codon-optimized PfCSP was amplified by PCR using primers having hexon-specific sequence at 5' and NANP-specific sequence at 3', and the resulting DNA fragment was inserted into the AgeI-NdeI region by second PCR.

[00149] For HVR5-modification, as illustrated in Fig. 3, XbaI site was introduced into HVR5 in the L1 Loop of Hexon in AdEasy-1 and then synthesized, phosphorylated double strand oligomer coding the Plasmodium circumsporozoite protein epitope was inserted into the XbaI site. The insertion was confirmed by sequencing (Fig 31; SEQ ID NO:23).

[00150] For Fiber-modification, as illustrated in Fig. 4, the SpeI-PacI fragment of AdEasy-1 was subcloned into EcoRI and PstI sites of pUC19 using EcoRI-PacI and PstI-SpeI linker oligomers. To insert a Plasmodium circumsporozoite protein B-cell epitope sequence into HI loop of Fiber knob, the region containing EcoNI (or NheI) and MfeI sites was amplified by two-step PCR using primers which have the epitope sequence. The PCR product was digested with EcoNI (or NheI) and MfeI, and then used to replace the native EcoNI (or NheI) -MfeI region of Fiber in SpeI-PacI/pUC19 vector. After confirming the sequence (Fig 32, SEQ ID NO:24; Fig 33, SEQ ID NO:25), the SpeI-PacI fragment of AdEasy-1 was replaced with the SpeI-PacI fragment containing the epitope sequence. The resulting Fiber-modified adenovirus DNA was used for homologous recombination with Plasmodium circumsporozoite protein coding adenovirus shuttle vector to produce Fiber-modified Plasmodium circumsporozoite protein adenovirus DNA.

[00151] To construct HVR1 and Fiber-modified adenovirus DNA which has two epitope insertions, SfiI-SfiI fragment of Fiber-modified adenovirus DNA was replaced with SfiI-SfiI fragment having the circumsporozoite protein epitope in HVR1 as illustrated in Fig. 5.

[00152] To modify the C-terminus of pVII, the region containing Sfi I and Sal I sites was amplified by two-step PCR using primers which have the circumsporozoite protein epitope sequence. The PCR product was digested with SfiI and Sall, and then used to replace the native SfiI-Sall region of SfiI/pUC19 vector (Fig. 6, 7 and 8). After confirming the sequence (Fig. 34, SEQ ID NO:26; Fig. 35, SEQ ID NO:27), the SfiI-SfiI fragment of HVR1 and/or Fiber-modified circumsporozoite protein adenovirus DNA was replaced with SfiI-SfiI fragment having the circumsporozoite protein epitope in pVII.

[00153] To insert the circumsporozoite protein CD4+ epitope sequence EYLNKIQNSLSTEWSPCSVT (SEQ ID NO:62) in the middle of pVII, about 7.7kb fragment of pAdEasy-1 was prepared by RsrII digestion and cloned between the EcoRI and HindIII sites of pUC19 plasmid using RsrII linker (RsrII/pUC19). The region containing Ascl and BglII sites in RsrII/pUC19 was amplified by two-step PCR using primers which have the epitope sequence. The PCR product was digested with Ascl and BglII, and then used to replace the native Ascl and BglII region in RsrII/pUC19 plasmid. After confirming the sequence of the replaced region (Fig. 36, SEQ ID NO:28; Fig. 37, SEQ ID NO:29), the RsrII fragment of HVR1-modified adenovirus DNA was replaced with the RsrII fragment containing the epitope sequence.

[00154] The recombinant adenoviruses listed in Table 1 (*P. yoelii*) and Table 2 (*P. falciparum*) below were produced to evaluate the effect of epitope insertion on infectivity, immunogenicity and sensitivity to pre-existing, anti-adenovirus immunity. Recombinant adenovirus vectors used were replication defective, E1 and E3-deleted adenovirus serotype 5 (STRATAGENE). Fig. 1 shows the schematic structure of capsid-modified Plasmodium circumsporozoite protein recombinant adenovirus.

Table 1. Recombinant adenoviruses (*Plasmodium yoelii* circumsporozoite protein)

Antigen	Recombinant Adenovirus	Promoter	Transgene	Adenovirus Protein	Insertion Site	Position (a.a.)	Inserted Sequence	Length
<i>P. yoelii</i> circumsporozoite protein (PyCS)	wt/Empty	CMV	None	Hexon	-	-	-	-
				Fiber	-	-	-	-
				pVII	-	-	-	-
	wt/GFP	CMV	GFP	Hexon	-	-	-	-
				Fiber	-	-	-	-
				pVII	-	-	-	-
	wt/PyCS-GFP	CMV	PyCS+GFP	Hexon	-	-	-	-
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₃ -HVR1/PyCS-GFP	CMV	PyCS+GFP	Hexon	HVR1	from138 to164	(QGPGAP) ₃	18
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₃ -HVR5/PyCS-GFP	CMV	PyCS+GFP	Hexon	HVR5	between 268 and 269	(QGPGAP) ₃	18
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₃ -Fib/PyCS-GFP	CMV	PyCS+GFP	Hexon	-	-	-	-
				Fiber	HI Loop	between 543 and 544	(QGPGAP) ₃	18
				pVII	-	-	-	-
	(QGPGAP) ₃ -HVR1/Fib/PyCS-GFP	CMV	PyCS+GFP	Hexon	HVR1	from138 to164	(QGPGAP) ₃	18
				Fiber	HI Loop	between 543 and 544	(QGPGAP) ₃	18
				pVII	-	-	-	-
	(QGPGAP) ₃ -Fib/PyCD4-pVII-1/PyCS-GFP	CMV	PyCS+GFP	Hexon	-	-	-	-
				Fiber	HI Loop	between 543 and 544	(QGPGAP) ₃	18
				pVII	C-terminus	between 198 and STOP Codon	YNRNIVNRLGDLNGKPEEK	21
	wt/cmv5-PyCS	CMV5	PyCS	Hexon	-	-	-	-
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₃ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₃	18
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₄ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₄	24
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₅ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₅	30
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₆ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₆	36
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₇ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₇	42
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₈ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₈	48
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₉ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₉	54
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₁₁ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₁₁	66
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(QGPGAP) ₁₂ -HVR1/cmv5-PyCS	CMV5	PyCS	Hexon	HVR1	from138 to164	(QGPGAP) ₁₂	72
				Fiber	-	-	-	-
				pVII	-	-	-	-

Table 2. Recombinant adenoviruses (*Plasmodium falciparum* circumsporozoite protein)

Antigen	Recombinant Adenovirus	Promoter	Transgene	Adenovirus Protein	Insertion Site	Position (a.a.)	Inserted Sequence	Length
P. falciparum circumsporozoite protein (PICSP)	wt/PICSP	CMV	PICSP	Hexon	-	-	-	-
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₄ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₄	16
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₄ -Fib/PICSP	CMV	PICSP	Hexon	-	-	-	-
				Fiber	HI Loop	between 543 and 544	(NANP) ₄	16
				pVII	-	-	-	-
	(NANP) ₄ -HVR1/Fib/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₄	16
				Fiber	HI Loop	between 543 and 544	(NANP) ₄	16
				pVII	-	-	-	-
	(NANP) ₆ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₆	24
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₈ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₈	32
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₁₀ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₁₀	40
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₁₂ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₁₂	48
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₁₄ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₁₄	56
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₁₆ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₁₆	64
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₁₈ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₁₈	72
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₂₀ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₂₀	80
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₂₂ -HVR1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₂₂	88
				Fiber	-	-	-	-
				pVII	-	-	-	-
	wt/cmv5-PICSP	CMV5	PICSP	Hexon	-	-	-	-
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₂₂ -HVR1/cmv5-PICSP	CMV5	PICSP	Hexon	HVR1	from138 to164	(NANP) ₂₂	88
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₂₈ -HVR1/cmv5-PICSP	CMV5	PICSP	Hexon	HVR1	from138 to164	(NANP) ₂₈ (NVDP) ₁ (NANP) ₁₀	112
				Fiber	-	-	-	-
				pVII	-	-	-	-
	(NANP) ₄ -HVR1/PICD4-pVII-1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₄	16
				Fiber	-	-	-	-
				pVII	C-terminus	between 198 and STOP Codon	EYLNKIQNSLSTEWSPCSVT	20
	(NANP) ₄ -Fib/PICD4-pVII-1/PICSP	CMV	PICSP	Hexon	-	-	-	-
				Fiber	HI Loop	between 543 and 544	(NANP) ₄	16
				pVII	C-terminus	between 198 and STOP Codon	EYLNKIQNSLSTEWSPCSVT	20
	(NANP) ₄ -HVR1/Fib/PICD4-pVII-1/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₄	16
				Fiber	-	-	-	-
				pVII	C-terminus	between 198 and STOP Codon	EYLNKIQNSLSTEWSPCSVT	20
	(NANP) ₄ -HVR1/PICD4-pVII-2/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₄	16
				Fiber	-	-	-	-
				pVII	Middle	between 92 and 93 Codon	EYLNKIQNSLSTEWSPCSVT	20
	(NANP) ₄ -HVR1/PICD4-pVII-3/PICSP	CMV	PICSP	Hexon	HVR1	from138 to164	(NANP) ₄	16
				Fiber	-	-	-	-
				pVII	Middle	between 140 and 141 Codon	EYLNKIQNSLSTEWSPCSVT	20
	(NANP) ₂₂ -HVR1/PICD4-pVII-3/cmv5-PICSP	CMV5	PICSP	Hexon	HVR1	from138 to164	(NANP) ₂₂	88
				Fiber	-	-	-	-
				pVII	Middle	between 140 and 141 Codon	EYLNKIQNSLSTEWSPCSVT	20
	(NANP) ₂₈ -HVR1/PICD4-pVII-3/cmv5-PICSP	CMV5	PICSP	Hexon	HVR1	from138 to164	(NANP) ₂₈ (NVDP) ₁ (NANP) ₁₀	112
				Fiber	-	-	-	-
				pVII	Middle	between 140 and 141 Codon	EYLNKIQNSLSTEWSPCSVT	20

[00155] The capsid-modified adenovirus genome DNA plasmid was purified, linearized by PacI digestion, and used for transfection of AD293 cells.

[00156] Adenovirus particles were prepared from the transfected AD293 cells by four rounds of freeze/thaw and used for further virus amplification. After the last amplification, adenovirus particles were purified by CsCl gradient

centrifugation. The band was then collected and dialyzed against dialysis buffer to remove CsCl. Virus particle (v.p.) was calculated based on O.D. 260 ($1 \text{ O.D.260} = 1.25 \times 10^{12} \text{ v.p./mL}$) (Bruna-Romero et al. 2003).

[00157] During the adenovirus amplification procedure, small differences in adenovirus growth were observed among capsid-modified adenoviruses, demonstrating that adenovirus infectivity and productivity was not adversely affected by the modification.

Example 2: *Plasmodium yoelii* circumsporozoite protein-specific immune response

Validation of *Plasmodium yoelii* recombinant adenoviruses

[00158] Plasmodium circumsporozoite protein coding adenovirus shuttle vectors were used for transient transfection to confirm Plasmodium circumsporozoite protein expression using AD293 cells (Fig. 38). 24 hours after transfection, cells were lysed in SDS sample buffer followed by SDS PAGE electrophoresis and western blotting with anti-PyCS monoclonal antibody (9D3).

[00159] To confirm the epitope insertion into adenovirus capsid proteins, purified recombinant adenoviruses were analyzed by SDS-PAGE ($2 \times 10^9 \text{ v.p./lane}$) and Western blot ($1 \times 10^9 \text{ v.p./lane}$) with anti-sporozoite antibody which recognizes the (QGPGAP)_n (SEQ ID NO:59) repeats were done as shown in Fig. 39A and 40A. The intensity of the bands in Fig. 39A correlated with the copy number of the capsid protein in an adenovirus virion: the copy number of Fiber (36 copies per virion) is twenty-times less than Hexon (720 copies per virion). The lower band in lane 4 in Fig. 39A is likely a degraded Hexon. The intensity of the bands in Fig. 40A correlated with the number of (QGPGAP)_n (SEQ ID NO:59) repeats inserted into HVR1.

[00160] To assess whether the PyCS-B epitope was exposed to the outside of adenovirus virion, serially diluted purified recombinant adenovirus particles were coated onto Enzyme-Linked Immunosorbent Assay (ELISA) plate and detected with anti-PyCS antibody that recognizes (QGPGAP)_n (SEQ ID NO:59) repeats. The antibody recognized all the capsid-modified adenoviruses (Fig. 39B

and 40B). The results of ELISA assay suggest that the PyCS-B epitope incorporated in capsid proteins were well exposed to the outside of adenovirus virions.

Plasmodium yoelii circumsporozoite protein-specific immune response after immunization with capsid-modified PyCS adenovirus

[00161] Six- to eight-week old female BALB/c mice were purchased from Taconic (Hudson, NY, USA) and maintained under standard conditions in the Laboratory Animal Research Center of The Rockefeller University. For immunization, adenoviruses were diluted in PBS and injected intramuscularly at indicated doses.

[00162] To evaluate the immunogenicity of recombinant adenoviruses after a single immunization, groups of naïve BALB/c mice (five per group) were immunized with 1×10^9 v.p. of various recombinant PyCS adenoviruses intramuscularly and PyCS-specific cell-mediated immune responses (CMI) were measured by ELISPOT 2 weeks after immunization (Fig. 41A).

[00163] The number of PyCS-specific, IFN- γ -secreting CD8⁺ T cells in the spleens of immunized mice were determined by an ELISPOT assay, using a synthetic peptide corresponding to the CD8⁺ T cell epitope (SYVPSAEQI; SEQ ID NO:66) within the PyCS protein. Briefly, 96 well nitrocellulose plates (Millititer HA, Millipore) were coated overnight with anti-mouse interferon γ mAb, R4. After overnight incubation at room temperature, the wells were washed repeatedly with culture medium and blocked with culture medium for 4 hours. 5×10^5 Splenocytes from immunized mice were added to the ELISPOT wells in the presence or absence of 10 μ g/mL CD8⁺ T cell epitope peptide and incubated 24 hours at 37°C and 5% CO₂. After extensive washing of the plates with PBS containing 0.05% Tween 20 (PBST), biotinylated anti-mouse interferon γ mAb, XMG1.2, in PBST were added and incubated overnight at 40°C. After washing with PBST, the plates will be incubated with peroxidase-labeled avidin (eBiosciences). The spots were developed by adding AEC substrate (BD Biosciences).

[00164] All of the capsid-modified adenoviruses induced comparable level of CMI to adenoviruses having intact capsid protein at this dose (Fig. 41B).

[00165] Next, naïve BALB/c mice were given multiple doses of recombinant adenoviruses with increasing doses, i.e. 1×10^8 , 1×10^9 , and 1×10^{10} v.p., at 3 week intervals, as shown in Fig. 42A. PyCS-specific humoral response was determined by ELISA. Five microliters of blood was collected from tail vein of the immunized mice and diluted in 495 μ l of PBS, and then the samples were centrifuged at 5,000 rpm for 5min to prepare diluted plasma samples (x100). Maxisorp ELISA plates were coated with 5 μ g/ml CS-specific peptide ((QGPGAP)₃; SEQ ID NO:59, n=3) in 0.1M Sodium Carbonate Buffer (pH 9.5) at 4°C for overnight. Plates were washed and blocked with 1x Diluent for 2 hours at room temperature. The plates were washed again and 100 μ l of serially twofold-diluted plasma or serum in 1x Diluent was added to the plates and the plates were incubated for one hour at room temperature. The plates were washed and incubated with 100 μ l of HRP-labeled goat anti-mouse IgG antibody. All of the peptides were synthesized by Biosyntheis (Lewisville, TX, USA).

[00166] Using this immunization regimen, all capsid-modified adenoviruses induced a significantly higher level of anti-(QGPGAP)₃ antibody response than wt/PyCS-GFP at week 10 (Fig. 42B).

[00167] To determine the vaccine efficacy of capsid-modified adenovirus, the immunized mice were challenged with 2×10^4 infectious *P. yoelii* sporozoites via tail vein injection at week 10. Parasite burden 42 hours after sporozoite challenge was determined by quantifying the amounts of parasite-specific ribosomal RNA in mouse liver and described as a ratio of the absolute copy number of parasite ribosomal RNA to that of mouse GAPDH mRNA. For statistical analysis, the values were log-transformed and then one-way ANOVA followed by a Dunnett's test was employed to determine the differences.

[00168] Vaccinations with (QGPGAP)₃-HVR1/PyCS-GFP, (QGPGAP)₃-Fib/PyCS-GFP or (QGPGAP)₃-HVR1/Fib/PyCS-GFP induced a higher level of

protection than wt/PyCS-GFP, resulting in a significantly lower parasite burden in the malaria challenged mice (Fig. 42C).

[00169] Next, the functionality of PyCS-specific antibody induced by capsid-modified adenoviruses was evaluated. First, to test whether the sera of adenovirus-immunized mice at week 10 (Fig. 42A) could recognize intact sporozoites, an indirect immunofluorescence assay (IFA) was performed. In IFA, air-dried sporozoites on multi-spot glass slides were incubated with 3% Bovine Serum albumin (BSA) in PBS for one hour and then incubated with diluted sera for one hour. After washing, the slides were incubated with fluorescent-labeled secondary antibody for one hour. The slides were washed and IFA titers were determined as the highest dilution producing fluorescence under a fluorescent microscope. Both (QGPGAP)₃-HVR1/PyCS-GFP and (QGPGAP)₃-HVR1/Fib/PyCS-GFP induced a highest IFA titer against sporozoites (Fig. 43A), indicating that the insertion of (QGPGAP)₃ epitope in HVR1 of adenovirus Hexon enabled PyCS adenovirus to elicit a robust antibody response against not only a synthetic peptide, but also a native epitope present in the malaria parasites.

[00170] Second, to determine whether mice immunized with capsid-modified adenovirus (Fig. 42A) developed “functional” antibodies that could neutralize the infectivity of sporozoites, an *in vitro* sporozoite neutralization assay was performed.

[00171] In the *in vitro* neutralizing assay, *P. yoelii* sporozoites were added to CD81/HepG2 in a 96-well plate in the presence of 30-fold diluted pooled serum from adenovirus-immunized mice. After a two-hour incubation, uninfected sporozoites were washed out with medium and then the cells were cultured for 42 hours. Relative amount of parasite ribosomal RNA to human GAPDH mRNA was measured by real-time PCR (Ophorst et al. 2006).

[00172] The pooled serum samples from mice immunized with capsid-modified adenovirus, particularly (QGPGAP)₃-HVR1/PyCS-GFP and (QGPGAP)₃-HVR1/Fib/PyCS-GFP, almost completely inhibited (99%) the sporozoite infectivity

in vitro (Fig. 43B). It is noted that the degree of inhibition in this assay was inversely correlated with the IFA titers shown in Fig. 43A.

Protection from blood stage malaria infection

[00173] Next it was determined whether immunization with capsid-modified rAd protects mice from developing a blood-stage malaria infection after sporozoite challenge. The experiments were performed twice and in each experiment, 20 BALB/c mice in each group were immunized three times with wt/PyCS-GFP or (QGPGAP)₃-HVR1/PyCS-GFP as shown in Figure 42A and at 4 weeks after the last immunization, the mice were intravenously challenged with 50 *P. yoelii* sporozoites. Giemsa-stained blood smears were analyzed from 3 to 12 days after challenge to detect blood stage malaria parasite infection. In the wt/CS-GFP immunized group, 30 out of 40 mice (75%) were infected whereas 35 out of 40 (87.5%) became infected in the naïve group (Table 3, below). (QGPGAP)₃-HVR1/CS-GFP immunized mice were more protected than wt/CS-GFP; only 15 out of 40 (37.5%) of which became infected, which is consistent with the result of protection experiment measured by parasite burden in liver (Figure 42C).

Table 3. Detection of blood stage malaria parasite infection after immunization with wt/PyCS-GFP or (QGPGAP)₃-HVR1/PyCS-GFP.

Immunization	No. of Mice (Challenged)	No. of Mice (Infected)	Protection (%)
Experiment 1			
None	20	18	10
wt/PyCS-GFP	20	14	30
(QGPGAP) ₃ -HVR1/PyCS-GFP	20	10	50
Experiment 2			
None	20	17	15
wt/PyCS-GFP	20	16	20
(QGPGAP) ₃ -HVR1/PyCS-GFP	20	5	75
Total			
None	40	35	87.5
wt/PyCS-GFP	40	30	75
(QGPGAP) ₃ -HVR1/PyCS-GFP	40	15	37.5

Prime-boost immunization 1

[00174] Next, naïve BALB/c mice were given “boosts” of HVR1-modified PyCS adenoviruses which have four or six repeats of (QGPGAP)_n (SEQ ID NO:59; n=4, 6) with or without the adjuvant at multiple increasing doses (i.e. 1×10^8 , 1×10^9 , and 1×10^{10} v.p.) at 3 week intervals, as shown in Fig. 44A. The adjuvant used in this experiment is Sigma Adjuvant System (Sigma-Aldrich) containing 200 µg/mL Saponin (Sigma-Aldrich). A vial of Sigma Adjuvant System (1mL) contains 0.5 mg Monophosphoryl Lipid A (detoxified endotoxin) from *Salmonella minnesota* and 0.5 mg synthetic Trehalose Dicorynomycolate in 2% oil (squalene)-Tween 80 in water. Adenovirus solution was mixed with the equal amount of the adjuvant before the immunization. One hundred microliters of the adenovirus-adjuvant mixture was injected intramuscularly. PyCS-specific humoral and cell-mediated immune responses were measured as described above. A trend was observed that HVR1-modified adenovirus having six repeats induced higher antibody titer than that having four repeats and the use of adjuvant augmented the antibody titer (Fig. 44B). In contrast, there was no effect of the adjuvant on CMI (data not shown).

[00175] To determine the vaccine efficacy of HVR1-modified PyCS adenovirus, five mice in each group were challenged with 2×10^4 infectious *P. yoelii* sporozoites via tail vein injection at week 9. Parasite burden 42 hours after sporozoite challenge was determined as described above. For statistical analysis, the values were log-transformed and then one-way ANOVA followed by a Dunnett's test was employed to determine the differences. There was a trend that HVR1-modified adenovirus having six repeats reduced parasite burden more than that having four repeats and the use of adjuvant augmented the protection (Fig. 44C).

[00176] To evaluate the functionality of antibody induced by HVR1-modified PyCS adenoviruses, we performed an *in vitro* sporozoite neutralization assay as described above. Pooled serum samples from mice immunized with HVR1-modified PyCS adenoviruses at week 9 neutralized sporozoite invasion at 50-fold dilution (Fig. 44D).

Prime-boost immunization 2

[00177] Naïve BALB/c mice were given “boosts” of HVR1-modified PyCS adenoviruses which have six, nine, or twelve repeats of (QGPGAP)_n (SEQ ID NO: 59; n=6, 9, 12) with or without the adjuvant at three doses of 1×10^{10} v.p. at 3 week intervals, as shown in Fig. 45A. The adjuvant used in this experiment is Sigma Adjuvant System (Sigma-Aldrich) containing 200 µg/mL Saponin (Sigma-Aldrich). Adenovirus solution was mixed with the equal amount of the adjuvant before the immunization. PyCS-specific humoral and cell-mediated immune responses were measured as described above. HVR1-modified PyCS adenovirus which has twelve repeats of (QGPGAP)_n (SEQ ID NO:59; n=12) with the adjuvant induced the highest antibody titer among the groups at week 9 (Fig. 45B). With respect to PyCS-specific CMI, there was no difference among the groups, indicating that the longer epitope insertion up to twelve does not impair adenovirus infectivity *in vivo* (Fig. 45C). Further, the adjuvant did not affect the ability of adenovirus to induce CMI (Fig. 45C).

[00178] To determine the vaccine efficacy of HVR1-modified PyCS adenovirus, five mice in each group were challenged with 2×10^4 infectious *P. yoelii* sporozoites via tail vein injection at week 9. Parasite burden 42 hours after sporozoite challenge was determined as described above. All of the HVR-1 modified PyCS adenovirus having (QGPGAP)_n repeats (SEQ ID NO:59, n=6, 9, 12), with or without adjuvant, showed increased protection. However, HVR1-modified PyCS adenovirus having twelve repeats of (QGPGAP)_n (SEQ ID NO:59, n=12) with the adjuvant showed the best protection (Fig. 45D), which was significantly more protective than any other treatment.

Example 3: *Plasmodium falciparum* circumsporozoite protein-specific immune response

[00179] Validation of *Plasmodium falciparum* recombinant adenoviruses
Plasmodium circumsporozoite protein coding adenovirus shuttle vectors were used for transient transfection to confirm Plasmodium circumsporozoite protein

expression using AD293 cells (Fig. 46A). 24 hours after transfection, cells were lysed in SDS sample buffer followed by SDS PAGE electrophoresis and western blotting with anti-NANP monoclonal antibody (2A10).

[00180] To confirm the epitope insertion into adenovirus capsid proteins, purified recombinant adenoviruses were analyzed by SDS-PAGE (2×10^9 v.p./lane) and Western blot (1×10^9 v.p./lane) with anti-sporozoite antibody which recognizes the (NANP)_n (SEQ ID NO:60) repeats were done as shown in Fig. 47A and 48A. The intensity of the bands in Fig. 47A correlated with the copy number of the capsid protein in an adenovirus virion: the copy number of Fiber (36 copies per virion) is twenty-times less than Hexon (720 copies per virion). The intensity of the bands in Fig. 48A correlated with the number of NANP repeat HVR1.

[00181] To assess whether the PfCSP-B epitope was exposed to the outside of adenovirus virion, serially diluted purified recombinant adenovirus particles were coated onto Enzyme-Linked Immunosorbent Assay (ELISA) plate and detected with anti-PyCS antibody that recognizes (NANP)_n (SEQ ID NO:60) repeats. The antibody recognized all the capsid-modified adenoviruses (Fig. 47B and 48B). The results of ELISA assay suggest that the PfCSP-B epitope incorporated in capsid proteins were well exposed to the outside of adenovirus virions.

Prime-Boost immunization 3

[00182] Naïve BALB/c mice were given multiple, increasing doses of recombinant PfCSP adenoviruses (i.e., 1×10^8 , 1×10^9 , and 1×10^{10} v.p.) at 3 week intervals as shown in Fig 49A. PfCSP-specific humoral response was determined by ELISA as described above using ELISA plates coated with $1 \mu\text{g/ml}$ (T1B)₄, a CS repeat peptide which contains a (NANP)_n repeat sequence (SEQ ID NO:60) (Calvo-Calle et al 2006). For statistical analysis, the values were log-transformed and one-way ANOVA followed by a Dunnett's test was employed to determine the differences between wt/PfCSP and capsid-modified adenoviruses. All capsid-modified adenoviruses induced statistically higher anti-NANP antibody titer than wt/PfCSP.

Prime-boost immunization 4

[00183] Next, naïve BALB/c mice were given “boosts” of HVR1-modified PfCSP adenoviruses which have four, six, eight, or ten repeats of (NANP)_n (SEQ ID NO:60; n=4, 6, 8, 10) with at multiple increasing doses (i.e., 1×10^8 , 1×10^9 , and 1×10^{10} v.p.) at 3 week intervals, as shown in Fig. 50A. PfCSP-specific humoral immune responses were measured as described above. All of the HVR1-modified adenoviruses induced significantly higher anti-NANP antibody titer than wt/PfCSP at week 9 (Fig. 50B). For statistical analysis, the values were log-transformed and then one-way ANOVA followed by a Dunnett's test was employed to determine the differences.

Prime-boost immunization 5

[00184] Naïve BALB/c mice were given “boosts” of HVR1-modified adenoviruses which have ten, sixteen, or twenty-two repeats of (NANP)_n (SEQ ID NO:60; n=10, 16, 22) with or without the adjuvant at three doses of 1×10^{10} v.p. at 3 week intervals, as shown in Fig. 51A. The adjuvant used in this experiment is Sigma Adjuvant System (Sigma-Aldrich) containing 200 µg/mL Saponin (Sigma-Aldrich). Adenovirus solution was mixed with the equal amount of the adjuvant before the immunization. PfCSP-specific humoral immune response was measured as described above, and it was determined that HVR1-modified adenoviruses with longer B cell epitope induced higher antibody titer (Fig. 51B).

