

The Research Group
Cellular and Molecular Immunology

has the honor to invite you to the public defence of the PhD thesis of

Emile Clappaert

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Dendritic cell-based cancer immunotherapy: increasing intratumoral dendritic cell abundance and potential for vaccination

Promotors:

Prof. dr. ir. Damya Laoui (VUB)

Prof. dr. ir. Jo Van Ginderachter (VUB)

The defence will take place on

**Friday, December 15, 2023 at 16h in the
Green Room (U-Residence)**

The defence can also be followed through a
live stream: [Click here](#)

Members of the jury

Prof. dr. ir. Wim Versées (VUB, chair)

Prof. dr. ir. Benoît Stijlemans (VUB, secretary)

Prof. dr. Kim De Veirman (VUB)

Prof. dr. Evelien Smits (UAntwerpen)

Dr. Barbara Maier (Austrian Academy of Sciences,
Austria)

Curriculum vitae

Emile Clappaert graduated as Master of Biology at KU Leuven in 2017, after which he joined the lab of BCIM at VUB in 2018 as assisting academic staff. During his PhD, he studied the use of dendritic cells as immunotherapy in cancer and discovered a dendritic cell subtype potent in inducing immune tolerance, resulting in a first author publication. Next to three other co-authorships, he also wrote a review on the potential of other myeloid cells in immunotherapy. He guided two Master thesis students and two Bachelor thesis students. As assistant, he organized and taught many practical courses, research rotations, seminars and workshops within the BCIM group for both students as a general audience and seated in both the Faculty Education Commission and the Department Education Council between 2020 and 2022.

Abstract of the PhD research

Receiving a cancer diagnosis has a major impact on the lives of millions of people each year. Although advancing therapeutical insights increased the life span of cancer patients, many people suffer from relapse and metastasis. For many cancers, chemotherapy remains the standard-of-care, with severe side-effects and without guarantee of success. Thus, there is a need for more effective therapies with less side-effects. The answer might lay within the patient's own body, even within the tumor itself. The tumor microenvironment is composed of cancer cells, but also contains immune cells, including cancer cell killing T cells. Increasing the amount and activity of T cells can be achieved by delivering tumor antigens, using the most potent antigen-presenting cells: tumor-associated conventional dendritic cells (TAcDCs). TAcDCs were used before as a cancer vaccine in mice, resulting in reduced tumor growth in melanoma and lung cancer. However, these results have been obtained in cancer models expressing a strong artificial antigen, leading to easier cancer cell recognition.

In this PhD thesis, we investigated the potential of TAcDCs as a vaccine and as a cell-based therapy in the aggressive mouse breast cancer model E0771, which does not express artificial antigens. TAcDCs could successfully arm the immune system against E0771 when used as a vaccine, but did not initiate an anti-tumoral effect when used as a therapy. Combinations with known immunotherapies did not improve the outcome. Surprisingly, TAcDC1s, a subtype of TAcDCs, counteracted the effect of successful immunotherapy, raising questions on the role of TAcDC1s in cancer.

The very low amount of TAcDCs in E0771 is an important hurdle for TAcDC research. The clinically established growth factor Flt3L was a valid candidate to increase TAcDC numbers, showing a significant increase of all TAcDC subtypes in E0771, but surprisingly without a decrease in tumor growth. In-depth analysis uncovered a new TAcDC subset in Flt3L-treated mice in several tumor models, the 'CD81⁺ migratory cDC1s'. We identified this subset as a potent inducer of 'regulatory T cells', a tumor-promoting T cell type. This shows that the use of Flt3L as cancer therapy could counter a potent immune response.

Altogether, my thesis contributed to the knowledge on the heterogeneity of TAcDCs in preclinical breast cancer and their use in cell-based cancer immunotherapy. My work also demonstrated that countering low TAcDCs numbers using Flt3L does not come without consequences and urges for a more careful consideration before its clinical application.