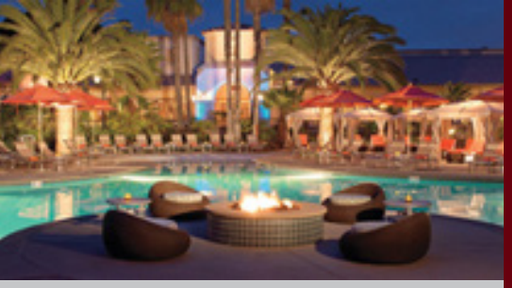

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OPTIMIZING SMALL MOLECULES FOR TOMORROW'S THERAPEUTICS

PLENARY KEYNOTE

Drug Discovery for Challenging Targets

James Wells, Ph.D., Professor, Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California San Francisco

EVENT FEATURES

- More than 100 presentations
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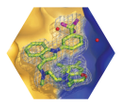
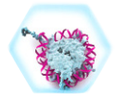


SEVENTH ANNUAL
Protein-Protein Interactions



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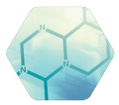
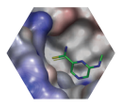
Epigenetic Inhibitor Discovery

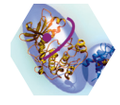
APRIL 24-25



SECOND ANNUAL
Macrocyclics and Constrained Peptides



NINTH ANNUAL
Fragment-Based Drug Discovery



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DrugDiscoveryChemistry.com

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TUESDAY, APRIL 22	SHORT COURSES*		
WEDNESDAY, APRIL 23	ANTI-INFLAMMATORIES	PROTEIN-PROTEIN INTERACTIONS	EPIGENETIC INHIBITOR DISCOVERY
	COMBINED PLENARY SESSION		
	WELCOME RECEPTION IN THE EXHIBIT HALL WITH POSTER VIEWING		
THURSDAY, APRIL 24	CONTINENTAL BREAKFAST & BREAKOUT DISCUSSIONS		
	ANTI-INFLAMMATORIES	PROTEIN-PROTEIN INTERACTIONS	EPIGENETIC INHIBITOR DISCOVERY
	MACROCYCLICS & CONSTRAINED PEPTIDES DRUG DISCOVERY	FRAGMENT-BASED DRUG DISCOVERY	KINASE INHIBITOR CHEMISTRY
	BREAKOUT DISCUSSIONS		
	DINNER SHORT COURSES*		
FRIDAY, APRIL 25	MACROCYCLICS & CONSTRAINED PEPTIDES DRUG DISCOVERY	FRAGMENT-BASED DRUG DISCOVERY	KINASE INHIBITOR CHEMISTRY
	WALK AND TALK LUNCHEON IN THE EXHIBIT HALL WITH POSTER VIEWING		

*Separate registration is required

TRACK-HOPPING

Attendees at **Drug Discovery Chemistry** are encouraged to "track-hop" between concurrent conference tracks. Register for one conference and gain access to three concurrent conference tracks, or for the best value, register for two conferences and gain access to all six conference tracks

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cbenton@healthtech.com

PLENARY KEYNOTE

Drug Discovery for Challenging Targets

James Wells, Ph.D., Professor, Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California San Francisco

James A. Wells and his research group focus on identifying or engineering proteins and small molecules that can facilitate drug discovery against challenging targets such as those involving allosteric regulation or protein-protein interactions. Such targets are often pursued for combating inflammation and cancer. The Wells lab has also recently focused on caspases which are proteases responsible for cell fate decisions in important biological processes such as apoptosis and innate inflammation. Caspases provide leads for developing new cancer therapeutics and biomarkers for cancer treatment.

Wells joined UCSF in 2005 where he directs and founded the Small Molecule Discovery Center (SMDC). Before UCSF, Wells co-founded Sunesis Pharmaceuticals and was a founding scientist in Genentech's Protein Engineering Department. Wells was elected to the National Academy of Sciences in 1999 and is the recipient of numerous other awards such as the Pfizer and Smissman Awards from the American Chemical Society, an award given by the American Peptide Society and the Merck Award from the ASBMB. Wells completed postdoctoral work in the laboratory of George Stark in 1982 at Stanford University School of Medicine and earned his Ph.D. in biochemistry from Washington State University.

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WELCOME TO **DRUG DISCOVERY CHEMISTRY**

Cambridge Healthtech Institute's **Drug Discovery Chemistry,** now in its ninth year, is a dynamic conference for medicinal chemists working in pharma and biotech. This three-day event focuses on discovery and optimization challenges of small molecule drug candidates, and offers many exciting opportunities for scientists to move between concurrent conference tracks to create a unique program according to personal interests.

New this year is **Epigenetic Inhibitor Discovery** which represents an area of biology where chemical tools are enabling progress against target types that offer new therapeutic intervention strategies. This topic nicely complements the most popular conference tracks from previous years: **Anti-Inflammatories, Protein-Protein Interactions, Macrocyclics and Constrained Peptides, Fragment-Based Drug Discovery**, and **Kinase Inhibitor Chemistry.**

We also offer a comprehensive selection of pre-conference and dinner short courses. Designed to be instructional and interactive, they are a great introduction for those new to a particular discipline or as a refresher for those who want to brush up on their knowledge. Maximize your time on site by adding one or more short courses that complement your conference track selections.

Learning opportunities are not limited to podium presentations, as delegates participate in informal roundtable breakout sessions and expert panel discussions. In addition, we have dedicated and robust poster sessions in the exhibit hall.

We invite you to review this brochure to see how this great lineup of speakers and synergistic topics come together to create the leading drug discovery chemistry event. In addition to staying abreast of the latest drug discovery advances, scientists from all levels and settings can network and enjoy spontaneous face-to-face interactions with one another.

We look forward to meeting you in San Diego!

Anjani Shah, Ph.D.
Conference Director
ashah@healthtech.com

Kip Harry
Conference Director
kharry@healthtech.com

Carolyn Benton
Business Development Manager
cbenton@healthtech.com

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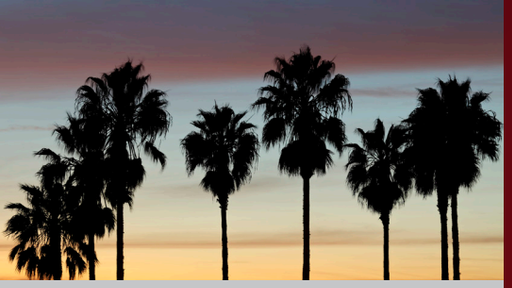

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Short Courses*

**Separate registration is required*

PRE-CONFERENCE
SHORT COURSES — TUESDAY, APRIL 22

Morning Course | 8:00 – 11:00 AM

Trends in Physical Properties of Drugs

Instructors: Terry Stouch, Ph.D., President, R&D, Science for Solutions, LLC

Additional Instructor(s) to be Announced

- Properties important for enhanced efficacy, delivery, and formulation
- pKa, tautomerism, crystallization, others
- Computational prediction: What works - what doesn't
- Experimental best practices

Noon Courses | 12:00 – 3:00 PM

GPCR Structure-Based Drug Discovery

Instructors: Arun Shukla, Ph.D., Assistant Professor, Medicine, Duke University Medical Center

Vsevolod (Seva) Katritch, Ph.D., Assistant Professor, Integrative Structural and Computational Biology, The Scripps Research Institute

Jan Steyaert, Ph.D., Director, Structural Biology Brussels Research Center, Vrije University Brussels

- Review of recent structures and their lessons
- Working with fragments
- Dealing with conformational states
- Antibodies as probes for structure

Epigenetic Assays and High-Throughput Screening

Instructors: Abdellah Allali-Hassani, Ph.D., Team Leader, Enzymatic Assays, Structural Genomics Consortium, University of Toronto

Karen Maegley, Ph.D., Associate Research Fellow, Integrative Biology and Biochemistry, Oncology, Pfizer, Inc.

Additional Instructor(s) to be Announced

- Overview of current screening strategies for hits
- Development of biochemical/biophysical assays
- Development of phenotypic/cell-based assays
- Application to Histone Methyltransferases, Demethylases & BET bromodomain

Predicting Sites of Protein-Protein Interactions: *In silico* Workshop

Instructor: Vinod Kurella, Ph.D., Visiting Research Fellow, BioInformatics, Harvard Medical School

- Bring your own laptop for a hands-on training session
- Learn capabilities and limitations of open-source software for protein-ligand docking prediction
- Applications to optimization of drug candidates (for the chemist) or target validation (for the biologist)
- Explorations/tutorials on: Rosetta, ClusPro, Zdock and others

Afternoon Courses | 3:30 – 6:30 PM

Immunology Basics for Chemists

Seng-Lai "Thomas" Tan, Ph.D., Head, Cellular and Translational Immunology, EMD Serono Research and Development Institute, Inc.

Additional Instructor(s) to be Announced

- Review of immune system's cellular players
- Review of inflammatory process
- Autoimmune & inflammation-related diseases
- Current treatment landscape and promising drug targets

Molecular Interactions and Drug Design

Instructor: Maricel Torrent, Ph.D., Senior Scientist, AbbVie

- Drug design principles generally applicable to all medicinal chemistry programs
- Interpretation of atomic-level protein X-ray and modeled structures of binding modes
- Understanding the relative amounts of potency gain from different interactions
- Case studies illustrate all of the design strategies

Dinner Course | 6:30 – 8:30 PM

Pharmacophore Discovery and Modeling Using Extended Hückel Theory

Sponsored by CHEMICAL COMPUTING GROUP

Instructor: Chris Williams, Ph.D., Principal Scientist, Chemical Computing Group

- Building pharmacophore models/queries
- Generating and using 3D information to search for novel active compounds
- Advantages of using Extended Hückel Theory (EHT), a semi-empirical method that takes into account electron donating and withdrawing effects for a given chemical structure
- Kinase-based case studies

DINNER
SHORT COURSES — THURSDAY, APRIL 24

Dinner Courses | 6:30 – 9:00 PM

Enabling Macrocyclic Compounds for Drug Discovery: Opportunities, Challenges and Strategies

Instructors: Mark L. Peterson, Ph.D., Vice President, Operations, Tranzyme Pharma

Eric Marsault, Ph.D., Professor, Pharmacology, University of Sherbrooke

- Unique characteristics of macrocycles
- Synthesizing and screening macrocyclic compound libraries
- Pros and cons of each methodology
- Drug discovery and development examples and challenges for macrocyclic molecules

Advancing Tools and Technologies for Fragment-Based Design

Instructors: Daniel A. Erlanson, Ph.D., Co-Founder, Carmot Therapeutics, Inc.

