SAVE $200! Register by April 4

20TH ANNUAL

APRIL 14 - 17, 2025

HILTON BAYFRONT | **SAN DIEGO, CA + VIRTUAL**

Drug Discovery Chemistry

Optimizing Small Molecules for Tomorrow's Therapeutics

APRIL 14, 2025	APRIL 15-16, 2025	APRIL 16-17, 2025
Degraders & Molecular Glues: Beyond Oncology	Degraders & Molecular Glues - Part 1	Degraders & Molecular Glues - Part 2
Covalent & Induced Proximity-Based Therapies	Fragment-Based Drug Discovery	Protein-Protein Interactions
Generative AI & Predictive Modeling	AI/ML for Early Drug Discovery - Part 1	AI/ML for Early Drug Discovery - Part 2
Drug Discovery in Women's Health	GLP1 & Oral Peptides	DNA-Encoded Libraries
RNA-Modulating Small Molecule Drugs	Emerging Technologies for Discovery Chemistry	Drugging Transcription Factors & Regulators
	Ts The Medicinal Chemistry-Pharmacology Interface	Ts Drug Exposure at the Target

PLENARY KEYNOTES

Applying Diverse Small Molecule Strategies to Difficult Targets: Drugging BTK for (Neuro)Immunology

Christopher J. Helal, PhD, Vice President & Head, Medicinal Chemistry, Biogen

Simplifying Synthesis with Radicals

Phil Baran, PhD, Chair & Professor, Department of Chemistry, Scripps Research Institute

PREMIER SPONSORS

eurofins | DISCOVERY

药明康德 WuXi AppTec

X-CHEM TAKE THE LEAD. DRIVE DISCOVERY.

DrugDiscoveryChemistry.com

CONFERENCE AT-A-GLANCE

APRIL 14, 2025	APRIL 15-16, 2025	APRIL 16-17, 2025
Degraders & Molecular Glues: Beyond Oncology	Degraders & Molecular Glues - Part 1	Degraders & Molecular Glues - Part 2
Covalent & Induced Proximity-Based Therapies	Fragment-Based Drug Discovery	Protein-Protein Interactions
Generative AI & Predictive Modeling	AI/ML for Early Drug Discovery - Part 1	AI/ML for Early Drug Discovery - Part 2
Drug Discovery in Women's Health	GLP1 & Oral Peptides	DNA-Encoded Libraries
RNA-Modulating Small Molecule Drugs	Emerging Technologies for Discovery Chemistry	Drugging Transcription Factors & Regulators
Pre-Conference In-Person Dinner Short Courses*	The Medicinal Chemistry-Pharmacology Interface	Drug Exposure at the Target

In-Person Dinner Short Courses*

**Premium or Separate Registration Required*

PLENARY KEYNOTES

Applying Diverse Small Molecule Strategies to Difficult Targets: Drugging BTK for (Neuro) Immunology

Christopher J. Helal, PhD

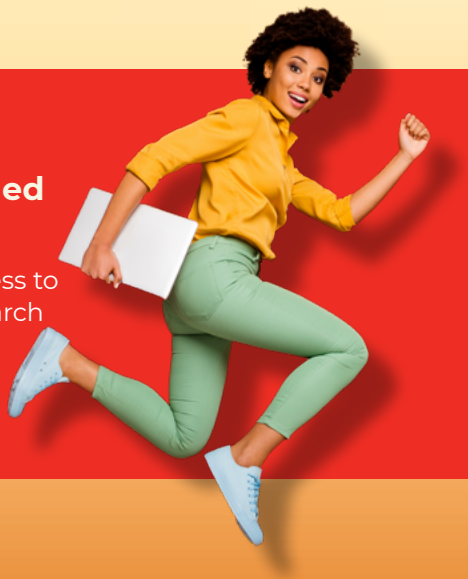
Vice President & Head, Medicinal Chemistry, Biogen

Simplifying Synthesis with Radicals

Phil Baran, PhD

Chair & Professor, Department of Chemistry, Scripps Research Institute

TRACK-HOPPING



Attendees at Drug Discovery Chemistry are encouraged to "track-hop" between concurrent sessions:

Though you register for a particular conference, in reality you gain access to all concurrent conferences. For the best value and to best fit your research needs, select a Premium registration that gives you access to all 10 conferences, 5 symposia, plus 2 short courses over four days of programming. Your registration also includes On-Demand access for one year to access these concurrent conferences.

DINNER SHORT COURSES*

APRIL 14 & 16, 2025
HILTON BAYFRONT | SAN DIEGO, CA

MONDAY, APRIL 14 6:00-8:30 PM

SC1: Protein Degraders: A Beyond Rule of Five Space and in vitro ADME Perspective

Instructors:

John Erve, PhD, President, Jerve Scientific Consulting

Stefanus Steyn, PhD, Research Fellow, Pharmacokinetics Dynamics & Metabolism, Pfizer

This course focuses on proteolysis targeting chimeras (PROTACs) and will cover topics relevant to developing them as oral therapeutics. Topics to be covered in this part of the course will include their physicochemical properties and how these influence solubility and permeability and assays to determine polarity. We will also examine ADME topics focusing on *in vitro* assays including stability assays, transporters, drug-drug interactions (DDIs), Cytochrome P450 (CYP450) inhibition, etc.

SC2: Fragment-Based Drug Design: Advancing Tools and Technologies

Instructors:

Ben J. Davis, PhD, Research Fellow, Biology, Vernalis R&D Ltd.

Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation

This course aims to introduce the fundamentals of Fragment-Based Lead Discovery (FBLD) to attendees. The first section will focus on the concepts of using fragments for hit generation. Special emphasis will be placed on practical pitfalls and the many ways to advance fragments to leads and drugs. The second part of the course will discuss the variety of fragment screening methods and when they are best applied. The composition of fragment libraries will also be discussed in detail. The attendees should come away from this course with a solid understanding of what FBLD is and how to apply it.

SC3: Fundamentals of Generative AI for Drug Discovery

Instructors:

Parthiban Srinivasan, PhD, Professor and Director, Centre for AI in Medicine, Vinayaka Mission's Research Foundation, India

Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

Deep generative modeling is rapidly transforming *de novo* drug discovery, streamlining the entire process. This course aims to explain the potential of AI, machine learning, and generative AI models in creating tailored molecules with specific properties. It explores the fundamentals of Variational Autoencoders, Generative Adversarial Networks, Transformers, Large Language Models (LLMs), BERT, and GPT models in the context of drug discovery, highlighting their crucial role in reshaping the pharmaceutical landscape. Along the way, we'll dissect three pivotal techniques for biopharma specific LLMs: prompt engineering, retrieval augmented generation (RAG), and fine-tuning. This course is designed for medicinal chemists, molecular modeling users, and project managers seeking to harness the capabilities of modern Generative AI concepts and integrate them into their work.

SC4: Detecting Target Engagement: Technology Innovations

Instructors:

Hans-Peter N. Biemann, PhD, Distinguished Scientist, Integrated Drug Discovery, Sanofi

Jonathan Brooks, Principal Scientist, Inflammation & Remodeling, Pfizer Inc.

Can Ozbal, PhD, CEO, Momentum Biotechnologies

Elmar Nurmemmedov, PhD, MBA, Co-Founder & CEO, CellarisBio

This course covers a range of biochemical or biophysical tools adapted to gauge interaction between a compound of interest (either a tool compound or potential therapeutic) with its intended disease-related molecular target. Most of the applications are employed at the hit-confirmation steps in the drug lead generation process, to discover small molecule compounds that engage difficult-to-drug protein targets. Applications to primary screening steps may also be covered.

WEDNESDAY, APRIL 16 6:15-8:45 PM

SC5: Protein Degraders: An in vivo ADME and Safety Perspective

Instructors:

Bin Ma, PhD, Sr Principal Scientist, Drug Metabolism & Pharmacokinetics, Genentech Inc

John Erve, PhD, President, Jerve Scientific Consulting

This course focuses on proteolysis targeting chimeras (PROTACs) and will cover topics relevant to developing them as therapeutics. Topics to be covered in this part of the course will include looking at what is known about how PROTACs are metabolized *in vivo* and strategies to deliver them with adequate PK/PD. The unique mechanism of action of PROTACs gives rise to some drug safety issues not seen in small molecules, which will be discussed. Finally, we will explore the possible relevance of circadian rhythm to protein degradation and PROTACs.

SC6: Chemical Biology for Covalent Drug Discovery, Phenotypic Screening, and Target Deconvolution

Instructors:

Paul Brennan, PhD, Professor, Nuffield Department of Medicine, University of Oxford

Jarrett R. Remsberg, PhD, Senior Scientist I, Platform and Proteomics, Belharra Therapeutics

Angelo Andres, Senior Scientist, Chemical Biology, AstraZeneca Pharmaceuticals

This course is designed to provide an overview and best practices in the use of chemical biology probes and assays that have been developed for applications in early drug discovery. Chemists and biologists working in lead generation, assay development, phenotypic screening, target discovery and deconvolution, target engagement and mechanism-of-action (MoA) studies will all benefit from attending this course. The instructors will share their knowledge and expertise around the use of various technologies and chemistries, and there will be time for open discussion and exchange of ideas.

SC7: AI Applications in Drug Development: Strategies for Innovation and Integration

Instructor:

Arvind Rao, PhD, Associate Professor, Department of Computational Medicine and Bioinformatics, University of Michigan

This course is intended to facilitate harnessing the transformative potential of artificial intelligence (AI) in pharmaceutical R&D. Through engagement with real-world case studies, we intend to collaboratively gain insights into state-of-the-art technologies and develop strategies to effectively integrate AI into pharma R&D processes. This course is intended to equip the attendee with the knowledge to optimize their R&D pipeline, enhance strategic decision-making, and position their organization at the forefront of AI-driven innovation in pharmaceuticals.

SC8: Principles of Drug Design: Ligand-Receptor Interactions and More

Instructor:

Maricel Torrent, PhD, Principal Research Scientist, Computational Drug Discovery, AbbVie, Inc.

This course provides an overview of protein-ligand interactions and drug design principles. The presentation is targeted to medicinal chemists. The course starts by covering hydrophobic, H-bonding and electrostatic interactions. Then the course moves into coverage of specialized topics such as conformation analysis, pi-stack, cation-pi, halogen bonding, protein-protein interface, and covalent inhibition. Medicinal chemistry case studies are incorporated.

SC9: DNA-Encoded Libraries

Instructors:

Svetlana Belyanskaya, PhD, Co-Founder, DEL Source; Former Vice President, Biology, Anagenex

Ghotas Evindar, PhD, Co-Founder & President, DEL Source; Former DEL Platform Senior Manager and Group Leader, GSK

This course provides an overview of DNA-Encoded Library (DEL) screening platforms, discusses common selection strategies for identifying novel hits from DEL campaigns and delves into parameters for building a library collection. The instructors will also cover strategic considerations in using DEL selection data to accelerate hit-to-lead steps in drug discovery.

SPONSORSHIP & EXHIBIT OPPORTUNITIES

CHI offers comprehensive packages that can be customized to your budget and objectives. Sponsorship allows you to achieve your goals before, during, and long after the event. Packages may include presentations, exhibit space and branding, as well as the use of delegate lists. Signing on early will maximize your exposure to qualified decision-makers and drive traffic to your website in the coming months.

PODIUM PRESENTATIONS — AVAILABLE WITHIN MAIN AGENDA!

