

Epigenetic and genetic determinants of resistance in the Pacific oyster *Crassostrea gigas* : A case study in natural population

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INTERACTION HOST PATHOGEN ENVIRONMENT



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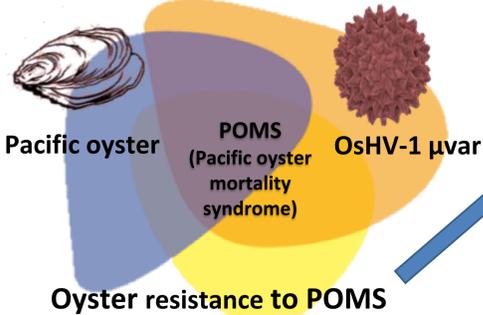
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Introduction



- Resistance of oyster to POMS (Pacific oyster mortality syndrome; caused by OsHV-1 μ var virus) are associated with:
- Early transcriptomic response to the viral infection (de Lorgeril et al. 2018)
- Genetic basis of the resistance (Dégremont et al. 2015; Azéma et al. 2017)
- Some evidences support a role of the microbiota and the epigenetic (DNA methylation in CpG context) as factors involved in resistance (Clerissi et al. 2020; Fallet et al. 2020)

Objectives

Here we propose to simultaneously study the potential role of genetics and epigenetics in the shaping of resistant or susceptible phenotypes in natural populations.

- Hypothesis 1:** Selective pressure is stronger in farming than in non-farming areas
- Hypothesis 2:** Oyster resistance is partly genetically and epigenetically encoded

Experimental design

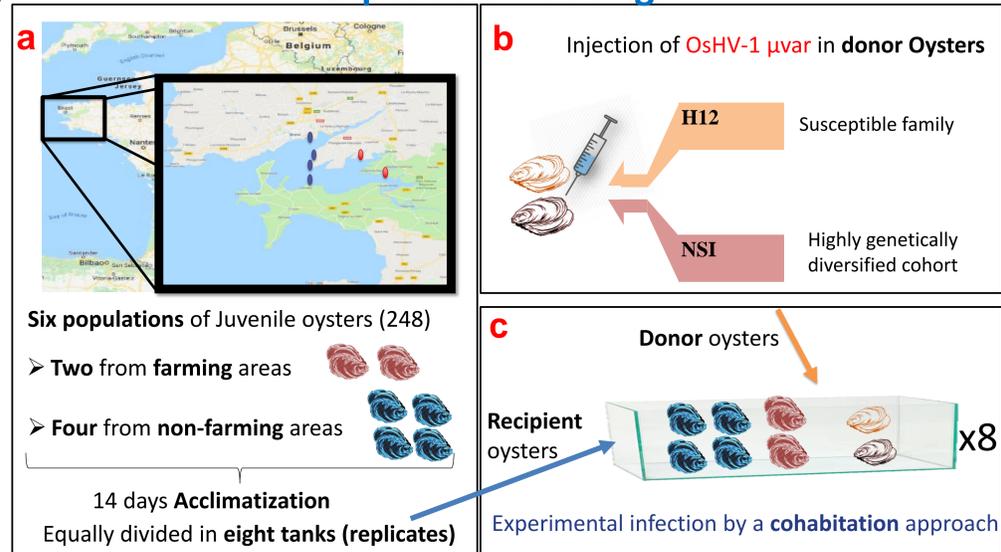


Figure 1: a) Sampling strategy of natural populations of the Pacific oyster (*Crassostrea gigas*) in the Rade of Brest from: Farming areas, Red circle (high densities of oysters, presence of the virus OsHV-1 μ Var and POMS) and non-farming areas, Blue circles (low densities of oysters, undetectable virus and absence of POMS). b) Injection in donor oyster with viral isolate from different location. c) Experimental infection in a randomized complete block design. The six populations of oyster were equally divided into eight replicates. Infection was induce by the cohabitation with infected donor oysters.

Phenotyping result

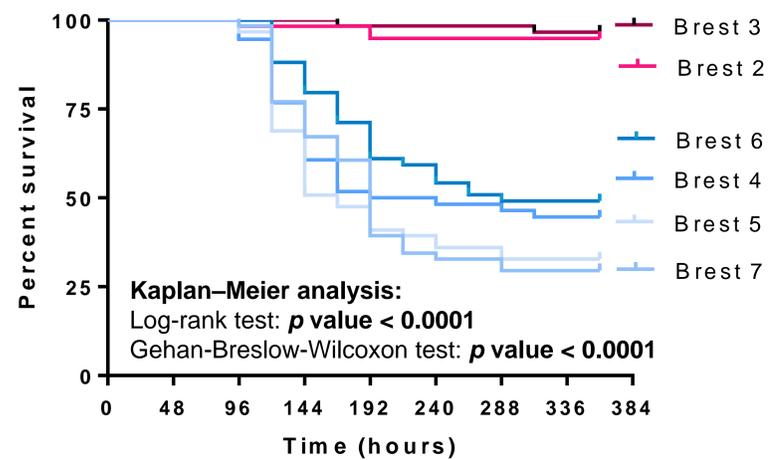


Figure 2: Survival curve for the 248 samples after 14 days of experimental infection.