Edward R. Zartler, Ph.D., President & CSO, Quantum Tessera Consulting

- Why fragments – pros and cons?
- What makes a good fragment?
- What to do with a fragment – growing, linking, and more
- Design of fragment libraries
- Importance of using orthogonal/multiple screening methods

Introduction to Targeted Covalent Inhibitors

Instructor: Christoph Zapf, Ph.D., Principal Scientist, Worldwide Medicinal Chemistry, Pfizer Research Labs

- Overview of covalent drugs, irreversible and reversible inhibitors
- Recent clinical developments and trial results
- Warhead considerations – reactivity, specificity
- Design considerations for targeted covalent inhibitors
- De-risking covalent inhibitors

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Brian Albrecht, Ph.D., Constellation Pharmaceuticals
Abdellah Allali-Hassani, Ph.D., University of Toronto
Dean Richard Artis, Ph.D., Elan
Prabhat Arya, Ph.D., DRILS University of Hyderabad Campus
Kate Ashton, Ph.D., Amgen, Inc.
Valerio Berdini, Ph.D., Astex Pharmaceutical
Paul Bonin, Pfizer, Inc.
Rogier C. Buijsman, Ph.D., Netherlands Translational Research Center B.V.
Lars Burgdorf, Ph.D., Merck KGaA
Julio Camarero, Ph.D., University of Southern California
Robert Carlson, Ph.D., Karyopharm Therapeutics
Zaneta Nikolovska-Coleska, Ph.D., University of Michigan
Stuart Conway, Ph.D., University of Oxford
Adrian Culf, Ph.D., Atlantic Cancer Research Institute
Max Cummings, Ph.D., Janssen
Dan Dairaghi, Ph.D., ChemoCentyrx
Helena Danielson, Ph.D., Uppsala University and Beactica
Ben Davis, Ph.D., Vernalis Ltd.
Gerald Denis, Ph.D., Boston University School of Medicine
Kurt Deshayes, Ph.D., Genentech, Inc.
Bruce Dorsey, Ph.D., Teva Pharmaceuticals
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Francisco X. Talamas, Ph.D., formerly Hoffmann-La Roche Inc.
Seng-Lai "Thomas" Tan, Ph.D., EMD Serono Research and Development Institute, Inc.
Steven J. Taylor, Ph.D., Boehringer Ingelheim Pharmaceuticals, Inc.
Nicholas Terrett, Ph.D., Ensemble Therapeutics Corp.
Marc Thommen, Ph.D., Polyphor
Paul R. Thompson, Ph.D., Scripps Florida
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Jennifer Venable, Ph.D., Johnson & Johnson Pharmaceutical R&D
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Chris Williams, Ph.D., Chemical Computing Group
Dietmar Wolf, Ph.D., AnalytiCon Discovery, LLC
Damian W. Young, Ph.D., Baylor College of Medicine
Wendy Young, Ph.D., Genentech, Inc.
Edward R. Zartler, Ph.D., Quantum Tessera Consulting
Christoph Zapf, Ph.D., Pfizer Research Labs
Qinghai Zhang, Ph.D., The Scripps Research Institute

"This meeting was an eye-opener for me to see how collectively drug delivery scientists can work with medicinal chemists to bring new pharmaceutical products more effectively to the market."
Hayat O., Professor, University of Illinois at Chicago

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Anti-Inflammatories: Small Molecule Approaches

Focusing on Medicinal Chemistry Optimizations

WEDNESDAY, APRIL 23

7:00 am Registration and Morning Coffee

KINASE INHIBITORS FOR INFLAMMATION

8:00 Chairperson's Opening Remarks

Seng-Lai "Thomas" Tan, Ph.D., Head, Cellular and Translational Immunology, EMD Serono Research and Development Institute, Inc.

» 8:10 FEATURED PRESENTATION: B Cell Receptor Signaling Inhibitors for Treatment of Inflammatory Diseases

Kamal Puri, Ph.D., Associate Director, Research, Gilead Sciences, Inc.

B-cell receptor (BCR) signaling plays a critical role in activation and function of self-reactive B cells that contribute to autoimmune diseases. Recent data have established an important role for PI3Kdelta in coupling BCR to B-cell activation and inhibition of this pathway may represent a promising new strategy. This talk will focus on recent achievements in the mechanism of action, pharmacological properties, and preclinical activity of PI3Kdelta inhibitors, with a focus on their emerging role in treating autoimmune disorders.

8:40 Discovery of BTK Inhibitors

Wendy Young, Ph.D., Director, Discovery Chemistry, Genentech

9:10 A Novel Class of Selective SYK Inhibitors for Inflammation

Lars Burgdorf, Ph.D., Principal Scientist, Medicinal Chemistry, Merck KGaA, Germany

Spleen Tyrosine Kinase (SYK) is a promising target for the treatment of autoantibody-mediated diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). We designed a new class of highly potent and selective SYK Inhibitors. We will present our drug discovery strategy for library design and compound optimization, including SAR, X-ray structures and selectivity profiles.

9:40 Coffee Break

10:05 Selective JAK1 Inhibition as a Therapeutic Strategy in Inflammation

Christel Menet, Ph.D., Senior Lead, Project Director, Autoimmune Disease, Galapagos

The lead compound, GLPG0634, is the first JAK1 selective compound that has demonstrated clinical efficacy and a favorable safety profile in two Phase IIA clinical studies in patients with rheumatoid arthritis. Discovery and SAR of the series will be presented.

10:35 Drug Discovery Strategy for the Identification of Potent and Selective RIP2 Kinase Inhibitors

Linda Casillas, Ph.D., Senior Scientific Investigator, Immuno-Inflammation Medicinal Chemistry, GlaxoSmithKline

11:05 Sponsored Presentation *(Opportunity Available)*

11:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:05 pm Session Break

TARGETING PROTEIN-PROTEIN INTERACTIONS FOR INFLAMMATION

1:15 Chairperson's Remarks

Wendy Young, Ph.D., Director, Discovery Chemistry, Genentech

1:20 Epigenetic BET Inhibitors and Inflammation

Gerald Denis, Ph.D., Associate Professor, Cancer Center, Boston University School of Medicine

The BET family of related proteins, comprised of BRD2, BRD3, BRD4 and BRDT, has recently been shown to co-activate NFkappaB-regulated cytokine genes, and to play opposite roles in cancer and HIV latency. Small molecule BET inhibitors ablate cytokine transcription, but are not selective for any co-expressed isoform. Lack of selectivity is a benefit in some cases and a hazard in others. Experiments to probe mechanism should now advance this field.

1:50 Targeting Areginie Deaminases (PADs) and Methyl Transferases for Inflammation

Paul R. Thompson, Ph.D., Associate Professor, Department of Chemistry, TSRI, Scripps Florida

The Protein Arginine Deiminases (PADs) are important regulators of extracellular trap formation and gene transcription, whose activity is upregulated in multiple inflammatory diseases, including rheumatoid arthritis, lupus, and cancer. Herein, I discuss PAD inhibitor development and our success in validating the PADs as therapeutic targets for multiple inflammatory diseases. Additionally, I describe our efforts to develop citrulline-specific probes that are used to visualize and isolate citrullinated biomarkers of disease.

2:20 Sponsored Presentation *(Opportunity Available)*

2:35 Refreshment Break in the Exhibit Hall with Poster Viewing

TARGETING PPIS FOR INFLAMMATION

(shared session with Protein-Protein Interactions)

3:20 Novel Small Molecular Ligands of KEAP1 Induce Protective NRF2-Dependent Anti-Inflammatory Responses in Neurodegenerative Models

Aleksey Kazantsev, Ph.D., Associate Professor, Neurology, Harvard Medical School and Massachusetts General Hospital

The study identified novel compounds, which induce canonical NRF2-dependent responses and are protective in Parkinson's and Huntington's disease models. In accord with the known anti-inflammatory effects of NRF2 activation, compounds potently repress an expression of inflammatory markers in activated microglial cells, macrocytes and in mouse brain. Reversible compound binding to the NRF2 inhibitor, KEAP1, was identified by a docking model and binding confirmed by mechanistic studies, suggesting a novel approach to activating the NRF2 pathway.

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3:50 Disrupting NRF2 and Keap1 Protein Interaction with Non-Covalent Inhibitors

Laura Silvian, Ph.D., Principal Scientist, Physical Biochemistry, Biogen Idec

Keap1 binds to the Nrf2 transcription factor to enable its ubiquitination; blocking this interaction would upregulate genes that protect against oxidative stress. Cell-active compounds that modify cysteines in Keap1 effect the Nrf2-dependent pathway. We have identified and characterized non-covalent compounds that bind to the Keap1 Kelch-DC domain and block Nrf2 binding. The non-covalent inhibition strategy presents a reasonable course of action to avoid toxic side effects due to non-specific cysteine modification.

4:20 Session Break

» 4:30 PLENARY KEYNOTE PRESENTATION

Drug Discovery for Challenging Targets

James Wells, Ph.D., Professor, Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California San Francisco

I will present work from our lab for two classes of challenging targets: protein-protein interfaces and novel allosteric sites, both to activate and inhibit protein function. We use a site-directed fragment-based discovery method, called Tethering, coupled to HTS approaches that are well-suited to probing these challenging surfaces. These approaches have led to the discovery of potent and selective compounds and some with surprising properties that will be discussed.

5:30 Welcome Reception in the Exhibit Hall with Poster Viewing

6:30 Close of Day

THURSDAY, APRIL 24

7:30 am Continental Breakfast and Breakout Discussions

In this session, attendees choose a specific roundtable discussion to join. Each group has a moderator to ensure focused conversations around key issues within the topic. The small group format allows participants to informally meet potential collaborators, share examples from their work and discuss ideas with peers. Check our website in February to see the full listing of breakout topics and moderators.

NEW APPROACHES FOR INFLAMMATION

8:40 Chairperson's Remarks *(Sponsorship Opportunity Available)*

8:45 Chemokine Receptors and Inflammation

Dan Dairaghi, Ph.D., Senior Director, Molecular Pharmacology and Biomarkers, ChemoCentyrx

The chemokine system, including chemokines and chemo-attractants, directs inflammatory responses, serving to precisely coordinate immune system cell movement. As drivers of the inflammatory response, chemokines and their receptors present opportunities for the development of new therapies. Each of ChemoCentryx's novel small molecule drug candidates is designed to target a specific chemokine receptor, thereby blocking the inflammatory response driven by that particular chemokine while leaving the rest of the immune system unaffected.

