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PhD in Medical Sciences
2014-2015

INVITATION to the Public defence of

Sarah MAENHOUT

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

Enhancing therapeutic vaccination in melanoma by alleviating STAT3-mediated immune suppression**Thursday 3 September 2015**

Auditorium **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>



Vrije Universiteit Brussel

Summary of the dissertation

Despite the fact that the immune system is able to recognize and kill tumor cells, immunotherapy rarely induces objective tumor regression. It has become clear that inhibitory cell types, such as myeloid-derived suppressor cells (MDSCs), are crucially involved in dampening effector T-cell functions.

Although the main site of action for MDSCs is most likely the tumor, so far the study of these cells has been largely restricted to the spleen. Therefore, we first compared the suppressive capacity and suppressive mechanisms used by splenic and tumor-derived MDSCs in different mouse tumor models. We showed that tumor-infiltrating MDSCs possess a stronger suppressive capacity than non-infiltrating MDSCs and that various suppressive mechanisms, including a higher nitrite production and arginase activity, account for this differences.

Given the important role these MDSCs play in the suppression of anti-tumor immune responses, different drugs are being developed to specifically target this cell population in order to alleviate their immunosuppressive function. In a second study we investigated the effects of AZD1480, a potent competitive small-molecule inhibitor of JAK1/2 kinases, on the function of different immune cell populations in a melanoma model. We showed that although AZD1480 has the ability to delay the tumor growth of MO4 tumor-bearing mice, this drug has detrimental effects on several aspects of the immune system, including an enhanced suppressive capacity of MDSCs and an impaired proliferation and cytokine secretion of T cells. Taken together, caution should be taken when treating cancer patients with JAK-STAT inhibitors, especially when combining them with immunotherapy.

Curriculum Vitae

In 2010, after a 1 year internship at the Laboratory of Molecular and Cellular Therapy (LMCT), Sarah Maenhout (° Jette, 25/11/1987) graduated, with great distinction, at the Vrije Universiteit Brussel as a Master in Biomedical Sciences. During her master thesis she developed a special interest in immunosuppressive mechanism preventing an effective immune response in cancer patients. She started her doctoral studies on this topic at the LMCT under the supervision of Prof. Dr. Kris Thielemans and Prof. Dr. Joeri Aerts and was funded by the Flanders agency for Innovation and Technology (IWT). The results of her research work were presented as oral and poster presentations at several national and international conferences. Moreover, her scientific research led to multiple publications in international, peer-reviewed journals, as first author and as co-author, and eventually led to the submission of a PhD thesis to obtain the degree of Doctor in Medical Sciences.