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

Phil Moon

to obtain the degree of Doctor of Bioengineering Sciences

Joint PhD with UGent

Title of the PhD thesis:

Assessing impacts of experimental trypanosome infections on B cell memory

Promotors:
Prof. dr. ir. Stefan Magez (VUB)
Prof. dr. Magdalena Radwanska (UGent)

The defense will take place on
Tuesday, December 20, 2022 at 11h at FSVM Research Building - Jozef Schell Seminar Room - Gent

Livestream via https://ugent-be.zoom.us/j/92291460436?pwd=bGoxeU9lT214SEk4a21uTHRkU2FtQT09

Members of the jury

Prof. dr. Rudi Beyaert (UGent, chair)
Prof. dr. ir. Benoit Stijlemans (VUB, secretary)
Prof. dr. Luc Leyns (VUB)
Prof. dr. Charlotte Scott (UGent)
Prof. dr. ir. Yann Sterckx (UAntwerpen)
Dr. ir. Philippe Holzmuller (CIRAD)

Curriculum vitae

Education:
M.Sc., Boise State University, 2017
B.Sc., Eastern Oregon University, 2014

Publications:
1. Moon P, Detrimental Effect of Trypanosoma brucei brucei Infection on Memory B Cells and Host Ability to Recall Protective B-cell Responses. J Infect Dis., Published in August 2022.

2. Establishment of a Standardized Vaccine Protocol for the Analysis of Protective Immune Responses During Experimental Trypanosome Infections in Mice. Book chapter: Methods Mol Biol., Published in March 2020.

During four years of doctorate training, Phil have given two oral and two poster presentations. He has taught molecular biology, immunology, and biochemistry to train hands-on laboratory skills to undergraduate students. He has supervised one master thesis and four bachelor thesis.

Abstract of the PhD research

Exposure to *Trypanosoma brucei brucei (T. b. brucei*), an extracellular salivarian parasite, triggers the destruction of the host B cell compartment, undermining the antibody production capacity. To gain a better understanding of the problem at hand, the first part of the work presented here is focused on unraveling the fate of vaccine-induced plasma cells (PCs) and memory B cells (MBCs). To understand how trypanosome infections trigger the loss of memory recall capacity, homologous and heterologous challenges were conducted. By combining infection models, we were able to show that while VSG vaccination itself can induce a protective antibody-mediated response against a homologous challenge, exposure to a heterologous variant not only gives rise to a successful infection but also results in the loss of protective responses against previously targeted VSG. Next, the antibody repertoire analysis was performed using V(D)J single-cell RNA sequencing (scRNAseq), using specific VSG-vaccinated mice followed by homologous and heterologous challenges. Results show that infections in the heterologous challenge group triggered an abundance of IgMs, indicating the induction of a poly-reactive response. However, limits in identifying paired clonotypes were observed, in which both the sequence of the antibody heavy chain and light chain could be obtained for a single B cell. Despite that, data demonstrate that mice protected mice against a homologous challenge, showed the generation of a more diverse repertoire of clonotypes undergoing processes of somatic hyper mutation (SHM) and class-switch recombination (CSR), as compared to mice that suffered an active infection after being challenged with heterologous parasites. In the final chapter of this work, the effect of a particular vaccine strategy was analyzed, targeting one of the main secreted proteins of *T. b. brucei*, pyruvate kinase (*Tb*PYK) The vaccinated mice with recombinant *Tb*PYK resulted in improved parasitemia control during the early stage of infection. This result sparked a scRNAseq analysis with a focus on germinal center (GC) B cells, PCs, and MBCs. The main finding here was that mock-vaccinated mice, with high parasitemia, had a signature gene expression indicative of polyclonal B cell activation. In contrast, the *Tb*PYK vaccinated group with low parasitemia had a very subdued gene expression profile. Finally, also in this setting vaccinated infected mice failed to mount MBCs and recall responses. As a result, the beneficial effect of the *Tb*PYK vaccination was short-lived.