SCIENCES & BIOENGINEERING SCIENCES

The Research Group

## Structural Biology Brussels

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

## Maria-Armineh TOSSOUNIAN

to obtain the degree of Doctor of Bio-Engineering Sciences

Title of the PhD thesis:

# Thiol-disulfide redox switches for the enzymatic reduction of protein methionine sulfoxide

**Promotor:**

Prof. dr. Joris Messens

The defence will take place on

**Wednesday September 25 2019 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. Henri De Greve (chairman)
Prof. dr. ir. Eveline Peeters (secretary)
Prof. dr. Gustavo Gutiérrez González
Prof. dr. Jean-François Collet (UCL)
Prof. dr. Haike Antelmann (Freie Univ. Berlin)

**Curriculum vitae**

Maria-Armineh Tossounian obtained her masters degree in molecular biology with greatest distinction at the VUB in 2014. With a VUB-bridging grant and an FWO-PhD aspirant grant she continued her research in the Redox signaling lab at SBB (VUB). Her PhD research focuses on the structural and functional characterization of different anti-oxidant enzymes, and an oxidant-specific biosensor. Her research led to three first-author and three co-author publications. She presented her results during international conferences, and she supervised a Master thesis project and several student practical courses.

**Abstract of the PhD research**

During phagocytosis, the human immune system releases oxidants to damage the macromolecules of pathogenic bacteria. During this period of oxidative stress, oxidation leads to alterations in protein function, and influences downstream signaling pathways of the pathogen. To counteract, bacteria have developed different types of anti-oxidant defense systems to overcome oxidative stress.

The main objective of my PhD thesis was to understand the impact of hydrogen peroxide induced methionine oxidation on two antioxidant enzymes, glutathione transferase Tau23 and Phi9. We showed that their function is regulated by a group of enzymes known as methionine sulfoxide reductases, MsrA and MsrB, which reduce oxidized methionine. Focus also went to understand the detailed mechanism of how these enzymes are recycled via thiol-disulfide switches. Further, this thesis also shows the kinetic and structural characterization of a biosensor. It consists of a circularly permuted fluorescent reporter protein (cpYFP) integrated into the flexible region of the *E. coli* transcription factor NemR, which senses hypochlorite via structural changes.

Overall, I mapped the details of the catalytic mechanism of Msr enzymes and how they regulate the function of different antioxidant enzymes. A cpYFP-based biosensor, which specifically senses oxidants that are released during bacterial phagocytosis, was structurally and kinetically characterized.