9:15 Targeting the Immunoproteasome

Dustin McMinn, Ph.D., Associate Director, Medicinal Chemistry, Onyx Pharmaceuticals

Selective inhibition of the immunoproteasome (iP) inhibits cytokine production and alters T cell plasticity yet with no effect on cell survival. ONX-0914, a selective inhibitor of the β5i subunit of iP, is efficacious in autoimmune disease models. Computational modeling reveals a related analogue, PR-924, adopts a distinct binding mode that enhances β5i selectivity. Data potentiating our design of lead structures with excellent selectivity for the immunoproteasome will be presented.

9:45 Coffee Break in the Exhibit Hall with Poster Viewing

10:30 Oral Peptide Therapies for Inflammation

David Y. Liu, Ph.D., CSO, Protagonist Therapeutics, Inc.

11:00 Discovery and Synthesis of FLAP Inhibitors for the Treatment of Inflammatory Diseases

Alec Lesback, Ph.D., Associate Scientific Director, Immunology Chemistry, Janssen Research & Development

11:30 Novel Selective Inhibitors of Nuclear Export (SINE) are Highly Effective in Models of Autoimmune Diseases

Robert Carlson, Ph.D., Vice President, Preclinical Development and Product Leadership, Karyopharm Therapeutics

Exportin 1 (XPO1) is a protein that controls nuclear export of over 200 cargo proteins. Selective Inhibitors of Nuclear Export (SINE) are XPO1 inhibitors that kill cancer cells through nuclear retention and activation of tumor suppressor proteins. SINEs also force nuclear retention of proteins that play key roles in inflammation. In this talk, the efficacy of SINEs in models for a variety of autoimmune diseases will be reviewed.

12:00 pm Close of Track

"Great opportunity to share and discuss cutting-edge approaches/aspects in drug discovery."

Fabrizio G., Principal Scientist, AstraZeneca

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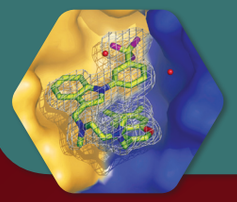

WEDNESDAY, APRIL 23

7:00 am Registration and Morning Coffee

TARGETING PPIs FOR CANCER

8:00 Chairperson's Opening Remarks

David Fry, Ph.D.,Vice President, Protein Chemistry, The Chemistry Research Solution (TCRS), LLC

» 8:10 FEATURED PRESENTATION: Treating Cancer by Disrupting Protein-Protein Interactions

Kurt Deshayes, Ph.D., Senior Scientist, Early Discovery Biochemistry, Genentech

The pro-survival IAP and BCL-2 proteins represent highly attractive PPI targets since their over-expression is associated with tumor progression and maintenance. We describe the discovery of completely novel series of small molecules that selectively target the IAP and select members of the BCL-2 proteins (BCL-2 and BCL-XL). Our work, guided by extensive structural information and supported by biochemical studies, illustrates the progression from initial lead to clinical candidate.

8:40 Discovery of Potent and Selective Piperidinone Inhibitors of the MDM2-p53 Interaction

Daqing Sun, Ph.D., Principal Scientist, Medicinal Chemistry, Amgen

This presentation will describe a successful approach for designing new scaffolds of MDM2 inhibitors based on the binding mode of known inhibitors with MDM2 protein. Through a combination of X-ray crystallography, molecular modeling, and iterative medicinal chemistry, we discovered highly potent, selective MDM2 inhibitors with excellent pharmacokinetic properties and *in vivo* anti-tumor activity in SJSA-1 osteo-sarcoma xenograft models.

9:10 The Design and Synthesis of A-Helix Mimetics as PPI Inhibitors

Sponsored by ASINEX inspired by Nature

Roman Kombarov, Ph.D., Project Manager, ASINEX

Protein-Protein interactions have great potential as therapeutic targets but are currently one of the most challenging areas in drug discovery. Through extensive research, Asinex has identified privileged structures which are effective mimics of protein secondary structural elements. In our talk, we present a chemical platform for the efficient design of novel alpha-helix mimetics as core structures decorated with poly-substituted hydrophobic substituents. These structures have the correct geometry and substitution characteristics to align the requisite functional groups in three dimensions; these structures are, in turn, are able to disrupt key elements of the PPI interface.

9:40 Coffee Break

10:05 Fragments for Tough Targets?

Roderick Hubbard, Ph.D., Senior Fellow, Research & Development, Vernalis; Professor, University of York

Fragments are an effective approach to initiate structure-based drug discovery for conventional targets such as kinases and other enzymes. In principle, the methods should also provide an important opportunity for targeting more challenging targets, such as protein-protein interactions. I will review progress in this area. As well as summarizing recent successes for targets such as Bcl-2 and Pin1, I will highlight the technical and conceptual challenges that remain.

10:35 Allosteric Regulators Targeting Higher-Order Proteasome Assemblies in the Treatment of Cancer

Maria Gaczynska, Ph.D., Associate Professor, Molecular Medicine, University of Texas Health Science Center at San Antonio

The proteasome is an essential human protease. Competitive inhibitors targeting proteasome's active sites are used to treat blood cancers, however they do not perform well with other cancers. Our novel small-molecule compounds binding to allosteric sites disrupt functional integrity of the catalytic core proteasome and its interactions with protein regulatory modules. The compounds work alone or in synergy with established competitive drugs and promise to provide access to treatment of solid cancers.

11:05 Direct Inhibition of β-Catenin with Small Molecules

Elmar Nurmemmedov, Ph.D., Scientist, Molecular Experimental Medicine, The Scripps Research Institute

β-catenin is an attractive therapeutic drug target for combating various cancers. We have employed a robust screening method against four allosteric sites (TCF4-, BCL9-binding sites, and two novel sites) on β-catenin. I will present significant findings of our drug development efforts, with potential therapeutic applications for treatment of various cancers.

11:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:05 pm Session Break

ALLOSTERIC INTERACTIONS

1:15 Chairperson's Remarks *(Sponsorship Opportunity Available)*

1:20 Allosteric Inhibitors of the Heat Shock Protein 70 (Hsp70) Complex

Jason E. Gestwicki, Ph.D., Associate Professor, Department of Pharmaceutical Chemistry, University of California, San Francisco

Heat shock protein 70 (Hsp70) is a molecular chaperone that plays critical roles in protein homeostasis. Hsp70 is assisted by co-chaperones, which bind Hsp70 and shape its activities. Our strategy is to screen for molecules that control the protein-protein interactions (PPIs) between Hsp70 and its critical co-chaperones. Using reconstituted multi-protein complexes, we have identified compounds that target PPIs in this system.

1:50 Talk Title to be Announced

Lee D. Fader, Ph.D., Principal Scientist, Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Inc.

2:20 Sponsored Presentation *(Opportunity Available)*

2:35 Refreshment Break in the Exhibit Hall with Poster Viewing

TARGETING PPIS FOR INFLAMMATION

(shared session with Anti-Inflammatories)

3:20 Novel Small Molecular Ligands of KEAP1 Induce

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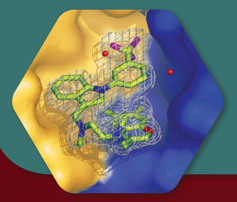

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NEW APPROACHES FOR DISRUPTING PPIs

8:40 Chairperson's Remarks

Edward R. Zartler, Ph.D., President & CSO, Quantum Tessera Consulting

8:45 Small Molecule Disruptors of the GK-GKRP Interaction

Kate Ashton, Ph.D., Senior Scientist, Medicinal Chemistry, Amgen, Inc.

Targeting the GK-GKRP pathway represents a novel approach to GK-mediated glucose metabolism. Since the kinetic parameters of the GK enzyme remain unchanged, the hypoglycemic risk is greatly reduced. We observed robust glucose lowering in animal models of diabetes, with no incidence of hypoglycemia. In addition, the novelty of targeting the protein-protein interaction of GK-GKRP using structure-based drug design will be of broad interest to scientists outside of the field of metabolic disorders.

9:15 Antibody-Guided Discovery of Small Molecule Protein-Protein Interaction Inhibitors

Wolfgang Fecke, Ph.D., Group Leader, Primary Pharmacology, UCB Pharma

Protein-protein interactions can be readily modulated by antibodies but remain challenging targets for small molecules. Antibodies can constrain target proteins in biologically relevant conformations which enables initial binding of low affinity small-molecule fragments. Binding of optimized hits will eventually become independent of antibody constraint. Examples of structure-constrained proteins will be used to introduce the strategy of antibody-stabilized fragment screening at UCB.

9:45 Coffee Break in the Exhibit Hall with Poster Viewing

10:30 Targeting Intracellular Protein-Protein Interactions with Engineered Cyclotides

Julio Camarero, Ph.D., Associate Professor, Pharmacology and Pharmaceutical Sciences & Chemistry, University of Southern California

Cyclotides are emerging as frameworks for design of peptide-based diagnostic and therapeutic compounds. They are large plant-derived backbone-cyclized polypeptides, 28-37 amino acids long. They share a disulfide-stabilized core characterized by an unusual knot. Cyclotides, in contrast to other circular poylpeptides, have a well-defined three-dimensional structure. The main features of cyclotides are a remarkable stability due to the cystine knot, a small size making them readily accessible to chemical synthesis, and an excellent tolerance to sequence variations.

11:00 How to Discover New Chemical Matter for PPIs: A New Approach to Protein-Ligand Binding From the Perspective of Water

José Duca, Ph.D., Head, CADD Cambridge, Novartis Institutes for BioMedical Research, Inc.

This presentation will cover prospective and retrospective examples on drug design efforts applied to PPIs and other relevant protein-ligand systems. We have applied our new ligand-binding concepts to all aspects of drug discovery, including hit finding, *de novo* design and lead optimization. Our model takes into account the intra- and inter-solute interactions that occur indirectly via perturbation of the aqueous medium. Our new binding ideas have immediate implications for drug discovery, as the solvation structure can be "reverse engineered" into ligand designs and ligand efficiency can redefined by the number/quality of H-bonds gained per ligand atom when water is transferred in or out of binding sites.

