

Maarit Hölttä-Vuori, Ph.D.  
Institute of Biomedicine, Anatomy  
University of Helsinki, Finland

**ESF-Euromembrane sponsored speaker at FEBS conference "From lipidomics to disease and green energy" (Spetses, Greece 23.-29.08.2012)**

**SCIENTIFIC REPORT**

**1. Summary**

The purpose of the trip was to attend the international workshop on lipid research, held on the island of Spetses, Greece, on August 23 - 29, 2012 (note that my departure was scheduled already for the morning of 28th). I work at the laboratory of prof. Elina Ikonen, and the focus of my recent studies has been the relation of cell stress and lipid droplet formation in a motor neuron disease. I presented the data of these recent unpublished results both as an oral presentation and a poster at the meeting.

**2. Final programme of the event**

Below is the final programme. My presentations are highlighted in yellow.

**Thursday, August 23**

Arrival, registration

16:00 - 20:30 Welcome drinks and snacks Co-sponsored by Agilent

**Friday, August 24**

08:45 - 09:00 Introduction

09:00 - 09:50 Opening lecture Karl Hostetler (San Diego, USA): Using Phospholipid Mimicry to Design Antiviral Drugs

Session 1: Lipids in inflammation

Morning Chair Bernd Helms

09:50 - 10:40 Edward Dennis (La Jolla, USA)

Evolution of Phospholipases A2 in Catalysis and Cellular Function on Membranes

10:40 - 11:00 Coffee break

11:00 - 11:50 Marco Lepore (Basel, Switzerland): Recognition of lipid antigens by the immune system

11:50 - 12:10 Marielle Klein (Vienna, Austria): The ceramidome and Toll-like receptor signaling

12:10 - 12:30 Vassilis Aidinis (Athens, Greece): Lysoglycerophospholipids in chronic inflammatory disorders

12:30 - 12:50 Hayley Gallagher (Cardiff, Wales): Molecular mechanisms underlying the anti-inflammatory and anti-atherogenic actions of dihomo-gamma-linolenic acid (DGLA)

13:00 Lunch

**15:30 - 17:30 Poster session A (even numbers)**

Enabling technology session: Progress in Lipidomics

Evening Chairs Gerhard Liebisch & David Russell

17:30 - 18:30 Markus Wenk (Singapore) Biochemical membrane lipidomics during Drosophila development

18:30 - 19:00 Round table discussion related to lectures

19:00 - 19:20 Karel Wirtz (Utrecht, The Netherlands) Spetses, a rich history

20:30 Dinner

**Saturday, August 25**

Session 2: Lipids in host-pathogen interactions

Morning Chair Frances Platt

09:00 - 9:50 David Russell (Ithaca, USA). Lipid metabolism, the common language of host and pathogen in tuberculosis

09:50 - 10:40 Kirstin Sandvig (Oslo, Norway): Entry of protein toxins into cells: Role of specific membrane lipids

10:40 - 11:00 Coffee break

11:00 - 11:50 Sergio Grinstein (Toronto, Canada): Phospholipids as regulators of phagosome formation and maturation

11:50 - 12:10 Luce Farine (Bern, Switzerland): Localization of enzymes involved in phosphatidylethanolamine synthesis in *Trypanosoma brucei*

12:10 - 12:30 Anne Bendt (Singapore): Mycolic acids as diagnostic markers for tuberculosis case detection and drug efficacy

12:30 - 12:50 Daniel Schlam (Toronto, Canada): Diacylglycerol kinases terminate diacylglycerol signalling during phagocytosis leading to heterogeneous phagosomal NADPH oxidase activity.

