



A Letter from the IEIIS President

Dear friends and colleagues!

Time is flying, and we are already well into 2017. IEIIS had a successful 2016 fall meeting in Hamburg, and I feel there is a lot of positive energy around the Society. We have to carry this forward to keep the core spirit of the Society, and also use this to develop IEIIS further.

Some updates:

2018 MEETING:

We are already well underway with planning the 2018 meeting, which will be held jointly together with the Society for Leukocyte Biology (SLB), similar to the meetings in 2006, 2010, and 2014. Organizers are David Underhill (SLB-IEIIS), Darren Lee (SLB) and me (Egil Lien) from IEIIS, and we already have a number of confirmed speakers. The site is Hotel Sheraton Grand at Wild Horse Pass in Chandler, close to Phoenix, Arizona (20 minutes from the airport), in a unique U.S. southwestern desert setting, and the meeting will be **October 14-16, 2018. SAVE THE DATE!**

2017 MEETING:

For 2017, we have already had local/satellite events with IEIIS involvement. One is the TOLLerant meeting and school especially directed towards trainees (students and postdocs), organized by Francesco Peri. Another is Innate Immunity Day at UMass Medical School. Ideas about further events are welcome. These events help maintain activities in main meeting off-years.

MEMBERSHIP DRIVE:

We are starting a membership drive to increase membership numbers. This will be coordinated with the help of our new Membership Chair, Tim Sellati. New for this year is the 2-year membership. There are many advantages with membership – ability to join interesting meetings and present your research, you will get a useful net of contacts, you can get advice on career choices and experiments, publish in the *Innate Immunity* journal, and more. This is a good opportunity for you and your friends to become or stay affiliated with the Society!

WEBSITE:

We have refreshed the website at www.ieiis.org with the direction of our new Web Coordinator Holger Heine. At the website you will find information about the Society; ability to join or re-join; contact information for officers, councilors and other people in key positions; information about upcoming events and meetings; awards, and more. If you have any input, please contact Holger at hheine@fz-borstel.de

InI JOURNAL:

Our great journal *Innate Immunity* continues to publish high quality reports. New developments are that *InI* will become an open access journal, which will make papers freely available.

THANKS:

Many contribute to the IEIIS. Special thanks to Otto Holst, President 2014-2016 and Editor-in-Chief of *InI*; our Treasurer Amy Hise; other councilors, and officers and key persons; including our Administrative Assistant, Nancy Pollman, for all the work benefiting IEIIS.

If you have any comments or ideas with regard to the Society, please contact me at egil.lien@umassmed.edu

Best regards,

Egil Lien

Egil Lien

IEIIS President 2016-2018

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NEWSLETTER EDITOR

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 **Oct. 14-16, 2018 · The Sheraton Grand, Chandler, AZ**
Joint Meeting of the Society for Leukocyte Biology &
The International Endotoxin and Innate Immunity Society 

Myeloid Cells: Development, Environment and Inflammation

Chairs: David Underhill (IEIIS/SLB), Darren Lee (SLB), Egil Lien (IEIIS)

We are excited to present the 15th biennial IEIIS meeting and 51st annual SLB meeting in a beautiful Southwestern US setting just 20-30 minutes outside of Phoenix. This will be the 4th time IEIIS and SLB (the Society for Leukocyte Biology) have joined forces – past joint meetings (2006, 2010, 2014) have been very successful.

We are assembling a great program. Proposed session topics include:

Inflammation and cell death in host-pathogen interactions; Myeloid cell development, differentiation and novel functions; Ligands of Innate Immunity: structure and function; Metabolism and physiology in inflammation; Best of JLB and Innate Immunity; Neutrophils and phagocyte functions; Metabolism and Physiology in inflammation; Leukocytes in immune privilege sites; inflammatory signaling; host receptors and microbes; the Microbiome in inflammation and immunity.

