MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2024

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

Global Health and Tropical Medicine (GHTM)/Instituto de Higiene e Medicina Tropical

RESEARCH GROUP AND URL

Vector-borne diseases and pathogens, GHTM-IHMT
https://ghtm.ihmt.unl.pt/research/research-groups/vector-borne-diseases-pathogens-vbd/

Malaria@GHTM (https://ghtm.ihmt.unl.pt/)

SUPERVISOR (NAME AND E-MAIL)

Pedro Cravo (pcravo@ihmt.unl.pt)

SHORT CV OF THE SUPERVISOR

Pedro Cravo (PC) earned a Bachelor's degree in Biotechnological Engineering, a Master's degree in Molecular and Biochemical Parasitology, and a Ph.D. in Genetics from the University of Edinburgh (UK), completed in 2001. PC has dedicated his career mainly to studying the molecular mechanisms of resistance to antimalarial drugs, using classical genetic tools combined with new genomic and bioinformatics concepts and technologies and to the discovery of new drugs through computational strategies. Currently, he is an Assistant Professor at the Institute of Hygiene and Tropical Medicine, at Universidade Nova de Lisboa (IHMT-NOVA), Portugal, where he continues researching into the mechanisms of resistance to antimalarial drugs and other infectious diseases of mostly tropical origin. At IHMT, he is a member of the Scientific Board of the Research Center "Global Health and Tropical Medicine" (GHTM), where he coordinates the cross-cutting issue "Antimicrobial Resistance and Drug Discovery". Within the scope of IHMT, he also coordinates the PT-OPENSCREEN infrastructure and the NOVA Green Labs initiative. PC has authored 70 publications in peer-reviewed journals, with more than 3000 citations and an holds an h-index of 33.

5 SELECTED PUBLICATIONS

- Cassiano, Gustavo Capatti; Martinelli, Axel; Mottin, Melina; Neves, Bruno Junior; Andrade, Carolina Horta; Ferreira, Pedro Eduardo; Cravo, Pedro. "Whole genome sequencing identifies novel mutations in malaria parasites resistant to artesunate (ATN) and to ATN + mefloquine combination". Frontiers in Cellular and Infection Microbiology 14 (2024): http://dx.doi.org/10.3389/fcimb.2024.1353057.
- Gonçalves, Adriana F.; Lima-Pinheiro, Ana; Teixeira, Miguel; Cassiano, Gustavo Capatti; Cravo, Pedro; Ferreira, Pedro E. "Mutation in the 26S proteasome regulatory subunit rpn2 gene in Plasmodium falciparum confers resistance to artemisinin". Frontiers in Cellular and Infection Microbiology 14 (2024): http://dx.doi.org/10.3389/fcimb.2024.1342856.
- Pedro Cravo. "On the contribution of the rodent model Plasmodium chabaudi for understanding the genetics of drug resistance in malaria". Parasitology International 91 (2022): https://novaresearch.unl.pt/en/publications/8e37eab0-1d13-49de-8274-8c5107aee37d
- Letícia Tiburcio Ferreira; Juliana Rodrigues; Gustavo Capatti Cassiano; Tatyana Almeida Tavella; Kaira Cristina Peralis Tomaz; Djane Clarys Baia-Da-Silva; Macejane Ferreira Souza; et al. "Computational chemogenomics drug repositioning strategy enables the discovery of epirubicin as a new repurposed hit for Plasmodium falciparum and P. vivax". Antimicrobial Agents and Chemotherapy Vol. 64 n.º 9 (2020): e02041-e02058. https://novaresearch.unl.pt/en/publications/bd0d6aa8-16ae-4e0e-96cb-e77348291f84
- Andrade, Carolina Horta; Neves, Bruno Junior; Melo-Filho, Cleber Camilo; Rodrigues, Juliana; Silva, Diego Cabral; Braga, Rodolpho Campos; Cravo, Pedro Vitor Lemos. "In Silico Chemogenomics Drug Repositioning Strategies for Neglected Tropical Diseases.". Current medicinal chemistry (2018): http://gateway.webofknowledge.com/gateway/Gateway.cgi?GWVersion=2&SrcAuth=ORCID&SrcA

pp=OrcidOrg&DestLinkType=FullRecord&DestApp=MEDLINE&KeyUT=MEDLINE:29521204&KeyUID=MEDLINE:29521204

PROJECT TITLE AND SHORT DESCRIPTION

Title: “Experimental Evolution, Genomics, and Transgenesis: A Triangular Approach to Understanding Primaquine and Tafenoquine Resistance in Malaria Parasites”

Description: Primaquine phosphate and tafenoquine are the only drugs available for preventing relapse of malaria caused by *Plasmodium vivax* and *Plasmodium ovale*, based on their ability to kill latent (hypnozoite) and developing liver stages of these parasites. In addition, both drugs are also used as transmission-blocking agents for *Plasmodium falciparum* malaria, due to their ability to kill gametocytes efficiently. Protecting the long-term efficacy of these unique drugs is crucial and is highly dependent on the understanding of their mechanism of action and of potential resistance. The mail goal of this project will be to to identify the genetic mutations responsible for resistance to primaquine and tafenoquine, using the rodent malaria model *Plasmodium berghei*. To do so, we will begin by experimentally evolving resistance to primaquine and tafenoquine *in vivo* by applying continuous drug pressure over asexual stages of *P. berghei* over many generations. We will then characterize the genetic variation in the resistant mutants selected above through comparison with their wild-type progenitors, using Whole Genome Sequencing (WGS). Finally we will evaluate the contribution of each mutation for the resistance phenotype through genetic transfection experiments both in *P. berghei* and in the human malaria parasite *P. falciparum*.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF)

***Scientific Area where the project fits best** – Please select/indicate the scientific area according to the panel evaluation areas: Chemistry (CHE) • Social Sciences and Humanities (SOC) • Economic Sciences (ECO) • Information Science and Engineering (ENG) • Environment and Geosciences (ENV) • Life Sciences (LIF) • Mathematics (MAT) • Physics (PHY)