

DISCOVERY OF NEW GLYCOSYLTRANSFERASES INVOLVED IN THE GLYCOSYLATION OF THE BACTERIAL FLAGELLUM

Keywords

Flagellin, glycosyltransferases, motility, biophysics, bacterial genetics

Summary

Flagellins (the individual subunits of the bacterial flagellar filament), are O-glycosylated [1] and this crucial post-translational modification takes place prior to the export of the flagellins to the cell surface. Indeed, we and others have shown the absence of formation of a functional flagellum when flagellin glycosylation is abolished [1-5], engendering adverse effects on motility, adherence, and invasion [6-7]. The so far best characterized flagellin glycosylation systems are those of pathogenic bacteria such as *Campylobacter jejuni* and *Helicobacter pylori*, which decorate their flagellins with quite original nonulosonic acid structures, related to sialic acid commonly decorating the surface of human cells [6]. Despite the thorough characterization of nonulosonic acid biosynthesis pathways reported for various bacterial species [8-9], knowledge on the mechanisms guiding transfer of these complex carbohydrate structures by glycosyltransferases (GTs) onto the flagellin acceptors, and the thereby arising effects on functional flagellum formation, remain largely elusive. Within this project, calling on our mastering of the model bacteria *Magnetospirillum magneticum* AMB-1 and *Magnetospira* QH-2, we aim to dissect the choreography of acceptor/donor/actor interplay leading to O-glycosylation of flagellins by nonulosonic acids, as well as by more common carbohydrate structures, in order to contribute to fill the void in knowledge of the global picture of flagellum formation.

The objectives of this project, situated at the interface between bacterial genetics and structural biology, consist in gene annotation to identify novel GTs, validate their function by deletion studies and phenotypic analyses of the mutants, and inspect the role of the GT gene products by proteomic studies and by X-ray crystallography, paralleled by the identification of the nature of all the sugars decorating the flagellin and the respective glycosylation sites.

Once the role and the mechanism of these enzymes will be established, they will become templates for new families of GTs within the CAZy database (<http://www.cazy.org/>). The experiments related to this project will be carried out in the laboratories LCB (<http://lcb.cnrs-mrs.fr/>) and AFMB (<http://www.afmb.univ-mrs.fr/>).

[1] M. Schirm *et al.*, *Mol. Microbiol.* **48**, 1579.

[2] P. Thibault *et al.*, *J. Biol. Chem.* **276**, 34862.

[3] W. K. Chou *et al.*, *J. Biol. Chem.* **280**, 35922.

[4] I. C. Schoenhofen *et al.*, *J. Biol. Chem.* **281**, 723.

[5] G. Sulzenbacher *et al.*, *Environ Microbiol* **20**, 228.

[6] M. J. Morrison *et al.*, *Biochemistry* **53**, 624.

[7] S. M. B. Tabei *et al.*, *J. Bacteriol.* **191**, 2851.

[8] I. C. Schoenhofen *et al.*, *Glycobiology* **16**, 8C.

[9] I. C. Schoenhofen *et al.*, *Glycobiology* **19**, 715.

The co-supervisors

Dr. François ALBERTO, LCB, UMR 7283. ✉ Francois.Alberto@univ-amu.fr

Dr. Gerlind SULZENBACHER, AFMB, UMR 7257. ✉ Gerlind.Sulzenbacher@univ-amu.fr

Locations

Research units LCB and AFMB, Campus Joseph Aiguier and Luminy, Marseille, France (in proximity of the beautiful Calanque Natural resort)

Doctoral school

Life and Health Sciences (ED 62), Aix-Marseille université (<https://ecole-doctorale-62.univ-amu.fr/>)

Expected profile of the candidate

Theoretical knowledge in molecular biology (DNA amplification, cloning method ...), biochemistry (protein expression and protein purification, ...) and structural biology, with a first practical experience (Master 2 internship) in one of these fields. Fluency, written and oral, in English. Knowledge in bio-informatics analyses and basic microbiology will be a plus.