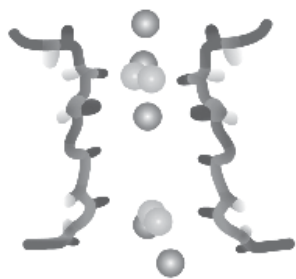


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Cambridge Healthtech Institute's Third Annual

Ion Channels as Therapeutic Targets

A Flood of Potential for Drug Discovery

October 21-22, 2008 • Boston, MA

KEYNOTE SPEAKERS:



George K. Chandy, Ph.D., Professor, Physiology & BioPhysics,
School of Medicine, University of California - Irvine



Michael Dabrowski, Ph.D., Head of Global Ion Channel
Initiative, AstraZeneca



Laszlo Kiss, Ph.D., Senior Research Fellow, Merck Research
Laboratories

SPECIAL EVENT FEATURE:

Ion Channels as Therapeutic Targets: An Industry Minireview

Peter Haddock, Ph.D., Group Leader, Ion Channel Group & CNS Biology, Pfizer

DISTINGUISHED FACULTY

Anindya Bhattacharya, Ph.D.,
Johnson & Johnson Pharmaceutical
Research and Development LLC

Neil A. Castle, Ph.D., Icagen Inc.

George K. Chandy, M.D., Ph.D.,
University of California - Irvine

Mark (Mao Xiang) Chen, Ph.D.,
GlaxoSmithKline Research and
Development

Chuan-Chu Chou, Ph.D.,
Schering Plough Research Institute

Michael Dabrowski, Ph.D.,
AstraZeneca

Gary Desir, M.D.,
Yale University School of Medicine

Jesus 'Tito' Gonzalez, Ph.D.,
Vertex Pharmaceuticals

Akihiko Kato, Ph.D.,
Eli Lilly and Company

Laszlo Kiss, Ph.D.,
Merck Research Laboratories

Roland Kozlowski, Ph.D., Lectus

Michael Mayer, Ph.D.,
University of Michigan

Dinah Misner, Ph.D., Roche Palo Alto

Birgit T. Priest, Ph.D.,
Merck Research Laboratories

Ken Stauderman, Ph.D.,
CalciMedica

Nuria Tamayo, Ph.D., Amgen

PRE-CONFERENCE SHORT COURSES:

MONDAY,
OCTOBER 20

Understanding the Structural Biology of Ion Channels to Guide Drug Discovery

Heike Wulff, Ph.D., University of
California - Davis

Boris S. Zhorov, Ph.D., D.Sc.,
McMaster University

Ion Channel Assays for Safety Screening

Gary Gintant, Ph.D., Abbott
Laboratories

Laszlo Urban, M.D., Ph.D.,
Novartis Institutes for Biomedical
Research

Harry Witchel, Ph.D., Brighton
and Sussex Medical School

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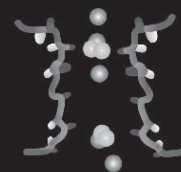
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Third Annual
Ion Channels as Therapeutic Targets
A Flood of Potential for Drug Discovery



October 21-22

PRE-CONFERENCE SHORT COURSES*

MONDAY, OCTOBER 20

9:00am-12:00pm

(SC2) Understanding the Structural Biology of Ion Channels to Guide Drug Discovery

During the past decade there have been two remarkable technological breakthroughs which have transformed ion channel-based drug discovery. The first advance is using X-ray crystallography and solid-state NMR to solve the structures of ion channels, which enabled structure-guided drug design of ion-channel blockers. The other advance is the development of automated assays such as FLIPR and Ionworks which have high throughput screening of ion channel blocking compounds a reality. This short course is an overview on the cutting-edge development of structure-based design of ion channel blockers. Several leading experts in the field will provide road maps to starters as well as contributing experiences of several complementary approaches.

