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Complex of malaria parasites and human proteins drive formation of cytoadherent assemblies at the surface of infected red blood cells

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Human red blood cells infected by the malaria parasite *Plasmodium falciparum* (iRBC) form dome-shaped ~120 nm-diameter protrusions on their surface, known as 'knobs'. Knobs provide essential presentation platforms for the parasite cytoadherence receptor family P*f*EMP1, which binds ligands on endothelial cells of the blood vessel wall thereby immobilizing iRBC in the microvasculature. The resulting obstruction of blood vessels and disruption of normal circulation causes inflammation and tissue damage that can lead to coma and death. iRBC cytoadherence constitutes the primary mechanism driving morbidity and mortality in *P. falciparum* infections, which account for over 90% of all malaria-related deaths. Despite their importance in malaria pathology the molecular mechanisms underpinning knob formation remain poorly understood. Here, I review recent progress in characterizing knob complexes formed between parasite and parasite-host proteins. Extensive flexibility is common among parasite knob components, which necessitated an integrative approach to resolve these complexes. I will focus on the development of novel *in silico* docking tools suitable for evaluating interactions between folded components and highly charged, very long and flexible protein segments. Our work offers the first glimpse of a molecular model for knobs.

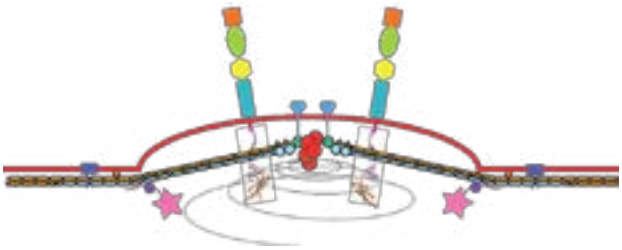

Figure1: *Model of a cytoadherent assembly ('knob') on the surface of P. falciparum-infected red blood cell, depicting recently characterized protein complexes that will be discussed here.*

Biography

John Vakonakis has completed his PhD in Biochemistry at Texas A&M University, where he pioneered the structural analysis of bacterial circadian clock proteins. His Postdoctoral work at the University of Oxford focused on the structural mechanisms underpinning cell adhesion and assembly of the extracellular matrix in animals. He did breakthrough work on the molecular architecture of the centriole organelle during a second Postdoc at the Swiss Light Source, prior to starting his own lab in Oxford Biochemistry. He has been a Marie Currie Fellow, Junior Research Fellow at Trinity College, Oxford, and a Wellcome Trust Research Fellow. He is now Associate Professor in Structural Biology and Biophysics at the University of Oxford, and Fellow in Biochemistry at Lincoln College. Over the last six years his research aims to understand how large molecular machines form in cells, such as the cytoadherence assemblies created upon *P. falciparum*-infection of human erythrocytes.

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