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Department of Medical Oncology
UZ Brussel

PhD in Medical Sciences
2015-2016

INVITATION to the Public defence of

Stephanie DU FOUR

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

The bidirectional link between tumor angiogenesis and immunity.**Wednesday 27 January 2016**

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

Melanoma brain metastases are associated with a poor prognosis and are characterized by excessive neo-angiogenesis, which frequently leads to intracranial hemorrhage. The dominant regulator of angiogenesis is the Vascular Endothelial Growth Factor (VEGF) and its main receptor VEGF receptor 2 (VEGFR-2). Tumor cells secrete high amounts of VEGF, which leads to uncontrolled formation of immature blood vessels. Besides its role in tumor angiogenesis, VEGF also has a strong immunosuppressive effect. Thus, targeting the VEGF-VEGFR pathway has become an important antitumoral strategy. Recently, immunotherapy has shown to increase the overall survival of patients with metastatic melanoma. However, in patients with melanoma brain metastases immunotherapy has limited activity due to the natural immunosuppressive environment present in the brain.

We investigated whether axitinib, a tyrosine kinase inhibitor against VEGFR-1, -2 and 3, can enhance the antitumor immune response in monotherapy or when combined with immunotherapy. Firstly, we showed that axitinib reduces tumor growth and increases survival through reduction of the immunosuppressive microenvironment in subcutaneous and intracranial mouse melanoma models. Secondly, when axitinib was combined with immunotherapy we observed a stronger reduction of tumor growth and an increased antitumor immune response. Thirdly, we demonstrate that axitinib has beneficial effects on the immune system of recurrent glioblastoma patients, however patients with progressive disease displayed an enhanced preexisting immunosuppression. In conclusion, we showed that combining antiangiogenesis with immunotherapy has beneficial effects on the antitumor immune response

Curriculum Vitae

Stephanie Du Four was born on the 23rd of May 1986 in Oostende. In 2011 she obtained her medical degree at the Vrije Universiteit Brussel, summa cum laude. Immediately after graduation she interrupted her internship in the department of Neurosurgery to start her PhD on the bidirectional link between tumor angiogenesis and immunotherapy in the Laboratory of Molecular and Cellular therapy (LMCT) at the Vrije Universiteit Brussel (VUB). During the first year of her research she obtained a research grant Emanuel Van Der Schueren from the Vlaamse Liga tegen Kanker and received the grant of the Medical Foundation Mathilde Horlait Dapsens for a research internship in Luxemburg. From February 2012 until August 2012 she developed an intracranial melanoma model under the surveillance of Dr. Simone Niclou at the Norlux laboratories in Luxemburg. In December 2012 she obtained a PhD grant from the Agency for Innovation by Science and Technology in Flanders (IWT) and performed the further research in the LMCT laboratory of the VUB. In August 2015 she resumed her medical training in neurosurgery.