

PhD position

An exciting opportunity to investigating the elusive flagellar pocket collar structure of the parasite *T. brucei* which causes the neglected tropical disease sleeping sickness.

Why and how trypanosomes build a flagellar pocket collar; a structure-function study.

Publication date: 03/03/2021

Employer: University of Bordeaux, France / ANR-FWF PRCI funding

Place of work: University of Bordeaux, CNRS UMR5234, Fundamental Microbiology and Pathogenicity.

<https://www.mfp.cnrs.fr/wp/>

Type of contract: PhD fellowship

Contract duration: 3 years

Expected starting date: Mai to October 2021

Work quota: Full time

Remuneration: minimum 1,422 euros (net)

Required diploma: Master's degree (M2)

Project:

We are seeking a highly motivated PhD candidate who desires to perform academic research of the highest standards with strong commitment in cell biology and structural studies and to be involved in a collaborative project aiming at studying how trypanosomes build a flagellar pocket collar (FPC). The host laboratory has identified several trypanosome-specific proteins, including BILBO1, involved in the structure and function of the FPC (1-4). However, more work is required to decipher the FPC composition and architecture. The project will be developed based on molecular and cell biology, and reverse genetics (gene replacement / tagging, RNAi, CRIPR/Cas9) approaches. This study also strongly relies on developing super-resolution light and cryo-EM/ET microscopy approaches to understand at the molecular level the role of the FPC in the formation of the flagellar pocket using state-of-the-art imaging and cryo-EM/ET in the [Bordeaux imaging centre](#) and [IECB](#).

Scientific context:

Trypanosomatids include many parasites of major medical and economic importance that cause several of the 20 World Health Organization's listed neglected tropical diseases. These flagellated parasites share several unique features: a single mitochondrion with its compact genome (the kinetoplast, K), a flagellar pocket (FP), and a microtubule-based cytoskeleton, to maintain cell shape and flagellar motility that plays crucial roles in life and cell cycle. The FP is an invagination of the plasma membrane enclosing the base of the flagellum. Because in most trypanosomes, endo- and exocytosis occur exclusively through the FP, it provides the sole surface for numerous important receptors and makes them inaccessible for components of the host innate immune system of the host. Moreover, the FP is also responsible for sorting all parasite surface glycoproteins targeted to, or recycling from, the pellicular membrane and for removal of host antibodies from the cell surface. As such, the FP is a key player in protein trafficking, cell signaling and immune evasion. Because it is hidden from the cell surface and sequesters important receptors, the FP is an attractive drug target. However, it has not been exploited as such because structural components of this organelle are still poorly characterized.

The FP is maintained enclosed by the flagellar pocket collar (FPC), a cytoskeleton structure. Despite extensive functional studies on BILBO1, the first FPC protein to be characterized (1-5), the mechanisms

underlying FPC *in vivo* macro-molecular assembly, biogenesis and roles remain elusive, mainly due to the poor knowledge of its molecular composition and assembly.

(1) Bonhivers M, et al. Biogenesis of the Trypanosome Endo-Exocytotic Organelle Is Cytoskeleton Mediated. PLOS Biol. 2008 May 6;6(5):e105.

(2) Florimond C, et al. BILBO1 Is a Scaffold Protein of the Flagellar Pocket Collar in the Pathogen Trypanosoma brucei. PLoS Pathog 2015, 11, doi:10.1371/journal.ppat.1004654.

(3) Perdomo D, et al. The Trypanosome Flagellar Pocket Collar and Its Ring Forming Protein—TbBILBO1. Cells. 2016 Mar 2;5(1):9.

(4) Vidilaseris K, et al. Crystal structure of the N-terminal domain of the trypanosome flagellar protein BILBO1 reveals a ubiquitin fold with a long structured loop for protein binding. J Biol Chem. 2020 Jul 2;295(6):1489–99.

(5) Isch, C.; Majneri, P.; Landrein, N.; Pivovarova, Y.; Lesigang, J.; Lauruol, F.; Robinson, D.R.; Dong, G.; Bonhivers, M. Structural and Functional Studies of the First Tripartite Protein Complex at the Trypanosoma Brucei Flagellar Pocket Collar. bioRxiv 2021, 2021.01.26.428227, doi:10.1101/2021.01.26.428227.

Professional environment

This exciting study will be based in Bordeaux, a beautiful, cosmopolitan city in the South-West of France, UNESCO World Heritage site and gateway to the vineyards and world-class surfing spots.

The student will join the [Protist Parasite Cytoskeleton team](#) headed by Dr Derrick Robinson and Dr Mélanie Bonhivers. The team is interested in the cytoskeleton and associated proteins and their roles in the biogenesis of specific structures of trypanosomes. The PhD student will be in close contact with the team members (3 CNRS researchers, 1 assistant professor, 1 engineer, 1 postdoc, 2 thesis students) and will collaborate with the group of Dr [Gang Dong](#) (MFPL Vienna) and of Dr [Rémi Fronzes](#) (IECB) with the Fundamental Microbiology and Pathogenicity department (<https://www.mfp.cnrs.fr/wp/>) .

Associated activities

- Participate in the general organization of the team (preparation of common solutions), equipment maintenance, general chemicals management
- Participate and present data to lab and department meetings

Expected skills

- General knowledge of cellular / molecular biology, cell culture
- General interest in cellular biology and parasitology
- Knowledge of fluorescence microscopy
- Expertise in super resolution microscopy, or electron microscopy or cryo-electron microscopy and image analysis would be an advantage.
- Rigor, experimental ethics
- Sense of organization, ability to manage multiple tasks in parallel
- Knowing how to work autonomously but in interaction with other members of the group
- Sense of teamwork,
- Ability to adapt / Quickness of mind / strong motivation
- Understanding of written and oral English.

Any questions : please contact melanie.bonhivers@u-bordeaux.fr.

Procedure to apply: send a full CV, a cover letter and the contact details of one or two referents to melanie.bonhivers@u-bordeaux.fr.