There are plenty of opportunities for presenting your work! We will have plenary sessions, break-out sessions, selected oral presentations, poster presentations, award presentations and of course plenty of time for networking and catching up with your colleagues and friends.

October 14-16, 2018
The Sheraton Grand at
Wild Horse Pass, Chandler, AZ

SAVE THE DATES!



A Tribute to Otto Lüderitz “The Decryption of the Secret of Bacterial Endotoxin”

by Jason Barker

A presentation by Ernst Th. Rietschel at the 14th biennial meeting, September 2016

Dr. Ernst Rietschel opened the IEIIS meeting in Hamburg with a tribute to the career of Dr. Otto Lüderitz, who passed away on November 30, 2015. In setting the stage for Dr. Lüderitz's contributions to the biochemical characterization of diverse species of LPS, Dr. Rietschel highlighted the technical and conceptual advances that appear frequently in the endotoxin story. An important early milestone was Richard Pfeiffer's discovery of the ability of a heat-stable substance derived from *Vibrio cholerae* cells to cause toxicity in animals. He termed this substance “endotoxin” to distinguish it from secreted toxins, and other researchers observed a similar material in a variety of medically-important bacteria. Another important conceptual advance was the discovery of the therapeutic value of fever (for the treatment of neurosyphilis, for example), thus providing a crucial link between clinical features of “toxicity” and host defense.



Dr. Otto Lüderitz

Otto Lüderitz joined the laboratory of Otto Westphal in 1943 at the University of Göttingen. While working on a vaccine against typhus, they noted the pyrogenic nature of *Proteus* extracts obtained by phenol-water isolation.

Eager to harvest the potential vaccine and therapeutic applications, they optimized the process further, resulting in the development of the phenol-water means of LPS isolation that is still used today. Over the next ~30 years, Dr. Lüderitz helped unravel the structure, biosynthesis, genetics, and serologic specificity of enterobacterial LPS. Now familiar aspects of LPS structure, such as the identification of structurally and serologically distinct lipid A, core, and O-antigen repeat regions, owe an immense debt to Dr. Lüderitz's work.

Dr. Rietschel's talk concluded with hypotheses about the evolutionary pressures that generated LPS structures beneficial to the Gram-negative bacterium expressing them—even as higher organisms generated increasingly complex means to detect LPS and mount microbicidal responses. Finally, recent work on the noncanonical inflammasome has revealed a new frontier in innate recognition of LPS—the cytosol. The opening talk thus served as a reminder of the importance of the LPS story to human health and of the important lessons it continues to provide for biomedical research. ▲

Bang Awardee: Kevin J. Tracey

by Jack Levin

As presented by Jack Levin at the 14th biennial meeting, September 2016

The Frederik B. Bang Award was established by the Stanley Watson Foundation to recognize a substantial body of significant research accomplishment by an outstanding senior investigator, whose contributions to the endotoxin and innate immunity fields extend over many years. The award honors Dr. Frederik B. Bang who spent his entire faculty career at the Johns Hopkins Univ. School of Medicine. He was an extraordinary biomedical investigator with an enormous range of interests which included hepatitis, parasitic diseases, and pertinently, bacterial endotoxins.

Dr. Kevin Tracey was unable to attend the meeting in Hamburg, but Dr. Tom Coleman was able to attend accept the award on his behalf. Dr. Jack Levin provided the following remarks at the occasion, outlining Dr. Tracey's many contributions to the field of innate immunity:

“This field is described as the interface between molecular medicine, neuroscience, and biology. Dr. Tracey's interest in and major ongoing contributions to this field result from his remarkable paper published in *Nature* in 2000 which demonstrated that activation of the vagus nerve modulated the systemic inflammatory responses to

endotoxin, inhibited the release of TNF from macrophages, and prevented the development of shock in rats during what would have been lethal endotoxemia. He has shown that acetylcholine is the mediator of the anti-inflammatory effect of vagal stimulation and identified the nicotinic acetylcholine receptor on macrophages. More recently, he demonstrated that acetylcholine was regulated innate immunity but not adaptive immunity.

