

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.

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The co-supervisors

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Locations

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

Doctoral school

Sciences de la vie et de la santé, Aix-Marseille Université (<https://ecole-doctorale-62.univ-amu.fr/>)

Extensive interdisciplinary training secured *via* the Plinius doctoral programme (<https://pliniuscursus.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.

The candidate must hold a Master2 degree by summer 2021 and been ranked in the top third of Master1 class. Applications, in English, including a CV (specifying the level of English), a motivation letter, two recommendation letters, grades and ranking of Master1 and grades for the first semester of Master2 must be sent to the supervisors by **May 10th 2021**.

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Currently there is no secured funding for this position. The candidate is expected to defend the application in English at the IM2B doctoral college mid of June 2021.

Starting date

October 2021

Salary

Net salary 1421 €/month + 4000 € allowance for training and conference fees.