

INTERNSHIP PROPOSAL

Institute and Group: **BIG/BCI/PBRC**

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Research project title:

Molecular basis of *Pseudomonas aeruginosa* exolysin A secretion

Keywords to describe the project:

protein trafficking, protein:protein interaction, protein folding, pore forming protein

Description of the project (15 lines max):

Pseudomonas aeruginosa is a major nosocomial bacterial pathogen. The virulence of recently isolated clinical strains depends on the secretion of a new toxin called ExlA, in the vicinity of host cell membranes. ExlA-mediated cytotoxicity has been extensively described but direct characterization of its properties has been hampered due to ineffective production in *P. aeruginosa* and despite improved secretion from *E. coli*. This project aims at identifying steps and partners in ExlA synthesis and trafficking. This will bring new data into the field of Type 5 secretion to which ExlA belongs, and will translate into new ways to maximize ExlA supply for biophysical characterization. As a safeguard, the search for limiting factor(s) in ExlA secretion will include functional complementation with select chaperones. Techniques span recombinant expression, bacterial cell fractionation, cross-linking, pull-down, chromatographic purification of a secretion intermediate and select factors to set up *in vitro* folding experiments and ExlA activity measurements on host cells and liposomes. For this project, a background in biochemistry or microbiology is recommended.

Justification that the internship's subject fits with the general theme of GRAL (3 lines max):

Type 5 secretion systems support the virulence of many bacterial pathogens. ExlA hijacks cell death signaling by forming a pore in target cell membranes and is thus a prime actor in host-pathogen interactions. ExlA-like proteins focus a collaboration with the Dessen lab (IBS).

Relevant publications of the team (3 max):

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



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Cell Lysis. (2017) Basso P, Ragno M, Elsen S, Reboud E, Golovkine G, Bouillot S, Huber P, Lory S, Faudry E, Attrée I. *m4Bio*

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.*