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Healthtech.com/Structure-Based-Drug-Design

Register by February 28
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What's New This Year:

- Coverage of novel targets and compounds including macrocycles, epigenetic targets, and BACE inhibitors
- Case studies and experimental follow-up - see how Constellation, Heptares, AstraZeneca, and others are leading the SBDD charge
- Expanded sessions on GPCR design and drug discovery
- Showcase of different approaches for working with the similar targets

Hear up-to-the-minute case studies from:

- Arena Pharmaceuticals
- Astex
- AstraZeneca
- Bristol-Myers Squibb
- Carmolex
- Carmot Therapeutics
- Constellation Pharmaceuticals
- Genentech
- Heptares Therapeutics UK
- Merck
- Novartis
- Structural Genomics Consortium
- Takeda
- Vernalis, Ltd.

Keynote Speaker

Chas Bountra, Ph.D.
Professor, Translational Medicine, Department of Clinical Medicine; Associate Head, Medical Sciences; Chief Scientist, Structural Genomics Consortium, University of Oxford

Fourteenth Annual

May 21 - 22, 2014 | Westin Boston Waterfront | Boston, MA

Structure-Based Drug Design

Using Structure and Rational Design to Accelerate Discovery

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About the Conference

Experimental methods such as X-ray crystallography, NMR, and computational chemistry techniques have led to a better understanding and larger knowledge base of 3-dimensional structures and binding events, encouraging rapid development of structure-based drug design. Cambridge Healthtech Institute's Fourteenth Annual **Structure-Based Drug Design** event will showcase informative, high-quality case studies, innovative techniques, and strategies to move from computation to experiment, and finally, to drug. Top scientists from pharma and biotech will address how they are hitting epigenetic targets, provide updates on the newest wave of GPCRs and other membrane proteins, and discuss the latest in fragment-based drug design. Attendees will return to their organizations with fresh perspectives and new ideas to maximize productivity and increase successes in drug discovery.

Present a Poster

- Your poster will be exposed to our international delegation
- Receive $50 off your registration
- Your poster abstract will be published in our conference materials
- Your research will be seen by leaders from top pharmaceutical, biotech, academic and government institutes

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WPC World Pharma Congress

Mastering Medicinal Chemistry

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Chemical Biology for Target Validation

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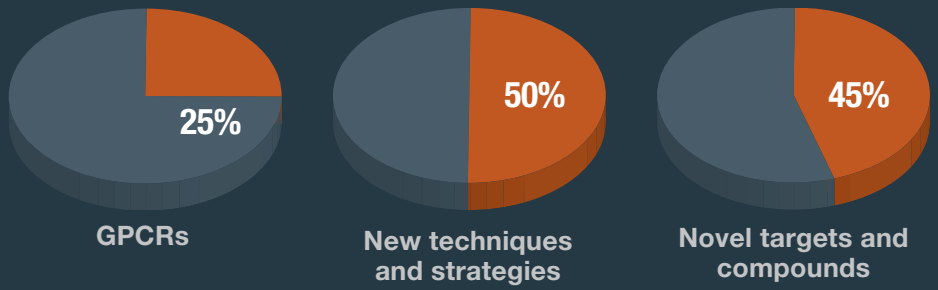
How will CHI's 14th Annual

