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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2021-2022

INVITATION to the Public defence of

Quentin LECOCQ

To obtain the academic degree of

'DOCTOR OF MEDICAL SCIENCES'

Developing nanobodies to advance immune checkpoint therapy that targets lymphocyte activation gene-3

The defence will take place on

Tuesday, **23 November 2021 at 5 p.m.**
In Auditorium Piet Brouwer

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

ADMITTANCE: Due to Covid restrictions, please contact the PhD candidate if you want to attend the public defence in person.

and will be organised online
via Zoom meeting, accessible through the following link:

https://qf.vub.ac.be/redirects/PhD_defense_Quentin_Lecocq.php

Summary of the dissertation

The activation of immune cells is controlled by, amongst others, inhibitory immune checkpoints (ICPs). ICPs can prevent excessive inflammation, tissue damage and ultimately autoimmunity. Unfortunately, cancer cells exploit ICPs to generate additional defense mechanisms against the host's immune system. Monoclonal antibodies targeting the ICP PD-1 are currently being administered to cancer patients in order to reinvigorate anticancer immune responses. However, some patients do not benefit from these expensive treatments. It is therefore of interest to develop tools that allow selection of patients that are likely to respond to treatment. Nanobodies (Nbs), the smallest antigen-binding fragment derived from camelid heavy-chain only antibodies, are ideal candidates for the development of imaging tracers and therapeutics. In this thesis, we report on the development of Nbs for non-invasive imaging of the next-generation ICP lymphocyte activation gene-3 (LAG-3) and provide first evidence for their potential as therapeutic agents. A total of 9 and 16 Nbs targeting mouse LAG-3 and human LAG-3 respectively were selected. SPECT/CT imaging using ^{99m}Tc-labeled Nbs allowed us to visualize LAG-3 in healthy and in tumor-bearing mice. Moreover, PD-1 treatment resulted in a compensatory upregulation of LAG-3, which could be detected using anti-LAG-3 Nbs. Subsequently, treatment of tumor-bearing mice with both PD-1 and LAG-3 blocking agents showed synergic effects on the control of tumor growth. Moreover, we also explored the ability of our Nbs to revert inhibitory effects of LAG-3 on the activation of reporter T cells. Taken together, our data indicate that Nbs targeting LAG-3 hold potential as theranostics in the field of immuno-oncology.

Curriculum Vitae

Quentin Lecocq was born on June 16th, 1993 in Brussels, Belgium. In 2014, he obtained a bachelor's degree in Biomedical sciences at the Vrije Universiteit Brussel. As part of his master's program, he followed a research internship at the University of Sheffield, United Kingdom, under the guidance of Prof. Dr. Shelly Lawson and Prof. Dr. Andrew Chantry. During his final year of studies, he performed an internship at the Laboratory for Molecular and Cellular Therapy (LMCT, VUB) under guidance of Prof. Karine Breckpot. There, he focused on evaluating the use of nanobodies targeting the immune checkpoint PD-L1 as cancer therapeutics. In 2016, he obtained his master's degree magna cum laude and started his PhD track at LMCT under the supervision of Prof. Karine Breckpot, Prof. Nick Devoogdt and Prof. Marleen Keyaerts. During his PhD, he focused on the development of nanobodies, targeting the immune checkpoint LAG-3, as nuclear imaging tracers and cancer therapeutics. His research led him to several international conferences which resulted in being awarded for his oral presentations.