SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Structural Biology Brussels (SBB)

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

Sotirios GKEKAS

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Unravelling the structure and function of the bacterial persistence regulator ObgE

Promotor:

Prof. Dr. ir. Wim Versées

The defence will take place on

Friday January 12 2018 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 (chairwoman)
Prof. Dr. Joris Messens (secretary)
Prof. Dr. Luc Leyns
Prof. Dr. Savvas Savvides (Universiteit Gent)
Prof. Dr. Arjan Kortholt (Rijksuniversiteit Groningen)

Curriculum vitae

Sotirios Gkekas obtained a BSc in Biology at the University of Crete (Greece) in 2009, and a MSc in Protein Biotechnology at the same University in 2011. In 2012, he was awarded a PhD scholarship by IWT and pursued his doctoral study in the Structural Biology Brussels (SBB) research group. During his PhD study period, he performed scientific research in the field of structural enzymology, which contributed so far to the publication of one peer-reviewed paper. In addition, he participated in several workshops and supervised 3 MSc thesis students.

Abstract of the PhD research

The last few decades, society is facing the problem that many pathogenic bacteria are becoming insensitive to the majority of existing antibiotics. An important cause of chronic bacterial infections is the presence of persister cells, and although the clinical relevance of persistence has been proven, the mechanisms leading to this phenomenon have largely remained unresolved.

Recent studies have uncovered the GTPase Obg as a central regulator of persistence in *Escherichia coli* and *Pseudomonas aeruginosa*. Thus, Obg forms a promising target for the development of anti-persister drugs. In the framework of my PhD research I set-out to structurally and functionally characterize the Obg protein from *E. coli*. Specifically, the first X-ray crystal structure of *E. coli* Obg in complex with GDP was solved and conformational changes regarding the functioning of the protein were mapped. A complete biochemical analysis of the protein provided new insights into the function of Obg and unraveled a role of its disordered C-terminal domain in nucleotide binding. In addition, the effect of *in vivo* identified mutants of Obg, that are affected in the persistence phenotype, on the mechanism and functioning of *E. coli* Obg was studied. Finally, I started investigating possible interactors that constitute the Obg persistence interactome. In particular, I have focused on the reported interaction between Obg and SpoT, a key regulator of the stringent stress response.

In conclusion, these findings contribute to our understanding of the detailed molecular mechanism of Obg proteins. Therefore, our results might lead to novel insights into the role of Obg in cellular physiology, including bacterial persistence.