Showcase your solutions to a guaranteed, targeted audience through a 15- or 30-minute presentation during a specific program, breakfast, lunch, or a pre-conference workshop. Package includes exhibit space, on-site branding, and access to cooperative marketing efforts by CHI. Lunches are delivered to attendees who are already seated in the main session room. Presentations will sell out quickly! Sign on early to secure your talk.

INVITATION-ONLY VIP DINNER/HOSPITALITY SUITE

Select specific delegates from the pre-registration list to attend a private function at an upscale restaurant or a reception at the hotel. From extending the invitations, to venue suggestions, CHI will deliver your prospects and help you make the most of this invaluable opportunity

For additional information, please contact:
Kristin Skahan
Senior Business Development Manager
781-972-5431 | kskahan@healthtech.com

ONE-TO-ONE MEETINGS

CHI will set up 6-8 in-person meetings during the conference, based on your selections from the advance registration list. Our staff will handle invites, confirmations and reminders, and walk the guest over to the meeting area. This package also includes a meeting space at the venue, complimentary main-conference registrations, branding, an 8'x10' exhibit space, and more.

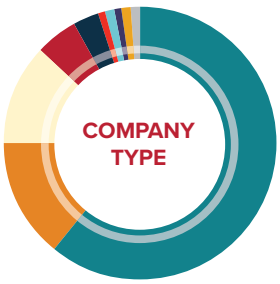
EXHIBIT

Exhibitors will enjoy facilitated networking opportunities with qualified delegates, making it the perfect platform to launch a new product, collect feedback, and generate new leads. Exhibit space sells out quickly, so reserve yours today!

ADDITIONAL BRANDING AND PROMOTIONAL OPPORTUNITIES ARE AVAILABLE, INCLUDING:

- » Conference Tote Bags
- » Literature Distribution (Tote Bag Insert or Chair Drop)
- » Badge Lanyards
- » Conference Materials Advertisement
- » Padfolios and More…

2024 ATTENDEE DEMOGRAPHICS



Biotech	61%
Pharma	14%
Academic	12%
Services	5%
Healthcare	3%
CRO	1%
Financial	1%
Government	1%
Press	1%
Societies	1%

USA	70%
Europe	15%
Asia	10%
Rest of World	5%

West Coast	46%
East Coast	40%
Midwest	14%

Scientist/Technologist	29%
Executive	20%
Director	18%
Sales & Marketing	18%
Manager	6%
Professor	6%
Assistant	3%

Reach these industry-leading companies through sponsorship

AbbVie Inc, Sr Dir Target Enabling Technologies
Amgen Inc, Scientist, Discovery Technology Platforms & Induced Proximity
Astex Pharmaceuticals Ltd, Sr Dir Computational Chemistry & Informatics
Boehringer Ingelheim Pharma GmbH & Co KG, Research Scientist, Medicinal Chemistry
Bristol Myers Squibb, Sr Principal Scientist, Medicinal Chemistry
Chugai Pharmaceutical Co Ltd, Researcher, Protein Science
Crinetics Pharmaceuticals Inc, Sr Scientist, Medicinal Chemistry
Cytokinetics Inc, Sr Dir Research DMPK
Daewoong Pharmaceutical Co Ltd, Researcher, Discovery Ctr
Daiichi Sankyo Co Ltd, Assoc Dir Research & Innovation Promotion, Medicinal Chemistry Research Labs
Deciphera Pharmaceuticals Inc, Principal Investigator, Chemistry Research
Eli Lilly & Co, Postdoctoral Researcher, Molecular Pharmacology
ENANTA Pharmaceuticals Inc, Principal Investigator, Medicinal Chemistry
Foghorn Therapeutics, Sr Dir & Head, Computational Chemistry
Frederick Natl Lab for Cancer Research, Scientific Project Mgr II, Applied & Dev Research
Frontier Medicines Corp, Chief Innovation Officer
Genentech Inc, Dir & Distinguished Scientist, Discovery Oncology
Gilead Sciences Inc, Sr Research Scientist, Structural Biology & Chemistry
GSK, Investigator, Cheminformatics
IBM Corp, Research Software Engineer, Accelerated Discovery
Incyte Corp, Sr Research Investigator, Discovery Chemistry
InSilico Medicine, VP & Global Head, AI Platforms
Janssen Pharmaceuticals, Sr Dir Synthetic Modality, DPDS External Innovation
Japan Tobacco Inc, Sr Dir, Central Pharmaceutical Research Institute
Jnana Therapeutics Inc, Sr VP & Head, Discovery Sciences
Johnson & Johnson Innovation Ctr, Sr Dir External Innovation
JW Pharmaceutical, Scientist, Drug Discovery Ctr
Mass General Brigham Innovation, Sr Program Mgr, Innovation
Massachusetts General Hospital, Asst Prof Psychiatry, Genetics & Aging Research
Mayo Clinic, Research Scientist, Hematology Oncology
MD Anderson Cancer Ctr, Principal Institute Research Scientist, Medicinal Chemistry & Immunology
Merck & Co, Assoc Principal Scientist, Quantitative Biosciences
Mirati A Bristol Myers Squibb Co, Exec Dir Structural Chemistry
MSD, Assoc Principal Scientist, Discovery Chemistry
NIH NCATS, Program Dir, Ofc of Drug Dev Partnership Programs
NIH NIAID, Administrator, Health Science
Nissan Chemical Corp, Scientist, Pharmaceutical Dev
Novartis Institutes for Biomedical Research, Dir & Head, Computer Aided Drug Design W Coast
OpenEye Cadence Molecular Sciences, Sr Application Scientist Mgr, Applications Science
Paraza Pharma Inc, Chief Strategy & Corp Development Officer, Chemical Sciences
Pfizer Inc, Sr Scientist, Biophysics
PTC Therapeutics Inc, Exec Dir
Sanford Labs for Innovative Medicine, Platform Leader, Machine Learning & Computational Biology
Sanofi, Distinguished Scientist & Scientific Dir, US Drug Discovery Structural Biology
Servier Pharmaceuticals, Principal Scientist, Mfg Science & Technology
St Jude Childrens Research Hospital, Grp Leader, Chemical Biology Ctr
Takeda, Dir & Toxicologist, Drug Safety Research & Evaluation
Tufts University, Assoc Prof, Chemistry
Vertex Pharmaceuticals Europe R&D Ltd, Scientist, Medicinal Chemistry & Chemical Biology

VIEW MORE ATTENDEES!

SPONSORS

PREMIER SPONSORS

eurofins | DISCOVERY

药明康德 WuXi AppTec

X-CHEM
TAKE THE LEAD. DRIVE DISCOVERY.

CORPORATE SPONSORS

ATOMBEAT
A DP TECHNOLOGY COMPANY

AURIGENE
PHARMACEUTICAL SERVICES

Axiom

CDD VAULT®
Complexity Simplified

Chemaxon

cresset

curia

cytiva

ELSEVIER

examol

Fidabio
The Power of 1st Principle

FOVUS

FUJIFILM
Value from Innovation

G/

HitChem

HITGEN

Johnson & Johnson Innovative Medicine

JUBILANT BIOSYS

MilliporeSigma

NEOsphere
BIOTECHNOLOGIES

PELAGO BIOSCIENCE
The home of CETSA®

QCWARE

QSIMULATE

Selvita

SYGNATURE™ DISCOVERY

XtalPi

CORPORATE SUPPORT SPONSORS

ATS
SCIENTIFIC PRODUCTS GENEVAC

AXCELEAD
Drug Discovery Partners

BioDuro

BIOGNOSYS
NEXT GENERATION PROTEOMICS

BIORTUS

Bi Biosensing Instrument

BIOSYNTH®

BirdoTech

BOC Sciences®
Best of Chemicals

BRUKER

carterra®

Chemify

CellarisBio

CHEMPARTNER
DEDICATED TO LIFESCIENCE

ChemScene

ChomiX
科络思
The ChemBio Company

Depixus™

eMolecules

excelra

FRONTAGE

FRONTIER
SPECIALTY CHEMICALS

GL Sciences
Separation Sciences for All

HITS

ICE Bioscience
Innovative CRO Explorer

INTONATION
Research Laboratories

LAXAI

Malvern Panalytical
a spectris company

MedChemica
CREATING A STEP CHANGE IN MEDICINAL CHEMISTRY

molport

Novalix

Oakwood Chemical
Enabling Discovery

PharmaBlock

Pion

PORTAL

proteome sciences

REACTION BIOLOGY

ReSync

Sai

SciY

Syngene
Putting Science to Work

TargetMol®
A DRUG SCREENING EXPERT

ThermoFisher SCIENTIFIC

Inaugural

Degraders & Molecular Glues: Beyond Oncology

Designing and Optimizing PROTACs and Glue Modalities for Diverse Therapeutic Indications

MONDAY, APRIL 14

12:00 pm Pre-Conference Symposium Registration

EXPLORING NEW DEGRADATION PATHWAYS & MODALITIES

1:00 Welcome Remarks

1:10 Chairperson's Remarks

Mary Matyskiela, PhD, Vice President, Molecular Sciences, Neomorph, Inc.

1:15 FEATURED PRESENTATION: Destruction with High Specificity: Mechanisms of Substrate Selection and Processing by the 26S Proteasome and p97/Cdc48

Andreas Martin, PhD, Professor and HHMI Investigator, Molecular & Cell Biology, University of California Berkeley

Our biochemical, single-molecule, and cryo-EM structural studies provide important mechanistic insights into the processing of ubiquitinated substrates by the 26S proteasome and the p97/Cdc48 protein unfoldase. We also recently characterized a novel mode of ubiquitin-independent, NUB1-cofactor mediated degradation by the human proteasome, whereby the ubiquitin-like modifier FAT10 functions in substrate delivery and engagement by the proteasomal ATPase motor, offering new opportunities for targeted protein degradation independent of ubiquitin or p97.

2:15 A Cellular Strategy for Interrogating TPD-Competent Sites on E3 Ligases

Justin M Reitsma, PhD, Principal Research Scientist I, Targeted Protein Degradation, AbbVie Inc

Discovering functionally active ligands within druggable pockets of novel E3 ligases has posed a significant challenge to targeted protein degradation efforts. We address this by using genetic code expansion to engineer ligases containing tetrazine-functionalized non-canonical amino acids. In living cells, click chemistry conjugates the tetrazine with a strained trans-cyclooctene linked to a target-binding ligand. This engineered ligase, featuring a covalent neosubstrate binder, is then analyzed for its protein degradation efficacy.

2:45 Leveraging Generative AI to Develop CRBN Molecular Glue Libraries for Efficient HTS and Rational Design

HongBo Zhang, VP, HitChem

The development of CRBN molecular glue (MG) degraders presents several key challenges:

1. Precision and Innovation in Rational Design – Achieving high precision to minimize off-target risks while incorporating innovative structures to ensure intellectual property (IP) advancement.
2. Optimized HTS Libraries – Designing libraries with validated warhead motifs while maintaining high structural diversity to maximize cost-effectiveness.

In this presentation, we will showcase how we have leveraged generative AI to develop a robust molecular generation model and its application in creating CRBN MG libraries—both virtual and ready-to-use. Additionally, we will share case studies demonstrating how the integration of these libraries with CADD tools, and lab chemistry capabilities has successfully led to the identification of novel degrader compounds and the discovery of hit compounds targeting multiple CRBN-degrading proteins.

