

ENDOTOXIN NEWSLETTER



IES NEWS FROM THE PRESIDENT

Here are updates from Dr. Robert Munford, President of the IES, on some items of interest to the IES membership:

- * Join us in Washington! Save the dates: IES 2002 will begin on Thursday, July 18, 2002, and continue through Sunday, July 21, 2002. The campus of the Uniformed Services University of the Health Sciences (USUHS), in Bethesda, Maryland, will be the primary venue. One or more sessions may be held in the Natcher auditorium, located nearby on the campus of the National Institutes of Health. Both USUHS and the NIH can be reached easily by metro from downtown Washington, D.C.
- * We have engaged a meeting management company, SHERIKON, to assist with the logistics of organizing and running the meeting.
- * Anthony Suffredini will chair the Local Host Committee, which will also include Stefanie Vogel, Matthew Pollack, and Carl Alving, plus others to be named. We are fortunate to have several active members in the Bethesda-Baltimore area who can participate in the organization of IES 2002.
- * Alan Cross will chair the Scientific Program Committee. Other members of the Scientific Program Committee are Peter Brandtzaeg, Chris Raetz, Steve Opal, Stefanie Vogel, Masahiro Nishijima, and Jean-Marc Cavaillon. Anthony Suffredini, as Local Host Committee Chair, will also serve on the committee. Members who have suggestions for the program are encouraged to contact Alan Cross at across@umm.edu.
- * Doug Golenbock is the new chair for Fundraising for IES 2002.
- * The next meeting of the IES Council will be in Chicago, Illinois, on Saturday, September 22, 2001, immediately prior to the ASM ICAAC meeting.
- * Work on the new edition of the IES membership directory is progressing, and the directory will soon be available for distribution to the membership. The on-line directory is also moving forward, but it is not quite ready to be implemented.
- * We have received web-links for a few companies that make endotoxin-related products. We will have a list of companies ready for evaluation by the Governing Council soon. We would like to receive responses from some additional companies who want to be listed on the IES Website. We will keep you updated on all of these topics in future issues of the newsletter. In the meantime, let us know if you have questions or desire more information on any of these IES topics, by contacting either Bob Munford (Robert.Munford@UTSouthwestern.edu) or Kent Myers (kmyers@corixa.com).

Volume 11, Number 1
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INSIDE:

IS THIS YOUR LAST ISSUE OF THE NEWSLETTER?

The mailing list for the IES newsletter has grown to include a large number of individuals who have not paid their dues for several years. This situation creates a significant expense for the Society and is unfair to those members who have made a point of keeping their memberships current. It was therefore decided at the last Council meeting to distribute the newsletter to only those members who are up-to-date on their dues payments. Under this new policy, which will go into effect starting with the next issue of the newsletter, any individual who has not paid their dues since 1998 will no longer be eligible to receive the newsletter. So, please take the time to confirm that you will not be dropped from our mailing list – we do not want to lose track of you!

(More information on paying your dues can be found on pages 3 and 6.)

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A Lesson From Paris: Use Defined Endotoxin Preparations

Jon A. Rudbach and Richard A. Proctor

Through posters and presentations at the IES Paris meeting, we learned about many new biological activities of endotoxins and the biochemical mechanisms of action thereof. These studies employed the most modern immunological and biochemical assays, as well as genetically modified animal models; such tools were not available to investigators 10 or 20 years ago. However, what were available to investigators 10 or 20 years ago were well-defined endotoxin preparations, like lipid A. Many of the elegant studies presented in Paris started with "endotoxins" that were ill-defined and probably contained multiple biologically active entities, including proteins (such as porins), oligosaccharides, lipids (such as lipoteichoic acid), and nucleic acids, in addition to the active principle of endotoxin, lipid A. This made interpretation of data from some of these studies very difficult for us and others at the meeting.

