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EDITORIAL

Neuroimmunology: reviews and perspectives on recent advances

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In an abstract sense, the immune system is tasked to monitor and interpret insults and potential threats from the external world and mount appropriate defensive actions accordingly. At the same time, it also monitors states of internal organs and facilitates resistance to perturbation and maintenance of homeostasis. The same abstraction applies to the nervous system, which processes information from the external and internal worlds and commands reactions to external and internal stimuli in order to maintain homeostasis. Increasingly, the seemingly autonomous immune system and nervous system are found to be subjected to monitoring, interpretation and regulation by each other. Immune cells and their complex behaviors are monitored, interpreted, and regulated by the nervous system, while neurons and glial cells in the nervous system are under immune surveillance and their physiological functions even depend on factors derived from immune cells. Therefore, it is critical to understand the rules and principles of neuro-immune crosstalk in physiology and disease, an area that has seen probably the most fast-growing development in contemporary immunology. In this issue, four leading experts in the field review recent advances and provide perspectives in several selected topics of neuroimmunology.

Dr. Hai Qi

The gastrointestinal (GI) tract is arguably the most complex organ system from the perspective of neuroimmunology. It interfaces with the external world and is in constant interactions with microbiota while mediating its physiological functions in food digestion and nutritional absorption. In his review [1], Chiu and colleagues explain in detail recent advances in understanding of how different types of neurons, namely, sensory, sympathetic, parasympathetic and enteric neurons interact with and functionally impact on various immune cells. As effects of different dopaminergic, cholinergic, and peptidergic neurotransmitters on GI immune cells are delineated in more precise detail genetically, biochemically and cell biologically, we begin to appreciate the principle of the most basic neuroimmune regulatory units that involve any nerve ending and any given type of immune cells. The authors nicely point out important gaps in our understanding, particularly with regards to whether and how immune status of the GI tract (or a segment) are represented in higher centers of the brain and whether and how the brain may then use that information to regulate the GI system in a top-down manner.

The first of the two broad but important questions above is summarily dealt with by Asya Rolls in her perspective [2]. Building on her recent discovery that specific neurons in the insular cortex is activated during colitis and, upon reactivation, can recall colitic inflammation, Rolls proposes the concept of immunoception to explain a potential way of representing immune status of internal organ systems in the insular cortex. Synthesized in this concept is a larger body of direct and indirect evidence for that immune information may be carried in afferents from the periphery, as opposed to or in addition to immune mediators acting on the central nervous system directly. The idea that an "immunengram" is composed of neurons in specific regions of the central nervous system in collaboration with cells in the target peripheral tissue will surely provoke new thoughts and experiments.

While it is important to understand how the brain perceive and represent in high centers the immune status of peripheral organs, the immune system certainly has a foothold inside the central nervous system as macrophages. Microglia are the most abundant and the most important macrophages in the brain. They can respond to blood-borne immune mediators and metabolites alike and modulate neuronal functions by their phagocytic activities and by various secreted factors. In the third review of the series [3], Ginhoux and colleagues summarize current understanding of the ontogeny, location, gene expression patterns and functional programming of brain macrophages as pertinent to the development and function of the nervous system. The authors prominently highlight the intimate involvement of microglia and other brain macrophages in major diseases of the central nervous system, from tumors to degeneration. They point to a future with a more holistic approach in dissecting the complex biology of brain macrophages and its impact on the interactions between the nervous and immune systems.

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If how immune cells other than macrophages regulate neuronal functions inside the brain is only alluded to in the aforementioned reviews, Kipnis and colleagues put it front and center in their piece [4]. They discuss how the type 2 response, which is primarily carried out by cytokines such as Interleukin 4, 5 and 13 and associated with allergy and parasitic infection, makes functional impacts on glial and neuronal biology and thereby regulates physiological and pathological processes in the brain.

Overall, this review series is not intended to be comprehensive on all contemporary topics of neuroimmunology. Instead, these four pieces should give our readers a glimpse of what has been accomplished in understanding basic biology of neuroimmune crosstalk and what lies in future investigation that may help in designing new ways to maintain health and treat diseases.

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COMPETING INTERESTS

The author declares no competing interests.

ADDITIONAL INFORMATION

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