

PhD PROPOSAL FOR THE DOCTORAL SCHOOL « Végétal, Animal, Aliment, Mer, Environnement »

GENERAL INFORMATION

Thesis title: Membrane switching: a colonization pathway for <i>Vibrio cholerae</i>
Acronym of the project: SWIT-CH
Disciplinary field 1: Biochemistry, molecular and cellular biology
Disciplinary field 2: Microbiology
Three keywords: Predation by heterotrophic protists, <i>Vibrio cholerae</i> , Phosphorus limitation
Registration establishment: Nantes université
Research unit: US2B, UMR CNRS 6286
Name of the thesis director HDR (Accreditation to supervise research) required: Delavat François
Email address of the thesis director: francois.delavat@univ-nantes.fr
Name of the thesis co-supervisor 1 (if applicable): Guillonneau Richard
Email address of the thesis co-supervisor 1 (if applicable): richard.guillonneau@univ-nantes.fr
Contact(s) (mailing address and E-mail): Laboratoire US2B, UFR sciences et techniques, 2 rue de la Houssiniere, 44322 Nantes cedex, France
<input type="checkbox"/> Doctoral school contest <input type="checkbox"/> Interview <input type="checkbox"/> Other (specify):

SCIENTIFIC DESCRIPTION OF THE PhD PROJECT

Socio-economic and scientific context: (10 lines)

To date, it is estimated that there are 2.9 million cases of cholera each year, resulting in 95,000 deaths. In an attempt to remedy this situation, the WHO has set an ambitious target: to eliminate cholera from high-risk areas by 2030.

One of the reasons for the success of *Vibrio cholerae*, the causative agent of cholera, is that this bacterium can precisely regulate the expression of its genes to thrive in nutrient-poor environments, and more particularly in phosphorus-poor environments. To survive inorganic phosphate (Pi) limitation, *V. cholerae* regulates genes belonging to the Pho regulon and remodels its membrane using the PhoBR two-component regulatory system. While the vast majority of marine waters are limited by essential nutrients such as Pi, coastal areas are subject to waves of Pi where *V. cholerae* often persists.

Assumptions and questions (8 lines)

Previous studies have shown that *V. cholerae* and other intestinal pathogenic bacteria that are unable to 'sense' low phosphate concentration in the intestine are less efficient at colonising it, an environment hitherto known to be rich in nutrients. Overall, a mechanistic understanding of the physiological trade-offs of *V. cholerae* membrane remodeling in response to Pi limitation remains to be investigated. The PhD student will focus on understanding the potential key role of the PhoBR system and membrane remodelling in the adaptation and persistence of *V. cholerae* in marine environments and during its interaction with heterotrophic protists which may lead to a transfer within the trophic chain.

The main steps of the thesis and scientific procedure (10-12 lines)

To answer this question, the PhD student will have to :

- i- Provide a complete picture of *V. cholerae* membrane remodelling in response to phosphate stress using 'omics' approaches such as lipidomics, glycomics and proteomics. This will allow us to generate mutants in the membrane remodelling pathway to identify the genes involved in this switching of the membrane.
- ii- determine the lifestyle of *Vibrio cholerae* in marine environment with respect to phosphate availability using wild type strains and mutants in membrane remodelling pathway. We will compare the ability to build biofilms quantitatively and qualitatively and the motility capacities of these strains in a defined low and high Pi media.
- iii- Identify the risk of transfer within the trophic chain using predatory heterotrophic protists. To check whether the ability to remodel the membrane is part of the strategy used by *V. cholerae* to avoid predation by protozoa, we will test mutants in the membrane remodelling pathway (unable to remodel their membrane) against different strains of heterotrophic protists.

Methodological and technical approaches considered (4-6 lines)

This thesis project will enable the student to learn all the techniques associated with lab-based microbiology and host-bacteria interactions. In addition, molecular biology techniques involving the creation of mutants, bioreporters and the biochemical analysis of the various biomolecules produced by these bacteria will also be used during this project, as will the use of high-resolution microscopy (confocal, electron).

Scientific and technical skills required by the candidate

Given the objectives set, the candidate should have a good knowledge of microbiology, cell biology and host-bacteria interactions, as well as some knowledge of biochemistry. From a technical point of view, he/she should also be interested in molecular biology tools, biochemical analyses and microscopy. *V. cholerae* is a pathogenic bacterium that will be handled in a cat-2 laboratory, so good organisation and strict compliance with hygiene and safety rules will be necessary.

Finally, the candidate should have a general interest in the transfer and persistence of pathogens in the

environment.