Topics to be covered:

- Pinpointing ion channel domains critical for specificity and activity
- Looking at 3-D structure for selectivity and specificity
- Oligomerization of ion channels – implications for tissue specificity
- Designing expression systems that produce truly representative channels for screening

Tutors: Heike Wulff, Ph.D., Assistant Professor, University of California - Davis
Boris S. Zhorov, Ph.D., D.Sc., Professor, Department of Biochemistry and Biomedical Sciences, McMaster University

1:30 – 2:00 Afternoon Pre-Conference Registration

2:00 – 5:00

(SC5) Ion Channel Assays for Safety Screening

Ion channels are involved in a complex and intricate signaling system that play an important role in affecting the cellular response to a drug and hence to the overall patient safety. For instance, the hERG potassium channel plays an important role in repolarization of cardiac myocytes and other sodium and calcium channels also control of ionic current flow in various cells. Drug-induced alterations in the translation and trafficking of the ion channel proteins and drug-induced blockade of channels resulting in reductions in ionic current are all thought to contribute to drug-related adverse events. *In vitro* assays using isolated cells, cell lines, and expression systems cloned for specific ion channels are now routinely used to predict the drug response. Electrophysiology experiments, using conscious or anaesthetized animals, are also conducted to identify potential drug liabilities. Over the years there have been significant improvements in both the technology and in the scientific understanding of how ion channels can impact drug safety. This course provides a detailed overview of the types of ion channel-based screening assays and technologies that are in use and how they are being applied to effectively monitor and predict drug safety.

Topics to be covered:

- Overview of current and emerging assays and methodologies
- Discussion on when and how to use these assays
- Use of automation and high-throughput techniques
- Comparison of platforms and applications
- Factors affecting sensitivity and specificity
- Emerging applications such as determining off-target adverse drug effects, looking beyond hERG channels, using action potentials as integrated test systems

Tutors:

Moderator: J. Rick Turner, Ph.D., PGCE, MICR, Chairman, Department of Clinical Research and Director, Cardiac Safety Education Center, Campbell University School of Pharmacy

Gary Gintant, Ph.D., Senior Group Leader, Department of Integrative Pharmacology, Abbott Laboratories

Dr Huabin Sun, Sr Research Investigator, Cardiovascular Safety Pharmacology & Discovery Tox, Bristol Myers Squibb Co

Laszlo Urban, M.D., Ph.D., Executive Director and Global Head, Preclinical Safety Profiling, Novartis Institutes for Biomedical Research Inc.

Harry Witchel, Ph.D., Senior Lecturer in Physiology, Brighton and Sussex Medical School

**separate registration required*

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Main Conference

TUESDAY, OCTOBER 21

7:00am – 6:30pm

Registration Open

7:30

Morning Coffee

PROGRESSING AT AN ACCELERATED PACE IN ION CHANNEL DRUG DISCOVERY

8:30 Ion Channels as Therapeutic Targets: Minireview & Chairperson's Remarks

Peter Haddock, Ph.D., Group Leader, Ion Channel Group & CNS Biology, Pfizer

This presentation will review a selected number of recent publications in the field of Ion Channel Biology and Drug Discovery. Dr. Haddock will present a synopsis of several papers in turn that have contributed to the Channel field in the last year and set the stage for the conference to follow.

KEYNOTE PRESENTATIONS:

9:00

Ion Channels as Therapeutic Targets to Modulate Cell Proliferation



George K. Chandy, M.D., Ph.D., Professor, Physiology & Biophysics, School of Medicine, University of California - Irvine

In 1984, potassium channels were discovered in lymphocytes and shown to regulate lymphocyte activation. Since then, ion channels have been described in diverse non-excitabile cells and their role in regulating cell proliferation, transformation and apoptosis is better understood. Ion channels in non-excitabile cells are viable therapeutic targets for many diseases. This presentation will highlight two potassium channels, Kv1.3 and KCa3.1, and the blockers we are developing as therapeutics for autoimmune diseases and atherosclerosis

9:35

Improving Ion Channel Lead Generation Capabilities by a Multi-Disciplinary Approach



Michael Dabrowski, Ph.D., Head of Global Ion Channel Initiative, AstraZeneca

We identified a number of scientific and technological gaps impairing the rational pursuit of ion channels as a target class. In order to rectify this situation, identify novel solutions and enable proper ion channel lead generation we employed nine senior postdoctorates in chemistry, electrophysiology, molecular and cellular biology. The group works as a team on common themes: Chemistry, Screening Technologies, Assay Refinement and Ion Channel Expression. In this talk several examples of novel solutions and technologies will be presented reflecting how the tractability of ion channels has improved.

