In 2014 we witnessed a rapid growth of the research and studies at the interface and intersection of neurosciences and immunology. This vast interdisciplinary area, often referred to as neuroendocrine immunology or neuroimmunology, also includes stress-immune interactions that may have complex and multifaceted impact on health and disease. Last year also brought some interesting developments and new conceptual trends to the field, and some of these were outlined here, on the BrainImmune site.

What we feel stimulating and important is now highlighted and summarized below.

**Neuroscience**

According to Kuti Baruch and colleagues from the Weizmann Institute of Science, Rehovot, Israel, and their study in *Science* magazine, overexpression of type I interferons (IFN-I) at the choroid plexus, induced by factors present in the cerebrospinal fluid, may contribute to age-linked cognitive decline. Of note, in this brain structure, interferons were

able to down-regulate the expression of **insulin-like growth factor** and **brain derived neurotrophic factor**, which are critical for neuronal growth and survival.

A prospective longitudinal population study in 800 women conducted by Lena Johansson and colleagues from the Sahlgrenska Academy at Gothenburg University in Sweden identified an association between psychological stress in middle age women and an increased risk of dementia and Alzheimer’s disease later in life.

**Immunology/Neuroimmunology**

Kathleen Kokolus and co-workers from the Roswell Park Cancer Institute, Buffalo, NY have found that an often overlooked ‘variable’ such as cool ambient housing temperature may influence the outcome of some experimental endpoints such as antitumor immunity and experimental tumor growth in mice. The norepinephrine (noradrenaline)-driven cold stress response is most likely the underlying mechanism involved in this phenomenon. The authors suggested that “it is important to consider ambient temperature when cancers (and perhaps other disorders) are modeled in mice”.

Radha Ramesh and colleagues showed that in contrast to the

NEWS

New Evidence that Peripheral Nerves Sense Infection and Drive IL-23 Production by Skin Dendritic Cells

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‘nonpathogenic T helper (Th)17 cells’, the highly pathogenic and ‘pro-inflammatory Th17 cells’ are not ‘canonical’ Th17 cells, and produce both Th17 and Th1 cytokines such as interleukin (IL)-17A and IFN-γ, respectively. The ‘signature’ or the typical profile of these Th17.1 cells include high level IL-23R expression and hypersensitivity to IL-23 stimulation, combined with a resistance to glucocorticoids. These cells may be important mediators of chronic inflammation and several autoimmune diseases.

Researchers from the Imperial College and the King’s College London, UK, provided perhaps the first evidence suggesting that asthmatics may overproduce IL-25 during asthma attacks triggered by common cold viruses. IL-25 (IL-17E) is known to induce Th2 cell immune responses, typically associated with asthma and its exacerbations.

The TRPV1 receptor (transient receptor potential vanilloid type 1 ion channel) is a classical nociceptor or pain receptor. Samuel Bertin and colleagues, however, identified a ‘non-canonical’ function of the TRPV1 receptor. This includes its expression, involvement in TCR signaling and pro-inflammatory activities of T cells, and cytokine productions such as IFN-γ, IL-17A and TNF.

A research group from Singapore has identified a new subset of Th cells that may play a key role in neuroinflammation and multiple sclerosis. The ‘new’ Th cells, referred to as Th-GM, are driven by the IL-7-STAT5 signaling axis and predominantly produce GM-CSF and IL-3.

Hematology/Bone Marrow Neuroendocrine Immunology

Nicole Powell et al. showed that neuromediators of the sympathetic nervous system (SNS) may enhance the myelopoietic output of immature pro-inflammatory CD14+CD16− monocytes. This selective expansion of immature, pro-inflammatory monocytes may drive, at least in part, the pro-inflammatory effects of psychological stress.