Example 4: PyCS CD4 epitope insertion into adenovirus core protein pVII

[00185] Antigen-specific CD4 T cells are required for antigen-specific B cell development and proliferation. Therefore to determine whether it would be possible to enhance PyCS-specific humoral immune response induced by capsid-modified adenovirus by inserting PyCS CD4 epitope in adenovirus protein, (QGPGAP)₃-Fib/PyCS-GFP that has PyCS CD4 epitope in pVII ((QGPGAP)₃-Fib/CD4-pVII-1/PyCS-GFP) was constructed. pVII is one of the adenovirus core proteins and the copy number per virion is 700-800, which is ideal for efficient

CD4 epitope presentation onto MHC class II molecule. As shown in Fig. 52A, the pVII band is shifted by PyCS CD4 epitope insertion into pVII on a SDS-PAGE gel.

[00186] To test the effect of PyCS CD4 epitope insertion into pVII, naïve BALB/c mice were immunized with (QGPGAP)₃-Fib/PyCS-GFP or (QGPGAP)₃-Fib/CD4-pVII-1/PyCS-GFP as shown in Fig. 42A and anti-QGPGAP antibody titer was determined by ELISA at week 10. (QGPGAP)₃-Fib/CD4-pVII-1/PyCS-GFP induced significantly higher anti-QGPGAP antibody titer than (QGPGAP)₃-Fib/PyCS-GFP (Fig. 52B), and that indicated PyCS CD4 epitope insertion into pVII augmented humoral immune response induced by capsid-modified adenovirus.

PfCSP CD4 epitope insertion into adenovirus core protein pVII

[00187] To evaluate the effect of PfCSP CD4+ epitope insertion into different positions in adenovirus core protein pVII on adenovirus-induced immune response, HVR1-modified PfCSP adenoviruses having the PfCSP CD4+ epitope just before the first Nuclear localization Signal (NLS) or between the two NLSs were constructed (Fig.53A).

[00188] To confirm the epitope insertion into pVII, purified recombinant adenoviruses were analyzed by SDS-PAGE as described above. As shown in Fig.53B, the pVII bands of (NANP)₄-HVR1/CD4-pVII-2/PfCSP and (NANP)₄-HVR1/CD4-pVII-3/PfCSP were shifted upward because of the epitope insertion.

PfCSP-specific immune response induced by HVR1and pVII-modified PfCSP adenovirus

[00189] Next, naïve BALB/c mice were given “boosts’ of HVR1and pVII-modified PfCSP adenoviruses which have four repeats of NANP in HVR1 and the PfCD4+ epitope in pVII with at multiple increasing doses (i.e., 1x10⁸, 1x10⁹, and 1x10¹⁰v.p.) at 3 week intervals, as shown in Fig. 54A. PfCSP-specific humoral immune responses were measured as described above. (NANP)₄-HVR1/CD4-pVII-2/PfCSP and (NANP)₄-HVR1/ CD4-pVII-3/PfCSP induced significantly higher anti-NANP antibody titer than (NANP)₄-HVR1/PfCSP at week 6 (Fig. 54B). In terms of CMI, (NANP)₄-HVR1/CD4-pVII-3/PfCSP induced significantly higher IFN γ

and IL-4-secreting PfCSP-specific CD4⁺ T cells than (NANP)₄-HVR1/PfCSP (Fig. 54C).

Example 5: Effect of capsid-modification on anti-adenovirus immunity

[00190] For the *in vitro* adenovirus neutralization experiments, serum was added to the AD293 cells at the indicated dilutions prior to the adenovirus infection. Caucasian serum samples were obtained from Innovative Research (Novi, MI, USA). All flow cytometry data was analyzed with FlowJo v8.8 software (Tree Star, Inc, Ashland, OR, USA). AD293 cells were infected with each capsid-modified adenovirus in the presence of human adenovirus neutralizing serum samples at the indicated dilution followed by measuring GFP expression by flow cytometry. A replacement of HVR1 with the PyCS-B epitope clearly made the adenovirus resilient to anti-adenovirus serotype 5 sera, whereas the modification of HVR5 or Fiber had no effect (Fig. 55).

[00191] Next, it was determined whether HVR1 is a critical molecule for the neutralization *in vivo*. For this purpose, mice were infected with 1×10^{10} v.p. wt/Empty adenovirus twice to mount sufficient pre-existing anti-adenovirus immunity (Fig. 56A) and randomized based on their anti-adenovirus antibody titers, as determined by ELISA. The mice were then given a single immunizing dose of capsid-modified adenovirus or unmodified adenovirus, and the level of PyCS-specific CD8⁺ T cell response was measured as described above. Only vaccination with (QGPGAP)₃-HVR1/PyCS-GFP or (QGPGAP)₃-HVR1/Fib/PyCS-GFP was able to induce a significantly more potent CS-specific CD8⁺ T cell response, compared to that induced by other capsid-modified or unmodified adenovirus (Fig. 56B).

[00192] The level of antibody response against (QGPGAP)₃ epitope was also measured, which is expressed on the capsid proteins of rAd, in mice infected with wt/Empty Ad followed by vaccination with capsid-modified rAd (Figure 57A). Only mice vaccinated with (QGPGAP)₃-HVR1/PyCS-GFP and (QGPGAP)₃-HVR1/Fib/PyCS-GFP were able to mount a significantly higher titer of anti-QGPGAP antibody than those vaccinated with wt/PyCS-GFP (Figure 57B).

[00193] The examples described above are meant to more fully illustrate the embodiments and are not to be interpreted as limiting the scope of any claimed embodiment. In addition, the references cited within the disclosure, and all references listed below are hereby incorporated by reference in their entirety as if fully set forth herein.

REFERENCES

- Abbink, P., Lemckert, A.A., Ewald, B.A., Lynch, D.M., Denholtz, M., et al. 2007. Comparative seroprevalence and immunogenicity of six rare serotype recombinant adenovirus vaccine vectors from subgroups B and D. *J Virol.* **81**:4654-4663.
- Alonso, P.L., Sacarlal, J., Aponte, J.J., Leach, A., Macete, E., et al. 2004. Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomised controlled trial. *Lancet.* **364**:1411-1420.
- Alonso, P.L., Sacarlal, J., Aponte, J.J., Leach, A., Macete, E., et al. 2005. Duration of protection with RTS,S/AS02A malaria vaccine in prevention of *Plasmodium falciparum* disease in Mozambican children: single-blind extended follow-up of a randomised controlled trial. *Lancet.* **366**:2012-2018.
- Anderson, R.J., Hannan, C.M., Gilbert, S.C., Laidlaw, S.M., Sheu, E.G., et al. 2004. Enhanced CD8+ T cell immune responses and protection elicited against *Plasmodium berghei* malaria by prime boost immunization regimens using a novel attenuated fowlpox virus. *J Immunol.* **172**:3094-3100.
- Athappilly, F.K., Murali, R., Rux, J.J., Cai, Z. & Burnett, R.M. The refined crystal structure of Hexon, the major coat protein of adenovirus type 2, at 2.9 Å resolution. *Journal of molecular biology* **242**, 430-455 (1994).
- Barrat, F.J., Meeker, T., Gregorio, J., Chan, J.H., Uematsu, S., et al. Nucleic acids of mammalian origin can act as endogenous ligands for Toll-like receptors and may promote systemic lupus erythematosus. *J Exp Med.* **202**, 1131-1139 (2005)
- Bejon, P., Lusingu, J., Olotu, A., Leach, A., Lievens, M., et al. 2008. Efficacy of RTS,S/AS01E vaccine against malaria in children 5 to 17 months of age. *N Engl J Med.* **359**:2521-2532.
- Belousova, N., Krendelchtchikova, V., Curiel, D.T. & Krasnykh, V. Modulation of adenovirus vector tropism via incorporation of polypeptide ligands into the Fiber protein. *Journal of virology* **76**, 8621-8631 (2002).
- Bergelson, J.M. et al. Isolation of a common receptor for Coxsackie B viruses and adenoviruses 2 and 5. *Science (New York, N.Y)* **275**, 1320-1323 (1997).
- Bewley, M.C., Springer, K., Zhang, Y.B., Freimuth, P. & Flanagan, J.M. Structural analysis of the mechanism of adenovirus binding to its human cellular receptor, CAR. *Science (New York, N.Y)* **286**, 1579-1583 (1999).
- Bruña-Romero, O., Schmieg, J., Del Val, M., Buschle, M. & Tsuji, M. The dendritic cell-specific chemokine, dendritic cell-derived CC chemokine 1, enhances protective cell-mediated immunity to murine malaria. *J Immunol* **170**, 3195-3203

(2003).Hong, S.S., Karayan, L., Tournier, J., Curiel, D.T. & Boulanger, P.A. Adenovirus type 5 Fiber knob binds to MHC class I alpha2 domain at the surface of human epithelial and B lymphoblastoid cells. *The EMBO journal* **16**, 2294-2306 (1997).

Bruña-Romero, O., González-Aseguinolaza, G., Hafalla, J.C., Tsuji, M., and Nussenzweig, R.S. 2001. Complete, long-lasting protection against malaria of mice primed and boosted with two distinct viral vectors expressing the same plasmodial antigen. *Proc Natl Acad Sci U S A*. **98**:11491-11496.

Bruña-Romero, O., Rocha, C.D., Tsuji, M. & Gazzinelli, R.T. Enhanced protective immunity against malaria by vaccination with a recombinant adenovirus encoding the circumsporozoite protein of Plasmodium lacking the GPI-anchoring motif. *Vaccine* **22**, 3575-3584 (2004).

Calvo-Calle, J.M., Oliveira, G.A., Watta, C.O., Soverow, J., Parra-Lopez, C., et al. 2006. A linear peptide containing minimal T- and B-cell epitopes of Plasmodium falciparum circumsporozoite protein elicits protection against transgenic sporozoite challenge. *Infect Immun*. **74**:6929-6939.

Clyde, D.F., Most, H., McCarthy, V.C., and Vanderberg, J.P. 1973. Immunization of man against sporozite-induced falciparum malaria. *Am J Med Sci*. **266**:169-177.

Chroboczek, J., Ruigrok, R.W. & Cusack, S. Adenovirus Fiber. *Current topics in microbiology and immunology* **199 (Pt 1)**, 163-200 (1995).

Chu, Y., Heistad, D., Cybulsky, M.I. & Davidson, B.L. Vascular cell adhesion molecule-1 augments adenovirus-mediated gene transfer. *Arterioscler Thromb Vasc Biol* **21**, 238-242 (2001).

Crawford-Miksza, L. & Schnurr, D.P. Analysis of 15 adenovirus Hexon proteins reveals the location and structure of seven hypervariable regions containing serotype-specific residues. *Journal of virology* **70**, 1836-1844 (1996).

Crompton, J., Toogood, C.I., Wallis, N. & Hay, R.T. Expression of a foreign epitope on the surface of the adenovirus Hexon. *The Journal of general virology* **75 (Pt 1)**, 133-139 (1994).

Crystal, R.G. Transfer of genes to humans: early lessons and obstacles to success. *Science (New York, N.Y)* **270**, 404-410 (1995).

Douglas, J.T. Adenoviral vectors for gene therapy. *Molecular biotechnology* **36**, 71-80 (2007).

Edelman, R., Hoffman, S.L., Davis, J.R., Beier, M., Sztein, M.B., et al. 1993. Long-term persistence of sterile immunity in a volunteer immunized with X-irradiated Plasmodium falciparum sporozoites. *J Infect Dis*. **168**:1066-1070.

Grillot, D., Valmori, D., Lambert, P.H., Corradin, G., and Del Giudice, G. 1993. Presentation of T cell epitopes assembled as multiple-antigen peptides to murine and human T lymphocytes. *Infect Immun.* **61**:3064-3067.

Graham, F.L. & Prevec, L. Adenovirus-based expression vectors and recombinant vaccines. *Biotechnology (Reading, Mass)* **20**, 363-390 (1992).

Gwadz, R.W., Cochrane, A.H., Nussenzweig, V., and Nussenzweig, R.S. 1979. Preliminary studies on vaccination of rhesus monkeys with irradiated sporozoites of *Plasmodium knowlesi* and characterization of surface antigens of these parasites. *Bull World Health Organ.* **57 Suppl 1**:165-173.

Hackett, N.R. *et al.* Use of quantitative TaqMan real-time PCR to track the time-dependent distribution of gene transfer vectors *in vivo*. *Mol Ther* **2**, 649-656 (2000).

Harvey, B.G. *et al.* Airway epithelial CFTR mRNA expression in cystic fibrosis patients after repetitive administration of a recombinant adenovirus. *The Journal of clinical investigation* **104**, 1245-1255 (1999).

Heemskerk, B. *et al.* Adenovirus-specific CD4⁺ T cell clones recognizing endogenous antigen inhibit viral replication *in vitro* through cognate interaction. *J Immunol* **177**, 8851-8859 (2006).

Henry, L.J., Xia, D., Wilke, M.E., Deisenhofer, J. & Gerard, R.D. Characterization of the knob domain of the adenovirus type 5 Fiber protein expressed in *Escherichia coli*. *Journal of virology* **68**, 5239-5246 (1994).

Hong, S.S., Habib, N.A., Franqueville, L., Jensen, S. & Boulanger, P.A. Identification of adenovirus (ad) penton base neutralizing epitopes by use of sera from patients who had received conditionally replicative ad (add1520) for treatment of liver tumors. *Journal of virology* **77**, 10366-10375 (2003).

Kester, K.E., Cummings, J.F., Ockenhouse, C.F., Nielsen, R., Hall, B.T., *et al.* 2008. Phase 2a trial of 0, 1, and 3 month and 0, 7, and 28 day immunization schedules of malaria vaccine RTS,S/AS02 in malaria-naïve adults at the Walter Reed Army Institute of Research. *Vaccine.* **26**:2191-2202.

Kirby, I. *et al.* Mutations in the DG loop of adenovirus type 5 Fiber knob protein abolish highaffinity binding to its cellular receptor CAR. *Journal of virology* **73**, 9508-9514 (1999).

Koizumi, N., Mizuguchi, H., Utoguchi, N., Watanabe, Y. & Hayakawa, T. Generation of Fiber-modified adenovirus vectors containing heterologous peptides in both the HI loop and C terminus of the Fiber knob. *The journal of gene medicine* **5**, 267-276 (2003).

Kozak M. 1987. An analysis of 5'-noncoding sequences from 699 vertebrate messenger RNAs. *Nucleic Acids Res.* **15**:8125-148.

- Krause, A., Joh, J.H., Hackett, N.R., Roelvink, P.W., Bruder, J.T., et al. 2006. Epitopes expressed in different adenovirus capsid proteins induce different levels of epitope-specific immunity. *J Virol.* **80**:5523-5530.
- Labow, D., Lee, S., Ginsberg, R.J., Crystal, R.G. & Korst, R.J. Adenovirus vector-mediated gene transfer to regional lymph nodes. *Human gene therapy* **11**, 759-769 (2000).
- Leen, A.M. et al. Identification of Hexon-specific CD4 and CD8 T cell epitopes for vaccine and immunotherapy. *Journal of virology* **82**, 546-554 (2008).
- Leopold, P.L. & Crystal, R.G. Intracellular trafficking of adenovirus: many means to many ends. *Advanced drug delivery reviews* **59**, 810-821 (2007).
- Mastrangeli, A. et al. "Sero-switch" adenovirus-mediated *in vivo* gene transfer: circumvention of anti-adenovirus humoral immune defenses against repeat adenovirus vector administration by changing the adenovirus serotype. *Human gene therapy* **7**, 79-87 (1996).
- Mathias, P., Wickham, T., Moore, M. & Nemerow, G. Multiple adenovirus serotypes use alpha v integrins for infection. *Journal of virology* **68**, 6811-6814 (1994).
- McConnell, M.J., Danthinne, X., and Imperiale, M.J. 2006. Characterization of a permissive epitope insertion site in adenovirus Hexon. *J Virol.* **80**:5361-5370.
- Meier, O. & Greber, U.F. Adenovirus endocytosis. *The journal of gene medicine* **5**, 451-462 (2003).
- Miyazawa, N. et al. Fiber swap between adenovirus subgroups B and C alters intracellular trafficking of adenovirus gene transfer vectors. *Journal of virology* **73**, 6056-6065 (1999).
- Miyazawa, N., Crystal, R.G. & Leopold, P.L. Adenovirus serotype 7 retention in a late endosomal compartment prior to cytosol escape is modulated by Fiber protein. *Journal of virology* **75**, 1387-1400 (2001).
- Mizuguchi, H. & Hayakawa, T. Targeted adenovirus vectors. *Human gene therapy* **15**, 1034-1044 (2004).
- Nakano, M.Y., Boucke, K., Suomalainen, M., Stidwill, R.P. & Greber, U.F. The first step of adenovirus type 2 disassembly occurs at the cell surface, independently of endocytosis and escape to the cytosol. *Journal of virology* **74**, 7085-7095 (2000).
- Nicklin, S.A. et al. Ablating adenovirus type 5 Fiber-CAR binding and HI loop insertion of the SIGYPLP peptide generate an endothelial cell-selective adenovirus. *Mol Ther* **4**, 534-542 (2001).

- Noureddini, S.C. & Curiel, D.T. Genetic targeting strategies for adenovirus. *Molecular pharmaceutics* **2**, 341-347 (2005).
- Nussenzweig, R.S., Vanderberg, J., Most, H., and Orton, C. 1967. Protective immunity produced by the injection of x-irradiated sporozoites of plasmodium berghei. *Nature*. **216**:160-162.
- Nussenzweig, R.S. & Long, C.A. Malaria vaccines: multiple targets. *Science (New York, N.Y)* **265**, 1381-1383 (1994).
- Onion, D. *et al.* The CD4+ T cell response to adenovirus is focused against conserved residues within the Hexon protein. *The Journal of general virology* **88**, 2417-2425 (2007).
- Ophorst, O.J., Radosević, K., Havenga, M.J., Pau, M.G., Holterman, L., *et al.* 2006. Immunogenicity and protection of a recombinant human adenovirus serotype 35-based malaria vaccine against Plasmodium yoelii in mice. *Infect Immun*. **74**:313-320.
- Oualikene, W., Gonin, P. & Eloit, M. Short and long term dissemination of deletion mutants of adenovirus in permissive (cotton rat) and non-permissive (mouse) species. *The Journal of general virology* **75 (Pt 10)**, 2765-2768 (1994).
- Priddy, F.H., Brown, D., Kublin, J., Monahan, K., Wright, D.P., *et al.* 2008. Safety and immunogenicity of a replication-incompetent adenovirus type 5 HIV-1 clade B gag/pol/nef vaccine in healthy adults. *Clin Infect Dis*. **46**:1769-1781.
- Roberts, M.M., White, J.L., Grutter, M.G. & Burnett, R.M. Three-dimensional structure of the adenovirus major coat protein Hexon. *Science (New York, N.Y)* **232**, 1148-1151 (1986).
- Roberts, D.M., Nanda, A., Havenga, M.J., Abbink, P., Lynch, D.M., *et al.* 2006. Hexon-chimaeric adenovirus serotype 5 vectors circumvent pre-existing anti-vector immunity. *Nature*. **441**:239-243.
- Rodrigues, E.G., Zavala, F., Eichinger, D., Wilson, J.M., and Tsuji, M. 1997. Single immunizing dose of recombinant adenovirus efficiently induces CD8+ T cell-mediated protective immunity against malaria. *J Immunol*. **158**:1268-1274.
- Rodrigues, E.G., Zavala, F., Nussenzweig, R.S., Wilson, J.M. & Tsuji, M. Efficient induction of protective anti-malaria immunity by recombinant adenovirus. *Vaccine* **16**, 1812-1817 (1998).
- Roelvink, P.W., Mi Lee, G., Einfeld, D.A., Kovesdi, I. & Wickham, T.J. Identification of a conserved receptor-binding site on the Fiber proteins of CAR-recognizing adenoviridae. *Science (New York, N.Y)* **286**, 1568-1571 (1999).
- Rux, J.J. & Burnett, R.M. Type-specific epitope locations revealed by X-ray crystallographic study of adenovirus type 5 Hexon. *Mol Ther* **1**, 18-30 (2000).

Rux, J.J. & Burnett, R.M. Adenovirus structure. *Human gene therapy* **15**, 1167-1176 (2004).

Roy, S. *et al.* Use of chimeric adenoviral vectors to assess capsid neutralization determinants. *Virology* **333**, 207-214 (2005).

Silvie, O., Greco, C., Franetich, J.F., Dubart-Kupperschmitt, A., Hannoun, L., *et al.* 2006. Expression of human CD81 differently affects host cell susceptibility to malaria sporozoites depending on the Plasmodium species. *Cell Microbiol.* **8**:1134-1146.

Sumida, S.M., Truitt, D.M., Lemckert, A.A., Vogels, R., Custers, J.H., *et al.* 2005. Neutralizing antibodies to adenovirus serotype 5 vaccine vectors are directed primarily against the adenovirus Hexon protein. *J Immunol.* **174**:7179-7185.

Sun, P., Schwenk, R., White, K., Stoute, J.A., Cohen, J., *et al.* 2003. Protective immunity induced with malaria vaccine, RTS,S, is linked to Plasmodium falciparum circumsporozoite protein-specific CD4+ and CD8+ T cells producing IFN-gamma. *J Immunol.* **171**:6961-6967.

Tao, D., Barba-Spaeth, G., Rai, U., Nussenzweig, V., Rice, C.M., and Nussenzweig, R.S. 2005. Yellow fever 17D as a vaccine vector for microbial CTL epitopes: protection in a rodent malaria model. *J Exp Med.* **201**:201-209.

Teramoto, S. *et al.* Investigation of effects of anesthesia and age on aspiration in mice through LacZ gene transfer by recombinant E1-deleted adenovirus vectors. *American journal of respiratory and critical care medicine* **158**, 1914-1919 (1998).

Top, F.H., Jr., Dudding, B.A., Russell, P.K. & Buescher, E.L. Control of respiratory disease in recruits with types 4 and 7 adenovirus vaccines. *American journal of epidemiology* **94**, 142-146 (1971).

Top, F.H., Jr. Control of adenovirus acute respiratory disease in U.S. Army trainees. *Yale J Biol Med* **48**, 185-195 (1975).

Tsuji, M., Romero, P., Nussenzweig, R.S., and Zavala, F. 1990. CD4+ cytolytic T cell clone confers protection against murine malaria. *J Exp Med.* **172**:1353-1357.

Tsuji, M., Rodrigues, E.G. & Nussenzweig, S. Progress toward a malaria vaccine: efficient induction of protective anti-malaria immunity. *Biol Chem* **382**, 553-570 (2001).

Wickham, T.J., Mathias, P., Cheresch, D.A. & Nemerow, G.R. Integrins alpha v beta 3 and alpha v beta 5 promote adenovirus internalization but not virus attachment. *Cell* **73**, 309-319 (1993).

Wohlfart, C. Neutralization of adenoviruses: kinetics, stoichiometry, and mechanisms. *Journal of virology* **62**, 2321-2328 (1988).

- Worgall, S. *et al.* Modification to the capsid of the adenovirus vector that enhances dendritic cell infection and transgene-specific cellular immune responses. *Journal of virology* **78**, 2572-2580 (2004).
- Worgall, S., Krause, A., Rivara, M., Hee, K.K., Vintayen, E.V., et al. 2005. Protection against *P. aeruginosa* with an adenovirus vector containing an OprF epitope in the capsid. *J Clin Invest.* **115**:1281-1289.
- Worgall, S., Krause, A., Qiu, J., Joh, J., Hackett, N.R., and Crystal, R.G. 2007. Protective immunity to *pseudomonas aeruginosa* induced with a capsid-modified adenovirus expressing *P. aeruginosa* OprF. *J Virol.* **81**:13801-13808.
- Wu, H., Dmitriev, I., Kashentseva, E., Seki, T., Wang, M., et al. 2002. Construction and characterization of adenovirus serotype 5 packaged by serotype 3 Hexon. *J Virol.* **76**:12775-12782.
- Wu, H. *et al.* Identification of sites in adenovirus Hexon for foreign peptide incorporation. *Journal of virology* **79**, 3382-3390 (2005).
- Xia, D., Henry, L., Gerard, R.D. & Deisenhofer, J. Structure of the receptor binding domain of adenovirus type 5 Fiber protein. *Current topics in microbiology and immunology* **199 (Pt 1)**, 39-46 (1995).
- Yang, Y., Li, Q., Ertl, H.C. & Wilson, J.M. Cellular and humoral immune responses to viral antigens create barriers to lung-directed gene therapy with recombinant adenoviruses. *Journal of virology* **69**, 2004-2015 (1995).
- Youil, R., Toner, T.J., Su, Q., Chen, M., Tang, A., et al. 2002. Hexon gene switch strategy for the generation of chimeric recombinant adenovirus. *Hum Gene Ther.* **13**: 311-320.

