

PhD proposal for the doctoral school
« Végétal, Animal, Aliment, Mer, Environnement »

INFORMATIONS GÉNÉRALES

Thesis title : Fostering and understanding, through epigenetic modifications, the lipid production in <i>P. tricornutum</i> .
Acronym : FUEL
Disciplinary field: Biochemistry, molecular and cellular biology
Three keywords: Epigenetic / Lipid metabolism / Diatom
Registration establishment: Université du Mans
Research unit : BiOSSE –Laval
Name of the thesis director HDR (Accreditation to supervise research) required: Ulmann Lionel Email address of the thesis director: lionel.ulmann@univ-lemans.fr Name of the thesis co-supervisor 1: Kwasiborski Anthony Email address: anthony.kwasiborski@univ-lemans.fr
Contact(s): Institut Universitaire de Technologie – Département Génie Biologique 52 Rue des Docteurs Calmette et Guérin BP 2045 - 53020 LAVAL CEDEX 09 - France
<input checked="" type="checkbox"/> Doctoral school contest

SCIENTIFIC DESCRIPTION OF THE PhD PROJECT

Socio-economic and scientific context: (10 lines)

Today's society faces different challenges. In the field of health, sedentarity leads to an increased risk of cardiovascular diseases. In terms of ecology, fossil fuels lead to an increase emission of greenhouse gas. In this context, microalgae become an important research stake mainly for the synthesis of high added value molecules such as pigments, antioxidants and long-chain polyunsaturated fatty acids. These molecules, used as food supplements or as biofuels, would improve the health of consumers or reduce the human ecological footprint. However, to

produce them, microalgae need to be cultivated under stressful conditions, which are incompatible with industrial use.

Assumptions and questions (8 lines)

Epigenetic studies the mechanisms inducing stable and heritable phenotypic modifications without modifications of the DNA sequence. At least three types of epigenetic regulations are present in microalgae (i) DNA methylation on cytosines, (ii) chromatin remodeling by histone modifications and (iii) RNA interference mediated by microRNAs. In microalgae, epigenetic regulates gene expression and is involved in adaptation to stress and in the production of metabolites. The aim of this thesis is to manipulate epigenetic in our model microalga, *P. tricornutum*, in order to improve the production of lipids of interest. In addition to the applied side, this thesis aims to study the involvement of epigenetic regulations in the lipid metabolism of microalgae under normal culture conditions and during abiotic stress such as nitrogen deficiency.

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

In this context, molecules exhibiting the capacity to modify the epigenome will be chosen on a bibliographic basis. Then their application conditions will be optimized during conventional cultures and during nitrogen stress. Thus, different concentrations of molecules will be applied to *P. tricornutum* and the effects on the phenotype (shape, size), on growth and on the epigenome (global DNA methylation level) of the microalga will be evaluated.

Secondly, *P. tricornutum* will be cultivated under the previously optimized conditions. From these cultures, biochemical parameters, such as the assay of the identified lipid classes will be carried out in order to identify the conditions allowing an increase their production. In parallel, molecular parameters such as the expression level and methylation of lipid metabolism genes as well as histone modifications will be evaluated in order to link a modification of epigenetic regulation and lipid production.

Methodological and technical approaches considered (4-6 lines)

Cultures of *P. tricornutum* will be developed to optimize the production of molecules with molecules that can modify the epigenome during nitrogen stress. Microscopy and molecular biology tools will be used to estimate the level of methylation and of gene expression (qPCR, Methylation Specific PCR, MSP) of lipid metabolism. HPLC and cytometry will be used to assay the lipid production by modified microalgae.

Scientific and technical skills required by the candidate

The candidate will have a background in epigenetic, cell biology and molecular biology. He must be able to carry out *in vitro* culture of microalgae, gene analysis technics (qPCR and MSP) and molecule's assays (HPLC).

