Editorial

Mexican Neuroimmunoendocrinology: What is Done and has to be Done

Ignacio Camacho-Arroyo[1] and Jorge Morales Montor*[,2]

[1]*Facultad de Química, Departamento de Biología and* [2]*Departamento de Inmunología, Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, AP 70228, México D.F. 04510, México*

Abstract: In this special issue of The Open Neuroendocrinology Journal, the reader will find reviewed some of the hottest topics in the field of Neuroendocrine-immune interactions, with emphasis on the work performed by Mexican Scientists in the field, celebrating the launching of The Mexican Society of Neuroimmunoendocrinology.

Cabrera-Muñoz *et al.*, describe the role of progesterone (P4) in the infection by the human immunodeficiency virus (HIV). Preeclampsia is a pregnancy-related disorder exclusive to human beings, and represents a public health problem worldwide whose etiology is still unknown. Sanchéz-Rodríguez *et al.*, make a very interesting overview of the role of immunological factors involved in this disease. Guzmán *et al.*, make a nice in depth review of the role that IL-6 plays during neuroimmunoendocrine interactions in mammals, and, point out the possible therapeutic use of specific targeting of the IL-6 pathway that can be a promising new approach for the treatment and prevention of neurodegenerative disorders in humans. Moreover, Morales reviews about neural plasticity induced by reproduction in the maternal brain, with special focus on lactation as a model for neuroprotection, and on the possible involvement of the immune system in this phenomenon. López-Meza *et al.*, discuss the role of prolactin effects on innate immune response to infection. Following the same line, Leff *et al.*, discuss the interacting neuroendocrine network in stress-inducing mood disorders in humans, that are important to understand the pathophysiological mechanisms that operate in these diseases. The contribution by Quintana and Salinas, shows the very important role that Gonadotropin-releasing hormone (GnRH) plays during experimental autoimmune encephalomyelitis. Another very important physiological function in vertebrates, is sleep. Velázquez-Moctezuma *et al.*, make an overview pointing out to that, sleep has an influence on the cellular and humoral immune response and, in turn, cytokines regulate the sleep pattern. Finally, Guzmán *et al.*, show that gonadal steroidogenesis is a fundamental process in the reproduction of mammlas, that is regulated not only by neuroendocrine products, but also by immune system molecules.

We hope that our readers will find fascinating and enticing, the first ever Special Issue devoted to Mexican Neuroimmunoendocrinology.

Keywords: Neuroimmunoendocrine network, neuroimmunology, immunoendocrinology, disease, health, neuroimmunomodulation.

INTRODUCTION

This issue of The Open Neuroendocrinology Journal is the result of the works presented to celebrate the foundation of The Mexican Society of Neuroimmunoendocrinology, carried out during the International Week of Brain, in March 24, 2009, in Mexico City. Why this special issue was devoted to present these works? The main reason for presenting this topic is due to the fact that this research field has vigorously progressed during the past decade. The proportion of the world's scientific publications devoted to neuroimmunoendocrine modulation has increased almost 100% in the past two decades. Notably, albeit at different rates, a growing number of scientists is dedicated to this field in different countries, including the so called underdeveloped countries. This fact is supported in this issue, in which work in this field is presented by authors of different Universities and Reseaarch Institutes around our country (Aguascalientes, Queretaro, México City), among others. It must be mentioned that the recognition or relative impact of this field, as measured by the average number of citations in published articles, is high in the world averages compared to other fields.

Infectious diseases are a huge health problem around the world. HIV caused disorders, as well as parasitic infections are among the most prevalent in humans. Due to the fact that it is well known that progesterone (P4) plays several non-reproductive actions, and particularly, a protagonical role in the regulation of the immune response, Cabrera-Muñoz *et al.*, [1], thoroughly describe how P4 is able to modulate the immune response during normal physiological processes, as well as in infectious diseases, particularly in parasitic and

*Address correspondence to this author at the Departamento de Inmunología, Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, AP 70228, México D.F. 04510, México;
Tel: + (5255)56223854; Fax: + (5255)56223369;
E-mails: jmontor66@biomedicas.unam.mx; jmontor66@hotmail.com

1876-5289/10

viral infections. Further investigations could open new application fields, where the differential effects of P4 upon the immune response represent the keystone of a successful hormonal therapy as well as the design of new drugs with more specific actions on parasites and virus [1].

