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The use of -omic tools in the study of disease processes in marine bivalve mollusks

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ABSTRACT

Our understanding of disease processes and host–pathogen interactions in model species has benefited greatly from the application of medium and high-throughput genomic, metagenomic, epigenomic, transcriptomic, and proteomic analyses. The rate at which new, low-cost, high-throughput -omic technologies are being developed has also led to an expansion in the number of studies aimed at gaining a better understanding of disease processes in bivalves. This review provides a catalogue of the genetic and -omic tools available for bivalve species and examples of how -omics has contributed to the advancement of marine bivalve disease research, with a special focus in the areas of immunity, bivalve–pathogen interactions, mechanisms of disease resistance and pathogen virulence, and disease diagnosis. The analysis of bivalve genomes and transcriptomes has revealed that many immune and stress-related gene families are expanded in the bivalve taxa examined thus far. In addition, the analysis of proteomes confirms that responses to infection are influenced by epigenetic, post-transcriptional, and post-translational modifications. The few studies performed in bivalves show that epigenetic modifications are non-random, suggesting a role for epigenetics in regulating the interactions between bivalves and their environments. Despite the progress -omic tools have enabled in the field of marine bivalve disease processes, there is much more work to be done. To date, only three bivalve genomes have been sequenced completely, with assembly status at different levels of completion. Transcriptome datasets are relatively easy and inexpensive to generate, but their interpretation will benefit greatly from high quality genome assemblies and improved data analysis pipelines. Finally, metagenomic, epigenomic, proteomic, and metabolomic studies focused on bivalve disease processes are currently limited but their expansion should be facilitated as more transcriptome datasets and complete genome sequences become available for marine bivalve species.

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Abbreviations: AIF-1, allograft inflammatory factor 1; AFLP, Amplified Fragment Length Polymorphism; AVNV, acute viral necrosis virus; C1qDC, C1q domain containing; EST, expressed sequence tags; FREPs, fibrinogen-related proteins; IL-17, interleukin-17; LC-MS, liquid chromatography with mass spectrometry; LC-MS/MS, liquid chromatography with tandem mass spectrometry; MAS, Marker Assisted Selection; MSX, multinucleated sphere X; NGS, next generation sequencing; OsHV-1, ostreid herpesvirus 1; PAMP, pathogen associated molecular pattern; PGRP, peptidoglycan recognition proteins; PRR, pattern recognition receptor; QPX, quahog parasite unknown; QTL, Quantitative Trait Loci; ROD, Roseovarius Oyster Disease; SNP, single nucleotide polymorphism; SSO, seaside organism; SRs, scavenger receptors cysteine-rich; SSR, single sequence repeats; VDAC, voltage-dependent anion channel.

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1. Introduction

The -omic-based disciplines focus on the analysis of structure and function of the genetic material (genomics and epigenomics), expressed genes (transcriptomics), proteins (proteomics), and low molecular weight metabolites (metabolomics) in an organism using an array of recently developed analytical high-throughput technologies. Additionally, these techniques allow for the study of species composition or expressed gene pathways in a complex mix of microorganisms (metagenomics/metatranscriptomics). These technologies have allowed researchers to better determine the complex relationships between genotypes, phenotypes, and the environment by simultaneously analyzing large numbers of individuals, genes, proteins, or metabolites in samples directly collected from the environment (reviewed in Carvalho and Creer, 2010). Therefore, these tools are particularly suited to study the complex interactions between hosts, pathogens, and the environment that lead to disease outbreaks (Fig. 1). In recent decades, there has been an explosion of the application of -omic technologies to address fundamental and applied research questions in human and veterinary medicine, from elucidation of novel mechanisms of immunity in model and non-model host species (Dheilly et al., 2014) to applications of whole-genome sequencing of pathogens to the development of diagnostic, prevention, and treatment tools (Firth and Lipkin, 2013). This explosion has been facilitated by the development of tools for the analysis of genomes of non-model species, as well as the decrease in the cost of high-throughput analysis technologies.

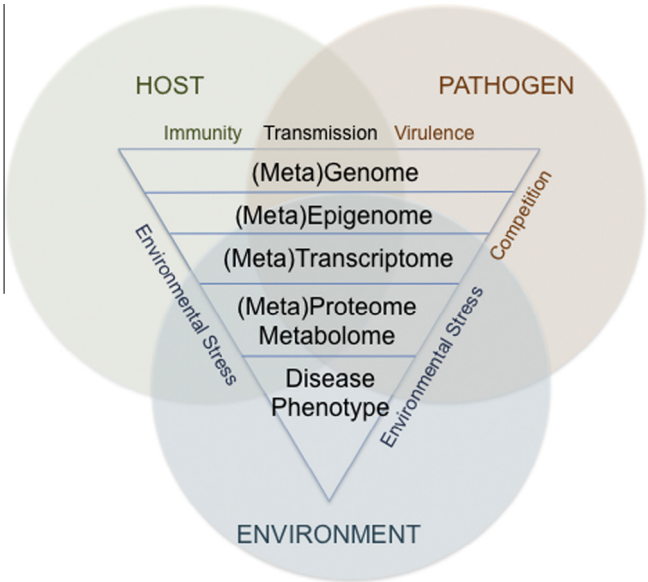

Fig. 1. The use of -omic tools to the study of disease processes. This figure integrates the traditional graphical definition of disease as the interaction between a host, a pathogen, and the environment (venn-diagram; Snieszko, 1974) With a triangle depicting the different -omic techniques that can be applied to the analysis of the structure and function of organisms involved in host–interactions, from the genes that inherently define hosts and pathogens (not directly affected by the environment), to the expression of these genes, proteins, and metabolites that define the phenotypes of the host and the pathogen (affected by the environment). All these -omic tools can be applied to either single organisms or the study of complex mixes of organisms (meta -omics).

The field of aquatic pathology has benefited from these major investments in studying the genomes, transcriptomes, and, to a lesser extent, the proteomes, metabolomes, and epigenomes of species of commercial and ecological interest. These tools have been also applied to the study of key pathogens causing major mortalities in these species. This review builds upon and expands several excellent reviews on the -omics of bivalve species (Cancela et al., 2010; Gestal et al., 2008; Guo et al., 2008; Peng, 2013; Rodrigues et al., 2012; Romero et al., 2012; Saavedra and Bachère 2006; Schmitt et al., 2012; Suárez-Ulloa et al., 2013; Wang et al., 2013; Yue, 2014) to provide some examples on how -omic tools have been used in the study of immunity and host–pathogen interactions in molluscan bivalves, and how this knowledge has been applied to two key areas in the management of the impact of infectious diseases on wild and cultured populations of these species: (a) the development of disease resistant strains (Section 5); and (b) the development of diagnostic tools (Section 8).

2. Genetic and genomic resources available for disease research and management in bivalve species

Most of the health management issues affecting marine bivalve molluscs can be addressed through improved knowledge of (1) the genetic mechanisms underlying relevant traits such as fast growth (which reduces risks to some disease-related losses by decreasing harvest time) and resistance/tolerance to diseases, (2) existing environmental stressors and anticipated stressors resulting from environmental change, and (3) the ability of bivalves to limit the uptake and accumulation of human pathogens and heavy metals in tissues and/or eliminate them under depuration (e.g. Camara et al., 2005). In particular, knowledge of underlying genetic