THESIS SUPERVISION

Unit name: BiOSSE – Biologie des Organismes, Stress, Santé et Environnement	Team name: MIMMA – Métabolisme et Ingénierie Moléculaire des Micro-algues et Applications Site de Laval – IUT de Laval
Unit director name: Jean-Luc Mouget	Name of the team director: Lionel Ulmann

<p>Address of the unit director :</p> <p>Faculté des Sciences et Techniques Avenue Olivier Messiaen 72085 LE MANS Cedex 09 - France</p>	<p>Address of the team director :</p> <p>Institut Universitaire de Technologie de Laval 52 Rue des Docteurs Calmette et Guérin BP 2045 - 53020 Laval Cedex 09 - France</p>
<p>Thesis director</p> <p>Name, first name: Ulmann Lionel Position: Professor Date of HDR: 18 october 2018 Employer : Le Mans Université Doctoral school affiliation: ED VAAME Rate of thesis supervision in the present project: 50% Actual rate of thesis supervision in ongoing theses (supervisions and co-supervisions): 50% Number of current thesis supervisions/co-supervisions: 1</p>	
<p>Thesis co-supervisor</p> <p>Name, first name: Kwasiborski Anthony Position : Assistant professor Accreditation to supervise research: <input type="checkbox"/> oui <input checked="" type="checkbox"/> non Employer: Le Mans Université Doctoral school affiliation: ED VAAME Rate of thesis supervision in the present project: 50% Actual rate of thesis supervision in ongoing theses (supervisions and co-supervisions): 0% Number of current thesis supervisions/co-supervisions: 0</p>	
<p>Professional status of previous PhD students supervised by both director and co-supervisors (from 5 years)</p> <p><i>Please provide the following information for <u>each</u> PhD students supervised</i></p> <p>Name, first name: Murison Victor 01/09/2020 - 13/12/2023 Thesis director: Ulmann Lionel Actually: Unemployed</p> <p>List of publications from the thesis work <u>Murison V.</u>, Hérault J., Côme M., Guinio S., Lebon A., Chamot C., Bénard M., Galas L., Schoefs B., Marchand J., Bardor M., Ulmann L. Comparison of two <i>Phaeodactylum tricornutum</i> ecotypes under nitrogen starvation and resupply reveals distinct lipid accumulation strategies but a common degradation process. <i>Front. Plant Sci.</i>, 14, 2023, doi: 1257500, 10.3389/fpls.2023.1257500.</p>	

Murison V., Hérault J., Schoefs B., Marchand J., **Ulmann L.** Bioinformatics-based screening approach for the identification and characterization of lipolytic enzymes from the marine diatom *Phaeodactylum tricornutum*. *Mar. Drugs*, 21, **2023**, 125, doi: 10.3390/md21020125

Name, first name: **Mohamad Ali Dalal**

01/10/2018 - 22/02/2022

Thesis director : Ulmann Lionel

Actually : contractual researcher at Toulouse Biotechnology Institut (TBI)

List of publications from the thesis work

Mohamad Ali D., Hogeveen K., Orhant R.M., Le Gal de Kerangal T., Ergan F., **Ulmann L.**, Pencreac'h G. Lysophosphatidylcholine-DHA specifically induces cytotoxic effects of the MDA-MB-231 human breast cancer cell line *in vitro* - Comparative effects with other lipids containing DHA. *Nutrients*, 15, **2023**, 2137, doi: 10.3390/nu15092137.

Name, first name: **Le Goff Manon**

thèse : 01/09/2016 – 10/03/2020

Thesis director: Ulmann Lionel

Actually: Clinic researcher

List of publications from the thesis work:

Le Goff M., Delbrut A., Quinton M., Pradelles R., Bescher M., Burel A., Schoefs B., Sergent O., Lagadic-Gossmann D., Le Ferrec E., **Ulmann L.** Protective action of *Ostreococcus tauri* and *Phaeodactylum tricornutum* extracts towards benzo[a]pyrene-induced cytotoxicity in endothelial cells. *Mar. Drugs*, 18, **2020**, doi: 10.3390/md18010003.

Le Goff M., Le Ferrec E., Mayer C., Mimouni V., Lagadic-Gossmann D., Schoefs B., **Ulmann L.** Microalgal carotenoids and phytosterols regulate biochemical mechanisms involved in human health and disease prevention. *Biochimie*, 167, **2019**, 106-118, doi: 10.1016/j.biochi.2019.09.012.

