UMR 5244 Université de Montpellier-CNRS-IFREMER- Université de Perpignan via Domitia
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DESCRIPTIF ANGLAIS

Context

This subject of these is funded by the CNRS and is part of the ANR project (**ANR-22-CPJ1-0056-01** - Tropical diseases of today, European diseases of tomorrow: a systems biology approach to understand, predict and control their emergence).

Project Title

Unveiling the Dark Secrets of Roommate Parasites: A Study on the Coinfection of Plasmodium and Schistosoma in Murine Models at a Biological and Molecular Level

Encadrants

Ronaldo DE CARVALHO AUGUSTO (CPJ, UPVD), encadrante principale (50%)
Jérôme BOISSIER (PU, UPVD), directeur de thèse (50%)

Contact

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Laboratory

UMR 5244 IHPE (Host-Pathogen-Environment Interaction), Perpignan http://ihpe.univ-perp.fr/

Doctoral School attached

ED 305 Energy and Environment, Perpignan
https://www.univ-perp.fr/recherche/doctorat-et-hdr/ecole-doctorale-energie-et-environnement-ed-305

Application

Online submission before November 01, 2023

Starting period

From 01 December to 01 February

Keywords

Malaria, Schistosomiasis, coinfection, epigenetic, immunopathology, drug development

Skills/qualifications:

- Holder of a master's degree in molecular biology, ecology/evolution, parasitology

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- Successful experience in the application of molecular biology techniques
- Comprehensive understanding of the ethical considerations with laboratory animal research and proficiency in the proper handling techniques, restraint methods, and observation of mice
- Experience or good knowledge of molecular and bioinformatics approaches (qPCR, ChIP-seq, RNA-seq, etc.) or a strong desire and ability to be trained
- Rigor, dynamism, diligence, and communication skills
- Level of English allowing you to read articles, to communicate orally and in writing on scientific aspects

Abstract

Background

Humans and other mammal populations frequently experience coinfections with a variety of parasites, leading to significant health risks across different systems (Cox 2001; Fenton 2013). Malaria and schistosomiasis are two major parasitic diseases that pose significant health risks to human populations, affecting over 500 million people worldwide, mainly in developing countries, often co-infecting the same individuals (Mazigo et al. 2010; McDowell et al. 2022). Coinfections investigations have been a topic of interest as geographic ranges of *Plasmodium* sp. and *Schistosoma* sp. overlap in tropical regions in several countries in South America and Africa, with estimates suggesting a coinfection rate of over 30% among children in Sub-Saharan Africa (Degarege et al. 2016). Current research on *Schistosoma-Plasmodium* coinfection has often produced contrasting results with some reports contending that *Schistosoma* infection can increase susceptibility to *Plasmodium* (Florey et al. 2012), whilst others document a protective effect on *Plasmodium* incidence (Doumbo et al. 2014). Differences in study design and the genetic background of parasite and host populations presumably contribute to these conflicting results. Although the immunopathological aspects of coinfections have been an object of previous studies, their possible impacts on parasite evolution and development are still neglected. In this project thesis, we propose to study (i) the immunopathological impacts of *Schistosoma-Plasmodium* coinfection in a murine model, (ii) the impact of coinfection on each parasite evolutionary development and their compatibility with subsequent hosts, (iii) the effect of new molecules against both parasites in an unprecedented coinfection approach.

Theme / Domain / Context

Parasitology, Ecology, Evolution

In this theses project, we aim to investigate the interplay between *P. yoelii* and *S. mansoni* in a murine model using cutting-edge biological and molecular approaches to advance knowledge into the underlying mechanisms of interaction and its potential implications for parasites' virulence and transmission. Schistosomes and Plasmodium are excellent experimental models to investigate coinfection since both systems offer stand-of-art molecular tools to be genetically manipulated allowing to explore parasite-parasite interaction from functional genomic to epidemiological hypothesis. By modifying the host's internal environment (immune system and metabolism) in a coinfection approach, we deem creating a complex and dynamic environment where each other pathogen must compete with coinfecting organisms while evading the host's defense mechanisms, making the understanding of these intricate interactions crucial in real-world situations. The present study will generate innovative data on the immunopathology of the murine host and on the possible long-term effects on the evolutionary dynamics of each parasite. For this, aspects of coinfection on parasite virulence, compatibility, and fitness will be investigated in a multiscale approach.

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Objectives

The primary objective of this project is to comprehensively investigate the intricate interplay between *P. yoelii* and *S. mansoni* in a murine model through advanced biological and molecular methodologies. Specific objectives include:

1. Characterizing Coinfection Effects: We will employ a murine model to study the impact of co-infection with *S. mansoni* and *P. yoelii* on both parasites. Through rigorous parasitological and functional genomic analyses, we will gain insights into the development and behavior of the two parasite populations in the presence of each other.
2. Evaluating Pathological and Immunological Impacts: The thesis will delve into the pathological and immunological consequences of coinfection in the murine model. By closely examining the host's immune responses and metabolic alterations, we aim to understand how the coinfecting organisms compete and evade host defense mechanisms in a complex and dynamic environment.
3. Insights into Evolutionary Dynamics: By investigating co-infection effects on parasite virulence, compatibility, and fitness, we hope to shed light on the long-term evolutionary dynamics of both *P. yoelii* and *S. mansoni*. This information may have implications for understanding the evolution and adaptation of these parasites in real-world scenarios.
4. Contribution to Drug Combination Approaches: As a part of our research, we will explore potential drug combination approaches for the treatment of co-infected mice. This investigation may contribute to the development of effective treatment strategies targeting multiple parasitic infections.

Methodology

- Genome-wide sequencing and diversity analysis of both *P. yoelii* and *S. mansoni;*
- Parasitological approaches to control and manipulate both parasites in acute and chronic infection scenarios in a murine model
- Epigenetics (ChIP-seq, ATAC-seq, and ChIPmentation)
- Transcriptomics (long-read RNA-seq)
- Histology
- Immunoparasitology (Flow cytometry, ELISA, and Bone Marrow-derived Macrophage development)
- Drug Combination Approaches

Expected outcomes

The expected outcomes of this study are to gain insights into the interplay between *Plasmodium* and *Schistosoma* in coinfected individuals and the possible consequences for both parasites' development. The study will contribute to our understanding of the molecular mechanisms behind the interaction between the two parasites and may help to identify potential targets for drug development. Additionally, the study may have implications for the design of control strategies for malaria and schistosomiasis in areas where these diseases are re-emerging due to climate change.

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