A Publication of the International Endotoxin and Innate Immunity Society

ENDOTOXIN NEWSLETTER

January 2023

IEIIS - INTERNATIONAL ENDOTOXIN & INNATE IMMUNITY SOCIETY

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A Letter from the IEIIS President

Amy Hise

Dear Friends and Colleagues,

As we slowly emerge from the restrictions of the pandemic it is a good time to reflect on the impact that it had on our scientific careers and institutions. Academia and industry have faced unique challenges over the past two years. Our society also faced challenges, including the difficulty of planning for and implementing our biennial meeting, which was delayed then held in a hybrid format with in-person attendees in Kobe, Japan and virtual attendees worldwide. A special thanks and recognition to our past President, **Koichi Fukase** who handled these challenges so well.

As researchers, we have been impacted in both positive and negative ways by the pandemic. Some investigators have been able to pivot their research to include SARS-CoV-2 focused projects, and in some cases obtain COVID specific funding. Others have struggled with difficulty completing funded projects or obtaining new funding, including challenges with staffing, lab/institutional shutdowns, restricted library hours, increased teaching or clinical responsibilities, lack of access to resources including human subjects, databases, clinical samples and supply chain issues. Overall, studies and surveys are showing a predominantly negative impact of the pandemic on research productivity. We have also faced challenges with teaching in virtual formats, increased student mental health and other needs, difficulty with recruiting and retaining post-docs and graduate students. Caregiving responsibilities have been a factor for many, especially women. Burnout, increased stress and mental health issues increased and are concerning. Many institutions were able to pivot to virtual or hybrid meeting formats and we have all attended virtual scientific conferences, allowing us to interact and stay connected; yet we missed in-person networking. Many have seen colleagues leave our institutions due to early retirement, changing to part time, changing careers, changing institutions or to illness. Many institutions have seen increased costs due to pandemic responses, decreased revenue from tuition and research funding and changes in staffing.

So, how can we best respond and prepare for the future? Several recent publications on the state of academia can give some guidelines. **Flexibility** is a key component; in scheduling, allowing work from home when appropriate, in hybrid meetings and conferences. For example, as principal investigator I hold most of my lab meetings via zoom in the late afternoon, which allows my lab members flexibility to participate from the lab or at home if they need to leave early to pick up kids or for other home responsibilities. We try to meet or talk regularly in person more informally as well to stay connected. As a chair of several committees, I also hold most meetings online, allowing participation from clinicians and faculty at our scattered affiliated institutions which diversifies our membership and increases participation. Many regularly scheduled weekly conferences and speakers have seen increased participation by allowing hybrid attendance. **Mentoring** and **Sponsorship** is also key to success as we move forward. Young scientists and those belonging to marginalized and/or underrepresented groups may have been hit hardest by the pandemic and may need additional support and encouragement. Graduate students who started during periods of institutional shutdowns missed out on critical daily interpersonal interactions that may have slowed their progress or led to burnout, anxiety and in some cases thoughts of other career options. All of us can reach out to colleagues and mentees to offer support and empathy. We can develop new collaborative research projects, including faculty as co-investigators or co-PI's that we may not have regularly worked with before, expanding potential funding and publications as well as developing new research directions. As IEIIS members, you can sponsor student membership(s) in our organization and refer and encourage colleagues to join. Like many scientific societies we have seen decreasing membership in recent years. One of the strengths of this society is the mentorship and leadership opportunities offered to early- and mid-stage investigators.

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LETTER FROM THE PRESIDENT

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Please consider running for one of the officer positions at the next call for nominations. Additionally, we still are seeking one or two motivated individuals to coordinate our social media postings (contact ieiis@aol.com if interested). We encourage all members to submit to our journal *Innate Immunity* and encourage members, including early-stage investigators to apply to be a reviewer. Opportunities are also available to write commentaries or reviews on current topics in innate immunity. Finally, taking active steps to address **Diversity**, **Equity** and **Inclusion** at local and institutional levels is important. The pandemic has impacted women and minority scientists/physicians greatly. Many studies have highlighted that diversity brings strength to our groups and organizations. Actively addressing bias and discrimination is a start, as well as emphasizing diversity in recruitment and hiring practices, providing flexibility in promotion and tenure and supporting faculty and staff retention. At our university, we have implemented mandatory bias and diversity training of search committees as well as promotion and tenure committees.

We have a new COVID-19 impact statement that is included with all promotion and tenure packages. We have surveyed our faculty to assess the impact of the pandemic and will re-survey again early next year. Creating a diverse and welcoming lab group, department and/or institution will enhance your science and create a vibrant and exciting workplace.