3:15 Networking Refreshment Break

3:30 Molecular Glue, Mitochondrial Biogenesis, Neurodegeneration, and Aging

Tauseef Butt, PhD, President & CEO, Progenra, Inc.

Misfolded proteins and protein aggregates damage mitochondria leading to cell death. Progenra has discovered a potent molecular glue that activates parkin (E3 ligase)/PINK1 (kinase) signaling pathway. Phosphorylation of ubiquitin and parkin E3 ligase by PINK1 orchestrates mitophagy as well as initiating mitochondrial gene transcription and translation (mitobiogenesis). Healthy mitochondrial function plays a critical role in protection against Alzheimer's and Parkinson's diseases and aging. Mechanisms of the glue will be discussed.

4:00 Targeting 14-3-3/CRAF Complexes with Molecular Glues: Applications in Oncology and RASopathies

Markella Konstantinidou, PhD, Staff Scientist, Laboratory of Dr. Michelle Arkin, Department of Pharmaceutical Chemistry, University of California, San Francisco

4th Annual

Covalent & Induced Proximity-Based Therapies

Innovative Chemistries and Assays for Studying and Modulating Cellular Interactions

MONDAY, APRIL 14

12:00 pm Pre-Conference Symposium Registration

EMERGING COVALENT INHIBITORS & STRATEGIES

1:00 Welcome Remarks

1:10 Chairperson's Remarks

Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation

1:15 Hydralazine Covalently Inhibits Cysteamine Dioxygenase to Attenuate GPCR Signaling and Glioblastoma Growth

Megan L. Matthews, PhD, Assistant Professor, Chemistry, University of Pennsylvania

Hydralazine (HYZ) has been used clinically for 70 years, but its mechanism of action (MOA) is still unknown. The talk will show how HYZ covalently and irreversibly inhibits a single target and achieves remarkable selectivity across cells and tissues. It connects an old drug to its target, reveals the mechanism of its therapeutic effect, and shows it can be now be repurposed and further optimized to treat neurological brain disorders.

1:45 Identification of VVD-214/RO7589831: A Clinical-Stage, Covalent Allosteric Inhibitor of WRN Helicase for the Treatment of MSI-High Cancers

Shota Kikuchi, PhD, Director, Chemistry, Vividion Therapeutics

WRN helicase is a promising target for treating cancers with microsatellite instability (MSI) due to its essential role in resolving deleterious non-canonical DNA structures that accumulate in cells with faulty mismatch repair mechanisms. Here we describe the medicinal chemistry optimization of potency, ADME, and PK properties of chemoproteomic screening hits, which resulted in identification of VVD-214/RO7589831 (Vividion/Roche), a clinical-stage, covalent allosteric inhibitor of WRN.

2:15 Discovery of RAS(ON) Mutant-Selective Covalent Tri-Complex Inhibitors

Allison Zhang, PhD, Senior Scientist I, Structural Biology & Biophysics, Revolution Medicines

We designed a series of natural product-inspired molecules that bind and remodel the surface of cyclophilin A to create a binary complex with high affinity for the active, GTP bound(ON) state of RAS. The resulting tri-complex sterically blocks RAS-effector interactions to disrupt downstream signaling. Structure-guided optimization enabled the development of orally bioavailable covalent inhibitors including the investigational agents, RMC-6291(RAS(ON) G12C-selective) and RMC-9805(RAS(ON)G12D-selective), both of which display profound antitumor activity in preclinical models.

2:45 In-Solution Quantification of Small-Molecule Protein Interactions Using FIDA Lambda Dynamics in Drug Discovery

David Myszka, Dir Drug Discovery, Fidabio

Based on "1st principle" biophysics, Flow Induced Dispersion Technology (FIDA) bridges the gap between structural and functional information of biomolecules. FIDA developed the capability of generating kon and koff rates in a fully in-solution assay without any immobilization to surfaces. Fida is able to measure in-solution small-molecule binding with 3 different orthogonal measurements in addition to quantifying molecule sizing (hydrodynamic radius), aggregation, PDI, and viscosity.

3:00 QuValent: QM/MM FEP & Transition State Analysis for Covalent Drug Design with Pharma-Suitable Throughput

David Pearlman, VP Product, Product, QSimulate

Despite increasing interest in covalent drugs, computational tools to help in lead optimization have lagged, due to the inherently quantum nature of covalent bond formation. We have developed the first QM/MM-based approach to FEP allowing throughput with a cost and timescale suitable for commercial drug discovery. QuValent allows far better predictions than classical methods. A complementary automated platform for assessing transition state energetics similarly provides for warhead optimization.

3:15 Networking Refreshment Break

3:30 Covalent Fragment-Based Ligand Discovery to Drug-Refractory Targets

Joe Patel, PhD, Vice President and Head of Discovery, Nexo Therapeutics

The presentation will discuss the design of CODON, our proprietary pan-amino-acid covalent fragment library and its ability to identify novel and induced pockets on relevant protein targets. The rich SAR generated during the screening phase enables rapid hit-to-lead progression and early confirmation of cellular target engagement.

4:00 Discovery and Characterization of Covalent Inhibitors

Brooke Brauer, PhD, Senior Research Scientist, Mass Spectrometry, AstraZeneca Pharmaceuticals

Covalent modulation of therapeutic targets is an increasingly important modality for drug discovery, particularly after recent success with historically challenging targets like KRAS G12C. In this talk, I'll present the work we have done to discover covalent inhibitors for an anti-apoptotic protein target and the targeted proteomics work done to profile the lead compounds effect in cells.

4:30 FEATURED PRESENTATION: Drug Discovery by Developing Heterobifunctional Molecules as Regulated Induced Proximity Targeting Chimeras (RIPTACs)

Jia Zhou, PhD, Professor, Chemical Biology Program, Department of Pharmacology & Toxicology, University of Texas Galveston

RIPTACs show promise in specifically targeting and eliminating disease cells while leaving healthy cells unharmed. As a unique drug discovery approach, RIPTACs work by forming a stable complex with target protein (TP) and effector protein (EP), selectively disrupting the EP function in disease cells and causing cell death. This presentation will introduce the proof of concept of the RIPTAC strategy and our efforts developing such heterobifunctional molecules as potential therapeutics.

5:15 Close of Symposium

5:30 Dinner Short Course Registration

6:00 Dinner Short Course*

SC2: Fragment-Based Drug Design: Advancing Tools and Technologies
*Premium Pricing or separate registration required. See Short Courses page for details.

APRIL 14, 2025 | 1:00-5:15 PM

2nd Annual

Generative AI & Predictive Modeling

Accelerating Drug Discovery by Improving Speed, Scale, and Accuracy

MONDAY, APRIL 14

12:00 pm Pre-Conference Symposium Registration

APPLICATIONS TO INNOVATIONS

1:00 Welcome Remarks

1:10 Chairperson's Remarks

Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.

1:15 Non-Human Intelligence in Drug Discovery

Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.

This talk summarizes our experience of developing non-human intelligent technologies for drug discovery. We created multiple temporally-validated machine learning (ML) models, and some LLM (large language model) agents to integrate and coordinate drug discovery activities. This platform includes 1) target-phenotype ML models; 2) target-based and property-based ML models; and 3) multiple LLM research assistant agents for drug discovery and repurposing.

1:45 Impact of Complementary Generative AI Methods and Absolute Binding Free Energy Applied to Drug Discovery

Romelia Salomon, PhD, Senior Project Leader, Drug Discovery, SandboxAQ

Discover how innovative generative AI and molecular simulation methods are revolutionizing drug discovery. This presentation will explore cutting-edge strategies for hit finding and lead optimization targeting unmet medical needs. Key highlights include AI-based ligand design, active learning absolute free energy perturbation (AQFEP) virtual screening, the Alchemical Transfer Method (ATM) for binding free energy estimation, and IDOLpro—a generative AI solution that integrates deep diffusion with multi-objective optimization.

2:15 Using Generative AI to Design Small Molecules That Can Engage Multiple Targets

Rayees Rahman, PhD, Co-Founder & CEO, Harmonic Discovery

Unlike conventional methods that focus on single-target selectivity, generative AI models leverage machine learning and deep learning algorithms to explore vast chemical spaces, optimizing molecules for polypharmacology. These models can integrate multi-target profiles, assessing potential off-target effects, efficacy, and safety considerations, ultimately facilitating the creation of compounds with desired therapeutic profiles. This study explores generative modeling for multi-target engagement and highlights its promise to address complex diseases through targeted polypharmacology.

2:45 Architecting AI Agent Networks for Scalable Cheminformatics

examol

Dennis Nenno, PhD, Chief Executive Officer & Co-Founder, Examol

Networks of AI agents can efficiently distribute complex cheminformatics workflows, but their effectiveness depends on connected data infrastructure and scalable, executable methods. Using a case study of ligand unbinding kinetics simulation, we demonstrate how a framework of coordinated AI agents can automate the experimental setup, identify key molecular events, and extract patterns across multiple timescales. We explore how this architecture enables chemists to tackle sophisticated lead optimization questions, while maintaining full reproducibility and scalability.

3:00 Selectivity and ADME Predictions with AI

Selvita

Michal Vieth, Group Leader, AI&CDD, Selvita

This presentation explores the application of AI/ML in drug discovery, focusing on a case study involving ADME and selectivity prediction. The study compares ligand-based and target-based AI models, their validation and highlighting their strengths and weaknesses in predicting ADME profiles and selectivity of a set of drugs. We compare their predicted selectivity with their mechanisms of action (MOA) using different AI approaches. Our findings contribute to a deeper understanding of how AI can be leveraged to improve the efficiency and success rate of drug discovery. This research exemplifies the type of cutting-edge computational approaches that Selvita's CADD group employs to support drug discovery projects.

3:15 Networking Refreshment Break

3:30 What Got Us Here Won't Get Us There: The Future of Drug Discovery with Generative AI

Sanaz Cordes, MD, Chief Advisor, Healthcare & Life Sciences, World Wide Technology Inc.

Ina Poecher, Data Scientist, World Wide Technology

This is an engaging and insightful talk on the transformative power of generative AI (GenAI) in drug discovery. It will explore how GenAI is reshaping the drug discovery process, driving efficiency, and unlocking new possibilities for innovation.

4:00 PANEL DISCUSSION: Session Speakers Discuss Current Gaps in Adopting GenAI for Drug Discovery

Moderator: Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.

4:45 Close of Symposium

5:30 Dinner Short Course Registration

6:00 Dinner Short Course*

SC3: Fundamentals of Generative AI for Drug Discovery

*Premium Pricing or separate registration required. See Short Courses page for details.

Inaugural

Drug Discovery in Women's Health

Where Innovation Meets Impact

MONDAY, APRIL 14

12:00 pm Pre-Conference Symposium Registration

LEVERAGING INNOVATIONS IN RESEARCH & TECHNOLOGIES

1:00 Welcome Remarks

1:10 Chairperson's Remarks

Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

1:15 Where Are All the Drugs in Women's Healthcare?

Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

Despite significant advancements in medicine, women's healthcare remains underserved, particularly in the realm of drug innovation. This talk will share the current landscape of drug approvals for women's health, highlight substantial unmet medical needs, and examine funding trends that impact innovation. Additionally, the extensive opportunities for novel drug discovery programs in this area will be emphasized.