SEQUENCE LISTING

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Moriya TSUJI

<120> MODIFICATION OF RECOMBINANT ADENOVIRUS WITH IMMUNOGENIC
PLASMODIUM CIRCUMSPOROZOITE PROTEIN EPITOPES

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Leu Phe Val Glu Ala Leu Phe Gln Glu Tyr Gln Cys Tyr Gly Ser Ser	

15	20	25	
agc aac act cgt gtg ctg aac gaa ctt aac tat gat aat gca gga aca 147			
Ser Asn Thr Arg Val Leu Asn Glu Leu Asn Tyr Asp Asn Ala Gly Thr			
30	35	40	45
aat tta tat aac gaa ctg gag atg aat tac tat ggt aag cag gaa aat 195			
Asn Leu Tyr Asn Glu Leu Glu Met Asn Tyr Tyr Gly Lys Gln Glu Asn			
50	55	60	
tgg tac tct ctg aaa aag aac tct aga tct ctg ggc gag aac gac gac 243			
Trp Tyr Ser Leu Lys Lys Asn Ser Arg Ser Leu Gly Glu Asn Asp Asp			
65	70	75	
ggc aat aat gaa gac aat gaa aag ctg agg aag cca aag cac aaa aaa 291			
Gly Asn Asn Glu Asp Asn Glu Lys Leu Arg Lys Pro Lys His Lys Lys			
80	85	90	
cta aag cag ccc gca gac ggc aat cca gac ccc aat gct aac cca aac 339			
Leu Lys Gln Pro Ala Asp Gly Asn Pro Asp Pro Asn Ala Asn Pro Asn			
95	100	105	
gtg gac ccc aat gct aat cca aac gtg gat cct aac gct aac ccg aat 387			
Val Asp Pro Asn Ala Asn Pro Asn Val Asp Pro Asn Ala Asn Pro Asn			
110	115	120	125
gtg gac cct aac gcc aat cca aat gcg aat ccc aac gct aat cct aac 435			
Val Asp Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn			
130	135	140	
gca aac ccg aat gct aac cct aac gca aac ccc aac gct aac ccc aac 483			
Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn			
145	150	155	
gcg aac ccc aat gcc aac ccc aac gcc aac ccg aac gcc aat cca aac 531			
Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn			
160	165	170	
gct aac cct aat gcc aat cct aat gcc aat ccg aac gcc aat cca aat 579			
Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn			
175	180	185	
gcc aat cca aat gct aat ccc aac gtg gac ccc aac gcg aac cct aat 627			
Ala Asn Pro Asn Ala Asn Pro Asn Val Asp Pro Asn Ala Asn Pro Asn			
190	195	200	205
gcc aac ccc aac gct aat cca aat gcg aac cct aac gcc aac ccg aat 675			
Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn			
210	215	220	
gct aat ccc aat gcc aac ccc aat gct aat ccc aat gcg aac cct aat 723			

Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn
 225 230 235

gcc aat ccc aac gcc aac ccc aac gca aac cct aat gct aac ccg aac 771
 Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn
 240 245 250

gcc aat ccg aac gca aat cct aat gct aat cct aac gct aac ccc aac 819
 Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn
 255 260 265

gcc aat cca aat aag aac aat caa ggc aac ggg cag ggg cac aat atg 867
 Ala Asn Pro Asn Lys Asn Asn Gln Gly Asn Gly Gln Gly His Asn Met
 270 275 280 285

cca aat gac cct aac cgg aat gtc gac gag aat gca aat gcc aat agc 915
 Pro Asn Asp Pro Asn Arg Asn Val Asp Glu Asn Ala Asn Ala Asn Ser
 290 295 300

gcc gtg aaa aat aat aat aac gag gag cca agt gac aaa cac att aag 963
 Ala Val Lys Asn Asn Asn Asn Glu Glu Pro Ser Asp Lys His Ile Lys
 305 310 315

gaa tat ttg aac aag att caa aac tcc ctc tca aca gaa tgg tct cct 1011
 Glu Tyr Leu Asn Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro
 320 325 330

tgc agc gtg act tgt gga aat ggc atc cag gtt cgt att aaa cca ggt 1059
 Cys Ser Val Thr Cys Gly Asn Gly Ile Gln Val Arg Ile Lys Pro Gly
 335 340 345

agt gcc aac aag ccc aag gat gaa cta gac tat gcg aat gat ata gag 1107
 Ser Ala Asn Lys Pro Lys Asp Glu Leu Asp Tyr Ala Asn Asp Ile Glu
 350 355 360 365

aaa aaa atc tgt aag atg gag aaa tgc tagcttctag a 1145
 Lys Lys Ile Cys Lys Met Glu Lys Cys
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<212> DNA

<213> Artificial Sequence

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<223> (QGPGAP)3-HVR1 modified Hexon protein

<220>

<221> CDS

<222> (1)..(2829)

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Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser

1 5 10 15

ggc cag gac gcc tcg gag tac ctg agc ccc ggg ctg gtg cag ttt gcc 96

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala

20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro

35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu

50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr

65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met

85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr

100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly

115 120 125

gcc cca aat cct tgc gaa tgg gat gaa cag ggc cct gga gct cca cag 432

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln

130 135 140

gga cca ggt gca cct caa ggg cct gga gcc cct aaa act cac gta ttt 480

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe

145 150 155 160

ggg cag gcg cct tat tct ggt ata aat att aca aag gag ggt att caa 528

Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln

165 170 175

ata ggt gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa 576

Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln

180 185 190

cct gaa cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat 624
 Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn
 195 200 205

cat gca gct ggg aga gtc cta aaa aag act acc cca atg aaa cca tgt 672
 His Ala Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys
 210 215 220

tac ggt tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att 720
 Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile
 225 230 235 240

ctt gta aag caa caa aat gga aag cta gaa agt caa gtg gaa atg caa 768
 Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln
 245 250 255

ttt ttc tca act act gag gca gcc gca ggc aat ggt gat aac ttg act 816
 Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr
 260 265 270

cct aaa gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac 864
 Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp
 275 280 285

act cat att tct tac atg ccc act att aag gaa ggt aac tca cga gaa 912
 Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu
 290 295 300

cta atg ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt 960
 Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe
 305 310 315 320

agg gac aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg 1008
 Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met
 325 330 335

ggt gtt ctg gcg ggc caa gca tcg cag ttg aat gct gtt gta gat ttg 1056
 Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu
 340 345 350

caa gac aga aac aca gag ctt tca tac cag ctt ttg ctt gat tcc att 1104
 Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile
 355 360 365

ggt gat aga acc agg tac ttt tct atg tgg aat cag gct gtt gac agc 1152
 Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser
 370 375 380

tat gat cca gat gtt aga att att gaa aat cat gga act gaa gat gaa 1200
 Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly Thr Glu Asp Glu

385	390	395	400	
ctt cca aat tac tgc ttt cca ctg gga ggt gtg att aat aca gag act				1248
Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr				
	405	410	415	
ctt acc aag gta aaa cct aaa aca ggt cag gaa aat gga tgg gaa aaa				1296
Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys				
	420	425	430	
gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga aat aat				1344
Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn				
	435	440	445	
ttt gcc atg gaa atc aat cta aat gcc aac ctg tgg aga aat ttc ctg				1392
Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu				
	450	455	460	
tac tcc aac ata gcg ctg tat ttg ccc gac aag cta aag tac agt cct				1440
Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro				
	465	470	480	
tcc aac gta aaa att tct gat aac cca aac acc tac gac tac atg aac				1488
Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn				
	485	490	495	
aag cga gtg gtg gct ccc ggg cta gtg gac tgc tac att aac ctt gga				1536
Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly				
	500	505	510	
gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt aac cac				1584
Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His				
	515	520	525	
cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg ctg ggc aat ggt				1632
His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly				
	530	535	540	
cgc tat gtg ccc ttc cac atc cag gtg cct cag aag ttc ttt gcc att				1680
Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile				
	545	550	560	
aaa aac ctc ctt ctc ctg ccg ggc tca tac acc tac gag tgg aac ttc				1728
Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe				
	565	570	575	
agg aag gat gtt aac atg gtt ctg cag agc tcc cta gga aat gac cta				1776
Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn Asp Leu				
	580	585	590	
agg gtt gac gga gcc agc att aag ttt gat agc att tgc ctt tac gcc				1824

Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala
 595 600 605

acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg ctt gag gcc atg 1872
 Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met
 610 615 620

ctt aga aac gac acc aac gac cag tcc ttt aac gac tat ctc tcc gcc 1920
 Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala
 625 630 635 640

gcc aac atg ctc tac cct ata ccc gcc aac gct acc aac gtg ccc ata 1968
 Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile
 645 650 655

tcc atc ccc tcc cgc aac tgg gcg gct ttc cgc ggc tgg gcc ttc acg 2016
 Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr
 660 665 670

cgc ctt aag act aag gaa acc cca tca ctg ggc tcg ggc tac gac cct 2064
 Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro
 675 680 685

tat tac acc tac tct ggc tct ata ccc tac cta gat gga acc ttt tac 2112
 Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr
 690 695 700

ctc aac cac acc ttt aag aag gtg gcc att acc ttt gac tct tct gtc 2160
 Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val
 705 710 715 720

agc tgg cct ggc aat gac cgc ctg ctt acc ccc aac gag ttt gaa att 2208
 Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile
 725 730 735

aag cgc tca gtt gac ggg gag ggt tac aac gtt gcc cag tgt aac atg 2256
 Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met
 740 745 750

acc aaa gac tgg ttc ctg gta caa atg cta gct aac tat aac att ggc 2304
 Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly
 755 760 765

tac cag ggc ttc tat atc cca gag agc tac aag gac cgc atg tac tcc 2352
 Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser
 770 775 780

ttc ttt aga aac ttc cag ccc atg agc cgt cag gtg gtg gat gat act 2400
 Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr
 785 790 795 800

aaa tac aag gac tac caa cag gtg ggc atc cta cac caa cac aac aac 2448
 Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn
 805 810 815

tct gga ttt gtt ggc tac ctt gcc ccc acc atg cgc gaa gga cag gcc 2496
 Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala
 820 825 830

tac cct gct aac ttc ccc tat ccg ctt ata ggc aag acc gca gtt gac 2544
 Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp
 835 840 845

agc att acc cag aaa aag ttt ctt tgc gat cgc acc ctt tgg cgc atc 2592
 Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile
 850 855 860

cca ttc tcc agt aac ttt atg tcc atg ggc gca ctc aca gac ctg ggc 2640
 Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly
 865 870 875 880

caa aac ctt ctc tac gcc aac tcc gcc cac gcg cta gac atg act ttt 2688
 Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe
 885 890 895

gag gtg gat ccc atg gac gag ccc acc ctt ctt tat gtt ttg ttt gaa 2736
 Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu
 900 905 910

gtc ttt gac gtg gtc cgt gtg cac cag ccg cac cgc ggc gtc atc gaa 2784
 Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu
 915 920 925

acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac gcc aca aca taa 2832
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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

gcc cca aat cct tgc gaa tgg gat gaa cag gga cca gga gca cca cag 432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

gga cca gga gca cca cag gga cca gga gca ccg caa ggt cct ggt gct 480
Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

cct aaa act cac gta ttt ggg cag gcg cct tat tct ggt ata aat att 528
Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile
165 170 175

aca aag gag ggt att caa ata ggt gtc gaa ggt caa aca cct aaa tat 576
Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr
180 185 190

gcc gat aaa aca ttt caa cct gaa cct caa ata gga gaa tct cag tgg 624

Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp	
195 200 205	
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Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr	
210 215 220	
acc cca atg aaa cca tgt tac ggt tca tat gca aaa ccc aca aat gaa	720
Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu	
225 230 235 240	
aat gga ggg caa ggc att ctt gta aag caa caa aat gga aag cta gaa	768
Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu	
245 250 255	
agt caa gtg gaa atg caa ttt ttc tca act act gag gca gcc gca ggc	816
Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly	
260 265 270	
aat ggt gat aac ttg act cct aaa gtg gta ttg tac agt gaa gat gta	864
Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val	
275 280 285	
gat ata gaa acc cca gac act cat att tct tac atg ccc act att aag	912
Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys	
290 295 300	
gaa ggt aac tca cga gaa cta atg ggc caa caa tct atg ccc aac agg	960
Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg	
305 310 315 320	
cct aat tac att gct ttt agg gac aat ttt att ggt cta atg tat tac	1008
Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr	
325 330 335	
aac agc acg ggt aat atg ggt gtt ctg gcg ggc caa gca tcg cag ttg	1056
Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu	
340 345 350	
aat gct gtt gta gat ttg caa gac aga aac aca gag ctt tca tac cag	1104
Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln	
355 360 365	
ctt ttg ctt gat tcc att ggt gat aga acc agg tac ttt tct atg tgg	1152
Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp	
370 375 380	
aat cag ctt cca aat tac tgc ttt cca ctg gga ggt gtg att aat aca	1200
Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr	
385 390 395 400	

gag act ctt acc aag gta aaa cct aaa aca ggt cag gaa aat gga tgg 1248
 Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
 405 410 415

gaa aaa gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga 1296
 Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
 420 425 430

aat aat ttt gcc atg gaa atc aat cta aat gcc aac ctg tgg aga aat 1344
 Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
 435 440 445

ttc ctg tac tcc aac ata gcg ctg tat ttg ccc gac aag cta aag tac 1392
 Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
 450 455 460

agt cct tcc aac gta aaa att tct gat aac cca aac acc tac gac tac 1440
 Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
 465 470 475 480

atg aac aag cga gtg gtg gct ccc ggg cta gtg gac tgc tac att aac 1488
 Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
 485 490 495

ctt gga gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt 1536
 Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
 500 505 510

aac cac cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg ctg ggc 1584
 Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
 515 520 525

aat ggt cgc tat gtg ccc ttc cac atc cag gtg cct cag aag ttc ttt 1632
 Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
 530 535 540

gcc att aaa aac ctc ctt ctc ctg ccg ggc tca tac acc tac gag tgg 1680
 Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
 545 550 555 560

aac ttc agg aag gat gtt aac atg gtt ctg cag agc tcc cta gga aat 1728
 Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
 565 570 575

gac cta agg gtt gac gga gcc agc att aag ttt gat agc att tgc ctt 1776
 Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
 580 585 590

tac gcc acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg ctt gag 1824
 Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
 595 600 605

gcc atg ctt aga aac gac acc aac gac cag tcc ttt aac gac tat ctc 1872
 Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
 610 615 620

tcc gcc gcc aac atg ctc tac cct ata ccc gcc aac gct acc aac gtg 1920
 Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
 625 630 635 640

ccc ata tcc atc ccc tcc cgc aac tgg gcg gct ttc cgc ggc tgg gcc 1968
 Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
 645 650 655

ttc acg cgc ctt aag act aag gaa acc cca tca ctg ggc tcg ggc tac 2016
 Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr
 660 665 670

gac cct tat tac acc tac tct ggc tct ata ccc tac cta gat gga acc 2064
 Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
 675 680 685

ttt tac ctc aac cac acc ttt aag aag gtg gcc att acc ttt gac tct 2112
 Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser
 690 695 700

tct gtc agc tgg cct ggc aat gac cgc ctg ctt acc ccc aac gag ttt 2160
 Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
 705 710 715 720

gaa att aag cgc tca gtt gac ggg gag ggt tac aac gtt gcc cag tgt 2208
 Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
 725 730 735

aac atg acc aaa gac tgg ttc ctg gta caa atg cta gct aac tat aac 2256
 Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
 740 745 750

att ggc tac cag ggc ttc tat atc cca gag agc tac aag gac cgc atg 2304
 Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met
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tac tcc ttc ttt aga aac ttc cag ccc atg agc cgt cag gtg gtg gat 2352
 Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
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gat act aaa tac aag gac tac caa cag gtg ggc atc cta cac caa cac 2400
 Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
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aac aac tct gga ttt gtt ggc tac ctt gcc ccc acc atg cgc gaa gga 2448
 Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly

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Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp			
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cgc atc cca ttc tcc agt aac ttt atg tcc atg ggc gca ctc aca gac	2592		
Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp			
850 855 860			
ctg ggc caa aac ctt ctc tac gcc aac tcc gcc cac gcg cta gac atg	2640		
Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met			
865 870 875 880			
act ttt gag gtg gat ccc atg gac gag ccc acc ctt ctt tat gtt ttg	2688		
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Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val			
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atc gaa acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac gcc aca	2784		
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Thr			

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 Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
 20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
 Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
 35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
 Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
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acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
 Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
 65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
 Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
 85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
 Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
 100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
 Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
 115 120 125

gcc cca aat cct tgc gaa tgg gat gaa cag gga cca gga gca cca cag 432
 Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
 130 135 140

gga cca gga gca cca cag gga cca gga gca ccg caa ggt cct ggt gct 480
 Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
 145 150 155 160

cct cag gga cca gga gca cca aaa act cac gta ttt ggg cag gcg cct 528
 Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe Gly Gln Ala Pro
 165 170 175

tat tct ggt ata aat att aca aag gag ggt att caa ata ggt gtc gaa 576
 Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly Val Glu
 180 185 190

ggt caa aca cct aaa tat gcc gat aaa aca ttt caa cct gaa cct caa 624
 Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln
 195 200 205

ata gga gaa tct cag tgg tac gaa aca gaa att aat cat gca gct ggg 672
 Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala Ala Gly
 210 215 220

aga gtc cta aaa aag act acc cca atg aaa cca tgt tac ggt tca tat 720
 Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr
 225 230 235 240

gca aaa ccc aca aat gaa aat gga ggg caa ggc att ctt gta aag caa 768
 Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val Lys Gln
 245 250 255

caa aat gga aag cta gaa agt caa gtg gaa atg caa ttt ttc tca act 816
 Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe Ser Thr
 260 265 270

act gag gca gcc gca ggc aat ggt gat aac ttg act cct aaa gtg gta 864
 Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys Val Val
 275 280 285

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 Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met Gly Gln
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caa tct atg ccc aac agg cct aat tac att gct ttt agg gac aat ttt 1008
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 325 330 335

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 Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn
 355 360 365

aca gag ctt tca tac cag ctt ttg ctt gat tcc att ggt gat aga acc 1152
 Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr
 370 375 380

agg tac ttt tct atg tgg aat cag ctt cca aat tac tgc ttt cca ctg 1200
 Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu
 385 390 395 400

gga ggt gtg att aat aca gag act ctt acc aag gta aaa cct aaa aca 1248
 Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro Lys Thr
 405 410 415

ggt cag gaa aat gga tgg gaa aaa gat gct aca gaa ttt tca gat aaa 1296
 Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys
 420 425 430

aat gaa ata aga gtt gga aat aat ttt gcc atg gaa atc aat cta aat 1344
 Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn Leu Asn
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gcc aac ctg tgg aga aat ttc ctg tac tcc aac ata gcg ctg tat ttg 1392
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ccc gac aag cta aag tac agt cct tcc aac gta aaa att tct gat aac 1440
 Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser Asp Asn
 465 470 475 480

cca aac acc tac gac tac atg aac aag cga gtg gtg gct ccc ggg cta 1488
 Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro Gly Leu
 485 490 495

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 Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met
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 Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His Ile Gln
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 Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly
 545 550 555 560

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 Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met Val Leu
 565 570 575

cag agc tcc cta gga aat gac cta agg gtt gac gga gcc agc att aag 1776
 Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser Ile Lys
 580 585 590

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 Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala His Asn
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acc gcc tcc acg ctt gag gcc atg ctt aga aac gac acc aac gac cag 1872
 Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn Asp Gln

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Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro			
625	630	635	640
gcc aac gct acc aac gtg ccc ata tcc atc ccc tcc cgc aac tgg gcg	1968		
Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala			
645	650	655	
gct ttc cgc ggc tgg gcc ttc acg cgc ctt aag act aag gaa acc cca	2016		
Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro			
660	665	670	
tca ctg ggc tgc ggc tac gac cct tat tac acc tac tct ggc tct ata	2064		
Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile			
675	680	685	
ccc tac cta gat gga acc ttt tac ctc aac cac acc ttt aag aag gtg	2112		
Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys Lys Val			
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gcc att acc ttt gac tct tct gtc agc tgg cct ggc aat gac cgc ctg	2160		
Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu			
705	710	715	720
ctt acc ccc aac gag ttt gaa att aag cgc tca gtt gac ggg gag ggt	2208		
Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly Glu Gly			
725	730	735	
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Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu Val Gln			
740	745	750	
atg cta gct aac tat aac att ggc tac cag ggc ttc tat atc cca gag	2304		
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755	760	765	
agc tac aag gac cgc atg tac tcc ttc ttt aga aac ttc cag ccc atg	2352		
Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met			
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Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val			
785	790	795	800
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Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala			
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ccc acc atg cgc gaa gga cag gcc tac cct gct aac ttc ccc tat ccg	2496		

Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro
820 825 830

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835 840 845

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Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe Met Ser
850 855 860

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865 870 875 880

gcc cac gcg cta gac atg act ttt gag gtg gat ccc atg gac gag ccc 2688
Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp Glu Pro
885 890 895

acc ctt ctt tat gtt ttg ttt gaa gtc ttt gac gtg gtc cgt gtg cac 2736
Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg Val His
900 905 910

cag ccg cac gcg ggc gtc atc gaa acc gtg tac ctg cgc acg ccc ttc 2784
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 Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
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cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
 Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
 35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
 Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
 50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
 Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
 65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
 Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
 85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
 Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
 100 105 110

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 Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
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 Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
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gga cca gga gca cca cag gga cca gga gca ccg caa ggt cct ggt gct 480
 Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
 145 150 155 160

cct cag gga cca gga gca cca cag gga cca gga gca cca aaa act cac 528
 Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His
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 180 185 190

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 195 200 205

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Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln			
245	250	255	
ggc att ctt gta aag caa caa aat gga aag cta gaa agt caa gtg gaa			816
Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu			
260	265	270	
atg caa ttt ttc tca act act gag gca gcc gca ggc aat ggt gat aac			864
Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn			
275	280	285	
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Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr			
290	295	300	
cca gac act cat att tct tac atg ccc act att aag gaa ggt aac tca			960
Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser			
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cga gaa cta atg ggc caa caa tct atg ccc aac agg cct aat tac att			1008
Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile			
325	330	335	
gct ttt agg gac aat ttt att ggt cta atg tat tac aac agc acg ggt			1056
Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly			
340	345	350	
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Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val			
355	360	365	
gat ttg caa gac aga aac aca gag ctt tca tac cag ctt ttg ctt gat			1152
Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp			
370	375	380	
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Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro			
385	390	395	400
aat tac tgc ttt cca ctg gga ggt gtg att aat aca gag act ctt acc			1248
Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr			
405	410	415	
aag gta aaa cct aaa aca ggt cag gaa aat gga tgg gaa aaa gat gct			1296

Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala
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 Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala
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 465 470 475 480
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 Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg
 485 490 495
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 515 520 525
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 545 550 555 560
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 565 570 575
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 Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe
 595 600 605
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aac gac acc aac gac cag tcc ttt aac gac tat ctc tcc gcc gcc aac 1920
 Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn
 625 630 635 640

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 Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu
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 Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr
 675 680 685

acc tac tct ggc tct ata ccc tac cta gat gga acc ttt tac ctc aac 2112
 Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn
 690 695 700

cac acc ttt aag aag gtg gcc att acc ttt gac tct tct gtc agc tgg 2160
 His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp
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cct ggc aat gac cgc ctg ctt acc ccc aac gag ttt gaa att aag cgc 2208
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tca gtt gac ggg gag ggt tac aac gtt gcc cag tgt aac atg acc aaa 2256
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gac tgg ttc ctg gta caa atg cta gct aac tat aac att ggc tac cag 2304
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 755 760 765

ggc ttc tat atc cca gag agc tac aag gac cgc atg tac tcc ttc ttt 2352
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 770 775 780

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 785 790 795 800

aag gac tac caa cag gtg ggc atc cta cac caa cac aac aac tct gga 2448
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ttt gtt ggc tac ctt gcc ccc acc atg cgc gaa gga cag gcc tac cct 2496
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 820 825 830

gct aac ttc ccc tat ccg ctt ata ggc aag acc gca gtt gac agc att 2544
 Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile
 835 840 845

acc cag aaa aag ttt ctt tgc gat cgc acc ctt tgg cgc atc cca ttc 2592
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 850 855 860

tcc agt aac ttt atg tcc atg ggc gca ctc aca gac ctg ggc caa aac 2640
 Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn
 865 870 875 880

ctt ctc tac gcc aac tcc gcc cac gcg cta gac atg act ttt gag gtg 2688
 Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val
 885 890 895

gat ccc atg gac gag ccc acc ctt ctt tat gtt ttg ttt gaa gtc ttt 2736
 Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe
 900 905 910

gac gtg gtc cgt gtg cac cag ccg cac cgc ggc gtc atc gaa acc gtg 2784
 Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu Thr Val
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ggc cag gac gcc tcg gag tac ctg agc ccc ggg ctg gtg cag ttt gcc 96

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
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cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
 Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
 35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
 Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
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acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
 Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
 65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
 Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
 85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
 Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
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ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
 Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
 115 120 125

gcc cca aat cct tgc gaa tgg gat gaa cag gga cca gga gca cca cag 432
 Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
 130 135 140

gga cca gga gca cca cag gga cca gga gca cca cag gga cca gga gca 480
 Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
 145 150 155 160

cca cag gga cca gga gca cca cag gga cca gga gca ccg caa ggt cct 528
 Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
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ggt gct cct aaa act cac gta ttt ggg cag gcg cct tat tct ggt ata 576
 Gly Ala Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile
 180 185 190

aat att aca aag gag ggt att caa ata ggt gtc gaa ggt caa aca cct 624
 Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro
 195 200 205

aaa tat gcc gat aaa aca ttt caa cct gaa cct caa ata gga gaa tct 672
 Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser
 210 215 220

cag tgg tac gaa aca gaa att aat cat gca gct ggg aga gtc cta aaa 720
 Gln Trp Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys
 225 230 235 240

aag act acc cca atg aaa cca tgt tac ggt tca tat gca aaa ccc aca 768
 Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr
 245 250 255

aat gaa aat gga ggg caa ggc att ctt gta aag caa caa aat gga aag 816
 Asn Glu Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys
 260 265 270

cta gaa agt caa gtg gaa atg caa ttt ttc tca act act gag gca gcc 864
 Leu Glu Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala
 275 280 285

gca ggc aat ggt gat aac ttg act cct aaa gtg gta ttg tac agt gaa 912
 Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu
 290 295 300

gat gta gat ata gaa acc cca gac act cat att tct tac atg ccc act 960
 Asp Val Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr
 305 310 315 320

att aag gaa ggt aac tca cga gaa cta atg ggc caa caa tct atg ccc 1008
 Ile Lys Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro
 325 330 335

aac agg cct aat tac att gct ttt agg gac aat ttt att ggt cta atg 1056
 Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met
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tat tac aac agc acg ggt aat atg ggt gtt ctg gcg ggc caa gca tcg 1104
 Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser
 355 360 365

cag ttg aat gct gtt gta gat ttg caa gac aga aac aca gag ctt tca 1152
 Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser
 370 375 380

tac cag ctt ttg ctt gat tcc att ggt gat aga acc agg tac ttt tct 1200
 Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser
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 Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile
 405 410 415

aat aca gag act ctt acc aag gta aaa cct aaa aca ggt cag gaa aat 1296
 Asn Thr Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn
 420 425 430

gga tgg gaa aaa gat gct aca gaa ttt tca gat aaa aat gaa ata aga 1344
 Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg
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 Val Gly Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp
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aga aat ttc ctg tac tcc aac ata gcg ctg tat ttg ccc gac aag cta 1440
 Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu
 465 470 475 480

aag tac agt cct tcc aac gta aaa att tct gat aac cca aac acc tac 1488
 Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr
 485 490 495

gac tac atg aac aag cga gtg gtg gct ccc ggg cta gtg gac tgc tac 1536
 Asp Tyr Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr
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 Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn
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cca ttt aac cac cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg 1632
 Pro Phe Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu
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 545 550 555 560

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 580 585 590

gga aat gac cta agg gtt gac gga gcc agc att aag ttt gat agc att 1824
 Gly Asn Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile
 595 600 605

tgc ctt tac gcc acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg 1872
 Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr
 610 615 620

ctt gag gcc atg ctt aga aac gac acc aac gac cag tcc ttt aac gac 1920
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625	630	635	640	
tat ctc tcc gcc gcc aac atg ctc tac cct ata ccc gcc aac gct acc				1968
Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr				
645	650	655		
aac gtg ccc ata tcc atc ccc tcc cgc aac tgg gcg gct ttc cgc ggc				2016
Asn Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly				
660	665	670		
tgg gcc ttc acg cgc ctt aag act aag gaa acc cca tca ctg ggc tcg				2064
Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser				
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ggc tac gac cct tat tac acc tac tct ggc tct ata ccc tac cta gat				2112
Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp				
690	695	700		
gga acc ttt tac ctc aac cac acc ttt aag aag gtg gcc att acc ttt				2160
Gly Thr Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe				
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gac tct tct gtc agc tgg cct ggc aat gac cgc ctg ctt acc ccc aac				2208
Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn				
725	730	735		
gag ttt gaa att aag cgc tca gtt gac ggg gag ggt tac aac gtt gcc				2256
Glu Phe Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala				
740	745	750		
cag tgt aac atg acc aaa gac tgg ttc ctg gta caa atg cta gct aac				2304
Gln Cys Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn				
755	760	765		
tat aac att ggc tac cag ggc ttc tat atc cca gag agc tac aag gac				2352
Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp				
770	775	780		
cgc atg tac tcc ttc ttt aga aac ttc cag ccc atg agc cgt cag gtg				2400
Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val				
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Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His				
805	810	815		
caa cac aac aac tct gga ttt gtt ggc tac ctt gcc ccc acc atg cgc				2496
Gln His Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg				
820	825	830		
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Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys
 835 840 845
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 Thr Ala Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr
 850 855 860
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 Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu
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 gac atg act ttt gag gtg gat ccc atg gac gag ccc acc ctt ctt tat 2736
 Asp Met Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr
 900 905 910
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 Val Leu Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg
 915 920 925
 ggc gtc atc gaa acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac 2832
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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala				
20	25	30		
cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc				144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro				
35	40	45		
acg gtg cgc cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg				192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu				
50	55	60		
acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac				240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr				
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aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg				288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met				
85	90	95		
gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act				336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr				
100	105	110		
ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt				384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly				
115	120	125		
gcc cca aat cct tgc gaa tgg gat gaa cag gga cca gga gca cca cag				432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln				
130	135	140		
gga cca gga gca cca cag gga cca gga gca cca cag gga cca gga gca				480
Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala				
145	150	155	160	
cca cag gga cca gga gca cca cag gga cca gga gca ccg caa ggt cct				528
Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro				
165	170	175		
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Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe Gly Gln				
180	185	190		
gcg cct tat tct ggt ata aat att aca aag gag ggt att caa ata ggt				624
Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly				
195	200	205		
gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa cct gaa				672

Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu	
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cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat cat gca	720
Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala	
225 230 235 240	
gct ggg aga gtc cta aaa aag act acc cca atg aaa cca tgt tac ggt	768
Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly	
245 250 255	
tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att ctt gta	816
Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val	
260 265 270	
aag caa caa aat gga aag cta gaa agt caa gtg gaa atg caa ttt ttc	864
Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe	
275 280 285	
tca act act gag gca gcc gca ggc aat ggt gat aac ttg act cct aaa	912
Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys	
290 295 300	
gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac act cat	960
Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His	
305 310 315 320	
att tct tac atg ccc act att aag gaa ggt aac tca cga gaa cta atg	1008
Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met	
325 330 335	
ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt agg gac	1056
Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp	
340 345 350	
aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg ggt gtt	1104
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355 360 365	
ctg gcg ggc caa gca tcg cag ttg aat gct gtt gta gat ttg caa gac	1152
Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp	
370 375 380	
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Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp	
385 390 395 400	
aga acc agg tac ttt tct atg tgg aat cag ctt cca aat tac tgc ttt	1248
Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe	
405 410 415	

cca ctg gga ggt gtg att aat aca gag act ctt acc aag gta aaa cct 1296
Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
420 425 430

aaa aca ggt cag gaa aat gga tgg gaa aaa gat gct aca gaa ttt tca 1344
Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
435 440 445

gat aaa aat gaa ata aga gtt gga aat aat ttt gcc atg gaa atc aat 1392
Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
450 455 460

cta aat gcc aac ctg tgg aga aat ttc ctg tac tcc aac ata gcg ctg 1440
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465 470 475 480