I welcome your thoughts on how IEIIS can better become a diverse and welcoming society (amy.hise@case.edu).

Best regards,

Amy Hise

Amy Hise
IEIIS President 2021-2023

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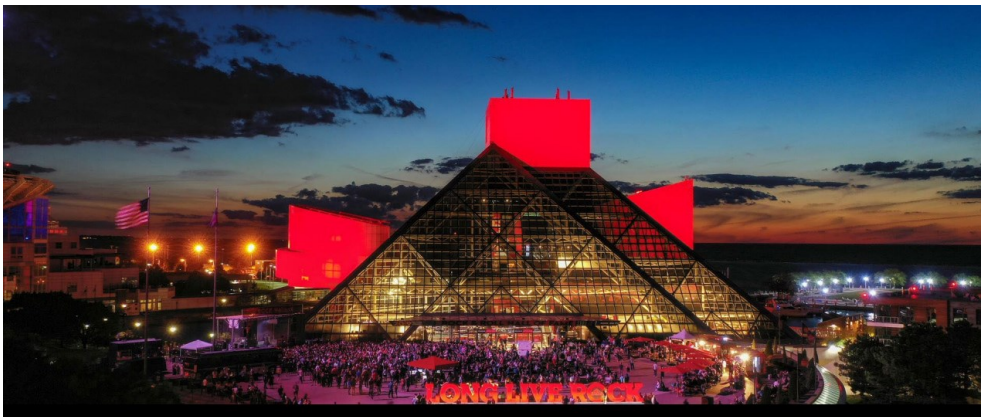
Stay tuned for more details on our 2023 IEIIS Meeting



IEIIS 2023 Meeting
Dates TBD (September 2023)
Cleveland, Ohio, USA

Louis Selim Chedid, MD PhD

IEIIS Honorary Life Member

by Jean-Mark Cavaillon

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Cavaillon J-M. Obituary Louis Selim Chedid, MD PhD IEIIS honorary life member. *Innate Immunity*. 2022;28(6):187-188. doi:10.1177/17534259221116799

Louis Selim Chedid was born in Cairo (Egypt) in June 1922 and died in Paris in March 2021 at the age of 98. After obtaining his bachelor's degree in Cairo, he started his medical studies in Beirut and completed them in Paris, defending his medical thesis on artificial estrogen in 1947. After being trained in Egypt and the United States, he joined the laboratory of Robert Courrier at the College de France (1946). In 1952, he was recruited by the CNRS (National Center for Scientific Research, France). In 1955, he defended his PhD on hormones and infection and started working at the Institut Pasteur (Paris) in the laboratory of Therapeutic Chemistry under André Lamensans. He joined the Institut Pasteur in 1961 and was promoted to Professor in 1972. In 1973, he became the head of the Experimental Immunotherapy laboratory. In 1986, he moved to the H. Lee Moffit Cancer Center and Research Institute at the University of South Florida, Tampa where he founded a startup working on vaccine adjuvants (VacSyn). Louis Chedid was the co-author of 26 patents.

He investigated immune mechanisms with the goal of boosting the defense against infections. Among his main contributions is the identification with Edgar Lederer (1908–1988) of the muramyl dipeptide (MDP), the smallest active part of the peptidoglycan of mycobacteria present in complete Freund adjuvant.[1,2] He then devoted part of his career to study homologs of MDP and their bioactivities, synthetic vaccines, and adjuvants.[3] He also performed numerous investigations on endotoxins including investigations on enhanced resistance to infection by endotoxins,[4,5] LPS-induced abortion, production of interleukin-1 and tumor necrosis factor in response to endotoxins, the synergy between MDP and LPS, prevention of endotoxin-induced lethality, the influence of endotoxin on bone marrow cells, endotoxin tolerance, polyclonal activation, LPS-induced radioresistance, localization of injected 51Cr-labeled LPS, and studies on alkalyl detoxified endotoxins. He offered the basis for an universal anti-endotoxin antibody: *"Thereafter, the presence of a few types of "R' (rough) antibodies or of serum factors reacting with rough antigens have the capability of coping, like masterkeys, with a wide range of infection due to serologically unrelated organisms."* [6]

