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Prof. Dr. Damya Laoui

Brussels Center for Immunology, VUB

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Liver Cell Biology Research Group, VUB

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Laboratory of Experimental Hematology, University of Antwerp, Belgium

Prof. Dr. Jo Van Ginderachter

Brussels Center for Immunology, VUB

Prof. Dr. Stefaan Verhulst

Liver Cell Biology Research Group, VUB

INVITATION to the Public defence of

Emma VERHEYE

To obtain the academic degree of

'DOCTOR OF MEDICAL SCIENCES'

Mapping the immune heterogeneity within the tumor microenvironment to identify novel target populations for immunotherapy in Multiple Myeloma

The public defence will take place on

Thursday, 11 September 2025 at 4 p.m.

In Auditorium Vanden Driessche

VUB Health Campus

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

Summary of the dissertation

Multiple myeloma (MM) is an incurable hematological cancer characterized by the uncontrolled proliferation of plasma cells in the bone marrow. Despite major advances in treatment, the complex and continually evolving tumor-immune microenvironment remains a major barrier to therapeutic success, allowing cancer cells to evade immune responses and acquire resistance.

In this thesis, advanced techniques such as single-cell RNA sequencing were employed to study how the immune system changes over time in a mouse model of MM. To ensure translational relevance, these findings were compared with patient-derived data. These results revealed substantial immune dysregulation in both mice and humans, including an increase in exhausted T cells (which are less effective at fighting cancer), expansion of tumor-supporting neutrophils, and impaired activation of conventional dendritic cells (cDCs), which are essential for initiating anti-tumor immune responses.

Therapeutic activation of cDCs using an anti-CD40 agonist (α CD40) restored their function, enhanced T-cell responses, and resulted in temporary tumor control. However, efforts to improve this effect by expanding cDCs using Flt3 ligand (Flt3L) did not enhance efficacy and instead led to an accumulation of regulatory T cells, providing no added benefit when combined with α CD40 therapy.

An alternative approach using the clinically approved MM drug, panobinostat, further activated cDCs and demonstrated additive effects when combined with α CD40, highlighting its potential for future therapeutic strategies.

In summary, this research offers new insights into the dynamic MM tumor-immune microenvironment and identifies cDCs as a promising therapeutic target for enhancing the efficacy of immune-based treatments.

Curriculum Vitae

Emma Verheye was born on March 15, 1998, in Anderlecht, Belgium. In 2021, she obtained a Master's degree in Biomedical Research from the Vrije Universiteit Brussel (VUB), graduating with great distinction. That same year, she began her PhD at VUB, conducting her research in the Laboratory of Hematology and Immunology and the Laboratory of Dendritic Cell Biology and Cancer Immunotherapy, under the supervision of Prof. Dr. Kim De Veirman and Prof. Dr. Ir. Damya Laoui.

Her doctoral research focused on characterizing the immune heterogeneity within the tumor microenvironment of multiple myeloma (MM), with the aim of identifying novel targets for immunotherapy.

Throughout her PhD, Emma strengthened her bioinformatics skills by applying single-cell technologies to investigate immune remodeling in MM. Her findings revealed that dendritic cells, which are key orchestrators of anti-tumor immunity, are functionally impaired in MM, but that their reactivation through targeted therapies can restore effective immune responses against the disease.

Her research was supported by an Emmanuel van der Schueren starter grant from Kom op tegen Kanker, as well as by an award from the VUB Oncology Research Center.

Emma is the author of eight peer-reviewed publications, including three as first author. She has presented her work at six national and international conferences, delivering two oral and four poster presentations. In addition to sharing her research with the scientific community, she also engaged with the general public by presenting her research to a non-scientific audience at "Dag van de Wetenschap" and the "Yamina Krossa Fund Day".