SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Structural Biology Brussels

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

Fanny COPPENS

to obtain the degree of Doctor of Sciences

Title of the PhD thesis:

Structural characterisation of the adhesins SabA from *Helicobacter pylori* and LpfD from *Escherichia coli*

Promotor:

Prof. dr. Han REMAUT

The defence will take place on

Wednesday June 21 2017 at 16.00h

in Auditorium D.2.01 at the Campus Humanities, Sciences and Engineering of the Vrije Universiteit Brussel, Pleinlaan 2 - 1050 Elsene, and will be followed by a reception.

Members of the jury

Prof. Dr. ir. Eveline PEETERS (chairman)
Prof. Dr. Peter TOMPA (secretary)
Prof. Dr. ir. Ronny WILLAERT
Prof. Dr. Gustavo Guttierez GONZALEZ
Prof. Dr. med. Markus GERHARD (TU Muenchen, D.)
Prof. Dr. Annemieke SMET (Univ. Antwerpen)

Curriculum vitae

Fanny Coppens obtained her Licence (Master) in Chemistry from the VUB in 2004 and her teacher's certificate in 2005. After various jobs, she started her PhD research in 2009 at the VUB. Since April 2015 she is working in the Unit for Biosafety and Biotechnology of the Scientific Institute for Public Health, where she is involved in biosafety expertise for activities of contained use and deliberate release of GMOs and/or pathogens. She also provides expertise to the competent authorities regarding the Cartagena Protocol on Biosafety to the Convention on Biological Diversity.

Abstract of the PhD research

The abundant usage of antibiotics in bacterial infection control leads to the appearance of resistance, and can cause a range of undesired side effects to the healthy microbiota. A promising approach to circumvent the appearance and spread of antibiotic resistance is the development of non-bactericidal therapies that target the pathogen's virulence traits, such as its ability to adhere to the host tissue. The detailed molecular description of the adhesins responsible for this host attachment, as well as the determination of their 3-dimensional structures form important first steps towards the development of such new therapeutics. In this project we investigate adhesins in *Helicobacter pylori* and *Escherichia coli*, two important intestinal pathogens in humans.

Long Polar Fimbriae (LPF) are adhesive surface appendages called pili, found in Adherent Invasive *E. coli* (AIEC) strains implicated in the intestinal disorder Crohn's Disease. Using binding assays of the purified soluble pilus proteins and murine intestinal tissue slides, LpfD was shown to be the adhesive factor in LPF. The X-ray structure of LpfD was shown to consist of two Ig-like domains, similarly to other well-known two-domain adhesins. The first steps were also taken in identifying LpfD's receptor as being a matrix-associated protein.

SabA is an adhesin of *H. pylori*, which is a causative agent of peptic ulcers and many gastric cancers. This adhesin is a member of a large family of *Helicobacter* outer-membrane proteins (HOPs), assumed to be autotransporters. The HOPs have a highly conserved C-terminal domain predicted to form a ß-barrel that anchors the adhesin domain in the bacterial outer membrane. The structure of the SabA adhesin domain was determined through X-ray crystallography and SAXS. It shows a characteristic 3+4 helix bundle that has since been seen also in other HOP adhesines such as BabA and HopQ. The overall topology of HOPs was determined to consist of a ß-barrel that is composed of one N-terminal and seven C-terminal ß-strands, interrupted with the bulky adhesin domain. This architecture is fundamentally different to the topology seen in classical autotransporters and provides an interesting route to develop inhibitors that specifically target HOP adhesins.