He collaborated with eminent US scientists including JJ Oppenheim, HS Warren, CA Dinarello, SM Wolff, and JM Krueger. With the latter three, he investigated the links between slow wave sleep and IL-1,7 his most cited paper (462 citations), and addressed the links between sleep and MDP. A Romanian scientist, Constantin Bona (1934–2015) worked for a while in his laboratory on so-called nonspecific immunity before joining the Mount Sinaï Hospital in New York, working on idiotypes and neonatal immunity. They are co-authors of 17 papers including reports on a *Nocardia* water soluble mitogen. Claude Leclerc started her bright career on vaccines and cancer at Institut Pasteur in his laboratory. Based on an idea of Agnès Ullman, she used the adenylate cyclase toxin from *Bordetella pertussis* to deliver antigen into the cytosol of the antigen presenting cell.[8] Her work was a continuation of the work on synthetic vaccines pioneered by Louis Chedid and Michael Sela (Weizman Institute), using peptides corresponding to fragments of diphtheria toxin.[9] In 1984, Claude Leclerc showed that intracellular delivery of MDP with the help of antibodies increased its adjuvanticity 10,000-fold.10 With Chedid, they hypothesized that the MDP receptor was intracellular: *"Specific receptors for MDP exist inside the macrophage […]. To be active, MDP has to be present inside the cells in sufficient concentration."*[11] before Dana Philpott's and Gabriel Nuñez' teams later identified the NOD1 & NOD2 cytoplasmic pattern recognition receptors in 2001/2002.

In 1964, he obtained French citizenship. He received the Bouchard Prize - Laureate of the Society of Biology (1954), and the Claude Bernard Prize of the City of Paris (1978). He was a Knight of the National Order of Merit, a member of many learned societies (The New York Academy of Sciences; The Royal Society (London); Société Française d'Immunologie…) and an honorary life member of the International Endotoxin and Innate Immunity Society. He was a member of editorial boards of journals (*Journal of the Reticulo-endothelial Society*, now the *Journal of Leukocyte Biology; Journal of Infectious Diseases*) and of various national committees (CNRS, Inserm, Scientific Council and Board of Directors of the Institut Pasteur of Lille, and the General Assembly of the Institut Pasteur).

He was the husband of Andrée Chedid (1920–2011), a famous Egyptian-French poet and novelist, the father of Louis Chedid a famous French singer, and the grand-father of Mathieu Chedid, also a famous singer. He wrote a memoir in 2004 (*Mémoires vagabondes*), sharing his passion for scientific adventures and recounting a life at the interface of two cultures. He was a enthusiastic and warm scientist, happy to share his discoveries and his passion.

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Obituary: Louis Selim Chedid, MD PhD

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Invitation to Review for *Innate Immunity*

Are you interested in reviewing for *Innate Immunity*? This helps you stay up-to-date on research in the innate immunity field, and gives you the opportunity to collaborate with our journal Editors. Early career researchers and senior researchers are equally welcome to review for us! Your help with this is greatly appreciated, and you will also benefit from free access to SAGE subscription journals for 90 days, and 25% discount on all SAGE books.

You can sign up to review by going to the *Innate Immunity* ScholarOne site, and creating an account. Then please ensure you've provided an institutional email address and provide full and accurate key words so you'll be sent the most relevant papers to review.

Changes in the Aims and Scope of *Innate Immunity*, the official journal of the International Endotoxin & Innate Immunity Society

Dirk Werling

Over the last months, *Innate Immunity*, the official journal of the International Endotoxin & Innate Immunity Society (IEIIS), has undergone some substantial changes in the Aims & Scope, which makes the journal hopefully again more attractive to Society members, and subsequently, open again to a wider audience.

The aim of the journal is still to provide a single, interdisciplinary forum for the dissemination of new information on innate immunity in humans, animals, but also fish and plants.

Thus, the journal welcomes manuscripts from researchers actively working on all aspects of innate immune responses, including humoral, cellular, and clinical topics.

The journal specifically welcomes submissions focusing on the interaction of cells with endotoxin- and exotoxin-related ligands from Gram-positive and Gram-negative bacteria, assessing the responses by multi-omics approaches such as, but not exclusively, RNASeq, lipidomic and metabolomic responses.

It also accepts manuscripts describing new immunologically active bacterial, viral, fungal, parasitic, and plant components, their receptors, signalling pathways, and induced mediators, as long as they describe a clear link between the identified and described component and the innate immune response.

Furthermore, *Innate Immunity* encourages submissions that take advantage of a wide array of model systems, including but not limited to humans, rodents, insects, plants and beyond, to probe the underlying principles involved. However, *Innate Immunity* is not accepting data that were generated in cell lines only. It has become increasing clear that such data vary widely between the same cell line used in different labs, and that the data are often impacted by the transformation of the cells used to generate the cell line. Thus, data generated in cell lines will only be accepted as part of a manuscript that assesses their biological relevance by reproducing the data in primary test systems, such as primary cells, organ cultures or indeed in vivo systems.