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Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
485 490 495

gat aac cca aac acc tac gac tac atg aac aag cga gtg gtg gct ccc 1536
Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
500 505 510

ggg cta gtg gac tgc tac att aac ctt gga gca cgc tgg tcc ctt gac 1584
Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
515 520 525

tat atg gac aac gtc aac cca ttt aac cac cac cgc aat gct ggc ctg 1632
Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
530 535 540

cgc tac cgc tca atg ttg ctg ggc aat ggt cgc tat gtg ccc ttc cac 1680
Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
545 550 555 560

atc cag gtg cct cag aag ttc ttt gcc att aaa aac ctc ctt ctc ctg 1728
Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
565 570 575

ccg ggc tca tac acc tac gag tgg aac ttc agg aag gat gtt aac atg 1776
Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
580 585 590

gtt ctg cag agc tcc cta gga aat gac cta agg gtt gac gga gcc agc 1824
Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
595 600 605

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Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
610 615 620

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 His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
 625 630 635 640

gac cag tcc ttt aac gac tat ctc tcc gcc gcc aac atg ctc tac cct 1968
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acc cca tca ctg ggc tgc ggc tac gac cct tat tac acc tac tct ggc 2112
 Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
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tct ata ccc tac cta gat gga acc ttt tac ctc aac cac acc ttt aag 2160
 Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
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aag gtg gcc att acc ttt gac tct tct gtc agc tgg cct ggc aat gac 2208
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 725 730 735

cgc ctg ctt acc ccc aac gag ttt gaa att aag cgc tca gtt gac ggg 2256
 Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
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 755 760 765

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 Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
 785 790 795 800

ccc atg agc cgt cag gtg gtg gat gat act aaa tac aag gac tac caa 2448
 Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln
 805 810 815

cag gtg ggc atc cta cac caa cac aac aac tct gga ttt gtt ggc tac 2496
 Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr

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Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro			
835	840	845	
tat ccg ctt ata ggc aag acc gca gtt gac agc att acc cag aaa aag			2592
Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys			
850	855	860	
ttt ctt tgc gat cgc acc ctt tgg cgc atc cca ttc tcc agt aac ttt			2640
Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe			
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Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala			
885	890	895	
aac tcc gcc cac gcg cta gac atg act ttt gag gtg gat ccc atg gac			2736
Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp			
900	905	910	
gag ccc acc ctt ctt tat gtt ttg ttt gaa gtc ttt gac gtg gtc cgt			2784
Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg			
915	920	925	
gtg cac cag ccg cac cgc ggc gtc atc gaa acc gtg tac ctg cgc acg			2832
Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr			
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Pro Phe Ser Ala Gly Asn Ala Thr Thr			
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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

gcc cca aat cct tgc gaa tgg gat gaa cag gga cca gga gca cca cag 432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

gga cca gga gca cca cag gga cca gga gca cca cag gga cca gga gca 480
Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

cca cag gga cca gga gca cca cag gga cca gga gca ccg caa ggt cct 528
Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
165 170 175

ggt gct cct cag gga cca gga gca cca cag gga cca gga gca cca aaa 576
Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys
180 185 190

act cac gta ttt ggg cag gcg cct tat tct ggt ata aat att aca aag 624
Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys

195	200	205	
gag ggt att caa ata ggt gtc gaa ggt caa aca cct aaa tat gcc gat			672
Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp			
210	215	220	
aaa aca ttt caa cct gaa cct caa ata gga gaa tct cag tgg tac gaa			720
Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu			
225	230	235	240
aca gaa att aat cat gca gct ggg aga gtc cta aaa aag act acc cca			768
Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr Thr Pro			
245	250	255	
atg aaa cca tgt tac ggt tca tat gca aaa ccc aca aat gaa aat gga			816
Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly			
260	265	270	
ggg caa ggc att ctt gta aag caa caa aat gga aag cta gaa agt caa			864
Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln			
275	280	285	
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Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly			
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Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile			
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gaa acc cca gac act cat att tct tac atg ccc act att aag gaa ggt			1008
Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly			
325	330	335	
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Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn			
340	345	350	
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Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser			
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acg ggt aat atg ggt gtt ctg gcg ggc caa gca tcg cag ttg aat gct			1152
Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala			
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gtt gta gat ttg caa gac aga aac aca gag ctt tca tac cag ctt ttg			1200
Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu			
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ctt gat tcc att ggt gat aga acc agg tac ttt tct atg tgg aat cag			1248

Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln
 405 410 415

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 Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr
 420 425 430

 ctt acc aag gta aaa cct aaa aca ggt cag gaa aat gga tgg gaa aaa 1344
 Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys
 435 440 445

 gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga aat aat 1392
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 450 455 460

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 Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro
 485 490 495

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 Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly
 515 520 525

 gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt aac cac 1632
 Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His
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 cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg ctg ggc aat ggt 1680
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 545 550 555 560

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 Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile
 565 570 575

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 Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe
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 agg aag gat gtt aac atg gtt ctg cag agc tcc cta gga aat gac cta 1824
 Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn Asp Leu
 595 600 605

agg gtt gac gga gcc agc att aag ttt gat agc att tgc ctt tac gcc 1872
Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala
610 615 620

acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg ctt gag gcc atg 1920
Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met
625 630 635 640

ctt aga aac gac acc aac gac cag tcc ttt aac gac tat ctc tcc gcc 1968
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645 650 655

gcc aac atg ctc tac cct ata ccc gcc aac gct acc aac gtg ccc ata 2016
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660 665 670

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Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr
675 680 685

cgc ctt aag act aag gaa acc cca tca ctg ggc tcg ggc tac gac cct 2112
Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro
690 695 700

tat tac acc tac tct ggc tct ata ccc tac cta gat gga acc ttt tac 2160
Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr
705 710 715 720

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Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val
725 730 735

agc tgg cct ggc aat gac cgc ctg ctt acc ccc aac gag ttt gaa att 2256
Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile
740 745 750

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755 760 765

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Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly
770 775 780

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Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser
785 790 795 800

ttc ttt aga aac ttc cag ccc atg agc cgt cag gtg gtg gat gat act 2448
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805 810 815

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 835 840 845

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 Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp
 850 855 860

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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg cgc cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

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Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

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Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

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Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

gga cca gga gca cca cag gga cca gga gca cca cag gga cca gga gca 480
Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

cca cag gga cca gga gca cca cag gga cca gga gca cca cag gga cca 528
Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
165 170 175

gga gca cca cag gga cca gga gca ccg caa ggt cct ggt gct cct cag 576
Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln
180 185 190

gga cca gga gca cca cag gga cca gga gca cca aaa act cac gta ttt 624
 Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe
 195 200 205

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 Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln
 210 215 220

ata ggt gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa 720
 Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln
 225 230 235 240

cct gaa cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat 768
 Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn
 245 250 255

cat gca gct ggg aga gtc cta aaa aag act acc cca atg aaa cca tgt 816
 His Ala Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys
 260 265 270

tac ggt tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att 864
 Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile
 275 280 285

ctt gta aag caa caa aat gga aag cta gaa agt caa gtg gaa atg caa 912
 Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln
 290 295 300

ttt ttc tca act act gag gca gcc gca ggc aat ggt gat aac ttg act 960
 Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr
 305 310 315 320

cct aaa gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac 1008
 Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp
 325 330 335

act cat att tct tac atg ccc act att aag gaa ggt aac tca cga gaa 1056
 Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu
 340 345 350

cta atg ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt 1104
 Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe
 355 360 365

agg gac aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg 1152
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 370 375 380

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 385 390 395 400

caa gac aga aac aca gag ctt tca tac cag ctt ttg ctt gat tcc att 1248
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 405 410 415

ggt gat aga acc agg tac ttt tct atg tgg aat cag ctt cca aat tac 1296
 Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr
 420 425 430

tgc ttt cca ctg gga ggt gtg att aat aca gag act ctt acc aag gta 1344
 Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val
 435 440 445

aaa cct aaa aca ggt cag gaa aat gga tgg gaa aaa gat gct aca gaa 1392
 Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu
 450 455 460

ttt tca gat aaa aat gaa ata aga gtt gga aat aat ttt gcc atg gaa 1440
 Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu
 465 470 475 480

atc aat cta aat gcc aac ctg tgg aga aat ttc ctg tac tcc aac ata 1488
 Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile
 485 490 495

gcg ctg tat ttg ccc gac aag cta aag tac agt cct tcc aac gta aaa 1536
 Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys
 500 505 510

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 Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val
 515 520 525

gct ccc ggg cta gtg gac tgc tac att aac ctt gga gca cgc tgg tcc 1632
 Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser
 530 535 540

ctt gac tat atg gac aac gtc aac cca ttt aac cac cac cgc aat gct 1680
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 545 550 555 560

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 565 570 575

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 580 585 590

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Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro			
625	630	635	640
atg gcc cac aac acc gcc tcc acg ctt gag gcc atg ctt aga aac gac			1968
Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp			
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Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr			
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Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr			
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 Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val
 835 840 845
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 Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn
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 Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln
 865 870 875 880
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 885 890 895
 aac ttt atg tcc atg ggc gca ctc aca gac ctg ggc caa aac ctt ctc 2736
 Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu
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 Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro
 915 920 925
 atg gac gag ccc acc ctt ctt tat gtt ttg ttt gaa gtc ttt gac gtg 2832
 Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val
 930 935 940
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 Val Arg Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu
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20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
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50 55 60

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65 70 75 80

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Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
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Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
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Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

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130 135 140

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Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

cca cag gga cca gga gca cca cag gga cca gga gca cca cag gga cca 528
Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro

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Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln			
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Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala			
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Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile			
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Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr			
225	230	235	240
gcc gat aaa aca ttt caa cct gaa cct caa ata gga gaa tct cag tgg			768
Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp			
245	250	255	
tac gaa aca gaa att aat cat gca gct ggg aga gtc cta aaa aag act			816
Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr			
260	265	270	
acc cca atg aaa cca tgt tac ggt tca tat gca aaa ccc aca aat gaa			864
Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu			
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Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly			
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Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val			
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Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys			
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 385 390 395 400

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595 600 605

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Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
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Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
725 730 735

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740 745 750

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Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
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Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
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Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

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Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
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Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu			
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cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat cat gca	624		
Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala			
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tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att ctt gta	720		
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Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met			
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Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp			
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aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg ggt gtt	1008		
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 580 585 590

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 Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu
 225 230 235 240

aat gga ggg caa ggc att ctt gta aag caa caa aat gga aag cta gaa 768
 Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu
 245 250 255

agt caa gtg gaa atg caa ttt ttc tca act act gag gca gcc gca ggc 816
 Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly
 260 265 270

aat ggt gat aac ttg act cct aaa gtg gta ttg tac agt gaa gat gta 864
 Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val
 275 280 285

gat ata gaa acc cca gac act cat att tct tac atg ccc act att aag 912
 Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
 290 295 300

gaa ggt aac tca cga gaa cta atg ggc caa caa tct atg ccc aac agg 960
 Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
 305 310 315 320

cct aat tac att gct ttt agg gac aat ttt att ggt cta atg tat tac 1008
 Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
 325 330 335

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 340 345 350

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 Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
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 370 375 380

aat cag ctt cca aat tac tgc ttt cca ctg gga ggt gtg att aat aca 1200
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 385 390 395 400

gag act ctt acc aag gta aaa cct aaa aca ggt cag gaa aat gga tgg 1248
 Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
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gaa aaa gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga 1296
 Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
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 Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
 465 470 475 480

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 Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
 485 490 495

ctt gga gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt 1536
 Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
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	565	570	575	
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Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu				
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tac gcc acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg ctt gag				1824
Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu				
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gcc atg ctt aga aac gac acc aac gac cag tcc ttt aac gac tat ctc				1872
Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu				
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tcc gcc gcc aac atg ctc tac cct ata ccc gcc aac gct acc aac gtg				1920
Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val				
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ccc ata tcc atc ccc tcc cgc aac tgg gcg gct ttc cgc ggc tgg gcc				1968
Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala				
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ttc acg cgc ctt aag act aag gaa acc cca tca ctg ggc tcg ggc tac				2016
Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr				
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Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr				
	675	680	685	
ttt tac ctc aac cac acc ttt aag aag gtg gcc att acc ttt gac tct				2112
Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser				
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Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe				
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Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn				
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 Asp Thr Lys Tyr Lys Asp Tyr Gln Val Gly Ile Leu His Gln His
 785 790 795 800

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 820 825 830

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 835 840 845

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 Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
 850 855 860

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 Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
 900 905 910

 atc gaa acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac gcc aca 2784
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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
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acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

gcc cca aat cct tgc gaa tgg gat gaa aat gca aat cca aat gca aat 432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

cca aat gca aat cca aat gca aat cca aac gcg aac ccg aat gct aat 480
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

cct aat gca aat cca aat gca aat cca aaa act cac gta ttt ggg cag 528
Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln
165 170 175

gcg cct tat tct ggt ata aat att aca aag gag ggt att caa ata ggt 576
Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
180 185 190

gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa cct gaa 624
Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
195 200 205

cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat cat gca 672
Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
210 215 220

gct ggg aga gtc cta aaa aag act acc cca atg aaa cca tgt tac ggt 720
Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
225 230 235 240

tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att ctt gta 768
Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
245 250 255

aag caa caa aat gga aag cta gaa agt caa gtg gaa atg caa ttt ttc 816
Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
260 265 270

tca act act gag gca gcc gca ggc aat ggt gat aac ttg act cct aaa 864
Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
275 280 285

gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac act cat 912
Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
290 295 300

att tct tac atg ccc act att aag gaa ggt aac tca cga gaa cta atg 960
Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
305 310 315 320

ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt agg gac 1008
Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
325 330 335

aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg ggt gtt 1056
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340 345 350

ctg gcg ggc caa gca tcg cag ttg aat gct gtt gta gat ttg caa gac 1104
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370	375	380	
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Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro			
405	410	415	
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Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser			
420	425	430	
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Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn			
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Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser			
465	470	475	480
gat aac cca aac acc tac gac tac atg aac aag cga gtg gtg gct ccc 1488			
Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro			
485	490	495	
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Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu			
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 580 585 590
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 Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
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 610 615 620
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20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro

35 40 45

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Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu

50 55 60

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Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr

65 70 75 80

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Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met

85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr

100 105 110

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Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly

115 120 125

gcc cca aat cct tgc gaa tgg gat gaa aat gca aat cca aat gca aat 432

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn

130 135 140

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Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn

145 150 155 160

cct aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat 528

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 325 330 335

 cct aat tac att gct ttt agg gac aat ttt att ggt cta atg tat tac 1056
 Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
 340 345 350

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 355 360 365

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Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
370 375 380

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Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
385 390 395 400

aat cag ctt cca aat tac tgc ttt cca ctg gga ggt gtg att aat aca 1248
Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
405 410 415

gag act ctt acc aag gta aaa cct aaa aca ggt cag gaa aat gga tgg 1296
Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
420 425 430

gaa aaa gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga 1344
Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
435 440 445

aat aat ttt gcc atg gaa atc aat cta aat gcc aac ctg tgg aga aat 1392
Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
450 455 460

ttc ctg tac tcc aac ata gcg ctg tat ttg ccc gac aag cta aag tac 1440
Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
465 470 475 480

agt cct tcc aac gta aaa att tct gat aac cca aac acc tac gac tac 1488
Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
485 490 495

atg aac aag cga gtg gtg gct ccc ggg cta gtg gac tgc tac att aac 1536
Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
500 505 510

ctt gga gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt 1584
Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
515 520 525

aac cac cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg ctg ggc 1632
Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
530 535 540

aat ggt cgc tat gtg ccc ttc cac atc cag gtg cct cag aag ttc ttt 1680
Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
545 550 555 560

gcc att aaa aac ctc ctt ctc ctg ccg ggc tca tac acc tac gag tgg 1728
Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
565 570 575

aac ttc agg aag gat gtt aac atg gtt ctg cag agc tcc cta gga aat 1776
 Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
 580 585 590

gac cta agg gtt gac gga gcc agc att aag ttt gat agc att tgc ctt 1824
 Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
 595 600 605

tac gcc acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg ctt gag 1872
 Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
 610 615 620

gcc atg ctt aga aac gac acc aac gac cag tcc ttt aac gac tat ctc 1920
 Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
 625 630 635 640

tcc gcc gcc aac atg ctc tac cct ata ccc gcc aac gct acc aac gtg 1968
 Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
 645 650 655

ccc ata tcc atc ccc tcc cgc aac tgg gcg gct ttc cgc ggc tgg gcc 2016
 Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
 660 665 670

ttc acg cgc ctt aag act aag gaa acc cca tca ctg ggc tcg ggc tac 2064
 Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr
 675 680 685

gac cct tat tac acc tac tct ggc tct ata ccc tac cta gat gga acc 2112
 Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
 690 695 700

ttt tac ctc aac cac acc ttt aag aag gtg gcc att acc ttt gac tct 2160
 Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser
 705 710 715 720

tct gtc agc tgg cct ggc aat gac cgc ctg ctt acc ccc aac gag ttt 2208
 Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
 725 730 735

gaa att aag cgc tca gtt gac ggg gag ggt tac aac gtt gcc cag tgt 2256
 Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
 740 745 750

aac atg acc aaa gac tgg ttc ctg gta caa atg cta gct aac tat aac 2304
 Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
 755 760 765

att ggc tac cag ggc ttc tat atc cca gag agc tac aag gac cgc atg 2352
 Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met

770	775	780	
tac tcc ttc ttt aga aac ttc cag ccc atg agc cgt cag gtg gat			2400
Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp			
785	790	795	800
gat act aaa tac aag gac tac caa cag gtg ggc atc cta cac caa cac			2448
Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His			
805	810	815	
aac aac tct gga ttt gtt ggc tac ctt gcc ccc acc atg cgc gaa gga			2496
Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly			
820	825	830	
cag gcc tac cct gct aac ttc ccc tat ccg ctt ata ggc aag acc gca			2544
Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala			
835	840	845	
gtt gac agc att acc cag aaa aag ttt ctt tgc gat cgc acc ctt tgg			2592
Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp			
850	855	860	
cgc atc cca ttc tcc agt aac ttt atg tcc atg ggc gca ctc aca gac			2640
Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp			
865	870	875	880
ctg ggc caa aac ctt ctc tac gcc aac tcc gcc cac gcg cta gac atg			2688
Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met			
885	890	895	
act ttt gag gtg gat ccc atg gac gag ccc acc ctt ctt tat gtt ttg			2736
Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu			
900	905	910	
ttt gaa gtc ttt gac gtg gtc cgt gtg cac cag ccg cac cgc ggc gtc			2784
Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val			
915	920	925	
atc gaa acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac gcc aca			2832
Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr			
930	935	940	
aca taa			2838
Thr			
945			

<213> Artificial Sequence

<220>

<223> (NANP)12-HVR1 modified Hexon protein

<220>

<221> CDS

<222> (1)..(2859)

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ggc cag gac gcc tcg gag tac ctg agc ccc ggg ctg gtg cag ttt gcc 96
Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg cgc cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

gcc cca aat cct tgc gaa tgg gat gaa aat gca aat cca aat gca aat 432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

cca aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat 480
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

cca aat gca aat cca aat gca aat cca aac gcg aac ccg aat gct aat 528
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
165 170 175

cct aat gca aat cca aat gca aat cca aaa act cac gta ttt ggg cag 576
Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln
180 185 190

gcg cct tat tct ggt ata aat att aca aag gag ggt att caa ata ggt 624
Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
195 200 205

gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa cct gaa 672
Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
210 215 220

cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat cat gca 720
Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
225 230 235 240

gct ggg aga gtc cta aaa aag act acc cca atg aaa cca tgt tac ggt 768
Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
245 250 255

tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att ctt gta 816
Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
260 265 270

aag caa caa aat gga aag cta gaa agt caa gtg gaa atg caa ttt ttc 864
Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
275 280 285

tca act act gag gca gcc gca ggc aat ggt gat aac ttg act cct aaa 912
Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
290 295 300

gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac act cat 960
Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
305 310 315 320

att tct tac atg ccc act att aag gaa ggt aac tca cga gaa cta atg 1008
Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
325 330 335

ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt agg gac 1056
Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
340 345 350

aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg ggt gtt 1104
Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
355 360 365

ctg gcg ggc caa gca tcg cag ttg aat gct gtt gta gat ttg caa gac 1152
Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
370 375 380

aga aac aca gag ctt tca tac cag ctt ttg ctt gat tcc att ggt gat 1200
Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
385 390 395 400

aga acc agg tac ttt tct atg tgg aat cag ctt cca aat tac tgc ttt 1248
Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
405 410 415

cca ctg gga ggt gtg att aat aca gag act ctt acc aag gta aaa cct 1296
Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
420 425 430

aaa aca ggt cag gaa aat gga tgg gaa aaa gat gct aca gaa ttt tca 1344
Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
435 440 445

gat aaa aat gaa ata aga gtt gga aat aat ttt gcc atg gaa atc aat 1392
Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
450 455 460

cta aat gcc aac ctg tgg aga aat ttc ctg tac tcc aac ata gcg ctg 1440
Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu
465 470 475 480

tat ttg ccc gac aag cta aag tac agt cct tcc aac gta aaa att tct 1488
Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
485 490 495

gat aac cca aac acc tac gac tac atg aac aag cga gtg gtg gct ccc 1536
Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
500 505 510

ggg cta gtg gac tgc tac att aac ctt gga gca cgc tgg tcc ctt gac 1584
Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
515 520 525

tat atg gac aac gtc aac cca ttt aac cac cac cgc aat gct ggc ctg 1632
Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
530 535 540

cgc tac cgc tca atg ttg ctg ggc aat ggt cgc tat gtg ccc ttc cac 1680
Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
545 550 555 560

atc cag gtg cct cag aag ttc ttt gcc att aaa aac ctc ctt ctc ctg 1728
Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu

565	570	575	
ccg ggc tca tac acc tac gag tgg aac ttc agg aag gat gtt aac atg 1776			
Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met			
580	585	590	
ggt ctg cag agc tcc cta gga aat gac cta agg gtt gac gga gcc agc 1824			
Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser			
595	600	605	
att aag ttt gat agc att tgc ctt tac gcc acc ttc ttc ccc atg gcc 1872			
Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala			
610	615	620	
cac aac acc gcc tcc acg ctt gag gcc atg ctt aga aac gac acc aac 1920			
His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn			
625	630	635	640
gac cag tcc ttt aac gac tat ctc tcc gcc gcc aac atg ctc tac cct 1968			
Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro			
645	650	655	
ata ccc gcc aac gct acc aac gtg ccc ata tcc atc ccc tcc cgc aac 2016			
Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn			
660	665	670	
tgg gcg gct ttc cgc ggc tgg gcc ttc acg cgc ctt aag act aag gaa 2064			
Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu			
675	680	685	
acc cca tca ctg ggc tcg ggc tac gac cct tat tac acc tac tct gcc 2112			
Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly			
690	695	700	
tct ata ccc tac cta gat gga acc ttt tac ctc aac cac acc ttt aag 2160			
Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys			
705	710	715	720
aag gtg gcc att acc ttt gac tct tct gtc agc tgg cct gcc aat gac 2208			
Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp			
725	730	735	
cgc ctg ctt acc ccc aac gag ttt gaa att aag cgc tca gtt gac ggg 2256			
Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly			
740	745	750	
gag ggt tac aac gtt gcc cag tgt aac atg acc aaa gac tgg ttc ctg 2304			
Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu			
755	760	765	
gta caa atg cta gct aac tat aac att ggc tac cag ggc ttc tat atc 2352			

Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile
 770 775 780

cca gag agc tac aag gac cgc atg tac tcc ttc ttt aga aac ttc cag 2400
 Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
 785 790 795 800

ccc atg agc cgt cag gtg gtg gat gat act aaa tac aag gac tac caa 2448
 Pro Met Ser Arg Gln Val Val Asp Thr Lys Tyr Lys Asp Tyr Gln
 805 810 815

cag gtg ggc atc cta cac caa cac aac aac tct gga ttt gtt ggc tac 2496
 Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr
 820 825 830

ctt gcc ccc acc atg cgc gaa gga cag gcc tac cct gct aac ttc ccc 2544
 Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro
 835 840 845

tat ccg ctt ata ggc aag acc gca gtt gac agc att acc cag aaa aag 2592
 Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys
 850 855 860

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 Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe
 865 870 875 880

atg tcc atg ggc gca ctc aca gac ctg ggc caa aac ctt ctc tac gcc 2688
 Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala
 885 890 895

aac tcc gcc cac gcg cta gac atg act ttt gag gtg gat ccc atg gac 2736
 Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp
 900 905 910

gag ccc acc ctt ctt tat gtt ttg ttt gaa gtc ttt gac gtg gtc cgt 2784
 Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg
 915 920 925

gtg cac cag ccg cac cgc ggc gtc atc gaa acc gtg tac ctg cgc acg 2832
 Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr
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ccc ttc tcg gcc ggc aac gcc aca aca taa 2862
 Pro Phe Ser Ala Gly Asn Ala Thr Thr
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<213> Artificial Sequence

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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

gcc cca aat cct tgc gaa tgg gat gaa aat gca aat cca aat gca aat 432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

cca aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat 480
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn

145	150	155	160	
cca aat gca aat cca aat gca aat cca aac gcg aac ccg aat gct aat				528
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn				
165	170	175		
cct aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat				576
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn				
180	185	190		
cca aaa act cac gta ttt ggg cag gcg cct tat tct ggt ata aat att				624
Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile				
195	200	205		
aca aag gag ggt att caa ata ggt gtc gaa ggt caa aca cct aaa tat				672
Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr				
210	215	220		
gcc gat aaa aca ttt caa cct gaa cct caa ata gga gaa tct cag tgg				720
Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp				
225	230	235	240	
tac gaa aca gaa att aat cat gca gct ggg aga gtc cta aaa aag act				768
Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr				
245	250	255		
acc cca atg aaa cca tgt tac ggt tca tat gca aaa ccc aca aat gaa				816
Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu				
260	265	270		
aat gga ggg caa ggc att ctt gta aag caa caa aat gga aag cta gaa				864
Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu				
275	280	285		
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Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly				
290	295	300		
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Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val				
305	310	315	320	
gat ata gaa acc cca gac act cat att tct tac atg ccc act att aag				1008
Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys				
325	330	335		
gaa ggt aac tca cga gaa cta atg ggc caa caa tct atg ccc aac agg				1056
Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg				
340	345	350		
cct aat tac att gct ttt agg gac aat ttt att ggt cta atg tat tac				1104

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
355 360 365

aac agc acg ggt aat atg ggt gtt ctg gcg ggc caa gca tcg cag ttg 1152
Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
370 375 380

aat gct gtt gta gat ttg caa gac aga aac aca gag ctt tca tac cag 1200
Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
385 390 395 400

ctt ttg ctt gat tcc att ggt gat aga acc agg tac ttt tct atg tgg 1248
Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
405 410 415

aat cag ctt cca aat tac tgc ttt cca ctg gga ggt gtg att aat aca 1296
Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
420 425 430

gag act ctt acc aag gta aaa cct aaa aca ggt cag gaa aat gga tgg 1344
Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
435 440 445

gaa aaa gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga 1392
Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
450 455 460

aat aat ttt gcc atg gaa atc aat cta aat gcc aac ctg tgg aga aat 1440
Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
465 470 475 480

ttc ctg tac tcc aac ata gcg ctg tat ttg ccc gac aag cta aag tac 1488
Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
485 490 495

agt cct tcc aac gta aaa att tct gat aac cca aac acc tac gac tac 1536
Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
500 505 510

atg aac aag cga gtg gtg gct ccc ggg cta gtg gac tgc tac att aac 1584
Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
515 520 525

ctt gga gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt 1632
Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
530 535 540

aac cac cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg ctg ggc 1680
Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
545 550 555 560

aat ggt cgc tat gtg ccc ttc cac atc cag gtg cct cag aag ttc ttt 1728
Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
565 570 575

gcc att aaa aac ctc ctt ctc ctg ccg ggc tca tac acc tac gag tgg 1776
Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
580 585 590

aac ttc agg aag gat gtt aac atg gtt ctg cag agc tcc cta gga aat 1824
Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
595 600 605

gac cta agg gtt gac gga gcc agc att aag ttt gat agc att tgc ctt 1872
Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
610 615 620

