# 8th Meeting of the German-Endocrine-Brain-Immune-Network (GEBIN)

The 8th Meeting of the German-Endocrine-Brain-Immune Network (GEBIN) took place from April 28th to 30th, 2010 at the Zeche Zollverein in Essen (Germany).

### *GEBIN Educational Short Course*

The GEBIN Educational Short Course for graduate students was organized for the fifth time by *Adriana del Rey (Philipps University, Marburg)* and was held on April 27th-28th, 2010 at the Institute of Medical Psychology and Behavioral Immunobiology, University Hospital Essen. A total of 25 students attended the course that consisted of seven lectures covering the basic elements of the communication between the nervous, endocrine and immune systems. The lectures were given by *Wiebke Hansen* (Medical Microbiology, Essen), *Sven Benson* (Medical Psychology and Behavioral Immunobiology, Essen), *Annemieke Kavelaars* (Neuroimmunology, Utrecht), *Adriana del Rey* (Physiology and Pathophysiology, Marburg), *Volker Stefanski* (Behavioral Physiology, Stuttgart-Hohenheim), *Richard Dodel* (Neurology, Marburg), and *Carsten Krüger* (Sports Medicine, Giessen).

### *GEBIN Meeting*

#### *Plenary talks*

The scientific program of the GEBIN Meeting was framed by three excellent plenary talks. The invited speakers outlined important parts of their research with particular relevance for the field of psychoneuroimmunology. *Fabrizio Benedetti (University of Turin, Italy)* highlighted the important role of the placebo effect as a major factor influencing physiological outcome in both human and animal studies. *Bente K. Pedersen (University of Copenhagen, Denmark)* summarized the effects on physical activity and exercise on the immune system and the specific role of cytokines including IL-6. Éadaoin Griffin *(Trinity College Dublin, Ireland)* illustrated that noradrenaline elicits anti-inflammatory actions in the central nervous system and has neuroprotective potential in conditions where inflammatory events contribute to CNS pathology.

The scientific program included more than 40 selected oral presentations covering the four major research areas of GEBIN:

#### *Stress, Behavior and Immune Function*

A set of studies was devoted to the prenatal origin of immunological and neuroendocrine reaction pattern in the adult organism and the potential relevance of disease susceptibility. *Byron Bitanihirwe (ETH Zürich, Switzerland)* suggested that maternal infection during pregnancy may be an environmental risk factor for the offspring to develop schizophrenia. The authors showed that late prenatal immune activation in mice with poly(I:C) produces behavioral, cognitive and neurochemical abnormalities which are related especially to the negative and cognitive symptoms of schizophrenia. *Christian Bruenahl (Charité Berlin)* focused on the fetal origin of allergic asthma: Stress during late gestation resulted in decreased serum levels of maternal progesterone and testosterone, and increased serum levels of estradiol associated with placental endocrine dysfunction. Offspring had increased vulnerability to asthma-like symptoms. Interestingly, supplementation of progesterone during stress-challenged pregnancies abrogates the increased disease susceptibility. *Hoang Thanh Ho (McMaster University Hamilton, Canada)* showed that prenatal stress can also enhance the severity of atherosclerosis in adult murine offspring. These authors exposed syngenic pregnant apolipoprotein E-deficient (apoE-/-) dams