Certainly, many investigators have tried to "clean-up" crude endotoxins by re-extraction, before using them in their studies. However, it was demonstrated in the 1960s that, once a

"denaturing" type of extraction step has been used, many of the contaminating proteins and other substances become "fixed" to the LPS and cannot be removed completely.

Methods for preparation of well-defined "endotoxin preparations" are available, and both lipid A and, as we learned in Paris, Re LPS are now available in purely synthetic form. We hope that future studies on biological activities of endotoxins will employ pure, defined starting materials to complement the power of today's modern assay techniques.

(Editors Note: We encourage reader response to this important comment. We especially invite suggestions for effective methods of obtaining highly defined preparations of lipopolysaccharides and lipid A.)

A Postcard from Paris!

I tend to think of each biennial IES meeting as defining a distinct chapter in the unfolding story of how endotoxins work, and I associate each meeting with a major plot development in this fascinating story. For example, the first IES meeting, in San Diego in 1990, highlighted for me the intimate link between biological activity and the aggregation properties of LPS and lipid A, and in so doing framed one of the central questions in this field, namely how an "insoluble" lipid can be taken up and recognized by cellular receptors. Subsequent meetings in Vienna, Helsinki, and Japan developed a partial answer to this question by introducing and developing two new characters in the story, LBP and CD14. The Santa Fe meeting brought forth the concept that LPS binding to LBP/CD14 is but one facet of a general system of innate immunity, in which early host responses are triggered by recognition of structural patterns that are characteristic of broad classes of microbes. This meeting also provided an exciting glimpse of the molecular details behind innate immune recognition, in a presentation in which TLR4 was identified as the LPS recognition and signaling element downstream from CD14. Continuing in this vein, the Paris 2000 meeting offered many excellent presentations that extended our understanding of the role of TLRs in the innate immune system. I was especially intrigued by the presentation of Dr. David Underhill (University of Washington, Seattle), in which he



described a model to account for the unusual recognition characteristics of the innate immune system. He proposed that TLRs act cooperatively to form homodimers and heterodimers with distinct ligand specificities and signaling characteristics. The existence of at least nine TLRs allows for a large number of pairwise TLR combinations and therefore a considerable repertoire of pattern recognition and responses. By sampling the contents of the phagolysosomal compartment, these TLR complexes can detect a broad range of microbial invaders and trigger the appropriate inflammatory response.

(For more information, see Ozinsky A, Underhill DM, Fontenot JD, Hajar AM, Smith KD, Wilson CB, Schroeder L, Aderem A., The repertoire for pattern recognition of pathogens by the innate immune system is defined by cooperation between toll-like receptors. *Proc. Natl. Acad. Sci. USA* **97**(25): 13766-71, 2000.)

Kent Myers
August 2000

Journal of Endotoxin Research Now Publishes Review Articles

Jack Levin, Editor-in-Chief of *Journal of Endotoxin Research*

With Volume 6, Issue 3 of the *Journal of Endotoxin Research*, an important new feature was inaugurated. We plan to publish a continuous series of invited Analytical Reviews. These Reviews will cover a wide range of topics, all of which will hopefully be of interest to the readers of the *Journal of Endotoxin Research*. Examples of review articles that have or will appear are shown below.

Although these Reviews will be invited, they will be subjected to the usual peer review by at least two reviewers, and will be revised when deemed appropriate by the reviewers and the Editor-in-Chief. It is our intent that the Reviews will be critical and balanced analyses of the field they describe.

Readers of the *Journal of Endotoxin Research* are encouraged to suggest potential topics for future Reviews. In addition, thoughtful brief critiques of published Reviews will be considered for future publication.

I believe that these Reviews will significantly add to the value of the *Journal of Endotoxin Research*, and collectively broaden our readership.

Suggestions for future review topics or comments regarding published reviews may be sent to me at the following address:

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Analytical Reviews in the *Journal of Endotoxin Research*

[Already Published]

Vol. 6, Issue 3

Title: Enteric bacteria, lipopolysaccharides and related cytokines in inflammatory bowel disease: biological and clinical significance.

