Board of examiners

Prof. dr. Anna Orlova
Department of Medicinal Chemistry
Theranostics & Department of Immunology
Genetics and Pathology, Medical Radiation Science
Uppsala University, Sweden

Dr. Benedicte Descamps
Infinity Lab (IMIT Ghent, MEDISIP)
Faculty of Engineering and Architecture
Ghent University

Prof. dr. Eline Menu
Laboratory of Hematology and Immunology
Vrije Universiteit Brussel

Prof. dr. Kiavash Movahedi
Laboratory for Molecular and Cellular Therapy
Vrije Universiteit Brussel

Prof. dr. Vicky Caveliers, Chair
Department of Medical Imaging, Vrije Universiteit Brussel
Department of Nuclear medicine, UZ Brussel

Prof. dr. Nick Devoogdt, Promoter
Department of Medical Imaging
Vrije Universiteit Brussel

Prof. dr. Matthias D'Huyvetter, Promoter
Department of Medical Imaging
Vrije Universiteit Brussel

VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2020-2021

INVITATION to the Public defence of

Janik PUTTEMANS

To obtain the academic degree of **'DOCTOR OF MEDICAL SCIENCES'**

Radiolabeled single-domain antibody fragments for targeted radionuclide therapy of difficult-to-treat cancers

The defence will take place on **Thursday, 4th March 2021 at 5 p.m.**

and will be organised **online** accessible through the following link:

Please click here to join the public defence.

Klik hier om deel te nemen aan de vergadering

Summary of the dissertation

Most cancer cells are characterized by the (over)expression of certain transmembrane proteins – so called tumor-associated antigens. This dissertation describes the application of targeted radionuclide therapy (TRNT) using single-domain antibody fragments (sdAbs) that recognize these tumor-associated antigens in 2 preclinical models that mimic difficult-to-treat cancers, namely brain metastasis and multiple myeloma. So far, TRNT has mainly been explored using β^--emitting radionuclides. However, their long range causes irradiation of neighboring non-target cells. The efficacy of low energy, long range β^-- and high energy, short range α-particle emitting radionuclides was compared in both preclinical models.

Firstly, we describe efforts to generate a novel sdAb targeting EGFRvIII - a mutated form of EGFR - for the targeted treatment of glioblastoma. Despite the implementation of a myriad of panning and screening techniques, no selective anti-EGFRvIII sdAbs could be generated.

Secondly, we evaluated an anti-HER2 sdAb for detection and treatment of HER2-positive brain metastases. We demonstrated the superior efficacy of sdAb-based TRNT compared to two clinically implemented HER2-directed treatments, trastuzumab and ado-trastuzumab-DM1.

Thirdly, we describe the generation and therapeutic potential of α- and β^--radiolabeled sdAbs as tumor-restrictive vehicles against the murine 5T33MM-idiotypic paraprotein.

Analogously, we assessed the transferability of this approach towards sdAb-based personalized medicine for multiple myeloma. Using patient blood samples, we were able to develop sdAbs targeting patient-specific anti-idiotypic paraproteins that could be used for the targeted eradication of residual, treatment-resistant myeloma cells.

Curriculum Vitae

Janik Puttemans was born on August 23rd, 1989 in Vilvoorde, Belgium. In 2014, he obtained a professional bachelor's degree in Biomedical Laboratory Technology at the Erasmus Hogeschool Brussel, for which he visited the University of Örebro, Sweden, where he completed his bachelor's thesis. Afterwards, he started a master's program in Industrial Engineering, majoring in Biochemistry. During his final year of studies, he performed research at the Laboratory for Molecular and Cellular Therapy (VUB) under guidance of prof. Karine Breckpot. There he focused of the development of polymer-mRNA nanoparticles as anti-cancer vaccines. In 2016, he obtained his master's degree cum laude and started his PhD track at the Department of Medical Imaging (VUB) under the supervision of prof. Nick Devoogdt and prof. Matthias D'Huyvetter. During his PhD, he focused on the development of single-domain antibody fragments for several molecular cancer markers, mainly in the context of brain malignancies and multiple myeloma. These antibody fragments were then evaluated in therapeutic applications using several types of radionuclides. His research led him to Göteborg, Sweden and Warsaw, Poland as visiting scientist to gain experience in several radiolabeling methods.