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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2017-2018

INVITATION to the Public defence of

Lukasz BIALKOWSKI

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

Combination therapy for a durable tumor rejection

Tuesday 16 January 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

The objective of cancer immunotherapy is to induce potent and long-lasting immune responses that allow the patients' own immune system to destroy large tumor masses and prevent disease recurrence over time. Recent advances in immunotherapy resulted in promising clinical anti-tumor responses. Nevertheless, an important challenge remains the development of tumor resistance and disease progression during or after therapy. Therefore, the focus of this thesis lies on the improvement of an mRNA-based immunotherapy in order to prevent tumor regrowth after a period of initially successful therapeutic activity.

In the first part, we demonstrated that immunotherapy efficacy largely depends on tumor location. Our findings showed that a highly suppressive TME of genital tract tumors could be abrogated by systemic use of cisplatin. Combination of the mRNA vaccine with cisplatin led to a complete and durable rejection of the majority of tumors.

In the second part, we demonstrated that immunotherapy was associated with an increase in the number of cancer stem cells. We therefore investigated the disruption of IL-6/TGF-β pathways, thought to promote cancer stem cells with the blockade of three immune checkpoint molecules. This combination therapy significantly improved the therapeutic outcomes of the mRNA vaccine, leading to a complete tumor rejection in part of treated mice.

In this thesis we demonstrate that there is still a need for the development of combination immunotherapies aiming at induction of potent tumor-specific immunity, boosting TILs and simultaneously targeting tumor escape mechanisms. Particularly for patients with advanced metastatic disease combinatorial immunotherapy may hold the greatest promise of success.

Curriculum Vitae

Lukasz was born on 14 May 1987 in Pila, Poland. He studied history at University of Gdansk and laboratory medicine at Medical University of Gdansk. In February 2011, he started his career at Vrije Universiteit Brussel by joining the Laboratory of Molecular and Cellular Therapy (LMCT) as Erasmus student. His primary focus was the induction of cellular immunity against cancer stem cells. After graduation, he continued working at the LMCT as PhD student. He obtained an IWT-SBO grant in December 2012. During his PhD, Lukasz investigated the combination of mRNA-based immunotherapy of HPV-associated tumors with chemotherapy or immunomodulaing monoclonal antibodies.