

## PHD PROPOSAL FOR THE DOCTORAL SCHOOL « Ecologie, Géosciences, Agronomie, ALimentation »

### GENERAL INFORMATION

<b>Thesis title:</b> Study of sulfotransferase from terrestrial and marine fungi
<b>Acronym:</b> SOFUN
<b>Disciplinary field 1:</b> Ecology <b>Disciplinary field 2:</b> Select an element
<b>Three keywords:</b> Sulfotransferases, Fungi, Biotechnology
<b>Research unit :</b> LUBEM
<b>Name of the thesis director:</b> MESLET-CLADIERE Laurence <b>Email address of the thesis director :</b> laurence.meslet@univ-brest.fr <b>Name of the thesis co-supervisor 1 (if applicable):</b> JANY Jean-Luc <b>Email address of the thesis co-supervisor 1 (if applicable):</b> jean-luc.jany@univ-brest.fr <b>Name of the thesis co-supervisor 2 (if applicable):</b> <b>Email address of the thesis co-supervisor 2 (if applicable):</b>
<b>Thesis grant (funding origin and amount):</b> CDE
<b>Contact(s) (mailing address and E-mail):</b> LUBEM-EA3882-Parvis Blaise Pascal-Technopôle Brest Iroise 29280 PLOUZANE
<b>Recruitment process:</b> Recruitment process depends on thesis funding. To select the corresponding recruitment process, please visit the EGAAL website <a href="#">here</a> . This information is needed for proposal publication. <input checked="" type="checkbox"/> <b>Doctoral school contest</b> <input type="checkbox"/> <b>Interview</b> <input type="checkbox"/> <b>Other (indicate) :</b>

**All sections must be filled. Once filled, please save the proposal form in pdf format using the following naming: Supervisor Name\_Unit\_Subject Acronym\_EN.pdf**

**ED EGAAL**

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## SCIENTIFIC DESCRIPTION OF THE PhD PROJECT

### **Socio-economic and scientific context : (10 lines)**

Sulphation is commonly associated to secondary metabolite bioactivity induction or enhancement. For example, a huge diversity of sulphated compounds is observed amongst the red algae cell wall polysaccharides, in particular within the carrageenan polysaccharide family. Carragenans have been widely used as thickening, gelling and stabilizing agents in the food industry, cosmetics or the pharmaceutical industry. Variable rheological properties of these carrageenan may vary depending, inter alia, on the sulphate number and position. In heparin/heparan, a member of the glycosaminoglycan family, N-sulphation at the S-domains play a role in the inflammatory response, blood thinning and cell differentiation. Heparin is a widely used anticoagulant (blood thinner) and its market is expected to accumulate revenues worth 16.3 US\$ billions by 2025.

### **Assumptions and questions (8 lines)**

Sulfotransferases (ST) occurs in multiple and numerous organisms. STs are transferase enzymes that catalyze the transfer of a sulfo group from a donor molecule to an acceptor alcohol or amine. The most common sulfo group donor is 3'-phosphoadenosine-5'-phosphosulfate (PAPS). Two different classifications coexist. The first one includes three different families : ST1 (with sub-families ST1.1 and ST1.2), ST2 and ST-proteins. The second one distinguishes cytosolic sulfotransferases which are involved in the exogenous or endogenous small molecules sulphation from cell-wall sulfotransferases (also called carbohydrate sulfotransferases) which are involved in larger molecules (most often polysaccharide) sulphation. Sulfotransferases have been widely described in animals, plants and algae, however, only few studies were designed to target fungal sulfotransferases. The aim of this project is therefore to address the question whether or not fungi harbour enzymes (and what type of enzymes) allowing for secondary metabolite and cell-wall polysaccharide sulphation.