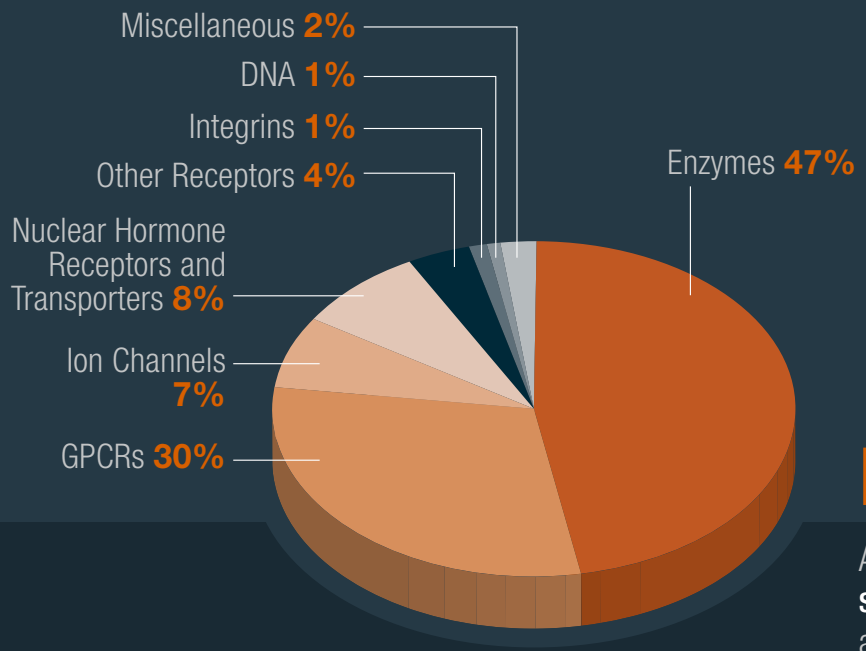
Structure-Based Drug Design

conference help to advance the drug discovery field?

By addressing topics that matter:

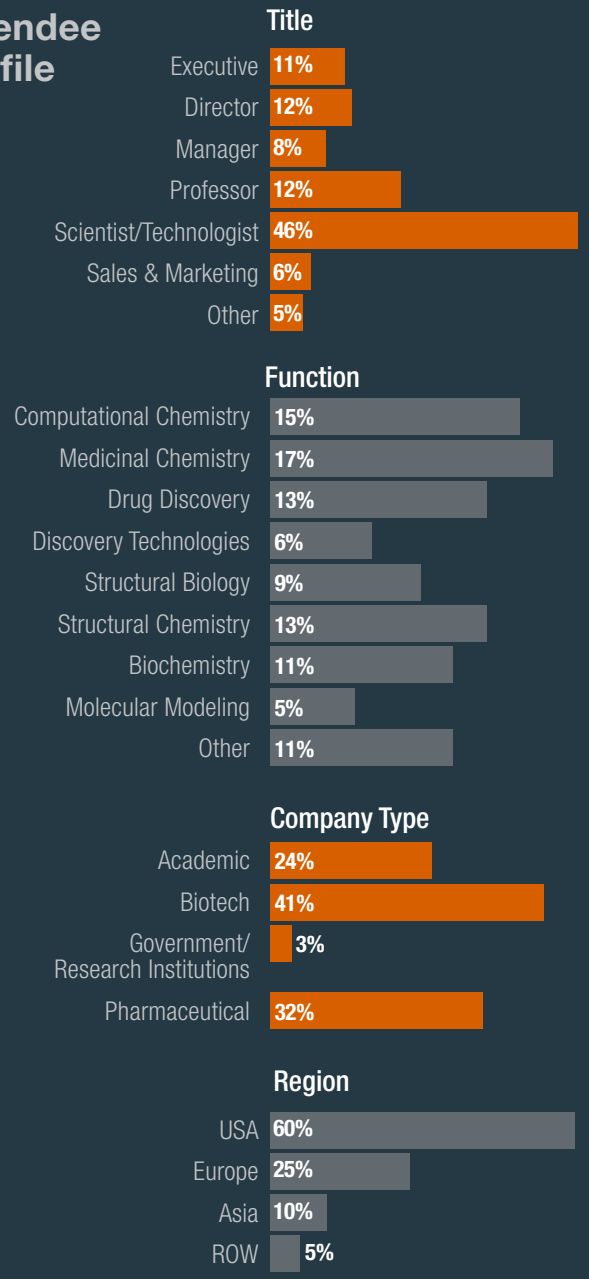


Current Drug Target Breakdown



By bringing together industry leaders:

Attendee Profile



FACT:

Among 32 pharma and biotech companies surveyed, **structure-based drug design** is the most prevalent activity with the most players emphasizing the fragment-based variation.