Authors: Caradonna, Amati, Magrone, Pellegrino, Jirillo, Caccavo

Vol. 6, Issue 4

Title: The search for *Lps*: 1993-1998.

Authors: Beutler, Poltorak

Vol. 6, Issue 5

Title: Lipopolysaccharides in the development of the Guillain-Barre syndrome and Miller Fisher syndrome forms of acute inflammatory peripheral neuropathies.

Authors: Prendergast, Moran

[In Press]

Title: The lipemia of sepsis: triglyceride-rich lipoproteins as agents of innate immunity.

Authors: Harris, Gosnell, Kumwenda

Title: Lipopolysaccharide biosynthesis: which steps do bacteria need to survive?

Authors: Gronow, Brade

Title: Bacterial lipopolysaccharides and innate immunity.

Authors: Alexander, Rietschel

Subscribe now to become better informed about these interesting areas of investigation.

Are your IES dues current?

If you wish to know/confirm the last year you have paid dues, send an email to Nancy Pollman, njpollman@hotmail.com, with the word "Year" in the Subject line and she will provide that information to you by return email.

AN INTRODUCTION TO JOHANNA SCHLOSSHART

Ernst Rietschel, Forschungsinstitut Borstel

Johanna Schlosshart belongs to the group of scientists who have paved the way for our current understanding of the genetic determination, chemical architecture and epitope structures of bacterial lipopolysaccharide. She lived in the former German Democratic Republic, was not allowed to travel or to publish in internationally-recognized journals or to officially cooperate with colleagues in the West. Thus, her important work remained largely unknown. In recognition of her contributions, she was elected in August 2000 by the members of the International Endotoxin Society as an Honorary Life Member of the Society. Johanna Schlosshart was very happy to receive this honor, which expresses best our estimate for her fundamental work and for her as an outstanding scientist and a wonderful colleague. After her retirement in 1985 she moved to a small town located close to Essen. I was in contact with Johanna Schlosshart and asked her to write a few sentences on her career and life. Her report is printed below.

MY LIFE IN SCIENCE

Johanna Schlosshart
IES Honorary Life Member

1932-1936	Elementary school
1937-1944	High School (Arbitur/Graduation/A-levels) [amer./brit.]
1946-1948	Study at the Technical College for Medical Technicians of the Land Berlin

After graduation from the Technical College I was employed at the Potsdam Veterinary Health Office of the Länder government Brandenburg in the field of microbiology.

Due to the lack of appropriate laboratory space, microbiological work was first carried out at this institute.

In 1948, the microbiologist Prof. Dr. Sartorius was instructed to establish an institute of hygiene in Potsdam which from 1950 on took over the human medical microbiological examinations. At that time I moved into this institute and took charge of the *Enterobacteriaceae* department. Facing numerous *Salmonella* and *Shigella* epidemics in that period of time, I always worked at full capacity. During those five years of work, Prof. Sartorius was asked to head the Institute for Serum and Vaccine Development in Berlin-Pankow, Wollankstr. 16. A central laboratory for *Enterobacteriaceae* for the diagnosis of *Salmonella* and *Shigella* was to be joined to this institute for the then-independent second German state, the German Democratic Republic.

Prof. Sartorius accepted this task and asked me to accompany him and to

establish this central laboratory in Berlin-Pankow, together with Dr. Kiesewalter as head of the department. To enlarge our knowledge, we were granted a study visit of three weeks at the Staatens Serum Institute in Copenhagen, the former seat of the International Salmonellae Center headed by Prof. Fritz Kauffmann. During this stay I had the opportunity to talk with Prof. Kauffmann about formation of mutations like the T- and R-types of *Salmonellae* in which I was very interested. About half a year later I received a letter from Dr. Lüderitz who was on a study visit in America. He had obtained my address from Prof. Kauffmann and stated his interest in cooperation in the field of S-R-T-type switching in *Salmonellae*. For this purpose he needed mutant forms allowing to elucidate the biosynthesis of bacterial lipopolysaccharides. Because of lack of time, Prof. Kauffmann was not able to offer his own help to the colleague from Frieberg and had recommended me to do the work. As I already knew of the team of Lüderitz and Westphal from the literature, I was very much prepared for such a collaboration.

