April 11 - 12, 2013  ■  Seaport Hotel, Boston, MA

Cambridge Healthtech Institute’s Inaugural

Molecular Pattern Recognition Receptors
Toll-like, NOD-like Receptors and Inflammasomes

Coverage Includes:
• NOD-Like Receptors (NLRs) and Soluble Receptors
• Damage Associated Molecular Patterns (DAMPs) and Pathogen Associated Molecular Patterns (PAMPs)
• TLR 2 and 4 and Their Role in the Immune System
• Pattern Recognition Receptors as Biomarkers
• Inflammasomes
• Therapeutic Potential for Inflammatory Diseases, Autoimmune Diseases, Infectious Diseases and Cancer

Presenting Companies:
• AC Immune SA
• Albert Einstein College of Medicine
  Department of Microbiology and Immunology
• Beth Israel Deaconess Medical Center
• Brunel University
  Centre for Infection, Immunity and Disease Mechanisms
• Centers for Disease Control and Prevention
• Children’s Hospital Boston
• Gilead Sciences
• Idera Pharmaceuticals
• Innate Pharma
• Nagasaki University
  Department of Molecular Pharmacology and Neuroscience
• National Heart & Lung Institute
• NovImmune SA
• Singapore Immunology Network
• University of Alabama at Birmingham
• VentiRx Pharmaceuticals
• Yale University
  And More!

Corporate Sponsor

healthtech.com/TLR
Molecular Pattern Recognition Receptors

THURSDAY, APRIL 11

7:30 am Registration and Morning Coffee

8:25 Chairperson’s Opening Remarks

INFLAMMASOMES

8:30 Inflammatory Monocytes Activate Memory CD8+ T and Innate NK Lymphocytes in an Inflammasome and Type I-Dependent Manner during Microbiological Pathogen Invasion

Gregoire Lauvau, Ph.D., Associate Professor, Microbiology and Immunology, Albert Einstein College of Medicine

Our work shows that Ly6C+CCR2+ inflammatory monocytes, a subset of monocytes, largely orchestrate memory CD8+ T and NK lymphocyte activation by differentiating into interleukin-18 (IL-18)- and IL-1β-producing cells in an inflammasome and type I interferon-IRF3-dependent manner. Memory CD8+ T cells became potent effector cells by sensing inflammation from monocytes independently of their cognate antigen. Like NK cells, they underwent rapid mobilization, upregulated intense and sustained effector functions during bacterial, viral and parasitic infections, and contributed to innate responses and protection in vivo.

9:05 Inhibition of Specific Endosomal Toll-like Receptors: A Novel Approach to the Treatment of Autoimmune Diseases

Robert Arbeit, MD, Vice President of Clinical Development, Idera Pharmaceuticals

Idera is developing candidates which inhibit specific endosomal Toll-like receptor-mediated immune activation. Two specific agents are currently in development for the treatment of autoimmune diseases: IMO-3100, a TLR7 and 9 antagonist, and IMO-8400, a TLR7 8, and 9 antagonist. A recently completed Phase 2a proof-of-concept trial of IMO-3100 in psoriasis successfully demonstrated the therapeutic effect of TLR antagonists in autoimmune disease.

9:40 Recombinant Surfactant Protein SP-D as a Therapeutic in Lung Inflammation and Allergy

Uday Kishore, Professor, Director, Centre for Infection, Immunity and Disease Mechanisms, Brunel University

SP-D is a lung collectin that has anti-allergic and anti-microbial properties. We have shown that recombinant SP-D can suppress allergic asthma in mouse models via suppression of IgE synthesis, histamine release, eosinophilia, inflammation and Th2 response. We understand the immunological mechanisms through which SP-D modulates eosinophils, dendritic cells, T and B cells. These studies have now led to setting up of clinical trials.

