Journal of Invertebrate Pathology 131 (2015) 121–136

Contents lists available at ScienceDirect

Journal of Invertebrate Pathology

journal homepage: www.elsevier.com/locate/jip

Review

Immune responses to infectious diseases in bivalves

Bassem Allam [a,*], David Raftos [b,c]

[a] School of Marine and Atmospheric Sciences, Stony Brook University, Stony Brook, NY 11794-5000, USA
[b] Department of Biological Sciences, Macquarie University, North Ryde, NSW 2109, Australia
[c] Sydney Institute of Marine Science, Chowder Bay Road, Mosman, NSW 2088, Australia

ARTICLE INFO

Article history:
Received 20 November 2014
Revised 7 April 2015
Accepted 5 May 2015
Available online 21 May 2015

Keywords:
Immunity
Innate
Mollusk
Bivalve
Hemocyte

ABSTRACT

Many species of bivalve mollusks (phylum Mollusca, class Bivalvia) are important in fisheries and aquaculture, whilst others are critical to ecosystem structure and function. These crucial roles mean that considerable attention has been paid to the immune responses of bivalves such as oysters, clams and mussels against infectious diseases that can threaten the viability of entire populations. As with many invertebrates, bivalves have a comprehensive repertoire of immune cells, genes and proteins. Hemocytes represent the backbone of the bivalve immune system. However, it is clear that mucosal tissues at the interface with the environment also play a critical role in host defense. Bivalve immune cells express a range of pattern recognition receptors and are highly responsive to the recognition of microbe-associated molecular patterns. Their responses to infection include chemotaxis, phagolysosomal activity, encapsulation, complex intracellular signaling and transcriptional activity, apoptosis, and the induction of anti-viral states. Bivalves also express a range of inducible extracellular recognition and effector proteins, such as lectins, peptidoglycan-recognition proteins, thioester bearing proteins, lipopolysaccharide and β1,3-glucan-binding proteins, fibrinogen-related proteins (FREPs) and antimicrobial proteins. The identification of FREPs and other highly diversified gene families in bivalves leaves open the possibility that some of their responses to infection may involve a high degree of pathogen specificity and immune priming. The current review article provides a comprehensive, but not exhaustive, description of these factors and how they are regulated by infectious agents. It concludes that one of the remaining challenges is to use new "omics" technologies to understand how this diverse array of factors is integrated and controlled during infection.

Contents

* Corresponding author.
E-mail address: Bassem.Allam@stonybrook.edu (B. Allam).

http://dx.doi.org/10.1016/j.jip.2015.05.005
0022-2011/

1. Introduction

Global production of bivalve mollusks reached over 13.2 million tons in 2012 representing a commercial value in excess of 16 billion US$ (FAO, 2014). This growing economic importance of bivalves has been associated with an increased awareness of, and attention to, infectious diseases affecting these animals. Currently, there are eight infectious diseases impacting mollusks that are listed by the Office International des Epizooties (OIE, the World Organization for Animal Health), including two viral infections, a prokaryote infection and five infections caused by protistan pathogens. Six out of these 8 infections impact bivalves. In parallel, there was a growing interest in the study of bivalve immunity and in the exploration of mechanisms used by these organisms to fight and resist infectious agents (Bachère et al., 2004; Bayne, 1983; Cheng, 1981; Chu, 1988; Song et al., 2010a). This was driven by 3 interrelated reasons: (1) thrive for basic understanding of immunity in bivalves in a comparative framework among the invertebrates, (2) generation of information for the development of disease-resistant varieties of cultured bivalves, and (3) discovery of new bioactive compounds for biotechnological applications. Since the pioneering work of Cuénot (1914) over a century ago, a large body of information has accumulated on the characteristics of cellular and humoral factors mediating immunity in bivalves, even though current knowledge remains for the most part descriptive. Functional characterization of the components of the bivalve immune system remains fragmentary and, when available, often circumstantial. The truth is that it is often difficult to identify immune responses proper towards an infection versus changes in a particular defense-related factor as an indirect, general, stress response. In this paper, highlights of the bivalve immune responses to some of the important infectious diseases affecting this group will be described. Focus will be given to provide information in a comparative framework to assess immune response towards infectious agents ranging from viruses to metazoans.