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Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
625 630 635 640

gcc atg ctt aga aac gac acc aac gac cag tcc ttt aac gac tat ctc 1968
Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
645 650 655

tcc gcc gcc aac atg ctc tac cct ata ccc gcc aac gct acc aac gtg 2016
Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
660 665 670

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Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
675 680 685

ttc acg cgc ctt aag act aag gaa acc cca tca ctg ggc tcg ggc tac 2112
Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr
690 695 700

gac cct tat tac acc tac tct ggc tct ata ccc tac cta gat gga acc 2160
Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
705 710 715 720

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

tct gtc agc tgg cct ggc aat gac cgc ctg ctt acc ccc aac gag ttt 2256
Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
740 745 750

gaa att aag cgc tca gtt gac ggg gag ggt tac aac gtt gcc cag tgt 2304
Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
755 760 765

aac atg acc aaa gac tgg ttc ctg gta caa atg cta gct aac tat aac 2352
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 770 775 780

att ggc tac cag ggc ttc tat atc cca gag agc tac aag gac cgc atg 2400
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 Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
 805 810 815

gat act aaa tac aag gac tac caa cag gtg ggc atc cta cac caa cac 2496
 Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
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 835 840 845

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cgc atc cca ttc tcc agt aac ttt atg tcc atg ggc gca ctc aca gac 2688
 Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
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 Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
 915 920 925

ttt gaa gtc ttt gac gtg gtc cgt gtg cac cag ccg cac cgc ggc gtc 2832
 Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
 930 935 940

atc gaa acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac gcc aca 2880
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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

gcc cca aat cct tgc gaa tgg gat gaa aat gca aat cca aat gca aat 432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

cca aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat 480
 Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 145 150 155 160

cca aat gca aat cca aat gca aat cca aac gcg aac ccg aat gct aat 528
 Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 165 170 175

cct aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat 576
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 180 185 190

cca aat gca aat cca aat gca aat cca aaa act cac gta ttt ggg cag 624
 Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln
 195 200 205

gcg cct tat tct ggt ata aat att aca aag gag ggt att caa ata ggt 672
 Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
 210 215 220

gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa cct gaa 720
 Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
 225 230 235 240

cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat cat gca 768
 Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
 245 250 255

gct ggg aga gtc cta aaa aag act acc cca atg aaa cca tgt tac ggt 816
 Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
 260 265 270

tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att ctt gta 864
 Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
 275 280 285

aag caa caa aat gga aag cta gaa agt caa gtg gaa atg caa ttt ttc 912
 Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
 290 295 300

tca act act gag gca gcc gca ggc aat ggt gat aac ttg act cct aaa 960
 Ser Thr Thr Glu Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
 305 310 315 320

gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac act cat 1008
 Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
 325 330 335

att tct tac atg ccc act att aag gaa ggt aac tca cga gaa cta atg 1056
 Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met

340 345 350
 ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt agg gac 1104
 Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
 355 360 365

 aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg ggt gtt 1152
 Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
 370 375 380

 ctg gcg ggc caa gca tcg cag ttg aat gct gtt gta gat ttg caa gac 1200
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 385 390 395 400

 aga aac aca gag ctt tca tac cag ctt ttg ctt gat tcc att ggt gat 1248
 Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
 405 410 415

 aga acc agg tac ttt tct atg tgg aat cag ctt cca aat tac tgc ttt 1296
 Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
 420 425 430

 cca ctg gga ggt gtg att aat aca gag act ctt acc aag gta aaa cct 1344
 Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
 435 440 445

 aaa aca ggt cag gaa aat gga tgg gaa aaa gat gct aca gaa ttt tca 1392
 Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
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 gat aaa aat gaa ata aga gtt gga aat aat ttt gcc atg gaa atc aat 1440
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 465 470 475 480

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 485 490 495

 tat ttg ccc gac aag cta aag tac agt cct tcc aac gta aaa att tct 1536
 Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
 500 505 510

 gat aac cca aac acc tac gac tac atg aac aag cga gtg gtg gct ccc 1584
 Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
 515 520 525

 ggg cta gtg gac tgc tac att aac ctt gga gca cgc tgg tcc ctt gac 1632
 Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
 530 535 540

 tat atg gac aac gtc aac cca ttt aac cac cac cgc aat gct ggc ctg 1680

Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
 545 550 555 560

cgc tac cgc tca atg ttg ctg ggc aat ggt cgc tat gtg ccc ttc cac 1728
 Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
 565 570 575

atc cag gtg cct cag aag ttc ttt gcc att aaa aac ctc ctt ctc ctg 1776
 Ile Gln Val Pro Gln Lys Phe Ala Ile Lys Asn Leu Leu Leu Leu
 580 585 590

ccg ggc tca tac acc tac gag tgg aac ttc agg aag gat gtt aac atg 1824
 Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
 595 600 605

gtt ctg cag agc tcc cta gga aat gac cta agg gtt gac gga gcc agc 1872
 Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
 610 615 620

att aag ttt gat agc att tgc ctt tac gcc acc ttc ttc ccc atg gcc 1920
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 625 630 635 640

cac aac acc gcc tcc acg ctt gag gcc atg ctt aga aac gac acc aac 1968
 His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
 645 650 655

gac cag tcc ttt aac gac tat ctc tcc gcc gcc aac atg ctc tac cct 2016
 Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
 660 665 670

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 675 680 685

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 Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
 705 710 715 720

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 Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
 725 730 735

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 740 745 750

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Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
755 760 765

gag ggt tac aac gtt gcc cag tgt aac atg acc aaa gac tgg ttc ctg 2352
Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu
770 775 780

gta caa atg cta gct aac tat aac att ggc tac cag ggc ttc tat atc 2400
Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile
785 790 795 800

cca gag agc tac aag gac cgc atg tac tcc ttc ttt aga aac ttc cag 2448
Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
805 810 815

ccc atg agc cgt cag gtg gtg gat gat act aaa tac aag gac tac caa 2496
Pro Met Ser Arg Gln Val Val Asp Thr Lys Tyr Lys Asp Tyr Gln
820 825 830

cag gtg ggc atc cta cac caa cac aac aac tct gga ttt gtt ggc tac 2544
Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr
835 840 845

ctt gcc ccc acc atg cgc gaa gga cag gcc tac cct gct aac ttc ccc 2592
Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro
850 855 860

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Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys
865 870 875 880

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885 890 895

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915 920 925

gag ccc acc ctt ctt tat gtt ttg ttt gaa gtc ttt gac gtg gtc cgt 2832
Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg
930 935 940

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 Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
 20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
 Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
 35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
 Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
 50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
 Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
 65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
 Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
 85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
 Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
 100 105 110

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 Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly

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cca aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat 528			
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165	170	175	
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225	230	235	240
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Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp			
245	250	255	
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260	265	270	
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275	280	285	
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Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly			
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Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val
 325 330 335

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 Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
 355 360 365

 cct aat tac att gct ttt agg gac aat ttt att ggt cta atg tat tac 1152
 Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
 370 375 380

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 385 390 395 400

 aat gct gtt gta gat ttg caa gac aga aac aca gag ctt tca tac cag 1248
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 405 410 415

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 Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
 420 425 430

 aat cag ctt cca aat tac tgc ttt cca ctg gga ggt gtg att aat aca 1344
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 450 455 460

 gaa aaa gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga 1440
 Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
 465 470 475 480

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 485 490 495

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 Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
 500 505 510

 agt cct tcc aac gta aaa att tct gat aac cca aac acc tac gac tac 1584
 Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
 515 520 525

atg aac aag cga gtg gtg gct ccc ggg cta gtg gac tgc tac att aac 1632
Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
530 535 540

ctt gga gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt 1680
Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
545 550 555 560

aac cac cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg ctg ggc 1728
Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
565 570 575

aat ggt cgc tat gtg ccc ttc cac atc cag gtg cct cag aag ttc ttt 1776
Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
580 585 590

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Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
595 600 605

aac ttc agg aag gat gtt aac atg gtt ctg cag agc tcc cta gga aat 1872
Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
610 615 620

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Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
625 630 635 640

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Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
645 650 655

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Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
660 665 670

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Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
675 680 685

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Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
690 695 700

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Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr
705 710 715 720

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Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
725 730 735

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740 745 750

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Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
755 760 765

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Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
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Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
785 790 795 800

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Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
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850 855 860

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Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
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Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
885 890 895

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900 905 910

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915 920 925

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Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly			
115	120	125	
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Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn			
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165	170	175	
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180	185	190	
cct aat gca aat cca aat gca aat cca aat gca aat cca aat gca aat			624
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Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln			
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Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly			
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gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa cct gaa			768
Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu			
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Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala			
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Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly			
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Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
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625 630 635 640

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675 680 685

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325 330 335

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tac gcc acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg ctt gag 2016
 Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu

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675	680	685	
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Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val			
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Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala			
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Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr			
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Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met			
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tac tcc ttc ttt aga aac ttc cag ccc atg agc cgt cag gtg gtg gat			2544
Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp			
835	840	845	
gat act aaa tac aag gac tac caa cag gtg ggc atc cta cac caa cac			2592
Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His			
850	855	860	
aac aac tct gga ttt gtt ggc tac ctt gcc ccc acc atg cgc gaa gga			2640

Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly
 865 870 875 880

cag gcc tac cct gct aac ttc ccc tat ccg ctt ata ggc aag acc gca 2688
 Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
 885 890 895

gtt gac agc att acc cag aaa aag ttt ctt tgc gat cgc acc ctt tgg 2736
 Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
 900 905 910

cgc atc cca ttc tcc agt aac ttt atg tcc atg ggc gca ctc aca gac 2784
 Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
 915 920 925

ctg ggc caa aac ctt ctc tac gcc aac tcc gcc cac gcg cta gac atg 2832
 Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
 930 935 940

act ttt gag gtg gat ccc atg gac gag ccc acc ctt ctt tat gtt ttg 2880
 Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
 945 950 955 960

ttt gaa gtc ttt gac gtg gtc cgt gtg cac cag ccg cac cgc ggc gtc 2928
 Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
 965 970 975

atc gaa acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac gcc aca 2976
 Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
 980 985 990

aca taa 2982
 Thr

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 Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser

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ggc cag gac gcc tcg gag tac ctg agc ccc ggg ctg gtg cag ttt gcc				96
Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala				
20	25	30		
cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc				144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro				
35	40	45		
acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg				192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu				
50	55	60		
acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac				240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr				
65	70	75	80	
aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg				288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met				
85	90	95		
gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act				336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr				
100	105	110		
ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt				384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly				
115	120	125		
gcc cca aat cct tgc gaa tgg gat gaa aac gcc aat cca aat gcg aat				432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn				
130	135	140		
ccc aac gct aat cct aac gca aac ccg aat gct aac cct aac gca aac				480
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn				
145	150	155	160	
ccc aac gct aac ccc aac gcg aac ccc aat gcc aac ccc aac gcc aac				528
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn				
165	170	175		
ccg aac gcc aat cca aac gct aac cct aat gcc aat cct aat gcc aat				576
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn				
180	185	190		
ccg aac gcc aat cca aat gcc aat cca aat gct aat ccc aac aat gcc				624
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn				
195	200	205		
ccc aac gcg aac cct aat gcc aac ccc aac gct aat cca aat gcg aac				672

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 210 215 220

cct aac gcc aac ccg aat gct aat ccc aat gcc aac ccc aat gct aat 720
 Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 225 230 235 240

ccc aat gcg aac cct aat gcc aat ccc aaa act cac gta ttt ggg cag 768
 Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln
 245 250 255

gcg cct tat tct ggt ata aat att aca aag gag ggt att caa ata ggt 816
 Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
 260 265 270

gtc gaa ggt caa aca cct aaa tat gcc gat aaa aca ttt caa cct gaa 864
 Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
 275 280 285

cct caa ata gga gaa tct cag tgg tac gaa aca gaa att aat cat gca 912
 Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
 290 295 300

gct ggg aga gtc cta aaa aag act acc cca atg aaa cca tgt tac ggt 960
 Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
 305 310 315 320

tca tat gca aaa ccc aca aat gaa aat gga ggg caa ggc att ctt gta 1008
 Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
 325 330 335

aag caa caa aat gga aag cta gaa agt caa gtg gaa atg caa ttt ttc 1056
 Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
 340 345 350

tca act act gag gca gcc gca ggc aat ggt gat aac ttg act cct aaa 1104
 Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
 355 360 365

gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac act cat 1152
 Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
 370 375 380

att tct tac atg ccc act att aag gaa ggt aac tca cga gaa cta atg 1200
 Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
 385 390 395 400

ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt agg gac 1248
 Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
 405 410 415

aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg ggt gtt 1296
 Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
 420 425 430

ctg gcg ggc caa gca tcg cag ttg aat gct gtt gta gat ttg caa gac 1344
 Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
 435 440 445

aga aac aca gag ctt tca tac cag ctt ttg ctt gat tcc att ggt gat 1392
 Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
 450 455 460

aga acc agg tac ttt tct atg tgg aat cag ctt cca aat tac tgc ttt 1440
 Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
 465 470 475 480

cca ctg gga ggt gtg att aat aca gag act ctt acc aag gta aaa cct 1488
 Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
 485 490 495

aaa aca ggt cag gaa aat gga tgg gaa aaa gat gct aca gaa ttt tca 1536
 Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
 500 505 510

gat aaa aat gaa ata aga gtt gga aat aat ttt gcc atg gaa atc aat 1584
 Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
 515 520 525

cta aat gcc aac ctg tgg aga aat ttc ctg tac tcc aac ata gcg ctg 1632
 Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu
 530 535 540

tat ttg ccc gac aag cta aag tac agt cct tcc aac gta aaa att tct 1680
 Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
 545 550 555 560

gat aac cca aac acc tac gac tac atg aac aag cga gtg gtg gct ccc 1728
 Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
 565 570 575

ggg cta gtg gac tgc tac att aac ctt gga gca cgc tgg tcc ctt gac 1776
 Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
 580 585 590

tat atg gac aac gtc aac cca ttt aac cac cac cgc aat gct ggc ctg 1824
 Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
 595 600 605

cgc tac cgc tca atg ttg ctg ggc aat ggt cgc tat gtg ccc ttc cac 1872
 Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
 610 615 620

atc cag gtg cct cag aag ttc ttt gcc att aaa aac ctc ctt ctc ctg 1920
 Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
 625 630 635 640

ccg ggc tca tac acc tac gag tgg aac ttc agg aag gat gtt aac atg 1968
 Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
 645 650 655

gtt ctg cag agc tcc cta gga aat gac cta agg gtt gac gga gcc agc 2016
 Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
 660 665 670

att aag ttt gat agc att tgc ctt tac gcc acc ttc ttc ccc atg gcc 2064
 Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
 675 680 685

cac aac acc gcc tcc acg ctt gag gcc atg ctt aga aac gac acc aac 2112
 His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
 690 695 700

gac cag tcc ttt aac gac tat ctc tcc gcc gcc aac atg ctc tac cct 2160
 Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
 705 710 715 720

ata ccc gcc aac gct acc aac gtg ccc ata tcc atc ccc tcc cgc aac 2208
 Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn
 725 730 735

tgg gcg gct ttc cgc ggc tgg gcc ttc acg cgc ctt aag act aag gaa 2256
 Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu
 740 745 750

acc cca tca ctg ggc tcg ggc tac gac cct tat tac acc tac tct ggc 2304
 Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
 755 760 765

tct ata ccc tac cta gat gga acc ttt tac ctc aac cac acc ttt aag 2352
 Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
 770 775 780

aag gtg gcc att acc ttt gac tct tct gtc agc tgg cct ggc aat gac 2400
 Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp
 785 790 795 800

cgc ctg ctt acc ccc aac gag ttt gaa att aag cgc tca gtt gac ggg 2448
 Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
 805 810 815

gag ggt tac aac gtt gcc cag tgt aac atg acc aaa gac tgg ttc ctg 2496
 Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu

820	825	830	
gta caa atg cta gct aac tat aac att ggc tac cag ggc ttc tat atc			2544
Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile			
835	840	845	
cca gag agc tac aag gac cgc atg tac tcc ttc ttt aga aac ttc cag			2592
Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln			
850	855	860	
ccc atg agc cgt cag gtg gtg gat gat act aaa tac aag gac tac caa			2640
Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln			
865	870	875	880
cag gtg ggc atc cta cac caa cac aac aac tct gga ttt gtt ggc tac			2688
Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr			
885	890	895	
ctt gcc ccc acc atg cgc gaa gga cag gcc tac cct gct aac ttc ccc			2736
Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro			
900	905	910	
tat ccg ctt ata ggc aag acc gca gtt gac agc att acc cag aaa aag			2784
Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys			
915	920	925	
ttt ctt tgc gat cgc acc ctt tgg cgc atc cca ttc tcc agt aac ttt			2832
Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe			
930	935	940	
atg tcc atg ggc gca ctc aca gac ctg ggc caa aac ctt ctc tac gcc			2880
Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala			
945	950	955	960
aac tcc gcc cac gcg cta gac atg act ttt gag gtg gat ccc atg gac			2928
Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp			
965	970	975	
gag ccc acc ctt ctt tat gtt ttg ttt gaa gtc ttt gac gtg gtc cgt			2976
Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg			
980	985	990	
gtg cac cag ccg cac cgc ggc gtc atc gaa acc gtg tac ctg cgc acg			3024
Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr			
995	1000	1005	
ccc ttc tcg gcc ggc aac gcc aca aca taa			3054
Pro Phe Ser Ala Gly Asn Ala Thr Thr			
1010	1015		

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<211> 2928
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ggc cag gac gcc tcg gag tac ctg agc ccc ggg ctg gtg cag ttt gcc 96
Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

cgc gcc acc gag acg tac ttc agc ctg aat aac aag ttt aga aac ccc 144
Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

acg gtg gcg cct acg cac gac gtg acc aca gac cgg tcc cag cgt ttg 192
Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

acg ctg cgg ttc atc cct gtg gac cgt gag gat act gcg tac tcg tac 240
Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

aag gcg cgg ttc acc cta gct gtg ggt gat aac cgt gtg ctg gac atg 288
Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

gct tcc acg tac ttt gac atc cgc ggc gtg ctg gac agg ggc cct act 336
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

ttt aag ccc tac tct ggc act gcc tac aac gcc ctg gct ccc aag ggt 384
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

gcc cca aat cct tgc gaa tgg gat gaa gct gct act gct ctt gaa ata 432
Ala Pro Asn Pro Cys Glu Trp Asp Glu Ala Ala Thr Ala Leu Glu Ile
130 135 140

aac cta gaa gaa gag gac gat gac aac gaa gac gaa gta gac gag caa 480
Asn Leu Glu Glu Glu Asp Asp Asp Asn Glu Asp Glu Val Asp Glu Gln

145	150	155	160	
gct gag cag caa aaa act cac gta ttt ggg cag gcg cct tat tct ggt				528
Ala Glu Gln Gln Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly				
165	170	175		
ata aat att aca aag gag ggt att caa ata ggt gtc gaa ggt caa aca				576
Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr				
180	185	190		
cct aaa tat gcc gat aaa aca ttt caa cct gaa cct caa ata gga gaa				624
Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu				
195	200	205		
tct cag tgg tac gaa aca gaa att aat cat gca gct ggg aga gtc cta				672
Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu				
210	215	220		
aaa aag act acc cca atg aaa cca tgt tac ggt tca tat gca aaa ccc				720
Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro				
225	230	235	240	
aca aat gaa aat gga ggg caa ggc att ctt gta aag caa caa aat gga				768
Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly				
245	250	255		
aag cta gaa agt caa gtg gaa atg caa ttt ttc tca gct agc cag ggc				816
Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe Ser Ala Ser Gln Gly				
260	265	270		
cct gga gct cca cag gga cca ggt gca cct caa ggg cct gga gcc cct				864
Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro				
275	280	285		
ggc act agc act act gag gca gcc gca ggc aat ggt gat aac ttg act				912
Gly Thr Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr				
290	295	300		
cct aaa gtg gta ttg tac agt gaa gat gta gat ata gaa acc cca gac				960
Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp				
305	310	315	320	
act cat att tct tac atg ccc act att aag gaa ggt aac tca cga gaa				1008
Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu				
325	330	335		
cta atg ggc caa caa tct atg ccc aac agg cct aat tac att gct ttt				1056
Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe				
340	345	350		
agg gac aat ttt att ggt cta atg tat tac aac agc acg ggt aat atg				1104

Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met
 355 360 365

ggt gtt ctg gcg ggc caa gca tcg cag ttg aat gct gtt gta gat ttg 1152
 Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu
 370 375 380

caa gac aga aac aca gag ctt tca tac cag ctt ttg ctt gat tcc att 1200
 Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile
 385 390 395 400

ggt gat aga acc agg tac ttt tct atg tgg aat cag gct gtt gac agc 1248
 Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser
 405 410 415

tat gat cca gat gtt aga att att gaa aat cat gga act gaa gat gaa 1296
 Tyr Asp Pro Asp Val Arg Ile Glu Asn His Gly Thr Glu Asp Glu
 420 425 430

ctt cca aat tac tgc ttt cca ctg gga ggt gtg att aat aca gag act 1344
 Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr
 435 440 445

ctt acc aag gta aaa cct aaa aca ggt cag gaa aat gga tgg gaa aaa 1392
 Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys
 450 455 460

gat gct aca gaa ttt tca gat aaa aat gaa ata aga gtt gga aat aat 1440
 Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn
 465 470 475 480

ttt gcc atg gaa atc aat cta aat gcc aac ctg tgg aga aat ttc ctg 1488
 Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu
 485 490 495

tac tcc aac ata gcg ctg tat ttg ccc gac aag cta aag tac agt cct 1536
 Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro
 500 505 510

tcc aac gta aaa att tct gat aac cca aac acc tac gac tac atg aac 1584
 Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn
 515 520 525

aag cga gtg gtg gct ccc ggg cta gtg gac tgc tac att aac ctt gga 1632
 Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly
 530 535 540

gca cgc tgg tcc ctt gac tat atg gac aac gtc aac cca ttt aac cac 1680
 Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His
 545 550 555 560

cac cgc aat gct ggc ctg cgc tac cgc tca atg ttg ctg ggc aat ggt 1728
His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly
565 570 575

cgc tat gtg ccc ttc cac atc cag gtg cct cag aag ttc ttt gcc att 1776
Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile
580 585 590

aaa aac ctc ctt ctc ctg ccg ggc tca tac acc tac gag tgg aac ttc 1824
Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe
595 600 605

agg aag gat gtt aac atg gtt ctg cag agc tcc cta gga aat gac cta 1872
Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn Asp Leu
610 615 620

agg gtt gac gga gcc agc att aag ttt gat agc att tgc ctt tac gcc 1920
Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala
625 630 635 640

acc ttc ttc ccc atg gcc cac aac acc gcc tcc acg ctt gag gcc atg 1968
Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met
645 650 655

ctt aga aac gac acc aac gac cag tcc ttt aac gac tat ctc tcc gcc 2016
Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala
660 665 670

gcc aac atg ctc tac cct ata ccc gcc aac gct acc aac gtg ccc ata 2064
Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile
675 680 685

tcc atc ccc tcc cgc aac tgg gcg gct ttc cgc ggc tgg gcc ttc acg 2112
Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr
690 695 700

cgc ctt aag act aag gaa acc cca tca ctg ggc tcg ggc tac gac cct 2160
Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro
705 710 715 720

tat tac acc tac tct ggc tct ata ccc tac cta gat gga acc ttt tac 2208
Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr
725 730 735

ctc aac cac acc ttt aag aag gtg gcc att acc ttt gac tct tct gtc 2256
Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val
740 745 750

agc tgg cct ggc aat gac cgc ctg ctt acc ccc aac gag ttt gaa att 2304
Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile
755 760 765

aag cgc tca gtt gac ggg gag ggt tac aac gtt gcc cag tgt aac atg 2352
 Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met
 770 775 780

acc aaa gac tgg ttc ctg gta caa atg cta gct aac tat aac att ggc 2400
 Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly
 785 790 795 800

tac cag ggc ttc tat atc cca gag agc tac aag gac cgc atg tac tcc 2448
 Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser
 805 810 815

ttc ttt aga aac ttc cag ccc atg agc cgt cag gtg gtg gat gat act 2496
 Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr
 820 825 830

aaa tac aag gac tac caa cag gtg ggc atc cta cac caa cac aac aac 2544
 Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn
 835 840 845

tct gga ttt gtt ggc tac ctt gcc ccc acc atg cgc gaa gga cag gcc 2592
 Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala
 850 855 860

tac cct gct aac ttc ccc tat ccg ctt ata ggc aag acc gca gtt gac 2640
 Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp
 865 870 875 880

agc att acc cag aaa aag ttt ctt tgc gat cgc acc ctt tgg cgc atc 2688
 Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile
 885 890 895

cca ttc tcc agt aac ttt atg tcc atg ggc gca ctc aca gac ctg ggc 2736
 Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly
 900 905 910

caa aac ctt ctc tac gcc aac tcc gcc cac gcg cta gac atg act ttt 2784
 Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe
 915 920 925

gag gtg gat ccc atg gac gag ccc acc ctt ctt tat gtt ttg ttt gaa 2832
 Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu
 930 935 940

gtc ttt gac gtg gtc cgt gtg cac cag ccg cac cgc ggc gtc atc gaa 2880
 Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu
 945 950 955 960

acc gtg tac ctg cgc acg ccc ttc tcg gcc ggc aac gcc aca aca taa 2928
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965 970 975

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<211> 1800

<212> DNA

<213> Artificial Sequence

<220>

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<220>

<221> CDS

<222> (1)..(1797)

