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Geneeskunde & Farmacie

GF

PhD in Medical Sciences
2014-2015

INVITATION to the Public defence of

Cleo GOYVAERTS

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

Targeting lentiviral vectors to antigen presenting cells

Friday 8 May 2015
Auditorium **P. Brouwer**, 16:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

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

Vrije Universiteit Brussel

Summary of the dissertation

Lentiviral vectors (LVs) represent multifunctional vaccine moieties as they can deliver a large genetic cargo to antigen presenting cells (APCs) *in situ*. However, systemic delivery of broad tropism LVs results in the infection of APCs as well as non-APCs, which brings along several safety concerns. Furthermore, in the past decade it became clear that APCs represent a heterogeneous population of cells with distinct functions, suggesting that not all APC subtypes are equally appropriate to stimulate a robust antitumor immune response. Therefore we proposed to target LVs to specific APC subtypes as we hypothesized that this could increase both their safety and efficacy profile. To generate APC subtype targeted LVs, we developed the nanobody (Nb) display technology. This strategy allows the inclusion of a fusogenic but binding-defective envelope glycoprotein together with an APC specific Nb on the LV's surface. The Nbs under investigation were Nb DC1.8, Nb DC2.1 and Nb R3_13. We characterized the transduction profile of the targeted LVs after *in vivo* or *ex vivo* intranodal injection of murine and human lymph nodes respectively. Furthermore, their potential to stimulate an ovalbumin specific immune response as well as their therapeutic benefit in murine tumor models was evaluated. We show that the Nb display technology allows the generation of APC subtype specific LVs with a safer kinetic profile. Furthermore, we demonstrated that the transduction of APCs alone is not enough to induce a robust and therapeutic cellular response but can suffice to stimulate $CD4^+$ T cells. While the latter may not be enough for antitumor immunotherapy, this could open possibilities for diseases in which the $CD4^+$ T cells play a leading role such as autoimmunity, allergy and transplantation rejection.

Curriculum Vitae

Cleo Goyvaerts (°Bonheiden, 29/10/1986) graduated in 2004 at the Heilig Hart College in Heist op den Berg. In that same year she started her education in Veterinary Sciences at the University of Ghent (UGent). Although she obtained her Bachelor in Veterinary Sciences three years later, she decided to switch to an education in Biochemistry and Biotechnology at the UGent for which she obtained her Master degree in 2010 with highest distinction. Her master dissertation was a joined cooperation between the UGent and Vrije Universiteit Brussel (VUB) under the supervision of Profs. Xavier Saelens, Johan Grooten, Kris Thielemans and Karine Breckpot. It was during this training period that she acquired a taste for research with targeted lentiviral vectors and antitumor immunotherapy. Therefore she was determined to start her scientific career with the PhD project entitled: 'Dendritic Cell Targeted Lentiviral vectors' at the Laboratory of Molecular and Cellular Therapy (VUB) under supervision of Profs. Karine Breckpot and Kris Thielemans. This PhD project was funded the first year by an OZR-VUB scholarship, followed by four years of funding through a FWO aspirant mandate (2010-2015). During her PhD she had the opportunity to guide master students and present her work on several national as well as international conferences. Furthermore she took the opportunity to perform a training period abroad at the Laboratory of Regenerative Immune Therapies Applied of Prof. Renata Stripecke at the Medizinische Hochschule Hannover in Germany (2014). Finally, her scientific research led to multiple publications in international, peer-reviewed journals, as author or co-author and eventually led to the submission of a PhD thesis to obtain the degree of Doctor in Medical Sciences.