After Dr. Lüderitz had returned to Germany, we agreed to a meeting in Spring of 1962. Meanwhile, the wall in Berlin had

been erected and therefore a journey from Berlin to Frieberg was no longer possible for me so that all of our following regular meetings took place in Berlin. Those meetings led to a collaboration that lasted for about 10 years and which, of course, had to be sanctioned by the next authority above us, the Ministry of Public Health. Unfortunately, the relationship between the two German states worsened so drastically during that time that our cooperation became more and more difficult and was finally prohibited in 1972.

At that moment, however, I had already been able to gain all intermediates of the S-R-type switching of *Salmonella minnesota* by mutations and placed them at the disposal of the Frieberg team. A characterization of *S. minnesota* had thus become possible, allowing new insights into the biosynthesis, structure, serology and immunology of bacterial lipopolysaccharide.

In the course of the following years, the central laboratory was removed from the institute in Pankow due to lack of space. Other tasks were given to me in the scope of bacterial and virological vaccines, antigens and antisera.

In 1985 I retired.



Final Report Confirms Paris 2000 Meeting a Financial Success

Kuni Takayama, IES Treasurer

The biennial IES 2000 Paris Conference, held in Paris, France on August 24-27, 2000, was a huge success in all categories that one could consider (finances, scientific quality of presentations, and overall conduct of the meeting). This was largely due to the dedicated efforts of our 1998-2000 IES President, Jean-Marc Cavaillon. The final financial results for the meeting are as follows: total expenses of US \$170,070, total revenues of US \$205,815, for a net profit of US \$35,745. (See the table below for a detailed summary of the meeting finances.)

The financial success of this meeting was attributable to several factors, including 1) close adherence to the budgeted figure of US \$167,000 for total expenses, 2) vigorous efforts by IES members to solicit funds from corporate sponsors, resulting in donations of US \$73,876, and 3) outstanding attendance at the meeting, with a total of 410 registered participants. Let us now all work hard to make the IES 2002 Bethesda Conference an equally successful endeavor.

The following table contains the final financial summary of IES 2000 Paris Conference. All figures are given in US dollars.

Category	Sub-Category	Description	Actual	Budgeted
Expenses:	from SOCFI/Colloquium	Site	25,662	25,350
		Lunch, Breaks, Cocktail party	27,471	28,500
		Printing	8,591	0
		Gala Dinner	26,174	20,700
		Bank Charges	1,472	2,000
		Management fees	24,669	20,100
		Miscellaneous	6,051	0
		Sub-Total	120,093	96,650
	outside SOCFI/Colloquium	Abstract books (JER 6[2])	6,441	5,000
		Awards, plaques	2,782	2,800
		Travel - invited speakers (40)	31,400	45,000
		Travel - IES officers (6)	9,354	0
		Proceedings	0	6,250
		Contingency	0	11,300
		JER expenses, manuscript handling	?	0
		Sub-total	49,977	70,350
		Revenues:	from SOCFI/Colloquium	Registration fees
Gala Dinner	9,939			5,000
Sub-total	131,939			120,500
outside SOCFI/Colloquium	Sponsors, collected in USA		73,876	30,000
	IES Support		0	14,000
	Social Fees		0	2,500
Sub-Total	73,876	46,500		
Total expenses			170,070	167,000
Total revenues			205,815	167,000
Net profit (expense)			35,745	0

Why and How to Join the International Endotoxin Society

Chris Hodgson, Membership Chair

Currently, members in the International Endotoxin Society range through academic staff and research workers in both universities and research institutions, medical researchers, and individuals in commerce and diagnostic laboratories. There are also a limited number of Honorary Members who have been rewarded for meritorious contributions to endotoxin research. All these individuals have in common a fascination with endotoxin.