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Pre-Conference Dinner Short Course*

Tuesday, May 20 | 6:00-9:00 pm

**Separate Registration Required*

Structure- and Dynamics-Based Design Strategies

Steven LaPlante, Ph.D., Founder & CEO, NMX Research & Solutions; Adjunct Professor, Institut National de la Recherche Scientifique (INRS)

This course will reveal design strategies that led to drugs currently in the clinic and on the market. An emphasis will be made on the exploitation of the bioactive ligand conformations using combinations of NMR, X-ray, calculations and SAR. Rational design and the implications of other properties will be addressed which include atropisomer chirality, drug self-aggregation and ADMET.

WEDNESDAY, MAY 21

7:00 am Registration and Morning Coffee

UPDATES ON NEW COMPOUNDS AND TARGETS

8:00 Chairperson's Opening Remarks

8:05 Tackling the Conformational Sampling of Larger Flexible Compounds and Macrocycles in Pharmacology and Drug Discovery

Nicolas Foloppe, Ph.D., Principal Scientist, Chemistry, Vernalis R&D Ltd.

Computational conformational sampling underpins much of molecular design in pharmaceutical work. We have tested in detail the sampling of larger more flexible compounds including therapeutic peptides, macrocycles, and inhibitors of protein–protein interactions. The tested mainstream low-mode based sampling approaches yielded very encouraging results, showing that one can productively tackle the computational the conformational search of larger flexible compounds for drug discovery.

8:35 Peptide Recognition of Bromodomain Reader Proteins

Yong Tang, Ph.D., Scientist, Structural Biology Department, Constellation Pharmaceuticals

High-resolution crystal structures of bromodomain reader proteins in complex with modified lysine peptide substrates have been determined. These studies have been complimented by solution biophysical assays as well as mutagenesis experiments. The molecular mechanism of these recognition events will be discussed.

9:05 Structure-Based Design of BACE Inhibitors for Alzheimer's Disease

Andrew W. Stamford, Ph.D., Executive Director, Discovery Chemistry, Merck Research Laboratories

Structure-based design applied to hits derived from a BACE1 fragment screen led to the discovery of the iminoheterocycle class of BACE inhibitors, foremost of which is MK-8931 currently in Phase 3 clinical trials for the treatment of Alzheimer's disease. This presentation will discuss the key role of X-ray crystallography-guided structure-based design in the discovery and optimization of novel, brain penetrant iminoheterocyclic BACE inhibitors.

9:35 Coffee Break in the Exhibit Hall with Poster Viewing

10:20 Structurally Informed Epigenetic Chemical Probe Design

Dafydd Owen, Ph.D., Associate Research Fellow, Biotherapeutics Worldwide R&D, Pfizer Worldwide Medicinal Chemistry

Pfizer is a member of a public-private partnership led by the Structural Genomics Consortium (SGC) to help identify a suite of high-quality chemical probes for epigenetic targets. Epigenetic proteins are amenable to structure based drug design and this has been a vital platform in the discovery of first in class tool compounds for bromodomains and histone methyl transferases. Our most recent progress in chemical probe discovery will be presented.

Sponsored by

10:50 Protein Active Site Comparison with SiteHopper: Phylogeny to Polypharmacology

Gregory L Warren, Ph.D., Senior Applications Scientist, OpenEye Scientific Software, Inc

Recent attempts to use sequence alignment to predict cross-reactivity and polypharmacology have been made with varying degrees of success. We present a new method, SiteHopper, which rapidly aligns and compares three-dimensional representations of protein active or binding sites. Case studies will be presented to show that SiteHopper is able to find similarity between binding sites for targets that bind the same ligand but have very different sequences.

PROPERTIES OF FRAGMENTS

11:20 Knowledge-Based Scoring Revisited – From Voronoi Tessellation to Non-Bonded Potentials

Marcel Verdonk, Director, Computational Chemistry & Informatics, Astex

The large number of available protein-ligand X-ray structures represents a wealth of information on non-bonded interactions. However, it is far from straightforward to convert this data into a form that is useful for structure-based design purposes. Here, we revisit the use of large numbers of protein-ligand complexes to derive knowledge-based potentials that provide superior performance in virtual screening, when compared to empirical scoring functions and force field based methods.

