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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2022-2023

INVITATION to the Public defence of

Hanne LOCY

To obtain the academic degree of

'DOCTOR OF MEDICAL SCIENCES'

In situ mRNA vaccination : bringing the fight to the tumor

The defence will take place on

Thursday, **1 December 2022 at 5:30 p.m.**

In Auditorium Vanden Driessche
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

and can be followed online, accessible through the following link**:**

https://gf.vub.ac.be/redirects/PhD_defense_Hanne_Locy.php

Summary of the dissertation

Breast cancer is the most common cancer in women worldwide. When diagnosed early, breast conserving surgery is the preferred therapy. As recurrence of breast cancer cells often occurs, treatment options that are minimally invasive and can activate the immune system, providing an immune memory, are required. Also, as breast cancer is a heterogeneous disease, there is an unmet need to (molecularly) portrait the disease to stratify patients for precision therapy. The current project aimed to locally deliver an immunomodulating mRNA mix, *i.e.,* TriMix, in early-stage breast cancer patients to turn the tumor into an auto-vaccine, enabling tumor associated dendritic cells to stimulate long-lasting antitumor immunity. Since the tumor is a complex and dynamic 'organ', it is important to comprehend the spatial and temporal changes that occur. This tumor immune contexture can be used to estimate cancer prognosis and therapy management and even so response. Since tumor infiltrating lymphocytes (TILs) reflect a favorable host antitumor immune response, this parameter is included in clinical practice, highlighting the need for robust assessment. Therefore, we combined immunohistochemistry with gene expression profiling to obtain spatial and semi-quantitative TIL data, while gaining insight in expressed genes and their relation to different immune contextures. To perform these assays, we optimized and validated start material and the subsequent data-analysis pipeline. Overall, we show that both technologies can help unravel cellular and transcriptome components of tumors and that intratumoral delivery of TriMix mRNA was feasible, well-tolerated in early stage breast cancer patients and suggestive for an immunomodulatory effect of the procedure as well as the investigational drug.

Curriculum Vitae

Hanne Locy was born on the 31st of December 1990. In 2008, she finished her secondary school at Sint-Pieters Instituut in Ghent, graduating Latin-Mathematics. She graduated with magna cum laude as a Master in the Biomedical Sciences at the University of Ghent with a specification 'Degeneration and Regeneration'. Subsequently, she obtained expertise during one year in the industry as a 'Contracts and Proposal Manager'. To intensify her scientific knowledge and to contribute to clinical applications, she joined the Laboratory for Molecular and Cellular Therapy, back then under the supervision of Prof. Dr. Kris Thielemans. She was awarded a personal VLAIO Baekeland mandate with the project 'In situ mRNA vaccination: bringing the fight to the tumor', the start of a joint PhD project between the Vrije Universiteit Brussel and eTheRNA Immunotherapies NV. The PhD project focused on the local delivery of the (proprietary) immunomodulatory TriMix mRNA in early stage breast cancer patients, making use of immunohistochemistry and nanoString gene expression profiling to investigate the immunomodulating capacity of the investigational drug. During her PhD, she published 4 manuscripts in peer-review journals as first author and co-authored 5 other articles. Her work has been presented at a national and international conference. In December 2022, Hanne can be found at the Pathology Department in the University Hospital of Brussels, where she will function as a Scientific Liaison between the University Hospital and the Vrije Universiteit Brussel.