<400> 24

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1 5 10 15

tat gac acg gaa acc ggt cct cca act gtg cct ttt ctt act cct ccc 96
Tyr Asp Thr Glu Thr Gly Pro Pro Thr Val Pro Phe Leu Thr Pro Pro
20 25 30

ttt gta tcc ccc aat ggg ttt caa gag agt ccc cct ggg gta ctc tct 144
Phe Val Ser Pro Asn Gly Phe Gln Glu Ser Pro Pro Gly Val Leu Ser
35 40 45

ttg cgc cta tcc gaa cct cta gtt acc tcc aat ggc atg ctt gcg ctc 192
Leu Arg Leu Ser Glu Pro Leu Val Thr Ser Asn Gly Met Leu Ala Leu
50 55 60

aaa atg ggc aac ggc ctc tct ctg gac gag gcc ggc aac ctt acc tcc 240
Lys Met Gly Asn Gly Leu Ser Leu Asp Glu Ala Gly Asn Leu Thr Ser
65 70 75 80

caa aat gta acc act gtg agc cca cct ctc aaa aaa acc aag tca aac 288
Gln Asn Val Thr Thr Val Ser Pro Pro Leu Lys Lys Thr Lys Ser Asn
85 90 95

ata aac ctg gaa ata tct gca ccc ctc aca gtt acc tca gaa gcc cta 336
Ile Asn Leu Glu Ile Ser Ala Pro Leu Thr Val Thr Ser Glu Ala Leu
100 105 110

act gtg gct gcc gcc gca cct cta atg gtc gcg ggc aac aca ctc acc 384
Thr Val Ala Ala Ala Ala Pro Leu Met Val Ala Gly Asn Thr Leu Thr
115 120 125

atg caa tca cag gcc ccg cta acc gtg cac gac tcc aaa ctt agc att 432

Met Gln Ser Gln Ala Pro Leu Thr Val His Asp Ser Lys Leu Ser Ile
130 135 140

gcc acc caa gga ccc ctc aca gtg tca gaa gga aag cta gcc ctg caa 480
Ala Thr Gln Gly Pro Leu Thr Val Ser Glu Gly Lys Leu Ala Leu Gln
145 150 155 160

aca tca ggc ccc ctc acc acc acc gat agc agt acc ctt act atc act 528
Thr Ser Gly Pro Leu Thr Thr Thr Asp Ser Ser Thr Leu Thr Ile Thr
165 170 175

gcc tca ccc cct cta act act gcc act ggt agc ttg ggc att gac ttg 576
Ala Ser Pro Pro Leu Thr Thr Ala Thr Gly Ser Leu Gly Ile Asp Leu
180 185 190

aaa gag ccc att tat aca caa aat gga aaa cta gga cta aag tac ggg 624
Lys Glu Pro Ile Tyr Thr Gln Asn Gly Lys Leu Gly Leu Lys Tyr Gly
195 200 205

gct cct ttg cat gta aca gac gac cta aac act ttg acc gta gca act 672
Ala Pro Leu His Val Thr Asp Asp Leu Asn Thr Leu Thr Val Ala Thr
210 215 220

ggt cca ggt gtg act att aat aat act tcc ttg caa act aaa gtt act 720
Gly Pro Gly Val Thr Ile Asn Asn Thr Ser Leu Gln Thr Lys Val Thr
225 230 235 240

gga gcc ttg ggt ttt gat tca caa ggc aat atg caa ctt aat gta gca 768
Gly Ala Leu Gly Phe Asp Ser Gln Gly Asn Met Gln Leu Asn Val Ala
245 250 255

gga gga cta agg att gat tct caa aac aga cgc ctt ata ctt gat gtt 816
Gly Gly Leu Arg Ile Asp Ser Gln Asn Arg Arg Leu Ile Leu Asp Val
260 265 270

agt tat ccg ttt gat gct caa aac caa cta aat cta aga cta gga cag 864
Ser Tyr Pro Phe Asp Ala Gln Asn Gln Leu Asn Leu Arg Leu Gly Gln
275 280 285

ggc cct ctt ttt ata aac tca gcc cac aac ttg gat att aac tac aac 912
Gly Pro Leu Phe Ile Asn Ser Ala His Asn Leu Asp Ile Asn Tyr Asn
290 295 300

aaa ggc ctt tac ttg ttt aca gct tca aac aat tcc aaa aag ctt gag 960
Lys Gly Leu Tyr Leu Phe Thr Ala Ser Asn Asn Ser Lys Lys Leu Glu
305 310 315 320

gtt aac cta agc act gcc aag ggg ttg atg ttt gac gct aca gcc ata 1008
Val Asn Leu Ser Thr Ala Lys Gly Leu Met Phe Asp Ala Thr Ala Ile
325 330 335

gcc att aat gca gga gat ggg ctt gaa ttt ggt tca cct aat gca cca 1056
Ala Ile Asn Ala Gly Asp Gly Leu Glu Phe Gly Ser Pro Asn Ala Pro
340 345 350

aac aca aat ccc ctc aaa aca aaa att ggc cat ggc cta gaa ttt gat 1104
Asn Thr Asn Pro Leu Lys Thr Lys Ile Gly His Gly Leu Glu Phe Asp
355 360 365

tca aac aag gct atg gtt cct aaa cta gga act ggc ctt agt ttt gac 1152
Ser Asn Lys Ala Met Val Pro Lys Leu Gly Thr Gly Leu Ser Phe Asp
370 375 380

agc aca ggt gcc att aca gta gga aac aaa aat aat gat aag cta act 1200
Ser Thr Gly Ala Ile Thr Val Gly Asn Lys Asn Asn Asp Lys Leu Thr
385 390 395 400

ttg tgg acc aca cca gct cca tct cct aac tgt aga cta aat gca gag 1248
Leu Trp Thr Thr Pro Ala Pro Ser Pro Asn Cys Arg Leu Asn Ala Glu
405 410 415

aaa gat gct aaa ctc act ttg gtc tta aca aaa tgt ggc agt caa ata 1296
Lys Asp Ala Lys Leu Thr Leu Val Leu Thr Lys Cys Gly Ser Gln Ile
420 425 430

ctt gct aca gtt tca gtt ttg gct gtt aaa ggc agt ttg gct cca ata 1344
Leu Ala Thr Val Ser Val Leu Ala Val Lys Gly Ser Leu Ala Pro Ile
435 440 445

tct gga aca gtt caa agt gct cat ctt att ata aga ttt gac gaa aat 1392
Ser Gly Thr Val Gln Ser Ala His Leu Ile Ile Arg Phe Asp Glu Asn
450 455 460

gga gtg cta cta aac aat tcc ttc ctg gac cca gaa tat tgg aac ttt 1440
Gly Val Leu Leu Asn Asn Ser Phe Leu Asp Pro Glu Tyr Trp Asn Phe
465 470 475 480

aga aat gga gat ctt act gaa ggc aca gcc tat aca aac gct gtt gga 1488
Arg Asn Gly Asp Leu Thr Glu Gly Thr Ala Tyr Thr Asn Ala Val Gly
485 490 495

ttt atg cct aac cta tca gct tat cca aaa tct cac ggt aaa act gcc 1536
Phe Met Pro Asn Leu Ser Ala Tyr Pro Lys Ser His Gly Lys Thr Ala
500 505 510

aaa agt aac att gtc agt caa gtt tac tta aac gga gac aaa act aaa 1584
Lys Ser Asn Ile Val Ser Gln Val Tyr Leu Asn Gly Asp Lys Thr Lys
515 520 525

cct gta aca cta acc att aca cta aac ggt aca cag gaa aca gga cag 1632
Pro Val Thr Leu Thr Ile Thr Leu Asn Gly Thr Gln Glu Thr Gly Gln
530 535 540

ggc cct gga gct cca cag gga cca ggt gca cct caa ggg cct gga gcc 1680
 Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
 545 550 555 560

cct gac aca act cca agt gca tac tct atg tca ttt tca tgg gac tgg 1728
 Pro Asp Thr Thr Pro Ser Ala Tyr Ser Met Ser Phe Ser Trp Asp Trp
 565 570 575

tct ggc cac aac tac att aat gaa ata ttt gcc aca tcc tct tac act 1776
 Ser Gly His Asn Tyr Ile Asn Glu Ile Phe Ala Thr Ser Ser Tyr Thr
 580 585 590

ttt tca tac att gcc caa gaa taa 1800
 Phe Ser Tyr Ile Ala Gln Glu
 595

<210> 25
 <211> 1794
 <212> DNA
 <213> Artificial Sequence

<220>
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<220>
 <221> CDS
 <222> (1)..(1791)

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 Met Lys Arg Ala Arg Pro Ser Glu Asp Thr Phe Asn Pro Val Tyr Pro
 1 5 10 15

tat gac acg gaa acc ggt cct cca act gtg cct ttt ctt act cct ccc 96
 Tyr Asp Thr Glu Thr Gly Pro Pro Thr Val Pro Phe Leu Thr Pro Pro
 20 25 30

ttt gta tcc ccc aat ggg ttt caa gag agt ccc cct ggg gta ctc tct 144
 Phe Val Ser Pro Asn Gly Phe Gln Glu Ser Pro Pro Gly Val Leu Ser
 35 40 45

ttg cgc cta tcc gaa cct cta gtt acc tcc aat ggc atg ctt gcg ctc 192
 Leu Arg Leu Ser Glu Pro Leu Val Thr Ser Asn Gly Met Leu Ala Leu
 50 55 60

aaa atg ggc aac ggc ctc tct ctg gac gag gcc ggc aac ctt acc tcc 240
 Lys Met Gly Asn Gly Leu Ser Leu Asp Glu Ala Gly Asn Leu Thr Ser

65	70	75	80	
caa aat gta acc act gtg agc cca cct ctc aaa aaa acc aag tca aac				288
Gln Asn Val Thr Thr Val Ser Pro Pro Leu Lys Lys Thr Lys Ser Asn				
85	90	95		
ata aac ctg gaa ata tct gca ccc ctc aca gtt acc tca gaa gcc cta				336
Ile Asn Leu Glu Ile Ser Ala Pro Leu Thr Val Thr Ser Glu Ala Leu				
100	105	110		
act gtg gct gcc gcc gca cct cta atg gtc gcg ggc aac aca ctc acc				384
Thr Val Ala Ala Ala Ala Pro Leu Met Val Ala Gly Asn Thr Leu Thr				
115	120	125		
atg caa tca cag gcc ccg cta acc gtg cac gac tcc aaa ctt agc att				432
Met Gln Ser Gln Ala Pro Leu Thr Val His Asp Ser Lys Leu Ser Ile				
130	135	140		
gcc acc caa gga ccc ctc aca gtg tca gaa gga aag cta gcc ctg caa				480
Ala Thr Gln Gly Pro Leu Thr Val Ser Glu Gly Lys Leu Ala Leu Gln				
145	150	155	160	
aca tca ggc ccc ctc acc acc acc gat agc agt acc ctt act atc act				528
Thr Ser Gly Pro Leu Thr Thr Thr Asp Ser Ser Thr Leu Thr Ile Thr				
165	170	175		
gcc tca ccc cct cta act act gcc act ggt agc ttg ggc att gac ttg				576
Ala Ser Pro Pro Leu Thr Thr Ala Thr Gly Ser Leu Gly Ile Asp Leu				
180	185	190		
aaa gag ccc att tat aca caa aat gga aaa cta gga cta aag tac ggg				624
Lys Glu Pro Ile Tyr Thr Gln Asn Gly Lys Leu Gly Leu Lys Tyr Gly				
195	200	205		
gct cct ttg cat gta aca gac gac cta aac act ttg acc gta gca act				672
Ala Pro Leu His Val Thr Asp Asp Leu Asn Thr Leu Thr Val Ala Thr				
210	215	220		
ggt cca ggt gtg act att aat aat act tcc ttg caa act aaa gtt act				720
Gly Pro Gly Val Thr Ile Asn Asn Thr Ser Leu Gln Thr Lys Val Thr				
225	230	235	240	
gga gcc ttg ggt ttt gat tca caa ggc aat atg caa ctt aat gta gca				768
Gly Ala Leu Gly Phe Asp Ser Gln Gly Asn Met Gln Leu Asn Val Ala				
245	250	255		
gga gga cta agg att gat tct caa aac aga cgc ctt ata ctt gat gtt				816
Gly Gly Leu Arg Ile Asp Ser Gln Asn Arg Arg Leu Ile Leu Asp Val				
260	265	270		
agt tat ccg ttt gat gct caa aac caa cta aat cta aga cta gga cag				864

Ser Tyr Pro Phe Asp Ala Gln Asn Gln Leu Asn Leu Arg Leu Gly Gln
 275 280 285

ggc cct ctt ttt ata aac tca gcc cac aac ttg gat att aac tac aac 912
 Gly Pro Leu Phe Ile Asn Ser Ala His Asn Leu Asp Ile Asn Tyr Asn
 290 295 300

aaa ggc ctt tac ttg ttt aca gct tca aac aat tcc aaa aag ctt gag 960
 Lys Gly Leu Tyr Leu Phe Thr Ala Ser Asn Asn Ser Lys Lys Leu Glu
 305 310 315 320

gtt aac cta agc act gcc aag ggg ttg atg ttt gac gct aca gcc ata 1008
 Val Asn Leu Ser Thr Ala Lys Gly Leu Met Phe Asp Ala Thr Ala Ile
 325 330 335

gcc att aat gca gga gat ggg ctt gaa ttt ggt tca cct aat gca cca 1056
 Ala Ile Asn Ala Gly Asp Gly Leu Glu Phe Gly Ser Pro Asn Ala Pro
 340 345 350

aac aca aat ccc ctc aaa aca aaa att ggc cat ggc cta gaa ttt gat 1104
 Asn Thr Asn Pro Leu Lys Thr Lys Ile Gly His Gly Leu Glu Phe Asp
 355 360 365

tca aac aag gct atg gtt cct aaa cta gga act ggc ctt agt ttt gac 1152
 Ser Asn Lys Ala Met Val Pro Lys Leu Gly Thr Gly Leu Ser Phe Asp
 370 375 380

agc aca ggt gcc att aca gta gga aac aaa aat aat gat aag cta act 1200
 Ser Thr Gly Ala Ile Thr Val Gly Asn Lys Asn Asn Asp Lys Leu Thr
 385 390 395 400

ttg tgg acc aca cca gct cca tct cct aac tgt aga cta aat gca gag 1248
 Leu Trp Thr Thr Pro Ala Pro Ser Pro Asn Cys Arg Leu Asn Ala Glu
 405 410 415

aaa gat gct aaa ctc act ttg gtc tta aca aaa tgt ggc agt caa ata 1296
 Lys Asp Ala Lys Leu Thr Leu Val Leu Thr Lys Cys Gly Ser Gln Ile
 420 425 430

ctt gct aca gtt tca gtt ttg gct gtt aaa ggc agt ttg gct cca ata 1344
 Leu Ala Thr Val Ser Val Leu Ala Val Lys Gly Ser Leu Ala Pro Ile
 435 440 445

tct gga aca gtt caa agt gct cat ctt att ata aga ttt gac gaa aat 1392
 Ser Gly Thr Val Gln Ser Ala His Leu Ile Ile Arg Phe Asp Glu Asn
 450 455 460

gga gtg cta cta aac aat tcc ttc ctg gac cca gaa tat tgg aac ttt 1440
 Gly Val Leu Leu Asn Asn Ser Phe Leu Asp Pro Glu Tyr Trp Asn Phe
 465 470 475 480

aga aat gga gat ctt act gaa ggc aca gcc tat aca aac gct gtt gga 1488
 Arg Asn Gly Asp Leu Thr Glu Gly Thr Ala Tyr Thr Asn Ala Val Gly
 485 490 495

ttt atg cct aac cta tca gct tat cca aaa tct cac ggt aaa act gcc 1536
 Phe Met Pro Asn Leu Ser Ala Tyr Pro Lys Ser His Gly Lys Thr Ala
 500 505 510

aaa agt aac att gtc agt caa gtt tac tta aac gga gac aaa act aaa 1584
 Lys Ser Asn Ile Val Ser Gln Val Tyr Leu Asn Gly Asp Lys Thr Lys
 515 520 525

cct gta aca cta acc att aca cta aac ggt aca cag gaa aca gga aac 1632
 Pro Val Thr Leu Thr Ile Thr Leu Asn Gly Thr Gln Glu Thr Gly Asn
 530 535 540

gct aat ccc aac gct aac cca aat gca aat cct aat gcc aac ccc gac 1680
 Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asp
 545 550 555 560

aca act cca agt gca tac tct atg tca ttt tca tgg gac tgg tct ggc 1728
 Thr Thr Pro Ser Ala Tyr Ser Met Ser Phe Ser Trp Asp Trp Ser Gly
 565 570 575

cac aac tac att aat gaa ata ttt gcc aca tcc tct tac act ttt tca 1776
 His Asn Tyr Ile Asn Glu Ile Phe Ala Thr Ser Ser Tyr Thr Phe Ser
 580 585 590

tac att gcc caa gaa taa 1794
 Tyr Ile Ala Gln Glu
 595

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 <211> 684
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> P. yoelii CD4+ epitope modified pVII sequence

<220>
 <221> CDS
 <222> (1)..(681)

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 Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg
 1 5 10 15

ttc cca agc aag atg ttt ggc ggg gcc aag aag cgc tcc gac caa cac	96
Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His	
20 25 30	
cca gtg cgc gtg cgc ggg cac tac cgc gcg ccc tgg ggc gcg cac aaa	144
Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys	
35 40 45	
cgc ggc cgc act ggg cgc acc acc gtc gat gac gcc atc gac gcg gtg	192
Arg Gly Arg Thr Gly Arg Thr Thr Val Asp Asp Ala Ile Asp Ala Val	
50 55 60	
gtg gag gag gcg cgc aac tac acg ccc acg ccg cca cca gtg tcc aca	240
Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Pro Val Ser Thr	
65 70 75 80	
gtg gac gcg gcc att cag acc gtg gtg cgc gga gcc cgg cgc tat gct	288
Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Arg Arg Tyr Ala	
85 90 95	
aaa atg aag aga cgg cgg agg cgc gta gca cgt cgc cac cgc cgc cga	336
Lys Met Lys Arg Arg Arg Arg Arg Val Ala Arg Arg His Arg Arg Arg	
100 105 110	
ccc ggc act gcc gcc caa cgc gcg gcg gcc ctg ctt aac cgc gca	384
Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Leu Leu Asn Arg Ala	
115 120 125	
cgt cgc acc ggc cga cgg gcg gcc atg cgg gcc gct cga agg ctg gcc	432
Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala Arg Arg Leu Ala	
130 135 140	
gcg ggt att gtc act gtg ccc ccc agg tcc agg cga cga gcg gcc gcc	480
Ala Gly Ile Val Thr Val Pro Pro Arg Ser Arg Arg Arg Ala Ala Ala	
145 150 155 160	
gca gca gcc gcg gcc att agt gct atg act cag ggt cgc agg ggc aac	528
Ala Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly Arg Arg Gly Asn	
165 170 175	
gtg tat tgg gtg cgc gac tcg gtt agc ggc ctg cgc gtg ccc gtg cgc	576
Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg Val Pro Val Arg	
180 185 190	
acc cgc ccc ccg cgc aac gtg cgc acc cgc ccc ccg cgc aac tac aac	624
Thr Arg Pro Pro Arg Asn Val Arg Thr Arg Pro Pro Arg Asn Tyr Asn	
195 200 205	
agg aac atc gtg aac agg ctg ctg ggc gac gcc ctg aac ggc aag ccc	672
Arg Asn Ile Val Asn Arg Leu Leu Gly Asp Ala Leu Asn Gly Lys Pro	

210	215	220	
gag gag aag tag			684
Glu Glu Lys			
225			
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<223> P. falciparum CD4+ epitope modified pVII-1 sequence			
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<221> CDS			
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<400> 27			
atg tcc atc ctt ata tcg ccc agc aat aac aca ggc tgg ggc ctg cgc			48
Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg			
1	5	10	15
ttc cca agc aag atg ttt ggc ggg gcc aag aag cgc tcc gac caa cac			96
Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His			
20	25	30	
cca gtg cgc gtg cgc ggg cac tac cgc gcg ccc tgg ggc gcg cac aaa			144
Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys			
35	40	45	
cgc ggc cgc act ggg cgc acc acc gtc gat gac gcc atc gac gcg gtg			192
Arg Gly Arg Thr Gly Arg Thr Val Val Asp Asp Ala Ile Asp Ala Val			
50	55	60	
gtg gag gag gcg cgc aac tac acg ccc acg ccg cca cca gtg tcc aca			240
Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Pro Val Ser Thr			
65	70	75	80
gtg gac gcg gcc att cag acc gtg gtg cgc gga gcc cgg cgc tat gct			288
Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Arg Arg Tyr Ala			
85	90	95	
aaa atg aag aga cgg cgg agg cgc gta gca cgt cgc cac cgc cgc cga			336
Lys Met Lys Arg Arg Arg Arg Arg Val Ala Arg Arg His Arg Arg Arg			
100	105	110	
ccc ggc act gcc gcc caa cgc gcg gcg gcc ctg ctt aac cgc gca			384

Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Leu Leu Asn Arg Ala
115 120 125

cgt cgc acc ggc cga cgg gcg gcc atg cgg gcc gct cga agg ctg gcc 432
Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala Arg Arg Leu Ala
130 135 140

gcg ggt att gtc act gtg ccc ccc agg tcc agg cga cga gcg gcc gcc 480
Ala Gly Ile Val Thr Val Pro Pro Arg Ser Arg Arg Arg Ala Ala Ala
145 150 155 160

gca gca gcc gcg gcc att agt gct atg act cag ggt cgc agg ggc aac 528
Ala Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly Arg Arg Gly Asn
165 170 175

gtg tat tgg gtg cgc gac tcg gtt agc ggc ctg cgc gtg ccc gtg cgc 576
Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg Val Pro Val Arg
180 185 190

acc cgc ccc ccg cgc aac gaa tat ttg aac aag att caa aac tcc ctc 624
Thr Arg Pro Pro Arg Asn Glu Tyr Leu Asn Lys Ile Gln Asn Ser Leu
195 200 205

tca aca gaa tgg tct cct tgc agc gtg act tag 657
Ser Thr Glu Trp Ser Pro Cys Ser Val Thr
210 215

<210> 28
<211> 741
<212> DNA
<213> Artificial Sequence

<220>
<223> P. falciparum CD4+ epitope modified pVII-2 sequence

<220>
<221> CDS
<222> (1)..(738)

<400> 28
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Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg
1 5 10 15

ttc cca agc aag atg ttt ggc ggg gcc aag aag cgc tcc gac caa cac 96
Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His
20 25 30

cca gtg cgc gtg cgc ggg cac tac cgc gcg ccc tgg ggc gcg cac aaa	144
Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys	
35 40 45	
cgc ggc cgc act ggg cgc acc acc gtc gat gac gcc atc gac gcg gtg	192
Arg Gly Arg Thr Gly Arg Thr Thr Val Asp Asp Ala Ile Asp Ala Val	
50 55 60	
gtg gag gag gcg cgc aac tac acg ccc acg ccg cca cca gtg tcc aca	240
Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Val Ser Thr	
65 70 75 80	
gtg gac gcg gcc att cag acc gtg gtg cgc gga gcc gaa tat ttg aac	288
Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Glu Tyr Leu Asn	
85 90 95	
aag att caa aac tcc ctc tca aca gaa tgg tct cct tgc agc gtg act	336
Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro Cys Ser Val Thr	
100 105 110	
cgg cgc tat gct aaa atg aag aga cgg cgg agg cgc gta gca cgt cgc	384
Arg Arg Tyr Ala Lys Met Lys Arg Arg Arg Arg Val Ala Arg Arg	
115 120 125	
cac cgc cgc cga ccc ggc act gcc gcc caa cgc gcg gcg gcc ctg	432
His Arg Arg Arg Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Leu	
130 135 140	
ctt aac cgc gca cgt cgc acc ggc cga cgg gcg gcc atg cgg gcc gct	480
Leu Asn Arg Ala Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala	
145 150 155 160	
cga agg ctg gcc gcg ggt att gtc act gtg ccc ccc agg tcc agg cga	528
Arg Arg Leu Ala Ala Gly Ile Val Thr Val Pro Pro Arg Ser Arg Arg	
165 170 175	
cga gcg gcc gcc gca gca gcc gcg gcc att agt gct atg act cag ggt	576
Arg Ala Ala Ala Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly	
180 185 190	
cgc agg ggc aac gtg tat tgg gtg cgc gac tcg gtt agc ggc ctg cgc	624
Arg Arg Gly Asn Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg	
195 200 205	
gtg ccc gtg cgc acc cgc ccc ccg cgc aac gtg cgc acc cgc ccc ccg	672
Val Pro Val Arg Thr Arg Pro Pro Arg Asn Val Arg Thr Arg Pro Pro	
210 215 220	
cgc aac tac aac agg aac atc gtg aac agg ctg ctg ggc gac gcc ctg	720
Arg Asn Tyr Asn Arg Asn Ile Val Asn Arg Leu Leu Gly Asp Ala Leu	
225 230 235 240	

acc cgc ccc ccg cgc aac tag 741
 Thr Arg Pro Pro Arg Asn
 245

<210> 29
 <211> 681
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> P. falciparum CD4+ epitope modified PVII-3 sequence

<220>
 <221> CDS
 <222> (1)..(678)

<400> 29
 atg tcc atc ctt ata tcg ccc agc aat aac aca ggc tgg ggc ctg cgc 48
 Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg
 1 5 10 15
 ttc cca agc aag atg ttt ggc ggg gcc aag aag cgc tcc gac caa cac 96
 Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His
 20 25 30
 cca gtg cgc gtg cgc ggg cac tac cgc gcg ccc tgg ggc gcg cac aaa 144
 Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys
 35 40 45
 cgc ggc cgc act ggg cgc acc acc gtc gat gac gcc atc gac gcg gtg 192
 Arg Gly Arg Thr Gly Arg Thr Thr Val Asp Asp Ala Ile Asp Ala Val
 50 55 60
 gtg gag gag gcg cgc aac tac acg ccc acg ccg cca cca gtg tcc aca 240
 Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Val Ser Thr
 65 70 75 80
 gtg gac gcg gcc att cag acc gtg gtg cgc gga gcc cgg cgc tat gct 288
 Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Arg Arg Tyr Ala
 85 90 95
 aaa atg aag aga cgg cgg agg cgc gta gca cgt cgc cac cgc cgc cga 336
 Lys Met Lys Arg Arg Arg Arg Val Ala Arg Arg His Arg Arg Arg
 100 105 110
 ccc ggc act gcc gcc caa cgc gcg gcg gcc ctg ctt aac cgc gca 384
 Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Ala Leu Leu Asn Arg Ala
 115 120 125

cgt cgc acc ggc cga cgg gcg gcc atg cgg gcc gct gaa tat ttg aac 432
 Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala Glu Tyr Leu Asn
 130 135 140

aag att caa aac tcc ctc tca aca gaa tgg tct cct tgc agc gtg act 480
 Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro Cys Ser Val Thr
 145 150 155 160

cga agg ctg gcc gcg ggt att gtc act gtg ccc ccc agg tcc agg cga 528
 Arg Arg Leu Ala Ala Gly Ile Val Thr Val Pro Pro Arg Ser Arg Arg
 165 170 175

cga gcg gcc gcc gca gca gcc gcg gcc att agt gct atg act cag ggt 576
 Arg Ala Ala Ala Ala Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly
 180 185 190

cgc agg ggc aac gtg tat tgg gtg cgc gac tcg gtt agc ggc ctg cgc 624
 Arg Arg Gly Asn Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg
 195 200 205

gtg ccc gtg cgc acc cgc ccc ccg cgc aac gtg cgc acc cgc ccc ccg 672
 Val Pro Val Arg Thr Arg Pro Pro Arg Asn Val Arg Thr Arg Pro Pro
 210 215 220

cgc aac tag 681
 Arg Asn
 225

<210> 30
 <211> 369
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 30

Met Lys Lys Cys Thr Ile Leu Val Val Ala Ser Leu Leu Leu Val Asp
 1 5 10 15

Ser Leu Leu Pro Gly Tyr Gly Gln Asn Lys Ser Val Gln Ala Gln Arg
 20 25 30

Asn Leu Asn Glu Leu Cys Tyr Asn Glu Glu Asn Asp Asn Lys Leu Tyr
 35 40 45

His Val Leu Asn Ser Lys Asn Gly Lys Ile Tyr Asn Arg Asn Ile Val
50 55 60

Asn Arg Leu Leu Gly Asp Ala Leu Asn Gly Lys Pro Glu Glu Lys Lys
65 70 75 80

Asp Asp Pro Pro Lys Asp Asp Asn Lys Asp Asp Leu Pro Lys Glu Glu
85 90 95

Lys Lys Asp Asp Leu Pro Lys Glu Glu Lys Lys Asp Asp Pro Pro Lys
100 105 110

Asp Pro Lys Lys Asp Asp Pro Pro Lys Glu Ala Gln Asn Lys Leu Asn
115 120 125

Gln Pro Val Val Ala Asp Glu Asn Val Asp Gln Gly Pro Gly Ala Pro
130 135 140

Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly
145 150 155 160

Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly
165 170 175

Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro
180 185 190

Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly
195 200 205

Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly
210 215 220

Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro
225 230 235 240

Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Glu Pro Pro

	245	250	255	
Gln Gln Pro Pro Gln Gln Pro Pro Gln Gln Pro Pro Gln Gln Pro Pro				
	260	265	270	
Gln Gln Pro Pro Gln Gln Pro Asn Asn Asn Asn Asn Asn Asn Gly Asn				
	275	280	285	
Asn Asn Glu Asp Ser Tyr Val Pro Ser Ala Glu Gln Ile Leu Glu Phe				
	290	295	300	
Val Lys Gln Ile Ser Ser Gln Leu Thr Glu Glu Trp Ser Gln Cys Ser				
	305	310	315	320
Val Thr Cys Gly Ser Gly Val Arg Val Arg Lys Arg Lys Asn Val Asn				
	325	330	335	
Lys Gln Pro Glu Asn Leu Thr Leu Glu Asp Ile Asp Thr Glu Ile Cys				
	340	345	350	
Lys Met Asp Lys Cys Ser Ser Ile Phe Asn Ile Val Ser Asn Ser Leu				
	355	360	365	

Gly

<210> 31
<211> 943
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 31

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala

20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe
145 150 155 160

Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln
165 170 175

Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln
180 185 190

Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn
195 200 205

His Ala Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys
210 215 220

Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile
225 230 235 240

Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln
 245 250 255

Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr
 260 265 270

Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp
 275 280 285

Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu
 290 295 300

Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe
305 310 315 320

Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met
 325 330 335

Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu
 340 345 350

Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile
 355 360 365

Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser
 370 375 380

Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly Thr Glu Asp Glu
385 390 395 400

Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr
 405 410 415

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

Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn
435 440 445

Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu
450 455 460

Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro
465 470 475 480

Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn
485 490 495

Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly
500 505 510

Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His
515 520 525

His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly
530 535 540

Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile
545 550 555 560

Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe
565 570 575

Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn Asp Leu
580 585 590

Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala
595 600 605

Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met
610 615 620

Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala
625 630 635 640

Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile
645 650 655

Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr
660 665 670

Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro
675 680 685

Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr
690 695 700

Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val
705 710 715 720

Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile
725 730 735

Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met
740 745 750

Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly
755 760 765

Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser
770 775 780

Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr
785 790 795 800

Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn
805 810 815

Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala
820 825 830

Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp

835	840	845	
Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile			
850	855	860	
Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly			
865	870	875	880
Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe			
885	890	895	
Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu			
900	905	910	
Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu			
915	920	925	
Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr Thr			
930	935	940	

<210> 32
 <211> 929
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 32

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile
165 170 175

Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr
180 185 190

Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp
195 200 205

Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr
210 215 220

Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu
225 230 235 240

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

Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly
260 265 270

Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val
275 280 285

Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
290 295 300

Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
305 310 315 320

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
325 330 335

Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
340 345 350

Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
355 360 365

Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
370 375 380

Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
385 390 395 400

Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
405 410 415

Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
420 425 430

Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
435 440 445

Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
450 455 460

Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
465 470 475 480

Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
 485 490 495

Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
 500 505 510

Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
 515 520 525

Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
 530 535 540

Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
545 550 555 560

Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
 565 570 575

Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
 580 585 590

Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
 595 600 605

Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
 610 615 620

Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
625 630 635 640

Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
 645 650 655

Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr

660 665 670

Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
675 680 685

Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser
690 695 700

Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
705 710 715 720

Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
725 730 735

Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
740 745 750

Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met
755 760 765

Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
770 775 780

Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
785 790 795 800

Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly
805 810 815

Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
820 825 830

Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
835 840 845

Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
850 855 860

Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
865 870 875 880

Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
 885 890 895

Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
 900 905 910

Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
 915 920 925

Thr

<210> 33

<211> 935

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 33

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
 20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
 35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
 50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe Gly Gln Ala Pro
165 170 175

Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly Val Glu
180 185 190

Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln
195 200 205

Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala Ala Gly
210 215 220

Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr
225 230 235 240

Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val Lys Gln
245 250 255

Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe Ser Thr
260 265 270

Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys Val Val
275 280 285

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

Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met Gly Gln
305 310 315 320

Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe
325 330 335

Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala
340 345 350

Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn
355 360 365

Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr
370 375 380

Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu
385 390 395 400

Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro Lys Thr
405 410 415

Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys
420 425 430

Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn Leu Asn
435 440 445

Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu
450 455 460

Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser Asp Asn
465 470 475 480

Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro Gly Leu

485	490	495
Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met		
500	505	510
Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu Arg Tyr		
515	520	525
Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His Ile Gln		
530	535	540
Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly		
545	550	560
Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met Val Leu		
565	570	575
Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser Ile Lys		
580	585	590
Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala His Asn		
595	600	605
Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn Asp Gln		
610	615	620
Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro		
625	630	640
Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala		
645	650	655
Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro		
660	665	670
Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile		
675	680	685

Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys Lys Val
690 695 700

Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu
705 710 715 720

Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly Glu Gly
725 730 735

Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu Val Gln
740 745 750

Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu
755 760 765

Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met
770 775 780

Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val
785 790 795 800

Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala
805 810 815

Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro
820 825 830

Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys Phe Leu
835 840 845

Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe Met Ser
850 855 860

Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser
865 870 875 880

Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp Glu Pro
885 890 895

Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg Val His
900 905 910

Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe
915 920 925

Ser Ala Gly Asn Ala Thr Thr
930 935

<210> 34

<211> 941

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 34

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His
165 170 175

Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly
180 185 190

Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr
195 200 205

Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu
210 215 220

Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys
225 230 235 240

Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln
245 250 255

Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu
260 265 270

Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn
275 280 285

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

Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser

305	310	315	320
Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile			
	325	330	335
Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly			
	340	345	350
Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val			
	355	360	365
Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp			
	370	375	380
Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro			
	385	390	395
			400
Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr			
	405	410	415
Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala			
	420	425	430
Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala			
	435	440	445
Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser			
	450	455	460
Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn			
	465	470	475
			480
Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg			
	485	490	495
Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg			
	500	505	510

Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg
515 520 525

Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr
530 535 540

Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn
545 550 555 560

Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys
565 570 575

Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val
580 585 590

Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe
595 600 605

Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg
610 615 620

Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn
625 630 635 640

Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile
645 650 655

Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu
660 665 670

Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr
675 680 685

Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn
690 695 700

His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp
705 710 715 720

Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg
725 730 735

Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys
740 745 750

Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln
755 760 765

Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe
770 775 780

Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr
785 790 795 800

Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly
805 810 815

Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro
820 825 830

Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile
835 840 845

Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe
850 855 860

Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn
865 870 875 880

Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val
885 890 895

Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe
900 905 910

Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu Thr Val
915 920 925

Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr Thr
930 935 940

<210> 35
<211> 947
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 35

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
165 170 175

Gly Ala Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile
180 185 190

Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro
195 200 205

Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser
210 215 220

Gln Trp Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys
225 230 235 240

Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr
245 250 255

Asn Glu Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys
260 265 270

Leu Glu Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala
275 280 285

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

Asp Val Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr
305 310 315 320

Ile Lys Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro
325 330 335

Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met
340 345 350

Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser
355 360 365

Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser
370 375 380

Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser
385 390 395 400

Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile
405 410 415

Asn Thr Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn
420 425 430

Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg
435 440 445

Val Gly Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp
450 455 460

Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu
465 470 475 480

Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr
485 490 495

Asp Tyr Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr
500 505 510

Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn
515 520 525

Pro Phe Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu
530 535 540

Leu Gly Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys
545 550 555 560

Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr
 565 570 575

Glu Trp Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu
 580 585 590

Gly Asn Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile
 595 600 605

Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr
 610 615 620

Leu Glu Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp
625 630 635 640

Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr
 645 650 655

Asn Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly
 660 665 670

Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser
 675 680 685

Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp
 690 695 700

Gly Thr Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe
705 710 715 720

Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn
 725 730 735

Glu Phe Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala

740 745 750

Gln Cys Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn
755 760 765

Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp
770 775 780

Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val
785 790 795 800

Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His
805 810 815

Gln His Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg
820 825 830

Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys
835 840 845

Thr Ala Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr
850 855 860

Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu
865 870 875 880

Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu
885 890 895

Asp Met Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr
900 905 910

Val Leu Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg
915 920 925

Gly Val Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn
930 935 940

Ala Thr Thr
945

<210> 36

<211> 953

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 36

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
 165 170 175

Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe Gly Gln
 180 185 190

Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
 195 200 205

Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
 210 215 220

Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
225 230 235 240

Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
 245 250 255

Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
 260 265 270

Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
 275 280 285

Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
 290 295 300

Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
305 310 315 320

Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
 325 330 335

Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
 340 345 350

Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
355 360 365

Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
370 375 380

Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
385 390 395 400

Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
405 410 415

Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
420 425 430

Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
435 440 445

Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
450 455 460

Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu
465 470 475 480

Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
485 490 495

Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
500 505 510

Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
515 520 525

Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
530 535 540

Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
545 550 555 560

Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
565 570 575

Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
580 585 590

Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
595 600 605

Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
610 615 620

His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
625 630 635 640

Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
645 650 655

Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn
660 665 670

Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu
675 680 685

Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
690 695 700

Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
705 710 715 720

Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp
725 730 735

Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
740 745 750

Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu

755	760	765	
Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile			
770	775	780	
Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln			
785	790	795	800
Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln			
805	810	815	
Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr			
820	825	830	
Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro			
835	840	845	
Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys			
850	855	860	
Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe			
865	870	875	880
Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala			
885	890	895	
Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp			
900	905	910	
Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg			
915	920	925	
Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr			
930	935	940	
Pro Phe Ser Ala Gly Asn Ala Thr Thr			
945	950		

<210> 37
<211> 959
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 37

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
165 170 175

Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys
180 185 190

Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys
195 200 205

Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp
210 215 220

Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu
225 230 235 240

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

Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly
260 265 270

Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln
275 280 285

Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly
290 295 300

Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile
305 310 315 320

Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly
325 330 335

Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn
340 345 350

Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser
355 360 365

Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala
370 375 380

Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu
385 390 395 400

Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln
405 410 415

Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr
420 425 430

Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys
435 440 445

Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn
450 455 460

Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu
465 470 475 480

Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro
485 490 495

Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn
500 505 510

Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly
515 520 525

Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His
530 535 540

His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly
545 550 555 560

Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile

565	570	575
Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe		
580	585	590
Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn Asp Leu		
595	600	605
Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala		
610	615	620
Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met		
625	630	635
Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala		
645	650	655
Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile		
660	665	670
Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr		
675	680	685
Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro		
690	695	700
Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr		
705	710	715
Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val		
725	730	735
Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile		
740	745	750
Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met		
755	760	765

Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly
770 775 780

Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser
785 790 795 800

Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr
805 810 815

Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn
820 825 830

Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala
835 840 845

Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp
850 855 860

Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile
865 870 875 880

Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly
885 890 895

Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe
900 905 910

Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu
915 920 925

Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu
930 935 940

Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr Thr
945 950 955

<210> 38

<211> 971

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 38

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
165 170 175

Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln
180 185 190

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Lys Thr His Val Phe
195 200 205

Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln
210 215 220

Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln
225 230 235 240

Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn
245 250 255

His Ala Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys
260 265 270

Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile
275 280 285

Leu Val Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln
290 295 300

Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr
305 310 315 320

Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp
325 330 335

Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu
340 345 350

Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe
355 360 365

Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met
370 375 380

Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu
385 390 395 400

Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile
 405 410 415

Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr
 420 425 430

Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val
 435 440 445

Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu
 450 455 460

Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu
465 470 475 480

Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile
 485 490 495

Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys
 500 505 510

Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val
 515 520 525

Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser
 530 535 540

Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala
545 550 555 560

Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro
 565 570 575

Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu

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

Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe
785 790 795 800

Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn
 805 810 815

Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp
 820 825 830

Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val
 835 840 845

Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn
 850 855 860

Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln
865 870 875 880

Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser
 885 890 895

Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu
 900 905 910

Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro
 915 920 925

Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val
 930 935 940

Val Arg Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu
945 950 955 960

Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr Thr
 965 970

<210> 39

<211> 977
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 39

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Gln Gly Pro Gly Ala Pro Gln
130 135 140

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
145 150 155 160

Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro
165 170 175

Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln
180 185 190

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
195 200 205

Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile
210 215 220

Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr
225 230 235 240

Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp
245 250 255

Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr
260 265 270

Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu
275 280 285

Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu
290 295 300

Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly
305 310 315 320

Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val
325 330 335

Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
340 345 350

Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
355 360 365

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr

370	375	380	
Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu			
385	390	395	400
Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln			
	405	410	415
Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp			
	420	425	430
Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr			
	435	440	445
Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp			
	450	455	460
Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly			
	465	470	480
Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn			
	485	490	495
Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr			
	500	505	510
Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr			
	515	520	525
Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn			
	530	535	540
Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe			
	545	550	560
Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly			
	565	570	575

Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
580 585 590

Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
595 600 605

Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
610 615 620

Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
625 630 635 640

Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
645 650 655

Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
660 665 670

Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
675 680 685

Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Leu Leu Thr
690 695 700

Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn
705 710 715 720

Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
725 730 735

Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser
740 745 750

Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
755 760 765

Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
770 775 780

Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
785 790 795 800

Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met
805 810 815

Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
820 825 830

Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
835 840 845

Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly
850 855 860

Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
865 870 875 880

Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
885 890 895

Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
900 905 910

Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
915 920 925

Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
930 935 940

Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
945 950 955 960

Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
965 970 975

Thr

<210> 40
<211> 975
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 40

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Ala Ala Thr Ala Leu Glu Ile
130 135 140

Asn Leu Glu Glu Glu Asp Asp Asp Asn Glu Asp Glu Val Asp Glu Gln
145 150 155 160

Ala Glu Gln Gln Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly
165 170 175

Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr
180 185 190

Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu
195 200 205

Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu
210 215 220

Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro
225 230 235 240

Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly
245 250 255

Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe Ser Ala Ser Gln Gly
260 265 270

Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro
275 280 285

Gly Thr Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr
290 295 300

Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp
305 310 315 320

Thr His Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu
325 330 335

Leu Met Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe
340 345 350

Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met

355	360	365	
Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu			
370	375	380	
Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile			
385	390	395	400
Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser			
405	410	415	
Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly Thr Glu Asp Glu			
420	425	430	
Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr			
435	440	445	
Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys			
450	455	460	
Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly Asn Asn			
465	470	475	480
Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu			
485	490	495	
Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro			
500	505	510	
Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn			
515	520	525	
Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly			
530	535	540	
Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe Asn His			
545	550	555	560

His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly
565 570 575

Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile
580 585 590

Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe
595 600 605

Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn Asp Leu
610 615 620

Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala
625 630 635 640

Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met
645 650 655

Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala
660 665 670

Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile
675 680 685

Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr
690 695 700

Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro
705 710 715 720

Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr
725 730 735

Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val
740 745 750

Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile
755 760 765

Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met
770 775 780

Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly
785 790 795 800

Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser
805 810 815

Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr
820 825 830

Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn
835 840 845

Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala
850 855 860

Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp
865 870 875 880

Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile
885 890 895

Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly
900 905 910

Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe
915 920 925

Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu
930 935 940

Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu
945 950 955 960

Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr Thr
965 970 975

<210> 41
<211> 599
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 41

Met Lys Arg Ala Arg Pro Ser Glu Asp Thr Phe Asn Pro Val Tyr Pro
1 5 10 15

Tyr Asp Thr Glu Thr Gly Pro Pro Thr Val Pro Phe Leu Thr Pro Pro
20 25 30

Phe Val Ser Pro Asn Gly Phe Gln Glu Ser Pro Pro Gly Val Leu Ser
35 40 45

Leu Arg Leu Ser Glu Pro Leu Val Thr Ser Asn Gly Met Leu Ala Leu
50 55 60

Lys Met Gly Asn Gly Leu Ser Leu Asp Glu Ala Gly Asn Leu Thr Ser
65 70 75 80

Gln Asn Val Thr Thr Val Ser Pro Pro Leu Lys Lys Thr Lys Ser Asn
85 90 95

Ile Asn Leu Glu Ile Ser Ala Pro Leu Thr Val Thr Ser Glu Ala Leu
100 105 110

Thr Val Ala Ala Ala Ala Pro Leu Met Val Ala Gly Asn Thr Leu Thr
115 120 125

Met Gln Ser Gln Ala Pro Leu Thr Val His Asp Ser Lys Leu Ser Ile
130 135 140

Ala Thr Gln Gly Pro Leu Thr Val Ser Glu Gly Lys Leu Ala Leu Gln

145 150 155 160

Thr Ser Gly Pro Leu Thr Thr Thr Asp Ser Ser Thr Leu Thr Ile Thr
 165 170 175

Ala Ser Pro Pro Leu Thr Thr Ala Thr Gly Ser Leu Gly Ile Asp Leu
 180 185 190

Lys Glu Pro Ile Tyr Thr Gln Asn Gly Lys Leu Gly Leu Lys Tyr Gly
 195 200 205

Ala Pro Leu His Val Thr Asp Asp Leu Asn Thr Leu Thr Val Ala Thr
 210 215 220

Gly Pro Gly Val Thr Ile Asn Asn Thr Ser Leu Gln Thr Lys Val Thr
225 230 235 240

Gly Ala Leu Gly Phe Asp Ser Gln Gly Asn Met Gln Leu Asn Val Ala
 245 250 255

Gly Gly Leu Arg Ile Asp Ser Gln Asn Arg Arg Leu Ile Leu Asp Val
 260 265 270

Ser Tyr Pro Phe Asp Ala Gln Asn Gln Leu Asn Leu Arg Leu Gly Gln
 275 280 285

Gly Pro Leu Phe Ile Asn Ser Ala His Asn Leu Asp Ile Asn Tyr Asn
 290 295 300

Lys Gly Leu Tyr Leu Phe Thr Ala Ser Asn Asn Ser Lys Lys Leu Glu
305 310 315 320

Val Asn Leu Ser Thr Ala Lys Gly Leu Met Phe Asp Ala Thr Ala Ile
 325 330 335

Ala Ile Asn Ala Gly Asp Gly Leu Glu Phe Gly Ser Pro Asn Ala Pro
 340 345 350

Asn Thr Asn Pro Leu Lys Thr Lys Ile Gly His Gly Leu Glu Phe Asp
355 360 365

Ser Asn Lys Ala Met Val Pro Lys Leu Gly Thr Gly Leu Ser Phe Asp
370 375 380

Ser Thr Gly Ala Ile Thr Val Gly Asn Lys Asn Asn Asp Lys Leu Thr
385 390 395 400

Leu Trp Thr Thr Pro Ala Pro Ser Pro Asn Cys Arg Leu Asn Ala Glu
405 410 415

Lys Asp Ala Lys Leu Thr Leu Val Leu Thr Lys Cys Gly Ser Gln Ile
420 425 430

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

Ser Gly Thr Val Gln Ser Ala His Leu Ile Ile Arg Phe Asp Glu Asn
450 455 460

Gly Val Leu Leu Asn Asn Ser Phe Leu Asp Pro Glu Tyr Trp Asn Phe
465 470 475 480

Arg Asn Gly Asp Leu Thr Glu Gly Thr Ala Tyr Thr Asn Ala Val Gly
485 490 495

Phe Met Pro Asn Leu Ser Ala Tyr Pro Lys Ser His Gly Lys Thr Ala
500 505 510

Lys Ser Asn Ile Val Ser Gln Val Tyr Leu Asn Gly Asp Lys Thr Lys
515 520 525

Pro Val Thr Leu Thr Ile Thr Leu Asn Gly Thr Gln Glu Thr Gly Gln
530 535 540

Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala Pro Gln Gly Pro Gly Ala
545 550 555 560

Pro Asp Thr Thr Pro Ser Ala Tyr Ser Met Ser Phe Ser Trp Asp Trp
565 570 575

Ser Gly His Asn Tyr Ile Asn Glu Ile Phe Ala Thr Ser Ser Tyr Thr
580 585 590

Phe Ser Tyr Ile Ala Gln Glu
595

<210> 42

<211> 227

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 42

Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg
1 5 10 15

Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His
20 25 30

Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys
35 40 45

Arg Gly Arg Thr Gly Arg Thr Thr Val Asp Asp Ala Ile Asp Ala Val
50 55 60

Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Pro Val Ser Thr
65 70 75 80

Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Arg Arg Tyr Ala
85 90 95

Lys Met Lys Arg Arg Arg Arg Val Ala Arg Arg His Arg Arg Arg
100 105 110

Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Ala Leu Leu Asn Arg Ala
115 120 125

Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala Arg Arg Leu Ala
130 135 140

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

Ala Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly Arg Arg Gly Asn
165 170 175

Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg Val Pro Val Arg
180 185 190

Thr Arg Pro Pro Arg Asn Val Arg Thr Arg Pro Pro Arg Asn Tyr Asn
195 200 205

Arg Asn Ile Val Asn Arg Leu Leu Gly Asp Ala Leu Asn Gly Lys Pro
210 215 220

Glu Glu Lys
225

<210> 43
<211> 374
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 43

Met Met Arg Lys Leu Ala Ile Leu Ser Val Ser Ser Phe Leu Phe Val
1 5 10 15

Glu Ala Leu Phe Gln Glu Tyr Gln Cys Tyr Gly Ser Ser Ser Asn Thr
180/247

20 25 30

Arg Val Leu Asn Glu Leu Asn Tyr Asp Asn Ala Gly Thr Asn Leu Tyr
35 40 45

Asn Glu Leu Glu Met Asn Tyr Tyr Gly Lys Gln Glu Asn Trp Tyr Ser
50 55 60

Leu Lys Lys Asn Ser Arg Ser Leu Gly Glu Asn Asp Asp Gly Asn Asn
65 70 75 80

Glu Asp Asn Glu Lys Leu Arg Lys Pro Lys His Lys Lys Leu Lys Gln
85 90 95

Pro Ala Asp Gly Asn Pro Asp Pro Asn Ala Asn Pro Asn Val Asp Pro
100 105 110

Asn Ala Asn Pro Asn Val Asp Pro Asn Ala Asn Pro Asn Val Asp Pro
115 120 125

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
130 135 140

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
145 150 155 160

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
165 170 175

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
180 185 190

Asn Ala Asn Pro Asn Val Asp Pro Asn Ala Asn Pro Asn Ala Asn Pro
195 200 205

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
210 215 220

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
225 230 235 240

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
 245 250 255

Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro
 260 265 270

Asn Lys Asn Asn Gln Gly Asn Gly Gln Gly His Asn Met Pro Asn Asp
 275 280 285

Pro Asn Arg Asn Val Asp Glu Asn Ala Asn Ala Asn Ser Ala Val Lys
 290 295 300

Asn Asn Asn Asn Glu Glu Pro Ser Asp Lys His Ile Lys Glu Tyr Leu
305 310 315 320

Asn Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro Cys Ser Val
 325 330 335

Thr Cys Gly Asn Gly Ile Gln Val Arg Ile Lys Pro Gly Ser Ala Asn
 340 345 350

Lys Pro Lys Asp Glu Leu Asp Tyr Ala Asn Asp Ile Glu Lys Lys Ile
 355 360 365

Cys Lys Met Glu Lys Cys
 370

<210> 44

<211> 941

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 44

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln
145 150 155 160

Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
165 170 175

Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
180 185 190

Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
195 200 205

Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
210 215 220

Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
225 230 235 240

Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
245 250 255

Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
260 265 270

Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
275 280 285

Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
290 295 300

Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
305 310 315 320

Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
325 330 335

Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
340 345 350

Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
355 360 365

Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser Tyr Asp
370 375 380

Pro Asp Val Arg Ile Ile Glu Asn His Gly Thr Glu Asp Glu Leu Pro
385 390 395 400

Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr

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

Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg
610 615 620

Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn
625 630 635 640

Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile
645 650 655

Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu
660 665 670

Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr
675 680 685

Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn
690 695 700

His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp
705 710 715 720

Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg
725 730 735

Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys
740 745 750

Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln
755 760 765

Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe
770 775 780

Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr
785 790 795 800

Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly
805 810 815

Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro
820 825 830

Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile
835 840 845

Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe
850 855 860

Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn
865 870 875 880

Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val
885 890 895

Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe
900 905 910

Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu Thr Val
915 920 925

Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr Thr
930 935 940

<210> 45

<211> 929

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 45

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile
165 170 175

Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr
180 185 190

Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp
195 200 205

Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr
210 215 220

Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu

225 230 235 240

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

Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly
 260 265 270

Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val
 275 280 285

Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
 290 295 300

Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
305 310 315 320

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
 325 330 335

Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
 340 345 350

Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
 355 360 365

Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
 370 375 380

Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
385 390 395 400

Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
 405 410 415

Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
 420 425 430

Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
435 440 445

Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
450 455 460

Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
465 470 475 480

Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
485 490 495

Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
500 505 510

Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
515 520 525

Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
530 535 540

Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
545 550 555 560

Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
565 570 575

Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
580 585 590

Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
595 600 605

Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
610 615 620

Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
625 630 635 640

Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
645 650 655

Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr
660 665 670

Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
675 680 685

Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser
690 695 700

Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
705 710 715 720

Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
725 730 735

Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
740 745 750

Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met
755 760 765

Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
770 775 780

Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
785 790 795 800

Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly
805 810 815

Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
820 825 830

Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
835 840 845

Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
850 855 860

Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
865 870 875 880

Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
885 890 895

Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
900 905 910

Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
915 920 925

Thr

<210> 46
<211> 937
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 46

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln
165 170 175

Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
180 185 190

Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
195 200 205

Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
210 215 220

Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
225 230 235 240

Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
245 250 255

Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
260 265 270

Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
275 280 285

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

Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
305 310 315 320

Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
325 330 335

Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
340 345 350

Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
355 360 365

Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
370 375 380

Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
385 390 395 400

Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
405 410 415

Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
420 425 430

Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
435 440 445

Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu
450 455 460

Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
465 470 475 480

Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
485 490 495

Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
500 505 510

Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
515 520 525

Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
530 535 540

Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
545 550 555 560

Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
565 570 575

Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
580 585 590

Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
595 600 605

His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
610 615 620

Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
625 630 635 640

Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn
645 650 655

Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu

660	665	670
Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly		
675	680	685
Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys		
690	695	700
Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp		
705	710	715
720		
Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly		
725	730	735
Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu		
740	745	750
Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile		
755	760	765
Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln		
770	775	780
Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln		
785	790	795
800		
Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr		
805	810	815
Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro		
820	825	830
Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys		
835	840	845
Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe		
850	855	860

Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala
865 870 875 880

Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp
 885 890 895

Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg
 900 905 910

Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr
 915 920 925

Pro Phe Ser Ala Gly Asn Ala Thr Thr
 930 935

<210> 47

<211> 945

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 47

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
 20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
 35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
 50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
165 170 175

Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile
180 185 190

Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr
195 200 205

Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp
210 215 220

Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr
225 230 235 240

Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu
245 250 255

Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu
260 265 270

Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly
275 280 285

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

Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
305 310 315 320

Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
325 330 335

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
340 345 350

Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
355 360 365

Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
370 375 380

Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
385 390 395 400

Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
405 410 415

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

Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
435 440 445

Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
450 455 460

Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
465 470 475 480

Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr

485	490	495
Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn		
500	505	510
Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe		
515	520	525
Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly		
530	535	540
Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe		
545	550	555
Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp		
565	570	575
Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn		
580	585	590
Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu		
595	600	605
Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu		
610	615	620
Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu		
625	630	635
Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val		
645	650	655
Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala		
660	665	670
Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr		
675	680	685

Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
690 695 700

Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser
705 710 715 720

Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
725 730 735

Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
740 745 750

Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
755 760 765

Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met
770 775 780

Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
785 790 795 800

Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
805 810 815

Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly
820 825 830

Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
835 840 845

Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
850 855 860

Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
865 870 875 880

Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
885 890 895

Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
900 905 910

Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
915 920 925

Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
930 935 940

Thr
945

<210> 48
<211> 953
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 48

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
165 170 175

Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln
180 185 190

Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly
195 200 205

Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu
210 215 220

Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala
225 230 235 240

Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly
245 250 255

Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
260 265 270

Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
275 280 285

Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys

290	295	300	
Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His			
305	310	315	320
Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met			
	325	330	335
Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp			
	340	345	350
Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val			
	355	360	365
Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp			
	370	375	380
Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp			
385	390	395	400
Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe			
	405	410	415
Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro			
	420	425	430
Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser			
	435	440	445
Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn			
	450	455	460
Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu			
465	470	475	480
Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser			
	485	490	495

Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
500 505 510

Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
515 520 525

Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
530 535 540

Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
545 550 555 560

Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
565 570 575

Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
580 585 590

Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
595 600 605

Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
610 615 620

His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
625 630 635 640

Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
645 650 655

Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn
660 665 670

Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu
675 680 685

Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
690 695 700

Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
705 710 715 720

Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp
725 730 735

Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
740 745 750

Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu
755 760 765

Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile
770 775 780

Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
785 790 795 800

Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln
805 810 815

Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr
820 825 830

Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro
835 840 845

Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys
850 855 860

Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe
865 870 875 880

Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala
885 890 895

Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp
900 905 910

Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg
915 920 925

Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr
930 935 940

Pro Phe Ser Ala Gly Asn Ala Thr Thr
945 950

<210> 49
<211> 961
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 49

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr

100	105	110
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly		
115	120	125
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn		
130	135	140
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
145	150	155
160		
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
165	170	175
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
180	185	190
Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile		
195	200	205
Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr		
210	215	220
Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp		
225	230	235
240		
Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr		
245	250	255
Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu		
260	265	270
Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu		
275	280	285
Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly		
290	295	300

Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val
305 310 315 320

Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
 325 330 335

Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
 340 345 350

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
 355 360 365

Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
 370 375 380

Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
385 390 395 400

Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
 405 410 415

Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
 420 425 430

Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
 435 440 445

Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
 450 455 460

Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
465 470 475 480

Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
 485 490 495

Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
 500 505 510

Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
515 520 525

Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
530 535 540

Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
545 550 555 560

Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
565 570 575

Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
580 585 590

Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
595 600 605

Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
610 615 620

Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
625 630 635 640

Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
645 650 655

Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
660 665 670

Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
675 680 685

Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr
690 695 700

Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
705 710 715 720

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

Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
740 745 750

Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
755 760 765

Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
770 775 780

Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met
785 790 795 800

Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
805 810 815

Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
820 825 830

Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly
835 840 845

Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
850 855 860

Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
865 870 875 880

Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
885 890 895

Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
900 905 910

Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu

915 920 925

Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
930 935 940

Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
945 950 955 960

Thr

<210> 50
<211> 969
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 50

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr

100	105	110
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly		
115	120	125
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn		
130	135	140
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
145	150	155
		160
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
165	170	175
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
180	185	190
Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln		
195	200	205
Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly		
210	215	220
Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu		
225	230	235
		240
Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala		
245	250	255
Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly		
260	265	270
Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val		
275	280	285
Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe		
290	295	300

Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys
305 310 315 320

Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
325 330 335

Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
340 345 350

Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
355 360 365

Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
370 375 380

Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
385 390 395 400

Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
405 410 415

Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
420 425 430

Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
435 440 445

Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
450 455 460

Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
465 470 475 480

Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu
485 490 495

Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
500 505 510

Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
515 520 525

Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
530 535 540

Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
545 550 555 560

Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
565 570 575

Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
580 585 590

Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
595 600 605

Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
610 615 620

Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
625 630 635 640

His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
645 650 655

Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
660 665 670

Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn
675 680 685

Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu
690 695 700

Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
705 710 715 720

Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
725 730 735

Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp
740 745 750

Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
755 760 765

Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu
770 775 780

Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile
785 790 795 800

Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
805 810 815

Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln
820 825 830

Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr
835 840 845

Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro
850 855 860

Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys
865 870 875 880

Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe
885 890 895

Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala
900 905 910

Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp

915 920 925

Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg
930 935 940

Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr
945 950 955 960

Pro Phe Ser Ala Gly Asn Ala Thr Thr
965

<210> 51
<211> 977
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 51

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
165 170 175

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
180 185 190

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
195 200 205

Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile
210 215 220

Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr
225 230 235 240

Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp
245 250 255

Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr
260 265 270

Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu
275 280 285

Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu
290 295 300

Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly
305 310 315 320

Asn Gly Asp Asn Leu Thr Pro Lys Val Val Leu Tyr Ser Glu Asp Val
325 330 335

Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
340 345 350

Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
355 360 365

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
370 375 380

Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
385 390 395 400

Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
405 410 415

Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
420 425 430

Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
435 440 445

Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
450 455 460

Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
465 470 475 480

Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
485 490 495

Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
500 505 510

Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
515 520 525

Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
530 535 540

Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
545 550 555 560

Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
565 570 575

Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
580 585 590

Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
595 600 605

Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
610 615 620

Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
625 630 635 640

Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
645 650 655

Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu
660 665 670

Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val
675 680 685

Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala
690 695 700

Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr

705 710 715 720

Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr
725 730 735

Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser
740 745 750

Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe
755 760 765

Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys
770 775 780

Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn
785 790 795 800

Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met
805 810 815

Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp
820 825 830

Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His
835 840 845

Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly
850 855 860

Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
865 870 875 880

Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
885 890 895

Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
900 905 910

Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
915 920 925

Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
930 935 940

Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
945 950 955 960

Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
965 970 975

Thr

<210> 52

<211> 985

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 52

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met

85	90	95
Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr		
100	105	110
Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly		
115	120	125
Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn		
130	135	140
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
145	150	155
160		
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
165	170	175
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
180	185	190
Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn		
195	200	205
Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln		
210	215	220
Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly		
225	230	235
240		
Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu		
245	250	255
Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala		
260	265	270
Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly		
275	280	285

Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val
290 295 300

Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe
305 310 315 320

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

Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His
340 345 350

Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met
355 360 365

Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp
370 375 380

Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
385 390 395 400

Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
405 410 415

Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
420 425 430

Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
435 440 445

Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
450 455 460

Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
465 470 475 480

Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
485 490 495

Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu
500 505 510

Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
515 520 525

Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
530 535 540

Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
545 550 555 560

Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
565 570 575

Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
580 585 590

Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
595 600 605

Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
610 615 620

Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
625 630 635 640

Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
645 650 655

His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
660 665 670

Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
675 680 685

Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn
690 695 700

Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu
705 710 715 720

Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
 725 730 735

Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
 740 745 750

Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp
 755 760 765

Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
 770 775 780

Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu
785 790 795 800

Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile
 805 810 815

Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
 820 825 830

Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln
 835 840 845

Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr
 850 855 860

Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro
865 870 875 880

Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys
 885 890 895

Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe

900	905	910
Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala		
915	920	925
Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp		
930	935	940
Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg		
945	950	955 960
Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr		
965	970	975
Pro Phe Ser Ala Gly Asn Ala Thr Thr		
980	985	

<210> 53
 <211> 993
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 53

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
 85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
 100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
 115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
 130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 165 170 175

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 180 185 190

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 195 200 205

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
 210 215 220

Pro Lys Thr His Val Phe Gly Gln Ala Pro Tyr Ser Gly Ile Asn Ile
225 230 235 240

Thr Lys Glu Gly Ile Gln Ile Gly Val Glu Gly Gln Thr Pro Lys Tyr
 245 250 255

Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Ile Gly Glu Ser Gln Trp
 260 265 270

Tyr Glu Thr Glu Ile Asn His Ala Ala Gly Arg Val Leu Lys Lys Thr
275 280 285

Thr Pro Met Lys Pro Cys Tyr Gly Ser Tyr Ala Lys Pro Thr Asn Glu
290 295 300

Asn Gly Gly Gln Gly Ile Leu Val Lys Gln Gln Asn Gly Lys Leu Glu
305 310 315 320

Ser Gln Val Glu Met Gln Phe Phe Ser Thr Thr Glu Ala Ala Ala Gly
325 330 335

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

Asp Ile Glu Thr Pro Asp Thr His Ile Ser Tyr Met Pro Thr Ile Lys
355 360 365

Glu Gly Asn Ser Arg Glu Leu Met Gly Gln Gln Ser Met Pro Asn Arg
370 375 380

Pro Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
385 390 395 400

Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
405 410 415

Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
420 425 430

Leu Leu Leu Asp Ser Ile Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
435 440 445

Asn Gln Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Val Ile Asn Thr
450 455 460

Glu Thr Leu Thr Lys Val Lys Pro Lys Thr Gly Gln Glu Asn Gly Trp
465 470 475 480

Glu Lys Asp Ala Thr Glu Phe Ser Asp Lys Asn Glu Ile Arg Val Gly
485 490 495

Asn Asn Phe Ala Met Glu Ile Asn Leu Asn Ala Asn Leu Trp Arg Asn
500 505 510

Phe Leu Tyr Ser Asn Ile Ala Leu Tyr Leu Pro Asp Lys Leu Lys Tyr
515 520 525

Ser Pro Ser Asn Val Lys Ile Ser Asp Asn Pro Asn Thr Tyr Asp Tyr
530 535 540

Met Asn Lys Arg Val Val Ala Pro Gly Leu Val Asp Cys Tyr Ile Asn
545 550 555 560

Leu Gly Ala Arg Trp Ser Leu Asp Tyr Met Asp Asn Val Asn Pro Phe
565 570 575

Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly
580 585 590

Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe
595 600 605

Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp
610 615 620

Asn Phe Arg Lys Asp Val Asn Met Val Leu Gln Ser Ser Leu Gly Asn
625 630 635 640

Asp Leu Arg Val Asp Gly Ala Ser Ile Lys Phe Asp Ser Ile Cys Leu
645 650 655

Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu
660 665 670

Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu

675	680	685	
Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val			
690	695	700	
Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ala			
705	710	715	720
Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser Gly Tyr			
725	730	735	
Asp Pro Tyr Tyr Thr Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr			
740	745	750	
Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ala Ile Thr Phe Asp Ser			
755	760	765	
Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe			
770	775	780	
Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys			
785	790	795	800
Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala Asn Tyr Asn			
805	810	815	
Ile Gly Tyr Gln Gly Phe Tyr Ile Pro Glu Ser Tyr Lys Asp Arg Met			
820	825	830	
Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp			
835	840	845	
Asp Thr Lys Tyr Lys Asp Tyr Gln Gln Val Gly Ile Leu His Gln His			
850	855	860	
Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Glu Gly			
865	870	875	880

Gln Ala Tyr Pro Ala Asn Phe Pro Tyr Pro Leu Ile Gly Lys Thr Ala
885 890 895

Val Asp Ser Ile Thr Gln Lys Lys Phe Leu Cys Asp Arg Thr Leu Trp
900 905 910

Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp
915 920 925

Leu Gly Gln Asn Leu Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met
930 935 940

Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr Val Leu
945 950 955 960

Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val
965 970 975

Ile Glu Thr Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr
980 985 990

Thr

<210> 54

<211> 1017

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 54

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ser
1 5 10 15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
20 25 30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Asn Asn Lys Phe Arg Asn Pro
35 40 45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
50 55 60

Thr Leu Arg Phe Ile Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65 70 75 80

Lys Ala Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
85 90 95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Thr
100 105 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ala Leu Ala Pro Lys Gly
115 120 125

Ala Pro Asn Pro Cys Glu Trp Asp Glu Asn Ala Asn Pro Asn Ala Asn
130 135 140

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
145 150 155 160

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
165 170 175

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
180 185 190

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
195 200 205

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
210 215 220

Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn
225 230 235 240

Pro Asn Ala Asn Pro Asn Ala Asn Pro Lys Thr His Val Phe Gly Gln

245	250	255
Ala Pro Tyr Ser Gly Ile Asn Ile Thr Lys Glu Gly Ile Gln Ile Gly		
260	265	270
Val Glu Gly Gln Thr Pro Lys Tyr Ala Asp Lys Thr Phe Gln Pro Glu		
275	280	285
Pro Gln Ile Gly Glu Ser Gln Trp Tyr Glu Thr Glu Ile Asn His Ala		
290	295	300
Ala Gly Arg Val Leu Lys Lys Thr Thr Pro Met Lys Pro Cys Tyr Gly		
305	310	315
		320
Ser Tyr Ala Lys Pro Thr Asn Glu Asn Gly Gly Gln Gly Ile Leu Val		
325	330	335
Lys Gln Gln Asn Gly Lys Leu Glu Ser Gln Val Glu Met Gln Phe Phe		
340	345	350
Ser Thr Thr Glu Ala Ala Ala Gly Asn Gly Asp Asn Leu Thr Pro Lys		
355	360	365
Val Val Leu Tyr Ser Glu Asp Val Asp Ile Glu Thr Pro Asp Thr His		
370	375	380
Ile Ser Tyr Met Pro Thr Ile Lys Glu Gly Asn Ser Arg Glu Leu Met		
385	390	395
		400
Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Ala Phe Arg Asp		
405	410	415
Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val		
420	425	430
Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp		
435	440	445

Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Ile Gly Asp
450 455 460

Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Leu Pro Asn Tyr Cys Phe
465 470 475 480

Pro Leu Gly Gly Val Ile Asn Thr Glu Thr Leu Thr Lys Val Lys Pro
485 490 495

Lys Thr Gly Gln Glu Asn Gly Trp Glu Lys Asp Ala Thr Glu Phe Ser
500 505 510

Asp Lys Asn Glu Ile Arg Val Gly Asn Asn Phe Ala Met Glu Ile Asn
515 520 525

Leu Asn Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ser Asn Ile Ala Leu
530 535 540

Tyr Leu Pro Asp Lys Leu Lys Tyr Ser Pro Ser Asn Val Lys Ile Ser
545 550 555 560

Asp Asn Pro Asn Thr Tyr Asp Tyr Met Asn Lys Arg Val Val Ala Pro
565 570 575

Gly Leu Val Asp Cys Tyr Ile Asn Leu Gly Ala Arg Trp Ser Leu Asp
580 585 590

Tyr Met Asp Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
595 600 605

Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
610 615 620

Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
625 630 635 640

Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
645 650 655

Val Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
660 665 670

Ile Lys Phe Asp Ser Ile Cys Leu Tyr Ala Thr Phe Phe Pro Met Ala
675 680 685

His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
690 695 700

Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro
705 710 715 720

Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn
725 730 735

Trp Ala Ala Phe Arg Gly Trp Ala Phe Thr Arg Leu Lys Thr Lys Glu
740 745 750

Thr Pro Ser Leu Gly Ser Gly Tyr Asp Pro Tyr Tyr Thr Tyr Ser Gly
755 760 765

Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
770 775 780

Lys Val Ala Ile Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp
785 790 795 800

Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
805 810 815

Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu
820 825 830

Val Gln Met Leu Ala Asn Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Ile
835 840 845

Pro Glu Ser Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
850 855 860

Pro Met Ser Arg Gln Val Val Asp Asp Thr Lys Tyr Lys Asp Tyr Gln
865 870 875 880

Gln Val Gly Ile Leu His Gln His Asn Asn Ser Gly Phe Val Gly Tyr
 885 890 895

Leu Ala Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Phe Pro
 900 905 910

Tyr Pro Leu Ile Gly Lys Thr Ala Val Asp Ser Ile Thr Gln Lys Lys
 915 920 925

Phe Leu Cys Asp Arg Thr Leu Trp Arg Ile Pro Phe Ser Ser Asn Phe
 930 935 940

Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln Asn Leu Leu Tyr Ala
945 950 955 960

Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp
 965 970 975

Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg
 980 985 990

Val His Gln Pro His Arg Gly Val Ile Glu Thr Val Tyr Leu Arg Thr
 995 1000 1005

Pro Phe Ser Ala Gly Asn Ala Thr Thr
 1010 1015

<210> 55

<211> 597

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 55

Met Lys Arg Ala Arg Pro Ser Glu Asp Thr Phe Asn Pro Val Tyr Pro
1 5 10 15

Tyr Asp Thr Glu Thr Gly Pro Pro Thr Val Pro Phe Leu Thr Pro Pro
20 25 30

Phe Val Ser Pro Asn Gly Phe Gln Glu Ser Pro Pro Gly Val Leu Ser
35 40 45

Leu Arg Leu Ser Glu Pro Leu Val Thr Ser Asn Gly Met Leu Ala Leu
50 55 60

Lys Met Gly Asn Gly Leu Ser Leu Asp Glu Ala Gly Asn Leu Thr Ser
65 70 75 80

Gln Asn Val Thr Thr Val Ser Pro Pro Leu Lys Lys Thr Lys Ser Asn
85 90 95

Ile Asn Leu Glu Ile Ser Ala Pro Leu Thr Val Thr Ser Glu Ala Leu
100 105 110

Thr Val Ala Ala Ala Ala Pro Leu Met Val Ala Gly Asn Thr Leu Thr
115 120 125

Met Gln Ser Gln Ala Pro Leu Thr Val His Asp Ser Lys Leu Ser Ile
130 135 140

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

Thr Ser Gly Pro Leu Thr Thr Thr Asp Ser Ser Thr Leu Thr Ile Thr
165 170 175

Ala Ser Pro Pro Leu Thr Thr Ala Thr Gly Ser Leu Gly Ile Asp Leu
180 185 190

Lys Glu Pro Ile Tyr Thr Gln Asn Gly Lys Leu Gly Leu Lys Tyr Gly
195 200 205

Ala Pro Leu His Val Thr Asp Asp Leu Asn Thr Leu Thr Val Ala Thr
210 215 220

Gly Pro Gly Val Thr Ile Asn Asn Thr Ser Leu Gln Thr Lys Val Thr
225 230 235 240

Gly Ala Leu Gly Phe Asp Ser Gln Gly Asn Met Gln Leu Asn Val Ala
245 250 255

Gly Gly Leu Arg Ile Asp Ser Gln Asn Arg Arg Leu Ile Leu Asp Val
260 265 270

Ser Tyr Pro Phe Asp Ala Gln Asn Gln Leu Asn Leu Arg Leu Gly Gln
275 280 285

Gly Pro Leu Phe Ile Asn Ser Ala His Asn Leu Asp Ile Asn Tyr Asn
290 295 300

Lys Gly Leu Tyr Leu Phe Thr Ala Ser Asn Asn Ser Lys Lys Leu Glu
305 310 315 320

Val Asn Leu Ser Thr Ala Lys Gly Leu Met Phe Asp Ala Thr Ala Ile
325 330 335

Ala Ile Asn Ala Gly Asp Gly Leu Glu Phe Gly Ser Pro Asn Ala Pro
340 345 350

Asn Thr Asn Pro Leu Lys Thr Lys Ile Gly His Gly Leu Glu Phe Asp
355 360 365

Ser Asn Lys Ala Met Val Pro Lys Leu Gly Thr Gly Leu Ser Phe Asp
370 375 380

Ser Thr Gly Ala Ile Thr Val Gly Asn Lys Asn Asn Asp Lys Leu Thr
385 390 395 400

Leu Trp Thr Thr Pro Ala Pro Ser Pro Asn Cys Arg Leu Asn Ala Glu
405 410 415

Lys Asp Ala Lys Leu Thr Leu Val Leu Thr Lys Cys Gly Ser Gln Ile
420 425 430

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

Ser Gly Thr Val Gln Ser Ala His Leu Ile Ile Arg Phe Asp Glu Asn
450 455 460

Gly Val Leu Leu Asn Asn Ser Phe Leu Asp Pro Glu Tyr Trp Asn Phe
465 470 475 480

Arg Asn Gly Asp Leu Thr Glu Gly Thr Ala Tyr Thr Asn Ala Val Gly
485 490 495

Phe Met Pro Asn Leu Ser Ala Tyr Pro Lys Ser His Gly Lys Thr Ala
500 505 510

Lys Ser Asn Ile Val Ser Gln Val Tyr Leu Asn Gly Asp Lys Thr Lys
515 520 525

Pro Val Thr Leu Thr Ile Thr Leu Asn Gly Thr Gln Glu Thr Gly Asn
530 535 540

Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asp
545 550 555 560

Thr Thr Pro Ser Ala Tyr Ser Met Ser Phe Ser Trp Asp Trp Ser Gly
565 570 575

His Asn Tyr Ile Asn Glu Ile Phe Ala Thr Ser Ser Tyr Thr Phe Ser
580 585 590

Tyr Ile Ala Gln Glu
595

<210> 56
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 56

Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg
1 5 10 15

Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His
20 25 30

Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys
35 40 45

Arg Gly Arg Thr Gly Arg Thr Thr Val Asp Asp Ala Ile Asp Ala Val
50 55 60

Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Pro Val Ser Thr
65 70 75 80

Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Arg Arg Tyr Ala
85 90 95

Lys Met Lys Arg Arg Arg Arg Arg Val Ala Arg Arg His Arg Arg Arg
100 105 110

Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Ala Leu Leu Asn Arg Ala
115 120 125

Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala Arg Arg Leu Ala
130 135 140

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

Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly Arg Arg Gly Asn
165 170 175

Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg Val Pro Val Arg
180 185 190

Thr Arg Pro Pro Arg Asn Glu Tyr Leu Asn Lys Ile Gln Asn Ser Leu
195 200 205

Ser Thr Glu Trp Ser Pro Cys Ser Val Thr
210 215

<210> 57

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 57

Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg
1 5 10 15

Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His
20 25 30

Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys
35 40 45

Arg Gly Arg Thr Gly Arg Thr Thr Val Asp Asp Ala Ile Asp Ala Val
50 55 60

Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Val Ser Thr
65 70 75 80

Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Glu Tyr Leu Asn
85 90 95

Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro Cys Ser Val Thr
100 105 110

Arg Arg Tyr Ala Lys Met Lys Arg Arg Arg Arg Arg Val Ala Arg Arg
115 120 125

His Arg Arg Arg Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Leu
130 135 140

Leu Asn Arg Ala Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala
145 150 155 160

Arg Arg Leu Ala Ala Gly Ile Val Thr Val Pro Pro Arg Ser Arg Arg
165 170 175

Arg Ala Ala Ala Ala Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly
180 185 190

Arg Arg Gly Asn Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg
195 200 205

Val Pro Val Arg Thr Arg Pro Pro Arg Asn Val Arg Thr Arg Pro Pro
210 215 220

Arg Asn Tyr Asn Arg Asn Ile Val Asn Arg Leu Leu Gly Asp Ala Leu
225 230 235 240

Thr Arg Pro Pro Arg Asn
245

<210> 58

<211> 226

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 58

Met Ser Ile Leu Ile Ser Pro Ser Asn Asn Thr Gly Trp Gly Leu Arg
1 5 10 15

Phe Pro Ser Lys Met Phe Gly Gly Ala Lys Lys Arg Ser Asp Gln His
20 25 30

Pro Val Arg Val Arg Gly His Tyr Arg Ala Pro Trp Gly Ala His Lys
35 40 45

Arg Gly Arg Thr Gly Arg Thr Thr Val Asp Asp Ala Ile Asp Ala Val
50 55 60

Val Glu Glu Ala Arg Asn Tyr Thr Pro Thr Pro Pro Val Ser Thr
65 70 75 80

Val Asp Ala Ala Ile Gln Thr Val Val Arg Gly Ala Arg Arg Tyr Ala
85 90 95

Lys Met Lys Arg Arg Arg Arg Arg Val Ala Arg Arg His Arg Arg Arg
100 105 110

Pro Gly Thr Ala Ala Gln Arg Ala Ala Ala Ala Leu Leu Asn Arg Ala
115 120 125

Arg Arg Thr Gly Arg Arg Ala Ala Met Arg Ala Ala Glu Tyr Leu Asn
130 135 140

Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro Cys Ser Val Thr
145 150 155 160

Arg Arg Leu Ala Ala Gly Ile Val Thr Val Pro Pro Arg Ser Arg Arg
165 170 175

Arg Ala Ala Ala Ala Ala Ala Ala Ala Ile Ser Ala Met Thr Gln Gly
180 185 190

Arg Arg Gly Asn Val Tyr Trp Val Arg Asp Ser Val Ser Gly Leu Arg
195 200 205

Val Pro Val Arg Thr Arg Pro Pro Arg Asn Val Arg Thr Arg Pro Pro
210 215 220

Arg Asn
225

<210> 59
<211> 6
<212> PRT
<213> Plasmodium yoelii

<400> 59

Gln Gly Pro Gly Ala Pro
1 5

<210> 60
<211> 4
<212> PRT
<213> Plasmodium falciparum

<400> 60

Asn Ala Asn Pro
1

<210> 61
<211> 21
<212> PRT
<213> Plasmodium yoelii

<400> 61

Tyr Asn Arg Asn Ile Val Asn Arg Leu Leu Gly Asp Ala Leu Asn Gly
1 5 10 15

Lys Pro Glu Glu Lys
20

<210> 62
<211> 20

<212> PRT

<213> Plasmodium falciparum

<400> 62

Glu Tyr Leu Asn Lys Ile Gln Asn Ser Leu Ser Thr Glu Trp Ser Pro

1 5 10 15

Cys Ser Val Thr

20

<210> 63

<211> 9

<212> PRT

<213> Plasmodium vivax

<400> 63

Ala Asn Gly Ala Gly Asn Gln Pro Gly

1 5

<210> 64

<211> 4

<212> PRT

<213> Plasmodium malariae

<400> 64

Asn Ala Ala Gly

1

<210> 65

<211> 4

<212> PRT

<213> Plasmodium yoelii

<400> 65

Gln Gln Pro Pro

1

<210> 66

<211> 9

<212> PRT

<213> Plasmodium yoelii

<400> 66

Ser Tyr Val Pro Ser Ala Glu Gln Ile
1 5

CLAIMS

1. A recombinant adenovirus derived from a recombinant adenovirus plasmid vector, wherein the recombinant adenovirus plasmid vector comprises a nucleotide sequence encoding:

a *Plasmodium* circumsporozoite protein gene, or antigenic portion thereof, operably linked to a heterologous promoter sequence, and

one or more modified capsid and/or core protein genes, wherein an immunogenic epitope sequence of *Plasmodium* circumsporozoite has been inserted into or replaces at least part of the one or more capsid or core protein genes; and

wherein the immunogenic epitope sequence is a B cell epitope sequence selected from (NANP)₁₂, (NANP)₁₄, (NANP)₁₆, (NANP)₁₈, (NANP)₂₀, or (NANP)₂₂.

2. The adenovirus according to claim 1, wherein the *Plasmodium* circumsporozoite protein gene further comprises a *Plasmodium falciparum* circumsporozoite protein gene.

3. The adenovirus according to claim 1, wherein the *Plasmodium* circumsporozoite protein gene further comprises a codon-optimized *Plasmodium falciparum* circumsporozoite protein gene.

4. The adenovirus according to claim 3, wherein the codon-optimized protein gene is encoded by SEQ ID NO:2.

5. The adenovirus according to any of claims 1-4, wherein the one or more modified capsid and/or core protein genes comprises a Hexon hypervariable region (HRV) sequence.

6. The adenovirus according to claim 5, wherein the HRV sequence comprises an HRV1 or HRV5 sequence and the B cell epitope sequence:

a) is inserted in the HVR1 or HVR5 sequence; or

b) replaces a portion of the HVR1 or HRV5 sequence.

7. The adenovirus according to claim 6, wherein the modified capsid protein gene is encoded by a nucleic acid sequence selected from the group consisting of, SEQ ID

NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, or SEQ ID NO:22.

8. The adenovirus according to claim 1, wherein the one or more modified capsid and/or core protein genes comprises a capsid Fiber protein gene and the B cell epitope sequence is inserted into the Fiber protein gene.

9. The adenovirus according to claim 8, wherein the modified capsid protein gene is encoded by SEQ ID NO:25.

10. The adenovirus according to claim 1, wherein the core protein gene further comprises a pVII protein gene and the CD4+ T cell epitope sequence is inserted into the pVII protein gene.

11. The adenovirus according to claim 10, wherein the modified core protein gene is encoded by SEQ ID NO:27, SEQ ID NO:28 or SEQ ID NO:29.

12. The adenovirus according to claim 10 or 11, wherein the CD4+ T cell epitope sequence is a *Plasmodium falciparum* circumsporozoite protein gene CD4+ T cell epitope sequence.

13. The adenovirus according to any one of claims 10 to 12, wherein the CD4+ T cell epitope sequence is EYLNKIQNSLSTEWSPCSVT (SEQ ID NO:62).

14. The adenovirus according to claim 1, wherein the adenovirus is produced from any one of the recombinant adenovirus plasmid vectors selected from the group consisting of an HVR1-modified adenovirus vector, a Fiber-modified adenovirus vector, an HVR1 and Fiber-modified adenovirus vector, a Fiber and pVII-modified adenovirus vector, an HVR1 and pVII-modified adenovirus vector and an HVR1, Fiber and pVII-modified adenovirus vector.

15. A recombinant adenovirus derived from a recombinant adenovirus plasmid vector, wherein the recombinant adenovirus plasmid vector comprises a nucleotide sequence encoding:

a *Plasmodium* circumsporozoite protein gene, or antigenic portion thereof, operably linked to a heterologous promoter sequence, and

one or more modified capsid and/or core protein genes, wherein an immunogenic epitope sequence of *Plasmodium* circumsporozoite has been inserted into or replaces at least part of the one or more capsid and/or core protein genes; and wherein the core protein gene comprises a pVII protein gene and a CD4+ T cell epitope sequence is inserted into the pVII protein gene.

16. The adenovirus according to claim 15 wherein the modified core protein gene is encoded by SEQ ID NO:27, SEQ ID NO:28 or SEQ ID NO:29.

17. The adenovirus according to claim 15 or claim 16, wherein the CD4+ T cell epitope sequence is a *Plasmodium falciparum* circumsporozoite protein gene CD4+ T cell epitope sequence.

18. The adenovirus according to claim 17, wherein the CD4+ T cell epitope sequence is EYLNKIQNSLSTEWSPCSVT (SEQ ID NO:62).

19. Use of a recombinant adenovirus according to any one of claims 1-18 in the manufacture of a medicament which induces a cellular and humoral response against a *Plasmodium* circumsporozoite protein for the treatment or prevention of malaria.

20. The use according to claim 19, wherein the medicament further comprises an adjuvant.

21. The use according to claim 19, wherein the medicament is prepared for administration of at least two doses of the medicament.

22. A pharmaceutical composition comprising a recombinant adenovirus according to any one of claims 1-18, wherein the recombinant adenovirus is produced from any one of the recombinant adenovirus plasmid vectors selected from the group consisting of an HVR1-modified adenovirus vector, a Fiber-modified adenovirus vector, an HVR1 and Fiber-modified adenovirus vector, a Fiber and pVII-modified adenovirus vector, an HVR1 and pVII-modified adenovirus vector and an HVR1, Fiber and pVII-modified adenovirus vector.

23. A vaccine for malaria infection comprising a recombinant adenovirus according to any one of claims 1-18, wherein the recombinant adenovirus is produced from any one of the recombinant adenovirus plasmid vectors selected from the group consisting of an HVR1-modified adenovirus vector, a Fiber-modified adenovirus vector,

an HVR1 and Fiber-modified adenovirus vector, a Fiber and pVII-modified adenovirus vector, an HVR1 and pVII-modified adenovirus vector and an HVR1, Fiber and pVII-modified adenovirus vector.

24. The vaccine for malaria infection according to claim 23, wherein the vaccine is administered to the subject intramuscularly, intradermally or subcutaneously.

25. The vaccine for malaria infection according to claim 23, wherein the vaccine is administered with an adjuvant to the subject.