

INTERNSHIP PROPOSAL

Institute and Group: Institut de biologie structurale - Group PatBac

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Research project title: Unraveling the link between pathogenic E. Coli and colorectal cancer

5 Keywords to describe the project: Escherichia coli, colorectal cancer, genotoxic agent, colibactin, megaenzyme

Description of the project (aims, experimental techniques, recommended background):

Certain commensal and Extraintestinal Pathogenic E. Coli strains have been shown to exhibit a genetic island called *pks* that encodes for a megadalton complex composed of NRPS (Non Ribosomal Peptide Synthase), PKS (Polyketide Synthetase) and hybrid NRPS/PKS domains. This complex is responsible for the production of a genotoxic product called colibactin that is known to break double strand DNA and induce G2 arrest of infected cells. This phenomenon has been linked to the development of colorectal cancer.

We propose to understand the colibactin production by studying the organisation of the NRPS and PKS assembly line by X-ray crystallography and electron microscopy in order to understand the link between colibactin production and colorectal cancer development.

The ideal candidate will have a background in biochemistry and protein purification and a strong interest for structural techniques such as X-ray crystallography and electron microscopy.

Justification that the internship's subject fits with the general theme of GRAL:

By looking at the link between colibactin production and colorectal cancer, this subject falls into the scope of host-pathogen interaction through a cellular structural biology approach that would perfectly fit with the general themes of GRAL.

Relevant publications of the team:

Contreras-Martel C, Martins A, Ecobichon C, Maragno Trindade D, Mattei PJ, El Ghachi M, Hicham S, Hardouin P, Boneca IG, Dessen A (2017) Molecular architecture of the PBP2:MreC core bacterial cell wall synthesis complex. **Nature Commun.**, 8, 776.

Dortet L, Lombardi C, Cretin F, Dessen A, Filloux A. (2018) Pore-forming activity of the *Pseudomonas aeruginosa* type III secretion system translocon alters the host epigenome. **Nature Microbiol.**, 3, 378.

Zouhir S, Robert-Genthon M, Trindade DM, Job V, Nedeljković M, Breyton C, Ebel C, Attrée I, Dessen A. (2018) Assembly of an atypical α -macroglobulin complex from *Pseudomonas aeruginosa*. **Sci. Rep.**, 8, 527.