SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Structural Biology Brussels (SBB)

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

Brandán PEDRE PÉREZ

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Thiol switches in *Corynebacterium glutamicum* that fight off oxidative stress

Promotor:
Prof. Dr. Joris Messens

The defense will take place on
Wednesday December 6 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. Eveline Peeters (chairman)
Prof. Dr. Henri De Greve (secretary)
Prof. Dr. Gustavo Gutiérrez González
Prof. Dr. Vsevolod Belousov
(IBCh, Russian Academy of Sciences)
Prof. Dr. Carsten Berndt
(Heinrich-Heine Univ. Düsseldorf)
Prof. Dr. Jean-François Collet (De Duve Inst., UCL)

Curriculum vitae

Brandán Pedre Pérez obtained a Master of Science in Research Methodology for Biosciences at the Universidad de León (Spain) in 2012, and worked for a brief period in the pharmaceutical industry. Subsequently, he became an IWT-PhD fellow in the Redox Signaling Lab of the SBB research group. He performed scientific research in the field of structural and functional redox biology. This research contributed to the publication of a book chapter and 8 papers in international peer-reviewed journals, and he presented his results at international conferences. During this period, he also supervised a Master thesis project.

Abstract of the PhD research

Excessive levels of reactive oxygen species are detrimental to normal cellular functions, as they cause oxidative damage to biomolecules. Cellular antioxidant systems keep the levels of reactive oxygen species under control, and bacteria have several antioxidant systems to fight off oxidative stress, including the ones in which cysteine thiols (-SH) are involved.

The main objective of my PhD was to disentangle the thiol-switches of *Corynebacterium glutamicum* that contribute to defense against oxidative stress. *C. glutamicum* is a model organism for human pathogens, such as *Corynebacterium diphtheriae* and *Mycobacterium tuberculosis*. These bacteria use a low-molecular-weight thiol, mycothiol, which is unique for this group. With an optimized method for the purification of mycothiol from bacterial cultures, we could demonstrate that mycothiol protects protein cysteine thiols from overoxidation. This protection is reversibly regulated through the action of a mycothiol-dependent enzyme, mycoredoxin-1, catalyzing the removal of mycothiol. In this research project, we uncovered a novel mycothiol-dependent enzyme, mycoredoxin-2, involved in arsenate detoxification. Furthermore, we unveiled the mechanisms of hydrogen peroxide sensing and transduction by OxyR, a bacterial transcription factor that regulates the response against oxidative stress.

In conclusion, this research showed that bacterial thiol switches on proteins are actively involved in the protection against excessive levels of reactive oxidative species.