1:45 FEATURED PRESENTATION BY A 2024 TIME WOMAN OF THE YEAR: Fighting Hyperemesis—A Geneticist's Story

Marlena Fejzo, PhD, Assistant Professor, Center for Genetic Epidemiology, Population and Public Health Sciences, Keck School of Medicine, University of Southern California; CSO, Harmonia Healthcare

Hyperemesis gravidarum (HG) is at the severe end of the spectrum of morning sickness and is associated with adverse maternal, fetal, and child outcomes. I dedicated my career to discovering the cause in hopes of improving treatment. We performed genetic studies of HG and identified the emetogenic hormone GDF15 is associated with the condition, elucidating new ways to treat and prevent HG and improve health of mothers, babies, and children.

2:15 Feedback from the Bench and Bedside Leading to the Discovery of Inavolisib (Itovebi), a Potent and Selective PI3K Alpha Inhibitor

Daniel Sutherlin, PhD, Senior Vice President, Small Molecule Drug Discovery, Genentech Inc.

Inavolisib, recently approved by the US FDA for endocrine resistant, PIK3CA mutated, HR-positive, HER2-negative, advanced breast cancer, in combination with palbociclib and fulvestrant, is a potent and selective inhibitor of PI3K alpha, one of the most commonly mutated oncogenes in cancer. The discovery of inavolisb, along with how the molecular properties were shaped by clinical and preclinical data from earlier molecules, will be discussed.

2:45 Advancing Clinical Research on Women's Health

Sarah Temkin, MD, Associate Director for Clinical Research, Office of Research on Women's Health, National Institutes for Health

The NIH Revitalization Act, passed in 1993 mandated inclusion of women into federally funded clinical research. More than three decades later, significant gaps remain in our understanding of the health of women. Opportunities to align research opportunities with the health needs of women will be discussed.

3:15 Networking Refreshment Break

3:30 A Public-Private Partnership Pathway to New, Non-Hormonal Contraceptives

Peter Meinke, PhD, Sanders Director & CEO, Sanders Tri-Institutional Therapeutics Discovery Institute

The nonprofit Sanders Tri-Institutional Therapeutics Discovery Institute (TDI) is a unique alliance created to remove the barriers that impede innovative, high risk translational drug discovery in academic settings. TDI's scientific contributions to the discovery, optimization, and validation of inhibitors of soluble adenylyl cyclase (sAC, ADCY10) for use as non-hormonal, on demand oral contraceptives for men (NewCo created: Sacyl Pharma) and as topical contraceptives for women (in IND-enablement) will be presented.

4:00 Prioritization of Targets for Non-Hormonal Contraception

Thomas Zollner, MD, Vice President & Lead, Reproductive Health, Bayer AG

Family planning is a human right. Nevertheless, almost half of all pregnancies are unintended and half of them end in abortion. In LMIC, 97% of those are unsafe, leading to 50,000 deaths of young women. User preferences worldwide indicate a preference of innovative, non-hormonal contraceptives. Compounds addressing the sperm proteome in women appear promising based on expected safety & efficacy. Prioritization of drug targets for R&D activities will be discussed.

4:15 Treating HPG Axis Disorders by Targeting KISS1R

Elizabeth Garner, MD, MPH, CEO, SeNa Therapeutics

SeNa Therapeutics is focused on developing innovative disease-modifying Kisspeptin receptor (KISS1R)-targeted therapies for hypothalamic-pituitary-gonadal (HPG) axis disorders in women. SeNa's novel KISS1R binding peptide-derived molecules therapeutically stimulate or attenuate Kisspeptin signaling, addressing both HPG hyperactivity and diminished activity.

4:30 Tackling New Therapies for PCOS with Machine Learning–Accelerated Medicinal Chemistry

Emily Hanan, Head, Medicinal Chemistry, PostEra

PCOS impacts 1 in 10 women of reproductive age, yet has no specifically approved therapeutics. In this heterogeneous endocrine disorder, androgen excess is linked to reproductive dysfunction and hirsutism. In our pursuit of novel therapies for PCOS, we have successfully applied our machine learning-driven medicinal chemistry platform to rapidly optimize a series of small molecules which affect the testosterone biosynthesis pathway, demonstrating *in vivo* reduction of testosterone with advanced leads.

4:45 Leveraging Multiomics Data to Identify and Prosecute Targets Implicated in Women's Health

Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

Endometriosis and alternative sources of non-hormonal contraception are neglected and challenging issues associated with women's health. Today, I will discuss how we leverage multi-omics data and AI to identify novel targets implicated in Endometriosis and how we contribute to the challenge of designing novel non-hormonal contraceptives using AI.

5:00 Leveraging Organoid Models for Drug Discovery in Women's Reproductive Health

Morgan Stanton, PhD, CEO, Opal Therapeutics

Opal Therapeutics is building a biotechnology platform dedicated to drug discovery in women's reproductive health. By integrating patient-derived uterine organoids for chemical screening and advanced image analysis, we are pioneering innovative therapeutic approaches for chronic gynecological conditions, including fibroids and endometriosis. Our platform aims to uncover novel pharmaceutical solutions, addressing the urgent need for targeted interventions in women's healthcare.

5:15 Close of Symposium

5:30 Dinner Short Course Registration

6:00 Dinner Short Courses*

*Premium Pricing or separate registration required. See Short Courses page for details.

6th Annual

RNA-Modulating Small Molecule Drugs

Novel Approaches to Target RNA Structure, Binding, Interactions, and Function

MONDAY, APRIL 14

12:00 pm Pre-Conference Symposium Registration

EMERGING CHEMISTRIES & SCREENING TECHNOLOGIES

1:00 Welcome Remarks

1:10 Chairperson's Remarks

Thomas Hermann, PhD, Professor, Department of Chemistry & Biochemistry, University of California, San Diego

1:15 Chemical Proteomic Profiling of RNA-Binding Protein Activity in Cells

Ken Hsu, PhD, Stephen F. and Fay Evans Martin Endowed Associate Professor, Department of Chemistry, The University of Texas at Austin

We developed photo-activatable-competition and chemoproteomic enrichment (PACCE) as global method for identifying RNA-binding sites on proteins. PACCE is complementary to existing RNA interactome capture methods and enables functional profiling of canonical RNA-binding domains as well as discovery of moonlighting RNA binding activity in the human proteome. Here, we provide an update on functional evaluation of non-canonical RBPs discovered using PACCE.

1:45 Visual Biology Drug Discovery

Generoso Ianniciello, Chief Business Officer, Anima Biotech

Lightning.AI, Anima's groundbreaking TechBio platform, uses Visual Biology to transform target and drug discovery. With PathwayLight, it generates deep, large-scale disease biology data by imaging cellular pathways in healthy and diseased cells. This data trains neural networks to identify "disease signatures," uncover novel targets, and discover small molecules that modulate mRNA biology. Validated through partnerships with Lilly, Takeda, and AbbVie, Lightning.AI now powers over 20 drug discovery programs.

2:15 An Integrative Structure-Based Approach to Discovering mRNA-Targeted Small Molecules

Elena Menichelli, PhD, Director & Head, Structural Biology, Arrakis Therapeutics

Using orally bioavailable small molecules to modulate the function of messenger RNAs offers a promising strategy for developing new therapies that extend beyond currently druggable protein targets. Here, we discuss our structure-based approach to discovering mRNA-targeted small molecules, touching on unique challenges in building a broad and robust platform.

2:45 Mirror-Image RNA-Targeted DEL Screens

X-CHEM

Zhen Chen, Senior Principal Research Scientist, Lead Discovery & Biochemistry, X-Chem, Inc.

We present mirror-image RNA-targeted DNA-encoded library (DEL) screening as a novel approach to discover small molecule ligands for RNA. Our strategy eliminates false enrichment from DNA:RNA hybridization, enhances the enrichment of genuine target engagers, and enabled the discovery of novel, specific binders to expansion repeat, splice site, and riboswitch targets. Our method unleashes the unparalleled throughput of DEL for RNA-targeted drug discovery.

3:15 Networking Refreshment Break

3:30 Enhancing Activation of a Novel Splice Site Sequence: Development of a Small Molecule Splicing Modifier Therapy for Genetic Diseases

Jigar Patel, PhD, Associate Director, Medicinal Chemistry, PTC Therapeutics

The viability of an emerging small molecule splicing program often depends on the ability to drive potency towards a particular target, while maintaining reasonable selectivity. This presentation highlights our hit-to-lead efforts towards the development of a splicing modifier of an undisclosed gene of high interest.

4:00 Recent Advances Developing RNA Splicing Modulators to Treat Incurable Diseases

Diane Hamann, PhD, Principal Scientist, Medicinal Chemistry, Rgenta Therapeutics

Rgenta Therapeutics has developed a proprietary, integrative RNA-targeting oral small molecule discovery platform to deliver first-in-class therapies. We are pursuing targets in the oncology and neurological diseases space, exemplified by the oncogenic transcription factor c-MYB and the PMS1 gene. In this presentation, we'll share an overview of our platform and recent progress on selected targets.

4:30 Identification of Functional Small Molecule Binders of UTRs in mRNAs Relevant to Human Disease

Thomas Roddy, PhD, Senior Vice President, Platform Technology, Atavistik Bio

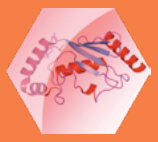
We have developed a technology using LC/MS-based metabolomics and an endogenous metabolite library to systematically discover functional binding pockets on RNA. These pockets enable an efficient drug discovery campaign using AI/ML-enabled structure-based drug design. This process has been successfully executed on several RNA targets in multiple therapeutic areas. Our discovery of compounds that bind to the UTR of human SERPINA1, which is implicated in Alpha-1-Antitrypsin (A1AT) deficiency, will be presented.

5:15 Close of Symposium

5:30 Dinner Short Course Registration

6:00 Dinner Short Courses*

*Premium Pricing or separate registration required. See Short Courses page for details.



8th Annual

Degraders & Molecular Glues — Part 1

Design, Delivery & Optimization of PROTACs and Glue Modalities

6:00 pm MONDAY, APRIL 14: Dinner Short Course*

SC1: Protein Degraders: A Beyond Rule of Five Space and *in vitro* ADME Perspective

*Premium Pricing or separate registration required. See Short Courses page for details.

TUESDAY, APRIL 15

7:00 am Registration Open and Morning Coffee

TARGETED PROTEIN DEGRADATION FOR ONCOLOGY

8:00 Welcome Remarks

8:05 Chairperson's Remarks

Josh Hansen, PhD, Senior Vice President, Chemistry, Treeline Biosciences Inc.

8:10 Strategies for Evaluating Novel E3 Ligases for Targeted Protein Degradation Applications

Reema Thalji, PhD, Medicinal Chemist, GSK

PROTACs are a rapidly evolving modality, currently sparking great excitement within the pharmaceutical industry. Due to limitations of the CRBN and VHL workhorse ligases, there is a desire to identify novel E3 ligase binders for targeted protein degradation applications. This talk will highlight our approach as well as the use of high-throughput chemistry to expedite this effort.

8:40 Degrading Siglecs for the Treatment of Anti-PD-1 and Anti-CTLA-4 Refractory Tumors

Peng Wu, PhD, Professor, Chemical Physiology, Scripps Research Institute

Siglec-7 and -9 are highly expressed on tumor-infiltrating myeloid cells to suppress their anti-tumor function, but with unclear roles in tumor-infiltrating T cells. We found that these Siglecs suppress T cell activity by inducing TCR dephosphorylation. Using a Siglec-7/9 degrader that targets both Siglecs to the lysosome for degradation, we rescued T cell effector function and reprogrammed tumor microenvironment, resulting in productive tumor control in anti-PD-1 and anti-CTLA-4 refractory mouse tumor models.