11:30 Fragment-Based Approach towards Inhibitors of the TPX2 - Importin-α Protein-Protein Interaction

Rhian Holvey, Ph.D., Postdoc, Department of Chemistry, University of Cambridge

TPX2-importin-α represents a promising anti-mitotic oncology target for which cancer cells have an increased reliance on over normal cells. We have identified fragments that bind this interaction representing the first compounds to show specificity between the two sites of importin-α. The ongoing development of these compounds has shown new information about the target interaction and helped in the development of more potent inhibitors.

12:00 pm Close of Track

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WEDNESDAY, APRIL 23

7:00 am Registration and Morning Coffee

SELECTIVE INHIBITION OF BET BROMODOMAINS

8:00 Chairperson's Opening Remarks *(Sponsorship Opportunity Available)*

8:10 Discovery and Optimization of BET Bromodomain Inhibitors

Brian Albrecht, Ph.D., Senior Director, Medicinal Chemistry, Constellation Pharmaceuticals

The BET bromodomain class of chromatin reading domains have emerged as new and exciting epigenetic targets for the potential treatment of cancer and immunological disorders. Inhibition of these targets leads to profound effects in relevant models of disease. The discovery and optimization of potent and selective BET bromodomain inhibitors will be presented.

8:40 Targeting Epigenetic Readers for Cancer Therapy

Jun Qi, Ph.D., Senior Research Scientist, Medical Oncology, Dana-Farber Cancer Institute

We have recently developed first-in-class, drug-like inhibitors of "bromodomain and extraterminal domain" epigenetic readers (BETs) for mechanistic study and therapeutic application in cancer and other diseases. We are continuously integrating the transcriptional consequences of BETi with changes in the epigenomic landscapes of cancer cells to elucidate the mechanisms underlying response to BETi using chemical and genetic perturbations.

9:10 Cracking the Histone Code: Development of Inhibitors of the Bromodomain-Histone Interaction

Stuart Conway, Ph.D., Associate Professor, Chemistry, University of Oxford

I will describe the development of our published BET bromodomain inhibitors and our unpublished work on the development of potent CREBBP bromodomain inhibitors.

9:40 Coffee Break

TRENDS IN BROMODOMAIN INHIBITOR SCREENING

10:05 Screening for Inhibitors of Bromodomain 4 … Have We Learned Something? … You BET!

Paul Bonin, Principal Scientist, Assay Development and Pharmacology, Primary Pharmacology Group, Pfizer, Inc.

To identify inhibitors of BRD4, a fluorescence polarization (FP) assay was developed that utilized a version of the novel BET family chemical probe PFI-1 labeled with a Cy5 dye. Binding of this probe to BRD4 as well as other BET family members (BRD2, BRD3, BRDT) was characterized. In addition, the ability of the BRD4 FP assay to identify legitimate fragment library hits will be compared to the ability of other assay technologies including surface plasmon resonance (SPR), time resolved fluorescence resonance energy transfer (TR FRET) and AlphaScreenTM.

10:35 Targeting Bromodomains - The Validity of High-Throughput Virtual Screening in Epigenetic Drug Discovery

Stefan Günther, Ph.D., Professor, Institute of Pharmaceutical Sciences, Pharmaceutical Bioinformatics, University of Freiburg

Bromodomains are acetyl-lysine epigenetic mark reader proteins. Small molecules inhibiting them have potential as anti-inflammatory, antiviral, and anticancer agents. We report the identification of novel scaffolds which potently inhibit specific bromodomains and exhibit antiproliferative activity against leukemia cell lines.

11:05 Sponsored Presentation *(Opportunity Available)*

11:35 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:05 pm Session Break

TARGETING HISTONE METHYLTRANSFERASES AND DEMETHYLASES

1:15 Chairperson's Remarks

Elisabeth Martinez, Ph.D., Assistant Professor, Pharmacology, University of Texas Southwestern Medical Center

1:20 Histone Methyltransferase Inhibitors: Fast-Acting Molecules against Blood and Liver Stage Malaria Parasites

Matthew Fuchter, Ph.D., Senior Lecturer, Synthetic and Medicinal Chemistry, Department of Chemistry, Imperial College London

We have pursued natural product and synthetic histone lysine methyltransferase (HKMT) inhibitors as novel therapeutics for malaria. We have identified highly active compounds that produce: rapid, stage- unspecific and irreversible killing of blood stage *P. falciparum* parasites with comparable potency against resistant strains; rapid activity *in vivo*; and unprecedented activating activity toward liver stage hypnozoites of P. cynomolgi parasites. Taken together this positions the HKMTs as a highly exciting new target class for the development of novel anti-malarials.

1:50 Discovery and Characterization of a Jumonji Histone Demethylase Inhibitor with *in vivo* Activity

Elisabeth Martinez, Ph.D., Assistant Professor, Pharmacology, University of Texas Southwestern Medical Center

I will discuss the development of a cell-based assay used in HTS to identify epigenetic modulators of gene expression. Using the small molecule JIB-04 as an example, I will describe the characterization of the mechanism of action of active compounds and their activity in cells and in animal models of disease, particularly in cancer.

2:20 Sponsored Presentation *(Opportunity Available)*

2:35 Refreshment Break in the Exhibit Hall with Poster Viewing

3:20 Chemical Probes for Histone Demethylases

Xiang Wang, Ph.D., Assistant Professor, Chemistry and Biochemistry, University of Colorado at Boulder

Histone demethylases are the latest class of histone modifying enzymes that have profound impacts on a variety of cellular processes and disease processes. Specific chemical probes are not only important to assist the elucidation of their cellular functions, but also critical to evaluate them as "druggable" targets to treat diseases. We have made and will continue to make significant progress in developing novel probes for both applications.

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3:50 Discovery of Histone Lysine Demethylase Inhibitors

Takayoshi Suzuki, Ph.D., Professor, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

As there is increasing evidence that lysine demethylases (KDMs) are associated with various disease states, they have emerged as attractive targets for the development of new therapeutic drugs. We have identified several classes of KDM inhibitors. This presentation will discuss the design, synthesis, and evaluation of our most recent KDM inhibitors and their possibility as anticancer agents will be presented.

4:20 Session Break

» 4:30 PLENARY KEYNOTE PRESENTATION

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James Wells, Ph.D., Professor, Pharmaceutical Chemistry and Cellular & Molecular Pharmacology, University of California San Francisco

I will present work from our lab for two classes of challenging targets: protein-protein interfaces and novel allosteric sites, both to activate and inhibit protein function. We use a site-directed fragment-based discovery method, called Tethering, coupled to HTS approaches that are well-suited to probing these challenging surfaces. These approaches have led to the discovery of potent and selective compounds and some with surprising properties that will be discussed.

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STRATEGIES FOR EPIGENETIC DRUG DISCOVERY

8:40 Chairperson's Remarks

Matthew Fuchter, Ph.D., Senior Lecturer, Synthetic and Medicinal Chemistry, Department of Chemistry, Imperial College London

» 8:45 FEATURED PRESENTATION: A Multifaceted Strategy for Discovering Chemical Probes of Histone Methyltransferases

Jian Jin, Ph.D., Associate Professor and Director, Medicinal Chemistry, Center for Integrative Chemical Biology and Drug Discovery, Division of Chemical Biology and Medicinal Chemistry, University of North Carolina at Chapel Hill

Histone methyltransferases (HMTs) have received great attention as a new class of potential therapeutic targets. However, very few chemical probes of HMTs have been created. To address this issue, our laboratory has pursued a multifaceted structure-based probe discovery strategy. Progress on discovering substrate-competitive probes of G9a and GLP, allosteric inhibitors of PRMT3, and cofactor-competitive probes of EZH2 and EZH1 will be presented.

9:15 Targeting the Recruitment of Histone Methyltransferase DOT1L

Zaneta Nikolovska-Coleska, Ph.D., Assistant Professor, Pathology, Medical School, University of Michigan

We have characterized the protein-protein interactions between DOT1L and MLL-fusion proteins, AF9/ENL, on a biochemical, biophysical and functional level. Our results strongly suggest that disruption of interaction between DOT1L and AF9/ENL is a promising therapeutic strategy with potentially fewer adverse effects than enzymatic inhibition of DOT1L for MLL-fusion protein-associated leukemia. Our studies for the first time have demonstrated novel approach for inhibiting the histone methyltransferase activity of DOT1L through blocking DOT1L.

9:45 Coffee Break in the Exhibit Hall with Poster Viewing

10:30 Fragment-Based Discovery of KDM Inhibitors

Helena Danielson, Ph.D., Professor, Biochemistry, Uppsala University; CSO, R&D, Beactica

This presentation will demonstrate the use of SPR biosensor analysis for fragment-based discovery of inhibitors targeting two different types of KDMs. Procedures for screening and characterisation of the hits, and their subsequent evolution into leads will be presented.

11:00 Chemical Probes to Explore Epigenetic Pathways

Susanne Muller-Knapp, Ph.D., Epigenetic Project Manager, Structural Genomics Consortium (SGC), Oxford

Recently described epigenetic probe molecules have opened new areas for targeting this new class of proteins. We have established a chemical biology platform for the development of highly specific and potent chemical tool compounds that target histone lysine demethylases and bromodomains. Recently developed probe molecules and their impact on target validation will be presented.

11:30 Defining the Functional Consequences of Isoform- Specific Inhibition of the Class I HDACs Using a Chemical Genetics Approach

Edward Holson, Ph.D., Director, Medicinal Chemistry, Stanley Center for Psychiatric Research, The Broad Institute of MIT and Harvard

Utilizing a chemical toolkit of highly selective HDAC inhibitors we have taken an unbiased approach to defining the biological outcome of small molecule inhibition of the individual HDAC isoforms. We have characterized and profiled a number of known and novel HDAC inhibitors and examined the effects on histone and non-histone acetylation, and gene expression and functional responses in a number of cell types. The focused application of highly selective inhibitors in non-oncology indications will be discussed.

12:00 pm Close of Track

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THURSDAY, APRIL 24

12:30 pm Registration

PROPERTIES OF A 'GOOD' MACROCYCLIC

1:30 Chairperson's Opening Remarks

Mark Peterson, Ph.D., Vice President, IP & Operations, R&D, Tranzyme Pharma, Inc.

