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PhD in Medical Sciences
2015-2016

INVITATION to the Public defence of

Jinheng WANG

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

**Exosomal communication in the bone marrow
microenvironment: a significant player in multiple
myeloma progression**

Promotors: Prof. Karin Vanderkerken,
Prof. Eline Menu

Friday 15 April 2016

Auditorium **Vandendriesche**, 14:30
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

Multiple Myeloma (MM) is an incurable plasma cell neoplasm characterized by an accumulation of malignant plasma cells in the bone marrow (BM). Its pathogenesis and progression largely rely on the cells and extracellular factors in the BM microenvironment. The interplay between bone marrow stromal cells (BMSCs) and MM cells plays a crucial role in MM pathogenesis by the secretion of growth factors, cytokines, and extracellular vesicles. Exosomes are 40-100 nm diameter membranous vesicles constitutively released by almost all cell types and they mediate local cell-cell communication by transferring mRNAs, miRNAs and proteins. However, the roles of BMSC- or MM cell-derived exosomes in the cell-to-cell communication and MM progression have not been elucidated yet.

In this thesis, we demonstrated the involvement of exosomes in the communication between BMSCs and MM cells, and revealed that BMSC-derived exosomes directly facilitated MM progression by promoting MM cell proliferation, migration, survival, and induction of drug resistance through multiple signaling pathways including JNK, p38, p53, and Akt. In addition, BMSC-derived exosomes activated MDSCs in the BM through STAT3 and STAT1 pathways, leading to increased immunosuppression which favors MM progression. Moreover, MM cell-derived exosomes can modify the BM microenvironment by promoting BMSC growth, angiogenesis, and enhancement of the immunosuppressive capacity of MDSCs. The modified BM microenvironment by both BMSC- and MM cell-derived exosomes will further facilitate MM cell growth, MM progression, and induction of drug resistance.

Curriculum Vitae

Jinheng Wang was born on 09/01/1986 in Henan, China. From 2003 to 2007, he studied Biotechnology at Henan Institute of Science and Technology in Henan and obtained his Bachelor degree in July 2007. Thereafter, he worked as a research staff at R&D Center of Caixin Sugar Co.Ltd until August 2009. From September 2009 to July 2012, he studied Immunology at Xinxiang Medical University in Henan and obtained Master degree. From October 2012, 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. Karin Vanderkerken, and Prof. Eline Menu. His research focused on identifying the role of exosomes in MM progression. His scientific research resulted in publications in international peer-reviewed journals. He has also presented his research data in some national and international congresses.