9:10 Systematic Discovery of Novel Degraders through Deep Proteomic Screening

NEOsphere BIOTECHNOLOGIES

Henrik Daub, CSO, NEOsphere Biotechnologies GmbH

Rational and systematic strategies are crucial for identifying molecular glue molecules for specific target proteins, essential for successful degrader drug discovery and fully realizing the potential of targeted protein degradation. This presentation will demonstrate how high-throughput proteomics can rapidly establish broad pipelines of novel, high-value degrader targets at scale and within native cells, employing a target and E3 ligase-unbiased approach. Identified targets were subsequently mechanistically validated; for instance, E3 ligase dependency was confirmed, and global ubiquitinomics was used to verify degrader-induced modifications, at an unparalleled depth of 50,000 ubiquitination sites.

9:40 Breakout Discussions (In-Person Only)

Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 1: New Strategies For Developing Next-generation Degraders and Glues

Anastasia Velentza, PhD, Vice President, Biology, Vilya Therapeutics

In-Person Only BREAKOUT DISCUSSION 2: PK/PD Considerations and Safety Assessments for Degraders

Robin Haid, PhD, Modeling & Simulation Expert, Preclinical Modeling & Simulation, Bayer AG

Dana Klug, PhD, Research Investigator, Medicinal Chemistry, Arvinas Inc.

10:25 Networking Coffee Break

10:50 Development of Orally Bioavailable MDM2 Degraders

Shaomeng Wang, PhD, Warner-Lambert/Parke-Davis Professor of Medicine, Pharmacology & Medicinal Chemistry; Co-Director, Molecular Therapeutics Program, University of Michigan

The human murine double minute 2 (MDM2) protein is a primary, endogenous cellular inhibitor of p53 and has been pursued as a cancer therapeutic target in the last 20 years. In this presentation, I will discuss the development of highly potent and orally efficacious MDM2 PROTAC degraders to overcome major clinical limitations of MDM2 inhibitors.

11:20 PROTAC Degraders of CDK8/CDK19 Mediator Kinases Potently Suppress Multiple Myeloma Proliferation

Campbell McInnes, PhD, Professor, Drug Discovery & Biomedical Sciences, University of South Carolina

CDK8 and CDK19 are kinase components associated with transcriptional Mediator complex. To extend the effects of CDK8/19 inhibition and to suppress kinase-independent activities, we have developed three series of PROteolysis TArgeting Chimeras (PROTACs) based on selective inhibitors of CDK8/19 kinases. CDK8/19 PROTACs were 10-fold more potent in the two CCNC-dependent MM lines (IC50 of 20-30 nM) than kinase inhibitors but not in the independent line.

11:50 Lessons Learned from Developing BTK Molecule Glue Degraders

Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

In this study, we discovered PS-10, a molecular glue targeting Bruton's tyrosine kinase (BTK). While PS-10 doesn't bind directly to BTK, it binds to E3 ubiquitin ligase CRBN, forming a ternary complex that leads to efficient BTK degradation. Cryo-EM analysis revealed unique protein interactions, and PS-10's mechanism extends to other kinases, demonstrating broader therapeutic potential.

12:20 pm Transition to Lunch

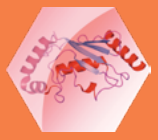
12:25 LUNCHEON PRESENTATION: Revolutionizing Screening for Molecular Glues: Unveiling WEE1 Degraders with High-Throughput Spectral Shift

eurofins | DISCOVERY

Olivier Mirguet, Scientific Dir Integrated Drug Discovery, DiscoveryOne, Eurofins Cerep

In this presentation, we introduce a high-throughput biophysical approach using Spectral Shift technology to identify a WEE1 molecular glue by directly characterizing ternary complex formation between WEE1, cereblon, and a library of degraders. The compound was then validated through orthogonal assays like E3scan™ and KinaseProfiler™ and profiled in cells for WEE1 degradation via Western blot and proteomics. This cutting-edge screening approach, combined with our Targeted Protein Degradation Platform, will significantly enhance successful molecular glue drug discovery.

12:55 Session Break



8th Annual

Degraders & Molecular Glues — Part 1

Design, Delivery & Optimization of PROTACs and Glue Modalities

OPTIMIZING PROTEIN DEGRADERS & GLUES

1:45 Chairperson's Remarks

Robin Haid, PhD, Modeling & Simulation Expert, Preclinical Modeling & Simulation, Bayer AG

1:50 PK/PD Model–Guided Design of Targeted Protein Degraders and Quantitative Translation of *in vitro* Data to *in vivo* Degradation Profiles

Robin Haid, PhD, Modeling & Simulation Expert, Preclinical Modeling & Simulation, Bayer AG

We present a mechanistic PK/PD modeling framework specifically tailored to Targeted Protein Degraders. Our approach enables a priori predictions to (1) guide compound design & optimization, (2) inform animal study design, and (3) assist in candidate selection. To explore the full potential and requirements we'll draw on experiences with our in-house degrader pipeline. Impact and potential of the fully model-informed degrader development shall inspire the audience for their own work.

2:20 Mechanistic and Machine Learning Tools for the Development of Orally Bioavailable PROTACs

Dana Klug, PhD, Research Investigator, Medicinal Chemistry, Arvinas Inc.

Proteolysis-targeting chimera (PROTAC) protein degraders are heterobifunctional small molecules that recruit a protein of interest to an E3 ubiquitin ligase, leading to proteasomal degradation of the target protein. This presentation will: 1) provide an overview of PROTAC technology, including properties distinguishing PROTACs from other modalities and 2) discuss physicochemical property guidelines and machine learning models for attaining oral absorption in the beyond Rule of 5 space occupied by PROTACs.

2:50 Application of Mechanistic Multiparameter Optimization to Predict *in vivo* Pharmacokinetics of Molecular Glues

Lei Jia, PhD, Associate Director, Drug Discovery Data Science, Johnson & Johnson

Mechanistic modeling approaches have advantages to predict *in vivo* properties: they are based on physiological relevance and can support additional scalars such as safety margins and drug-drug interaction risk assessment; they are interpretable to guide molecular design; and are less likely to be influenced by human bias. This work incorporates recent approaches to predict *in vivo* PK properties and dose projection, and also validates *in vitro* to *in vivo* correlation.

3:20 *In Silico* Techniques to Design and Rank Degraders

Trung Kien Nguyen, Application Scientist, Solutions, Cresset

To improve the performance of heterobifunctional degraders, we present advances in our CADD platform that enable more precise and efficient discovery. We highlight the use of Spark™ for linker replacement in degraders, facilitating the exploration of analogous or novel ideas that may vary in composition and length. To precisely capture design impact, this virtual screening evaluates candidates based on a highly detailed description of electrostatics and shape. In addition to entire linker replacement, we also showcase a workflow that generates lead variants, each carrying only a single, small functional group change in the linker. This allows one to dissect the effect of each modification, enabling systematic lead optimization. To help triage variants, we demonstrate how Electrostatic Complementarity™ analysis uncovers clashes or matches with the target protein, arising from linker modifications. Finally, we outline how guided protein-protein docking and molecular simulations can further enhance the development of heterobifunctional degraders.

3:35 Grand Opening Refreshment Break in the Exhibit Hall with Poster Viewing and Best of Show Voting Begins

PLENARY KEYNOTE SESSION

4:35 Plenary Welcome Remarks from Lead Content Director

Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

4:50 PLENARY KEYNOTE: Applying Diverse Small Molecule Strategies to Difficult Targets: Drugging BTK for (Neuro)Immunology

Christopher J. Helal, PhD, Vice President & Head, Medicinal Chemistry, Biogen

Bruton's Tyrosine Kinase (BTK) plays a central role in certain cancers which has led to the identification and approval of several covalent inhibitors. Despite this progress, challenges exist in identifying BTK inhibitors with improved safety profiles and brain penetration to address both peripheral and central immunological diseases. In this talk we will share application of diverse strategies to inhibit or degrade BTK for optimal efficacy and safety.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:35 Close of Day

WEDNESDAY, APRIL 16

7:15 am Registration Open and Morning Coffee

DESIGNING MOLECULAR GLUES

8:00 Chairperson's Remarks

Maricel Torrent, PhD, Principal Research Scientist, Computational Drug Discovery, AbbVie, Inc.

8:05 Rational Molecular Glue Discovery Based on High-Throughput Screening for Novel Ligase-Target Pairs

Abhishek Dogra, Director, Medicinal Chemistry & Induced Proximity, A Alpha Bio Inc.

We describe the application of AlphaSeq, a high-throughput, highly sensitive experimental platform for measuring protein-protein interactions, to elucidate >100 novel interactions between therapeutically relevant targets and diverse set of ligases. We further characterize these PPIs through site-directed mutagenesis to prioritize actionable pairs for rational molecular glue discovery. Finally, we depict the systematic AlphaSeq validation and hit-finding approaches we have employed to identify small molecules that enhance these weak ligase-target interactions.

8:35 Prospective Discovery of Molecular Glues by High-Throughput Chemical Diversification

Michael Erb, PhD, Associate Professor, Department of Chemistry, The Scripps Research Institute

Molecular glues function by binding to a target and reconfiguring its surface to cooperatively engage another target. Motivated by the largely serendipitous nature of molecular glue discovery, we developed a high-throughput chemistry (HTC)-based approach to prospectively discover molecular glues. By systematically installing structural modifications onto a pre-existing ligand of interest, we can discover rare modifications that enable a ligand to function as a molecular glue.

9:05 Discovery of Highly Selective and Potent Casein Kinase 1a (CK1a) Degraders for the Treatment of Hematologic Malignancies

Weilin Xie, PhD, CEO, Innovo Therapeutics

Molecular glue degraders (MGD) represent a transformative class of small-molecule drugs that selectively degrade disease-driving proteins. The orally active CK1α MGDs show potent anti-tumor activity against AML and DLBCL

even in those with acquired genetic resistance to standard-of-care treatment. Our results highlight CK1α molecular glues as a promising class of anti-cancer agents.

9:35 Coffee Break in the Exhibit Hall with Poster Awards Announced

10:30 A Molecular Glue Degrader of HuR/ELAVL1 to Treat Debilitating Diseases

Yong Cang, PhD, Professor, ShanghaiTech University; Co-Founder & CSO, Degron Therapeutics

Leveraging induced proximity and degradation proteomics, we discovered a novel CRBN-based molecular glue degrader of HuR/ELAVL1, an RNA binding protein abnormally activated in cancer and other diseases. The MGD is moving to the clinics to treat BRAF mutant cancers as a monotherapy, while its efficacy in other disease models, including cancer cachexia, has been validated. The mechanistic studies of HuR degrader in these diseases are going to be discussed.

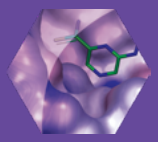
11:00 PANEL DISCUSSION: Session Speakers Share Insights on Discovery and Optimization of Molecular Glues

Moderator: Mary Matyskiela, PhD, Vice President, Molecular Sciences, Neomorph, Inc.