10:10

Grand Opening Coffee Break in the Exhibit Hall

10:40

Effective Screening Strategies to Expand the Pharmacology of Ion Channels and Pave the Way for the Next Generation of Ion Channel Therapeutics



Laszlo Kiss, Ph.D., Senior Research Fellow, Merck Research Laboratories

11:10

***in-vitro* and *in-vivo* Pharmacology of Novel TRPV1 Antagonists**

Anindya Bhattacharya, Ph.D., Senior Scientist, Pain & Related Disorders, Johnson & Johnson Pharmaceutical Research and Development LLC

TRPV1 is a polymodal nociceptor that offers hope as an analgesic drug target. The objective of this presentation will be to review industrial TRPV1 drug discovery efforts including ours, discuss challenges and explore opportunities/benefits of TRPV1 intervention by small molecule antagonists. One of the key focus areas will be to discuss TRPV1 *in-vitro* screens used during HTS and/or lead optimization with a view of predictability/translatibility of the pharmacology to *in-vivo* efficacy either in a pharmacodynamic or 'diseased' model of pathology. Some of the practical issues in a screening paradigm (species difference, recombinant versus native TRPV1, hemi-equilibrium versus equilibrium pharmacology, PK-PD and ADMET) will be presented in context of the continuum of TRPV1 drug discovery.

11:40

PANEL DISCUSSION

Progressing at an Accelerated Pace in Ion Channel Drug Discovery—Meeting the Top Two Challenges:

- Selectivity & Off-Target Effects – Using Technology to Get Past the Bottleneck
- Toward Predictive Pre-Clinical Models for Ion Channels – Translation from *in vitro* to *in vivo*

Facilitator:

Peter Haddock, Ph.D., Group Leader, Ion Channel Group & CNS Biology, Pfizer

Panelists:

Anindya Bhattacharya, Ph.D., Senior Scientist, Pain & Related Disorders, Johnson & Johnson Pharmaceutical Research and Development LLC

George K. Chandy, M.D. Ph.D., Professor, Physiology & BioPhysics, School of Medicine, University of California - Irvine

Michael Dabrowski, Ph.D., Head of Global Ion Channel Initiative, AstraZeneca

Laszlo Kiss, Ph.D., Senior Research Fellow, Merck Research Laboratories

LEADING-EDGE PHARMACEUTICAL TARGETS

12:10pm High-Throughput Profiling of Ion Channels in Primary Human Cells

Michael Mayer, Ph.D., Department of Biomedical Engineering and Department of Chemical Engineering, University of Michigan

This talk presents a high-throughput method to quantify the functional activity of potassium ion channels in primary human lymphocytes. This method is rapid, automated, specific (here for the voltage-gated Kv1.3 ion channel), and capable of measuring, in parallel, the electrical currents of over 200 individual lymphocytes isolated from freshly drawn blood. The statistics afforded by high-throughput measurements allowed direct comparison of Kv1.3 activity in different subsets of lymphocytes, including CD4+ and CD8+ T cells, γδ T cells, regulatory T cells, and B cells. Moreover, the results suggest that Kv1.3 ion channel activity can be used as a functional activation marker in T cells. High-throughput measurements made it possible to compare the activity of Kv1.3 channels in lymphocyte samples from multiple sclerosis (MS) patients and from rheumatoid arthritis (RA) patients with lymphocyte samples from healthy control subjects. We show that patients with progressive forms of MS have significantly increased Kv1.3 activity in peripheral T cells compared to controls. In the context of RA, preliminary data demonstrate that Kv1.3 activity may be a better biomarker for disease activity than existing markers such as C-reactive protein. We propose that profiling ion channel activity in primary human cells presents an enabling methodology that may be useful for diagnostic applications, therapeutic monitoring, drug screening, and drug safety testing.