- Significant higher survival rates in farming than non-farming populations
- We sequenced 248 libraries prepared by exome capture “Seq Cap Epi Enrichment System”, to get the genetic (SNPs) and epigenetic (DNA methylation) information..

Genome / Epigenome wide association studies (GWAS / EWAS)

GWAS and EWAS were performed on 56,474 SNPs and 596,065 CpG sites, respectively.

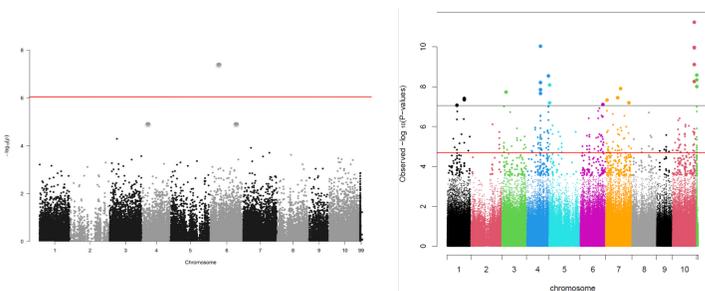


Figure 3: Manhattan plot of GWAS (left) / EWAS (right) analysis for Pacific oyster resistance to POMS. Genome-wide significance threshold (FDR) was represented by the red line.

- In EWAS analysis, 251 CpG sites were identified as significantly associated to the resistance (hyper and hypo methylation).
- Interestingly, 41 of these CpGs (highlighted in red in fig.4) were located in genes involved in oyster's innate immune response pathways such as TLR/NF-kB, JAK/STAT, Apoptosis, Autophagy, RIG-like receptors and STING dependent pathways.

- In GWAS analysis, only one (FDR threshold) SNP was significantly associated to resistance. This SNP was located in the UBA2 gene, known to be involved in the antiviral pathway JAK/STAT. SNPs
- Other SNPs with suggestive threshold (0.005 P-value) were located in genes involved in TLR/NF-kB, JAK/STAT, Apoptosis and Autophagy pathways.

Immune pathways involve in POMS resistance

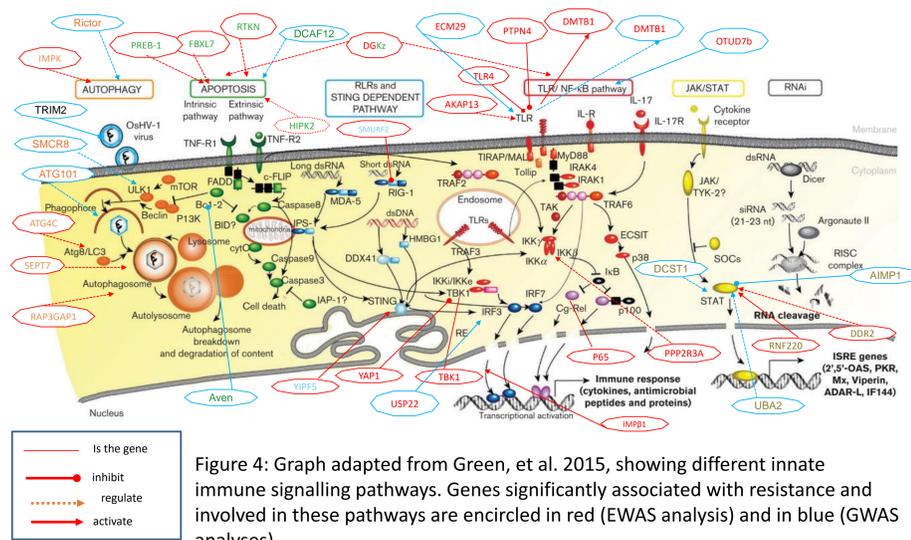


Figure 4: Graph adapted from Green, et al. 2015, showing different innate immune signalling pathways. Genes significantly associated with resistance and involved in these pathways are encircled in red (EWAS analysis) and in blue (GWAS analyses).

Conclusion and perspectives

- Oyster populations from farming areas are more resistance to POMS comparing to the population from non-farming areas. This hypothesis is supported by the fact that in non-farming area there is no POMS (or little POMS) and therefore no selective pressures rub off on oyster population.
- The first EWAS study associating DNA methylation to resistance to POMS.
- Genetic and epigenetic mechanisms are likely to contribute to heritable variation in oyster resistance.

References

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