» 1:40 FEATURED PRESENTATION: Unexpected Structure-Permeability Relationships in Cyclic Peptides Inspired by Natural Products: Charting Islands of Bioavailability Beyond the Rule of 5s

Scott Lokey, Ph.D., Professor, Department of Chemistry and Biochemistry, University of California, Santa Cruz

Many cyclic peptide natural products share a common chemical feature, backbone N-methylation, which serves to enhance lipophilicity and proteolytic stability, although the impact of N-methylation on passive membrane diffusion in cyclic peptides has not been investigated in detail. I will present our latest research on the use of NMR and computational methods to examine the interplay between structure and conformation to determine membrane permeability in natural product-inspired cyclic peptides.

2:10 Building a Natural Product-Inspired Macrocyclic Toolbox to Hunt for Modulators of Protein-Protein Interactions

Prabhat Arya, Ph.D., Professor, Chemistry and Chemical Biology, DRILS University of Hyderabad, India

A case study of a novel macrocyclic molecule that prevents mitochondrial damage in beta cells through a gain/correction of function will highlight our approach of targeting PPIs with natural product-inspired small molecules that are 3D in shape with 2-4 stereogenic centres and acceptable pharma complexity. The more traditional flat, aromatic chemical toolbox, while fine for accessing the deep and well-defined pockets of traditional enzyme targets, is proving inadequate for signaling pathway-based targets, such as protein-protein or protein-DNA/RNA- interactions.

2:40 Design and Synthesis of Macrocyclic Tera-Peptide Mimetics for PPI and Antibacterial Applications

Sponsored by ASINEX Inspired by Nature

Dmitry Genis, Ph.D., CEO, ASINEX

Compounds with mid- and large-sized rings have long been considered by medicinal chemists as a discrete class of molecules, not only due to their interesting physico-chemical and biological properties, but also due to the challenge of their synthesis. In this talk, we present the design of novel medchem-like macrocyclic scaffolds based on non-conventional macrocyclization chemistries and the use of pre-designed macrocycles for lead generation with special emphasis on protein-protein interaction targets and antibacterial research.

3:10 Macrocycles in Small Molecule Drug Discovery

Max Cummings, Ph.D., Principal Scientist, Discovery Sciences, Janssen

Macrocycles are receiving increased attention in small molecule drug discovery. Macrocyclization allows for larger small molecules that may not meet standard calculated property criteria, and macrocycles are frequently invoked as a magic bullet for the vast frontier of protein-protein interactions. A discussion around the topic of macrocycles in small-molecule drug discovery will be presented, with the HCV compounds Simeprevir and TMC647055 as examples to frame the more general discussion.

3:40 Refreshment Break in the Exhibit Hall with Poster Viewing

4:20 Modulation of the Pharmacodynamic and Pharmacokinetic Profiles of Small Molecule Macrocycles

Mark Peterson, Ph.D., Vice President, IP & Operations, R&D, Tranzyme Pharma, Inc.

Starting from diverse libraries of conformationally-defined macrocyclic small molecules, multiple lead series have been successfully generated against GPCR targets. A comparison of these structures demonstrates that selectivity and binding activity can vary greatly depending primarily on the stereochemistry around the ring for a given scaffold. Using these examples as case studies, the significance and implications of the findings on drug discovery and lead optimization using macrocyclic templates will be discussed.

4:50 Structure-Based Design of Macrocyclic Kinase Inhibitors leading to the Clinical Candidates SB1317, SB1518 & SB1578

*Anders Poulsen, Ph.D., Senior Research Scientist, Experimental Therapeutics Centre, A*STAR*

An HTS against Aurora A kinase revealed several promising pyrimidine-aniline leads. Macrocycle formation was proposed to achieve novelty and selectivity. In a kinase panel selected macrocycles were active on other kinase targets. Subsequently these compounds became leads in our CDK2/Flt3 and JAK2 projects. This presentation will concentrate on the structural biology and conformational properties of our macrocyclic kinase inhibitors as an explanation for their selectivity and SAR.

5:20 Breakout Discussions

In this session, attendees choose a specific roundtable discussion to join. Each group has a moderator to ensure focused conversations around key issues within the topic. The small group format allows participants to informally meet potential collaborators, share examples from their work and discuss ideas with peers. Check our website in February to see the full listing of breakout topics and moderators.

6:20 Close of Day

6:30 Dinner Short Courses*

*Separate registration required; please see page 4 for details

FRIDAY, APRIL 25

7:45 am Morning Coffee

TARGETING MEMBRANE PROTEINS WITH MACROCYCLICS

8:00 Chairperson's Remarks

Nicholas Terret, Ph.D., CSO, Ensemble Therapeutics

8:05 Synthetic Macrocyclic, Protease-Resistant Peptides that Mimic Endocrine Hormones and Bind Receptors

Danielle Guarracino, Ph.D., Assistant Professor, Chemistry, The College of New Jersey

A deficiency of cyclic peptide hormone vasopressin poses the continuous threat of dehydration and loss of electrolyte balance in a rare form of diabetes. In contrast, overactive cyclic peptide hormone oxytocin, similar in structure, has been linked to prostate enlargement, autism, and anxiety disorders. We developed macrocyclic compounds that structurally mimic these hormones, with changes intended to promote stability and potency. Each mimicking compound had moderate abilities to compete with immobilized vasopressin for binding its G-protein coupled receptor (GPCR).

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8:35 Structures of P-Glycoprotein in Complex with Cyclopeptide Inhibitors and Stimulators Reveal Flexible Binding Sites and Conformations

Qinghai Zhang, Ph.D., Associate Professor, Integral Structural and Computational Biology, The Scripps Research Institute

P-glycoprotein is a primary ATP-binding cassette (ABC) transporter causing multidrug resistance in many cancer cells. We describe the design, library synthesis and screening of conformationally constrained cyclopeptides, from which we characterized potent inhibitors and transporters for P-glycoprotein. Several new crystal structures revealed flexible binding sites and conformations. We also describe structural dynamics studies of ABC transporters correlating conformational changes with various states. The study will shed light on strategies to overcome P-glycoprotein-mediated drug transport.

9:05 Engineering Scorpion Venom Peptides to Generate High Potent and Selective Therapeutics Targeting a Potassium Channel

ChiChi Huang, Ph.D., Scientific Director, Antibody Drug Discovery, Janssen R&D, LLC

Selectively blocking Kv1.3, a voltage-gated potassium channel involved in mediating active T cell responses, has been suggested as an approach for treating autoimmune diseases. However generating selective inhibitors remains a challenge. We present a series of highly selective and potent Kv1.3 blockers we identified by making an extensive chimeric peptide library of native peptide toxins, OsK1, a potent Kv blocker, and OdK2, a weak but specific Kv1.3 blocker.

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

DIFFERENT TYPES OF MACROCYCLICS

10:20 Selective Histone Deacetylase Inhibitors (HDACi) based on Cyclic Peptoids

Adrian Culf, Ph.D., Research Scientist, Medicinal Chemistry, Atlantic Cancer Research Institute

Peptoids are peptide mimics, providing a large structural diversity of hydrolytically stable, membrane permeable molecules that are at the boundary between synthetic chemicals and biologics. These molecules are good candidates for exploring targets of medicinal interest. We present our work in automated peptoid synthesis (N-substituted glycine oligomer), macrocyclization for 9 to 15 atom rings, lead identification, molecular modelling, *in vitro* recombinant enzymatic and cellular activity of hydroxamate and thiol-capped cyclic peptoids.

10:50 Novel Natural Product-Based Macrocycles for Efficient Drug Discovery

Sponsored by AnalytiCon discovery The Natural Product Company

Dietmar Wolf, Ph.D., Executive Vice President, AnalytiCon Discovery, LLC

In addition to successful natural products as an inspirational source for new drugs, there is a high demand for diverse, suitable macrocyclic libraries with tractable chemistry. New concepts for the generation of macrocyclic compounds with superior diversity will be described including the integration of natural product building blocks into the modular synthesis of macrocycles.

11:20 2-CLIPS Peptides: Discovery and Optimization of a New Class of Biopharmaceuticals

Sponsored by PEPSCAN

Peter Timmerman, Ph.D., CSO, Pepscan Therapeutics

2-CLIPS peptides constitute a unique class of constrained, bicyclic peptides that display affinities and selectivities comparable to those of antibodies. Their chemical synthesis is compatible with high-diversity screening in genetically-encoded libraries for identifying lead binders to a variety of different target proteins. Structural optimization via (non)-natural amino acid replacements using our high-sensitivity SIMPLIS-array platform improves their performance with orders of magnitude.

11:35 PANEL DISCUSSION: Library Design Strategies

Moderator: Nicholas Terret, Ph.D., CSO, Ensemble Therapeutics

12:05 pm Walk and Talk Luncheon in the Exhibit Hall with Poster Viewing (last chance for viewing)

CASE STUDIES: TARGETING INTRACELLULAR PROTEIN-PROTEIN INTERACTIONS

1:25 Chairperson's Remarks *(Sponsorship Opportunity Available)*

1:30 Stapled Peptide Reactivating Wild-Type p53 towards Clinical Development

Vincent Guerlavais, Ph.D., Distinguished Scientist, Aileron Therapeutics

This presentation discusses the structure-based discovery of the first example of a negatively charged amphipathic stapleda-helical peptide having potent and selective biological activities: ATSP-7041, a dual MDM2/MDMX inhibitor, achieves sub-micromolar *in vitro* activity, and demonstrates robust tumor growth suppression in xenograft cancer models. ATSP-7041 is a precursor to a more potent molecule that is currently undergoing IND enabling studies and is planned for entry into clinical trials in 2014.

2:00 A Cyclic Peptide Hit Optimized to a Non-Peptidic Macrocycle that Targets an Intracellular PPI

Marc Thommen, Ph.D., Head, Technology Platforms, Polyphor

We will describe a successful drug discovery case study of applying two complementary parts of our proprietary macrocycle platform that identifies and optimizes potent and selective modulators of intra- and extracellular protein-protein interactions (PPIs). In particular we highlight a successful case study for the structural transfer of a cyclic peptide hit to a non-peptidic macrocycle to address an intracellular PPI.

