Study of Fe-S dependent secondary-metabolites of myxobacteria

Keywords: Secondary metabolites, Myxobacteria, iron-sulfur protein, antibiotics, synthetic biology.

Summary

Natural product discovery from microorganisms provided important sources for drugs (antibiotics, anti-cancer agents, immune-modulators...). Myxobacteria, a group of common soil-dwelling bacteria, produce a prolific number of secondary metabolites and in this regard are similar to actinomycetes and certain fungi. Interestingly, whole-genome sequencing of several myxobacterium species, has revealed that 10% of their genomes is a large reservoir of secondary-metabolite-Biosynthetic Gene Clusters (BGCs)[1]. Importantly, myxobacterial secondary metabolites frequently have novel structures and distinct modes of action (MOAs) such as the myxovirescin, an antibiotic used against human pathogens[2].

In the past decade, it has been shown that many biosynthetic pathways for secondary-metabolites involve Fe-S cluster-containing proteins for a core biosynthesis reaction *per se* or for modification of the metabolite itself[3]. Secondary metabolite biosynthetic pathways of *Myxococcus xanthus* DK1622 follow this rule, as illustrated by the fact that Fe-S proteins are associated to half of the secondary-metabolite BGCs of *M. xanthus*, including those for myxovirescin, myxoprincomide and myxalamide.

Medical and industrial exploitation of secondary-metabolites require high titer production which could prevent their exploitation from the biodiversity since they are often produced in low amount from natural producing strains, such as the myxobacteria. To overcome this barrier synthetic biology is a key approach. Nevertheless, the involvement of Fe-S proteins is often a major bottleneck since they are frequently inactive when produced in heterologous host. In this project, we will study ways to exploit Fe-S dependent secondary-metabolites from myxobacteria.

[1.] Wenzel and Müller, Mol. Biosyst. (2009) Myxobacteria 'microbial factories' for the production of bioactive secondary metabolites. [2.] Olatunji et al., Nat. Commun. (2020) Structures of lipoprotein signal peptidase II from S. aureus complexed with antibiotics globomycin and myxovirescin. [3.] Langraf et al., Ann. Rev. Biochem. (2016) Radical S-Adenosylmethionine Enzymes in Human Health and Disease.

The co-supervisors

Béatrice PY, Laboratoire de Chimie Bactérienne (LCB)- py@imm.cnrs.fr
Marc MARESCA, Institut des Sciences Moléculaires de Marseille (iSm2) - m.maresca@univ-amu.fr

Location

LCB, 31 Chemin Joseph Aiguier, Marseille, France
iSm2, Saint-Jérôme Campus, Marseille, France

Doctoral school

Life and Health Sciences (ED 62), Aix-Marseille Université

Expected profile of the candidate

Candidate should be a Master M2 with a microbiology, biology molecular and biochemistry background. He/she should be motivated, serious, innovative and autonomous. Candidate should also be able to integrate easily into various scientific environments.