SCIENCES & BIOENGINEERING SCIENCES

The Research Group
Structural Biology Brussels

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

Jessie Vandierendonck

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Isolation, characterization and genetic modification of toxin-bearing bacteriophages from enterohemorhaggic *E. coli*

Supervisor:
Prof. dr. ir. Remy Loris (VUB)
Co-supervisor:
Em. prof. dr. Henri De Greve (VUB)

The defence will take place on

Friday, October 31, 2025 at 5 p.m.

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

Members of the jury

Prof. dr. Charles van der Henst (VUB, chair)
Prof. dr. ir. Eveline Peeters (VUB)
Prof. dr. Kim Roelants (VUB)
Prof. dr. ir. Rob Lavigne (KU Leuven)
Prof. dr. Hedvig Tamman (University of Tartu, EE)

Curriculum vitae

Jessie obtained a degree of Master of Science in Biology at the Vrije Universiteit Brussel in 2020. After graduating, she started a PhD in the research group of Prof. dr. ir. Remy Loris (Structural Biology Brussels). Her research focused on a phage-based delivery system for bacterial toxins as antimicrobial strategy. During her doctoral research, Jessie published two first-author articles in peer-reviewed journals. She attended multiple phage conferences, a phage workshop and she supervised three master's theses and assisted in practical courses for both bachelor's and master's programs.

Abstract of the PhD research

The rise of multidrug resistant bacteria currently threatens human health worldwide. Hence, the search for new antimicrobial strategies to cure bacterial infections is urgent as conventional antibiotics are becoming ineffective. According to WHO, pathogenic *Escherichia coli* is ranked as "critical" species to find new antimicrobial treatments for their infections. *E. coli* is an intestinal bacterium that is mostly harmless, but some pathotypes exist that can cause intestinal infections (e.g. enterohemorrhagic *E. coli*), but also urinary tract and bloodstream infections. As alternative treatment to fight such microbial infections, (bacterio)phage therapy is often proposed. Bacteriophages are bacterial viruses that were discovered a decade before the first antibiotic's discovery. By producing new phage progeny inside a bacterial cell, lytic phages can lyse and thereby kill bacteria, making them suitable for therapy.

Another promising antibacterial strategy lies within the exploitation of antibacterial toxins from bacterial toxin-antitoxin (TA) systems. TA-systems are bacterial genetic elements that encode a toxin protein, which causes cell death, and a cognate antitoxin that neutralizes the toxin. The combination of phage therapy and antibacterial toxins is an interesting approach for the treatment of *E. coli* infections. By engineering toxin genes into the genome of phages, the temperate phage can serve as a vehicle to deliver exogenous toxins into the pathogenic bacterial cell. There, the toxin will be expressed during the lysogenic cycle. Ultimately, these recombinant bacteriophages can be used as a powerful tool to combat infectious, multi-resistant bacteria, both in the lytic and lysogenic cycle.

However, engineering toxin-bearing phages is challenging as this involves cloning of the harmful toxins, which leads to growth arrest in the bacterial host cell. Therefore, cloning strategies were developed where toxin expression is regulated on multiple layers by replicational, transcriptional and translational control. Furthermore, phages were isolated from enterohemorrhagic *E. coli* and fully characterized both genomically and morphologically, including the identification of their host receptors. Finally, a characterized EHEC phage was recombined with toxins and validated *in vitro* for its toxicity to the host cell as a proof of concept.