PhD proposal on host-parasite interactions

Research project: The roles of *Leishmania* and *Eimeria* exo-kinases in subversion of host cell signalling. Intracellular parasites successfully survive because they modify the cellular functions of their host cell to their benefit through the secretion of virulence factors such as kinases. Despite their phylogenetic distance, most pathogens directly regulate similar host pathways through interactions with similar host proteins, suggesting that there is a signature for host cell subversion during infection. We propose to identify the host pathways regulated during parasite infection focusing on cell signalling to establish a host cell-signalling signature for parasite infection. Two parasitic effectors, LdCK1.2 (*Leishmania donovani*) and EtROP1 (*Eimeria tenella*), whose essential role for intracellular parasite survival has been previously demonstrated, will be studied. The aim of the PhD project is to identify common mechanisms used by the two parasites to regulate host cell signal transduction, validate their importance for parasite survival and determine the implication of LdCK1.2 and EtROP1 in these regulations. The PhD student will apply systems-level analyses on *L. donovani* and *E. tenella* infections: phospho-proteomic to assess the short-term impact of parasites on host cell signalling regulations, and transcriptomic to assess the long-term consequences of host signalling subversion on cellular phenotype. Next, he will perform a functional analysis of candidate host-signalling targets and their downstream pathways using genome editing to determine their importance for intracellular parasite survival. Studying very divergent host-parasite systems will reveal the basic mechanisms that govern host cell subversion and establish the host cell-signalling signature for parasite infection. This project is funded by the Labex Parafrap, for details see http://www.labex-parafrap.fr/en/

Teams: The project will be developed under the supervision of Dr Najma Rachidi, senior researcher of the parasitology molecular and signalisation unit at the institut Pasteur in Paris and Dr Anne Silvestre, senior researcher of the ISP unit at INRAE in Tours. Institut Pasteur and INRAE are both international and multi-disciplinary research centres with access to state of the art technologies.

Candidate eligibility requirements:
Applicants must have achieved academic excellence and be highly motivated to pursue a Ph.D. project in Parasitology. They should have obtained a 'Masters 2' degree or an equivalent (5 years after high/secondary school) in Sciences by July 2021; out of this format, only exceptional applications (upon justification) will be considered by the program director. English language skills are mandatory and the PhD program does not have an age restriction, but most accepted candidates are 24-26 years old and start their Ph.D. within a year of finishing their M.Sc., a few of them within 3 years. Mobility between the Master's lab and the Ph.D. host lab is mandatory, meaning that the applicants must change from their present Research Director and Institute to another one for the Ph. D. training. **Applicants must apply before April 10th, 2021 at https://parafrap.application.systems/site/index.php**

Starting date for the PhD and Salary: September 1st, 2021. The net monthly salary, for 36 months, will be in the range of 1500-1900 € according to French national rules and depending on the Research Institutions. The Ph.D. students will receive private health insurance and social security entitlements.

Publication of the teams

N. Rachidi, J.F. Taly, E. Durieu, O. Leclercq, N. Aulner, E. Prina, P. Pescher, C. Notredame, L. Meijer and G.F. Späth. 2014. Pharmacological assessment defines the *Leishmania donovani* casein kinase 1 as a drug target and reveals important functions in parasite viability and intracellular infection. Antimicrob Agents Chemother, 58 (3) 1501-1515.

Smirlis D., Dingli, F., Pescher, P., Prina E., Loew, D., Rachidi, N. and Spath, G. F. 2019. SILAC-based quantitative proteomics reveals pleiotropic, phenotypic modulation in primary murine macrophages infected with the protozoan pathogen *Leishmania donovani*. J Proteomics 213, 103617.

Diallo MA, Sausset A, Gnahoui-David A, Silva ARE, Brionne A, Le Vern Y, Bussière FI, Tottey J, Lacroix-Lamandé S, Laurent F, Silvestre A. 2019. Eimeria tenella ROP kinase EtROP1 induces G0/G1 cell cycle arrest and inhibits host cell apoptosis. Cell Microbiol. Jul; 21(7):e13027.