13:00 Lunch

### **15:30 - 17:30 Poster session A (even numbers)**

#### Enabling technology session: Progress in Lipidomics

Evening Chairs Isabelle Dugail & Konrad Sandhoff

17:30 - 17:50 Joost Brandsma (Southampton, UK)

Predictive lipid biomarkers for severe asthma phenotypes: Unbiased lipidomics analysis for U-BIOPRED

17:50 - 18:50 Edward Dennis (La Jolla, USA)

Understanding omega-3 fatty acid functioning through lipidomics analysis of the macrophage and plasma lipodomies

18:50 - 19:30 Round table discussion related to lectures

20:30 Dinner

### **Sunday, August 26**

#### Session 3: Lipid droplets

Morning Chair Markus Wenk

09:00 - 9:50 John McLauchlan (Glasgow, United Kingdom): The role of lipids and lipid droplets in Hepatitis C Virus infection

09:50 - 10:40 Isabelle Dugail (Paris, France): Caveolin and adipocyte lipid droplet storage

10:40 - 11:00 Coffee break

11:00 - 11:50 Bernd Helms (Utrecht, The Netherlands): Lipid droplet dynamics in hepatic stellate cells

11:50 - 12:10 Maja Radulovic (Graz, Austria): Novel approaches to lipid droplet biology in the yeast *Saccharomyces cerevisiae*

12:10 - 12:30 Barbara Koch (Graz, Austria): Topology of triacylglycerol lipases of the yeast *Saccharomyces cerevisiae*

12:30 - 13:00 Maarit Holtta-Vuori (Helsinki, Finland): Alleviation of seipinopathy related ER stress by neutral lipid storage. Lecture sponsored by ESF-Euromembrane

13:00 Lunch

### **15:30 - 17:30 Poster session B (odd numbers)**

#### Enabling technology session: Progress in Lipidomics

Evening Chairs Sergio Grinstein & Marco Lepore

17:30 - 17:50 Silke Matysik (Regensburg, Germany): Gas chromatography coupled to tandem mass spectrometry: A rapid and reliable method for the simultaneous determination of oxysterols, plant sterols, and cholesterol precursors

17:50 - 18:50 Markus Wenk (Singapore): Application of lipidomics to host-pathogen interactions

18:50 - 19:30 Round table discussion related to lectures

20:30 Dinner

Monday, August 27

#### Session 4: Lipid disorders

Morning Chair Karel Wirtz

09:00 - 9:50 Konrad Sandhoff (Bonn, Germany): Sphingolipid digestion and storage in disease

09:50 - 10:40 Frances Platt (Oxford, United Kingdom). Glycosphingolipid storage disorders

10:40 - 11:00 Coffee break

11:00 - 11:50 Thijn Brummelkamp (Amsterdam, The Netherlands): Haploid genetic screens decipher lipid biology hijacked by pathogens

11:50 - 12:10 Jitka Rybova (Prague, Czech Republic): Blood group B antigens are major glycosphingolipids accumulated in the pancreas of a patient with Fabry disease, blood group B secretor

12:10 - 12:30 Ajay Kumar Mahalka (Aalto, Finland): Molecular mechanisms of lipid-protein interactions in pathologically stressed conditions

12:30 - 12:50 Joanna Siedlecka (Warsaw, Poland): Lipid profile of *Ercc1*<sup>-/-</sup> mouse model of accelerated aging

13:00 Lunch

### **15:30 - 17:30 Poster session B (odd numbers)**

#### Enabling technology session: Progress in Lipidomics

Evening Chairs John McLaughlan & Kirstin Sandvig

17:30 - 17:50 Feven Sahle (Helsinki, Finland): Lipidomics for aging human bone marrow mesenchymal stem cells

17:50 - 18:50 Gerhard Liebisch (Regensburg, Germany): Lipidomics - Tools to find lipid biomarker and study cellular lipid metabolism

18:50 - 19:30 Round table discussion related to lectures

20:30 Dinner

## **Tuesday, August 28**

09:00 - 09:50 Special Lecture Karl Hostetler (San Diego, USA): Changing Phospholipid Structure to Change Drug Behavior