The journal includes Original Research articles, Research Notes, Reviews and Mini-reviews. In addition, *Innate Immunity* has introduced a new article type 'Technical Note' which gives authors the opportunity to describe novel methods, reagents, software, codes or databases, techniques, or significant improvements to established protocols, taken into account how time-consuming some of these processes are.

These technical notes can have some of the following formats:

1. Genome sequences and chemical characterisation of new ligands. *Innate Immunity* considers papers that announce a sequence of a newly identified ligand that stimulates the innate immune response. The manuscript should provide detailed information about the organism the ligand has identified, and a brief description of the identification method used to identify the ligand, with an emphasis on the detailed methodology and protocols used to characterize the ligand genetically and chemically. Accession numbers associated with publicly available data, for both raw reads and assemblies, should be provided with submission. Announcement of genome sequences, and raw data associated with them, will not be considered for publication until this is publicly available via GenBank, RefSeq and TPA, as well as records from SwissProt, the Protein Information Resource, the Protein Research Foundation, and the Protein Data Bank. By publishing a resource in *Innate Immunity*, authors agree, within reason, to make their materials available to the community, barring security restrictions. Authors are encouraged to submit their new ligands in expression plasmids or deposit them in a public repository such as Addgene.

2. Databases and software: *Innate Immunity* considers papers that announce the development of novel databases and software related to the identification of new innate immune stimulating ligands. The manuscript must describe the implementation of the software used. For a full 10 years following publication, the authors must make the software available to the community either via Weblink if hosted on a specific server or via the GitHub repository. In this case, the authors must also be available for technical support.

3. Protocols and workflows: *Innate Immunity* considers manuscripts describing novel wet or dry lab protocols used to generate and identify substances that stimulate an innate immune response in mammals, fish, birds, insects and plants. The protocol and required reagents and software used need to be described in detail, and authors must ensure that all protocols/reagents/ software are available to the wider community, either through purchase or public repository before the manuscript will be considered.

We hope that these changes will make *Innate Immunity* more attractive again for IEIIS members. For pre-submission enquiries, please contact the Editor-in-Chief Prof Dirk Werling (dwerling@rvc.ac.uk)

Lab Updates from Dr. Stefanie Vogel:
E6020, a TLR4 Agonist Adjuvant


Stefanie Vogel

Gopalakrishnan A, Richard K, Wahid R, Harley R, Sztein MB, Hawkins LD, Vogel SN. E6020, a TLR4 Agonist Adjuvant, Enhances Both Antibody Titers and Isotype Switching in Response to Immunization with Hapten-Protein Antigens and Is Diminished in Mice with TLR4 Signaling Insufficiency. *J Immunol.* 2022 Oct 5:ji2200495. doi: 10.4049/jimmunol.2200495. Epub ahead of print. PMID: 36198422

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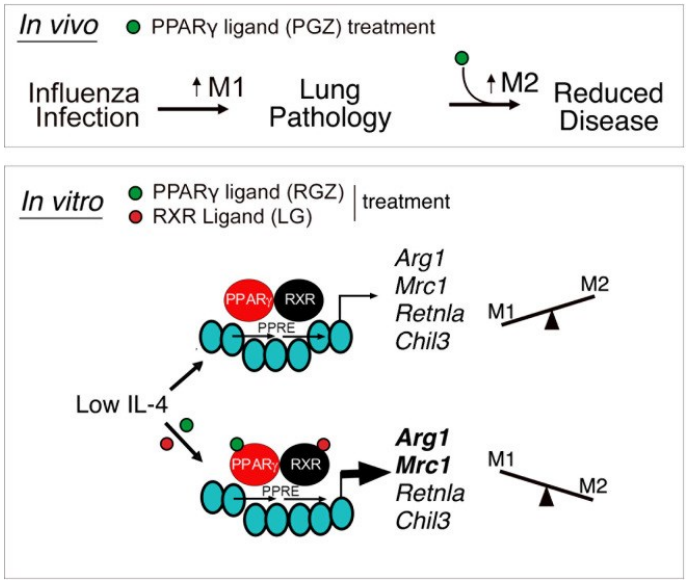
A Gopalakrishnan

