UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Internship project Master 2
Year 2018-2019

Laboratory/Institute: IBS **Director:** Winfried Weissenhorn
Team: Structure and Stability of Integral Membrane Protein and Phage Assemblies
Head of the team: Cécile Breyton

Name and status of the scientist in charge of the project: **HDR: yes X no ☐**
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Program of the Master's degree in Biology:

☐ Neurosciences and Neurobiology ☐ Immunology, Microbiology, Infectious Diseases
X Integrative Structural Biology ☐ Physiology, Epigenetics, Differentiation, Cancer

Title of the project: Investigation of phage T5 tails using mass spectrometry

Objectives (up to 3 lines):

We aim to study bacteriophage T5 using mass spectrometry (MS). In particular, we will investigate the composition of the tail of T5 before and after its interaction with its *E. coli* receptor FhuA. Indeed, it has been suggested that phage proteins might be expelled to perforate the *E. coli* cell wall.

Abstract (up to 10 lines):

Bacteriophages, viruses infecting bacteria, are the most abundant biological entity of Earth. Phage therapy is an attractive alternative to treat antibiotic-resistant bacterial infections in humans, animals and plants. The Breyton team focuses its studies on the T5 tail, composed of eleven proteins. Using native MS, we will study the tail of T5 and its interaction with its *E. coli* receptor FhuA to determine the stoichiometry of each protein and to understand the re-organization of the tail upon its interaction with the receptor. This represents a great challenge for native MS because the mass change might represent only ~10 % of the total mass of the tail. These data will be confirmed by MS-based proteomics, whereby we can assess the composition of the tail before and after receptor interaction. Overall, we will decipher the composition and stoichiometry of the tail of T5 before and after binding to its receptor FhuA.

Methods (up to 3 lines):

T5 tails will be produced using the infection of *E. coli* cultures by mutant phages. T5 tails will be purified by classical biochemistry methods (PEG/salt precipitation, chromatography, density gradient), and characterised (SDS-PAGE). T5 tails will be analysed by different kinds of Mass Spectrometry (proteomics, native).

Up to 3 relevant publications of the team:

- Arnaud et al., (2017) Bacteriophage T5 tail tube structure suggests a trigger mechanism for Siphoviridae DNA ejection. Nat Commun. 8:1953.
- Noirclerc-Savoye et al., (2015) Tail proteins of phage T5: investigation of the effect of the His6-tag position, from expression to crystallisation. Protein Expr Purif. 109:70
- Flayhan et al., (2014) Crystal structure of pb9, the distal tail protein of bacteriophage T5: A conserved structural motif among all siphophages. *J. Virol*. 88:820

Requested domains of expertise (up to 5 keywords):

Biochemistry, Structure Biology