GENEESKUNDE & FARMACIE

**INVITATION to the Public defence of**

## Promotors

**Prof. Dr. Karine Breckpot**
Translational Oncology Research Centre, VUB

**Prof. Dr. Nick Devoogdt**
Molecular Imaging and Therapy Research Group, VUB

**Prof. Dr. Cleo Goyvaerts**
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## Chair

**Prof. Dr. Eline Menu**
Translational Oncology Research Centre, VUB

## Board of examiners

**Prof. Dr. Eva Lion**
Laboratory for Experimental Hematology, University of Antwerp

**Prof. Dr. Sarah Gerlo**
Inflammation and Immunomodulation laboratory, Ghent University

**Prof. Dr. Thierry VandenDriessche**
Department of Gene Therapy and Regenerative Medicine, VUB

**Prof. Dr. Johnny Duerinck**
Center for Neuroscience, VUB

**Prof. Dr. Geert Raes**
Brussels Center for Immunology, VUB

# Fien MEEUS

To obtain the academic degree of

**'DOCTOR OF MEDICAL SCIENCES'**

## Advancing CAR-T cell therapy for solid tumors using nanobodies: Developing nanobody-based CARs and nanobody-displaying lentiviral vectors

The public defence will take place on

**Wednesday**, **29 April 2026 at 5 p.m.**

**In Auditorium Piet Brouwer**
VUB Health Campus
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

**and can be followed online**, accessible through the following link:
https://gf.vub.ac.be/redirects/PhD_defense_Fien_Meeus.php

## Summary of the dissertation

CAR-T cell therapy is a form of immunotherapy in which a patient's T cells are isolated and genetically engineered in the lab to express chimeric antigen receptors (CARs). CARs are synthetic receptors that give T cells the ability to recognize and kill cancer cells when they are reinfused into patients. While CAR-T cells have shown promising potential for treatment of blood cancers, their efficacy in solid tumors remains limited. To advance CAR-T cell therapy for solid tumors, we used camelid-derived antibody fragments, called nanobodies. We developed nanobody-based (nano)CARs that target B7-H3 and HER2, proteins that are highly expressed on cancer cells. Targeting B7-H3 on glioblastoma cells, we observed that nanoCARs were associated with potent antitumor function *in vitro* and *in vivo*, but showed a limiting reactivity towards healthy mouse tissue. Targeting HER2, we evaluated 12 nanoCARs for antitumor function towards glioblastoma, breast cancer and melanoma cells, and showed the potential of the lead nanoCAR to control tumor growth in mice. Finally, a major challenge in CAR-T therapy relates to accessibility owing to the high cost and complex manufacturing process associated with autologous CAR-T cell products. *In situ* CAR engineering represents a promising approach, to generate CAR-T cells within the patient's body, providing an off-the-shelf product. We used nanobodies to develop vehicles that can deliver CARs to T cells after their injection into the patient's bloodstream. We showed that these vehicles are able to generate functional HER2 CAR-T cells *in vitro*, providing promising potential for their further evaluation in mouse models to optimize dose and efficacy. Altogether, this study contributes to the advancement of CAR-T cell therapies for the treatment of solid tumors, laying a foundation for the implementation of this work in follow-up projects.

## Curriculum Vitae

Fien Meeus was born on the 17th of November 1997 in Ukkel, Belgium and grew up in Brussels where she went to high school, studying Latin and Mathematics. In 2015, she started studying biomedical sciences at the Vrije Universiteit Brussel (VUB), where she graduated her master's in 2020 with greatest distinction. Her interest in applied immunology, cancer immunotherapy and genetic engineering, brought her to the Molecular and Cellular Therapy research group and the Hematology and Immunology research group, to perform two master's internships. She performed her thesis internship at the Molecular Imaging and Therapy research group, where she focused on evaluating nanobodies as nuclear imaging tracers and for their implementation in CAR-T cell therapy for the treatment of multiple myeloma. After this, she pursued a PhD in Medical Sciences as part of a collaborative project performed at the Molecular and Cellular Therapy research group, under guidance of Prof. Dr. Karine Breckpot and the Molecular Imaging and Therapy research group, under guidance of Prof. Dr. Nick Devoogdt and Prof. Dr. Cleo Goyvaerts. She was supported by personal fellowships of the research foundation Flanders (FWO) and Kom op tegen Kanker and focused on advancing CAR-T cell therapy using nanobodies for the treatment of solid tumors, and on increasing accessibility to CAR-T cell products by developing an off-the-shelf alternative. She presented her research on national and international conferences, and her work led to two first-authored research papers, two co-first authored review papers and seven additional co-authored research publications. Performing this project fueled her continued interest in further advancing therapeutic strategies for the treatment of brain tumors, using cell therapies and genetic engineering.