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<https://www.ibs.fr/spip.php?lang=en>

Title of the M2 research internship:

Persistence of *Pseudomonas aeruginosa* in blood

Project summary:

Bacterial blood stream infections (BSI) are the leading cause of health-care associated infections in hospitals. Some BSI are impossible to treat due to an increased number of pathogens resisting antibiotics, as well as the emergence of bacterial persistence. *Pseudomonas aeruginosa* (Pa) is one of the five major causes of BSI. Once in the human blood, Pa faces several elements of innate immune system. An important mechanisms to kill bacterial cells is via activation of the complement system (CS) which leads to the formation of the Membrane Attack Complex (MAC) pore in the bacterial envelope.

We showed that the survival of Pa isolates facing the CS in whole blood is strain-dependent, ranging from elimination to full resistance. In addition, we made a breakthrough discovery in pinpointing of a third pathogen subpopulation that escapes CS-mediated bactericidal activity by forming rare phenotypic variants, that we named evaders (Pont S, Fraikin N, Caspar Y, Van Melderen L, Attrée I, Cretin F. PLoS Pathog. 2020 Dec 16;16(12):e1008893). The evaders appear at low rates (0.01-0.1%) in the clonal populations and share some characteristics with antibiotic persisters, notably biphasic killing curves.

The specific aims of this internship project are to: 1/ purify the evaders after labelling with vital dyes, 2/ study of the ability of the evaders to interact with the different protein of the CS. The flow cytometry and the bacteriology techniques will be the cornerstone of the approach. These two parts are included in a larger project on which a final year thesis student and an additional researcher are participating, giving the opportunity for additional supervision in genetics and microscopy.

The understanding of bacterial mechanisms leading to evasion of the innate immune system in blood will provide fundamental knowledge and tools to develop in future new strategies to combat some of the main pathogens causing bacteremia.

Keywords:

Pseudomonas aeruginosa, complement, host-pathogen interaction

Relevant publications of the team:

Pont S, Fraikin N, Caspar Y, Van Melderen L, Attrée I, Cretin F. PLoS Pathog. 2020 Dec 16;16(12):e1008893

Golovkine G, Faudry E, Bouillot S, Elsen S, Attrée I, Huber P. PLoS Pathog. 2016 Jan 4;12(1):e1005377