Expression, Purification and Efficacy Testing of Synthetic Plasmodium falciparum Apical Membrane Antigen 1 Expressed in Pichia pastoris

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Technology description

Summary

A challenge facing the biotechnology industry involves finding robust systems for the expression of large amounts of recombinant protein. Extra technological hurdles are faced when these proteins are required for therapeutic usages.
Malaria remains one of the leading causes of both morbidity and mortality in the tropical and sub-tropical world. Currently, there is no malaria vaccine. This invention relates to both of these issues.
Two recombinant forms of the malaria asexual blood stage antigen Apical Membrane Antigen 1 (AMA1) were produced in Pichia pastoris using totally defined, synthetic medias and a fermentation methodology that has been reproducibly scaled over a 10-fold range to 60L. High levels of secreted recombinant protein were obtained (300mg/L secreted protein in the supernatant, and >50mg/L final purified bulk protein), and a purification strategy developed to remove Host cell-derived lipids. Highly purified forms of both types of AMA1 produced appear to produce antibodies in vivo in rabbits that block homologous parasites from invading red blood cells in vitro . The combination of the two allelic forms made appears potent at inducing antibodies capable of blocking the invasion of many heterologous parasite strains in vitro , suggesting that the combination of these two alleles of AMA1 will provide sufficient coverage from the diverse field populations of parasites. One of the two AMA1's, based on the FVO allelic variant of AMA1, was emulsified with complete and incomplete Freund's adjuvant.
Vaccination of highly susceptible Aotus vociferans monkeys with this formulation conferred significant protection from a subsequent lethal challenge with the virulent FVO Plasmodium falciparum parasite. Five of eight animals whose primary immune response was directed against AMA1 were completely protected. These two recombinant forms of AMA1 may be an effective malaria vaccine. The production and purification methodologies may be suitable to other therapeutic proteins where large-scale, inexpensive production methodologies are required.

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