11:50 Inhibiting Protein-Protein Interactions Using Fragments and Structure-Based Drug Design

Steve Swann, Ph.D., Senior Scientist, Fragment Based Drug Discovery, Takeda

My talk will focus on several narratives describing the use of biophysical techniques to identify low molecular weight, yet efficient chemical starting points that bind at a protein-protein interface. Each of these fragment starting points, were optimized using structure-based drug design to yield potent inhibitors which ultimately modulated cell signalling and apoptosis.

"All relevant topics on structure-based drug design with excellent speakers and a well run conference."

- Associate Professor, Physics, University of North Carolina, Charlotte

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12:20 pm Fishing for Fragments to Complement Known Binders
Daniel A. Erlanson, Ph.D., President, Carmot Therapeutics, Inc.
Finding fragments is now routine, but advancing them to leads can be difficult. Linking two fragments is complicated by getting the linker just right. In contrast, using a known binder as an anchor from which to "fish" for fragments identifies only those connected by suitable linkers. Chemotype Evolution applies this strategy to provide a general solution to the problem of how to turn promising fragments into promising leads.

12:50 Luncheon Presentations *(Sponsorship Opportunity Available)* **or Lunch on Your Own**

GPCRS AND OTHER MEMBRANE PROTEINS

2:00 Chairperson's Remarks

2:05 High End GPCR Design: Crafted Ligand Design and Druggability Analysis Using Protein Structure, Lipophilic Hotspots and Explicit Water Networks
Jonathan S. Mason, Ph.D., FRSC, Senior Research Fellow, Heptares Therapeutics UK
Full SBDD for GPCRs is now possible using a combination of advanced experimental and computational data: Conformational thermostabilisation of StaR® proteins enable biophysical screening and crystal structures with both potent and weak ligands. Explicit water networks are a critical 'third dimension' for SBDD, key for understanding ligand binding energies and kinetics. Binding site energetic surveys using GRID for lipophilic hotspots are found to be key drivers for binding.

2:35 Low-End GPCR Design: Ligand Steered Homology Models as Tools for Virtual Screening
Kerim Babaoglu, Ph.D., Associate Principal Scientist, Computational Chemistry, Merck
Multiple GPCR models can be built using different templates in various states. However, one still needs some way to discern which model is the most "correct" or which is the most useful. One strategy is the use of molecular docking along with available ligand binding data to gauge the validity of the models created. This methodology was applied in an attempt to reproduce a model of the recently solved CCR5 Receptor. The resulting model serves as viable template for virtual screening and recapitulates the binding mode of Maraviroc. This methodology has also been applied prospectively against an in-house target and the metrics of that virtual screen will be discussed.

3:05 Challenges in GPCR Drug Discovery: Ligands, Orphans and Homology Modeling
Carleton Sage, Ph.D., Fellow, Computational Systems, Arena Pharmaceuticals
As the number of crystal structures for GPCRs increases rapidly, the promise of applying homology modeling to GPCR drug discovery with high fidelity becomes a reality. However, the number of orphan receptors still remains significant and ligand-based approaches reign supreme. This talk will present the use and limitations of ligand and homology based approaches in GPCR ligand discovery.

3:35 GPCR Mutagenesis: Leveraging Data to Aid in Drug Discovery
Karen A. Rossi, MS, Senior Research Investigator, Computer-Assisted Drug Design, Bristol-Myers Squibb Company
The recent emergence of several pharmaceutically relevant GPCR crystal structures has led to a heightened interest in GPCR homology modeling and mutagenesis. We have developed a system for capturing, analyzing and mapping mutagenesis data onto 3D structures. This has improved the translation of the experimental data into structural insights, such as binding pocket identification and homology model refinement. In this presentation, we will describe this system and its application to drug discovery.

4:05 Refreshment Break in the Exhibit Hall with Poster Viewing

WATER IN DRUG DESIGN

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5:00 A Robust Solution for Accurate Binding Energy Predictions Using Free Energy Perturbation
Woody Sherman, Ph.D., Vice President, Applications Science, Schrödinger, Inc.