Le Goff M., Lagadic-Gossmann D., Latour R., Podechard N., Grova N., Gauffre F., Chevance S., Burel A., Appenzeller B.M.R., **Ulmann L.**, Sergent O., Le Ferrec E. PAHs increase the production of extracellular vesicles both *in vitro* in endothelial cells and *in vivo* in urines from rats. *Environ. Pollut.*, 255, **2019**, 113171, doi: 10.1016/j.envpol.2019.113171.

Five main recent publications of the supervisors on thesis subject

Thesis director

Bhattacharjya R., Tyagi R., Rastogi S., **Ulmann L.**, Tiwari A. Response of varying combined nutrients on biomass and biochemical composition of marine diatoms *Chaetoceros gracilis* and *Thalassiosira weissflogii*. *Bioresour. Technol.*, 394, **2024**, 130274, doi.org/10.1016/j.biortech.2023.130274.

Murison V., Hérault J., Côme M., Guinio S., Lebon A., Chamot C., Bénard M., Galas L., Schoefs B., Marchand J., Bardor M., **Ulmann L.** Comparison of two *Phaeodactylum tricornutum* ecotypes under nitrogen starvation and resupply reveals distinct lipid accumulation strategies but a

common degradation process. *Front. Plant Sci.*, 14, **2023**, doi: 1257500, 10.3389/fpls.2023.1257500.

Murison V., Hérault J., Schoefs B., Marchand J., **Ulmann L.** Bioinformatics-based screening approach for the identification and characterization of lipolytic enzymes from the marine diatom *Phaeodactylum tricornutum*. *Mar. Drugs*, 21, **2023**, 125, doi: 10.3390/md21020125.

Thesis co-supervisor

A. Kwasiborski, F. Bastide, B. Hamon, P. Poupard, P. Simoneau, T. Guillemette. 2022. *In silico* analysis of RNA interference components and miRNAs-like RNAs in the seed-borne necrotrophic fungus *Alternaria brassicicola*. *Fungal Biology*. 126, pp224-234.

G. Quang N'guyen, R. Raulo, A. Porquier, B. Iacomì, S. Pelletier, J-P. Renou, N. Bataillé-Simoneau, C. Champion, B. Hamon, **A. Kwasiborski**, J. Colou, A. Benamar, P. Hudhomme, D. Macherel, P. Simoneau, T. Guillemette. 2021. Responses of the Necrotrophic Fungus *Alternaria brassicicola* to the Indolic Phytoalexin Brassinin. *Frontiers in Plant Science*. 11, 611-643.

J. Colou, G. Quang N'Guyen, O. Dubreu, K. Fontaine, **A. Kwasiborski**, F. Bastide, F. Manero, B. Hamon, S. Aligon, P. Simoneau, T. Guillemette. 2019. Role of membrane compartment occupied by Can1 (MCC) and eisosomes subdomains in plant pathogenicity of the necrotrophic fungus *Alternaria brassicicola*. *BMC Microbiology*. 19:295.

G. Quang N'Guyen, R. Raulo, M. Marchi, C. Agussach, B. Iacomì, S. Pelletier, J-P. Renou, N. Bataillé-Simoneau, C. Champion, F. Bastide, B. Hamon, C. Mouchès, B. Porcheron, R. Lemoine, **A. Kwasiborski**, P. Simoneau, T. Guillemette. 2019. Responses to Hydric Stress in the Seed-Borne Necrotrophic Fungus *Alternaria brassicicola*. *Frontiers in Microbiology*. 10, 1969.

FINANCEMENT DE LA THÈSE

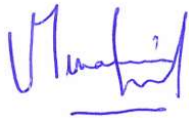
Origin(s) of the thesis funding: Collectivités Locales Mayennaises
Gross monthly salary: 2956.17 €
Thesis funding state Acquired
Funding beginning date/duration of the thesis funding 01/10/24 – 30/09/27

Date : 18 March 2024

Nom, signature du directeur d'unité : Jean-Luc MOUGET



Nom, signature du responsable de l'équipe : Lionel ULMANN



Nom, signature du directeur de thèse : Lionel ULMANN

