



AQUATIC AND FISHERY SCIENCES
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Dear Editors,

We are pleased to submit the enclosed manuscript, "Epigenetic and genetic population structure is coupled in a marine invertebrate," for consideration in *Genome Biology and Evolution*.

Recent studies have considerably shifted our understanding of the contributions of epigenetic markers, specifically DNA methylation patterns, in shaping heritable traits. Now, a growing body of research is associating methylation variation with environmental exposures in marine invertebrates, particularly in trans-generational studies that suggest methylation changes in progenitors can be inherited. Few studies have controlled for (or described) the relationship between methylotype and genotype in test organisms, and those that do typically use summary statistics that may not fully capture such interactions, potentially resulting in an overestimation of environmentally-induced methylation changes.

Here, we address this gap using a multi-omic approach to characterize the interactions between genetic variation and epigenetic variation in a marine invertebrate. We leverage two genetically distinct populations of *Olympia* oysters that were bred and reared in common conditions to control for within-generational changes to the methylome.

Our novel study shows that genetic variation explains 27% of the variation in inter-individual DNA methylation patterns, which was not evident in the population-level approaches used previously in marine invertebrates. We provide a framework for future studies in environmental epigenetics to take genetic variation into account when teasing apart the drivers of phenotypic variation. Additionally, this study introduces the first publicly available draft genome and characterization of genome-wide methylation patterns in the oyster genus *Ostrea*, and to our knowledge, this is the first methylation QTL analysis in a marine invertebrate.

This manuscript is not under consideration by another journal, and all authors approve of the manuscript and its submission to *Genome Biology and Evolution*.

Thank you for your consideration.

Sincerely,
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