SCIENCES & BIOENGINEERING SCIENCES

The research group
Brussels Center for Immunology

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

Ahishakiye Neema Jumapili

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Targeting immune checkpoint receptors in cancer: Insights into Neuropilin-1 and VSIG4

Supervisor:
Prof. dr. Jo Van Ginderachter (VUB)

The defence will take place on
Thursday, July 2, 2026, at 2.00 p.m.

VUB Etterbeek campus, Pleinlaan 2, Elsene, Auditorium **D, Promotiezaal D2.01**.

The defence can be followed through a live stream:
https://us02web.zoom.us/j/88072978678?pwd=XJqNRYIlURBk2hVO0IITSqepaqtl2g.1

Members of the jury

Prof. dr. Damya Laoui (VUB, chair)
Prof. dr. Karine Breckpot (VUB)
Prof. dr. Sandra Tuyaerts (VUB)
Prof. dr. Jan Gettemans (UGent)
Prof. dr. Luca Tamagnone (The Catholic University of Sacred Heart, IT)

Curriculum vitae

Neema Jumapili obtained a BSc degree in biochemistry from Egerton University, Kenya and a Msc degree in Molecular Biology from the Vrije Universiteit Brussel in 2021. She subsequently pursued a PhD in the Brussels Center for Immunology lab under the supervision of Prof. Jo Van Ginderachter. Her PhD research was supported by Fonds Wetenschappelijk Onderzoek.
Throughout her PhD, Neema contributed to teaching activities and supervised two master students. She presented her research at several national and international conferences. Neema is a co-author to four publications, including one (co-) first article.

Abstract of the PhD research

Immune checkpoint blockade has revolutionized cancer treatment. However, many patients are still refractory to the treatment, underscoring the need for the identification and validation of novel targets that regulate anti-tumor immunity. We sought to explore the therapeutic potential of targeting two emerging immune checkpoint markers in the tumor microenvironment, Neuropilin-1 (NRP1) and VSIG-4, as modulators of immune suppression in cancer.
Neuropilin-1 plays an emerging role in the regulation of immune responses. Beyond its established function in cancer cell behavior, angiogenesis and neuronal development, through its interaction with semaphorins and vascular endothelial growth factors (VEGF), NRP1 is also highly expressed on immunosuppressive immune populations, particularly regulatory T cells and macrophages. To therapeutically target NRP1, we generated and optimized half-life extended Nanobody (Nb) constructs with a prolonged *in vivo* circulation time and tumor delivery. These constructs block both the NRP1-VEGF and NRP1-Sema3a interactions, and their therapeutic use was evaluated in murine melanoma models, both as monotherapy and in combination with anti-PD-1 immune checkpoint blockade. Targeting NRP1 resulted in a delay in tumor growth, confirming its functional role in melanoma progression. To elucidate the underlying mechanism, we performed comprehensive immune profiling of the tumor infiltrate at the single cell level. This revealed that NRP1 blockade, in combination with PD1 blockade, modulates the abundance and functional states of immune populations, providing a mechanistic insight into how NRP1 targeting can alleviate tumor-associated immunosuppression.
In addition, we assessed the role of the macrophage-associated receptor VSIG4 in cancer, based on the finding that VSIG4 expression on macrophages is associated with a poor prognosis in a variety of human cancers. In mouse models of colorectal and breast cancer, we showed that tumor-associated macrophages do not express VSIG4 and, consequently, VSIG4-deficiciency did not affect primary tumor growth and metastasis.
Altogether, this thesis underscores both the promise and challenge of the identification and targeting of immune checkpoint receptors in cancer. While NRP1 represents a viable and functionally relevant target with demonstratable anti-tumor effects, the study of VSIG4 reveals the limitations of preclinical models in recapitulating human biology. This thesis therefore contributes to a more nuanced understanding of immune checkpoint targeting, emphasizing the importance of mechanistic validation and careful model selection in the development of next-generation cancer immunotherapies.