**M2 Internship proposal**

**2023 - 2024**

**Team**

Team: Regulatory RNAs in Clostridia

Team website: https://www.i2bc.paris-saclay.fr/regulatory-rnas-in-clostridia/

Head of the team: Olga Soutourina

Address: 1 avenue de la Terrasse, 91190 Gif-sur-Yvette

Supervisor of the internship: Olga Soutourina

Tel: 01 69 82 62 06

@:olga.soutourina@i2bc.paris-saclay.fr

**Title of the M2 project**

**Characterisation of regulatory RNAs in the human pathogen *Clostridioides difficile***

**Project description**

*Clostridioides difficile* is the major cause of nosocomial infections associated with antibiotic therapy. The disruption of the colonic microbiota by broad-spectrum antibiotics promotes colonization of the intestinal tract by this pathogen. Due to the increase of severe forms associated with a strong inflammatory response and higher recurrence rates, a current imperative is to develop synergistic and alternative treatments of *C. difficile* infections. The mechanisms controlling infection cycle of this major human enteropathogen remain largely unexplored. Noncoding RNAs (ncRNA) are in the centre of networks controlling virulence and antibiotic resistance in major pathogens. This project is built upon our genome-scale data on a large diversity of ncRNAs in *C. difficile*, the majority being specific to this pathogen, their expression during infection and interactions with the RNA chaperone protein Hfq. Our goal is to uncover the biological roles and the molecular mechanisms of action of most promising selected ncRNAs in *C. difficile*. We will use an integrative interdisciplinary strategy combining genome-wide and targeted molecular biology and genetics, bioinformatics approaches to identify ncRNA targets and regulatory networks and study the impact of riboregulation in *C. difficile* and during infection in host. We expect to identify RNA-based mechanisms that contribute directly to the control of *C. difficile* pathogenicity. These data can be used to develop novel RNA-based diagnostic and therapeutic strategies to limit the development of *C. difficile* infection.

During this internship the student will acquire strong background in the RNA-based mechanisms for regulation of gene expression, in particular for pathogenesis control. The student will get new skills to manipulate strictly anaerobic bacteria with particular growth requirements using specific equipment available in the host laboratory and learn to use advances genetic approaches for genome engineering and mutagenesis in Clostridia we developed.

**Keywords**

**Regulatory RNAs, pathogenesis control, molecular mechanisms, regulation of gene expression, anaerobic bacteria**

**Publications of the team (selection of 5)**

1. Soutourina O.\*, Monot, M., Boudry, P., Saujet, L., Pichon, C., Sismeiro, O., Semenova, E., Severinov, K., Le Bouguenec, C., Coppée, J.-Y., Dupuy, B. and Martin-Verstraete, I. Genome-wide identification of regulatory RNAs in the human pathogen *Clostridium difficile*. (2013). PLoS Genetics. 9(5) :e1003493.
2. O. Soutourina\* « RNA-based control mechanisms of *Clostridium difficile*» in special section on Cell regulation in Current Opinion in Microbiol (2017). 36C :62-68.
3. Maikova A, Peltier J, Boudry P, Hajnsdorf E, Kint N, Monot M, Poquet I, Martin-Verstraete I, Dupuy B, Soutourina O\*. (2018) Discovery of new type I toxin-antitoxin systems adjacent to CRISPR arrays in *Clostridium difficile*. Nucleic Acids Res. 46(9):4733–4751.
4. Peltier, J., Hamiot, A., Garneau, J., Boudry, P., Maikova, A., E. Hajnsdorf, Fortier, L.C., Dupuy, B. and Soutourina, O.\* Type I toxin-antitoxin systems contribute to the maintenance of mobile genetic elements in *Clostridioides difficile* (2020) Communications Biology (Nature group). **3:** 718
5. Boudry P., Piattelli E., Drouineau E., Peltier J., Boutserin A., Lejars M., Hajnsdorf E., Monot M., Martin-Verstraete I., Dupuy B., Gautheret D., Toffano-Nioche C., Soutourina, O.\* Identification of RNAs bound by Hfq reveals widespread RNA partners and a sporulation regulator in the human pathogen *Clostridioides difficile.* (2021) RNA Biology 18(11): 1931-1952

**Perspectives**

* Could this internship be followed by a thesis?

⌧ Yes

🞏 No

Remark: depending on the level and motivation of the student

* Doctoral School of reattachment: SDSV n°577