Collectively his studies have demonstrated that this pathway can attenuate systemic inflammatory responses.

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Bang Awardee: Kevin J. Tracey

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Just this year, he reported in *PNAS* that stimulation of the vagus nerve inhibited cytokine production and attenuates the severity of rheumatoid arthritis in humans, thus establishing an impressive example of the potential therapeutic effect of vagal stimulation, and thereby justifying the validity of the term 'bioelectronic medicine'.

Early in his career when he worked in Anthony Cerami's lab he definitively established the major deleterious role of TNF (then called cachectin) in sepsis and shock, and which produced many of the pathological effects of endotoxin. He described molecules of potential interest that prevent LPS-induced TNF production and inflammation, including an alpha-7 nicotinic receptor agonist.

Another major achievement was the discovery of HMGB-1 as a late mediator of endotoxin-induced lethality and sepsis. This observation led to the idea that this molecule was a link between necrosis observed in sepsis and endotoxin-induced shock and deleterious effects leading to organ dysfunction. Nowadays, with the key role played by DAMPS (damage associated molecular patterns), the discovery of HMGB1 appears as a major step in our understanding of inflammation.

Although as indicated, Dr. Tracey cannot be with us today, he has shown his recognition of the stature of the Bang Award and his respect for our society by asking his colleague Dr. Tom Coleman to come to Hamburg to accept the Bang Award on his behalf." ▲

Spotlight on Outer Membrane Vesicles

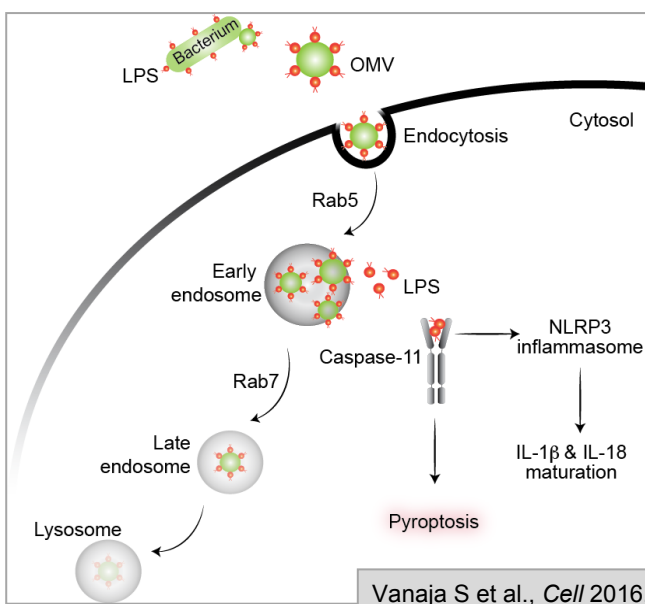
At the 2016 IEIIS meeting in Hamburg, one of the sessions focused on outer membrane vesicles. In this newsletter, we highlight the novel work of one of the presenters, Dr. Vijay Rathinam.

Immune monitoring of the cytosol for non-self signals allows the host to defend itself from microbial threats. Studies over the last few years have revealed that lipopolysaccharide (LPS) from Gram-negative bacteria gains access to the cytosol, and signals independently of TLR4 by binding directly to inflammatory caspases (caspase-11 in mice and caspase-4/5 in humans). The detection of bacterial LPS in the cytosol by caspase-11 and caspase-4/5 elicits two main outcomes via gasdermin D; proteolytic maturation of caspase-1/IL-1 β /IL-18 and pyroptosis, an inflammatory form of cell death. Whereas the receptor for cytosolic LPS and the downstream responses have been delineated, remarkably little was known about how LPS gains access to the cytosol during infection, which is the most defining event in this pathway. The mechanism of cytosolic localization of LPS becomes more intriguing given that this phenomenon is not just limited to cytosolic bacteria, but is a general feature of several extracellular Gram-negative bacteria that do not reside in the cytosol. Gram-negative bacteria secrete outer membrane vesicles (OMV), which are lipid bilayer vesicles of 20-200 nanometers in diameter. Bacteria secrete OMV to