2:30 Macrocycle Analogs of Natural Products as Promising Antimalarial and Anti-Trypanosomal Agents: Synthesis and Biological Evaluation

Gloria Serra, Ph.D., Professor, Medicinal Chemistry, Organic Chemistry, Facultad de Química, Universidad de la República

Azolic and non-azolic cyclohexapetides analogs of antimalarial and/or antytripanosomal natural products were obtained in very good yields combining solid-phase peptide synthesis and solution synthesis. Seven of the synthesized macrocycles showed submicromolar EC50 against *Plasmodium falciparum* K1 and a high selectivity (SI > 125) for the parasite. In addition, five compounds displayed low micromolar EC50 against T. brucei brucei and good selectivity. Interestingly, several cyclohexapeptides exhibited satisfactory mutual anti-parasitic activities.

3:00 New Learnings about Macrocycles in Drug Discovery: Progress Towards Lead Series

Nicholas Terrett, Ph.D., CSO, Ensemble Therapeutics Corp

Macrocycles are found widely in nature and several of these natural products are marketed as drugs with good drug-like properties. As it is difficult to readily generate analogs of natural products, the popularity of synthetic macrocycles for drug discovery has been steadily increasing. This presentation will update on recent findings on the druggabilty of macrocycles and will illustrate with examples of lead discovery programs from Ensemble.

3:30 Close of Conference

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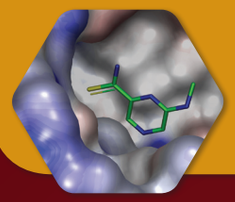

THURSDAY, APRIL 24

12:30 pm Registration

ADDRESSING CHALLENGES IN FRAGMENT-BASED APPROACHES

1:30 Chairperson's Opening Remarks

Daniel A. Erlanson, Ph.D., President & Co-Founder, Carmot Therapeutics, Inc.

1:40 Using Fragments with Confidence

Ben Davis, Ph.D. Research Fellow, Biology, Vernalis

In fragment-based ligand design, it is vital to have a high level of confidence in the initial fragment hits in order to exclude potentially misleading artifacts. I will discuss ways of avoiding some of the common pitfalls which can bedevil an FBLD campaign, in order to define a well validated set of hits. I will also discuss examples where FBLD has been integrated with other approaches to generate novel, optimized lead compounds.

2:10 Fragment-Based Approaches for Drugging Proteases

Steven J. Taylor, Ph.D., Director, Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Inc.

Fragments are components of drug-like molecules that are low molecular weight and can be pre-filtered for favorable physicochemical properties. The Boehringer Ingelheim fragment deck contains approximately 3000 fragments that have been screened against a number of difficult to drug targets including proteases. In this talk we describe our Fragment to Lead efforts that resulted in potent, selective MMP-13 and Chymase inhibitors. Lessons learned from these efforts are transferrable to other lead identification campaigns.

2:40 Evolution of Fragments in the Absence of Crystal Structures

Peter Kutchukian, Ph.D., Associate Principal Scientist, ChemInformatics, Merck and Co.

While FBS offers an efficient avenue to sample chemical space, FBS campaigns are primarily executed for targets that can be readily crystallized, ultimately limiting its scope. A new strategy that extracts information from fragment campaigns, and leverages the information to identify small molecules with enhanced potency and diverse chemotypes without using any target structural information will be described, as well as its application to specific case studies.

3:10 Targeting Specific Interactions to Improve Binding Properties of EGFR-Kinase Ligands

Sponsored by CHEMICAL COMPUTING GROUP

Chris Williams, Ph.D., Principal Scientist, Chemical Computing Group

A structure-based drug design modeling program, combined with PDB data-mining, protein structural fingerprints and pharmacophore searches was used to help identify and characterize linkers for connecting EGFR-binding moieties to DNA and Src targeting functionalities. The resulting compounds showed EGFR inhibitory potency in the low micromolar to nM range and retained significant activity against their divergent targets.

3:40 Refreshment Break in the Exhibit Hall with Poster Viewing

4:20 Fishing for Fragments to Complement Known Binders

Daniel A. Erlanson, Ph.D., President and Co-Founder, 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.

4:50 Fragment vs. HTS Hits: Does it Have to be a Competition?

Nicholas J. Skelton, Ph.D., Senior Scientist, Department of Discovery Chemistry, Genentech, Inc.

Fragment-based approaches are often viewed as a being in competition with high-throughput biochemical screening to identify hits to initiate drug discovery programs. Combining data from both approaches can often be beneficial. I will describe recent fragment-based lead discovery efforts at Genentech that have complemented results from biochemical screening.

5:20 Breakout Discussions

In this session, attendees choose a specific roundtable discussion to join. Each group has a moderator to ensure focused conversations around key issues within the topic. The small group format allows participants to informally meet potential collaborators, share examples from their work and discuss ideas with peers. Check our website in February to see the full listing of breakout topics and moderators.

6:20 Close of Day

6:30 Dinner Short Courses*

*Separate registration required; please see page 4 for details

FRIDAY, APRIL 25

7:45 am Morning Coffee

EMERGING METHODS FOR GENERATING AND SCREENING FRAGMENTS

8:00 Chairperson's Remarks

Peter Kutchukian, Ph.D., Associate Principal Scientist, ChemInformatics, Merck and Co.

8:05 Fragment-Based Discovery in 3D Utilizing Diversity-Oriented Synthesis

Damian W. Young, Ph.D., Assistant Professor, Departments of Pathology and Immunology and Pharmacology; Assistant Director, Center of Drug Discovery, Baylor College of Medicine

Fragment chemical space has traditionally relied heavily on the use of highly sp2 carbon atom enriched aromatic compounds. Accordingly, it is rational to consider that a limited subset of biological space can be targeted with such compounds. We have utilized diversity-oriented synthesis as a guiding algorithm to produce fragments having greater sp3/sp2 carbon atom ratios toward the goal of engaging a wider spectrum of biological targets using fragment-based drug discovery.

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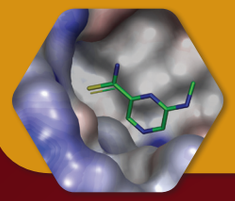


8:35 New Developments in NMR

Isabelle Krimm, Ph.D., Fragment-Based Screening & NMR Team, Institute of Analytical Sciences, University of Lyon, CNRS

Fragment screening resides in the identification of minimal motifs responsible for the specific protein-ligand recognition. Once fragment hits have been identified, one needs to ensure that the fragments exhibit a specific binding mode. We will see how NMR can be used, if crystallographic resolution of protein-fragment complexes fails. In addition, we will see how to assess whether the protein undergoes conformational changes upon fragment binding.

9:05 Getting the Most out of Your Fragments: Synergistic Approaches to Fragment-Based Drug Discovery

Brad Jordan, Ph.D., Senior Scientist, Molecular Structure and Characterization, Amgen

This talk will discuss the utility and advantages of 19F-NMR based fragment screening. The data shown will detail approaches using both NMR and SPR in a synergistic manner for the detection of fragment hits.

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

NEW TARGETS FOR FRAGMENT-BASED APPROACHES

10:20 Fragment-Based Approaches to Study GPCR Biased Signaling

Iwan de Esch, Ph.D., Professor, Medicinal Chemistry, VU University, Amsterdam

We have performed fragment library screening on a list of GPCR targets and not only determined binding affinities but also agonist and antagonist activity on both G-protein mediated signalling and on b-arrestin mediated signalling. The data illustrates the delicate differences in biased signalling when performing FBDD on GPCR targets. The presentation will also reflect on remarkable differences in binding kinetics during fragment growing.

10:50 Fragment-Based Drug Discovery on G Protein-Coupled Receptors and Their Signaling Complexes

Arun Shukla, Ph.D., Assistant Professor, Medicine, Duke University Medical Center

We present a surface plasmon resonance biosensor approach that enables, cell-free, label-free, fragment screening that directly measures fragment interactions with wild-type GPCRs. We exemplify the method by the discovery of novel, selective, high affinity antagonists of human β2 adrenoceptor. Moreover, we apply this approach to screen fragments against preformed signaling complexes of GPCRs.

11:20 Targeting Low-Druggability Bromodomains (e.g. BAZ2B): Fragment-Based Screening and Inhibitor Design

Fleur Ferguson, Ph.D. Student, Laboratory of Christopher Abell, Department of Chemistry, University of Cambridge

Bromodomain-containing proteins play important roles in transcriptional regulation and disease. The BET bromodomains have been validated as therapeutic targets through development of chemical probes, however many others remain untargeted. The BAZ2B bromodomain is predicted to be the least druggable. We have used fragment-based screening to discover and characterize highly ligand-efficient hits with novel scaffolds. We solved crystal structures of fragments bound to BAZ2B and used structure-based design to optimize and merge the fragments.

11:50 Sponsored Presentation

Sponsored by SCHRÖDINGER.

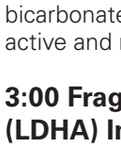
Speaker to be Announced

12:05 pm Walk and Talk Luncheon in the Exhibit Hall with Poster Viewing (last chance for viewing)

DEVELOPING DRUG CANDIDATES FROM FRAGMENT HITS

1:25 Chairperson's Remarks *(Sponsorship Opportunity Available)*

» 1:30 FEATURED PRESENTATION: Fragment-Based Discovery of BACE Inhibitors for Alzheimer's Disease



Andrew Stamford, Ph.D., Executive Director, Medicinal Chemistry, Merck

A fragment screening approach leading to the discovery of the BACE inhibitor MK-8931 currently in clinical trials for the treatment of Alzheimer's disease will be described. This presentation will discuss the discovery of fragments binding to the active site of the aspartyl protease BACE1 by HSQC NMR screening and the molecular design principles applied to the triaging and optimization of these fragments facilitated by X-ray crystallography-driven structure-based design.

2:00 Fragment Success Story: Case Study of an HCV Drug Candidate

Francisco X. Talamas, Ph.D., former Associate Director and Head, Virology Chemistry, F. Hoffmann-La Roche, Inc.

In this talk, the approaches used to design fragments that bind to the HCV Polymerase NS5B and the process used to select the starting point for our lead expansion efforts will be presented. Also, it will be elaborated upon how structure-based design was used to increase the affinity of the fragment to single digit nanomolar potency. During the optimization process, several liabilities were addressed allowing us to identify a candidate for clinical development.

2:30 Exploiting New Crystal Structure of Human Soluble Adenylate Cyclase for the Identification of Novel Allosteric Inhibitors through Fragment-Based Drug Discovery

Valerio Berdini, Ph.D., Associate Director, Computational Chemistry, Astex Pharmaceutical

I present a series of fragment inhibitors we identified based on the crystal structure of human adenylate cyclase (AC), which we were the first to crystallize. AC catalyzes the synthesis of a second messenger, cAMP. The crystal structure of AC revealed a pseudo-symmetrical arrangement of two catalytic domains with a single competent active site and a novel discrete bicarbonate binding pocket. Our fragments bind the bicarbonate pocket and have been optimized to allow a high level of flexibility of AC's active and regulatory sites.

