SCIENCES & BIOENGINEERING SCIENCES

The Research Group
Structural Biology Brussels

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

Arne Janssens

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Another brick in the wall: understanding and exploiting the novel outer membrane stress protein SlyB

Promotor:
Prof. dr. Han Remaut

The defense will take place on

Wednesday, October 2, 2024 at 4 p.m.

VUB Etterbeek campus, Pleinlaan 2, Elsene in auditorium I.0.02

The defense can be followed through a live stream here

Members of the jury

Prof. dr. Eveline Peeters (VUB, chair)
Prof. dr. Jo Van Ginderachter (VUB, secretary)
Prof. dr. Janine Brunner (VUB)
Prof. dr. Kim Roelants (VUB)
Prof. dr. Xavier De Bolle (UNamur)
Prof. dr. Olivier Dussurget (Institut Pasteur, FR)

Curriculum vitae

Arne Janssens obtained a degree of Master of Science in Bioengineering Sciences: Chemistry and Bioprocess technology at the Vrije Unversiteit Brussel in 2018. After graduating, he started a PhD funded by an FWO fellowship, within the lab of Prof. dr. Han Remaut (Structural Biology Brussels). During his PhD, Arne presented his work at different international conferences and scientific meetings. His research resulted in a first-author paper in the peer-reviewed journal Nature, while he also contributed to an additional publication as co-author. Finally, he guided three master thesis students while also assisting in practical courses for bachelor and master students.

Abstract of the PhD research

Antimicrobial resistance is fast rising to become one of the top challenges to modern healthcare. Inherently hard to combat are the Gram-negative or 'diderm' bacteria, which are surrounded by a second membrane called the outer membrane (OM). As the first line of defense and an indispensable layer crucial for survival, the OM forms an appealing target for novel antibacterial therapies to combat diderm pathogens. In this PhD work, I sought a better insight into how the OM accommodates stress conditions by external assaults and how to use this information in devising new strategies for the development of novel antibacterial therapies.

In the first part of this work, two molecular mechanisms were unveiled which underpin the essential role of the OM. The study of the lipoprotein SlyB shows how diderms protect the integrity and content of their OM when its specialized lipids are destabilized. A novel function is described, where SlyB becomes essential in such conditions, as it seals off deleterious lipid rafts. Next, the role of the OM in protecting cells against osmotic shock was investigated. Breaking the molecular links between the OM and the cell wall sensitizes diderms to osmotic downshift. Both studies contradict the current dogma that it is the cell wall of bacteria that confers osmoresistance. A new model is therefore proposed, where the combination of OM and cell wall counter osmotic downshift as a single mechanical device.

In a second part of this PhD, the property of SlyB to capture surface antigens was explored in the development of a novel vaccination platform. Using these complexes, the humoral immune response in mice was shown to greatly benefit from this formulation. Furthermore, SlyB domains were shown to evoke a broad response even against low abundant valuable antigens. Finally, a microfluidics set-up was developed, aiming to generate a high-throughput selection platform for growth inhibiting biologicals. Here, the rapid detection and manipulation of picodroplets allowed to enrich clonal populations of Nanobody-secreting yeast cells.

The work in this thesis uncovered two new fundamental processes occurring in the diderm envelope. It also illustrated the need for a better fundamental understanding of the OM, as it translated into the development of two promising novel antibacterial strategies. As such, it lays the foundation for the design of new tools and therapies in the combat against problematic bacterial pathogens.