Title : Structural and functional analysis of VAR2CSA adhesive properties in the context of pregnancy associated malaria

Project description:

Plasmodium falciparum is the main causative agent of malaria still causing around 400 000 deaths each year. The key feature of *P. falciparum* pathogenesis is the way in which it modifies the surface of the erythrocytes so that parasites can adhere to host cells.

Adhesion of *P. falciparum*-infected erythrocytes (PEs) to chondroitin-4-sulfate (CSA) present in the placental intervillous vascular spaces has been linked to the severe disease outcome of **placental malaria** (PM). After multiple pregnancies, women acquire protective antibodies that block CSA-binding and cross-react with geographically diverse placental isolates. Evidence strongly suggests that VAR2CSA, a member of the variant *P. falciparum* Erythrocyte Membrane protein 1 (PfEMP1) family, has an important role in PM and immunity. Although VAR2CSA is the main candidate for a pregnancy malaria vaccine, experimental evidence suggests that antigenic polymorphism, the lack of structural information and gaps in our understanding of placental sequestration may pose a challenge for vaccine and therapeutic development. The overall objective of this project is **to determine the high-resolution structure of the extracellular region of VAR2CSA** and its individual domains in order to **characterize the high affinity CSA-binding site** as well as conserved epitopes that can be used for vaccine and therapeutic strategies.

This ambitious structure-function study will unravel details on the molecular interactions involved in placental sequestration. This knowledge will be very helpful in the design of novel CSA-binding PfEMP1 antigens capable of inducing broad and potent neutralizing antibodies to a wide variety of strains. This will be a crucial step towards the **structure-based design of novel vaccine and therapeutic strategies** to provide protection against negative outcomes of PAM.

Supervisor:

Zaineb FOURATI KAMMOUN : zaineb.kammoun@parisdescartes.fr
UMR 8038, laboratoire CiTCOM. Directeur : Nicolas LEULLIOT. Université de Paris.

Références:

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