Post-doctoral position: Genetic and non-genetic basis of oyster resistance to Pacific oyster mass mortality syndrome (POMS)

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Laboratory, localization	UMR IHPE, Montpellier, France
Application dead line	September 15th 2021
Starting	November 1th 2021
Duration	18 months
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Mots-clés –
Genetic, Epigenetics, Transcriptomics, Heredity, Aquaculture, Host/pathogen interactions

Mission –
Host/pathogen interactions are characterized by a co-evolutionary dynamics through which the two partners impose strong selective pressures on each other. Among the mechanisms involved, recent studies have shown that genetic and epigenetic inheritance should be taken into account as a driver of phenotypic variation and therefore of host / pathogen coevolution. *Crassostrea gigas*, the most exploited oyster species in the world, has been facing the Pacific Oyster Mortality Syndrome (POMS) since 2008. This disease, which has become panzootic, represents a threat to oyster farming worldwide but display all the characteristics of a good model for studying the mechanisms of rapid adaptation to pathogen emergence. Indeed, recent data have shown that the resistance of oysters to OsHV-1 µvar virus rely on several inherited but non-exclusive molecular mechanisms, involving genetic and non-genetic (epigenetics and microbiota) bases. The objectives of this project will be to study the molecular bases of oyster resistance to POMS through the triptych genome, epigenome and transcriptome. The responses to this objective will provide resistance markers that would be used in marker-assisted selection programs and, new empirical data to enrich the knowledge on the role of genetic and non-genetic inheritance in species adaptability to pathogen emergence

Activity-
To study the molecular basis of oyster resistance to POMS we will study the triptych genome, epigenome and transcriptome. This will require carrying out: i) experiments in controlled environments , ii) molecular biology (DNA / RNA extraction, sequencing library construction, etc.), iii) bioinformatic processing of sequence data (filtering, mapping, SNP calling, Methylation calling…), iv) implementation of biostatistical approaches for the identification of the association between CpG / SNP / DEGs / molecular phenotype/ Resistance to the disease, v) result presentation in team meetings and congresses, vi) writing of scientific reports and articles.

Expected skills –
The candidate will hold a PhD in genomics, (epi)genetics, molecular ecology or bioinformatics. He / she will have good knowledge in (epi)genomics, quantitative genetics and bioinformatics. Experience in phenotype / (epi)genotype association studies (EWAS, GWAS, QTL, eQTL, methQTL…) will be appreciated. The candidate will be involved in a multidisciplinary consortium; he / she should be curious about other disciplines and have good oral and written

communication skills.

Work context -

The candidate will join the Microevolution of Interactions team of the Hosts Pathogens Interactions laboratory at the Montpellier area. He / she will have to interact regularly with the participants of the GestInnov project within the laboratory but also with the external partners.

Constraint and risks –

Field trips and travel for meetings will have to be carried out. The candidate will have to handle potentially hazardous chemicals and biological agents but these won't represent a danger if good laboratory practices are respected.

Detailed scientific program

1 Context -

Host/pathogen interactions are characterized by a coevolutionary dynamics through which the two protagonists impose strong selective pressures on each other. Thus, populations of pathogens go through natural selection to acquire new mechanisms allowing them to counter the defense strategies of hosts, which themselves undergo perpetual adaptations.

Among the mechanisms involved, only those encoded by changes in the genome sequence have been considered for a very long time. Recent studies have shown that non-genetic inheritance, in particular epigenetics, must be taken into account as a motor of phenotypic variation [1]. Thus, it is now necessary to consider that the phenotype of the host, encoded by the genotype and the epigenotype (under environmental influence), is the material on which selection by the pathogen acts (and vice versa) and that it is this phenotype that will be transmitted to the offspring [2].

Recent works conducted in a controlled environment have combined the study of genetic and epigenetic factors; they were able to explain phenomena hitherto misunderstood, particularly in invertebrates, such as the induction of resistance during the lifetime of an initially sensitive genotype and then the transmission of this trait to subsequent generations (transgenerational priming / shaping ; [3,4]).

The concerted implication of these genetic and epigenetic mechanisms must now be understood in natural populations and in many biological models in order to determine their validity in an ecological context. This is a necessary prerequisite to determine the relative weight of genetics and epigenetics in the adaptability of species in natural environment especially in response to the emergence of diseases, an increasingly frequent and problematic phenomenon in the Anthropocene era [5].

In the context of intensification and globalization of aquaculture, epidemics have had a considerable impact on many aquaculture industries. The main species of oyster exploited in the world and in France, *Crassostrea gigas,* is a good example of this trend. Indeed, during the last twenty years, events of recurrent mortalities have been recorded in the production of *C. gigas* [6]. In 2008, the farmers had to deal with an unprecedented event of massive mortalities, which has now become annual and that can locally reach up to 80% of juveniles mortality [7]. In 2016, this mortality rate reached in France 66.7% of juveniles less than one year old [8].

