Grenoble Alliance for Integrated Structural & Cell Biology

INTERNSHIP PROPOSAL

Institute and Group: **BIG/BCI/PBRC**
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Research project title:
Investigating the molecular determinants of *Pseudomonas aeruginosa* exolysin A activity

Keywords to describe the project:
toxin, pore forming protein, membrane damage, protein:protein interaction

Description of the project:
Pseudomonas aeruginosa is a major nosocomial bacterial pathogen. The virulence of recently isolated clinical strains depends on the secretion of a new pore-forming toxin called ExlA. ExlA-mediated cytotoxicity and membrane damage induction have been described but the determinants of these functions have been only partially characterized.
This project aims at identifying molecular determinants of ExlA activities by investigating the function of ExlA variants on cells and liposomes. The kinetic assessment of ExlA activity will also be used to infer the stoichiometry of the functional unit of ExlA, which is not known. Relevant techniques include recombinant expression, protein separation, challenge of cultivated cells, cross-linking and phylogeny-based site-directed mutagenesis. For this project, a background in biochemistry or microbiology is recommended.

Justification that the internship's subject fits with the general theme of GRAL:
ExlA is a powerful virulence factor that shapes host-pathogen interactions by hijacking cell death signaling. ExlA belongs to the type 5 secretion systems that broadly contribute to bacterial pathogenesis. ExlA-like proteins focus a collaboration with the Dessen lab at the IBS.

Relevant publications of the team:

Exolysin Shapes the Virulence of *Pseudomonas aeruginosa* Clonal Outliers. (2017) Reboud E, Basso P, Maillard AP, Huber P, Attrée I. *Toxins (Basel)*

Pseudomonas aeruginosa Pore-Forming Exolysin and Type IV Pili Cooperate To Induce Host Cell Lysis. (2017) Basso P, Ragno M, Elsen S, Reboud E, Golovkine G, Bouillot S, Huber P, Lory S, Faudry E, Attrée I. *mBio*

Multiple *Pseudomonas* species secrete exolysin-like toxins and provoke Caspase-1-dependent macrophage death. (2017) Basso P, Wallet P, Elsen S, Soleilhac E, Henry T, Faudry E, Attrée I. *Environ Microbiol*.