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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2019-2020

INVITATION to the Public defence of

Katrijn BROOS

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

Evaluating single domain antibodies specific for PD-L1 as cancer nuclear imaging and therapy agents

Friday, 11 October 2019 at 5:30 p.m.
In Auditorium **Vanden Driessche**
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

How to reach the campus Jette:
http://www.vub.ac.be/english/infoabout/campuses

Summary of the dissertation

The immune checkpoints programmed death-1 (PD-1) and its ligand PD-L1 are major players in the escape of cancer cells from anticancer immune responses. Monoclonal antibodies targeting PD-1 and PD-L1 have shown unprecedented efficacy to treat advanced stage cancer, admitting in subsets of patients and selected cancer types. Therefore, developing innovative and efficacious theranostics that allow patient selection and monitoring next to effective treatment is warranted. Single domain antibodies (sdAbs), also-called nanobodies, are small sized, antigen-binding moieties that efficiently penetrate into tumors, and moreover generate high contrast in noninvasive imaging, making them prime candidates for development of novel theranostics. In this thesis, we report on the generation and validation of mouse or human PD-L1-specific sdAbs. Screening of alpaca immune libraries followed by further characterization using ELISA, flow cytometry and surface plasmon resonance (SPR), led to the selection of lead sdAbs that bind selectively and with high affinity to either mouse or human PD-L1. SPECT/CT imaging in mice using Technetium-99m-labeled sdAbs that target mouse or human PD-L1 revealed that the selected sdAbs generate high signal-to-noise ratios and have the strong ability to specifically detect mouse or human PD-L1 expression in multiple tumor models. Furthermore, we showed that sdAb K2, that binds with high affinity to human PD-L1, competes with the FDA-approved antibody avelumab for the binding to PD-L1 and has the ability to block the interaction between PD-L1 and PD-1, thereby facilitating *de novo* activation of antigen-specific T cells and enhancing the functionality of T cells. Taken together, these data indicate that sdAb K2 has a high potential as a theranostic agent in cancer management.

Curriculum Vitae

Katrijn Broos was born on the 1st of February 1991. In 2013 she finished her master of science in engineering, cum laude, at the Katholieke Universiteit Leuven. She wrote her Master thesis on the applicability of tSMAC mRNA to induce immunogenic cell death.

After that, she started her PhD program under supervision of Prof. Dr. Karine Breckpot, Prof. Dr. Nick Devoogdt and Prof. Dr. Marleen Keyaerts at the Laboratory for Molecular and Cellular therapy at the Vrije Universiteit Brussel. She obtained a doctoral grant from the "Agentschap voor Innovatie door Wetenschap en Technologie-Vlaanderen (IWT)" and an Emmanuel Van der Schueren scholarship from "Kom op tegen kanker" to finance her research. Her research focused on the evaluation of single domain antibodies specific for the immune checkpoint ligand PD-L1 as cancer nuclear imaging and therapy agents. Her research has been presented at several national and international scientific conferences and has resulted in 5 peer-reviewed publications as first author and a patent application. Furthermore, for her research on single domain antibodies as theranostic agents, she received the poster award at the Knowledge for Growth conference in Ghent.