3:00 Fragment-Based Approach toward Lactate Dehydrogenase A (LDHA) Inhibitors

Mark Elban, Ph.D., Investigator, CSC Chemistry, RD Platform Technology & Science, GlaxoSmithKline

A fragment-based approach was used to identify a unique series of LDHA inhibitors with good ligand efficiencies. Subsequent optimization delivered a novel lead series with LDHA cellular activity of 10 μM, selectivity against LDHB, and good physicochemical properties. The overall strategy of identification and optimization, lessons learned, and some guiding principles of the FBDD effort will be presented in the context of the discovery of a fragment-derived lead series for the inhibition of LDHA.

3:30 Close of Conference

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THURSDAY, APRIL 24

12:30 pm Registration

OPTIMIZING NEXT-GENERATION KINASE INHIBITORS

1:30 Chairperson's Opening Remarks

Rogier C. Buijsman, Ph.D., Head, Chemistry, Netherlands Translational Research Center B.V. (NTRC)

1:40 Combining Cellular and Biochemical Panel Profiling for the Development of Selective Kinase Inhibitors

Rogier C. Buijsman, Ph.D., Head, Chemistry, Netherlands Translational Research Center B.V. (NTRC)

Selective kinase inhibitors are optimized for increased target residence time and profiled on large panels of biochemical and cell-based assays. Genotypic, phenotypic and pathway information are combined to determine the optimal compound for a particular patient responder population. This presentation will discuss an in-depth knowledge concerning the relationship between cellular and biochemical profiles of marketed kinase inhibitors as well as insight in genetic susceptibility of these inhibitors.

2:10 Binding Kinetics as Optimization Parameter for Kinase and Epigenetic Enzyme Inhibitors: The Discovery of Slowness

Gerhard Mueller, Ph.D., Senior Vice President, Medicinal Chemistry, MercaChem BV

To improve the correlation between biochemical and cellular or *in vivo* efficacy, it is advantageous to consider the lifetime of the ligand-target complex by determining and optimizing the residence time of compound-target complexes. In this presentation the relevance of binding kinetic attributes of inhibitors against kinases, as well as a variety of epigenetic targets, such as histone-deacetylases (HDACs) and histone-lysinemethyl-transferases (HKMTs) is emphasized.

2:40 The Use of Solvent Mapping for Improving Docking and Scoring

Istvan Enyedy, Ph.D., Senior Scientist, Chemistry, Biogen Idec

Target structure-based "hit" optimization in a drug discovery project is challenging from the computational point of view. Scoring functions cannot predict binding affinity, thus computational chemists must use their intuition or prior knowledge about the target class to prioritize compounds for synthesis. This talk will focus on how we can use solvent mapping and information from co-crystal structures in guiding docking and scoring. Test results using FRED and HYBRID docking protocol from OpenEye into nine kinases, more than 200 structures, will be presented.

3:10 The Discovery and Profile of Narrow Spectrum Kinase Inhibitors as Novel Treatments for Inflammatory Pulmonary Diseases

Sponsored by SYGNATURE discovery

Stuart Onions, Ph.D., Director, Research Management, Sygnature Discovery Ltd.

COPD affects 65 million people worldwide and by 2030 could be the third largest cause of death. Corticosteroids are the current front line therapy, but cannot prevent disease progression and new, improved therapies are required. This presentation details the discovery of narrow spectrum kinase inhibitors which directly target the lung, have optimal duration of action and reduced toxicity by minimizing systemic exposure.

3:40 Refreshment Break in the Exhibit Hall with Poster Viewing

4:20 Design of Oral Bioavailable, Type2 Inhibitors of Discoidin Domain-Containing Receptor 1/2 (DDR1/DDR2) Using Fragment-Based Drug Discovery

Valerio Berdini, Associate Director, Computational Chemistry, Astex Pharmaceutical

A fragment-based drug discovery screening identified a weak hit. Followed by X-Ray the complex showed the ligand bound in the "back-pocket" of DDR1. As a result a 'Back-to-Front' fragment-to-lead campaign aimed to reach the hinge region of the kinase ATP pocket. The talk will focus on this unconventional fragment-based approach to kinases, showing a quick progression of one of the initial hits into very potent leads. It will then give an overview of the lead optimization phase towards orally bioavailable, selective DDR1 and DDR2 inhibitors.

4:50 Next-Generation Protein Kinase Inhibitors When Selectivity Counts

Stefan Laufer, Ph.D., Chairman, Pharmaceutical & Medicinal Chemistry, Pharmacy & Biochemistry, University of Tuebingen

Highly selective PKIs are valuable probes and tools in anti-cancer and anti-inflammatory drug discovery. We have developed a platform for kinase inhibitors with extreme selectivity, leading to the development of ATP-independent type 1 1/2 inhibitors. This presentation will discuss a design approach for highly selective protein kinase inhibitors (selectivity > 1000), generally suitable for 46 out of 518 kinases. A case study for p38 and further perspectives will also be discussed.

5:20 Breakout Discussions

In this session, attendees choose a specific roundtable discussion to join. Each group has a moderator to ensure focused conversations around key issues within the topic. The small group format allows participants to informally meet potential collaborators, share examples from their work and discuss ideas with peers. Check our website in February to see the full listing of breakout topics and moderators.

6:20 Close of Day

6:30 Dinner Short Courses*

*Separate registration required; please see page 4 for details

FRIDAY, APRIL 25

7:45 am Morning Coffee

EMERGING APPROACHES FOR INHIBITION

8:00 Chairperson's Remarks *(Sponsorship Opportunity Available)*

» 8:05 FEATURED PRESENTATION: Conformationally Constrained Diaminopyrimidines: Identification of Potent ALK Inhibitors

Bruce Dorsey, Ph.D., Senior Director, Medicinal Chemistry, Teva Pharmaceuticals

Deregulated ALK acts through over expression in human glioblastoma or chromosome translocation in both anaplastic large cell lymphoma (NPM-ALK) and non-small cell lung cancer (EML4-ALK). Interest in ALK has increased significantly with the recent FDA approval of crizotinib for the treatment of locally advanced or metastatic NSCLC that is ALK positive. Here we present the results of our efforts to design and synthesize clinically relevant ALK inhibitors.

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8:35 Modulating JAK Kinase Activity and Selectivity through the Intervention of Small Molecule Macrocycles: Discovery of SB1518 (Pacritinib)

*Anthony D. William, Ph.D., Senior Scientist, The Agency for Science, Technology and Research (A*STAR)-ICES*

The most advanced small molecule macrocycle Pacritinib has shown promising activity in late phase clinical trials for the treatment of Myelofibrosis. Here, the design and optimization of macrocyclic Jak2/Flt3 inhibitors will be discussed.

9:05 Development of Highly Potent and Selective Reversible Covalent BTK Inhibitors

Erik Verner, Ph.D., Director, Chemistry, Principia Biopharma

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

DEVELOPMENT OF NOVEL KINASE INHIBITORS

10:20 The Discovery of Novel Selective Anaplastic Lymphoma Kinase Inhibitors

Pierre-Yves Michellys, Ph.D., Director, Medicinal Chemistry, The Genomics Institute of the Novartis Research Foundation (GNF)

Anaplastic lymphoma kinase (ALK) is a receptor tyrosine kinase belonging to the insulin receptor superfamily. Presented is the discovery of novel and selective anaplastic lymphoma kinase inhibitors that emerged from the parallel medicinal chemistry effort done on LDK378. Synthesis, structure activity relationships (SAR), preclinical profile and *in vivo* efficacy xenograft models are described as well as the rational design strategy employed.

10:50 Novel IRAK4 Inhibitors for Oncology and Inflammation

Susanta Samajdar, Ph.D., Research Director, Medicinal Chemistry, Aurigene Discovery Technologies Limited

This presentation will discuss the discovery and optimization of hit series, some preliminary *in vivo* data, combination therapy strategy, present focus and further advancements.

11:20 Discovery of a Selective PI3Kβ Clinical Candidate - Rationales for Selectivity

Laurent Schio, Ph.D., Director, Medicinal Chemistry, Oncology, Sanofi

Most PI3K inhibitors currently in clinical development inhibit the four class I PI3K isoforms resulting in side effects and dose limitations in patients. We report here the discovery of selective PI3Kβ inhibitors from high throughput screening and drug design approaches. X-Ray analysis of co-structures obtained with different PI3K isoforms could not explain the level selectivity observed. Further biophysical studies and state of the art *in silico* calculations have allowed the establishment of a rationale for selectivity despite high sequence similarity in the ATP binding site.

11:50 Sponsored Presentation *(Opportunity Available)*

12:05 pm Walk and Talk Luncheon in the Exhibit Hall with Poster Viewing (last chance for viewing)

EXPANDING THE DRUGGABLE KINOME - BEYOND ONCOLOGY

1:25 Chairperson's Remarks

Jan Hoflack, Ph.D., CSO, Oncodesign Biotechnology

1:30 Selective and Brain-Permeable Polo-Like Kinase-2 (Plk-2) Inhibitors

Dean Richard Artis, Ph.D., Senior Vice President, Molecular Discovery, Elan

2:00 Nanocyclix Approach towards Unexplored Kinases: Identification of RIP2 and SIK2 Inhibitors for Application in Auto-Immune and CNS Disorders

Jan Hoflack, Ph.D., CSO, Oncodesign Biotechnology

Oncodesign's chemical biology approach using its macrocyclic chemistry platform has allowed the identification of potent and selective inhibitors for RIP2 and SIK2 kinases. The molecules have been used as chemical probes to validate the potential of these novel targets. Data will be presented that demonstrate the potential role of RIP2 as a target of interest in auto-immune diseases and for SIK2 in neuroprotection/ageing. The discovery and optimization of the inhibitors will be presented.

2:30 Identification of Potent, Selective and Orally Bioavailable TYK2 Inhibitors for Psoriasis

Jun Liang, Ph.D., Scientist, Discovery Chemistry, Genentech, Inc.