Another disease exclusive to human beings is preeclampsia, which is a pregnancy-related disorder, and represents a public health problem worldwide. Interestingly, etiology of this disorder is still unknown. Sanchéz-Rodríguez EN *et al.,* [2] discuss that understanding the onset and course of this disorder depends on the knowledge about the interaction among several systems of the organism, such as the immune, vascular and endocrine systems. For instance, particularly in Mexican women with preeclampsia, authors point out to *KIR* genes, together with the phenotype of NK cells in peripheral blood and the decidua, are important factors related with ethiology of the disease.

Interleukin 6 (IL-6) is a typical pleiotropic cytokine that modulates a variety of physiological events in vertebrates, including cell proliferation, differentiation, survival, and apoptosis, among other functions. IL-6 plays roles in the immune, the endocrine, the nervous, and the hematopoietic systems, in bone metabolism, regulation of blood pressure and inflammation. IL-6 exerts its effects on different tissues and organ systems. Thus, Guzman *et al.,* [3], review in depth the participation of the IL-6 in the neuroimmunoendocrine network. Authors speculate that specific targeting of the IL-6 pathway can be a promising approach for the treatment and prevention of neurodegenerative disorders in humans.

Steroids can regulate some functions of the immune system, and, viceversa, molecules secreted by the immune system modulate steroid synthesis. This is the case of cytokines. These molecules participate in the immune response and are secreted by different immunological cells. Gonadal and adrenal steroidogenesis regulation by bidirectional communication between the immunologic and neuroendocrine systems has been well established. Cytokines production is influenced by the direct action of hormones and neurotransmitters in immune system cells. Thus, Guzmàn *et al.,* thoroughly review the action of some of the main cytokines produced by the immunologic system on the regulation of gonadal (ovarian and testicular), adrenal and neural steroidogenesis [4].

One of the most important functions of mammals is motherhood. It has been suggested that the maternal brain undergoes a collection of adaptive changes including behavioral, neuroendocrine, and autonomic responses related to maternal behavior and milk production. Furthermore, recent reports from Morales *et al.,* have documented neuroprotection in the hippocampus of lactating rats against excitotoxic damage induced by kainic acid. Thus, Morales [5] presents recent studies about neural plasticity induced by reproduction in the maternal brain, with special focus on lactation as a model for neuroprotection, and on the possible involvement of the immune system in this phenomenon.

Prolactin (PRL) has been considered as a cytokine able to modulate immune response in mammals. In addition, particular effects of this hormone on inflammatory response have been documented in autoimmune diseases, whereas its effects on innate immune response during infectious diseases are in general, unknown. Lòpez-Meza *et al.,* [6], present the state of art of the role of PRL on innate immune response during the establishment and progress of different infectious diseases caused by bacteria, fungi and protozoa in mammals. They show convincing evidence that PRL effects on innate immune response to infection depend on the pathogenic microorganism, host, immunological state of organisms, PRL variant involved, as well as its concentration [6].

Neurotransmitters, peptide hormones and cytokines act through the hypothalamic-pituitary-adrenocortical (HPA) axis forming a regulatory loop that maintains homeostasis in response to different stressors. Thus, Leff *et al.,* [7], describe the functional interactions between HPA axis activity and the neural pathways that impinge on forebrain-limbic structures under stressful conditions. Authors conclude that interactions between immune-borne cytokines and HPA axis activity, and glucocorticoid receptors are extremely important to understand the pathophysiological mechanisms that operate in mood-related disorders, such as the stress-inducing altered changes in brain morphology, neuronal atrophy and neurogenesis in brain areas involved in learning processing and memory [7].

