Instituto de Medicina Molecular João Lobo Antunes

Master's Project Proposal

Title: *In vitro* characterization of a *Pb*Wsp transmission-blocking vaccine candidate

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Synopsis:

Malaria remains one of the most prevalent parasitic diseases worldwide, affecting 219 million and killing 435 000 people every year. The complexity of the parasite's life cycle, which includes two obligatory hosts and multiple parasite forms, has hindered efforts to eliminate malaria. Sor far, no vaccine is available, and RTS,S, a subunit vaccine that targets the circumsporozoite protein (CSP) is, currently, the most advanced malaria vaccine candidate. However, it has shown only moderate success and rapidly waning efficacy. Conversely, whole-sporozoite (Wsp) vaccines have shown the most success among current malaria vaccine candidates. The host laboratory has previously developed a WSP vaccine, termed *Pb*Vac, that consists of genetically modified sporozoites of *P. berghei* (*Pb*) expressing *P. falciparum* antigens, more specifically *P. falciparum* (*Pf*) CSP, the most abundant antigen on the surface of sporozoites. The results of phase I/IIa clinical trials have warranted the generation of new vaccine candidates expressing multiple antigens able to elicit immune responses against additional stages of the parasite's life cycle, including inhibiting of parasite transmission to the mosquito vector. Transmission-blocking vaccines could reduce the spread of the parasite in the community, by targeting molecules present during the sexual development of parasites in the mosquito. *Pfs*48/45 is a *Pf* molecule essential for male gametocyte fertility. Previous standard membrane feeding assays have shown that chimeric *Pfs*48/45 proteins induced 80% reduction on oocyst load compared to the control, identifying this antigen as one of the most promising candidates for transmission-blocking interventions.

In this project, the student will work on the characterization of a chimeric Wsp vaccine expressing not only *Pf*CSP but also the transmission-blocking candidate antigen *Pfs*48/45. The student will employ techniques such as immunofluorescence microscopy, quantitative real time PCR and Western blot to assess the correct expression of the inserted antigens, and will assess parasite infectivity in the mosquito, and in human and rodent hepatic cells. The knowledge generate by this project is expected to contribute to the identification of a multi-stage malaria vaccine.

Bibliography:

WHO. World Malaria Report. 2019
Draper, S.J. *et al*. "Malaria Vaccines: Recent Advances and New Horizons", *Cell Host & Microbe* **24**, 43-56 (2018)
Mendes, A.M. *et al.* "A *Plasmodium berghei* Sporozoite-Based Vaccination Platform Against Human Malaria", *npj Vaccines* **3**, 1-11 (2018)

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