to sound stress and evaluated the presence of atherosclerotic lesions in the offspring. *Stefan Reber (University of Regensburg)* summarized parts of his interesting findings on the effects of chronic psychosocial stress on spontaneous colonic inflammation in mice. Stress promotes systemic immune activation and the development of inflammatory Th cell responses. *Ulrike Gimsa (Leibniz Institute for Farm Animal Biology, Dummerstorf)* showed that psychological stress affects anxiety-like behavior and stress reactivity more strongly in the mitochondrial uncoupling protein (UCP2)-deficient than in wildtype mice. UCP2 is a protein which protects against oxidative stress. Results of a case-cohort study (MONICA/KORA) on coronary heart disease were reported by *Rebecca Thwing Emeny (Helmholtz Center, Munich)*. The results suggest that work stress associated inflammatory burden contributes to coronary heart disease. High work stress is associated with elevated IL-18, IL-8 and monocyte chemoattractant protein (MCP)-1. Two reports dealt which the question whether inflammation effects brain function with respect to social cognition and memory function in humans. *Jan S. Grigoleit* and *Jennifer Kullmann (University Hospital Essen)* showed that acute experimental endotoxemia (induced by lipopolysaccharide (LPS) injection) evokes changes in brain activation during emotional processing, but does not impair ability to perceive emotions of others. Classical conditioning of immunosuppression in humans is a well-known phenomenon; however, some patients respond while others do not. *Kirstin Ober (University Hospital Essen)* analyzed the possible psychological and neuroendocrine parameters distinguishing subjects that are responsive or non-responsive to the conditioning paradigm. Nicolas Rohleder (Brandeis University, USA) showed that diurnal salivary alpha-amylase activity, a non-invasive marker for sympathetic activity, is relatively robust against short-term influences and useful for the assessment of chronic stress. A further set of reports was devoted to the association between diurnal rhythms and sleep on endocrine and immune parameters. *Tanja Lange (University of Lübeck)* reviewed animal and human data highlighting underlying mechanisms of this adjuvant like action of sleep. Sleep enhances the immune response after vaccination in humans. *Christiane Berndt (University of Technology, Dresden)* reported on the influence of day and night sleep on basal activity of the hypothalamic pituitary adrenal axis. This session was closed by *Sigrid Elsenbruch (University Hospital Essen)* who reported on neural and behavioral effects of expectation in an experimental visceral placebo analgesia paradigm in humans.

***Neuro-Endocrine-Immune Network in Psychiatric Disease***

The section was opened by a report of *Stéphanie Vuillermot (ETH Zürich, Switzerland)* on the effects of prenatal immune challenge (poly-I:C mouse model) relevant to schizophrenia. The authors suggest that dopaminergic mal-development may represent a primary etiopathological mechanism in the development of long-lasting dopaminergic dysfunctions relevant to schizophrenia. *Aye Mu Myint* (*Ludwig-Maximilians-University Munich)* confirmed previous findings that indicate an imbalance in kynurenine pathways in mood disorder patients. A fascinating relationship between glucocorticoid receptor binding to peripheral blood mononuclear cells and posttraumatic stress disorder (PTSD) was demonstrated by *Mirjam van Zuiden (University Medical Center, Utrecht, NL).* These results indicate that high GR binding to PBMCs before military deployment might be associated with an increased risk to develop PTSD symptoms in the aftermath of a traumatic experience.

***Neuroimmunology of the CNS***

*Cobi Heijnen (University Medical Center, Utrecht, NL)* demonstrated that mesenchymal stem cells (MSC) may be suitable to treat neonatal hypoxic-ischemic brain damage. Treatment with MSC at three days after neonatal hypoxic-ischemic brain injury induced formation of new neurons and ogligodendrocytes. A second treatment at 10 days enhanced axonal remodeling and MBP formation. These processes may contribute to the pronounced reduction in lesion size and strongly improved sensorimotor function. *Kirsten Oesterwind (Goethe-University, Frankfurt)* reported on the potential of hematopoietic cells to contribute to the generation of non-hematopoietic tissues including Purkinje neurons. A set of talks was devoted to the role of immune components in pain. *Annemieke Kavelaars (University Medical Center, Utrecht, NL)* showed that neuropathic pain is associated with a decrease in the intracellular level of G protein coupled receptor kinase 2 (GRK2) in microglia/macrophages from spinal cord in rodents. Following these findings, *Hanneke Willemen (University Medical Center, Utrecht, NL)* tested the hypothesis that reduced GRK2 in microglia/macrophages is critical for prolonging the duration of