What are the benefits of membership in the IES?

*** IES Newsletter**

Official quarterly IES newspaper containing news about members and meetings, special articles, important information for members.

*** Reduced subscription rate to the official IES journal, the *Journal of Endotoxin Research*, published by Maney Publishing UK.**

The editorial aim of the *JER* is to disseminate new information on endotoxin to researchers in all relevant scientific disciplines, both basic and clinical. The Journal is indexed abstracted and/or published online in the following media: *Biochemistry and Biophysics Citation Index™*, *BIOSYS®*, *Cambridge Scientific Abstracts*, *Chemical Abstracts*, *Current Awareness in Biological Sciences (CABS)*, *Current Contents*, *Excerpta Medica (EMBASE)*, *MEDLINE*, *Research Alert®*, and *Science Citation Index*. In addition, all subscribers with a fully paid subscription have on-line access via the Web to the full text version of each article.

*** IES Membership Directory**

A hardcopy directory of all IES members is supplied at no charge to members in good standing. In addition, the Society's comprehensive membership database will soon be available online so that searches for member information by name, location, affiliation can be made and member's own information updated easily.

How do I join the IES?

Anyone wishing to join the IES should acquire a form from either the Membership Chair (see below for contact information), a current IES Newsletter, or on the IES website (<http://www.kumc.edu/IES/ieshome.htm>). Prospective members should have an interest in endotoxin or related areas, as evident from publications, presentations, etc., and their application for membership must be endorsed by an IES member in good standing. The application process is as follows:

- 1) The completed application form, including payment, should be sent to the IES Treasurer (see Contacts), who will forward it to the Membership Chair for review, and place the payment in escrow;
- 2) Membership Chair notes the applicant's details and, if appropriate, makes a recommendation of acceptance to the Governing Council of the IES and notifies the applicant and the Treasurer;
- 3) Treasurer deposits or refunds the dues payment, depending on the decision, and forwards details for inclusion in the IES membership database.

Please note that membership of the IES entitles you to a reduced personal subscription rate to the *Journal of Endotoxin Research*. You are encouraged to enter your subscription at the same time you apply for membership.

Nominated members receive IES newsletters, intimations of future meetings, substantial reductions in registration fees for the biennial IES meetings, and, if requested, the *Journal of Endotoxin Research* from the time their application reaches the Membership Chair.

How much does it cost?

- * Annual membership \$50 US
- * Student membership \$15 US
- * Subscription to *Journal of Endotoxin Research* \$88 US

Contact information:

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THE CLASSIFIEDS

Editor's Note: The newsletter is pleased to include notices for positions, services, meetings, etc. that are of potential interest to the membership. This service is available to members at no charge for non-profit items. Please direct all inquiries or submissions to the Newsletter Editor at the address shown on p. 1.

POSTDOCTORAL POSITION

A postdoctoral position is available immediately in microbial pathogenesis to investigate the role of the lipopolysaccharide of *Helicobacter pylori* in virulence. Research will involve structural analysis of the defined mutants of *H. pylori* generated through specific mutations using functional analysis approach. Specifically, the project work will require the candidate to have demonstrated expertise in physical and chemical methods of molecular level structural analysis of bacterial polysaccharides and immunochemical techniques. Knowledge of mass spectrometry and nuclear magnetic resonance techniques will be considered an asset.

