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

Ema Romão

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Development of Nanobodies with a therapeutic and diagnostic potential in cancer

Supervisor:
Prof. Dr. Ir. Jo Van Ginderachter (VUB)
Co-supervisors:
Prof. Dr. Nick Devoogdt (VUB)
Emeritus Prof. Dr. Serge Muyldermans (VUB)

The defence will take place on

28 April 2026 at 13h30

VUB Etterbeek campus, Pleinlaan 2,
Elsene, Building LIC: Learning Theater

The defence can be followed through a live stream:
https://zoom.us/j/99000024261

Members of the jury

Prof. Dr. Ir Stefan Magez (VUB, chair)
Prof. Dr. Els Pardon (VUB)
Dr. Ir. Sophie Hernot (VUB)
Dr. Mike Taussig (Cambridge Protein Arrays)
Prof. Dr. Maarten Dewilde (KULeuven)

Curriculum vitae

Ema Romão obtained a Master's degree in Biomolecular Sciences from the VUB in 2013. She subsequently started her doctoral studies in bioengineering sciences under Professor Dr. Serge Muyldermans with the support of first a FWO fellowship and then a KOTK Scholarship, with which she conducted research in the field of Nanobody engineering with particular focus on oncological targets. Her research led to 3 own articles and contributed to another 17 international peer-reviewed journals. She also presented her results in international conferences and was a supervisor to seven master students.

Abstract of the PhD research

Since their discovery, antibodies have been central to immunological research, facilitating the development of innovative research, diagnostic, and therapeutic tools. Their high specificity and capacity to elicit and engage immune effector mechanisms have enabled their successful application as tools across a very wide repertoire of pathologies. Despite their very valuable and established successes, full length monoclonal antibodies also have some intrinsic limitations. They have a large molecular weight (~150 kDa), which hinders penetration in solid tumors or complex tissues. In addition, their Fc part can result in off-target effects, and their production is complex and expensive. Together, these limitations drove research into alternative antibody-based fragments with improved biophysical, biochemical, or pharmacokinetic profiles.

Among those alternative fragments, there are Nanobodies , single domain antigen-binding fragments derived from the heavy-chain-only antibodies naturally found in camelids. They have emerged as versatile and robust tools in a wide range of applications. Nanobodies have several advantageous properties, such as a small molecular weight (~ 15 kDa), which contributes to deep and rapid tissue penetration, high solubility, thermal and chemical stability, ease of engineering and economic production, retention of full antigen recognition with high specificity and affinity and a low immunogenic profile.

The present work describes the generation and preclinical characterization of Nanobodies targeting two clinically relevant pathways in oncology. This thesis first describes the isolation and comprehensive characterization of Nanobodies targeting the CD47-SIRPα immune checkpoint axis, a pathway exploited by many cancer types to evade macrophage-mediated phagocytosis. Nanobodies were generated against both CD47 and SIRPα and then evaluated for binding affinity, specificity, cross-reactivity, thermostability and ability to modulate phagocytosis. A small subset of SIRPα specific Nanobodies was radiolabeled and examined for in vivo biodistribution and tumor accumulation in mouse models. Second, this thesis also describes the generation, characterization, and in vivo validation of Nanobodies against CD33, a biomarker for acute myeloid leukemia. Twelve Nanobodies were generated, six of which demonstrated specific binding to native CD33 expressed on leukemic cells, with nanomolar-range affinity and a favourable thermostability profile. These candidates were then radiolabeled and tested in vivo in mice bearing xenograft THP-1 tumors.

Collectively, the findings presented in this thesis further reinforce the versatility and translational promise of Nanobodies in cancer research. Through rigorous selection, engineering, and both in vitro and in vivo validation, this work contributes to the expanding body of evidence supporting Nanobodies as next-generation precision tools in oncology.