inflammatory pain. They suggest that the level of GRK2 in microglia may determine the chronicity of the inflammatory hyperalgesia by preventing silencing of microglia/macrophage activity. *Harald Engler (University Hospital Essen)* investigated the effect of peripheral lipopolysaccharide (LPS) administration on the amygdala in rats. The group provides evidence that LPS increased neural activity in the amygdala as indicated by increased amygdaloid noradrenaline levels as well a significant increase in total EEG activity about 2 hrs post injection. Conzeptializing the brain a sensory organ, *Timo Wirth (University Hospital Essen)* investigated fingerprints of neural activity after peripheral immune challenge. The effects of an immune challenge with staphylococcal enterotoxin B (SEB) were investigated by implanted deep brain monopolar electrodes in the amygdala and the insular cortex. The findings indicate that the brain is able to express specific electrical activity patterns related to the modality of a peripheral immune activation (SEB naïve vs. SEB experienced).

***Peripheral Neuro-Immune Interactions***

Recent data show a higher concentration of the cytokine IL-7 in synovial fluid of patients with rheumatoid arthritis (RA) as compared to osteoarthritis. *Georg Pongratz (University Hospital Regensburg)* showed that beta2-adrenergic receptor stimulation at the time-point of B cell activation increases expression of functional IL-7 receptors. The authors conclude that a sympathetic stimulus at the time-point of B cell activation might increase a proinflammatory B cell population in arthritis. The alpha-melanocyte-stimulating hormone (MSH)-related tripeptide derivative KdPT is an anti-inflammatory, anti-oxidative small molecule as *Markus Böhm (University of Münster)* demonstrated in his presentation. KdPT is devoid of any pigmentary effect but maintains significant anti-inflammatory activity. It may be therefore a promising anti-inflammatory molecule for the treatment of various human diseases. Furthermore, *Agatha Kokot (University of Münster)* showed that alpha-MSH increases the expression of suppressors of cytokine signaling in human melanocytes. *Anne Wagner (Philipps-University, Marburg)* demonstrated that immune-cell products (supernatants from cultures of lymphocytes) have significant effects on apoptosis, proliferation and metabolism of pC12 cells, which resemble an in vitro model of mouse sympathetic neurons. These results strengthen the possibility that immune-derived products contribute to the alterations in splenic sympathetic innervations observed during the development of the autoimmune disease in lpr/lpr mice. *Jürgen Kraus (University of Magdeburg)* provided novel evidence that opioids inhibit NFkappaB-signaling in neuronal and immune cells by diverse mechanisms. A final series of reports were focused on the neuroendocrine-immunology in rheumatoid arthritis (RA). *Silvia Capellino (University Hospital Regensburg)* demonstrated an upregulation of dopamine pathway in RA as compared to osteoarthritis, and *Torsten Lowin (University Hospital Regensburg)* provided evidence that the endocannabinoid system in influenced by steroid hormones in RA. *Stefanie Haas (University Hospital Regensburg)* showed a significant impact of IL-1 beta and TNF on the circadian rhythm of synoviocytes in osteoarthritis and RA. The last presentation of the meeting was given by Alexander Fassold who reported on his search for neutralizing ligands to soluble neuropilin-2, a nerve repellent receptor that is increased in RA synovium and aggravates sympathetic fiber repulsion and arthritis.

The Steering Committee of the GEBIN greatly acknowledges the excellent scientific organization of the meeting by *Sigrid Elsenbruch* and *Harald Engler* and the supporting team from the Institute of Medical Psychology and Behavioral Immunobiology, University Hospital Essen (University of Duisburg-Essen). The World Heritage Site Zeche Zollverein – a centre of the creative industry in the Ruhr area – turned out to be a very stimulating site for many scientific discussions for the participants. Many thanks also for the fantastic social program which helped to make this meeting a very special one.

***Volker Stefanski, Harald Engler, and the Steering Committee of the GEBIN***