

Publication

Antigenicity and immunogenicity of a novel chimeric peptide antigen based on the *P. vivax* circumsporozoite protein

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 2184865

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Year 2013

Title Antigenicity and immunogenicity of a novel chimeric peptide antigen based on the *P. vivax* circumsporozoite protein

Journal Vaccine : the official journal of the International Society for Vaccines

Volume 31

Number 42

Pages / Article-Number 4923-30

Keywords Malaria, Plasmodium vivax, Vaccine, CS protein, Long synthetic peptide, Mice

Plasmodium vivax circumsporozoite (PvCS) protein is a major sporozoite surface antigen involved in parasite invasion of hepatocytes and is currently being considered as vaccine candidate. PvCS contains a dimorphic central repetitive fragment flanked by conserved regions that contain functional domains.; We have developed a chimeric 137-mer synthetic polypeptide (PvCS-NRC) that includes the conserved region I and region II-plus and the two natural repeat variants known as VK210 and VK247. The antigenicity of PvCS-NRC was tested using human sera from PNG and Colombia endemic areas and its immunogenicity was confirmed in mice with different genetic backgrounds, the polypeptide formulated either in Alum or GLA-SE adjuvants was assessed in inbred C3H, CB6F1 and outbred ICR mice, whereas a formulation in Montanide ISA51 was tested in C3H mice.; Antigenicity studies indicated that the chimeric peptide is recognized by a high proportion (60-70%) of residents of malaria-endemic areas. Peptides formulated with either GLA-SE or Montanide ISA51 adjuvants induced stronger antibody responses as compared with the Alum formulation. Sera from immunized mice as well as antigen-specific affinity purified human IgG antibodies reacted with sporozoite preparations in immunofluorescence and Western blot assays, and displayed strong in vitro inhibition of sporozoite invasion (ISI) into hepatoma cells.; The polypeptide was recognized at high prevalence when tested against naturally induced human antibodies and was able to induce significant immunogenicity in mice. Additionally, specific antibodies were able to recognize sporozoites and were able to block sporozoite invasion in vitro. Further evaluation of this chimeric protein construct in preclinical phase e.g. in Aotus monkeys in order to assess the humoral and cellular immune responses as well as protective efficacy against parasite challenge of the vaccine candidate must be conducted.

Publisher Elsevier ; [Online:] Amsterdam

ISSN/ISBN 0264-410X

edoc-URL <http://edoc.unibas.ch/dok/A6183911>

Full Text on edoc Available;

Digital Object Identifier DOI 10.1016/j.vaccine.2013.05.082

PubMed ID <http://www.ncbi.nlm.nih.gov/pubmed/23954378>

ISI-Number WOS:000326772100038

Document type (ISI) Journal Article