

**2<sup>nd</sup> INTERNATIONAL WORKSHOP ON  
MOLECULAR MEDICINE OF SPHINGOLIPIDS**  
12-17 October 2014 | Kloster Banz | Germany

in conjunction with an ISN Symposium on  
Sphingolipids In Neurochemistry, Neurobiology and Psychiatry



Report on the  
ISN-SYMPOSIUM ON SPHINGOLIPIDS IN NEUROCHEMISTRY,  
NEUROBIOLOGY AND PSYCHIATRY  
Kloster Banz, Germany, 12-17 October 2014

[www.sphingolipids2014.com](http://www.sphingolipids2014.com)

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The 2nd International Workshop/Leopoldina Symposium on Molecular Medicine of Sphingolipids focused on the biomedical role and application of sphingolipids. 150 scientists attended from a total of 18 countries (Australia, Canada, Finland, Germany, Israel, Italy, Japan, Poland, Portugal, Republic of Korea, Russia, Singapore, Spain, Sweden, Switzerland, Netherlands, UK, USA ). The symposium consisted of 6 main seminars/sessions, i.e. SPHINGOLIPID BIOLOGY, METABOLISM, ONCOLOGY, IMMUNE SYSTEM, INFLAMMATION AND INFECTION, THERAPIES and the ISN-SYMPOSIUM ON SPHINGOLIPIDS IN

NEUROCHEMISTRY, NEUROBIOLOGY AND PSYCHIATRY. There were also two formal poster sessions. The full scientific program is attached to this report.

The ISN-symposium covered a broad spectrum of neurobiological and neurochemical aspects of sphingolipids. It clearly showed the outstanding significance of sphingolipids in many, very diverse diseases ranging from lysosomal storage disease to autoimmune disorders of the central nervous system, pain and alcohol addiction, but also from enzyme replacement therapy to direct targeting of specific receptors to prevent some of the diseases. The symposium very clearly indicated the outstanding significance of sphingolipids for neurobiology and neuro-psychiatric diseases. It also indicated that sphingolipids are novel and very promising targets to treat many of these diseases.

The meeting was chaired by **Johannes Kornhuber**, Universitätsklinikum Erlangen, Germany

The presentations were as following:

**Volkmar Gieselmann**, University of Bonn, Germany, gave a talk entitled TREATMENT OPTIONS FOR METACHROMATIC LEUKODYSTROPHY. He reported new enzyme replacement strategies to treat metachromatic leukodystrophy. In particular, recent developments and novel approaches to deliver aryl sulfatase A were presented and discussed.

**Paola Bruni**, University of Florence, Italy, presented a seminar on NEW INSIGHTS ONTO THE ROLE OF S1P SIGNALING AXIS IN THE ACTION OF PROFIBROTIC AGENTS IN MYOBLASTS. She presented our current knowledge on the role of S1P and the different S1P receptors in neuro-muscular biology, the role of S1P in muscle repair and damage, in particular fibrosis.

**Einat Vitner**, Weizmann Institute of Science, Rehovot, Israel, presented data on RIPK3 AS A POTENTIAL THERAPEUTIC TARGET FOR GAUCHER'S DISEASE. Some of this work was recently published in which Dr. Vitner showed that neuronal death in Gaucher disease (GD), the most common lysosomal storage disease, is caused by a pathway that involves the receptor-interacting protein kinase 3 (Ripk3) protein. Ablation of this pathway markedly improves neurological and visceral disease in a mouse model of GD, and *Ripk3* deficiency dramatically improved the clinical course of GD mice with increased survival, motor coordination and salutary effects on cerebral as well as hepatic injury. Additional data was shown documenting a role for the interferon alpha and beta pathway in neuroinflammation.

**May Han**, Stanford University, Stanford, CA, United States, gave a talk on S1P IN NEUROINFLAMMATION. She elaborated the role of S1P in experimental multiple sclerosis. In particular she showed that S1P-receptor 1 is phosphorylated in multiple sclerosis lesions,

which results in an alteration of receptor internalisation. Mutations of this phosphorylation site resulted in severe experimental autoimmune encephalomyelitis. The disease was driven by interleukin 17 (IL-17)-producing helper T cells (TH17 cells). A lack of S1P1 phosphorylation promoted TH17 polarization and thereby exacerbated experimental multiple sclerosis.

