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Editorial Note on Neuroendocrine Immune System

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Editorial

The neuroendocrine-immune (NEI) regulatory network is a complex system, which plays an indispensable role in the immunity of the host. In the present study, the bio informatical analysis of the transcriptomic data from oyster Crassostrea gigas and further biological validation revealed that oyster TNF could activate the transcription factors NF-κB and HSF (heat shock transcription factor) through MAPK signaling pathway, and then regulate apoptosis, redox reaction, neuro-regulation and protein folding in oyster haemocytes. The activated immune cells then released neurotransmitters including acetylcholine, norepinephrine and [Met5]-enkephalin to regulate the immune response by arising the expression of three TNF and translocating two NF-κB (Cgp65,) between the cytoplasm and nuclei of haemocytes. Neurotransmitters exhibited the immunomodulation effects by influencing apoptosis and phagocytosis of oyster haemocytes. Acetylcholine and norepinephrine could down-regulate the immune response, while [Met5]-enkephalin up-regulate the immune response. These results suggested that the simple neuroendocrine-immune regulatory network in oyster might be activated by oyster TNF and then regulate the immune response by virtue of neurotransmitters, cytokines and transcription factors.

The neuroendocrine-immune (NEI) regulatory network consists of nervous system, endocrine system and immune system, which carries a reciprocal regulation to maintain homeostasis in the host with the involvement of signaling molecules, such as neurotransmitters, hormones and cytokines. The accumulating evidences in the last decades have clearly documented the vital importance of NEI network in the regulation of physiological homeostatic mechanisms, in particular with regard to immunomodulation functions.

The structure and function of the NEI regulatory network in vertebrates have been well understood, and the connections between neuroendocrine system and immune system are mediated by nerve pathways, hormonal circuits, cytokines, neuropeptides and chemokines. The central nervous system (CNS) mediates both innate and adaptive immunity through systemic, regional and local routes. The peripheral nervous system provides the first line of defense at local sites, while the sympathetic (or adrenergic) nervous system (SNS) and the parasympathetic (or cholinergic) nervous system generally inhibit inflammation at a regional level.

Once the host is invaded by pathogenic microorganisms, the immune system will be activated immediately by immune surveillance cells, and then generate immune mediators to activate peripheral sensory afferent neurons. The activated neurons release neurotransmitters, such as neuropeptides, to up-regulate the immune response level and transfer the immune signals to the CNS at the same time. When the immune response exceeds a certain threshold or the pathogens are completely removed, the CNS releases immune mediators such as glucocorticoids, acetylcholine and catecholamines by controlling adrenal or autonomic nervous system to suppress immune response in case of an immune injury. Meanwhile, energy is re-allocated in the above processes to maintain the immune response and homeostasis There are various kinds of neuroendocrine-immune axes and neuroendocrine cells in mammals to impinge on neuro-immunomodulation.

Analogous NEI network has also been found in invertebrates. The structure of nervous system in invertebrates is relatively simple, and its diversity and complexity increases along with the evolution. A primitive nervous system consisting of two neurons exists in the most primitive multicellular organisms sponges, and there are neither synaptic contacts nor motion-control functions between neurons. In Cnidaria, neurons contact with each other through synapses within a reticular nervous system, while there is a trapezoidal nervous system in Platyhelminthes, indicating a dramatic progress in evolution. A chain nervous system consisting of pharyngeal ganglia and abdominal ganglia occurs in Annelida and Arthropoda, dominating contractile activity of muscles [1-5].

Molluscs have the well-developed nervous system in invertebrates 14 with the presence of cephalic ganglia, pleural ganglia, visceral ganglia and pedal ganglia. For example, the nervous system of oyster Crassostrea virginica consists of two cerebral ganglia (CG) under the palps, and one visceral ganglia (VG) near the posterior adductor muscle with the nerve fibers connecting them. Although the nervous systems vary dramatically in structure, a growing number of ancestral molecules have been found in invertebrates sharing similar roles in the immune regulation of vertebrates, which makes it believable that hormonal and neuronal immune-regulating routes do exist in invertebrates.

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