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

Máté Kiss

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Cancer-induced local and systemic reprogramming of myeloid cells and its impact on disease progression

Supervisors:
Prof. dr. ir. Jo Van Ginderachter
Prof. dr. ir. Damya Laoui

The defense will take place on

Friday, April 23, 2021 at 15h30

The defense can be followed through a live stream. Contact Mate.Kiss@vub.be for more information

Members of the jury

Prof. dr. Joris Messens (VUB, chair)
Dr. Antonella Fioravanti (VUB, secretary)
Prof. dr. Karine Breckpot (VUB)
Prof. dr. Karin De Visser (The Netherlands Cancer Institute)
Prof. dr. Michele De Palma (Swiss Institute for Experimental Cancer Research)

Curriculum vitae

Máté Kiss (1990) obtained his medical degree at the University of Debrecen, Hungary in 2015. He began his PhD at the VUB in 2016 after receiving the FWO Strategic Basic Research Doctoral Grant. He is the author of 17 scientific papers and 1 book chapter. In 2019, he was the recipient of the Germaine Eisendrath-Dubois Foundation Award in Cancer Research.

Abstract of the PhD research

Myeloid cell types, such as monocytes, macrophages and neutrophils, are abundant in most tumors and can show tumor-promoting activities. Myeloid cells are also key in establishing an immunosuppressive microenvironment that decreases the ability of T cells to recognize and kill cancer cells, ultimately posing a major obstacle to efficient immunotherapy.

During my PhD work, I studied two aspects of the tumor-myeloid cell interplay. One aspect of my work was examining the impact of the inflammatory signal interleukin-1β (IL1β) on myeloid cell accumulation and antitumor immunity. I found that IL1β release promoted tumor progression and accumulation of immunosuppressive neutrophils in two distinct mouse cancer models. The inflammasome pathway that typically safeguards IL1β release in tissues and thereby prevents unnecessary inflammation was not required for this process in tumors, indicating the presence of alternative release pathways. Thus, an important clinical implication of my work is that drugs targeting the inflammasome will likely not inhibit IL1β release in certain cancer types. Another aspect of my PhD work was investigating how cancer affects the phenotype of circulating monocytes which represent a key source of immunosuppressive macrophages in tumors. Using several mouse cancer models, I found that the cancer-induced systemic environment causes extensive changes in the gene expression profile of circulating monocytes before they reach the tumor. This was associated with cancer-induced changes in chromatin accessibility that did not cause alterations in gene expression but can potentially influence the cells' response to future stimuli. Among the genes showing cancer-induced activation in monocytes, I found the gene encoding Junctional Adhesion Molecule-A (JAM-A) whose role in monocytes is ill-defined in the context of cancer. To investigate the function of this molecule, I generated a mouse model with myeloid cell-specific deletion of JAM-A. I found that JAM-A was not required for monocyte accumulation in tumors but played a role in fine-tuning the gene expression of tumor-infiltrating hypoxic neutrophils.

Altogether, my PhD work contributes to a deeper understanding of how cancer alters the phenotype of myeloid cells both locally and systemically and defines several candidate pathways for therapeutic targeting and future investigation.