12:40 Luncheon Technology Workshop Development And Validation of Compound Profiling Assays For Voltage-Gated Sodium Channels Using Automated Electrophysiology

Sponsored by:



Jeff Clare, Ph.D., Director, Ion Channel Group, Millipore

Voltage-gated sodium channel (NaV) inhibitors are an important class of drugs used to treat a variety of indications including arrhythmia, pain, local anaesthesia, epilepsy and bipolar disorder. Despite the indispensable role of NaV channels in mediating action potentials throughout nervous, cardiac and muscle tissues, drugs that inhibit these channels are remarkably well tolerated. This is thought to be largely due to their voltage- and use-dependent mechanism of action whereby the extent of block is greatly increased during periods of repetitive firing or sustained depolarisation as may occur, for example, during seizure activity or pain signalling. Interest in NaV channels within the pharmaceutical industry has been intensified by the discovery of human mutations in NaV1.7 that confer remarkable inability to sense pain in otherwise healthy individuals. Other subtypes have previously been implicated in pain signalling (e.g. NaV1.8 and 1.3) but, until recently, the development of subtype selective inhibitors has proved extremely challenging and the therapeutic utility of such blockers remains an important issue. This presentation will describe the development and use of a panel of robust assays for profiling the selectivity of compounds against each of the NaV subtypes, from 1.1 to 1.8. These assays use two different automated electrophysiology platforms (Ionworks and PatchXpress) and have been validated for detecting use- and voltage-dependent inhibition.

1:40 Session Break

LEADING-EDGE PHARMACEUTICAL TARGETS (CON'T)

2:20 Chairperson's Remarks

Michael Mayer, Ph.D., Assistant Professor, Biomedical Engineering and Chemical Engineering, University of Michigan

2:25 Antagonism of the TRPV1 Channel and Thermoregulation

Nuria Tamayo, Ph.D., Principal Scientist, Amgen

The vanilloid receptor 1 (VR1, TRPV1) is a non-selective cation channel that can be activated by a variety of noxious stimuli, including capsaicin, extracellular acidity and heat. It is expressed in primary afferent neurons and is upregulated following inflammation and nerve injury. Antagonism of this channel is considered an attractive approach for the treatment of chronic pain and inflammatory hyperalgesia. We have recently advanced a TRPV1 antagonist, AMG 517, into clinical trials as a new therapy for

the treatment of pain. However, in addition to the desired analgesic effects, AMG 517 significantly increased body core temperature following oral administration. Here we will discuss our two approaches to eliminate or minimize the on-target hyperthermic effect.

2:55 Discovering Small Molecule CRAC Channel Inhibitors

Ken Stauderman, Ph.D., Vice President, Research, CalciMedica

CalciMedica's drug discovery strategy targets CRAC channels. CRAC channels are key components of the Ca²⁺ signaling pathway in immune cells, which is essential for adaptive immune responses. CalciMedica has acquired exclusive rights to the molecular components of CRAC channels (Orai1-3 and STIM1-2) and is using these molecules to screen for novel small molecule inhibitors for the treatment of autoimmune diseases.

3:25 Technology Watch E Unum Pluribus: One Platform, Three Programs

Sponsored by:



Arthur M. "Buzz" Brown, M.D., Ph.D., President and CEO, ChanTest Corporation

ChanTest's 120-member ion channel library (ICL) is being validated and optimized for PatchXpress 7000A, IonWorks Quattro and FLIPRTetra (Automated Patch Clamp-Fluorescence). The single ICL-APC/FI platform supports three programs: services, supplies and drug discovery. For services, ICL "books" can be arranged for screening according to tissue (Cardiac or CNS Channel Panels), therapeutic area (Pain or Seizure Panels) or channels family (Nav 1.x, Cav x.y). For supplies, "books" are customized by instrument for purchase. For discovery, the ICL-APC/FI platform can be screened with diversity or ion channel-focused compound libraries or repurposed drug libraries. Examples of the different program applications will be presented.

3:55 Networking Refreshment Break in the Exhibit Hall

4:30 Sodium Channel Drug Discovery in the Era of Automated High-Throughput Electrophysiology

Neil A. Castle, Ph.D., Director of Biology, Senior Research Advisor, Icaegen Inc.

Voltage-Gated sodium channels are excellent targets for development of drugs to treat neuroexcitatory disorders like pain and epilepsy. Identifying novel drug candidates has historically been a challenge due in part to the complex structural conformational changes that occur during Na channel gating, and the fact that many compounds only interact with specific gating states. The development of high-throughput planar patch clamp electrophysiology technologies like the PatchXpress™ and more recently the Ionworks Quattro™ have provided opportunities to effectively use automated electrophysiology in the hit and lead identification stages of sodium channel drug discovery. In this presentation we will describe how we use both of these platforms to support target and assay development, as well as screening and hit to lead progression.