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

In order to address the latter questions, a preliminary study investigated a large bunch of genome sequence available in public databases for the occurrence of sulfotransferases. The very first results unravel the occurrence of cytosolic sulfotransferases in fungi (in particular in marine fungi and phytopathogens), but also heparan sulfotransferase which would be exclusively found within the early diverging fungal phylum Mucoromycota (in particular in Mucor which is a model genus at LUBEM). The PhD project comprises two major parts. The first one will target the fungal cytosolic sulfotransferases, already described in species such as *Aspergillus sydowii* and *Hortaea werneckii*, aiming to purify these proteins to unravel their structure and activity. In addition, sulfated fungal metabolites will be isolated to test for putative antimicrobial or anticarcinogen activities. The second part will focus on the heparin sulfotransferase identified in the Mucoromycotina phylum and more particularly in Mucor spp.. In order to decipher their functions, plasmalemma and cell-wall will be extracted, purified and analyzed to address the question whether sulfate groups were transferred to proteins or polysaccharides, what is the role of the sulphation and tentatively answer the question why such heparin transferases are specific to certain groups of early diverging fungi. The heparin sulfotransferases will be purified prior to enzymatic assays on different substrates.

### **Methodological and technical approaches considered (4-6 lines)**

The different approaches aiming to address the scientific question will consist in bioinformatic analyses (including genome mining), molecular biology (including sulfotransferase cloning and transformation, protein overexpression), biochemistry (enzymatic assays). Partnerships have already been established with the Lipidocean platform (LEMAR-UBO) and the NMR facility (UBO) in order to analyze cell wall composition of the different fungal species investigated.

### **Scientific and technical skills required by the candidate**

PhD applicants will need knowledge in Mycology, Molecular Biology and Biochemistry. Bioinformatic and chemistry skills will be an asset.

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## THESIS SUPERVISION<sup>1</sup>

<b>Unit name:</b> LUBEM-EA3882	<b>Team name:</b>
<b>Unit director name:</b> COTON Emmanuel	<b>Team director name:</b> MOUNIER JÉRÔME
<b>Mailing address of the unit director:</b> Emmanuel.coton@univ-brest.fr	<b>Mailing address of the team director:</b> Jerome.mounier@univ-brest.fr
<b>Thesis director</b> Surname, first name: MESLET-CLADIERE Laurence Position: Associated Professor Obtained date of the HDR (Habilitation thesis to supervise research): 31 march 2017 Employer: UBO-ESIAB Doctoral school affiliation: EGAAL Rate of thesis supervision in the present project (%): 50% Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%): 50% Number of current thesis supervisions/co-supervisions: 1	
<b>Thesis co-supervisor 1 (if applicable)</b> Surname, first name: JANY Jean-Luc Position: Associated Professor Habilitation thesis to supervise research <input type="checkbox"/> yes <input checked="" type="checkbox"/> no If yes, date diploma received: Employer: UBO ESIAB Doctoral school affiliation: EGAAL Rate of thesis supervision in the present project (%): 50% Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%): 50% Number of current thesis supervisions/co-supervisions: 2	
<b>Thesis co-supervisor 2 (if applicable)</b> Surname, first name:	

<sup>1</sup> In EGAAL Doctoral School, if only one scientist in thesis supervision = 100% of supervision rate; if 2 people involved in thesis supervision = from 50% to 70% of supervision rate for the director; if 3 people involved in thesis supervision = 40% / 30% / 30% of supervision rate distribution among supervisors.

Position:

Habilitation thesis to supervise research  yes  no If yes, date diploma received:

Employer:

Doctoral school affiliation:

Rate of thesis supervision in the present project (%):

Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):

Number of current thesis supervisions/co-supervisions:

**Private partner (if CIFRE funding, private funding,...)**

Surname, first name:

Position:

Employer:

Rate of thesis supervision in the present project (%):

Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):

Number of current thesis supervisions/co-supervisions:

**International partner (if Cotutelle thesis)**

Surname, first name:

Position:

Employer:

Rate of thesis supervision in the present project (%):

Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):

Number of current thesis supervisions/co-supervisions:

**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: LEBRETON Annie

Date of PhD beginning and PhD defence: 10/2015 au 12/2018

Thesis supervision: Pr. Georges BARBIER

Professional status and location: Post doc between Beijing (China) and Nancy (France)

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

List of publications from the thesis work:

Lebreton, A., Meslet-Cladiere, L., Morin-Sardin, S., Coton, E., Jany, J.L., Barbier, G. and Corre, E. (2019). Comparative analysis of five *Mucor* species transcriptomes. Genomics. 10.1016/j.ygeno.2018.09.003.

