Postdoctoral fellowship: Heme homoeostasis in *Trypanosoma cruzi* as a target to inhibit parasite proliferation

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Based at: IBR Instituto de Biología Molecular y Celular de Rosario. Fac. de Cs. Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario. Laboratorio de Biología y Bioquímica del Trypanosoma cruzi (http://www.ibr-conicet.gov.ar/laboratorios/serra/). Rosario, Santa Fe. Argentina

Starting: April 1st, 2019 and extended for 24 months (fellowship stipend equivalent to CONICET postdoctoral fellowship, transportation and installation expenses are not included).

Closing date for applications: February 25th, 2019.

Project Description

Trypanosoma cruzi is a parasite that causes Chagas disease, the most relevant parasitic disease in several South American countries, and which has become a relevant health problem in many non-endemic countries through migration of infected individuals and spread of its insect vector, the 'kissing bug'.

T. cruzi, as well as other trypanosomatids relevant for human health, rely upon their hosts to supply essential metabolites and cofactors. These parasites do not produce heme, but they have several heme proteins involved in essential metabolic pathways. T. cruzi is able to import heme from its hosts during the replicative stages; the protein TcHTE is essential for this heme transport activity. Heme is also a highly toxic molecule, meaning that the parasite must strictly control its heme homeostatic processes (importation, trafficking and detoxification) where TcHTE and other unknown proteins are directly involved.

The aim of this project is to elucidate the molecular mechanisms for heme homeostasis. Considering that known heme chaperones, transporters and detoxifying enzymes have not been yet identified in *T.* cruzi, the project would identify the novel proteins fulfilling these essential roles, and which may prove suitable as new targets for new drug development against Chagas disease.

References:

- Tripodi KEJ, Menendez Bravo SM, Cricco JA. Role of heme and heme-proteins in trypanosomatid essential metabolic pathways. *Enzyme Res* 2011; 2011: 873230.
- Merli ML, Pagura L, Hernández J, Barisón MJ, Pral MF, Silber AM, et al. The *Trypanosoma* cruzi Protein TcHTE Is Critical for Heme Uptake. *PLoS Negl Trop Dis* 2016;1–18.
- Merli ML, Cirulli BA, Menendez-Bravo SM, Cricco JA. Heme A synthesis and CcO activity are essential for Trypanosoma cruzi infectivity and replication. *Biochem J England* 2017; 474: 2315–2332.

Keywords – heme transport, heme homeostasis, drug targets, Chagas disease, neglected tropical diseases

Eligibility

Applicants require a PhD in Biological Sciences or similar (to be completed by March 31st, 2019) and experience in one or more of the following: microbiology, molecular biology or parasitology, along with good written and spoken English.

How to apply

Interested applicants should send a full CV, an intention letter and 2 (two) references, to Julia Cricco (cricco@ibr-conicet.gov.ar)