Topics to be discussed:

- Strategies to identify and screen molecular glues
- Value of serendipitous discovery versus rational design
- How to drive structure-activity relationships for molecular glues
- Design and screening of glue libraries in multiple assay formats

12:00 pm Close of Degraders – Part 1 Conference



20th Annual

Fragment-Based Drug Discovery

Towards Small Molecule Therapeutics from Smaller Hits on 'Difficult Targets'

6:00 pm MONDAY, APRIL 14: Dinner Short Course*

SC2: Fragment-Based Drug Design: Advancing Tools and Technologies

*Premium Pricing or separate registration required. See Short Courses page for details.

TUESDAY, APRIL 15

7:00 am Registration Open and Morning Coffee

FRAGMENT-BASED DRUG DISCOVERY (FBDD) BEST PRACTICES & INNOVATIONS

8:00 Welcome Remarks

8:05 Chairperson's Remarks

Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation

8:10 FEATURED PRESENTATION: From Fragments to Drugs: FBDD Tips for Success

Stephen W. Fesik, PhD, Professor of Biochemistry, Pharmacology & Chemistry; Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University

We've used Fragment-Based Drug Discovery (FBDD) for nearly 30 years and have had success in finding high affinity ligands for some of the most challenging targets. In this presentation, I will reveal the details of the methods, approaches, and best practices that we use in FBDD. Topics include: fragment libraries, screening methods, hit-to-lead fragment optimization, and structure-based design.

9:10 Poster Spotlight(s)

9:40 Breakout Discussions (In-Person Only)

Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 3: Covalent Drug Discovery

Giulia Alboreggia, PhD, Postdoctoral Fellow, Pellecchia Lab, University Of California Riverside

Maurizio Pellecchia, PhD, Professor, Biomedical Sciences Division, University of California, Riverside

In-Person Only BREAKOUT DISCUSSION 4: 25 Years and Counting – What Have We Learned so Far?

Dean G. Brown, PhD, Vice President & Head, Chemistry, Jnana Therapeutics

Mark Murcko, PhD, Principal, Disruptive Biomedical LLC

10:25 Networking Coffee Break

10:50 Next-Generation Fragment Screening: Revealing Hidden Insights through Parallel SPR Detection on Large Target Arrays

John Quinn, PhD, Distinguished Scientist, Biophysical Group, Biochemical and Cellular Pharmacology, Genentech

Transformative high-throughput SPR-based fragment screening over large target panels can now be completed in days rather than years, enabling rapid, cost-effective ligandability testing and general pocket finding. Unlike conventional single-target fragment screens, this new approach reveals fragment hit selectivity and allows affinity cluster mapping across many targets. This helps identify selective fragments driven by favorable enthalpic contributions which possess more development potential towards favorable drug-like leads.

11:20 Avidity-Aided Fragment Discovery and Maturation

Thomas Kodadek, PhD, Professor, Department of Chemistry, University of Florida, Scripps Biomedical Research

Protein-binding fragments represent an attractive starting point for drug development. However, due to the weak affinity of these complexes, methods for their discovery are limited. We present here a facile new approach for fragment discovery that leverages avidity effects between bead-displayed fragments and a multimeric target protein to stabilize these complexes and allow large libraries of bead-displayed fragments to be easily screened for binding to a protein of interest.

11:50 The Fragment-Based Discovery of Novel, Reversible, Pan-RAS Inhibitors

John Taylor, Group Leader, Medicinal Chemistry, Cancer Research Horizons

We describe the fragment-based discovery process behind a novel series of pan-RAS inhibitors, binding in the Switch I/II pocket. Through structure-enabled design, we develop these into a series of macrocyclic analogues, which effect inhibition of the RAS/RAF interaction and downstream phosphorylation of ERK. We will discuss some of the learnings gleaned from running a fragment screen against a target of this kind, and how best to follow up such hits.

12:20 pm Transition to Lunch

12:25 LUNCHEON PRESENTATION: F-SAPT: A Unique Quantum Chemistry Method to Quantify both the "What" and the "Why" of Intermolecular Interactions in Drug Design

QCWARE

Kirk Pearce, Director of Customer Success, QC Ware

In this presentation, we will examine F-SAPT (Functional-group Symmetry-Adapted Perturbation Theory), a powerful quantum chemistry method that provides unprecedented insight into protein-ligand interactions. Unlike traditional methods, F-SAPT not only quantifies the strength of interactions but also explains the why behind them by breaking down intermolecular interactions into their fundamental components. We will also discuss other common molecular design workflows such as conformer search, torsion scan, intrinsic reaction coordinate optimization, and transition state optimization. All of these methods, including F-SAPT, are implemented in Promethium, a high-performance quantum chemistry engine built to accelerate drug discovery research. Our user-friendly platform was designed for both computational chemists and non-specialists alike, allowing for more informed decisions throughout the entire molecular design process.

12:55 Session Break

FBDD-SPURRED PROGRESS

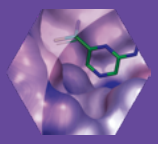
1:45 Chairperson's Remarks

Chaohong Sun, PhD, Senior Director, Target Enabling Technologies, AbbVie, Inc.

1:50 Discovery of Pyrazolocarboxamide RIP2 Kinase Inhibitors

Mark A. Elban, Scientific Leader, Discovery Chemistry, GSK

A fragment based screening and design program leading to the discovery of pyrazolocarboxamides as novel inhibitors of receptor interacting protein 2 kinase (RIP2). Fragment evolution, robust crystallography, and structure based



20th Annual

Fragment-Based Drug Discovery

Towards Small Molecule Therapeutics from Smaller Hits on 'Difficult Targets'

design were used to afford advanced pyrazolocarboxamides with excellent biochemical and whole blood activity and improved kinase selectivity enabling investigation of RIP2 inhibition as a viable modality for the treatment of inflammatory indications.

2:20 Identification and Development of Fragment-Derived Chemical Matter in Previously Unknown Allosteric Sites of WRN

Justyna Sikorska, PhD, Associate Principal Scientist, Mass Spectrometry & Biophysics, Merck

Werner Syndrome helicase (WRN) targets mismatch repair deficiency in cancer cells, making it a key target for MSI-H or MMRd tumors. In this presentation, we will describe the identification of a novel allosteric binding pocket using fragment-based screening. Moreover, we will discuss in more detail the chemical progression of one of the fragments hit and underscore the challenges faced in targeting this dynamic helicase.

2:50 Optimization of a Fragment Hit Yields ABBV-973, a Potent, Pan-Allele Small Molecule STING Agonist for Intravenous Administration

Andrew S. Judd, Medicinal Chemist, Abbvie

Optimization of a fragment hit yields ABBV-973, a potent, pan-allele small molecule STING agonist for intravenous administration.

3:20 Accelerating and Advancing Therapeutics with Biacore™ Insight Software 6.0

cytiva

Cynthia Shuman, Biacore & Reagents Field Application Specialist, Discovery & Medical, Cytiva

Accelerating drug discovery requires efficient and scalable data analysis. Biacore™ Insight Software 6.0, powered by Biacore Intelligent Analysis™, automates binding and affinity screening using machine learning, reducing analysis time by over 80% while enhancing reproducibility and flexibility. This session will explore how AI-driven automation, enhanced data integration, and advanced analytical tools streamline SPR workflows, enabling faster and more reliable therapeutic development.

3:35 Grand Opening Refreshment Break in the Exhibit Hall with Poster Viewing and Best of Show Voting Begins

PLENARY KEYNOTE SESSION

4:35 Plenary Welcome Remarks from Lead Content Director

Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

4:50 PLENARY KEYNOTE: Applying Diverse Small Molecule Strategies to Difficult Targets: Drugging BTK for (Neuro)Immunology

Christopher J. Helal, PhD, Vice President & Head, Medicinal Chemistry, Biogen

Bruton's Tyrosine Kinase (BTK) plays a central role in certain cancers which has led to the identification and approval of several covalent inhibitors. Despite this progress, challenges exist in identifying BTK inhibitors with improved safety profiles and brain penetration to address both peripheral and central immunological diseases. In this talk we will share application of diverse strategies to inhibit or degrade BTK for optimal efficacy and safety.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:35 Close of Day

WEDNESDAY, APRIL 16

7:15 am Registration Open and Morning Coffee

COVALENT APPROACHES FOR DRUG DISCOVERY

8:00 Chairperson's Remarks

Phillip Schwartz, PhD, Director, Biophysics, Septerna

8:05 FEATURED PRESENTATION: Unlocking Difficult-to-Drug Targets with Covalent Fragments

Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation

Frontier Medicines unites fragment-based and covalent drug discovery to unlock previously intractable targets. This presentation will describe how we apply Frontier's platform to important biological problems including validating a novel E3 ligase and finding leads against other challenging targets.

9:05 Expanding the Chemical Tractability of the Human Proteome

Christopher G. Parker, PhD, Associate Professor, Chemistry, Scripps Research Institute

In this talk, I will describe our lab's efforts to develop powerful photoaffinity-based chemical proteomic strategies to broadly map ligandable sites on proteins directly in cells, and how this information can be advanced into useful chemical probes for targets that play critical roles in human health and disease.

9:35 Coffee Break in the Exhibit Hall with Poster Awards Announced

10:30 Photo-Affinity Probes for Drug Discovery

Jarrett R. Remsberg, PhD, Senior Scientist I, Platform and Proteomics, Belharra Therapeutics

Belharra Therapeutics applies a novel chemistry-enabled non-covalent probe library and quantitative mass spectrometry to identify chemical probes that selectively bind any pocket, on any protein, in live cells. This next-gen chemoproteomics discovery engine identifies chemical probes that selectively engage diverse protein classes including transcription factors, adaptors, ion channels, and transporters, dramatically increasing the scope of the druggable proteome.

11:00 Histidine and Tyrosine Targeting for Covalent Fragment Discovery

Maurizio Pellecchia, PhD, Professor, Biomedical Sciences Division, University of California, Riverside

The design of covalent drugs targeting residues other than Cys, such as His, or Tyr, is gaining significant traction. I will discuss strategies and opportunities to design covalent ligands targeting those residues using both ligand-first structure-based design or covalent-fragment screening. I will present our successful implementations of both approaches.

11:30 Proteomic and Direct-to-Biology-Based Covalent-Fragment Discovery

Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

We introduce COOKIE-Pro (COvalent Occupancy KInetic Enrichment via Proteomics), a novel method for quantifying covalent inhibitor binding kinetics proteome-wide. The method accurately determines kinact and KI values using a desthiobiotin probe and mass spectrometry. By integrating direct-to-biology synthesis with COOKIE-Pro, we enabled rapid screening of covalent fragments without purification, generating high-confidence hits within days. This approach overcomes limitations of traditional methods and accelerates development of selective covalent therapeutics.

12:00 pm Close of Fragment Conference

7th Annual

AI/ML for Early Drug Discovery — Part 1

AI-Driven Drug Design and Lead Optimization for Small Molecule and Peptide Therapeutics

6:00 pm MONDAY, APRIL 14: Dinner Short Course*

SC3: Fundamentals of Generative AI for Drug Discovery

*Premium Pricing or separate registration required. See Short Courses page for details.

TUESDAY, APRIL 15

7:00 am Registration Open and Morning Coffee

ACCELERATING DRUG DISCOVERY USING AI/ML

8:00 Welcome Remarks

8:05 Chairperson's Remarks

Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

8:10 FEATURED PRESENTATION: A Quantum Leap from Physics to AI- 15 years of Transforming Drug Discovery

Jose Duca, PhD, Global Head Computer Aided Drug Discovery, Global Discovery Chemistry, Novartis Institutes for Biomedical Research Inc.

