Humanized mice models and host-human Plasmodium interactions - Plasmodium Infection and Transmission Biology Unit
INSERM U1347 & Department of Parasites and Insect Vectors

Post-doctoral position

A 36-month post-doctoral position starting on November 1st 2025 and funded by the French National Research Agency (ANR) is available in the Plasmodium Infection and Transmission Biology Unit at Institut Pasteur in Paris (Humanized mice models and host-human Plasmodium interactions: https://research.pasteur.fr/en/team/group-sylvie-garcia/

Project:
Plasmodium vivax infection, the main cause of malaria in Latin America and Asia, affects 14.3 million people annually, with 3.3 billion people at risk worldwide. No effective vaccine is available. *P. vivax* entry into red blood cells (RBCs) requires sequential ligand- receptor interactions and parasites can only invade immature RBCs (reticulocytes) expressing high levels of CD71, which account for up to 1.5% of circulating RBCs. CD71 is the receptor for PvRBP2b, a member of the *P. vivax* reticulocyte-binding protein (PvRBP) family, while CD98 heavy chain (CD98hc) is a reticulocyte-specific receptor for another PvRBP family member, PvRBP2a. Encoded by the SLC3A2 gene, CD98hc is part of a multifunctional complex involved in amino acid transport, cell adhesion, immune activation, and murine erythropoiesis. We hypothesize that CD98hc might be a key modulator of vivax malaria risk. Naturally occurring polymorphisms at the SLC3A2 locus that affect CD98hc expression or function might inhibit blood-stage *P. vivax* infection (1) by accelerating reticulocyte maturation, reducing CD71 expression and therefore inhibiting entry via the CD71-PvRBP2b pathway and (2) by decreasing PvRBP2a binding affinity to its host-cell receptor, therefore reducing entry via the alternative CD98hc- PvRBP2a pathway.
In collaboration with the team of Marcelo U. Ferreira in São Paulo University, Brazil, we will explore in vivo the dual role of CD98hc in human erythropoiesis and *P. vivax* infection. We will examine (1) the role of CD98 in human erythropoiesis and *P. vivax* infection, (2) whether genetic diversity at the SLC3A2 locus and levels of anti-PvRBP2a antibodies in Amazonians are associated with their vivax malaria risk, and (3) the effects of CD98hc-targeted interventions in vivo on erythropoiesis and *P. vivax* infection. In our team, we will specifically address questions 1 et 3, exploiting unique humanized mice, that support both human erythropoiesis and blood-stage *P. vivax* infection, with a focus on the bone marrow (primary erythropoietic organ and extravascular reservoir of *P. vivax*). This collaborative project will generate new insights into *P. vivax* interactions with a key host-cell receptor, opening new opportunities to devise new therapeutics using anti-CD98hc strategies and anti-PvRBP2a-based vaccines.

Experimental approaches: CRISPR-cas9 and lentiviral genetic engineering, experimental infections in mice, sc-RNA sequencing, Flowcytometry and FlowImaging.

Requirements: Candidates with a recent PhD in Biological Science, especially in Parasitology or Cell Biology, are encouraged to postulate. Experience in molecular biology is required. Highly motivated and autonomous candidates are wanted. Skills in mouse models or in vivo imaging or Flowcytometry would be appreciated.

Application: Applicants should send a CV, a bibliography, a motivation letter and the names of two references in a single pdf file to Dr. Sylvie Garcia (sylvie.garcia@pasteur.fr) before November 2025.