We recently published a study, using the novel "TLR4-SNP" knock-in mouse strain, that homozygously expresses two single-nucleotide polymorphisms (SNPs), homologous to human TLR4 SNPs (299/399), to explore the role of TLR4 in antibody responses. In this study, we compared the role of TLR4-adjuvanted immunogens in WT and the LPS-hyporesponsive TLR4-SNP mice. We observed comparable antibody titers in WT and TLR4-SNP mice when immunized with either T-independent (NP-Ficoll) or T-dependent (NP-Ova) antigens alone. Interestingly, inclusion of E6020 (a TLR4 adjuvant) in immunizations enhanced antibody responses to a greater extent in WT mice than in TLR4-SNP mice. We also observed that in the T-dependent immunization model, E6020-mediated isotype class switching from IgG1 to IgG2c was sustained in WT mice after the second immunization but was significantly compromised in the TLR4-SNP mice. Our data support the efficacy of the TLR4 agonist adjuvant, E6020, in WT mice to increase not only antibody titers, but also to mediate isotype class switching. The results suggest that individuals expressing TLR4 SNPs may require additional immunizations to achieve optimal antibody responses.

Protection Against Influenza-Induced Acute Lung Injury

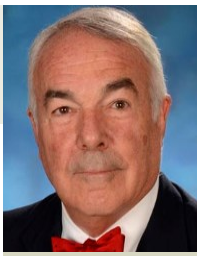
Gopalakrishnan A, Joseph J, Shirey KA, Keegan AD, Boukhvalova MS, Vogel SN, Blanco JCG. Protection against influenza-induced Acute Lung Injury (ALI) by enhanced induction of M2a macrophages: possible role of PPARγ/RXR ligands in IL-4-induced M2a macrophage differentiation. *Front Immunol.* 2022 Aug 16;13:968336. doi: 10.3389/fimmu.2022.968336. PMC9424652.

We recently published a study to demonstrate that mice lacking the IL-4Rα receptor, required for IL-4 and IL-13 mediated M2 macrophage differentiation, are more susceptible to influenza-induced lethality, while mice lacking the gene that encodes for COX-2, an M1 macrophage inflammatory mediator, are more resistant. Therapeutic administration of pioglitazone (a ligand of the nuclear hormone receptor and transcription factor, Peroxisome Proliferator Activated Receptor gamma PPARγ) increased survival of mice from influenza PR8 infection and reversed influenza-induced suppression of PPARγ mRNA in lungs. Importantly, we noted that conditional knockout mice expressing PPARγ-deficient macrophages were significantly more sensitive to PR8-induced lethality. These findings were extended in cotton rats infected with a non-adapted human influenza strain. Mechanistically, we observed that macrophages from WT mice responded to IL-4 treatment by induction of M2a genes- *Arg1, Mrc1, Chil3*, and *Retnla*. However, IL-4 treatment induced *Chil3* and *Retnla* genes in PPARγ-deficient macrophages, while expression of Arg1 and Mrc1 mRNA were not significantly elevated. PPARγ forms a heterodimer with Retinoid X Receptor (RXR), also a nuclear hormone receptor, to activate M2 macrophage gene expression. In WT macrophages, PPARγ and/or RXR ligands, rosiglitazone and LG100758, respectively, significantly enhanced IL-4-induced expression of *Arg1* and *Mrc1*, but not *Chil3* and *Retnla.* Similar enhancement of IL-4-induced genes was also observed in PPARγ-deficient macrophages in the presence of LG100758, but not rosiglitazone, albeit to a significantly lower extent than in WT macrophages. Our study supports a model in which PPARγ/RXR heterodimers control IL-4-induced M2a differentiation and suggest that PPARγ/RXR agonists should be considered as potential therapies for clinical intervention against influenza-induced ALI.



Graphical abstract from the recently published manuscript in *Frontiers in Immunology*.

Lab Update from Dr. Alan Cross:
Impact of Non-Lethal Burn Injury on Innate Host Defenses