A research team from Harvard Medical School, Boston, Massachusetts, reported that SNS neurotransmitters such as norepinephrine (noradrenaline) through an inhibition of CXCL12 expression in the hematopoietic stem cell niche are able to amplify the hematopoietic
stem cells (HSCs) proliferation, thus, increasing the output of neutrophils and inflammatory monocytes from the bone marrow. This mechanism may help explain the stress-induced increase of blood leukocytes (e.g. neutrophils and monocytes) or their traffic to experimental atherosclerotic lesions, as demonstrated by these researchers.

Lorena Arranz and colleagues from the Spanish National Cardiovascular Research Center in Madrid found that an excessive production of IL-1β can cause sympathetic neuropathy by damaging the Schwann cells that provide a protective shield to sympathetic nerve endings in the bone marrow. This cytokine-induced neuropathy enhances the susceptibility of mesenchymal stem cells (MSC) in the haematopoietic niche to cell death and may represent a key mechanism in the development of myeloproliferative neoplasms (MPNs).

Cardiology

Researchers from Duke University Medical Center, Durham, NC, have linked a polymorphism of the 5HTR2C serotonin receptor gene to an increased cardiovascular disease risk. Interestingly, the same research group has also reported that this polymorphism may also contribute to enhanced stress-induced cortisol response.

A research team from University of Alabama, AL, demonstrated a connection between splenic microenvironment and cells, and the development of heart failure, showing that activated mononuclear splenocytes in chronic heart failure traffic to the heart to induce immune cell-mediated injury.

Endocrinology/Neuroendocrine-Immunology

In the female reproductive tract, sperm is ‘stored’ for several days, and, in humans, fertilization usually occurs in case the intercourse took place up to 6 days before ovulation. A Spanish team led by Miguel Relloso found that in dendritic cells (DCs) estradiol is able to suppress the NF-kb translocation to the nucleus, explaining the suppressed DCs’ function observed during ovulation. Thus, it appears that DCs are ‘shutdown’ during estrus (high estradiol) so that spermatozoa can survive; the allogeneic spermatozoa could reach and be stored at the oviduct in order to acquire the ability to fertilize. This ‘window of opportunity’, as shown by the same
research team could be also linked to the restraint exerted by high estrus levels of estradiol on sperm-induced Th17 responses.

Graves’ disease (GD) is considered typically a Th2 autoimmune condition, but Peng and coworkers showed that patients with Graves’ disease also have higher percentages of Th22 and Th17 cells, accompanied by higher concentrations of plasma IL-22 and IL-17. Thus, Th22 cells may contribute to organ-specific autoimmunity in humans in addition to their involvement in epidermal immunity.

Dermatology

According to Lorena Riol-Blanco and colleagues from the Department of Microbiology and Immunobiology at Harvard, and their Nature report, skin dendritic cells are in direct contact to sensory nerves. Their study may represent a breakthrough in dermatology research as the authors proposed a model explaining some key mechanisms that may contribute to the development of psoriasis. This model includes skin sensory neurons triggering IL-23 production by dendritic cells, acting on T cells to induce IL-17 and IL-22, which, in turn, recruit locally leukocytes to drive a psoriasiform skin inflammation.

asthma, autoimmune diseases, autoimmune thyroid disease, bone marrow, cold stress, dementia, estrogens, Graves’ disease, heart attack, hematopoiesis, IL-17, IL-22, IL-23, IL-25, inflammation, multiple
Neuroendocrine Immunology – What Was Hot in 2014 | The BrainImmune Resource: Opinions & views in neuroendocrine immunology, stress-immun...
sclerosis, psoriasis, psychological stress, sex hormones, Th17, Th22

Source: Cover Image: Medical Discovery. Author: Teena Marie; Deviant Art http://teena-marie.deviantart.com/ Credit: http://www.deviantart.com/#/art/Medical-Discovery-49699821?hf=1
Note from the author: “This is an actual advertisement that was painted back in the late 1800’s. (I’m guessing sometime on the 1890’s.) It was actually common practice in the 19th and 20th centuries to paint advertisements on the side of barns. I’m sure you’d probably find more of these painted barns in the Midwest. It would make for an interesting project though, capturing a bit of America such as these”.

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