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A review of the immune molecules in the sea cucumber

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ABSTRACT

It is very important to identify and characterize the immune-related genes that respond to pathogens. Until recently, only some of the immune-related genes in sea cucumbers had been characterized. Their expression patterns after pathogen challenges have been analyzed via expressed sequence tag libraries, microarray studies and proteomic approaches. These genes include lectins, antimicrobial peptides, lysozyme, enzymes, clotting protein, pattern recognition proteins, Toll receptors, complement C3 and other humoral factors that might participate in the innate immune system of sea cucumbers. Although the participation of some of these immune molecules in the sea cucumber's innate immune defense against invading pathogens has been demonstrated, the functions of many of the molecules remain unclear. This review focuses on the discovery and functional characterization of the immune-related molecules from the sea cucumber for the first time and provides new insights into the immune mechanisms of the sea cucumber, which opens new possibilities for developing drugs for novel anti-bacterial and antiviral applications in fisheries.

1. Introduction

Marine invertebrates rely solely on innate immunity, which includes both humoral and cellular responses, as they lack an adaptive immune system. Various methods employed to counteract infectious agents include coagulation, cell agglutination, encapsulation and phagocytosis [1,2]. The microbial load in the natural marine habitat can number up to 10^6bacteria per mL and 10^9 viruses per mL of seawater [3]. It is therefore imperative that animals develop a robust innate immune system for survival.

The sea cucumber is a marine animal belonging to the Holothuroidea. As a food, it has many widely accepted benefits as a candidate source of novel drugs [4]. Sea cucumber numbers have reached billions, making it one of the most numerous aquaculture species in China. In recent years, sea cucumber disease has become a serious issue for the increasing number of sea cucumbers in the aquaculture industry. The emergence of a large number of reports about sea cucumber diseases that could impact the national economy [5,6]. Bacterial disease is the most reported and the most serious disease in the current aquaculture production.

A sea cucumber has a cavity between its digestive tract and body wall that is filled with fluid and suspended coelomic cells that are similar to blood cells. The cellular immunity of the sea cucumber is accomplished by coelomocytes, and the humoral immune response is based on the secretion of various immune factors into the coelomic cavity by coelomocytes [7–10]. When sea cucumbers are attacked by pathogens, they rely on their effective cellular and humoral innate immune responses to identify and exclude invading microbes and repair wounds, but many defense mechanisms are still unknown. Therefore, the immune factors of sea cucumber are the main receptors in the host defense against the invasion of pathogenic bacteria. These immune molecules include lectins, antimicrobial peptides, lysozyme, enzymes, clotting protein, pattern recognition proteins, Toll receptors, complement C3 and other humoral factors that might participate in the innate immune system of sea cucumber.

In this review, we describe the discovery of immune-related molecules by the high-throughput technologies of genomics and proteomics and the characterization of these immune molecules that participate in the major immune reactions against invading pathogens in the sea cucumber.

2. Expressed sequence tag (EST) and proteomic analysis of immune genes in sea cucumber

Sea cucumber is an economically important aquaculture species in China. Diseases are major issues that cause serious economic

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Table 1
Immune-related genes of sea cucumber initially identified by expressed sequence tag (EST) and proteins as well as their characterized functions.