5:00 Voltage-gated Sodium Channels as Targets for Pain Treatment

Dr Alexander Binshok, Instructor in Anaesthesia, Anesthesia Clinics 309, Harvard Medical School

5:30 Panel Discussion with Speakers

6:00 Happy Hour in the Exhibit Hall

7:30 End of Day

Advisory Board

Chuan-Chu Chou, Ph.D., Fellow, Schering Plough Research Institute

Jesus "Tito" Gonzalez, Ph.D., Senior Director, Biology, Vertex Pharmaceuticals Inc.

Peter Haddock, Ph.D., Group Leader, Ion Channel Group & CNS Biology, Pfizer Inc.

Laszlo Kiss, Ph.D., Research Fellow, Neuroscience Drug Discovery, Automated Biotechnology Group, Merck Research Laboratories

7:30 Continental Breakfast Breakout Discussion Sessions

Table 1: Correlating *in vitro* Potency with *in vivo* Efficacy for Ion Channel Modulators

Moderator: Birgit Priest Ph.D., Primary Research Fellow, Ion Channels, Merck Research Labs

Table 2: Primary Cell Lines and Automated Patch Clamp Systems for Screening

Moderator: Dinah Misner, Associate Director, Discovery and Investigative Safety, Roche Palo Alto

Table 3: Outside the Box: Are There Non-Conventional Ways for Ion Channel-Based Drug Discovery?

Moderator: Chuan-Chu Chou, Ph.D., Fellow, Schering Plough Research Institute

ION CHANNEL CARDIAC SAFETY ASSAYS

8:30 Chairperson's Remarks

Chuan-Chu Chou, Ph.D., Fellow, Schering Plough Research Institute

8:40 Strategies to Predict QT Prolongation and Arrhythmias: Assessing hERG and Other Cardiac Ion Channels Early in Drug Development

Dinah Misner, Associate Director, Discovery and Investigative Safety, Roche Palo Alto

Preclinical strategies to assess new chemical entities (NCEs) for cardiovascular liabilities early in the development process, with an emphasis on detection of QT prolongation and arrhythmias, will be presented. Topics to be discussed include an overview of the current regulatory guidelines around pre-clinical cardiovascular assessment, discussion of state-of-the-art technologies for *in vitro* testing (specifically around ion channels) and translation to *in vivo* results, and development of customized strategies to de-risk cardiovascular liabilities of NCEs. Additionally, specific examples will be provided where these new technologies have benefited projects to identify liabilities early, enabling selection of the "best" NCE moving forward.

9:10 Addressing the Challenges in Recombinant Expression for Higher Throughput Screens of Ion Channels with Cardiac Liability

Mao Xiang Chen, Ph.D., Biological and Cellular Targets, BR&AD, GlaxoSmithKline Research and Development

Ion channels of the cardiac action potential, particularly hERG, arguably carry the biggest liability in drug development. Recent years have seen the advent of a number of assay technologies which enabled higher throughput early profiling of individual cardiac ion channels. However, the data quality and throughput obtained with these platforms is critically dependent on the robustness of the expression reagent being used. The generation of high quality, recombinant cell lines and optimization of expression is therefore a key step in developing these assays and this can present significant challenges due to the diversity and organizational complexity of many channel types. This presentation focuses on several difficult to express cardiac ion channels, and demonstrates improved assays can be obtained by integration of expression and optimization strategies with planar array electrophysiology systems.

9:40 Networking Coffee Break in the Exhibit Hall

TARGETING ION CHANNEL MODULATORS OR AUXILIARY SUBUNITS – AN EXCITING ROUTE

10:35 Chairperson's Remarks

Chuan-Chu Chou, Ph.D., Fellow, Schering Plough Research Institute

10:40 Functional Modulation of AMPA Receptors by Auxiliary Subunits, TARPs

Akihiko S. Kato, Ph.D., Research Scientist, Neuroscience Discovery Research, Eli Lilly and Company

Many ion channels comprise principal and auxiliary subunits. Auxiliary subunits are effective drug targets, e. g. sulfonylureas for SUR subunit of K_{ATP} , and gabapentin for $\alpha 2\delta$ subunit of calcium channels. We will describe TARPs (Transmembrane AMPA receptor Regulatory Proteins) auxiliary subunits of AMPA-type glutamate receptors. TARPs dramatically regulate trafficking and pharmacology of AMPA receptors. Recently, we discovered another family of TARPs, whose regulation is different from conventional TARPs. Understanding of receptor auxiliary subunits provides further dimensions for therapeutic strategies.