Alan Cross

Alan Cross, Professor of Medicine
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Two graduate students in my laboratory, Jerod Brammer and Adrienne Kambouris, have been studying the impact of a non-lethal burn injury on innate host defenses. Nearly 500,000 burn injuries occur each year in the United States, with over 3,000 fatalities. Bacterial-derived sepsis is a leading cause of death following burns. Jerod used a 10% total body surface area nonlethal full-thickness flame burn model in outbred mice with and without *Pseudomonas aeruginosa* (PA) infection at the burn site that was originally described by Alan Holder. Jerod found that the following the burn the PA LD50 decreased 6 logs compared to PA-infected mice without the burn. Bacteria were detected in distal organs by 18 hr, concurrent with the onset of clinical signs of sepsis. Serum pro-inflammatory cytokines as well as IL-10 were first detected at 12 h postburn and increased until death, usually by 24 hr. With burn alone, there was a relatively low, transient increase in serum HMGB-1 levels; however, with burn and infection the HMGB1 concentration increased >10-fold and increased until death. Treatment of infected, burned mice with P5779, a peptide inhibitor of HMGB1, increased mean survival time from 23 to 42 h ($P<0.0001$). In a follow-up paper Jerod reported that even in the absence of infection, a subeschar seroma formed post-burn that was filled with ~500 ul of fluid, nearly 25% of the blood supply, that supported the robust growth of PA and contained inflammatory cytokines and chemokines which recruited immature PMNs and monocytes to the seroma in the absence of endothelial breakdown. These immune cells failed to limit PA growth and dissemination. This sequestering of critical immune cells away from other tissues, created a functional systemic neutropenia, thereby facilitating PA-mediated sepsis. These studies show that therapeutic targeting of HMGB-1 during burn wound infection may improve outcome and that seroma formation post-burn contributes importantly to immune dysfunction that facilitates disseminated bacterial infection.

Adrienne has continued this work and was struck by the observation that in the seroma a large number of PA were in close proximity, but not within, activated PMNs. She has been trying to identify why these phagocytes appear to be so dysfunctional. To do this she has been comparing the ability of PMNs from the seroma to those from the peripheral circulation of those same burned and burned and infected mice to generate reactive oxygen species (ROS) and ingest and kill PA (i.e., opsonophagocytic assays). She has compared the functional activity of both groups of mice to sham mice that underwent clipping of fur and isoflurane anesthesia but did not receive either a burn or infection. These studies are ongoing. Concurrently, she has used NanoString® technology to identify mRNA expression of host immune proteins in blood, liver, spleen and burn site skin at various points in time post-burn. She also is simultaneously examining the expression of PA virulence factors in bacteria at these same anatomic sites. These studies are ongoing, but an early finding from the Nanostring data is that arginase expression in mice is markedly and persistently upregulated. One report in the literature claims that the source is myeloid derived suppressor cells (MDSC) generated by the burn and finds that the administration of arginine ameliorates burn wound PA sepsis, perhaps by acting on the PA. Another finding of interest in Adrienne's study is that following the burn and PA infection, the skin remains a reservoir for ongoing PA dissemination, however, there is a general quiescence in PA gene expression until ~12 hrs at which time there is a marked expression of nearly every PA gene included in the analysis. Adrienne is preparing manuscripts describing her findings. ▲

Brammer J, Choi M, Baliban SM, Kambouris AR, Fiskum G, Chao W, Lopez K, Miller C, Al-abed Y, Vogel SN, Simon R, Cross AS. A non-lethal murine flame burn model leads to a transient reduction in host defenses and enhanced susceptibility to lethal Pseudomonas aeruginosa infection. *Infect Immun.* 2021; 89::e0009121.doi.10.1128/IAI00091-21. PMID:34152806

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Lab Update from Dr. Susu Zughaier:
Endotoxin Detection Using SERS from Silver Nanorods and Advanced Machine Learning

Susu Zughaier

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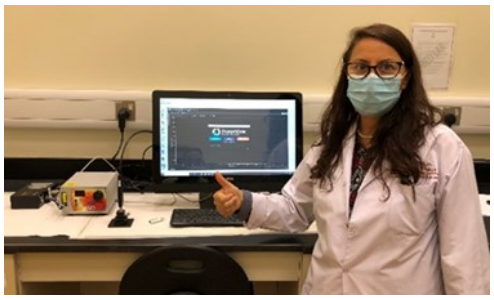
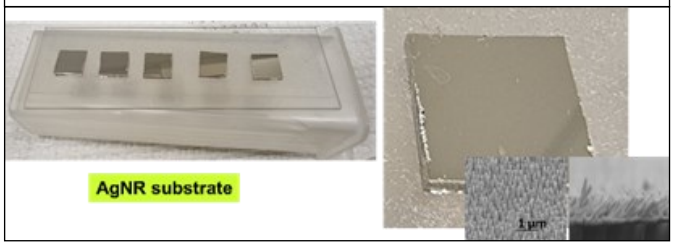
Collaborative research between Dr Susu Zughaier Lab at Qatar University and Prof. Yiping Zhao lab at University of Georgia is ongoing to develop a potential smart pathogen sensor or (sepsis sensor). The sensor utilizes silver nanorods substrate to enhance signal detected by Raman spectroscopy (SERS). Two papers were recently published as a proof-of-concept demonstrating the high sensitivity of this method in detecting physiologically relevant low endotoxin concentrations from various Gram-negative strains. Data were used to train machine learning algorithm (RamanNet). The measurements are adapted to portable and compact Raman spectroscopes.



