
Contribution ID : **253** Type : **Oral**

# Structural basis of Plasmodium vivax specificity towards reticulocytes

*Friday, 25 November 2016 14:30 (15)*

Understanding the process of invasion is essential for developing strategies to stop blood stage infection. An important feature of *Plasmodium* invasion is the host cell selectivity that the different species have for cells of the erythroid lineage. Indeed, *Plasmodium vivax* preferentially invades reticulocytes which are immature red blood cells. Several members of *P. vivax* Reticulocyte Binding Protein (PvRBP) family have been shown to bind specifically to reticulocytes. One of the major unanswered questions in *P. vivax* biology is the identity of the reticulocyte specific receptor required for invasion.

We report the first crystal structures of the erythrocyte-binding domain from two members of the PvRBP family, PvRBP2a and PvRBP2b, which were solved at 2.12 and 1.71 angstrom resolution respectively. Both structures share a strikingly similar fold with PfRh5, an essential invasion ligand in *P. falciparum* and a leading vaccine candidate for blood stage infection.

While PvRBP2a binds both mature and immature erythrocytes, PvRBP2b exhibits strong specificity towards reticulocytes. We have identified the reticulocyte-specific receptor for PvRBP2b. We characterized the ligand-receptor complex in solution using small angle X-ray scattering and analytical ultracentrifugation. We generated monoclonal antibodies toward PvRBP2b that inhibit the interaction with its receptor and solved crystal structure of reticulocyte-binding domain in complex with three different Fab fragments.

This study provides the fundamental characterization of the structural features that govern *P. vivax* red blood cell binding as a framework for generating new therapeutics and answers the long standing question of the reticulocyte-specific receptor for *P. vivax* invasion.

## Keywords or phrases (comma separated)

crystal structure, SAXS, AUC, Plasmodium vivax, malaria, invasion, receptor, antibody

## Are you a student?

No

## Do you wish to take part in</br>the Student Poster Slam?

No

## Are you an ECR? (<5 yrs</br>since PhD/Masters)

No

## What is your gender?

Male

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**Session Classification :** Concurrent Session 4: Structural Biology II - Sponosred by DECTRIS

**Track Classification :** Structural Biology