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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2021-2022

INVITATION to the Public defence of

Sven DE MEY

To obtain the academic degree of

'DOCTOR OF MEDICAL SCIENCES'

Barriers in radiobiology : Hypoxic radiosensitization by modifying the metabolism of the tumor

The public defence will take place on

Tuesday, **28 June 2022 at 7 p.m.**

In Auditorium Piet Brouwer
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_Sven_De_Mey.php

Summary of the dissertation

Cancer is one of the most common diseases in the developed world. One in six deaths are due to cancer, ranking this disease as the second leading cause of death, only preceded by heart diseases. Radiotherapy represents an essential treatment modality in cancer management, either alone or combined with other therapies. Over the past few decades, technological advances and clinical research have given radiation oncologists the capability to personalize treatments for accurate delivery of radiation dose based on clinical parameters and anatomical information. However, there is a lot of heterogeneity in the clinical responses to radiotherapy between different cancer types and even within the same cancer type. Resistance to radiotherapy is polymodal and associated with several biological alterations both within the tumor and the surrounding microenvironment.

In this work, we used a practical research approach to find genetic prognostic indicators (pathways or biological processes) that influence the radioresistance of three different cancer types. We found that gene signatures linked to radiobiological pathways, metabolism and proliferation for the cells had prognostic associations with overall survival of the patients.

In a next step, we demonstrated that multiple possible metabolic paths can be taken to radiosensitize hypoxic cancer cells. We have first demonstrated that dichloroacetate (DCA) can shift glycolysis to OXPHOS of the cancer cells even under hypoxic conditions, which leads to enhanced radiorespons of both aerobic and hypoxic tumor cells through increased reactive oxgyen species (ROS).

We continued on the alteration the metabolism of tumor cells by showing that the anti-diabetic drugs metformin and phenformin could block the mitochondrial complex I. By blocking the OXPHOS of the cells, we reduced their OCR. The reduced oxygen consumption of the cells counteracted the hypoxic radioresistance both in cells and tumor-bearing mice.

Lastly, we discussed the possibility of using metformin and modified IL-2 as a potential immunocorrective drug in colorectal cancer. DCA, metformin and phenformin are all under clinical investigation. The data from our studies will provide new insight into their development of them as radiosensitizes and accelerate the design of clinical trials in combination with radiotherapy.

Curriculum Vitae

Sven de Mey was born on 21st February 1991. In 2009, he finished his secondary school at Maria Boodschaplyceum in Brussels. He graduated as a Master of Bioscience Engineering at the Katholieke Universiteit Leuven (KUL) with a specialization in Cellular and genetic engineering. Afterwards, he joined the Translational Radiation Oncology and Palliative Care (TROP) lab under the supervision of Prof. Dr. Mark De Ridder in 2015 as a PhD researcher. He focused during his PhD research on how to radiosensitize cancer cell by influencing the metabolism. During his PhD, he published 5 manuscripts in peer-review journal as first author and co-authored 5 other articles. His work has also been presented at several national and international conferences. In April 2021, Sven made the switch from academia to industry and is active as a medical advisor at Sandoz.