“A human monoclonal antibody prevents malaria infection by targeting a new site of vulnerability on the parasite”

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Development of a highly effective vaccine or antibodies for the prevention and ultimately elimination of malaria is urgently needed. Here we report the isolation of a number of human monoclonal antibodies directed against the Plasmodium falciparum (Pf) circumsporozoite protein (PfCSP) from several subjects immunized with an attenuated Pf whole-sporozoite (SPZ) vaccine (Sanaria PfSPZ Vaccine). Passive transfer of one of these antibodies conferred high-level, sterile protection in two different mouse models of malaria infection. The antibody binds to a unique ‘junctional’ epitope positioned between the N terminus and the central repeat domain of PfCSP. Moreover, it prevented proteolytic cleavage of PfCSP on PfSPZ. Analysis of crystal structures of Fab in complex with the junctional epitope determined the molecular interactions of binding and revealed the epitope’s conformational flexibility. This antibody is highly effective for passive prevention of malaria, which has potential application for use in travelers, military personnel and elimination campaigns and identifies a new and conserved site of vulnerability on PfCSP for next-generation rational vaccine design.