5:30 Water Modeling: A Safe-Conduct to Understand Protein-Ligand Interactions
Jose Duca, Ph.D., Head, Computer-Aided Drug Discovery, Novartis
For many years it has been well appreciated that water plays a key role in governing protein structure and function. However, a true grasp of the full extent and nature of water's role is only now beginning to emerge. This talk will overview a new paradigm that attributes protein structure and function largely to the structure-free energy relationships of solvating water, including a description of the theory and its reduction to practice in drug design settings.

6:00 Welcome Reception in the Exhibit Hall with Poster Viewing

THURSDAY, MAY 22

8:00 am Morning Coffee

INNOVATIVE APPROACHES TO ENABLE DISCOVERY

8:40 Chairperson's Remarks

8:45 Google™-Like Technologies as Alternative to Fragment-Based Drug Discovery
Carlos J. Camacho, Ph.D., Associate Professor, Computational Biology, University of Pittsburgh; Co-Founder & Co-Chairman, Scientific Advisory Board, Carmolex
We present a novel pharmacophore-based interactive screening technology that builds on the role anchor residues, or deeply buried hot spots, have in PPIs, to increase hit rates by redesigning these entry points with anchor-biased virtual multicomponent reactions (MCR). This chemistry delivers hundreds of millions of readily synthesizable novel compounds especially suitable to disrupt PPIs, which typically are not amenable to traditional small molecule intervention.

"Good quality, up-to-date presentations made this a stimulating and informative conference."
- Chief Scientific Officer, *De Novo* Pharmaceuticals Ltd.

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9:15 Identification of Novel Weak Agonists for PPARg through Virtual Screening

Anders Hogner, Ph.D., Associate Director, Computational Chemistry, CVMD Innovative Medicines, AstraZeneca

This presentation will give an overview of the hit identification process targeting PPARg at AstraZeneca using various virtual screening approaches. Crystal structures of the hits in complex with PPARg demonstrates (as predicted) that the compound utilizes a binding mode distinct from other classical PPARg ligands, presumably explaining the compound's weak agonistic effect as well as the efficacy in inhibiting phosphorylation.

9:45 Sponsored Presentations *(Opportunities Available)*

10:15 Coffee Break in the Exhibit Hall with Poster Viewing

10:45 Structure-Based Design and Property Optimization of Potent and Selective Pyrazole Carboxamide Interleukin-2 Inducible T-Cell Kinase (ITK) Inhibitors for the Treatment of Inflammatory Diseases

Jason Burch, Ph.D., Scientist, Medicinal Chemistry, Genentech

X-ray crystallography and computational methods were used to evolve a double-digit nanomolar pyrazole carboxamide HTS hit into a selective sub-nanomolar ITK inhibitor (>300X potency improvement). Highlights included optimization of the pi-stacking and lipophilic interactions with the phenylalanine "sentinels" of the active site. Further evolution of this scaffold involved optimization of the pharmaceutical properties of the lead matter through the use of calculated properties (e.g. TPSA, solubility index) to guide target selection.

» 11:15 KEYNOTE PRESENTATION: Structures, Chemical Probes, New Biology, New Targets for Drug Discovery: Is This the Right Sequence?

Chas Bountra, Ph.D., Head, Structural Genomics Consortium (SGC); Professor, Translational Medicine; Associate Head, Medical Sciences, University of Oxford

In my presentation, I will discuss our partnership with nine large pharmaceutical companies to generate structure enabled, freely available, chemical probes; our collaborations with a network of academic labs to use these probes to dissect biological and disease networks; our plans to further improve target validation by using patient derived primary cells, and a new initiative to advance new clinical candidates into Phase IIa studies, pre-competitively.

12:00 pm Close of Conference

"The selection of speakers and presentations strongly demonstrated the expansive breadth and impact of structure-based drug design."

- Director of Bioinformatics, ActivX Biosciences

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CHI offers comprehensive sponsorship packages which include presentation opportunities, exhibit space, branding and networking with specific prospects. Sponsorship allows you to achieve your objectives before, during, and long after the event. Any sponsorship can be customized to meet your company's needs and budget. Signing on early will allow you to maximize exposure to qualified decision-makers.

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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!

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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, helping you to make the most out of this invaluable opportunity. Evening will be customized according to sponsor's objectives i.e.:

- Purely social
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Exhibitors will enjoy facilitated networking opportunities with qualified delegates. Speak face-to-face with prospective clients and showcase your latest product, service, or solution.

