



Grenoble Alliance for Integrated
Structural & Cell Biology

GRAL MSc RESEARCH SCHOLARSHIP 2020-2021 RESEARCH INTERNSHIP PROPOSAL

Institute / Group

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Research Project Title

Interactions between *Pseudomonas aeruginosa* toxin ExoU and its eukaryotic partners

Description of the project

Pseudomonas aeruginosa is a multi-resistant bacterial pathogen that uses an arsenal of virulence factors to infect human cells. Its major weapon is the Type III secretion system (T3SS), a nano-syringe that allows the injection of different toxins directly into the cytoplasm of the host cell. Previously, we studied structure-function relationship of ExoU [1] which is one of the most aggressive T3SS toxins with phospholipase activity inducing membrane rupture and cell death. Recently we identified, by genetic approaches, a host “receptor” for ExoU toxin and demonstrated that epithelial cells depleted for this human protein become resistant to ExoU intoxication. In the proposed project, we will study the interaction between ExoU and its host “receptor(s)”. By overexpressing the two proteins in *E. coli* and by performing pull-down assays and biochemical assays (gel filtration, crosslinking, ELISA) as well as crystallography if a complex is identified. In parallel, we will perform immunoprecipitation on epithelial cells infected by *P. aeruginosa* carrying ExoU-HA to find other potential partners. The work will include mainly biochemistry, microbiology and characterisation of protein-protein interaction, and it will be conducted in collaboration with cellular biologists for *in vivo* host-bacteria interaction test.

Keywords

Type III secretion system, toxin activation mechanism, Protein-protein interaction, Chromatography, pull-down

Relevant publications of the team

Gendrin, C, C Contreras-Martel, S Bouillot, S Elsen, D Lemaire, DA Skoufias, P Huber, I Attree, and A Dessen. Structural basis of cytotoxicity mediated by the type III secretion toxin ExoU from *Pseudomonas aeruginosa*. PLoS Pathog, 2012. 8(4): p. e1002637

Discola KF, Förster A, Boulay F, Simorre JP, Attree I, Dessen A, Job V. Membrane and chaperone recognition by the major translocator protein PopB of the type III secretion system of *Pseudomonas aeruginosa*. J Biol Chem (2014) DOI: 10.1074/jbc.M113.517920