Please send CV and the names of three references to:

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PROCALCITONIN OFFERED FOR RESEARCH USE

Dr. Shaul Kornfeld
Brahms Diagnostica GmbH

Procalcitonin is known to be a diagnostic marker for the determination of severe bacterial infection and sepsis (see www.procalcitonin.com for more information). This protein has now been cloned and the Human and Mouse peptides are available for research purposes. Research groups that have an interest in using either the Human or the Mouse Procalcitonin in their investigations of severe infection and sepsis should contact Dr. Wolfgang Weglöhner (weglöhner@invivo.de) for further information. Supplies of the peptide are available for research purposes only at no charge. Interested researchers may consult the web site www.procalcitonin.com, which contains a list of all publications on this topic as well as a chat site for the exchange of thoughts and experience between research and clinical groups in the field of infection and sepsis.

Thank you in advance for your courtesy and if you need more information do not hesitate to contact me.

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Nicola Laws, BVSc
Univ of Southern Queensland
Queensland, Australia

Miroslav Prucha, MD
Hospital Homolka
Prague, Czechoslovakia

Welcome

Also, welcome back to all past members that have re-joined!

Greetings from Paris!

There were an extraordinary number of fascinating presentations at the meeting. Although much of the meeting was focused on the role of TLRs in signal transduction by Gram negative and positive bacterial ligands, one of the most intriguing presentations that I saw was work presented by Dr. Ulrich Seydel and colleagues from Borstel, suggesting that activation of a high conductance Ca^{++} - and voltage-dependent potassium channel (MaxiK) is a very early step in signal transduction in macrophages. Moreover, paxilline, a selective K^+ channel blocker, inhibited both TNF- α and IL-6 gene expression, and TNF- α release from human macrophages. Both Lipid IV_A and anti-CD14

antibody blocked channel activation induced by LPS. Thus, the induction of TNF- α via TLR4/MD-2 must be considered as potentially interacting with this MaxiK channel.

(For more information, see Blunck R, Scheel O, Muller M, Brandenburg K, Seitzer U, Seydel U.J, New insights into endotoxin-induced activation of macrophages: involvement of a K^+ channel in transmembrane signaling. *J. Immunol* **166**(2), 1009-15, 2001.)

Stefanie N. Vogel
August 2000



IES Contact Information

Need to update your address information? Wondering why you have not received a copy of the newsletter?(It probably has not been mailed yet!) Want to pay your dues but are not sure how? You can get answers to these and all other questions related to your IES membership from the following individuals. See your directory for other means of contact, i.e. mailing addresses and phone numbers.

Membership: Dr J. Chris Hodgson (UK) IES Membership Chairman Phone: 0131 445 6133 Email: hodgc@mri.sari.ac.uk	Change of address: Dr. Richard Silverstein (USA) IES Secretary Phone: 001 913 588 6954 Email: rsilvers@kumc.edu
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Dues and subscription payments: Dr. Kuni Takayama (USA) IES Treasurer Phone: 001 608 256 1901 Email: takayama@itis.com	Missing newsletter: Dr. Kent Myers (USA) IES Editor Phone: 001 406 375 2135 Email: kmyers@corixa.com
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Been to Paris Recently?

If so, the Newsletter would love to hear from you! We are looking for articles of any length from members about whatever session, symposium, or experience at the IES meeting made a particularly strong impression on them. These articles can be as short as a few sentences, much like a postcard to the membership, and so do not need to take more than a few minutes to write. Or, since a picture is worth a thousand words, instead of sending a written article you can just email us any photographs you have of IES members at work or at play. Of course, we always welcome submissions of any sort, such as news items, announcements or summaries of other meetings, announcements of available positions, historical matters, photographs, and other pertinent (or otherwise) drogeries of potential interest to the membership. Note that the Newsletter is an appropriate forum for discussion of any and all issues related to the endotoxin community; however, we are not the place for publication of original research articles (that is what the *JER* is for). Please submit all items for publication in the Newsletter to the Editor at the address shown on p. 1.



Email Directory in Progress

A Second Reminder: The IES is striving to create an email directory. A message was sent to all members with known

email addresses. If you did not receive a message, please take this opportunity to provide an updated address, phone, fax, and/or email address for your listing by sending a brief email immediately to njpollman@hotmail.com.

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