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Structural basis of Plasmodium vivax specificity towards reticulocytes

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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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