

PROPOSITION SUJET DE THESE

Concours d'attribution des Contrats Doctoraux 2018 - 2021

A renvoyer par email **format Pdf** à edsvs-direction@univ-amu.fr

Avant le 16 mai 2018

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PRESENTATION DU SUJET (1/2 page maximum avec courte bibliographie)	
Titre en anglais:	Molecular mechanisms of phage infection and pathogenic conversion in the human pathogen <i>Vibrio cholerae</i> .
Spécialité:	Microbiology
Liens URL éventuel du sujet:	http://lism.cnrs-mrs.fr/RL_files/fr/index.html

Filamentous phages are ubiquitous viruses that infect bacteria with high specificity in order to inject their genetic material, which results in the acquisition of virulence factors for some host. One example is the marine bacterium *Vibrio cholerae* that convert to a human pathogen upon infection by the CTX phage carrying the cholera toxin genes. To initiate the infection process, filamentous phages sequentially parasitize two bacterial structures of their host envelope: a pilus and the Tol-Pal system. The Tol-Pal system is a conserved macrocomplex connecting the inner membrane (IM), the peptidoglycan and the outer membrane (OM) in a proton-motive force (PMF)-dependent manner in Gram-negative bacteria. The Tol-Pal system plays an essential role in cell viability, as it maintains the envelope integrity and participate in OM constriction during cell division.

While more than 70 filamentous phages have been reported in the literature, mechanistic data

on the initial host/phage interaction are still scarce. Overall, the conservation of the infection process among these phages is a question that has not been clearly addressed in the literature, as data are available for only two host/phage couples so far: F-specific *E. coli* phages (such as M13) and, to a lesser extent, *V. cholerae* infected by CTX. Recent experimental data obtained in our lab and in others labs call into question the current infection model.

The proposed Ph.D project aims to decipher the molecular, structural and energetic events involved in the early steps of filamentous phage infection thanks to a multidisciplinary approach. By extending the study to other host/phage couples, the project will provide new insights into bacterial pathogenic conversion, and may enhance phage engineering strategies for therapeutics.

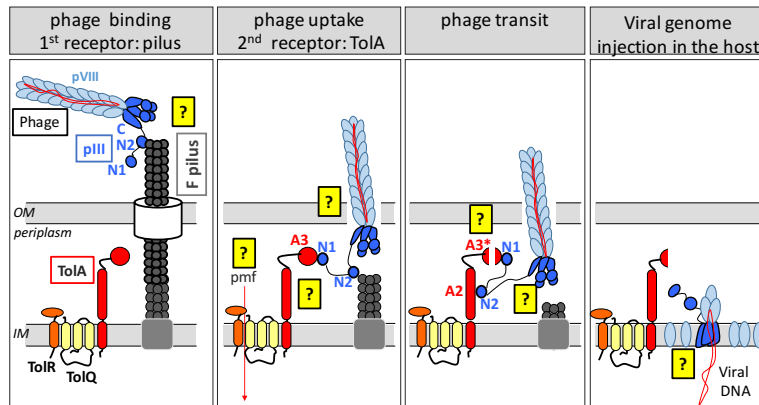


Figure 1. Working model for filamentous phage infection in *E. coli*. Yellow question marks highlight unclear events in the process. OM: outer membrane, IM inner membrane, pVIII: phage major coat protein, pIII: phage minor coat protein.

Ph.D project: The PhD student will use molecular biology, biochemistry, fluorescent microscopy and phenotypic analysis in order to answer the following questions:

- How do the pilus and the Tol-Pal machineries interplay during phage translocation across the cell envelope (protein-protein interaction, colocalization, coordination with the cell cycle...)?
- What is the sequence of events and the role of the pmf during phage uptake?
- Is the process conserved for other filamentous phages?

Candidate profile: We are seeking for an enthusiastic and strongly motivated student with a Master degree in Molecular biology, biochemistry or Microbiology (expected before July 2018), with teamwork spirit. Knowledge in phage manipulation and/or fluorescent microscopy is a “plus”.

Requirements: The PhD student will have to defend the project orally in front of the doctoral college of Aix- Marseille University. The attribution of the scholarship will depend on her/his rankings. The candidate's application and attached documents (as specified here: <https://ecole-doctorale-62.univ-amu.fr/fr/futur-doctorant/financements/concours-lecole-doctorale>), must be submitted before May 31 and the defense will take place around June 24th.

Informations complémentaires