Silver nanorods substrate and compact Raman spectroscope



Advanced machine learning algorithm

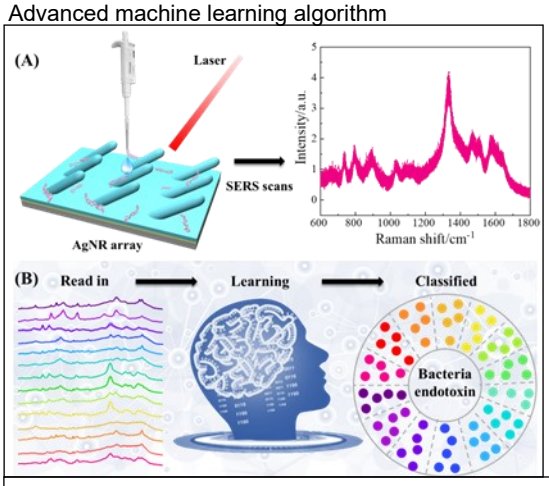


Figure. 1 The general schematic strategy for classification of bacterial endotoxins using SERS and MLA.
(A) Sample preparation and SERS measurements; and
(B) spectra pretreatments and classification using an MLA.

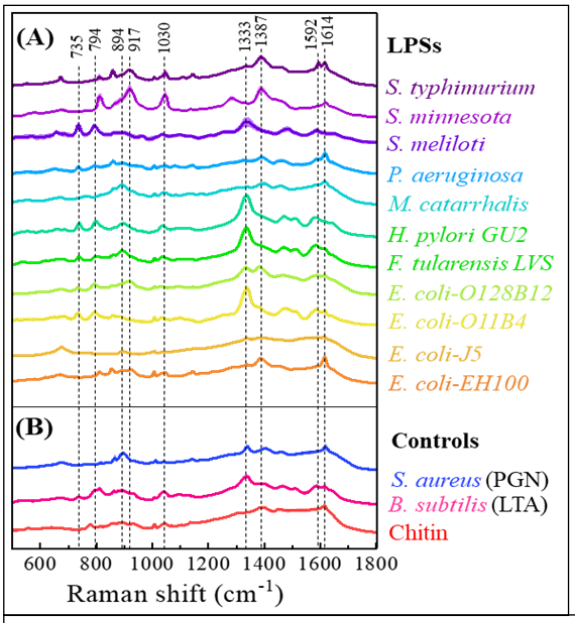


Figure. 2 (A) Typical average SERS spectra of eleven bacterial endotoxin samples. The mean SERS spectra are shown by the solid line, and the standard deviations are marked by the shadow. (B) SERS spectra of S. aureus peptidoglycan (PGN) and B. subtilis lipoteichoic acid (LTA) as well as chitin are used as controls since their structure is very distinct from LPS structures.

Nanoscale. 2022 Jun 23;14(24):8806-8817. DOI: 10.1039/d2nr01277d
Differentiation and classification of bacterial endotoxins based on surface enhanced Raman scattering and advanced machine learning. Yang Y, Xu B, Haverstick J, Ibtehaz N, Muszyński A, Chen X, Chowdhury MEH, Zughaier SM*, Zhao Y*

Biosensors (Basel). 2021 Jul 11;11(7):234. DOI: 10.3390/bios11070234
Highly Sensitive Detection and Differentiation of Endotoxins Derived from Bacterial Pathogens by Surface-Enhanced Raman Scattering. Xiaomeng Wu, Yiping Zhao*, Susu M Zughaier*

Lab Update from Dr. Robert Munford:
Interested in Studying Acyloxyacyl Hydrolase (AOAH)?


Robert Munford

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AOAH is the eukaryotic lipase that deacylates/inactivates many LPSs and several host lipids. There is new evidence that AOAH plays a significant role in preventing gut-derived endotoxemia, LPS-induced inflammation and fat storage in the liver (steatohepatitis), LPS-induced arterial foam cell formation (atherosclerosis), and oxidized phospholipid-induced pulmonary injury. Originally found in myeloid cells (monocyte-macrophages, neutrophils, dendritic cells) and renal proximal tubule cells, the enzyme has recently been found in NK cells, ILC1 cells, microglia, recent T cell emigrants, and other cell types.

