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Et al.

Human monoclonal antibodies to *Plasmodium falciparum* circumsporozoite protein for transient passive protection of malaria travelers to endemic areas

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Plasmodium falciparum, is a protozoa that causes over 214 million cases of Malaria worldwide and the World Health Organization reported an estimated 438,000 deaths attributed to malaria in 2015. Current prevention strategies have reduced malaria cases but they are either costly, have poor efficacy or resistance has begun to develop. There is a global need for an effective pre-exposure prophylaxis treatment.

The leading Malaria vaccine candidate is RTS,S which contains a monovalent *Plasmodium falciparum* circumsporozoite protein (CSP). The goal of this vaccine is to induce anti-CSP antibodies that would block sporozoite invasion of hepatocytes and thereby hinder parasite development into a blood-stage infection that causes malaria morbidity and mortality. Antibodies isolated from individuals who have received the RTS,S vaccine have been shown to prevent infection of hepatocytes, suggesting that CSP antibodies could be used prophylactically. However, phase III trial results of the vaccine have shown underwhelming efficacy in children.

Growing resistance to transient protection strategies for travelers and low efficacy in vaccine trials suggest there is a need for a new treatment strategy. The generation of CSP specific human monoclonal antibodies (mAbs) would be useful as prevention especially for individuals that are temporarily exposed to Malaria in endemic regions such as travelers or military personnel.

Isolation and production of therapeutic mAbs traditionally utilizes a handful of techniques including antibody engineering, phage display or hybridoma generation from transgenic mice. We have sorted antigen-specific memory B-cells from the peripheral blood of children naturally infected with malaria to isolate CSP-specific memory B-cells. These cells were individually sorted and PCR was performed to amplify antibody variable regions of the B-cell's antibody mRNA. Samples that produced heavy and light chain antibody sequence were cloned and transiently expressed. We plan to characterize these mAbs for binding and neutralization of CSP to identify functional therapeutic mAbs.

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