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Hematology and Immunology
Vrije Universiteit Brussel

Prof. dr. Rik Schots, Promoter

Hematology and Immunology
Vrije Universiteit Brussel



PhD in Medical Sciences
2018-2019

INVITATION to the Public defence of

Sylvia FAICT

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

**Exosomal Communication in Multiple Myeloma
-Friend or Foe-**

Monday, 23 September 2019 at 5 p.m.

In Auditorium **Piet Brouwer**

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>

Summary of the dissertation

Multiple Myeloma (MM) is a plasma cell malignancy in which monoclonal plasma cells accumulate in the bone marrow (BM). The interaction between the BM cells and MM is pivotal to the progression of MM and forms therefore an attractive target. The BM aids in the growth of these malignant cells by providing them with necessary growth factors & nutrients, creating an immune compromised environment and inducing drug resistance.

In this dissertation, we aimed to explore the role and function of exosomes in MM. We first demonstrated that exosomes are implicated in MM bone disease by inhibiting osteoblast differentiation and stimulating osteoclast function.

More importantly, we also showed an added effect in vivo of exosome inhibition to bortezomib on tumor load in the 5TGM1 mouse model.

Secondly, we performed a lipidomic analysis on peripheral plasma of MM patients. We found several differences in lipid composition between healthy and MM human plasma. This led to the discovery and evaluation of a new therapeutic target in MM, i.e. acid sphingomyelinase (ASM), which can be transported between cells by MM exosomes. The inhibition of this enzyme by amitriptyline led to an increased drug sensitivity to both melphalan and bortezomib.

This study further uncovers the role of exosomes secreted by MM cells in inducing osteolysis and drug resistance and confirms that these exosomes present an attractive target in the treatment of MM.

Curriculum Vitae

Sylvia Faict finished her medical education, summa cum laude, at the Vrije Universiteit Brussel in 2015. She wrote her Master's thesis on the quality of life after autologous stem cell transplantation in Lymphoma and received the Nedeljkovic award for outstanding results in her Master of Medicine.

Next, she obtained a research grant from the Research Foundation Flanders (FWO Vlaanderen) and started her PhD at the lab of Hematology and Immunology, under the expert supervision of Prof. Dr. E. Menu, Prof. Dr. K. Vanderkerken and Prof. Dr. R. Schots. Her research is focused around the role of extracellular vesicles and exosomes in Multiple Myeloma.

Simultaneously, she has been working as a resident-in-training for Internal Medicine / Hematology at the University Hospital UZ Brussel.

During the four years of her doctoral training, she published two papers as a first author and co-authored four other papers. A final paper as first author is currently still under review.

For her research on Multiple Myeloma she received various awards, including the New Investigator Award from the Cancer and Bone Society in June 2018. Her work was presented at different European and Transatlantic conferences.