### Session 5: Lipid-based biofuels

Morning Chair Bernd Helms

09:50 - 11:00 John Harwood (Cardiff, United Kingdom): Algal-based lipids: regulation and implications

11:00 - 11:20 Coffee break

11:20 - 12:20 John Harwood (Cardiff, United Kingdom): Crops as sustainable sources of oils, chemical feedstocks and biofuels

12:20 - 12:40 Lital Davidi (Rehovot, Israel): Characterization and origin of two types of lipid droplets in *Dunaliella bardawil*

12:40 - 13:00 Angeliki Bourtsala (Athens, Greece): Study of cotton (*Gossypium hirsutum*) phospholipase D and its involvement in wound stress responses

13:00 Lunch

15:00 - 18:00 Excursion by boat including Meet the Expert sessions in subgroups on the beach

20:30 Conference Dinner Co-sponsored by Avanti

## **Wednesday, August 29**

Departure

### **3. Description of the scientific content**

The topics of the meeting covered a wide range of lipid research spanning from cell biology to lipidomics, pathogens, and biofuels. The data was presented both in oral presentations (invited speakers as well as selected topics from poster abstracts) and poster sessions. At the end of each day, there was time allocated for "round table discussions" that allowed more informal discussion of the topics presented at the sessions. Also the evening dinners were arranged in subgroups, which enabled free discussion on both scientific topics as well as career development etc. For the presentations, there was a lot of unpublished data and the whole meeting was very well received by all the participants.

### **4. Presentations by the applicant**

Below is my abstract for the meeting. I had both an oral presentation as well as a poster.

#### **Alleviation of seipinopathy related ER stress by neutral lipid storage**

Maarit Hölttä-Vuori<sup>1,4</sup>, Veijo T. Salo<sup>1</sup>, Yuki Ohsaki<sup>1,2</sup>, Maximiliano L. Suster<sup>3</sup> and Elina Ikonen<sup>1,4</sup>

<sup>1</sup>Institute of Biomedicine, Anatomy, University of Helsinki, Finland; <sup>2</sup>Department of Anatomy and Molecular Cell Biology, Nagoya University Graduate School of Medicine, Japan; <sup>3</sup>Sars International Center for Marine Molecular Biology, University of Bergen, Norway; <sup>4</sup>Minerva Foundation Institute for Medical Research, Helsinki, Finland.

Mutations affecting the N-glycosylation site in Berardinelli-Seip lipodystrophy associated gene *BSCL2/seipin* lead to a dominantly inherited spastic paraplegia termed seipinopathy. While seipin loss of function leads to severe congenital lipodystrophy, the effect of seipin N-

glycosylation mutations on lipid balance in the nervous system is unknown. In this study, we show that seipin N88S mutant expression led to a decreased triglyceride content in astrocytoma and motor neuron cell lines. This imbalance was corrected by supplementation with exogenous oleic acid. Upon oleic acid loading, seipin N88S protein was relocated from the ER to the surface of lipid droplets and this was paralleled by alleviation of ER stress induced by the mutant protein. This effect was not limited to seipin N88S, as oleic acid loading also reduced tunicamycin induced ER stress in motor neuron cells. Furthermore, both seipin N88S and tunicamycin induced ER stress was decreased by inhibiting lipolysis, suggesting that the presence of lipid droplets protected neuronal cells from ER stress. In developing zebrafish larvae, seipin N88S expression led to triglyceride imbalance and reduced spontaneous free swimming. Importantly, supplementation with exogenous oleic acid increased fish motility and reduced ER stress in the zebrafish head. We propose that decreased triglyceride storage contributes to the pathology induced by seipin N88S, and that rescuing triglyceride levels may provide a new therapeutic strategy in seipinopathy.

### **5. In relation to EUROCORES programme**

The idea of EUROCORES is to promote collaborative research, networking and dissemination between colleagues of European countries and beyond. This workshop met that goal excellently, offering numerous chances for interaction and forming collaborations between different disciplines of lipid research.