11:10 Inhibitors of Ion Channel Accessory Protein Interactions as Novel Therapeutics for Neuropathic and Inflammatory Pain

Loic L'Huillier, Ph.D., Team Leader, Electrophysiology, Lectus Therapeutics, Ltd.

Accessory proteins confer key functional properties to ion channels such as regulation of biophysical properties, and/or channel trafficking. We have identified, through the use of novel protein-protein interaction assays, series' of compounds that modulate ion channel function through exploiting the interaction between (i) Kv1.1 channels and their regulatory Kv β 1 accessory protein subunits, and (ii) Cav2.2 channels and their regulatory Cav β 3 accessory protein subunits. We will present an introduction to the development and performance of robust, high-throughput Kv1.1/Kv β 1 and Cav2.2/Cav β 3 protein-protein interaction assays demonstrating the identification of novel series of ion channel modulators. We will also present subsequent functional *in vitro* electrophysiological characterization and *in vivo* evaluation of these novel ion channel modulators in models of inflammatory and neuropathic hyperalgesia.

EMERGING ION CHANNEL TARGETS FOR TREATING TYPE II DIABETES

11:40 Regulation of Glucose Metabolism by the Voltage-Gated Potassium Channel Kv1.3 and the Intracellular Calcium Sensor Synaptotagmin-7

Gary Desir, M.D., Professor, Department of Medicine, Section of Nephrology, Yale University School of Medicine

The voltage-gated potassium channel Kv1.3 plays a key role in the regulation of peripheral glucose metabolism. Channel inhibition in adipocytes leads to membrane depolarization, calcium release from intracellular stores, increased intracellular calcium, and ultimately to GLUT4 translocation to the plasma membrane. Channel deletion results in constitutive expression of GLUT4 at the plasma membrane. Synaptotagmin-7 (Syt-7) also modulates peripheral glucose homeostasis through its action on both insulin secretion and GLUT4 traffic. Syt-7 deletion in mice leads to a diabetic state characterized by decreased insulin secretion by the pancreatic β cell, constitutive expression of GLUT4 at the plasma membrane, and decreased responsiveness to insulin in adipocytes. Since Kv1.3 modulates intracellular calcium, Syt-7 senses intracellular calcium, and are both expressed on GLUT4 vesicles, we speculate that Kv1.3 and Syt VII are components of the machinery that regulates calcium-dependent GLUT4 traffic and glucose metabolism.

12:10 Kv1.3 Channels as Targets for Genetic-Induced Obesity and Intranasal Insulin Delivery

Debra Fadool, Ph.D., Department of Biological Science, Programs in Neuroscience and Molecular Biophysics, The Florida State University

Previously, it has been demonstrated that mice with Kv1.3 gene-targeted deletion (Shaker subfamily of ion channels) fail to gain weight when placed on a high-fat diet and have increased peripheral insulin sensitivity via augmentation of GLUT4 translocation to the plasma membrane. We now show that channel deletion in a genetic model of obesity and late-onset diabetes (MC4R-null mice) reduces body weight by decreasing fat deposition and subsequent fasting leptin levels, significantly extends lifespan and increases reproductive success, and abrogates obesity by increasing locomotor activity and mass-specific metabolism. Intranasal insulin delivery (IND; inhaled insulin) to awake, wild-type mice robustly phosphorylates the channel in the olfactory bulb and increases protein-protein interactions with receptor tyrosine kinases and adaptor proteins that regulate channel biophysics. IND-treated mice had an increased short- and long-term object memory recognition, increased anxiolytic behavior, and an increased odor-discrimination using an odor habituation protocol but no change in odor threshold using a two-choice paradigm. Unlike Kv1.3 gene-targeted deletion that alters metabolism, adiposity, and axonal targeting to defined olfactory glomeruli to generate a "super-smeller" phenotype, suppression of Kv1.3 via IND had no effect on olfactory anatomy that would predict changes in odorant coding.