This disease, called Pacific Oyster Mortality Syndrome (POMS), has a complex etiology. Recently, our group has developed a holistic approach to characterize its pathogenesis. We have shown that this disease is polymicrobial. The process begins with a viral infection caused by the herpes virus OsHV-1 µvar. This infection partially affecting the immune cells of the oyster induces

immune suppression of the host and microbiota dysbiosis, paving the way for a secondary bacterial infection leading to death by a bacteraemia [9].

In this same study, we demonstrated that, at the molecular phenotype level, the resistant oyster families developed a faster and more intense antiviral response than the sensitive ones [9]. In addition, the level of basal transcription of certain genes seems to be able to predict the resistance or the sensitivity of an individual [9-12].

While this disease is polymicrobial, the determinants of resistance are also multifactorial. Quantitative genetic studies have shown that resistance is an inherited trait, [13] based in part on the DNA sequence thanks to the identification of QTL [14,15]. Other studies focused on the microbiota showed that certain microorganisms (in particular a species of cyanobacteria) are specifically associated with resistant or sensitive oysters and can be used as predictors of the disease outcome [16]. It has also been shown that exposure during embryonic development to a diversified microbial flora improves the resistance rate of the exposed cohort by 50% thanks to an immunomodulatory effect [17].

In this last work, it was shown that this enhanced phenotype was transgenerationally inherited, suggesting the involvement of epigenetic mechanisms in the expression of this resistance [17]. This last hypothesis was recently strengthen in natural environments where wild populations of genetically undifferentiated oysters showed significant contrasts in resistance although distant by only a few hundred meters [18].

2 Aims of the project -

The objective of this project is to study the molecular bases of oysters' resistance to POMS through the study of the triptych genome, epigenome and transcriptome. This will provide markers of resistance that would be used in marker-assisted selection programs. In addition, this empirical data will enrich the knowledge on the role of genetic and non-genetic inheritance in species adaptability to pathogen emergence.

3 Methods -

1 Sampling and biological material (in progress)

Populations of wild oysters will be sampled in 5 production basins (Brittany, Marennes-Oléron, Arcachon basin, Leucate lagoon, Thau lagoon). Within these basins, two oyster populations, one from areas with high infectious pressure, one free from disease, will be sampled. The adult oysters sampled will be used for the production of juveniles. Viral populations living in sympatry with oyster populations sampled in infectious zones will also be sampled.

2 : Experimental and *in natura* infection (November 2021)

Experimental infections in allopatric and sympatric interactions will be carried out, with the objective of characterizing in a standardized way the resistance of the hosts in the case of sympatric (host and virus of the same geographical location) and allopatric (host and virus from localizations) interactions (different geographic areas). This experiment will also produce the samples that will be used for the characterization of the molecular phenotypes (transcriptome) of resistance/susceptibility and the molecular determinants (genetic/epigenetic) of these phenotypes. In parallel with this controlled experiment, each oyster population produced will be deployed in Marennes-Oléron and in the Thau lagoon in order to validate the phenotypes obtained in natural environment.

3 Integrative Omics

The characterization of the molecular phenotype in "naïve" condition and during the immune response of the hosts (early stages) will be carried out by a Quant-seq approach.

The characterization of the genotype and the epigenotype of the oysters will be done jointly by a WGBS-seq approach.

4 Bioinformatics and biostatistics

The project will benefit from Ifremer's computing infrastructure for the sea, the super calculator Datarmor. After an initial analysis which will be carried out at each level of organization, the association between the resistant phenotype, the molecular phenotype, the genotype and the epigenotype will be made according to existing methodologies. This will include approaches such as the detection of expression QTL [19], the detection of QTL by mixed linear model approaches [20] or that of methQTL [21]. We will take into account the population structure using nested GLM-type models. Population-based approaches using GWAS and EWAS will also be considered [22,23].

4 Means available to develop the project -

The funding necessary for the development of this Post-Doctoral project has already been obtained (FEAMP 2020 GestInnov project and Ifremer GT-Huitre project). The GT-Huitre project started in September 2020 and will run until September 2024. The Gestinnov project will start in October 2021 and end in June 2024. The entire duration of the post-doctoral period will therefore be covered. All the material resources of the IHPE laboratory necessary for the development of the project [notably bioinformatics and genomics resources] will be made available to the young researcher.

5 Expected results and valorization -

This Post-doctoral fellow will help to decipher the molecular basis beyond the resistance of oysters to the POMS. The results will be valued by at least one high impact publication and presentations in international congresses. In combination with the other works conducted at the IHPE lab, this post-doctoral project will contribute to the complete elucidation of POMS complexity.

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