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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2019-2020

INVITATION to the Public defence of

## Anke MAES

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

# Exploring the therapeutic potential of targeting mitotic exit in combination with standard of care agents in high grade B cell malignancies.

**Monday, 18 November 2019 at 5 p.m.**
In Auditorium **Vanden Driessche**
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

Diffuse large B cell lymphoma (DLBCL), multiple myeloma (MM) and mantle cell lymphoma (MCL) are among the most common B cell malignancies. Despite recent advances in disease management, virtually all MCL and MM patients and ±30-40% of the DLBCL patients still relapse. These 3 malignancies are all characterized by a high proliferation index, especially in the high risk/relapse setting. Blocking this uncontrolled proliferation might therefore be an interesting approach in the treatment of these diseases.

In this thesis, we aim to explore the therapeutic potential of targeting proteins involved in mitotic exit in MM, DLBCL and MCL.

First, the therapeutic potential of blocking the anaphase promoting complex/cyclosome (APC/C) and its co-activator Cdc20 was explored in MM, DLBCL and MCL, using the small molecule inhibitor proTAME. This inhibition resulted in a metaphase arrest, subsequently leading to (caspase-3 dependent) cell death. Secondly, the biological role of maternal embryonic leucine zipper kinase (MELK) and the therapeutic potential of MELK inhibition was examined in DLBCL and MCL. Blocking MELK, using the small molecule OTSSP167, impaired cell growth, induced caspase-mediated apoptosis and sensitized the cells to venetoclax. Moreover, OTSSP167 treatment of A20-inoculated mice resulted in a significant prolonged survival. Taken together, this study indicates that both APC/C ad MELK could be potential new targets in the treatment of these high grade B cell malignancies.

## Curriculum Vitae

Anke Maes finished her master in the Biomedical sciences, cum laude, at the Vrije Universiteit Brussel in 2014. She wrote her master thesis on the inhibition of the E3 ubiquitin ligases IAP and APC/C in multiple myeloma.

After that, she started her PhD at the laboratory of Hematology an Immunology, under the supervision of Prof. Dr. Karin Vanderkerken and Prof. Dr. Elke De Bruyne. Her research focused on the inhibition of the mitotic progression in the high grade B cell malignancies diffuse large B-cell lymphoma and mantle cell lymphoma. Simultaneously, she has been working as coordinator of the Oncology Research Center at the Vrije Universiteit Brussel since 2018.

During the five years of her doctoral training, she presented her work at multiple (inter)national conferences and published three peer-reviewed papers as a first author and co-authored four other papers. For her research on blocking the APC/C as a therapeutic target in lymphoma, she received the Abstract Achievement Award at the American Society of Hematology in Atlanta.