10:15 Coffee Break with Exhibit and Poster Viewing

10:55 Transcriptome Analysis of Cigarette Smoke Extract Induced TLR2-Dependent Activation of Human Cells

Mark J. Paul-Clark, Ph.D., Lecturer in Cardiothoracic Pharmacology, National Heart & Lung Institute, Imperial College

We have previously shown that oxidants and cigarette smoke extract (CSE) activate cells in vitro and in vivo, in part via the pattern recognition receptor TLR2. Transfected HEK293 cells with TLR2/6 or control vector were treated with H2O2, CSE and control media for 8h. Expression patterns in HEK293 cells were similar to those obtained from THP-1 cells and PBMCs. Pathway analysis of these cells revealed that inflammation was associated with NFR2-mediated and aryl hydrocarbon receptor signaling pathways. The study suggests that chronic pathologies caused by smoking cigarettes are driven by persistent episodes of inflammation and oxidative stress and also provides a gene list for the cellular response to oxidants.

11:30 A Nonredundant Role for Tlr9 and the Nalp3 Inflammasome in Acetaminophen-Induced Liver Injury

Wajhat Z. Mehal, Ph.D., Associate Professor, Section of Digestive Diseases, Yale University

12:05 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

NOD-LIKE RECEPTORS

1:45 Chairperson’s Remarks

1:50 Activation of Cytosolic Pathogen Sensor RIG-I for Prophylactic and Therapeutic Applications against Infectious Diseases

Prakash Sambhara, D.V.M., Ph.D., Chief, Immunology Section, Influenza Division, Centers for Disease Control and Prevention

Retinoic acid-inducible gene-I (RIG-I) is a pattern recognition receptor that is present in the cytosol. Interaction of RIG-I with its ligand leads to the activation of type 1 interferon. Type 1 interferon plays a major role in the induction of antiviral immunity by activating interferon responsive gene families. I will discuss latest developments with RIG-I and its ligands, and their utility as antiviral agents and adjuvants.

2:25 Development of STING-Specific Cyclic Dinucleotide Adjuvants for Cancer and Infectious Disease Vaccines

Thomas Dubensky, Jr., Ph.D., CSO, Aduro Biotech

Cyclic dinucleotides (CDNs) are bacterial intracellular messengers that have been shown to also function as PAMPs (Pathogen Associated Molecular Patterns) that activate innate immunity through triggering the mammalian host cell protein STING (Stimulator of Interferon Genes). Direct binding of CDNs to STING initiates a signaling cascade through the TBK-1/IRF3 axis to induce type I interferon and other co-regulated genes. We demonstrate that vaccination with CDN-adjuvanted recombinant protein formulated to facilitate cytosolic trafficking induced STING-dependent, antigen-specific CD4 and CD8 T cell responses, together with Th1-based antibodies correlated with protective immunity in a viral challenge model. When co-formulated with an irradiated GM-CSF secreting tumor cell vaccine (STINGVAX) to mobilize and activate dendritic cells in vivo, CDNs promoted a significant reduction of tumor growth in a stringent B16 melanoma treatment model. STING represents a significant new adjuvant target for the development and clinical translation of effective vaccines for infectious and malignant diseases.

2:55 Talk Title to be Announced

Andreas Muhs, Ph.D., CSO, AC Immune SA

3:30 Refreshment Break with Poster and Exhibit Viewing

4:05 Therapeutic Potential of Dectin-1 Agonists

Anshu Agrawal, Ph.D., Associate Adjunct Professor, Medicine/Immunology, University of California Irvine

Beta glucans, found in natural products such as mushrooms, oat, and fungi can activate the dendritic cells of the immune system via the dectin-1 receptor which belongs to the family of C-type lectin receptors. Activation of dendritic cells via dectin-1 results in cytosolic trafficking induced STING (Stimulator of Interferon Genes). Direct binding of CDNs to STING initiates a signaling cascade through the NLRP3 inflammasome and type I interferon-IRF3 dependent, antigen-specific CD4 and CD8 T cell responses, together with Th1-based antibodies correlated with protective immunity in a viral challenge model. When co-formulated with an irradiated GM-CSF secreting tumor cell vaccine (STINGVAX) to mobilize and activate dendritic cells in vivo, CDNs promoted a significant reduction of tumor growth in a stringent B16 melanoma treatment model. STING represents a significant new adjuvant target for the development and clinical translation of effective vaccines for infectious and malignant diseases.

