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PhD in Medical Sciences
2017-2018

INVITATION to the Public defence of

Nathan DE BEULE

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

Bone marrow-induced survival: identifying novel targets in multiple myeloma.

Tuesday April 24th, 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

Along with the continuous introduction of new therapeutic agents, overall survival of multiple myeloma (MM) patients has significantly improved. However, the majority will eventually relapse and become refractory to treatment. Both cellular and non-cellular components of the bone marrow microenvironment play a crucial role in the development of resistance, including a complex (BM) interplay of cytokines, chemokines, growth factors, exosomes, proteolytic enzymes and adhesion molecules. A better insight in these processes may lead to new therapeutic strategies.

We explored different BM microenvironment targeting strategies in the immunocompetent 5TMM model. In a first project, we explored the role of tumor-associated macrophages (TAMs) on myeloma cell survival and drug resistance. We found that the macrophage-induced pro-survival effect was associated with activation of the STAT3 pathway in 5T33MM cells. In a second project, we found that *T. brucei* induced intrinsic apoptosis of 5T33MM cells *in vivo*, and that this effect was associated with reduced endogenous unfolded protein response (UPR) activation.

The effect of novel therapeutic agents was also investigated in the 5TMM model. Treatment with the integrin inhibitor G038887 had no direct effect on tumor load but was able to prolong survival. We also examined the effect of the Bruton tyrosine kinase inhibitor ibrutinib on MM cell survival and the BM microenvironment but were not able to detect a significant impact on tumor load or bone destruction.

Curriculum Vitae

Nathan De Beule was born on 14/01/1987 in UZ Brussel hospital, Jette. In 2005 he started his studies in medicine at the Vrije Universiteit Brussel. The interest for hematology arose through a combination of a scientific/clinical internship at the hematological department of Aarhus University, Aalborg, Denmark in 2011 under supervision of Prof. Dr. Hans. E. Johnsen and the making of a master thesis entitled: "Multiple myeloma in the era of novel agents: a single center experience." under supervision of Prof. Dr. Rik Schots, head of the department of Hematology, UZ Brussel in 2012. In June 2012 he obtained his MD with maxima cum laude.

In October 2012, after obtaining a grant from the FWO, he started his PhD research in the Laboratory of Hematology and Immunology (HEIM) at the Myeloma Center Brussels of the Vrije Universiteit Brussel (VUB) under the supervision of Prof. Dr. Karin Vanderkerken, Prof. Dr. Eline Menu, Prof. Dr. Els Van Valckenborgh and in close collaboration with the department of Hematology under supervision of Prof. Dr. Rik Schots. Research focused on revealing mechanisms involved in BM-induced survival of myeloma cells. His scientific research resulted in publications in international peer-reviewed journals. He has also presented his research data during various national and international congresses.

From October 2016 until today, he has been working as a clinician to further specialize in clinical hematology.