SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Cellular and Molecular Immunology

has the honor to invite you to the public defense of the PhD thesis of

Joar Esteban PINTO TORRES

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Glycolytic enzymes from *Trypanosoma* as targets for parasite detection and control

Promotors:

Prof. Dr. ir. Stefan Magez

The defence will take place on

Monday January 15 2018 at 16:00h

in Auditorium D.2.01 at the Campus Humanities, Sciences and Engineering of the Vrije Universiteit Brussel, Pleinlaan 2 - 1050 Elsene, and will be followed by a reception.

Members of the jury:

Prof. Dr. ir. Wim Versées (chairman)
Prof. Dr. Gustavo Guiterrez (secretary)
Prof. Dr. Peter Tompa
Dr. Philippe Holzmuller (CIRAD,Montpellier, Fr.)
Prof. Dr. Wendy Gibson (Univ. of Bristol, UK)

Curriculum vitae

Joar Pinto obtained a Master in Molecular Biology at the Vrije Universiteit Brussel (2014). He was granted a VUB doctoral scholarship to perform scientific research in the group of Structural and Functional Immunoparasitology at the CMIM lab. His work resulted in two first-author publications in a peer reviewed journal, 2 oral presentations and 1 poster presentation at national and international scientific conferences. He also gave a workshop in biochemistry at the Ghent University Global Campus Korea. Mr. Pinto collaborated in a bilateral project with the University of Edinburgh and obtained a NSE travel grant to conduct experiments in Clinvet (South-Africa). He supervised 2 master thesis projects.

Abstract of the PhD research

Animal trypanosomosis (Nagana) is a chronic wasting disease that causes severe pathological conditions in the afflicted animals. In Sub-Saharan Africa, Nagana is spread within the so-called 'Tsetse belt", a territory that extends for 8.7 million km^2 and roughly represents one-third of Africa. The vastness of the disease hinders the continent's potential for agricultural expansion. Due to major roadblocks in vaccine development, control of animal trypanosomosis mostly relies on chemotherapy. However, drug resistant parasite strains have emerged during the last decades driven by the long-term and indiscriminate use of drugs in endemic regions. Exacerbated drug usage is linked to the lack of easy-to-use rapid diagnostic tests (RDTs) that can be used under field conditions such as lateral flow assays (LFA).

LFAs are rapid and easy to use diagnostic tests that can be applied in resource-constrained settings. Most LFAs fall into two categories; those aimed to directly target antigens from the parasite (antigen-based) and those aimed to detect host's antibodies generated against the pathogens (antibody-based). The last, are less preferred for follow-up studies as they are not able to distinguish between cured or ongoing infections. For that reason antigen-based LFA are desired. Unfortunately, not enough suitable biomarkers are currently available for the expansion of those diagnostic tests.

This study had three main aims: (i) the identification of new biomarkers for the diagnosis of animal trypanosomosis, (ii) the development of a sandwich ELISA as a proof of principle for the design of a LFA prototype using Nanobodies (Nb) as assay reagents; and (iii) the structural and functional characterization of the Nb-biomarker complex.

The results gathered in this work describe: (i) the identification of the glycolytic enzyme pyruvate kinase (PYK) as a suitable biomarker for Nagana, using *Trypanosoma congolense* as a model; (ii) the development of a Nb-based sandwich ELISA targeting PYK as a first step towards the design of an LFA assay, and finally, (iii) the specific Nb-based inhibition of *T. congolense* PYK.