Immune-related genes	Tissue distribution	Function	Reference
Pattern recognition receptors and signaling			
Mannan-binding C-type lectin	RT,CM	Agglutination	Bulgakov et al. 2007;Yang et al. 2009; Yang et al.2010; Dong et al.2014
Rhamnose-binding lectin(SAL)	BW	ND	Yang et al. 2009
GalNAc-specific lectin	BW	ND	Yang et al. 2009
Secreted lectin homolog; HeEL-1	BW, Int	ND	Yang et al. 2009
Serum lectin	BW	ND	Yang et al. 2009
NACHT leucine-rich repeat and PYD containing protein	Int	ND	Yang et al. 2009
Peptidoglycan recognition protein SC2	Int	ND	Yang et al. 2009
Ficolin-like	BW,Int	Agglutination	Francisco et al. 2008;Yang et al. 2009
Fibrinogen-like protein	BW, RT, Int	ND	Francisco et al. 2008;Yang et al. 2009; Dong et al. 2014
Ficolin	CM	ND	Zhang et al. 2014
Tenascin R	RT	ND	Yang et al. 2009
Myp	Int	ND	Yang et al. 2009; Francisco et al. 2009;
Ahcy	Int	ND	Yang et al. 2009
Gnmt	Int	ND	Yang et al. 2009
Angiopoietin-like 7	Int	ND	Yang et al. 2009
Thymosin beta	RT,Int	ND	Francisco et al. 2008; Francisco et al. 2009; Yang et al. 2009; Yang et al.2010; Dong et al. 2014
Heat shock protein	Int, BW	ND	Yang et al. 2009; Yang et al.2010; Dong et al. 2014
Ferritin	Int, BW, RT	ND	Francisco et al. 2008;Yang et al. 2009; Yang et al.2010
Echinonectin	BW,Int	ND	Francisco et al. 2008;Yang et al. 2009
Cyclophilin A	RT	ND	Yang et al. 2009
Mannose receptor, C-type 1-like 1	BW	ND	Yang et al. 2009
Nectin	BW	ND	Yang et al. 2009
Thioredoxin	BW	Antioxidant activity	Yang et al. 2009
Cysteine-rich secretory protein-2	Int	ND	Yang et al. 2009
Nesprin-1 beta	Int	ND	Yang et al. 2009
Cellular retinol-binding protein type 1b	Int	ND	Yang et al. 2009
Serine proteinase inhibitor	RT, Int	Protease inhibitor	Francisco et al. 2008;Yang et al. 2009; Yang et al.2010
Blood island enriched Kruppel-like factor	BW	ND	Yang et al. 2009
Suppressor of defective silencing 3 homolog	Int	ND	Yang et al. 2009
Zonadhesin	BW	ND	Yang et al. 2009
MyD88	Int, RT	ND	Lu et al.2013
TRAF6	CM	ND	Lu et al.2013
Phenoloxidase	CM	ND	Jiang et al.2014
Toll-like receptor	Int, CM, RT, BW	ND	Sun et al. 2013;Lu et al. 2013; Dong et al. 2014
NF-κB	CM	ND	Wang et al.2013
Complement system			
Complement component C3	RT, Int	ND	Yang et al. 2009; Zhou et al.2011; Dong et al. 2014
Complement component Bf	BW	ND	Yang et al. 2009;Dong et al. 2014
Complement regulator factor H	BW		Yang et al. 2009; Dong et al. 2014
Cytokines and growth factors			
Receptor (TNFRSF)-interacting serine−threonine kinase 1	RT	ND	Yang et al. 2009
Interleukin enhancer binding factor 3	RT	ND	Yang et al. 2009
Macrophage differentiation protein	BW	ND	Yang et al. 2009
Transferrin superfamily members			
Major yolk protein	RT, Int	ND	Francisco et al. 2008; Francisco et al. 2009; Yang et al. 2009
Toposome	RT, Int, BW	ND	Francisco et al. 2008;Yang et al. 2009
Effector genes			
Lysozyme	Int, RT	Antimicrobial activity	Cong et al. 2009; Yang et al. 2009; Yang et al.2010; Dong et al.2014
V-fos transformation effector protein, transcript variant 1	RT	ND	Yang et al. 2009
Dual oxidase	Int	ND	Yang et al. 2009
1DD104	Int	ND	Francisco et al. 2008; Francisco et al. 2009; Yang et al. 2009; Yang et al.2010
Cathepsin C/J	Int, CM	ND	Francisco et al. 2008; Francisco et al. 2009
Melanotransferrin	BW, RT, CM	ND	Francisco et al. 2008; Francisco et al. 2009; Yang et al. 2009;Qiu et al. 2014
Calreticulin	CM	Ca^{2+} modulation	Zhang et al. 2014
Phospholipase C-gamma	CM	Ca^{2+} modulation	Zhang et al. 2014
Chaperone protein DnaK	CM	Molecular chaperones	Zhang et al. 2014
Calumenin	CM	Ca^{2+} modulation	Zhang et al. 2014
Guanine nucleotide binding protein (G protein)	CM	Ca^{2+} modulation	Zhang et al. 2014
Glutathione S-transferase	CM	ROS elimination	Zhang et al. 2014