2. General organization of the bivalve defense system

The bivalve defense system includes several layers of physical and biological barriers. The most obvious physical barrier is provided by the shell that supports and protects the soft tissue from biological and physico-chemical insults. The second physical barrier beyond the shell is provided by the skin and the mucosal layer that covers it and that entraps microbes facilitating their elimination via ciliary activity. Internal defense is ensured by the effectors of the innate immunity. Like most invertebrates, bivalves have an open circulatory system populated by hemocytes (molluscan blood cells, previously and sometimes still referred to as amoebocytes) that circulate in hemolymph vessels and sinuses as well as throughout soft tissues. The circulation is mainly ensured by a systemic heart, which in bivalves is often located near the posterior adductor muscle, lodged in a pericardial coelom delimited by the pericardium. Most prior work on molluscan immunobiology targeted internal immune factors and activities associated with circulating hemocytes and dissolved humoral factors of the plasma which work in a complementary fashion to neutralize invading organisms. Invaders are detected via humoral and hemocyte-bound recognition factors, triggering the production of cytokines that mediate the recruitment of additional hemocytes, activation of phagocytosis and the production and/or release of a wide range of antimicrobial compounds. Recent research suggests a certain level of specific immune priming in mollusks (Wang et al., 2013; Zhang et al., 2014b). Even though precise mechanisms for "immune memory" have not been fully established in the invertebrates, they are thought to involve recognition factors such as thioester-containing proteins (Rodrigues et al., 2010), C-type lectins (Wang et al., 2013) or the Down syndrome cell adhesion molecule, Dscam (Ng et al., 2014).

In addition to internal defense ensured by circulating hemocytes and plasma factors, a growing body of evidence highlights the role of immune factors associated with mucosal surfaces in interactions with microbes. Peripheral compartments such as bivalve's extrapallial cavity (space between mantle and shell) have been shown to contain abundant hemocytes that contribute to the immune protection of these compartments (Allam et al., 2001, 2000a; Allam and Paillard, 1998) in addition to their role in biomineralization and shell deposition (Beedham, 1965; Fisher, 2004; Mount et al., 2004; Wilbur, 1964). Hemocytes have been also described in association with mucosal secretions covering pallial surfaces (Allam, 1998; Lau et al., 2013a,b; Takatsuki, 1934). These "peripheral" hemocytes are functionally active as demonstrated by their ability to phagocytose biotic and abiotic particles and to secrete hydrolytic and antimicrobial compounds (Allam, 1998; Allam and Paillard, 1998; Lau et al., 2013b; Takatsuki, 1934). They can move bi-directionally via trans-epithelial migration (Allam, 1998; Lau et al., 2013a), providing the animal with a sentinel system similar to that played by dendritic cells in vertebrates. The extrapallial fluid has also been shown to contain hydrolytic enzymes such as lysozyme and peptidases (Allam and Paillard, 1998) that contribute to pathogen neutralization. Similarly, humoral defense factors associated with bivalve pallial mucus have been suggested to represent the first line of immune defense in these animals extending the defensive role of mucus beyond that of a simple physical barrier. Mucosal secretions covering bivalve pallial organs were shown to contain a wide range of antimicrobial factors (Allam and Pales Espinosa, 2015; Pales Espinosa et al., 2014). Previous studies have shown that oyster pallial mucus contains agglutinins (a functional but generic term that encompasses proteins that agglutinate non-self entities) that interact with various bacterial species (Fisher, 1992). More recent work showed that some of these agglutinins are lectins that bind microbes through protein-carbohydrate interactions (Pales Espinosa et al., 2009; Xing et al., 2011). Previous studies also reported the presence in pallial mucus of hydrolytic enzymes that likely contribute to host protection, such as lysozyme (McDade and Tripp, 1967) and proteases (Brun et al., 2000). The contribution of these external immune factors to bivalve health is greatly under-investigated and very likely under-estimated. While a rich body of literature exists on host-pathogen interactions in mollusks once infection is established, the interactions of microbes and their hosts at these water-tissue interfaces during initial encounters remain poorly characterized. This lack of information is exacerbated by the fact that virtually all economically important infections affecting these animals initiate at mucosal surfaces.