4:40 Moderated Breakout Discussion Groups

5:45 Reception in the Exhibit Hall with Poster Viewing

7:00 pm End of Day One
12:05 Luncheon Presentation (Sponsorship Opportunity Available) or Lunch on Your Own

1:45 Chairperson’s Remarks

1:50 The Significance of Toll-Like Receptor-9 in Triple Negative Breast Cancer
Katri Selander, M.D., Ph.D., Assistant Professor, Medicine, University of Alabama at Birmingham
TLR9 is an innate immunity DNA-receptor which is also widely expressed in various cancers. We demonstrated recently that low tumor TLR9 expression is a poor prognosis marker specifically in triple negative breast cancer. The aim of our continuing work is to characterize at the molecular level how the lack of tumor TLR9 promotes poor survival in these patients.

2:25 The Unique Biology and Clinical Relevance of Toll-Like Receptor 8
Robert Hershberg, M.D., Ph.D., CEO, VentiRx Pharmaceuticals
The biology of TLR8 is unique in humans given its expression on myeloid-derived dendritic cells, monocytes and NK cells. In addition, TLR8 can be targeted using small molecule agonists and antagonists. Preclinical and clinical data are emerging which highlight TLR8 as an important target in human disease.

3:30 Inflammasomes Are Important Mediators of Bladder Inflammation
Francis M. Hughes, Jr., Ph.D., Staff Scientist II, Urology, Medical University of South Carolina
The NLRP3 inflammasome mediates production of inflammatory mediators such as IL-1b and IL-18 and as such is implicated in a variety of inflammatory processes including infection, sepsis, autoinflammatory diseases and metabolic diseases. The proximal steps in NLRP3 inflammasome activation are not well understood. Here we elucidate a critical role for Ca2+ mobilization in activation of the NLRP3 inflammasome by multiple stimuli. We demonstrate that blocking Ca2+ mobilization inhibits assembly and activation of the NLRP3 inflammasome complex, and that Ca2+ signaling is pivotal in promoting mitochondrial damage. Our findings support a model for NLRP3 inflammasome activation by Ca2+-mediated mitochondrial damage.

8:00 am Morning Coffee

8:25 Chairperson’s Opening Remarks

TOLL-LIKE RECEPTORS

8:30 Blockade of TLR4 Activation Represents a Promising Strategy in Diabetes
Limin Shang, Ph.D., Head, Exploratory Science Section, Exploratory Science and Translational Medicine, NovImmune SA
Dysregulation of Toll-like receptor 4 (TLR4) signaling via numerous ligands appears to play an underlying role in the pathogenesis of multiple inflammatory diseases. Thus, NI-0101, an anti-human TLR4 monoclonal antibody, was generated to have the capacity to interfere with LPS-induced signaling of TLR4 as well as other activators (i.e., endogenous or chemical ligands). To evaluate the role of TLR4 in beta islet cell biology, NI-0101 was shown to block human islet-induced immune cell activation. Furthermore, using an anti-mouse TLR4 mAb in vivo, blockade of TLR4 was efficient in protecting grafted islets from rejection in a mouse islet transplantation model as well as in murine models of diabetes. Taken together, these data promote blockade of TLR4 activation as a promising strategy in diseases associated with islet cell pathogenesis.

9:05 Therapeutic Antibody against Toll-Like Receptor 3 (TLR3) for the Treatment of Inflammation
Canine Paturel, Ph.D., Director, R&D, Innate Pharma
Innate Pharma is developing a therapeutic antibody against Toll-like Receptor 3 (TLR3), an immune checkpoint controlling inflammation. We have generated a panel of mouse anti-human TLR3 antibodies and humanization of several candidates is ongoing. In addition, Innate Pharma generated efficacy data in animal models of COPD, Colitis, Rheumatoid Arthritis and sepsis with surrogate rat anti-mouse TLR3.

9:40 Mechanisms of HIV-Mediated Inhibition of TLR4 Triggered Macrophage Activation
Souvenir Tachado, M.D., Assistant Professor, Medicine, Beth Israel Deaconess Medical Center
Alveolar macrophages (AM) express Toll-like receptors (TLRs) such TLR4, and we found significant derangement of TLR4-mediated activation of AM from asymptomatic HIV+ subjects. Furthermore, this derangement is specific, may represent AM reprogramming to an LPS-tolerant phenotype and is independent of HAART. In summary, HIV infection of AM results in targeted and specific impairment of macrophage TLR-mediated signaling pathways, impairing critical components of first line host defenses in the lungs.

