Macromolecular dynamics of malaria parasite adhesion

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Survival of the human malaria parasite *Plasmodium falciparum* within the host relies on its ability to drastically alter its red blood cell (RBC) host. Parasite derived modifications of the RBC membrane skeleton alter the deformability properties of the RBC. These modifications underpin cytoadherence based virulence and severe disease states such as cerebral and placental malaria. This adhesion is driven by the assembly of a parasite derived structure at the RBC membrane skeleton called the knob which acts as a scaffold for the presentation of the major virulence antigen PfEMP1 at the RBC surface. The knob is composed of the knob associated his-rich protein (KAHRP) and together with PfEMP1 they form the virulence complex. In this work, we have defined the protein trafficking networks and the structural remodelling events that underpin parasite virulence. Using a mass spec based approach, we identify the protein composition of important PfEMP1 trafficking structures called Maurer's clefts. We GFP tagged 9 of the most abundant proteins and using an immunoprecipitation and mass spectrometry approach we build a comprehensive protein interaction network of proteins at the Maurer's clefts, which includes the virulence protein PfEMP1. We have developed a correlative light and electron microscopy technique which combines dSTORM super resolution microscopy and scanning electron microscopy, to visualise host cell remodelling events. Using this technique, we have tracked the trafficking of KAHRP to the RBC membrane skeleton and its sequential assembly into donut shaped structures which insert into the membrane forming the knobs. Further to this we also track the delivery of PfEMP1 to the virulence complex.