We will explore the transformative journey of drug discovery over the past 15 years, driven by advancements in AI, quantum mechanics, and physics-based methods. We will highlight the importance of creating a dry lab (Computer-Aided Drug Discovery, CADD group) grounded in physics and first principles, showcasing innovative techniques that have revolutionized drug design. Additionally, we will demonstrate how a relentless focus on delivering the portfolio has led to groundbreaking discoveries.

9:10 Accelerating Drug Discovery Success with Integrated Computational and Experimental Sciences

Douglas Kitchen, Head, Computational Chemistry, Curia

Curia was founded in 1992 and the Computer-assisted drug discovery group began in 1997. The CADD group has applied computational and cheminformatics calculations to dozens of projects as part of project teams from Curia and multiple drug discovery entities. We have found that the expert use of computational chemistry in collaboration with experimentalists leads to successful projects with the generation of novel chemical matter and preclinical leads. Several example projects will illustrate the use of virtual screening, traditional physics-based modeling, reaction modeling and library design in early drug discovery.

9:40 Breakout Discussions (In-Person Only)

Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 5: AI/ML for ADME/Tox and Safety Predictions

Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals, Inc.
Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.

In-Person Only BREAKOUT DISCUSSION 6: AI/ML for Hit Finding and Lead Optimization

Emily Hanan, Head, Medicinal Chemistry, PostEra
Dmitri Kireev, PhD, Professor, Department of Chemistry, University of Missouri
Ella Morishita, PhD, CSO, Veritas In Silico Inc.

10:25 Networking Coffee Break

10:50 Leveraging Organoid Models and AI for Drug Discovery in Women's Reproductive Health

Morgan Stanton, PhD, CEO, Opal Therapeutics

Opal Therapeutics is expanding its women's health discovery platform with a molecular modeling program focused on identifying and optimizing non-hormonal therapeutics. Built alongside our patient-derived uterine organoids and AI imaging tools, this in-progress effort will enable virtual screening and structure-based drug design for gynecological conditions like endometriosis and fibroids.

11:20 Leveraging Multiomics Data to Identify and Prosecute Targets Implicated in Women's Health

Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

Endometriosis and alternative sources of non-hormonal contraception are neglected and challenging issues associated with women's health. Today, I will discuss how we leverage multiomics data and AI to identify novel targets implicated in Endometriosis and how we contribute to the challenge of designing novel non-hormonal contraceptives using AI.

11:50 Tackling New Therapies for PCOS with Machine Learning–Accelerated Medicinal Chemistry

Emily Hanan, Head, Medicinal Chemistry, PostEra

PCOS impacts 1 in 10 women of reproductive age, yet has no specifically-approved therapeutics. In this heterogeneous endocrine disorder, androgen excess is linked to reproductive dysfunction and hirsutism. In our pursuit of novel therapies for PCOS, we have successfully applied our machine learning–driven medicinal chemistry platform to rapidly optimize a series of small molecules which affect the testosterone biosynthesis pathway, demonstrating *in vivo* reduction of testosterone with advanced leads.

12:20 pm Transition to Lunch

12:25 LUNCHEON PRESENTATION: Accelerating Drug Discovery with AI and Next-Generation Automation

Michael Bellucci, Sr Dir R&D, R&D, XtalPi Inc

In this presentation we will examine XtalPi's philosophy, which integrates AI with physics-based methods to achieve the goal of accurate and efficient exploration of chemical space. Our discussion will highlight the synergy between these computational strategies and how they contribute to more accurate predictions and streamlined drug development processes. Furthermore, we will introduce our cutting-edge automation platform, a beacon of innovation in automated chemical synthesis. Automated chemical synthesis is not only reshaping the landscape of drug discovery but also setting new standards for efficiency and innovation. Through multiple case studies, we will showcase our tailored approach to harnessing AI & Automation capabilities, illustrating how XtalPi's platform drives innovation and efficiency across specific drug discovery projects for our clients.

12:55 Session Break

SMALL MOLECULE DRUG DESIGN USING AI/ML

1:45 Chairperson's Remarks

Jose Duca, PhD, Global Head Computer Aided Drug Discovery, Global Discovery Chemistry, Novartis Institutes for Biomedical Research Inc.

1:50 AI/ML-Based Discovery of Novel 5-HT2A Receptor Agonists with Non-Hallucinogenic Potential

Tanweer A. Khan, PhD, Senior Director & Head, Discovery Chemistry, ATAI Life Sciences

We identified non-hallucinogenic 5-HT2AR agonists with antidepressant-like activity through AI-driven drug design. These molecules showed strong *in vitro* 5-HT2AR activation, high brain penetration in rodents, and antidepressant-like effects in behavioral and EEG tests without hallucinogenic responses.

7th Annual

AI/ML for Early Drug Discovery — Part 1

AI-Driven Drug Design and Lead Optimization for Small Molecule and Peptide Therapeutics

2:20 Using AI for mRNA-Targeted Small Molecule Drug Discovery: Tips, Tricks, and Pitfalls

Ella Morishita, PhD, CSO, Veritas In Silico Inc.

Discovering mRNA-targeted small molecule drugs presents challenges in identifying optimal targets and developing potent, specific modulators. This presentation will explore how advanced experimental tools and computational techniques, including AI, integrated within our ibVIS platform can enhance target identification, screening, hit-to-lead, and lead optimization. New data and effective strategies will be shared to advance drug discovery programs while avoiding potential pitfalls.

2:50 AI-Powered Hit Finding and Beyond

Dmitri Kireev, PhD, Professor, Department of Chemistry, University of Missouri

Lead discovery is shifting toward hard-to-drug targets, while fast-growing chemical spaces offer new hit-finding opportunities. Yet, technologies for exploiting vast spaces to identify leads against challenging targets are yet to emerge. We present our effort on addressing these challenges by enhancing our FRASE-bot platform to include 3D pharmacophore searches on multi-billion datasets, ABFE simulations, and new strategies for extracting from phenotypic data, with a focus on lead identification and optimization.

3:20 Uni-FEP: A high-accuracy and efficient free energy perturbation tool for drug discovery

Hang Zheng, Senior Researcher, Atombeat

Uni-FEP is an accurate and efficient alchemical free energy perturbation (FEP) tool designed for absolute and relative binding free energy calculations. It overcomes traditional FEP limits with improved force fields (RESP charges, QM-derived torsions) and enhanced sampling (adaptive lambda scheduling, Hamiltonian replica exchange, GCMC water sampling). The integrated platform streamlines setup, simulation, and analysis, supporting cloud/on-premises use. Benchmarked against Schrödinger, Merck, and 20+ patent cases, Uni-FEP shows high prediction accuracy, proving its reliability in drug design.

3:35 Grand Opening Refreshment Break in the Exhibit Hall with Poster Viewing and Best of Show Voting Begins

PLENARY KEYNOTE SESSION

4:35 Plenary Welcome Remarks from Lead Content Director

Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

4:50 PLENARY KEYNOTE: Applying Diverse Small Molecule Strategies to Difficult Targets: Drugging BTK for (Neuro)Immunology

Christopher J. Helal, PhD, Vice President & Head, Medicinal Chemistry, Biogen

Bruton's Tyrosine Kinase (BTK) plays a central role in certain cancers which has led to the identification and approval of several covalent inhibitors. Despite this progress, challenges exist in identifying BTK inhibitors with improved safety profiles and brain penetration to address both peripheral and central immunological diseases. In this talk we will share application of diverse strategies to inhibit or degrade BTK for optimal efficacy and safety.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:35 Close of Day

WEDNESDAY, APRIL 16

7:15 am Registration Open and Morning Coffee

DIVERSIFYING AI/ML APPLICATIONS

8:00 Chairperson's Remarks

Fred Manby, DPhil, Co-Founder & CTO, Iambic Therapeutics

8:05 Creating and Using Enchant, the Multi-Modal Transformer for Drug Discovery

Fred Manby, DPhil, Co-Founder & CTO, Iambic Therapeutics

Many companies have worked on laboratory automation to generate large volumes of high-quality data. At Iambic we have built Enchant—a multimodal transformer trained on dozens of modalities and data sources. It can be deployed on a huge range of highly relevant issues in drug discovery. Here we'll discuss what it took to create Enchant, and how we leverage this and other AI technologies in our drug discovery pipeline.

8:35 PANEL DISCUSSION: How Drug Discovery Applications Drive AI Innovations and Vice Versa

Moderator: Fred Manby, DPhil, Co-Founder & CTO, Iambic Therapeutics
Panelists:
Bryce Allen, PhD, Co-Founder & CEO, Differentiated Therapeutics
Jose Duca, PhD, Global Head Computer Aided Drug Discovery, Global Discovery Chemistry, Novartis Institutes for Biomedical Research Inc.
Brian Loyal, Principal Solutions Architect, Artificial Intelligence & Machine Learning, Amazon Web Services
Ashwini Ghogare, PhD, Executive Director and Head of AI & Automation for Drug Discovery, MilliporeSigma
Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

9:35 Coffee Break in the Exhibit Hall with Poster Awards Announced

10:30 Axiom: Towards Eliminating Small Molecule Toxicity with AI for Clinical Safety Assessment

Alex Beatson, CoFounder, AxiomBio Inc.

Toxicity causes many drug candidate failures and costs the industry billions of dollars each year. Axiom has built an AI system for clinical drug-induced liver injury risk assessment which is more accurate than existing *in vitro* assays. We screened >100k molecules in primary hepatocytes with high-content imaging and collected clinical data from thousands of trials. Our AI models trained across these data outperform *in vitro* assays on many clinical benchmarks at a fraction of the cost.

11:00 Applications of Machine Learning in Target-Based Drug Discovery

Sean Ekins, PhD, Founder & CEO, Collaborations Pharmaceuticals, Inc.

Collaborations Pharmaceuticals, Inc. is a small drug discovery company that has developed its own suite of machine learning tools. These technologies have been applied to various drug discovery (Glycogen Synthase Kinase 3 beta as well as Chemokine receptors CCR3, CCR4, and CCR5) and toxicology targets (steroidogenesis, seizure inducers) to build and validate models prior to screening drug or compound libraries and eventual *in vitro* testing with implications for human health.

11:30 AI/ML-Based Discovery of Novel Allosteric MALT1 inhibitors for the Treatment of Hematology Indications

Peter C. Ray, PhD, Executive Director, Drug Design, Recursion

MALT1 inhibition may have benefits for hematological malignancies, where MALT1 is constitutively activated, such as activated B-cell (ABC)-DLBCL, as a single agent or in combination with BCR signalling pathway modulators such as BTK inhibitors. Design of novel allosteric MALT1 inhibitors using MD, ML and AI generative design approaches will be described, leading to REC-3565 development candidate, with selectivity over UGT1A1, which distinguishes it from other MALT1 inhibitors in clinical development.

12:00 pm Close of AI/Machine Learning – Part 1 Conference

TUESDAY, APRIL 15

7:00 am Registration Open and Morning Coffee

GLP1, GIP1 PEPTIDE-BASED DRUG DESIGN & DEVELOPMENT

8:00 Welcome Remarks

8:05 Chairperson's Remarks
Hao Wu, PhD, Director of Chemistry, Pinnacle Medicines

8:10 Biased Agonism at GLP-1R and GIPR for Treating T2D and Obesity
Ruben Rodriguez, PhD, Senior Scientist, In Vitro Pharmacolgy, Carmot/Roche
Obesity and diabetes are major public health concerns. Incretin-like therapeutics have proven highly effective in treating both conditions and their associated complications. We are exploring the next generation of higher efficacy compounds through biased signaling of cAMP over ß-arrestin on both GLP-1R and GIPR. Our findings demonstrate that biased agonists provide longer-lasting glucose reduction, greater food intake suppression, and weight loss, highlighting their potential in treating these conditions.