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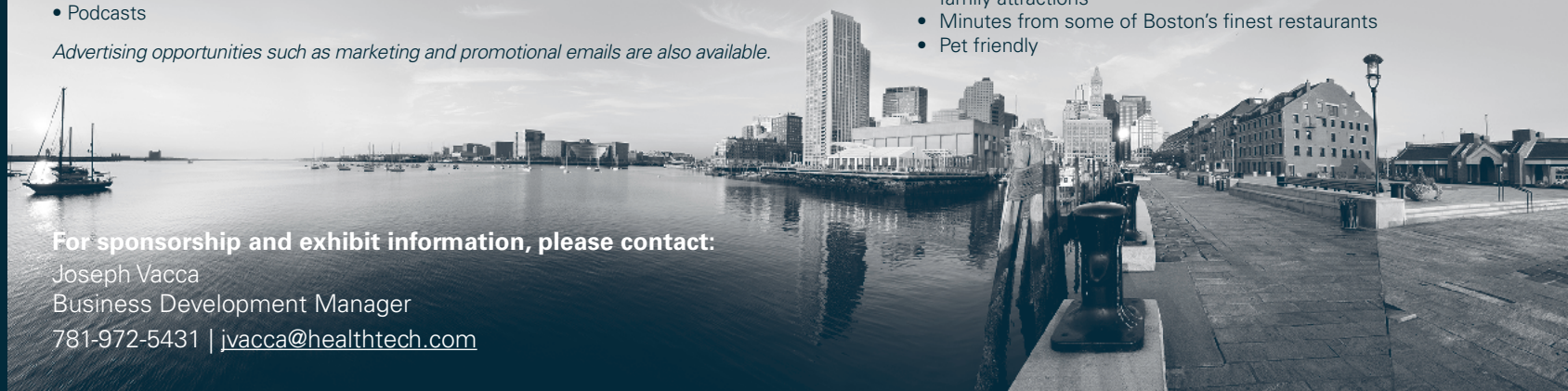

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Room Rate: $269 s/d
Reservation Cutoff: April 23, 2014

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Flight Discounts:
Special discounts have been established with American Airlines. Please use one of the following methods:

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- Go online www.aa.com/group enter Conference code 7654AA in promotion discount box
- Contact our designated travel agent Rona Meizler at 1-617-559-3735 or rona.meizler@protravelinc.com.

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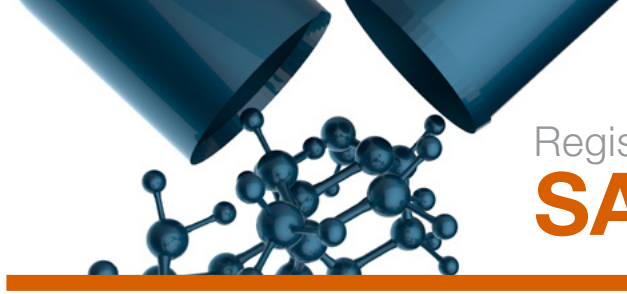

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Structure- and Dynamics-Based Strategies (May 20, 6:00-9:00 pm)	$699	$399

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Early Registration Discount until February 28, 2014	$1399	$649
Advance Registration Discount until April 18, 2014	$1599	$729
Registrations after April 18, 2014, and on-site	$1799	$799

Poster Submission - Discount ($50 Off): Poster abstracts are due by April 4, 2014. Once your registration has been fully processed, we will send an email containing a unique link allowing you to submit your poster abstract. If you do not receive your link within 5 business days, please contact jring@healthtech.com. *CHI reserves the right to publish your poster title and abstract in various marketing materials and products.

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Alumni Discount: Cambridge Healthtech Institute (CHI) appreciates your past participation at Structure-Based Drug Design. As a result of the great loyalty you have shown us, we are pleased to extend to you the exclusive opportunity to save an additional 20% off the registration rate.

Group Discounts: Discounts are available for multiple attendees from the same organization. For more information on group rates contact David Cunningham at +1-781-972-5472

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Please use keycode SBD F when registering

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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.

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