SCIENCES & BIOENGINEERING SCIENCES

The Research Group
Cellular and Molecular Immunology

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

Sana Arnouk

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Nanobody-mediated targeting of immunoregulatory cells for cancer therapy

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

The defence will take place on

Tuesday, December 19, 2023 at 13h in auditorium D.2.01

The defence can also be followed through a live stream: Click here

Members of the jury

Prof. dr. ir. Jan Steyaert (VUB, chair)
Prof. dr. ir. Stefan Magez (VUB, secretary)
Prof. dr. Eline Menu (VUB)
Prof. dr. Leila Akkari (Nederlands Kankerinstituut, NL)
Prof. dr. Susan Mariola Schlenner (KULeuven)

Curriculum vitae

Sana Arnouk obtained the degree of Master of Molecular Biology with great distinction at the VUB in 2018. Afterwards, she started as a PhD student in the Brussels Center for Immunology with Prof. Jo Van Ginderachter as her promotor. During her PhD, Sana was supported by funding from Kom Op Tegen Kanker and Fonds Wetenschappelijk Onderzoek. Sana is a co-author of eight research articles including one first co-authorship. She is also a co-author on three review articles including one first authorship. She supervised two master thesis students and two bachelor thesis students.

Abstract of the PhD research

In the recent years, major breakthroughs have been achieved in cancer treatment such as the development of immune checkpoint blockade (ICB) therapy. This therapy unleashes the brakes imparted on anti-tumoral T cells by the tumor. Nevertheless, a large fraction of patients remains refractory to such therapies accentuating the need to concomitantly address other tumor-promoting characteristics, such as immunosuppression. Tumor-infiltrating regulatory T cells (tiTregs) and tumor associated macrophages (TAMs) are notorious for their contribution to immunosuppression. Therefore, targeting those cell types in combination with ICB is highly promising. Nevertheless, those cell types are essential in the periphery for the normal functioning of the human body. Hence, the targeting needs to be specific to the tumor-infiltrating counterparts.

Interleukin 1 receptor 2 (IL1R2) has been highlighted as a marker for tiTregs by several groups. In this PhD, we verified the upregulation of IL1R2 on murine tiTregs and its absence from peripheral Tregs. We verified that IL1R2$^+$ tiTregs are protumoral and investigated the signals implicated in the upregulation of IL1R2 on tiTregs. We explored the possible role of IL1R2 in the tumor in general and on tiTregs specifically and we generated immunotherapeutic compounds against IL1R2. On the other hand, we showed that a molecule called IMDQ is able to re-educate the TAMs (modify their phenotype from protumoral to antitumoral). As our own anti-MMR nanobody has been shown to penetrate solid tumors and deliver a therapeutic payload to TAMs, we conjugated it to IMDQ and showed that the conjugation did not interfere with the targeting capacity of the nanobody. Then we showed *in vivo* that the conjugate was able to delay tumor growth, remodel the immune infiltrate and enhance the response to ICB.