**Klaus Scholich**, University Hospital Frankfurt, Goethe University, Frankfurt am Main, Germany, reported on S1P RECEPTORS AS TARGETS FOR THE TREATMENT OF NEUROPATHIC PAIN. He presented the role of lipids in pain regulation. He was able to apply these basic insights to chemotherapy-induced pain and to show the role of specific S1P receptors in this severe clinical complication.

**Christian Mueller**, Universitätsklinikum Erlangen, Germany, gave a presentation on FROM DEPRESSION TO ALCOHOLISM: THE ROLE OF ACID SPHINGOMYELINASE. Dr. Müller reported that alcohol addiction is a very common psychiatric disorder with severe health consequences for the individual and detrimental effects for social environment and society. A common pathway into alcoholism is depression-induced alcohol addiction. Thereby, adverse life events, stress, or a particular susceptibility lead to a primary depression. In an attempt to reduce stress and counteract primary depression, controlled alcohol consumption can develop into a high frequency compulsive use and, finally, alcohol addiction. In contrast, high alcohol consumption may also induce a secondary depression in non-depressed individuals. At present, there are no specific therapies available to selectively treat different types of alcohol addiction. A new lipid-regulating signalling pathway in the brain has been shown to control the balance between continuous generation of new nervous cells and controlled cell death in the brain. The enzyme acid sphingomyelinase (Asm) generates the lipid, ceramide, which is an important regulator of synaptic plasticity in the brain. In his seminar he presented novel, yet unpublished data on the role of the acid sphingomyelinase in alcohol dependence with comorbid depression/anxiety disorder.

After these plenary talks the meeting continued with several short talks:

**Victoria A. Blaho**, Weill Cornell Medical College, New York, NY, United States, discussed in her talk entitled SPHINGOSINE 1-PHOSPHATE BOUND TO ApoM<sup>+</sup>HDL RESTRAINS LYMPHOPOIESIS AND AUTOIMMUNE NEUROINFLAMMATION the interaction between ApoM lipoproteins in the plasma and the regulation of the immune system and autoimmune responses by S1P and the S1P1 receptor.

**Kristina Friedland**, Molecular and Clinical Pharmacy, Erlangen, Germany, reported the role of TRPC6 CHANNELS AND ASM – TWO PARTNERS IN CRIME. She discussed the interaction of antidepressants with brain TRCP6 channels and delineated functional consequences of this interaction.

**Michelle M. Mielke**, Mayo Clinic, Rochester, MN, United States, reported on PLASMA

SPHINGOLIPIDS ARE ASSOCIATED WITH NEUROIMAGING MEASURES OF AMYLOID-BETA AND NEURODEGENERATION. The studies aim to define and establish sphingolipids as predictive biomarkers for Alzheimer disease, studies with obviously very high clinical impact.

**Viola Nordstroem**, DKFZ Heidelberg, Heidelberg, Germany, described the REGULATION OF HYPOTHALAMIC NEURONAL FUNCTION BY GLUCOSYLCERAMIDE SYNTHASE (GCS)-DERIVED GANGLIOSIDES. In particular, she indicated that GCS-derived gangliosides are important components for hypothalamic regulation of insulin signaling and subsequent adipose tissue homeostasis. Impaired ganglioside expression in neurons therefore provides a potentially new mechanistic concept for the development of obesity in humans.

**Franziska Peters**, University of Cologne, Germany, described in her talk entitled CERAMIDE SYNTHASE 4 - DEFICIENCY CAUSES AGE RELATED HAIR LOSS the biochemical and clinical phenotype of mice lacking ceramide synthase 4. The mice show very interesting neuro-ectodermal phenotypical alterations.

**Ying Sun**, Cincinnati Children's Hospital Research Foundation and University of Cincinnati College of Medicine, Cincinnati, OH, United States analysed in her seminar on NEW INSIGHTS IN THE PATHOLOGICAL MECHANISMS OF NEURONOPATHIC GAUCHER DISEASE BY FUNCTIONAL STUDY OF IPSC-DERIVED NEURONS AND TRANSCRIPTOME PROFILING OF THE GAUCHER DISEASE MICE BRAIN the role of abnormalities of mRNAs and microRNAs in the brain of Gaucher-mice.

**Gerhild van Echten-Deckert**, University of Bonn, Germany, analysed in her talk SPHINGOSINE-1-PHOSPHATE LYASE DEFICIENCY IN THE BRAIN: IMPLICATIONS FOR NEURODEGENERATION the neuroanatomical and biochemical changes of mice lacking sphingosine-1-phosphate lyase (S1PL).



**Johannes Kornhuber**, University of Erlangen, Introducing the session



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