and removal of sequences in the p33 regions that suppress the immunogenic potential of p19 epitopes, ("suppressing sequences") and (3) demonstrate the ability to produce recombinant subunit protein products based on the linking of discontinuous enhancing sequences from the p33 region with the p19 core region in such a manner that the products can be efficiently expressed in a cell based system. Recombinant subunit proteins produced in this manner have the potential to overcome the issues seen with previous p42 based vaccines and to consistently induce specific anti-merozoite antibodies that provide protective immunity against malaria in animal models and humans. Therefore, the overall technical problem to be solved is: the design, construction, and expression of novel recombinant subunit proteins based on sequences derived from the MSP-1 C-terminal region that result in enhanced immunogenicity and improved protective efficacy.

SUMMARY OF THE INVENTION

[019a] In one aspect, there is provided MSP-1 C-terminal recombinant subunit proteins with enhanced immunogenic properties comprising:

the p19 core region of the *Plasmodium falciparum* MSP-1 protein of the C-terminal region to which a segment of the p33 region is operably linked, wherein

said segment of the p33 region does not include the amino acid sequence LVQNFPNTIISKLIEGK and, wherein all animals immunized with said protein have an immunologic response that results in parasite growth inhibition activity greater than 50%.

[019b] In another aspect, there is provided vaccine formulations comprising MSP-1 C-terminal subunit proteins as defined herein.

[019c] In another aspect, there is provided the use of vaccine formulations comprising MSP-1 C-terminal subunit proteins as defined herein in the manufacture of a medicament for eliciting protection from malaria infection.

[019d] In another aspect, there is provided the vaccine formulations as defined herein, wherein the segment of the p33 region segment of the MSP-1 C-terminal subunit protein is selected from the group consisting of SEQ. ID. NO: 8, SEQ ID. NO: 14, SEQ. ID. NO: 16 and SEQ. ID. NO: 18.

[020] The present disclosure~~invention~~ provides recombinant subunit proteins that have enhanced immunogenic properties that make them suitable as vaccines to protect against malaria in animal models and humans. The recombinant subunit proteins are comprised of the MSP-1 C-terminal p19 core region of the protein and selected segments from the MSP-1 C-terminal p33 region. The addition of the selected p33 segments results in enhanced immunogenic properties. Specifically the enhanced immunogenic potential is in the ability to elicit consistent and protective antibody responses. These enhanced antibody responses have the potential to inhibit parasite growth *in vitro* and *in vivo* provide protection against disease caused by malaria parasites. The recombinant subunit proteins of the invention are expressed from transformed insect cells that contain integrated copies of the appropriate expression cassettes within the genome of the cells. The insect cell expression system provides high yields of recombinant subunit proteins with native-like conformation. Specifically, the recombinant subunit proteins are secreted from the transformed insect cells and represent novel forms of the malaria MSP-1 C-terminal region that are not found in nature. More specifically, the recombinant subunit proteins are novel derivatives that have been created to provide improved immunogenic potential to protect against disease caused by malaria parasites. In animal models, the antibodies that result from vaccination with the recombinant subunit proteins that have enhanced immunogenic potential are capable of inhibiting parasite growth *in vitro*.

[021] The present disclosure~~invention~~ also provides methods for utilizing the recombinant subunit proteins described as vaccines to elicit the production of antibodies capable of conferring protection against malaria in mammalian hosts.

BRIEF DESCRIPTION OF THE DRAWINGS

[022] **FIG. 1.** Amino acid sequence of MSP-1 p42 from the *P. falciparum* strain FUP (Uganda Palo Alto) of the MAD type. The p33 region is in regular type face and the p19 core region is shown in bold and italics.

[023] **FIG. 2.** Alignment of the MSP-1 p42 amino acid sequences from the three *P. falciparum* strains FUP, 3D7, and FVO. Amino acids in 3D7 and FVO that are the same as FUP strain are indicted with a + symbol, amino acids differing from of the FUP strain are shown, those in the p19 core region are in bold. Gaps in alignments are indicated by a – symbol. The p19 core region is shown in bold and italics

[024] **FIG. 3.** Alignment of the amino acid sequences from three N-terminally truncated subunits, Construct A, Construct B and Construct C relative to the FUP p42 sequence. The CT, C72, and p33-7 epitopes in the p33 sequence are indicated as bold and underlined. The p19 core region is shown in bold and italics

[025] **FIG. 4.** Alignment of the amino acid sequences from all MSP-1 C-terminal subunit protein constructs relative to the FUP MSP-1 p33 sequence.

[026] **FIG. 5.** Diagram of all MSP-1 C-terminal subunit constructs – ordered by Name

[027] **FIG. 6.** Diagram of all MSP-1 C-terminal subunit constructs – ordered by Group

[028] **FIG. 7.** ELISA antibody titers for Group 2 MSP-1 C-terminal constructs.

[029] **FIG. 8.** ELISPOT analysis of Group 1 and Group 2 MSP-1 C-terminal subunits

DETAILED DESCRIPTION OF THE INVENTION

[030] The invention provides malaria MSP-1 C-terminal recombinant subunit proteins that comprise the p19 core region and selected segments of the p33 region. These recombinant subunit proteins are produced and secreted from a stable insect cell lines that have been transformed with the appropriate expression plasmid. Immunization of animals with the recombinant subunit proteins of the invention is effective in inducing a consistent antibody response. Specifically, these antibody responses are capable of inhibiting the growth of *Plasmodium falciparum*. The combination of the selected p33 segments with the p19 core is