10:15 Coffee Break with Exhibit and Poster Viewing

10:55 Development of a TLR7 Agonist to Treat Chronic Hepatitis B Virus (HBV) Infection
Simon Fletcher, Ph.D., Principal Scientist, Biology, Gilead Sciences
GS-9620 is a potent, selective agonist of human TLR7 being developed to treat chronic HBV (CHB). It has demonstrated promising antiviral activity in both the woodchuck and chimpanzee models of CHB, and single dose safety has been demonstrated in healthy volunteers. Data from these preclinical and clinical studies will be presented.

11:30A Critical Role for Calcium Mobilization in Activation of the NLRP3 Inflammasome
Tiffany Horng, Ph.D., Assistant Professor, Department of Genetics and Complex Diseases, Harvard School of Public Health
**SPONSORSHIP, EXHIBIT, AND LEAD GENERATION OPPORTUNITIES**

CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space and branding, as well as the use of the pre and post-show delegate lists. Customizable sponsorship packages allow you to achieve your objectives before, during, and long after the event. Signing on early will allow you to maximize exposure to hard-to-reach decision makers!

**Agenda Presentations**
Showcase your solutions to a guaranteed, highly-targeted audience. Package includes a 15 or 30-minute podium presentation within the scientific agenda, exhibit space, on-site branding and access to cooperative marketing efforts by CHI.

**Breakfast & Luncheon Presentations**
Opportunity includes a 30-minute podium presentation. Boxed lunches are delivered into the main session room, which guarantees audience attendance and participation. A limited number of presentations are available for sponsorship and they will sell out quickly. Sign on early to secure your talk!

**Invitation-Only VIP Dinner/Hospitality Suite**
Sponsors will select their top prospects from the conference pre-registration list for an evening of networking at the hotel or at a choice local venue. CHI will extend invitations and deliver prospects. Evening will be customized according to sponsor’s objectives i.e.:
- Purely social
- Reception style
- Focus group
- Plated dinner with specific conversation focus

**Exhibit**
Exhibitors will enjoy facilitated networking opportunities with high-level conference delegates. Speak face-to-face with prospective clients and showcase your latest product, service, or solution.

*Inquire about additional branding opportunities!

**Looking for additional ways to drive leads to your sales team? CHI can help!**
We offer clients numerous options for custom lead generation programs to address their marketing and sales needs, including:
- Live Webinars
- White Papers
- Market Surveys
- Podcasts and More!

To customize your participation at this event, please contact:
Tim McLucas - Manager, Business Development
781-972-1342  |  tmclucas@healthtech.com

**TRAVEL & HOTEL INFORMATION**

**Seaport World Trade Center**
200 Seaport Boulevard
Boston, MA 02210
T: 617-385-5049

Please visit our conference website to reserve your room or call the hotel directly to reserve your sleeping accommodations. You will need to identify yourself as a CHI conference attendee to receive the discounted room rate with the host hotel. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space and rate-availability basis. Rooms are limited, so please book early to take advantage of the discount we have negotiated. We understand that you have many choices when making your travel arrangements, and may ultimately decide to stay at another hotel. Please understand that reserving your room in the CHI room block allows you to take full advantage of the conference sessions, events and networking opportunities, and ensures that our staff will be available to help should you have any issues with your accommodations.

**Flight Discounts:**
Special discounts have been established with American Airlines for this conference. Please use one of the following methods:
- Call 1-800-433-1790 and use Conference Code 9243BM
- Go online at www.aa.com/group enter Conference code 9243BM in promotion discount box
- Contact our designated travel agent at 1-877-559-5549 or Wendy.Levine@protravelinc.com

**Car Rental Discounts:**
Special discount rentals have been established with Hertz for this conference. Please use one of the following methods:
- Call HERTZ, 800-654-3131, use our Hertz Convention Number (CV): 04KL0004
- Go online www.hertz.com, use our Hertz Convention Number (CV): 04KL0004

healthtech.com/TLR
Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

Handicapped Equal Access: In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

To view our Substitutions/Cancellations policy, go to http://www.healthtech.com/regdetails

Video and audio recording of any kind is prohibited onsite at all CHI events.