12:40 Close of Ion Channels Conference



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October 22-23 RNAi for Therapeutics HDAC Inhibitors Targeting Diabetes

Multiple Conference Pricing

Includes access to three conference days (excludes short courses)

Early Registration until July 25, 2008 \$1645 \$795
Advanced Registration until September 12, 2008 \$1795 \$875
Registration after September 12, 2008 or On-Site \$1995 \$945

REQUIRED- Please select the two conferences you will most likely attend:

October 21-22 (choose one)

RNAi for Screening Kinase Inhibitors **ION CHANNELS**
October 22-23 (choose one) RNAi for Therapeutics HDAC Inhibitors Targeting Diabetes

Poster Discount \$50 off

CD PURCHASING INFORMATION: All Discovery on Target conferences included.

I cannot attend but would like to purchase the conference CD for \$750 (plus shipping). Massachusetts deliveries will include 5% sales tax.
 Please send information on exhibiting and opportunities to present workshops.

PAYMENT INFORMATION

Enclosed is a check or money order payable to Cambridge Healthtech Institute, drawn on a U.S. bank, in U.S. currency.

Invoice me, but reserve my space with credit card information listed below.

Invoices unpaid two weeks prior to conference will be billed to credit card at full registration rate. Invoices must be paid in full and checks received by the deadline date to retain registration discount. If you plan to register on site, please check with CHI beforehand for space availability.

Please charge: AMEX (15 digits) Visa (13-16 digits) MasterCard (16 digits)

Card # _____ Exp. Date _____

Cardholder _____

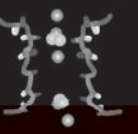
Signature _____

Cardholder's Address (if different from above) _____

City/State/Postal Code _____

Country _____

Please refer to the Registration Code below:



PRESENT A POSTER AND SAVE \$50
Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure a poster board and inclusion in the conference CD, your abstract must be submitted, accepted and registration paid in full by **September 22, 2008**. Register online to use the Poster Abstract Submission form or, if you register by phone, fax, or mail, you will receive Poster Abstract Submission guidelines via email. I am interested in presenting a poster at:

Discovery on Target and will submit a completed one-page abstract by **September 22, 2008** (Please Note: Registration must be paid in full to present poster.)

Title _____



Yes! I would like to receive a **FREE** eNewsletter subscription to:

- Weekly Update**
The latest industry news, commentary and highlights from Bio-IT World
- eCliniqua**
Innovative management in clinical trials
- Systems Biology**
Tools, strategies and companies driving integrative biology

Please send information about related conferences and reports:

- Drug Discovery Chemistry (DCH)
- Beyond Genome (BYG)
- World Pharmaceutical Congress (WPC)

CHI INSIGHT PHARMA REPORTS

A series of reports that evaluate the salient trends in pharmaceutical technology, business, and therapy markets. Keep abreast of the latest advances in pharmaceutical R&D, their potential applications and business impacts, and their current and future position in the marketplace. For a list of reports, visit Insightpharma.com, or contact Rose LaRaia, rlaraia@healthtech.com, 781-972-5444

ADDITIONAL REGISTRATION DETAILS

Each registration includes all conference sessions, posters and exhibits, food functions, and a copy of the conference CD.

GROUP DISCOUNTS

Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 781-972-5472 to discuss your options and take advantage of the savings.



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.

SUBSTITUTION/CANCELLATION POLICY

- In the event that you need to cancel a registration, you may:
- Transfer your registration to a colleague within your organization
 - Credit your registration to another Cambridge Healthtech Institute program
 - Request a refund minus a \$100 processing fee per conference
 - Request a refund minus the cost (\$750) of ordering a copy of the CD

NOTE: Cancellations will only be accepted up to two weeks prior to the conference.

Program and speakers are subject to change.

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

FAX or MAIL your registration to:

Cambridge Healthtech Institute
250 First Avenue, Suite 300, Needham, Massachusetts 02494
T: 781-972-5400 or
Toll-free in the U.S. 888-999-6288
F: 781-972-5425 • www.healthtech.com