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PhD in Medical Sciences
2018-2019

INVITATION to the Public defence of

Ahmet KRASNIQI

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

**Targeted radionuclide therapy of non-Hodgkin lymphoma
with anti-CD20 single domain antibody fragments.**

Friday 24 May 2019

Auditorium Vanden Driessche, 17:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>

Summary of the dissertation

Anti-CD20 radioimmunotherapy has been shown to be an effective approach for the treatment of relapsed or refractory CD20-positive lymphomas. However, the prolonged circulation time of radiolabelled antibodies can lead to severe radiation exposure of healthy organs, causing side effects and myelotoxicity as an important dose-limiting factor.

Single-domain antibody fragments (sdAbs) are small fragments that bind their target very fast and specific, penetrate tumours and tissues very efficiently, and might circumvent the limitations of radiolabelled antibodies.

In this thesis, we described the generation of sdAbs against human CD20 antigen. Based on *in vitro* and *in vivo* characterization experiments, a lead compound was selected. When radiolabelled with Gallium-68 for imaging and with Lutetium-177 for targeted radionuclide therapy, the lead anti-CD20 sdAb showed specific tumour targeting in mice bearing human CD20 tumours, with low accumulation in non-target organs. Targeted radionuclide therapy with Lutetium-177 radiolabeled anti-CD20 sdAb significantly prolonged median survival of treated mice, without signs of toxicity. Finally, to recapitulate the human situation, the biodistribution of anti-CD20 sdAb was evaluated in human CD20 transgenic mice bearing human CD20 tumours.

In conclusion, in preclinical tumour models, we showed that radiolabelled anti-CD20 sdAb can be used as a theranostic tool for the treatment of CD20-positive lymphomas, and this with a very low toxicity profile compared to radiolabeled anti-CD20 antibodies.

Curriculum Vitae

Ahmet Krasniqi was born on 27th of November 1986 in Peje, Kosovo. After obtaining his Master degree in Biomedical Sciences at Vrije Universiteit Brussel, he started his PhD programme under supervision of Prof. Dr. Nick Devoogdt and Prof. Dr. Matthias D'Huyvetter at In Vivo Cellular and Molecular Imaging (ICMI) Laboratory of the Vrije Universiteit Brussel.

He obtained a doctoral grant from the Agentschap voor Innovatie door Wetenschap en Technologie-Vlaanderen (IWT) and Wetenschappelijk Fonds Willy Gepts to finance his research. During his PhD, he has been focusing on evaluating the potential of radiolabeled single domain antibody fragments for radionuclide-based imaging and targeted radionuclide therapy of Non-Hodgkin lymphoma. His research has been presented at several national and international scientific conferences and has resulted in 6 peer-reviewed publications, of which 3 as first author, and 1 patent application.