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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2020-2021

INVITATION to the Public defence of

Yannick De Vlaeminck

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

TAMING cancer:
TArgeting Myeloid cells using INnovative Gene-based technologies

The defence will take place on **Wednesday, 3rd March 2021 at 4:30 p.m.**

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

Public PhD defence

QR-code:

Summary of the dissertation

The immune system developed as a way to protect the body from infectious agents. However, the immune system also plays multiple roles in diseases such as cancer, being implicated in its initiation and progression as well as its control. This is explained by the multitude of immune cells that can intricately communicate with malignant cells. On the one hand, professional antigen-presenting cells (APCs) can instruct T cells to eliminate cancer cells while on the other hand tumor-associated macrophages (TAMs) can elicit tumor progression, metastasis and therapy resistance. This knowledge instigated us to develop lentiviral vectors (LVs) encoding an antigen and display APC targeting nanobodies (Nbs) on their surface allowing to restrict their tropism to these cell types. However, a lack of efficacy of APC targeted LVs was seen due to the cytokine milieu resulting from the transduction of only APCs, which was characterized by a type I interferon response as well as the lack of stromal cells that assist in antigen presentation. This lack of efficacy prompted us to develop TAM targeted Nb fusion proteins containing the pro-apoptotic second mitochondria-derived activator of caspase linked with a macrophage mannose receptor targeting Nb. We showed that the majority of TAMs could be depleted and that surviving TAMs adopted an anti-tumor phenotype. Finally, we identified Nbs that bind and antagonize neuropilin-1, a co-receptor expressed on TAMs that is involved in several cancer related processes. Using a gene-based strategy, we showed a delay in growth of tumors, which might be explained by a shift from alternatively activated TAMs to classically activated TAMs as well as an increase in tumor-specific T cells. These findings pave the road for selective manipulation of APCs and TAMs using a gene-based approach, thereby favoring anti-cancer immune responses, while reducing tumor-promoting events.

Curriculum Vitae

Yannick De Vlaeminck started working as a lab technician in 2009 at the Center of Medical Genetics (UZBrussel, Belgium), performing research in neurogenetics. In 2015, he finished his Master of Biomedical Sciences, magna cum laude, at the Vrije Universiteit Brussel. He wrote his thesis on gene-based strategies to manipulate myeloid cells in cancer which was awarded as best master thesis by the "Stichting tegen Kanker".

After that, he started a PhD program under supervision of Prof. Karine Breckpot, Prof. Jo Van Ginderachter and Prof. Cleo Goyvaerts at the Laboratory for Molecular and Cellular Therapy (LMCT). He obtained doctoral grants from "Kom op tegen Kanker" (Emmanuel Van der Schueren), ORC (Oncology Research Center) and the "Fonds voor Wetenschappelijk Onderzoek" (FWO-SB) to finance his research.

His research focused on the development of gene-based myeloid cell targeting therapies using innovative tools such as lentiviral vectors and nanobodies. His work has been presented at several national and international scientific conferences and resulted in several awards and 5 peer-reviewed publications as first author.