Many AOAH details were summarized in a 2020 review: Munford RS, Weiss JP, and Lu M., Biochemical transformation of bacterial lipopolysaccharides by acyloxyacyl hydrolase reduces host injury and promotes recovery. *The Journal of Biological Chemistry.* 2020;295(51):17842-51

Investigators who would like to study Aoah$^{-/-}$ C57Bl/6J mice may obtain them from Jackson Labs.

Mingfang Lu and Bob Munford can provide interested colleagues with unpublished Word files that summarize new and old information regarding the enzyme's expression, structure, etc., and provide criteria to help investigators validate purified AOAH and anti-AOAH antibodies. Email robertmunford@gmail.com or mingfanglu@fudan.edu.cn ▲

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SCHOOL OF MEDICINE

CASE WESTERN RESERVE UNIVERSITY

Faculty Positions in Global Infectious Disease Research

Center for Global Health and Diseases
Case Western Reserve University

The Center for Global Health and Diseases (CGHD) in the Department of Pathology at Case Western Reserve University (CWRU) is recruiting Assistant, Associate, or Professor faculty to expand its clinical research programs. Applications are encouraged from physician-scientists and PhD scientists whose research involves international patient cohorts, international field work and immunity and pathogenesis of infectious disease. These positions will be supported by substantial start-up packages. The CGHD has clinical and translational research programs in adult and pediatric infectious disease (including malaria, schistosomiasis, filariasis and onchocerciasis, SARS-CoV2, Influenza, HIV, HPV, the microbiome and bacterial pathogens) with domestic and international partnerships in Africa, Asia, Europe, and Latin America. The CGHD and Department of Pathology together support research from basic immunology to international clinical trials, an Immunology Training Program, and multiple NIH training grants. Annual research funding in immunology and infectious diseases exceeds $100M across CWRU and affiliates. The Pathology Department is ranked in the top 10-13 nationally for NIH funding. Other assets include the Tuberculosis Research Unit, Division of Infectious Diseases and HIV Medicine, Department of Molecular Biology and Microbiology, and programs at our 4 affiliated medical centers: University Hospitals Cleveland Medical Center, Cleveland Clinic, MetroHealth Medical Center and Louis Stokes Cleveland VA Medical Center. CWRU values interdisciplinary thinking, creative collaboration and entrepreneurship. CWRU supports the importance of diversity within its faculty and staff, both in terms of gender and underrepresented minorities.

CWRU is located in University Circle in Cleveland, Ohio, a hub for art, culture, and sports with a low cost of living and outstanding schools, making it ideal for family life. University Circle houses the world-famous Cleveland Orchestra, the Cleveland Museum of Art, the Cleveland Museum of Natural History and the Crawford Auto-Aviation Museum. Cleveland is home to Major League baseball, football and basketball teams and is surrounded by a ring of parks and Lake Erie, ideal locations for hiking, sailing and other outdoor activities. Cleveland is home to the Rock and Roll Hall of Fame, a stunning lakeshore building designed by I.M. Pei (https://www.thisiscleveland.com/).

Candidates for Assistant Professor should have a demonstrated record of research success with substantial potential to obtain external funding. Candidates for Associate/full Professor should have robust funded research programs, national/international reputations and skills to be effective mentors and leaders. Candidates should submit a cover letter, CV, statement of research interests, diversity and equity statement, and names of 3 referees in a single pdf file to cghdsearch@case.edu. The diversity and equity statement (approximately 1/2 page) should explain how their research, teaching, and/or service have **contributed** to diversity, equity and inclusion within their scholarly field(s) and/or how their individual and/or collaborative efforts have promoted structural justice inside and outside institutions of higher learning. This statement should reflect on how the candidate's continued efforts will foster a culture of diversity, pluralism, and individual difference at CWRU into the future.

In employment and education, CWRU is committed to Equal Opportunity and Diversity. Women, veterans, members of underrepresented minority groups, and individuals with disabilities are encouraged to apply. CWRU provides reasonable accommodations to applicants with disabilities (contact the Office of Inclusion, Diversity and Equal Opportunity at 216-368-8877 to request an accommodation at any point in the application and hiring process; determinations will be made on a case-by-case basis).

As our society grapples with the history, legacy and persistence of entrenched racism and its impact on communities of color, we reaffirm our mission to expand opportunities for underrepresented groups; to provide a multifaceted education for our students; foster a culture of diversity, pluralism and recognition of individual difference; and realize our ideals within the university and in the larger world.

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