We have sought potent and selective TYK2 inhibitors, in order to inhibit the interleukin-12 (IL-12) pathway. A fragment-like hit was identified through high throughput screening of the Genentech library and it was optimized using structure-based and property-guided design. The resulting potent and selective TYK2 inhibitor blocked interferon-gamma production *in vitro* and *in vivo*, demonstrating for the first time that selective TYK2 inhibition is an effective strategy to inhibit IL-12 signaling pathway.

3:00 Novel Triazolopyridine Compounds as Selective JAK1 Inhibitors: From Target Discovery to GLPG0634

Christel Menet, Ph.D., Senior Therapeutic Area Lead & Project Director, Galapagos NV

We have identified a series of compounds that showed good activity in biochemical and cellular assays against the novel drug target JAK1. This series demonstrated promising ADME/PK properties and several compounds showed activity in *in vivo* models of RA. The lead compound, GLPG0634, is the first JAK1 selective compound that has demonstrated clinical efficacy and a favorable safety profile in two Phase IIA clinical studies in patients with rheumatoid arthritis. Discovery and SAR of the series will be presented.

3:30 Close of Conference

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Sponsorship, Exhibit, and Lead Generation Opportunities

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.

Podium Presentations – *Within the Main Agenda!*

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

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

- Purely social
- Focus group
- Reception style
- Plated dinner with specific conversation focus

Exhibit

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

Additional branding and sponsorship opportunities available!

Looking for additional ways to drive leads to your sales team? One move can make all the difference!

CHI's Lead Generation Programs will help you obtain more targeted, quality leads throughout the year. We will mine our database of 800,000+ life science professionals to your specific needs. We guarantee a minimum of 100 leads per program! Opportunities include:

- **Whitepapers**
- **Web Symposia**
- **Custom Market Research Surveys**
- **Podcasts**

Advertising opportunities such as marketing and promotional emails are also available.

For additional information please contact:

Carolyn Benton
Business Development Manager
781-972-5412 | cbenton@healthtech.com

2014 Exhibitors & Sponsors

(As of December 3, 2013)

American Peptide Company, Inc.
AMRI
AnalytiCon Discovery
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Chemical Computing Group
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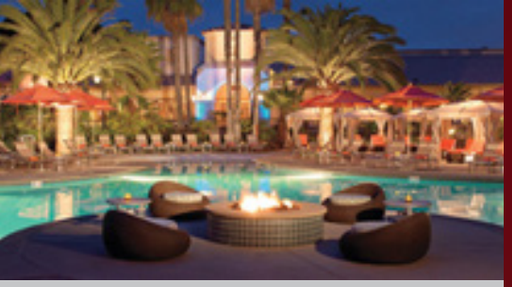
SensiQ Technologies
Sygnature Discovery
Synthonix, Inc.



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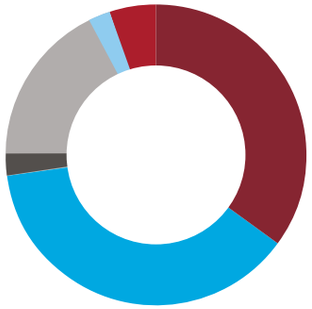
Attendee Profile

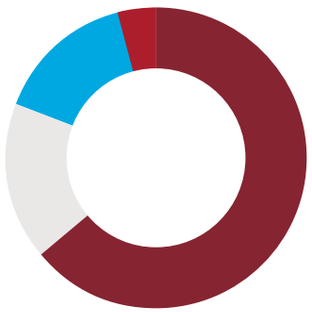
2013 ATTENDEE DEMOGRAPHICS

COMPANY TYPE



Pharma	35%
Biotech/Commercial	29%
Academic	24%
Healthcare/Hospital	6%
Government	3%
Other	3%

GEOGRAPHIC BREAKDOWN



USA	64%
Europe	17%
Asia	15%
Other	4%

USA Breakdown	
West Coast	44%
East Coast	39%
Midwest	17%

ATTENDEE TITLES

Scientist/Technologist	50%
Professor	15%
Director	14%
Executive	9%
Manager	4%
Sales & Marketing	4%
Other	4%

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Imgenex Corporation
Jubilant Discovery
Kalexsyn
LipoScience
OpenEye Scientific Software
PharmaCore, Inc.
Polyphor
Schrödinger
Selcia
SensiQ Technologies
Simulations Plus
Sygnature Discovery
SYNlthesis
Synthonix, Inc.
TC Scientific
Topharman USA

"Speakers were great and presented valuable data. Comprehensive conference and overview of most current inflammation targets and therapies."
Tina T., Associate Scientist, Biogen Idec

"Great conference – CHI conference organizers achieved a good balance of coverage of the most exciting topics in HCV drug discovery and development."
Mike M., Director, Southern Research Institute

"A mutli-disciplinary gathering where you can gain new insights and refresh on new ideas through networking and presentations."
Djamal B., Arisan Therapeutics

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Hotel & Travel Information

Conference Hotel:

Hilton San Diego Resort & Spa
1775 East Mission Bay Drive
San Diego, CA 92109
Phone: 619-276-4010
Discounted Room Rate: $199 s/d
Discounted Cut-off Date: March 25, 2014

The Hilton San Diego Resort & Spa is a TripAdvisor Certificate of Excellence recipient. It is located directly on Mission Bay and is a short, 10 minute taxi ride from the San Diego International Airport. In addition to its stunning location, our conference attendees will enjoy:

- Newly renovated guest rooms
- Unlimited use of the resort's modern, state-of-the-art Fitness Center
- World class swimming pool
- Breathtaking views and award winning restaurants
- Beachside firepits for evening relaxation
- Complimentary shuttle to Historic Old Town and Gaslamp Quarter

We understand that you have many choices when making your travel arrangements. Please understand that reserving your room in the CHI room block at the conference hotel 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 questions about your accommodations.

Flight Discounts:

Special discounts have been established with American Airlines for this conference:

- Call 1-800-433-1790 and use Conference code 1844AB
- Go to www.aa.com/group and enter Conference code 1844AB in promotion discount box
- Contact our designated travel agent, Rona Meizler at (617) 559-3735 or rona.meizler@protravelinc.com

Car Rental Discounts:

Special discount rentals have been established with Hertz for this conference.

- Go to www.hertz.com and enter Convention Number (CV): 04KL0005

Or Call Hertz directly at 800-654-3131 and reference our Discount Number 04KL0005

With its great weather, miles of sandy beaches, and major attractions, San Diego is known worldwide as one of the best tourist destinations. International and commercial air service for the region is provided by the San Diego International Airport. The Online Transit Information System ("Otis") lets you find out how to get around San Diego using the Metropolitan Transit System's buses, trolleys, or trains.

Some San Diego Highlights

- **The Gaslamp Quarter** is Southern California's premier dining, shopping and entertainment district, where you'll find a truly eclectic blend of food, fun and culture all within one of San Diego's most historic areas.
- Just south of Mission Valley and known as the birthplace of California, **Old Town** teems with a lively, authentic atmosphere, boasting museums, historical sites and restaurants.
- At the world-famous **San Diego Zoo**, you'll see some of the world's rarest wildlife including giant pandas and koalas. A visit to the San Diego Wild Animal Park is like a safari to many of the world's most exotic places.
- World-renowned **Balboa Park** is home to fifteen museums, various arts and international culture associations, as well as the San Diego Zoo, making it one of the nation's largest cultural and entertainment complexes.
- **SeaWorld San Diego** entertains, amazes and educates, creating memories that will last a lifetime. See live shows, ride the rides, and get up-close to beluga whales, polar bears, sharks and penguins.

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How to Register: **DrugDiscoveryChemistry.com**

reg@healthtech.com • P: 781.972.5400 or Toll-free in the U.S. 888.999.6288

Please use keycode DCH F when registering

SHORT COURSES

	Commercial	Academic, Government, Hospital-affiliated
1 Short Course	$699	$399
2 Short Courses	$999	$599
3 Short Courses	$1199	$699
4 Short Courses	$1299	$799
5 Short Courses	$1399	$899

Pre-Conference Short Courses (April 22)

SC1: Trends in Physical Properties of Drugs
SC2: GPCR Structure-Based Drug Discovery
SC3: Epigenetic Assays and High-Throughput Screening
SC4: Predicting Sites of Protein-Protein Interactions: In silico Workshop
SC5: Immunology Basics for Chemists
SC6: Molecular Interactions and Drug Design
SC7: Pharmacophore Discovery and Modeling using Extended Hückel Theory

Dinner Short Courses (April 24)

SC8: Enabling Macrocyclic Compounds for Drug Discovery
SC9: Advancing Tools and Technologies for Fragment-Based Design
SC10: Introduction to Covalent Inhibitors

CONFERENCE PRICING

STANDARD PACKAGE *(Includes Access to Two Conferences, Excludes Short Courses)*

Early Registration Deadline until January 31, 2014	**$2199**	**$1049**
Advance Registration Deadline until March 21, 2014	$2399	$1149
Registrations after March 21, 2014 and on-site	$2599	$1249

BASIC PACKAGE *(Includes Access to One Conference, Excludes Short Courses)*

Early Registration Deadline until January 31, 2014	**$1649**	**$829**
Advance Registration Deadline until March 21, 2014	$1749	$899
Registrations after March 21, 2014 and on-site	$1849	$1019

CONFERENCE SELECTIONS:

April 23-24 (Wednesday-Thursday)

Track 1: Anti-Inflammatories
Track 2: Protein-Protein Interactions
Track 3: Epigenetic Inhibitor Discovery

April 24-25 (Thursday-Friday)

Track 4: Macrocyclics and Constrained Peptides
Track 5: Fragment-Based Drug Discovery
Track 6: Kinase Inhibitor Chemistry

CONFERENCE DISCOUNTS

POSTER DISCOUNT ($50 Off) Poster abstracts are due by March 21, 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.*

REGISTER 3 - 4th IS FREE: Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply.

ALUMNI DISCOUNT: Cambridge Healthtech Institute (CHI) appreciates your past participation at Drug Discovery Chemistry. 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. *Please note: Our records must indicate you were an attendee of Drug Discovery Chemistry in the past in order to qualify.*

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 **Alumni, Group, and 'Register 3 & 4th is Free' discounts cannot be combined.**

If you are unable to attend but would like to purchase the entire **Drug Discovery Chemistry** CD for $750 or a single conference track for $350 (plus shipping), please visit www.drugdiscoverychemistry.com. Massachusetts delivery will include sales tax.

ADDITIONAL REGISTRATION DETAILS

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