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Structure of human IgM in complex with the malaria protein PfEMP1

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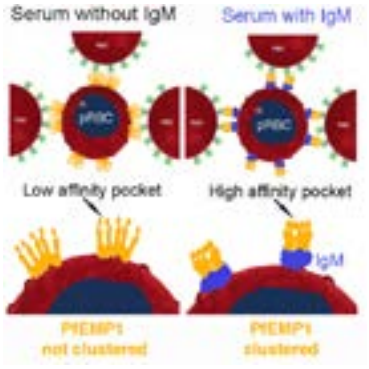
Children under the age of 5 years have huge malaria burden in endemic area. Increased death in complicated malaria is due to increased sequestration to tissues and agglutination with erythrocytes and cells of our immune system. It is known that parasites that bind to non-immune IgM cause severe malaria due to increased rosetting (agglutination). Using biochemical, parasitology and electron tomography techniques we have identified that PfEMP1, a crescent shaped molecule interacts with human IgM through its bulky C-terminus (membrane proximal) in 1:1 and 2:1 ratio. While the bulky C terminus limits the stoichiometry of this interaction yet clusters parasite molecule PfEMP1 (*P. falciparum* Erythrocyte Membrane Protein-1) to mediate robust host parasite interaction. Structural analysis revealed that PfEMP1 could also preclude the activation of complement mediated lysis of parasite despite IgM deposition on parasitized RBC surface. We also found that IgM although not a rosetting factor enhances this interaction by increasing the strength of this interaction by at least four-fold. In terms of physiological relevance, we need to understand that new born babies have elevated level of IgM and could be more prone to agglutination and hence more deaths due to malaria.



Biography

Ulf Skoglund received his PhD in 1969 at Stockholm University, Sweden. He was a Professor during the years 1996 – 2009 at Karolinska Institute, Stockholm, Sweden. Since 2010, he is a Professor in Structural Cellular Biology at Okinawa Institute of Science and Technology, Okinawa, Japan. He has developed electron-tomographic technologies allowing for images of proteins to be generated so that e.g. X-ray structures can be fitted into the 3D densities. This technique is termed COMET (Constrained Maximum Entropy Tomography). His unit has also developed a large-scale dynamics method that allows for quantitative calculations of molecular movements in solution. Current developments concern the mathematics and improvements of the basic 3D reconstruction principles, as well as work on reconfigurable and high-performance computing. His unit has also been actively pursuing several cell biology projects.

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