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Department of Hematology and Immunology
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Doctoraat Medische Wetenschappen
PhD in Medical Sciences
2011-2012

Openbare verdediging van/*Public defence of*

Song XU

Voor het behalen van de academische graad van
'DOCTOR IN DE MEDISCHE WETENSCHAPPEN'
To obtain the academic degree of
'DOCTOR IN MEDICAL SCIENCES'

Biological properties of mesenchymal stem cells in the multiple myeloma tumor microenvironment

Promotor: prof. Ivan Van Riet

Co-promotor: prof. Karin Vanderkerken

Thursday 13 September 2012

Auditorium 1, 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>

Please confirm your presence to songxu@vub.ac.be



Situering van het proefschrift/*Summary of the dissertation*

Multiple Myeloma (MM) is a hematological malignancy characterized by a clonal proliferation of plasma cells in the bone marrow (BM). The crosstalk between BM stromal cells and MM cells supports the proliferation, survival, migration and drug resistance of MM cells, as well as osteoclastogenesis and angiogenesis. Mesenchymal stem cells (MSCs) are multipotent progenitors that can differentiate into a variety of cell types and are the main precursor cells of the BM stroma. However, the direct involvement of MSCs in the pathophysiology of MM has not been well addressed.

With this research work we determined that MSCs can be attracted by MM cell produced CCL25 and favor MM cell growth in vitro and in vivo. Moreover, we demonstrated that dysregulated Notch signaling and miR-135b expression are two possible mechanisms involved in the impaired osteogenic differentiation of MSCs from MM patients. In addition, we developed an optimal protocol to culture murine MSCs in vitro, and discovered that HDAC inhibitor Vorinostat does not induce bone loss in contrast to previous findings.

Collectively, our data suggest that MSC-based cytotherapy has a potential risk for MM disease progression or relapse. Targeting endogenous MSCs osteogenesis by inhibiting Notch signaling or miR-135b expression might be a promising strategy to control bone disease in MM patients.

Curriculum Vitae

Song Xu was born on January 18, 1982 in Tianjin, P.R. China. Since 2000, he was enrolled in the Faculty of Clinical Medicine in Tianjin Medical University. Besides his study and training in clinical medicine he was also devoted to scientific research. From 2006 to 2007, he worked on gene therapy in glioma for his master thesis in the Neuro-oncology Laboratory, Neurological Institution of Tianjin Medical University General Hospital. This work was published in (inter) national peer-reviewed journals. In June 2007, he obtained his master degree (M.D.) with great distinction, and was subsequently appointed as a surgeon in the department of lung cancer surgery, Tianjin Medical University General Hospital. In October 2007, Song Xu got a scholarship from the China Scholarship Council (CSC) and started his PhD study at the Vrije Universiteit Brussel (Belgium) in the research group Hematology and Immunology under the supervision of Prof. Dr. Ivan Van Riet and Prof. Dr. Karin Vanderkerken. His research work was focused on the role of mesenchymal stem cells in the tumor microenvironment of multiple myeloma. His findings have been presented during several (inter)national meetings and were published in peer-reviewed journals.