Lebreton, A., Corre, E., **Jany, J.L.**, Brillet-Guéguen, L., Pèrez-Arques, C., Garre, V., Monsoor, M., Debuchy, R., Le Meur, C., Coton, E., Barbier, G., & **Meslet-Cladière, L.** (2020) Comparative genomics applied to *Mucor* species with different lifestyles. *BMC genomics*, 21(1), 135. doi.org/10.1186/s12864-019-6256-2.

**Five main recent publications of the supervisors on thesis subject:**

Navarri, M., Jégou, C., **Meslet-Cladière, L.**, Brillet, B., Barbier, G., Burgaud, G., and Fleury, Y. (2016). Deep Subseafloor Fungi as an Untapped Reservoir of Amphipathic Antimicrobial Compounds. *Marine drugs* 14, 50.

Gillot, G., **Jany, J.L.**, Dominguez-Santos, R., Poirier, E., Debaets, S., Hidalgo, P.I., Ullan, R.V., Coton, E., & Coton, M. (2017). Genetic basis for mycophenolic acid production and strain-dependent production variability in *Penicillium roqueforti*. *Food Microbiology*. 62, 239-250.

Gillot, G., **Jany, J.L.**, Dominguez-Santos, R., Poirier, E., Maillard, M.E., Debaets, S., Thierry, A., Coton, E., & Coton, M. (2017). Functional diversity within the in *Penicillium roqueforti* species. *International Journal of Food Microbiology*. 241, 141-150.

Lebreton, A., **Meslet-Cladière, L.**, Morin-Sardin, S., Coton, E., **Jany, J.L.**, Barbier, G. and Corre, E. (2019). Comparative analysis of five *Mucor* species transcriptomes. *Genomics*. 10.1016/j.ygeno.2018.09.003.

Lebreton, A., Corre, E., **Jany, J.L.**, Brillet-Guéguen, L., Pèrez-Arques, C., Garre, V., Monsoor, M., Debuchy, R., Le Meur, C., Coton, E., Barbier, G., & **Meslet-Cladière, L.** (2020) Comparative genomics applied to *Mucor* species with different lifestyles. *BMC genomics*, 21(1), 135. doi.org/10.1186/s12864-019-6256-2.

Martinelli L, Redou V, Cochereau B, Delage L, Hymery N, Poirier E, Le Meur C, Le Foch G, Cladière L, Mehiri M, Demont-Caulet N, **Meslet-Cladière L.** (2020) Identification and Characterization of a New Type III Polyketide Synthase from a Marine Yeast, *Naganishia uzbekistanensis*. *Mar Drugs*. 2020 Dec 11;18(12):637. doi: 10.3390/md18120637. PMID: 33322429; PMCID: PMC7763939

Rédou, V., Vallet, M., **Meslet-Cladière, L.**, Kumar, A., Pang, K.-L., Pouchus, Y.-F., Barbier, G., Grovel, O., Bertrand, S., and Prado, S. (2016). Marine Fungi. In *The Marine Microbiome* (Springer), pp. 99-153.

Burgaud, G., Mehiri, M. and **Meslet-Cladière, L.** (2019). Les champignons marins et leurs potentiels biotechnologiques. *Les Techniques de l'Ingénieurs*.

## THESIS FUNDING

<b>Origin(s) of the thesis funding: CDE</b>
<b>Gross monthly salary: 1758€</b>
<b>Thesis funding state : Acquired</b>
<b>Funding beginning date/Funding ending date: 10-2021 (3 years)</b>

**Date: 11 march 2021**

**Name, signature of unit director: Emmanuel COTON**



**Name, signature of team director: Jérôme MOUNIER**

**Name, signature of thesis project director: Laurence MESLET-CLADIERE**

A handwritten signature in black ink, appearing to read "Meslet", is written below the text.