**Master 2 internship project**

**Year 2024-2025**

**Laboratorys/Institutes:** IAB and TIMC **Directors:** Pierre Hainaut & Alexandre Moreau-Gaudry

**Teams:** Apicolipide and TrEE **Heads of the team:** Cyrille Botté & Fabien Pierrel

**Name and status of the scientist in charge of the project:**

Dr Cyrille Botté and Prof. Ludovic Pelosi

**HDR: yes X no ☐**

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**Program of the Master’s degree in Biology:**

**X** Microbiology, Infectious Diseases and Immunology

**Title of the project: Characterization of the coenzyme Q biosynthesis pathway in Toxoplasma gondii**

Objectives (up to 3 lines): The project aims to identify the proteins involved in the coenzyme Q biosynthesis pathway in *Toxoplasma gondii*, using cell biology (inducible mutant, mitochondrial location) and biochemistry (functional analysis in yeast or in *E. coli*) approaches.

Abstract (up to 10 lines): Apicomplexa are obligate intracellular parasites responsible for major human infectious diseases such as toxoplasmosis, caused by *Toxoplasma gondii*, and malaria, caused by *Plasmodium* spp, which pose social and economic burdens around the world. To combat these infections, atovaquone, a major antiparasitic used to treat or prevent toxoplasmosis, is used. Atovaquone is a coenzyme Q analogue that has been indicated to specifically target the cytochrome bc1 complex of the mitochondrial respiratory chain in protozoan. However, the rapid emergence of resistance to atovaquone resulted in a costly combination with proguanil, limiting its widespread use in resource-poor disease-endemic areas. Cheaper alternatives that can overcome resistance are desperately required. To this end, we propose to explore the coenzyme Q biosynthetic pathway in *T. gondii*. Although poorly documented in the literature, it appears to differ significantly from the human pathway, since no homologues of the COQ6, COQ7 and COQ9 proteins have been identified. During the course of this internship, the putative function of COQ proteins in *T. gondii* will be checked by complementation assays in *Saccharomyces cerevisiae* or in *Escherichia coli*, and a candidate likely to substitute for both COQ6 and COQ7 in *T. gondii* will be studied in particular.

Methods (up to 3 lines): Aim 1. Task1-2: Tagging and inducible knock-down (iKD) in virulent type I strain (task1) and cystogenic type II strainparasites (Task2); Task3: Phenotyping, impact on growth viability. Task4: Lipidomic and fluxomic analyses to identifying the function of lipid modulators. Aim2: expression of proteins in yeast or in *E. coli*, lipids extraction and quinone analysis (HPLC-MS).

Relevant publications of the teams:

Charital *et al*. mBio (2024) mBio. 2024 Apr 10;15(4):e0042724. doi: 10.1128/mbio.00427-24.

Sheokand *et al*. Cell Rep. 2023 Apr 25;42(4):112251. doi: 10.1016/j.celrep.2023.112251.

Pelosi L. *et al*., Mol. Cell 84 (2024) 981. DOI: 10.1016/j.molcel.2024.01.003.

Kazemzadeh K. *et al*., PNAS (2024) 121(13):e2321242121. DOI: 10.1073/pnas.2321242121.

Requested domains of expertise: cellular biology, molecular biology, biochemistry, host-pathogen interactions, metabolism, lipidomics/metabolomics, metabolic adaptation.