Multi-omics approach to improve the understanding of toxicity mechanisms linked to lipid metabolism alterations in the sentinel species *Gammarus fossarum*.

Introduction

Implementing molecular and physiological approaches in ecotoxicology is both essential and feasible today. This interdisciplinary framework will improve our understanding of pollutants impact in freshwater environments and will foster ecotoxicology towards a more holistic vision.

Molecular and analytical methods currently allow measuring the expression of thousands of genes and the presence of hundreds metabolites (e.g. lipids) in each sample. When these molecular information are linked with physiological or pathological parameters (in the context of laboratory or field exposures), they are expected to improve the comprehension of the mechanisms of toxicity at both individual and population levels.

Integrating different molecular and physiological levels is thus possible and it offers new perspectives in predictive ecotoxicology and for the evaluation of freshwater quality.

State of the art

One of the major obstacles to predict potential toxic effects of chemicals in aquatic species is the absence of knowledge on the metabolic pathways involved in the maintain of the populations, in particular for environmentally relevant species.

Our laboratory has shown the usefulness of the freshwater crustacean *Gammarus fossarum* as sentinel organism to evaluate energetic and endocrine perturbations, through physiological and biochemical approaches, in particular in the context of biomonitoring of aquatic environments (Geffard et al. 2010, Coulaud et al. 2015). We have also recently shown the interest in using –omics approaches, notably proteogenomics, in order to identify key proteins of the reproductive system and potential biomarkers of toxicity of heavy metals and pesticides in *G. fossarum* (Trapp et al. 2015, Gouveia et al. 2017).

Lipid metabolism is one of the main metabolic pathways for the energy homeostasis in all metazoans. In crustaceans, lipids play a major role in molt cycle, reproduction, growth or hormone synthesis (e.g. ecdystéroïdes) (Tessier et al. 1983).Some chemicals known to interfere with lipid metabolisms in vertebrates (also known as obesogens, e.g. tributylétain) have been shown to affect lipid distribution and synthesis in the model crustacean *Daphnia magna* (Jordao et al. 2015; Jordao et al. 2016). Moreover, some drugs used to treat dyslipidemias in humans, such as fibrates or statins, have been detected in effluents of wastewater treatment plants at concentrations of ng/l (Jelic et al. 2011). Notably, statins act by inhibiting the rate limiting step enzyme of mevalonate synthesis (HMG-CoA reductase), a highly conserved protein in eukaryotes (Istvan, 2001).

Thus, lipid metabolism may be the toxicity target of many chemicals in various species. However, there is an important lack of knowledge, in particular for aquatic species, about molecular interactions between some lipid species and the activation/inhibition of signaling/metabolic pathways associated with observed phenotypes or life traits.

Objective

In order to address these gaps, this PhD project propose an innovative multi –omics approach in ecotoxicology, consisting in obtaining transcriptomics and lipidomics profiles in the sentinel species *Gammarus fossarum.* These multi –omics data will be integrated using network analysis approaches, notably for gene expression data (Degli Esposti et al. 2016), and multivariate statistical approached specifically developed for –omics feature selection and multiple data integration (Rohart et al. 2017).

The general objective of the project is the **characterization of metabolic pathways involved in lipid biosynthesis/transport/degradation through a multi-omics approach** (transcriptomics and lipidomics) in the crustacean *Gammarus fossarum*. This approach will be developed in a well-characterized physiological context (male and female reproductive stages of gammarids) (Geffard et al. 2010). This approach will allow to understand the molecular plasticity of energy metabolism, identifying the key genes and lipids associated with reproduction.

The work will be organized following 3 research axes :

1 : Molecular characterization of lipid metabolism linked with the reproductive stage of the organisms.

2 : Modulation of lipid metabolism following to starvation

3 : Identification of molecular targets of disruption of the lipid metabolism following exposure to statins..

The PhD candidate will join the project at a time when the data acquisition for axe 1 will be completed and while the data for the other two axes will be under acquisition. This will allow the student to benefit of important datasets since the start of his/her PhD project.

Organisation

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Candidate profile : bioinformatician or biochemist with proved experience in bioinformatics (e.g. Master level, experience in RNA-seq analysis) and statistics. Good knowledge of R and programming language Python. Interest in applying –omics approaches in environmental contexts will be an asset.

Essential bibliography

Coulaud R, et al. 2015. Environ Toxicol Chem 34 : 1031-1038.
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