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

Hannah Van Hove

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:
A combination of ontogeny and environment drives macrophage identity across brain regions

Promotors:
Prof. dr. Kiavash Movahedi (VUB)
Prof. dr. ir. Jo Van Ginderachter (VUB)

The defense will take place on
Wednesday, June 8, 2022 at 15:00h in auditorium D.0.08 and will be followed by a reception in the Q Foyer.

The defense can also be followed through a live stream. Contact hannah.van.hove@vub.be for more information.

Members of the jury

Prof. dr. ir. Eveline Peeters (VUB, chair)
Prof. dr. Janine Brunner (VUB, secretary)
Prof. dr. Ilse Smolders (VUB)
Prof. dr. Diego Gomez-Nicola (University of Southampton)
Prof. dr. Steffen Jung (Weizmann Institute of Science)

Curriculum vitae

Hannah obtained her Master degree in Biomolecular Sciences at the Vrije Universiteit Brussel in 2017. She started her PhD in 2017 under the promotorship of Prof. Dr. Ir. Kiavash Movahedi and Prof. Dr. Ir. Jo Van Ginderachter and was funded by a Fonds Wetenschappelijk Onderzoek predoctoral fellowship. Hannah co-authored six scientific papers, published in peer-reviewed international journals, amongst which three as a first author. She presented her work in (inter)national conferences and symposia. Finally, she supervised one bachelor and two master thesis students.

Abstract of the PhD research

All tissues within the body contain tissue-resident macrophages that are crucial for tissue homeostasis. Tissue-resident macrophages are remarkably plastic and can change their phenotype and functions depending on environmental signals. The central nervous system contains various tissue-resident macrophages. Historically the central nervous system was considered immune privileged. However, recent studies uncovered that the brain consists of different regions that are all associated with their own degree of steady-state privilege. Access to parenchymal tissues is restricted by the blood-brain barrier, while border tissues are more accessible to the blood circulation.

While parenchymal microglia have been extensively studied in both homeostasis and disease, less is known about border-associated macrophages. In this thesis the remarkable diversity of border-associated macrophages was uncovered that displayed tissue-specific transcriptional signatures. Border-associated macrophages were derived from both embryonic precursors and monocytes. Interestingly, the apical side of the choroid plexus epithelium harbored a unique microglial population with a signature of microglia in neurodegenerative conditions, called DAM.

Circumventricular organs are parenchymal regions lacking a blood-brain barrier. Parenchymal microglia have a unique embryonic origin and do not receive monocyte input which is attributed to the early closure of the blood-brain barrier during development. Interestingly both embryonic- and monocyte-derived microglia were found within the circumventricular organs. These entered the circumventricular organs around birth after which they persisted. Surprisingly, embryonic- and monocyte-derived microglia were transcriptionally equivalent. The circumventricular organ environment profoundly influenced the transcriptional signature of microglia that were heterogenous and distinct from other parenchymal microglia due to their activated phenotype. One of these populations expressed a DAM-like signature and localized around astrocyte and tanycyte processes in a region rich in myelinated axons.

Altogether my PhD work revealed the remarkable diversity of tissue-resident macrophages across brain regions and how different environments influenced the phenotype and origin of tissue-resident macrophages within the central nervous system.