UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2020-2021

Laboratory/Institute: IAB - Institute for Advanced Biosciences. **Director:** Pierre HAINAUT
Team: Host-Pathogen Interactions & Immunity to Infections **Head of the team:** Mohamed-Ali HAKIMI

Name and status of the scientist in charge of the project:
HAKIMI Mohamed-Ali (DR1 INSERM) **HDR: yes ⊗ no ☐**

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Program of the Master's degree in Biology:

⊗ Immunology, Microbiology, Infectious Diseases ☐ Integrative Structural Biology
☐ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology
☐ Planta International

Title of the project: Lifelong Persistence Strategies of Toxoplasma gondii : Conquering the Host Cell and Evading Innate Immunity

Objectives (up to 3 lines):

The project aims to investigate how *Toxoplasma* deploys sophisticated mechanisms to profoundly modify the cells it infects and to promote parasite persistence. The student will explore the function of parasite-derived effectors that share the ability to reach the host nucleus and to regulate gene expression.

Abstract (up to 10 lines):

Toxoplasma is a prevalent single-celled eukaryotic parasite causing toxoplasmosis, a food-borne zoonotic disease potentially life-threatening in immune-suppressed individuals and in the unborn fetus. For those interested in the interaction between a pathogen and the host cell in which it grows, the last decade or so has been an exciting one in Toxoplasma research. We uncovered a new family of parasite-derived effector proteins that are singularly exported post-invasion into the host cell. Some appear to be clear counter-defenses that neutralize innate immune responses, while others are subtler in their effects, tweaking host functions to optimize the intracellular niche for parasite growth. The project aims i) to explore the synergistic and/or antagonist effects of parasite effectors on host gene regulation, following their delivery in the nuclei of the infected cell, but also to ii) decipher the extent to which they contribute to immune evasion and/or sustained parasitism.

Methods (up to 3 lines):

The student will use a multidisciplinary approach to study two novel effector proteins including, cellular biology, genetic engineering in Toxoplasma (CRISPR-Cas9, AID KD…), innovative gene expression analysis (Nanopore RNA sequencing) and biochemistry coupled to mass spectrometry proteomics.

Up to 3 relevant publications of the team:

1- Braun L, Brenier-Pinchart MP, Hammoudi PM, Cannella D, Kieffer-Jaquinod S, Vollaire J, Josserand V, Touquet B, Coute Y, Tardieux I, Bougdour A and Hakimi MA@. The Toxoplasma effector TEEGR promotes parasite persistence by modulating NF-kB signalling via EZH2. Nature Microbiology, 2019 Jul;4(7):1208-1220.
2- Hakimi MA, Olias P and Sibley DL. Toxoplasma Effectors Targeting Host Signaling and Transcription. Clinical Microbiology Reviews, 2017 Jul;30(3):615-645.
3- Gay G, Braun L, Brenier-Pinchart MP, Vollaire J, Josserand V, Curt-Bertini RL, Curt-Varesano A, Pelloux H, Coute Y, Bougdour A and Hakimi MA@ Toxoplasma TgIST co-opts Host Chromatin Repressors dampening STAT1-dependent gene regulation and IFN-γ-mediated host defenses. J. Exp. Med. 2016 Aug 8. pii: jem.20160340.

Requested domains of expertise (up to 5 keywords):

Immunity, cell biology, epigenetic, microbiology, parasitology