VUB SCIENCES &
BIOENGINEERING SCIENCES

The Research Group
Microbiology

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

# Veerke De Kock

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

## Tuning the genome: Lrs14 DNA-binding proteins link global gene regulation and chromatin organization in Sulfolobales

Supervisor:
**Prof. dr. ir. Eveline Peeters (VUB)**
Co-supervisor:
**Dr. Rani Baes (VUB)**

The defence will take place on
**Friday, December 12, 2025 at 5 p.m.**

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

## Members of the jury

Prof. dr. ir. Jo Van Ginderachter (VUB, chair)
Prof. dr. Charles Van der Henst (VUB)
Prof. dr. Anastassia Vorobieva (VUB)
Prof. dr. Laurence Van Melderen (ULB)
Prof. dr. Remus Dame (Universiteit Leiden, NL)

## Curriculum vitae

Veerke obtained a Master’s degree in Biology from the Vrije Universiteit Brussel in 2020. After graduating, she started a PhD in the research group of Microbiology under the supervision of Prof. Dr. ir. Eveline Peeters. Her research focused on characterizing Lrs14-like DNA-binding proteins. During her doctoral research, Veerke published two first-author articles in peer-reviewed journals and contributed as a co-author to three additional publications. She presented her work at seven national and international conferences, supervised three master’s students in their thesis research, and assisted in practical courses for both bachelor's and master's programs.

## Abstract of the PhD research

Archaea occupy a unique position in the tree of life as the closest prokaryotic relatives of eukaryotes. In these organisms, transcription, its regulation and chromatin organization are tightly interconnected processes. In the thermoacidophilic archaea of the Sulfolobales, this interplay relies on a diverse repertoire of DNA-binding proteins, ranging from nucleoid-associated proteins to basal and specific transcription factors. Within this context, the Lrs14 family of DNA-binding proteins has long stood out as an intriguing yet poorly understood group: while some members act as transcriptional regulators, others display features reminiscent of chromatin-organizing nucleoid-associated proteins.

This doctoral research investigates the functional role of Lrs14-like proteins across the Sulfolobales. Comparative phylogenetic and structural analyses show that these proteins constitute a conserved, archaeal-specific family, with several homologs encoded in each genome. All homologs share a highly conserved winged-helix–turn–helix fold and lack ligand-binding domains—hallmarks of canonical chromatin proteins. Structural predictions further suggest that they may bridge distinct DNA regions and contribute to higher-order genome architecture.

Functional analyses in the model organism *Sulfolobus acidocaldarius* demonstrate that Lrs14-like proteins exert broad, genome-wide regulatory effects. RNA-seq profiling of single-gene deletion mutants reveals that the expression of up to one third of all genes is altered upon deletion of an Lrs14-like protein, affecting nearly all functional categories. Notably, the *lrs14*-like genes themselves are highly responsive to environmental stress and physiological transitions.

In *Metallosphaera sedula*, an in-depth study of one Lrs14 homolog reveals extensive, non-sequence-specific genome binding *in vivo* and the ability to condense and aggregate DNA *in vitro*, providing direct evidence for a structural role in chromatin organization.

Together, these findings position Lrs14-like proteins as dual-function chromatin organizers and global transcriptional regulators. This duality suggests that they represent an archaeal strategy for higher-order genome organization in the absence of histones, integrating chromatin architecture with adaptive gene regulation.