Targeting *Plasmodium* oocyst rupture in mosquito to block malaria transmission

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Plasmodium parasites, the protozoa responsible of malaria disease in humans, are transmitted by *Anopheles* mosquitoes causing an estimated **241 million malaria cases** and **627 000 malaria deaths** worldwide in 2020 (WHO) mostly children below 5. *Plasmodium falciparum* is responsible for the majority of malaria deaths globally and is the most prevalent species in sub-Saharan Africa. The difficulty to control the mosquito populations, the lack of effective vaccine and the development of parasites drug resistance highlight the urgent need for new interventions that would both alleviate the symptoms and cure the disease and also block malaria transmission.

The long-term goal of research in the laboratory is to obtain knowledge of basic molecular processes that can be exploited for novel intervention strategies and identification of new targets for drug development. Specifically, the laboratory focuses on the mosquito stages of the parasite with the aim to develop transmission blocking approaches, that will target the parasite in the mosquito. The oocyst, localized at the mosquito midgut, is a cell within which a replicative phase takes place, resulting in formation of thousands of sporozoites, the infectious form of the parasite, during roughly 14 days. The oocyst is surrounded by a structure called capsule (or cyst wall) whose composition remains largely unknown. For the sporozoites to transfer to the salivary gland of the mosquito from which they will be injected into a new host, the oocyst must rupture breaching the capsule and releasing the sporozoites. **We investigate factors involved in oocyst rupture, a process being essential for transmission and thus a putative target for transmission blocking approaches.**

In the laboratory three proteins have been identified named Oocyst Rupture Protein 1 -3 (ORP), which are all essential for oocyst rupture (Curra' et al. 2016, Siden-Kiamos et al, 2018 and unpublished data). The three proteins are expressed in the oocyst and located at the capsule. They have similarities to the trimeric DNA binding factor Nuclear Factor Y (NF-Y), although they are not expressed in the nucleus. Our current hypothesis based on experimental data suggest that the three proteins form a complex similar to NF-Y, and this complex is directly involved in destabilization of the oocyst capsule during rupture. We intend to identify potential candidates able to inhibit the trimer formation blocking the mechanism of oocyst rupture in infected mosquitoes.

Short biosketch

Dr Curra' after completing her joint Ph.D. in the Ponzi lab (ISS, Rome) and Braun-Breton lab (Universite'de Montpellier, France) joined the IMBB malaria group in 2013 as a Marie Curie post-doctoral fellow. She then continued her post-doctoral training at the University of Sao Paulo Brazil, where she initiated work on the ORP proteins. She was awarded a Stavros Niarchos Foundation fellowship at IMBB in 2018 to continue work on this project. From the beginning of 2021 the project is supported by an ELIDEK post-doctoral grant. Dr Curra' has published 18 papers in peer-reviewed journals, of which three as corresponding author.