Review of: "Investigation of liposomal self-adjuvanting peptide epitopes derived from conserved blood-stage Plasmodium antigens"

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This is an interesting paper related to development of rational designed synthetic vaccine candidates for malaria. The relevance of this work lies on the fact that up to date a fully protective vaccine against this deadly disease does not exist. Methodology can be separated into three items: 1- selection and boc-chemistry strategy applied to solid phase peptide synthesis (SPPS) of some peptide constructs containing three Plasmodium falciparum sequences, amongst a central (merozoite surface protein-1) MSP-1 epitope, a well-known N-terminal MSP-1 sequence, as well as a third epitope derived from the (ring-infected erythrocyte surface antigen) RESA antigen, all derived from P. falciparum merozoite blood -stages strategically located into different presenting systems amongst one forming part of a large consecutive three epitope linear arrangement so-named multi epitope P1 and three polyleucine -epitope independent constructs named pL1, pL2 and pL3 respectively useful also for producing mannose- conjugates and liposomes. All molecules were produced on standard yields between 40% to 51%.

2- Physical and chemical characterization of all molecules by mass spectrometry, circular dichroism and particle size analysis and 3- animal model (female BALB/c mice) for antigenicity and immunogenicity studies after being s.c. immunized with adjuvant assisted formulations (Freund´s and alum) and others administered as liposome conjugates. A subsequent challenged by intravenous injection of an inoculum of 1 x 10^5 P. yoelii 17X infected erythrocytes was performed to all immunize animal groups.

Despite an apparently well-conceived molecular design some contradictions can be detected. First, a homology analysis (for example multiple sequences alignment on remote servers) for sequences derived from MSP-1 and RESA antigens from both origins P. falciparum and P. yoelii 17X is lacking in the rationale. Therefore, one could not expect any protective efficacy data after performing a heterologous challenging of vaccinated mice due to those epitope sequences low homology and similarity percentages. Secondly, no clear explanations regarding criteria about how each epitope was chosen for this study are neither providing nor argued. Perhaps a design considering only MSP-1 and RESA from P. yoelii 17X sequences for all constructs and their immunogenicity tests by a homologous challenging with an inoculum of P. yoelii 17X would be sufficient to face an interesting hypothesis. A later step consisting in a P. falciparum model to be tested in a humanized environment would lead to more reliably conclusions useful for a malaria vaccine candidate development.

Third, circular dichroism and 3D-structure prediction experiments do not represent an immuno-active conformation for a given epitope however these are valuable tools towards potential bio-active molecular conformations.