PhD student position for a biostatistician (genomic and transcriptomic in malaria) at Institut Pasteur in Paris (2019- 2023)

Our research

Erythrocyte invasion is a complex process involving multiple interactions between *Plasmodium* merozoites and host erythrocytes. Unlike *P. falciparum*, which can use multiple erythrocyte receptors for invasion and has merozoite proteins with overlapping and redundant receptor-binding functions, invasion of human erythrocytes by *P. vivax* merozoites primarily relies on the interaction between the *P. vivax* Duffy Binding Protein (PvDBP) and the erythrocyte Duffy antigen receptor for chemokines (DARC). Consequently, PvDBP is considered a promising candidate for a *P. vivax* malaria vaccine.

However, recently, a growing body of studies (including ours), have reported PCR-positive vivax malaria cases in Duffy-negative individuals around the world, specifically across Africa and South America. These novel observations highlight the emerging issue of *P. vivax* infection in Duffy-negative populations, which questions the essential role of the PvDBP-DARC interaction and raises the possibility of alternative invasion mechanism(s) with implications for the design of blood-stage vaccines for *P. vivax* malaria.

The VIPeRs project, supported by ANR, aims **to identify *P. vivax* ligands involved in host cell invasion and understand how *P. vivax* has gained the capacity to infect reticulocytes from Duffy-negative individuals.**

Our strategy is based on a 2-step approach by taking full advantage of next-generation sequencing and functional biological analysis (including *in vitro* invasion assays and infection in humanized mice) and by availing our access to *P. vivax* isolates from both Duffy-negative and Duffy-positive vivax malaria patients in Madagascar. This strategy should overcome the main weakness of previous investigations by exploring and characterizing the full repertoire of parasite ligands involved in invasion of human reticulocytes in Malagasy malaria endemic settings where two human populations with distinct Duffy blood group phenotypes (Duffy-negative and Duffy-positive) are frequently exposed to *P. vivax*.

The PhD student will be strongly involved in the first part of the project. Our objective is to explore the natural variation of the reticulocyte invasion protein repertoire. To this end, we will compare the characteristics of the genes/alleles (single nucleotide polymorphisms (SNPs) and copy number variations (CNVs)) encoding proteins involved in invasion pathways in P. vivax isolates collected from Duffy-negative and Duffy-positive patients. We will search for enrichment of specific traits in genes encoding invasion-related proteins in P. vivax strains isolated from Duffy-negative reticuloctyes. A special focus will be dedicated to PvDBP, PvEBP and PvRBPs genes. Any novel genes identified, not belonging to PvEBP or PvRBP families, will also be studied.

The IP Paris provides an optimal environment for the proposed type of research, including the skills for NGS sequencing platforms and bioinformatics and statistical analysis support (https://research.pasteur.fr/en/center/c3bi/)

Your skills

- M2 in bioinformatics, or in molecular biology with bioinformatics skills
- Ability to work in a team and on own initiative

- Excellent leadership and communication skills in English
- Have an analytical approach to problem solving.

- Other appreciate skills are: Knowledge on malaria biology and population genetics, experience in molecular biology and in cells culture, willing to share its expertise and supervise students

Who we are

The project will be co-ordinated by Didier MENARD (https://research.pasteur.fr/fr/member/didier-menard/). Didier MENARD is a malariologist with a long-standing field experience through his different positions in the Institut Pasteur International Network, in Africa (Central African Republic and Madagascar) and in Southeast Asia (Cambodia). He has been one of the pioneers to study epidemiological associations between the human host and susceptibility to *P. vivax* malaria and discovered that *P. vivax* in Madagascar can cause blood stage infection and clinical disease in Duffy-negative individuals. He also used comparative genomic studies of P. vivax field isolates to reveal duplication of PvDBP in Malagasy P. vivax strains and identify a novel gene encoding a homolog of PvDBP referred to as PvEBP. He is currently based at IP Paris and leads the 'Malaria Genetics and Resistance Group' hosted by the 'Biology of Host-Parasite Interactions Unit' (Head: Artur Scherf).

This project brings other groups working on parasite biology (Chetan Chitnis) and humanized mouse model (S. Garcia) along with malaria experts located in vivax malaria endemic area (I. Vigan-Womas at IP Madagascar).

Contact

Interested in applying? Send an email to dmenard@pasteur.fr