exert several biological functions: OMV enable bacteria to communicate with host cells in a contact-independent manner and modulate their function in favor of the bacteria. Notably, OMV can fuse with the host cell membranes releasing their contents into the cytosol. LPS is the most abundant and potent component of OMV and is displayed on the outer surface of OMV. Recent work by Dr. Rathinam and colleagues discovered that OMVs produced by

Gram-negative bacteria function as vehicles to mediate the cytosolic localization of LPS during infections. Consequently, OMVs activate the cytosolic LPS sensing pathway leading to pyroptosis, caspase-1 activation, and IL-1 cytokine release in vitro as well as in vivo. Demonstrating a necessary role for OMVs for intracellular LPS release during bacterial infections, genetic attenuation of bacterial OMV production diminishes their ability to activate caspase-11-dependent cell death and IL-1 responses. Collectively,

these findings reflect OMVs as a biologically relevant means by which LPS enters the cell during bacterial infections. OMVs with the cargo of immunostimulatory PAMPs may represent a cardinal sign of infection with not only viable but also multiplying bacteria. The finding of OMV activation of cytosolic LPS sensing pathway may have significant implications for OMV-based vaccine development. Future experimental evaluation of whether the activation of cytosolic LPS sensing by OMVs is beneficial or harmful in OMV vaccine applications will be key in the rational design of OMV-based vaccines and in improving their safety and adjuvanticity. ▲



MEMBERSHIP / CONTACT US

Join or Renew Your Membership Now

The success of the organization requires a constant infusion of new talented investigators, so please reach out to young trainees and investigators who would benefit from membership and contribute to the group. To inform these conversations, we'd like to remind you of the benefits of joining the IEIIS.

IEIIS members are entitled to a 20% reduced article processing rate for the society's official journal *Innate Immunity* as well as a discounted registration rate to attend the society's highly-regarded biennial international scientific and business meeting. The meeting sites alternate between the USA, Japan, and Europe, providing international opportunities for scientific interaction with researchers in wide-ranging and related areas of work.

Other benefits of membership include:

- **Joining a network of experienced scientists who can give advice and help on project and career issues/development**
- **Speaking/presenting at internationally attended meetings**
(2018 meeting joint with SLB: October 14-16, Arizona, US)
- **New 2-year discounted membership rate**
- **Involvement in smaller meetings during main meeting off-years**
A unique opportunity for trainees, and young and mid-level investigators to meet with highly accomplished scientists whose seminal discoveries underpin the fields of endotoxin biology and innate immunity
- **Ability to apply for student travel grants for the IEIIS biennial meetings**
Includes up to \$750 USD and a waiver of registration fees
- **IEIIS Newsletter**
News about members and meetings; special articles and contact information
- **Opportunities**
Become involved via Council or committee membership

Our Newest IEIIS Members

Dr. Christian Alexander
Research Center Borstel
Borstel, Schleswig-Holstein
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Univ Paris-Saclay
Orsay, Ile-De-France
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Dr. Nicole Reisinger
Biomim Research Center
Tulln, Lower Austria
AUSTRIA

Elena Vassilieva, PhD
Emory Univ School of Medicine
Atlanta, GA
USA

Welcome to our newest members.



We look forward to your continued participation in our Society and invite you, along with our current membership, to share your studies on our website, in our newsletter, and at our 2018 biennial meeting.

Where to Ask ...

Need to update your address information? Want to pay your dues but are not sure how? You can get answers to these and all other questions related to your IEIIS membership from the following locations:

Email us at IEIIS@aol.com or contact one of these individuals directly:

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