THESIS SUPERVISION

Unit name: Biological Sciences and Biotechnologies Unit, US2B, UMR CNRS 6286	Team name: Team 2 : Molecular Engineering and Glycobiology
Unit director name: Bernard Offmann	Team director name: Cyrille Grandjean
Mailing address of the unit director: direction.us2b@univ-nantes.fr	Mailing address of the team director: Cyrille.grandjean@univ-nantes.fr
Thesis director Surname, first name: Delavat François Position: Associate professor Obtained date of the HDR (Accreditation to supervise research):15/10/2021 Employer: Nantes université Doctoral school affiliation: VAAME Rate of thesis supervision in the present project (%): 50 Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%): 70 Number of current thesis supervisions/co-supervisions: 1	
Thesis co-supervisor 1 (if applicable) Surname, first name: Guillonneau, Richard Position: Assistant professor Accreditation to supervise research <input type="checkbox"/> yes <input type="checkbox"/> no If yes, date diploma received: Employer: Nantes université Doctoral school affiliation: Biologie santé Rate of thesis supervision in the present project (%): 50 Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%): 0 Number of current thesis supervisions/co-supervisions: 0	
Professional status of previous PhD students supervised by both director and co-supervisors	

(from 5 years)

Please provide the following information for each PhD students supervised

Surname, first name: Rahmani, Alexandra

Date of PhD beginning and PhD defence: from 01/10/2016 to 4/11/2019

Thesis supervision: Pichereau Vianney (UBO associate professor), Paillard christine (CNRS UBO research director, professor) et Delavat François (UBO assistant professor)

Professional status and location: Assistant professor (UBO – ESIAB LUBEM)

Contract profile (post-doc, fixed-term, permanent): permanent

List of publications from the thesis work:

#Article **A. Rahmani, F. Delavat**, C. Lambert, N. Le Goic, E. Dabas, C. Paillard and V. Pichereau. Implication of the type IV secretion system in the pathogenicity of *Vibrio tapetis*, the etiological agent of Brown Ring Disease affecting the Manila clam *Ruditapes philippinarum*. *Frontiers in Cellular and Infection Microbiology* 2021, 11:e634427.

#patent : V. Pichereau, C. Paillard, **F. Delavat, A. Rahmani**, P. Le Chevalier (20% each). Biological Control of Vibriosis in aquaculture. EP21306334 deposited 27/09/2021

Surname, first name: Morot Amandine

Date of PhD beginning and PhD defence: from 01/10/2019 to 17/03/2023

Thesis supervision: Dufour Alain (UBO professor), Paillard christine (CNRS UBO research director, professor) et Delavat François (Nantes université - associate professor)

Professional status and location: Post-doc at Dublin City University (Ireland)

Contract profile (post-doc, fixed-term, permanent): fixed-term

List of publications from the thesis work:

#Article D. Oyanedel, A. Lagorce, M. Bruto, P. Haffner, **A. Morot, (...) F. Delavat, (...)**, and D. Destoumieux-Garzón. Cooperation and cheating orchestrate *Vibrio* assemblages and polymicrobial synergy in oysters infected with OsHV-1 virus. *Proceedings of the National Academy of Sciences of the United States of America* 2023, 120(40) e2305195120

#Article **A. Morot, F. Delavat**, A. Bazire, C. Paillard, A. Dufour, and S. Rodrigues. Genetic insights into biofilm formation by a pathogenic strain of *Vibrio harveyi*. *Microorganisms* 2024, 12(1), 186

#Article : **A. Morot**, S. El Fekih, A. Bidault, A. Le Ferrand, A. Jouault, J. Kavousi, A. Bazire, V. Pichereau, A. Dufour, C. Paillard, **F. Delavat**. Virulence of *Vibrio harveyi* ORM4 toward the European abalone *Haliotis tuberculata* involves both quorum sensing and a type III secretion system. *Environmental Microbiology* 2021, 23(9):5273-5288

#Article : A. Joublin-Delavat, K. Touahri, P. Créatin, **A. Morot**, S. Rodrigues, B. Jesus, F. Trigodet, **F. Delavat**. Genetic and physiological insights into the diazotrophic activity of a non- cyanobacterial marine diazotroph. *Environmental Microbiology* 2022, 24, 6510-6523.

Five main recent publications of the supervisors on thesis subject:

Shropshire, H., **Guillonau, R.**, Han, Z., Jones, R. A., Ahmed, S., García-Romero, I., ... & Chen, Y. (2023). Glyceroglycolipids are essential for *Burkholderia cenocepacia* intracellular survival by preventing phagolysosome acidification. *bioRxiv*, 2023-05.



Guillonnet, R., Murphy, A. R., Teng, Z. J., Wang, P., Zhang, Y. Z., Scanlan, D. J., & Chen, Y. (2022). Trade-offs of lipid remodeling in a marine predator-prey interaction in response to phosphorus limitation. *Proceedings of the National Academy of Sciences*, 119(36), e2203057119.

Stirrup, R., Mausz, M. A., Silvano, E., Murphy, A., **Guillonnet, R.**, Quareshy, M., ... & Chen, Y. (2023). Aminolipids elicit functional trade-offs between competitiveness and bacteriophage attachment in *Ruegeria pomeroyi*. *The ISME Journal*, 17(3), 315-325.

THESIS FUNDING

Origin(s) of the thesis funding: ANR
Gross monthly salary: 2100 €
Thesis funding state:
Funding beginning date/duration of the thesis funding: 01/10/24

Date: 23/07/2024

Name, signature of unit director: OFFMANN Bernard



Name, signature of team director:

Cyrille Grandjean



Name, signature of thesis project director:

François Delavat



All sections must be filled in. Once completed, please save the proposal form in PDF format using the following naming: Supervisor Name_Unit_Subject Acronym_EN.pdf
Please also send a Word version to make it easier to change the layout if necessary.

Documents to be send to: ed-vaame@doctorat-paysdelaloire.fr