SCIENCES & BIOENGINEERING SCIENCES

The research group
Brussels Center for Immunology

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

Maida Živalj

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Assessing the role of Lipocalin-2 (Lcn-2) and the blocking potential of anti-Lcn-2 nanobodies (Nbs) in cancer and infectious diseases

Supervisor:
Prof. dr. ir. Jo Van Ginderachter (VUB)
Co-supervisor:
Prof. dr. ir. Benoit Stijlemans (VUB)

The defence will take place on
Thursday, September 17, 2026 at 4 p.m.

VUB Etterbeek campus, Pleinlaan 2, Elsene, Auditorium D.2.01.

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

Members of the jury

Prof. dr. ir. Geert Raes (VUB, chair)
Prof. dr. Eveline Peeters (VUB)
Prof. dr. Cleo Goyvaerts (VUB)
Prof. dr. Guy Caljon (UAntwerpen)
Prof. dr. Ralf Weiskirchen (Uniklinik RWTH Aachen, DE)

Curriculum vitae

Maida Živalj obtained her Master's degree in Molecular Biology with great distinction at the VUB in 2020. She subsequently started her PhD at the Brussels Center for Immunology (BCIM) with Prof. Jo Van Ginderachter and Prof. Benoit Stijlemans as her promotors. During her PhD, Maida was supported by funding from the Research Foundation – Flanders (FWO). Maida is a co-author of four research articles, including one as first author. She is also a co-author of two review articles, including one as first author. In addition, she supervised two master's thesis students and two bachelor's thesis students.

Abstract of the PhD research

Lipocalin-2 (Lcn-2) is a secreted glycoprotein that regulates iron homeostasis by binding iron-loaded siderophores, thereby limiting bacterial growth. The resulting complex is internalized via its receptor (24p3R), contributing to cellular iron handling. Produced mainly by neutrophils and macrophages, Lcn-2 plays a key role in iron recycling, immune regulation, and macrophage polarization. Its expression is upregulated in cancer and inflammatory diseases, where it can disrupt iron homeostasis. Reflecting its pleiotropic nature, Lcn-2 serves as both a prognostic biomarker in cancer and a potential target to enhance erythropoietic recovery in inflammatory conditions such as African trypanosomiasis, although its precise mechanisms remain unclear.

This study aimed to investigate the role of Lcn-2 in macrophage iron homeostasis and its impact on cancer and inflammatory diseases, focusing on the Lcn-2/IL-10 axis and to evaluate the therapeutic potential of nanobody (Nb)-based targeting.

In the E0771 triple-negative breast cancer model, using *Lcn2*-deficient mice and a *Lcn2*-deficient E0771 cell line, it was shown that although the Lcn-2 expression was upregulated systemically it did not affect tumor growth or immune responses. Mechanistically, Lcn-2 was found to promote iron export from macrophages, whereas its deficiency led to iron retention. This effect appears to be mediated through the Lcn-2/IL-10 axis, which is also relevant in inflammatory settings such as African trypanosomiasis.

In a *Trypanosoma brucei brucei* (*T. b. brucei*) infection model, *Lcn2*-deficient mice showed improved anemia recovery and reduced weight loss during early-stage disease. These findings also highlighted the importance of the IL-10/IFN-γ balance in regulating inflammation and erythropoiesis, with IL-10 likely exerting protective effects through modulation of Lcn-2.

Finally, Nbs targeting Lcn-2 were developed and shown to inhibit multiple aspects of its function, likely by interfering with its siderophore-binding region. In addition, several Nbs blocked Lcn-2-mediated fibroblast activation and, in the *T. b. brucei* infection model, proved effective as *in vivo* imaging tools for monitoring Lcn-2 expression.

Collectively, these results support the development of Nb-based Lcn-2-targeted diagnostic and therapeutic strategies.