The role that Gonadotropin-releasing hormone (GnRH) plays as a possible immunomodulator during experimental Autoimmune Encephalomyelitis (EAE), a model of Multiple Sclerosis (MS), is extensiveley in depth reviewed by Quintanar and Salinas [8]. MS is a disorder characterized by the infiltration of lymphocytes and monocytes, the activation of the microglia, demyelination and axonal loss. It has been established that GnRH is expressed in many non-hypothalamic tissues. Interestingly, authors describe that administration of GnRH to animals with EAE reduces the severity of the disease, inducing a significant recovery in the clinical signs of locomotion, an increase in both the level of the proteins involved in the process of neuroregeneration and in the axonal diameter of spinal cord neurons. They suggest that this knowledge could lead to the generation of novel therapies against MS [8].

One of the most important physiological process of animals is sleep. It is well known that sleep restriction or impairment results in an increased risk of getting an infectious disease. Also, once a subject is sick due to an infectious disease, his sleep pattern completely changes. For a number of years these facts have been interpreted as the result of the alteration or loss of the main sleep function, the restoration of the defense system. Nevertheless, experimental evidence to support this idea is surprisingly scarce. Thus, Velázquez-Moctezuma *et al.,* [9] review all literature concerning this subject. Authors suggest that sleep has an influence on the cellular and humoral immune response and, in turn, cytokines regulate the sleep pattern. Full understanding of this relationship could enable us to open new approaches in the therapeutic management of immune diseases [9].

Finally, present reviews suggest that not only immune-mediated mechanisms affect the course of the different diseases presented in here, but the neuroendocrine system produces a specific outcome for such diseases. Also, these molecular mechanisms involved in the communication among the immune and neuroendocrine systems may be crucial for the design of more specific drugs that affect pathogens, but spare the host, and have critical implications for the host-

parasite relationship at molecular and evolutionary levels, in addition to the benefits that concern human health.

REFERENCES

[1] Cabrera-Muñoz E, Escobedo G, Guzmán C, Camacho-Arroyo I. Role of progesterone in HIV and parasitic infections. Open Neuroendocrinol J 2010; 3: 136-42.

[2] Sánchez-Rodríguez EN, Nava-Salazar S, Mendoza-Rodríguez CA, Romero-Arauz F, Morán C, Cerbón MA. Immune-endocrine alterations during preclampsia. Open Neuroendocrinol J 2010; 3: 143-51.

[3] Guzmán C, Hallal-Calleros C, López-Griego L, Morales-Montor J. Interleukin-6: a cytokine with a pleiotropic role in the neuroimmunoendocrine network. Open Neuroendocrinol J 2010; 3: 152-60.

[4] Guzmán C, Hernández-Bello R, Morales-Montor J. Regulation of steroidogenesis in reproductive, adrenal and neural tissues by cytokines. Open Neuroendocrinol J 2010; 3: 161-69.

[5] Morales T. Hippocampus neuroprotection during lactation: a model to study neuroendocrine-immune interactions. Open Neuroendocrinol J 2010; 3: 170-74.

[6] López-Meza, JE, Lara-Zárate L, Ochoa-Zarzosa A. Effects of prolactin on innate immunity of infectious diseases. Open Neuroendocrinol J 2010; 3: 175-79.

[7] Leff P, Hernández-Gutiérrez ME, Becerril LE, *et al*. The interacting neuroendocrine network in stress-inducing mood disorders. Open Neuroendocrinol J 2010; 3: 180-207.

[8] Quintanar JL, Salinas E. Experimental autoimmune encephalomyelitis: a neurological challenge for gonadotropin-releasing hormone (GnRH). Open Neuroendocrinol J 2010; 3: 208-14.

[9] Velázquez-Moctezuma J, Esqueda-León E, Ibarra-Coronado EG. Reciprocal relationship between sleep and the immune response: a survey. Open Neuroendocrinol J 2010; 3: 215-20.