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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2018-2019

INVITATION to the Public defence of

Inès DUFAIT

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

Myeloid-derived suppressor cells as a novel therapeutic target in colorectal cancer.

Wednesday 19 December 2018
Auditorium **Piet Brouwer**, 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

In this PhD thesis, we mainly focused on the immunosuppressive aspects of the tumor micro-environnement (TME), more specifically on myeloid-derived suppressor cells (MDSCs). It is becoming increasingly clear that MDSCs hamper anti-tumor immune responses across different tumor types. Using multiple platforms, we generated mouse *in vitro* MDSCs and provided a proof-of-concept that the generated MDSCs resembled those found within the TME. Additionally, targeting these MDSCs was shown to be predictive for the outcome in tumor-bearing mice. Furthermore, we demonstrated that depletion of L-arginine by Arg-1^{+} MDSCs, as is the case in the TME, contributes to enhanced protection of tumor cells to irradiation. Simultaneously, we provided a proof-of-concept of the potential to identify new targets using our *in vitro*-generated mouse MDSCs. Perforin and granzyme B were shown, for the first time, to be present on MDSCs of mouse and human origin.

Although the availability of a platform to generate mouse MDSCs is of high importance, it would be even more substantial to translate this into a human setting. Therefore, we validated different human precursor cells as a starting point for MDSC cultures using a similar differentiation strategy as proven successful in the murine setting.

To conclude, we made considerable advances in the field of MDSC research by developing an *in vitro* MDSC platform that allows in depth analysis of these MDSC's biology and strategies to manipulate these cells, thereby enhancing both basic and applied immunological research.

Curriculum Vitae

Inès Dufait initiated her career at the VUB in 2007, when she started studying biomedical sciences. During this period she performed one short internship abroad, at the division of infection and immunology of the University College London. She concluded her education with her master thesis "Myeloid-derived suppressor cells as a biomarker of tumor growth and radiosensitivty: Role of hypoxia-inducible arginase-1", which she defended in June 2013.

For her PhD she returned to the field of cancer immunology and obtained in December 2013 an IWT SBO grant, which allowed her to perform basic research for four years. An additional grant from Kom op Tegen Kanker prolonged this period with another 6 months. During this period, she published three first author papers and contributed to several other manuscripts. She presented her work on national and international congresses.