8:40 Tuning Multi-Receptor Peptide Agonists through Molecular Design
Krishna Kumar, PhD, Professor, Chemistry, Tufts University
We describe here the design and development of potent peptide analogs that are completely refractory to hydrolytic enzyme action while retaining full biological activity, potency, and efficacy. This lecture will describe the fundamental design principles, molecular pharmacology, and *in vivo* data detailing, fine tuning such activity by simple chemical modification of peptides. Some of the compounds described rival or better those used in the clinic.

9:10 Advancing Obesity Drug Discovery from Bench to Bedside with Qualified Cell-based Assays for GLP-1 & Beyond
Gaurav Agrawal, Director of Scientific Applications, Market Dev & Scientific Applications, Eurofins DiscoverX
Obesity, a global chronic disease, has seen breakthroughs with GLP-1 and GIP therapeutics, sparking interest in next-generation drugs targeting additional receptors like glucagon, amylin, NPY2R, apelin, and others. This presentation highlights challenges and opportunities in obesity drug discovery, leveraging well-characterized assay solutions used to accelerate 100+ programs globally. We will explore pre-qualified functional assays — measuring cAMP, β-arrestin, and receptor internalization — for effective screening, characterization, and commercial development of obesity-related therapeutics.

9:40 Breakout Discussions (In-Person Only)
Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 7: Macrocyclic Peptides: Discovery to Delivery
Rumit Maini, PhD, Director - Business Development, Peplib

In-Person Only BREAKOUT DISCUSSION 8: Peptide Drug Conjugates (PDCs)
Avinash Muppidi, PhD, Director, Peptide Therapeutics, Eli Lilly & Co.
Keykavous Parang, PhD, Professor, Biomedical and Pharmaceutical Sciences, Chapman University

10:25 Networking Coffee Break

10:50 Novel Unimolecular Tetra-Agonists for the Treatment of Obesity and Related Disorders
Cristina M. Rondinone, PhD, Founder & CEO, Pep2Tango Therapeutics
We describe the characterization of a novel long-acting peptide agonist for GLP-1, GIP, Amylin, and Calcitonin Receptors, and assessed its efficacy against the dual GIPR/GLP-1R agonist Tirzepatide. Multiple metabolic endpoints were examined, including acute food intake and calcium regulation effects in lean rats, acute glucose-lowering effects in lean mice, and its chronic effects in diet-induced obesity (DIO) rats compared to Tirzepatide.

11:20 Supporting a Peptide Pipeline: Enabling Development of an Orally Bioavailable PCSK9 Inhibitor
Scott Pollack, PhD, Associate Principal Scientist, Merck & Co., Inc.
The growth of peptide-based programs in drug discovery, and in particular those developed through mRNA display, has required the parallel development of new chemistries to enable access to non-canonical amino acids (ncAAs) and ultimately macrocyclic peptides. We describe our efforts to prepare a novel orally bioavailable PSCK9 inhibitor and how these approaches can be used to enable other peptide programs.

11:50 PANEL DISCUSSION: Peptide Therapeutics Opportunities and Challenges
Moderator: Hao Wu, PhD, Director of Chemistry, Pinnacle Medicines
Panelists:
Tahnee J. Dening, PhD, Principal Scientist, Genentech Inc.
Katerina Leftheris, PhD, formerly Chief Scientific Officer, Vilya Therapeutics
Mark Murcko, PhD, Principal, Disruptive Biomedical LLC
Scott Pollack, PhD, Associate Principal Scientist, Merck & Co., Inc.

12:20 pm Enjoy Lunch on Your Own

SMALL MOLECULE & OTHER ANTI-OBESITY APPROACHES

1:45 Chairperson's Remarks
Robert D. Mazzola, PhD, Director & Principal Scientist, Chemical Research, Merck & Co.

1:50 Developing Small Molecule Agonists of GLP-1R and Other Obesity-Related Peptide-Binding GPCRs
Yingli Y. Ma, PhD, CTO, Platform Technology, Structure Therapeutics
I will present on the development of small molecule agonist versions of peptides that bind G protein-coupled receptors (GPCRs) such as GLP-1R that play a role in obesity

2:20 Discovery and Development of Orally Available GLP1 Receptor Small Molecule Agonist and Sensitizer
Jiayu Liao, PhD, Professor, Bioengineering, University of California, Riverside
Small molecule modulators for the GLP1 receptor offer complementary chemical tools and therapeutic agents as a novel mode of action. We pioneered the discovery and development of a non-peptide and orally available small molecule GLP1 receptor agonist and an utterly novel action of the GLP1 peptide sensitizer. This represents a novel opportunity for the GLP1 receptor and Class B GPCRs as therapeutics to treat metabolic diseases in the future.

2:50 The Promise of Synergistic Pharmacology: LY3457263, a Novel NPY2 Receptor Agonist for Type 2 Diabetes and Obesity
Avinash Muppidi, PhD, Director, Peptide Therapeutics, Eli Lilly & Co.
Nisotirostide is a novel NPY2 receptor agonist that enhances the effects of GLP-1 receptor agonists in T2D and obesity. Selective activation of NPY2 receptor signaling leads to significant reductions in food intake and body weight in mice. Chronic administration in obese mice resulted in dose-dependent weight loss and improved glucose homeostasis, suggesting its potential to improve glycemic control and reduce body weight in patients. Clinical evaluation is ongoing.

3:20 Poster Spotlight(s)

3:35 Grand Opening Refreshment Break in the Exhibit Hall with Poster Viewing and Best of Show Voting Begins

PLENARY KEYNOTE SESSION

4:35 Plenary Welcome Remarks from Lead Content Director
Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

4:50 PLENARY KEYNOTE: Applying Diverse Small Molecule Strategies to Difficult Targets: Drugging BTK for (Neuro)Immunology
Christopher J. Helal, PhD, Vice President & Head, Medicinal Chemistry, Biogen
Bruton's Tyrosine Kinase (BTK) plays a central role in certain cancers which has led to the identification and approval of several covalent inhibitors. Despite this progress, challenges exist in identifying BTK inhibitors with improved safety profiles and brain penetration to address both peripheral and central immunological diseases. In this talk we will share application of diverse strategies to inhibit or degrade BTK for optimal efficacy and safety.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:35 Close of Day

WEDNESDAY, APRIL 16

7:15 am Registration Open and Morning Coffee

MAKING ORAL PEPTIDES

8:00 Chairperson's Remarks
Anastasia Velentza, PhD, Vice President, Biology, Vilya Therapeutics

8:05 Development of Orally Available Cyclic Peptides
Manuel L Merz, PhD, Postdoctoral Fellow, Broad Institute
I present work completed in the Christian Heinis laboratory as part of my graduate studies where we developed synthesis and screening tools for generating large chemical libraries of small cyclic peptides, enabling the discovery of target-specific, orally bioavailable peptides. This generalizable workflow, applicable to interactions with a functional readout, yielded sub-1 kDa peptides with high-affinity binding to proteases and good oral bioavailability in rats.

8:35 Presentation to be Announced

9:05 Design of Bicyclic Peptide Tandems Mimicking the Homodimeric GDF15 Protein to Modulate the GDF15-GFRaL-RET Receptor Complex Cell Signaling
Anais FM Noisier, PhD, Associate Principal Scientist, AstraZeneca R&D
The GDF15-GFRaL-RET protein complex is involved in appetite control and is an attractive target for disease states such as obesity and cachexia. We describe the discovery of Bicycle peptides and the design of Bicycle tandems capable of mimicking the homodimeric GDF15 ligand and modulating the intracellular signaling response driven by the hexameric complex assembly.

9:35 Coffee Break in the Exhibit Hall with Poster Awards Announced

10:30 Formulation & Delivery Considerations in Early Drug Discovery for Oral Peptides
Tahnee J. Dening, PhD, Principal Scientist, Genentech Inc.
Although once considered highly infeasible, oral administration of peptide drugs is now a reality, as evidenced by oral semaglutide (Rybelsus) and oral octreotide (Mycapssa) drug products. In this presentation, we will discuss formulation strategies (and peptide design rules) to enable the oral absorption of both high solubility/low permeability peptides and low solubility/high permeability peptides, with an emphasis on early drug discovery.

11:00 Advancements in Peptide Late-Stage Functionalization for Drug Discovery
Jennifer Hanisak, Associate Principal Scientist, Peptide Chemistry, Merck & Co., Inc.
In macrocyclic peptide (MP) drug discovery, fine-tuning structural features and physical chemical properties is crucial for developing drug-like candidates. Commercial non-canonical amino acids (ncAAs) are of limited availability, making the discovery of novel ncAAs paramount. Late-stage functionalization (LSF) is an efficient strategy for identifying novel ncAAs but is restricted to chemistries compatible with MPs. This presentation will highlight some of our recent accomplishments in expanding the LSF toolbox for MPs.

11:30 Next-Generation, Orally Bioavailable, PD-L1-Targeted Macrocyclic Peptide
Paul M. Scola, PhD, Senior Director, Drug Discovery, Bristol Myers Squibb Co.
The discovery of BMS-986238, a second-generation macrocyclic peptide and a potent inhibitor of PD-L1, is described. The targeted profile of this asset included the property of tight binding kinetics to the PD-L1 receptor, but with a significantly modified pharmacokinetic profile and specifically a long plasma half-life. These properties were predicted to reduce the frequency of QD-dosing as compared to the first-generation inhibitor BMS-986189 and likewise enable oral administration.

12:00 pm Close of GLP1 & Oral Peptides Conference

Inaugural

Emerging Technologies for Discovery Chemistry

Covalent Approaches and New Biophysical Tools

6:00 pm MONDAY, APRIL 14: Dinner Short Course*

SC4: Detecting Target Engagement: Technology Innovations

*Premium Pricing or separate registration required. See Short Courses page for details.

TUESDAY, APRIL 15

7:00 am Registration Open and Morning Coffee

BIOPHYSICAL METHODS FOR LEAD GENERATION

8:00 Welcome Remarks

8:05 Chairperson's Remarks

Sujatha Gopalakrishnan, Director, Research Fellow, Head of HTS & Molecular Characterization, AbbVie

8:10 Affinity Selection-Mass Spectrometry (ASMS) for Drug Lead Generation

Hans-Peter N. Biemann, PhD, Distinguished Scientist, Integrated Drug Discovery, Sanofi

Affinity Selection-Mass Spectrometry (ASMS) identifies small molecule ligands for soluble and membrane proteins via a mass-encoded readout. Additionally, this binding assay approach enables compound competition binding assessments and binding site mapping with membrane proteins without purifying the target. This presentation reviews several applications across diverse ASMS platforms at distinct service labs, including studies with poorly ligandable proteins.

8:40 Implementation of an IR-MALDESI-Based ASMS Platform: Learnings from Screening and Affinity Ranking Applications

Nathaniel L. Elsen, PhD, Principal Research Scientist, Discovery, AbbVie, Inc.

Affinity Selection Mass Spectrometry (ASMS) has been implemented at AbbVie for screening, hit confirmation, and direct-to-biology applications. Learnings based on our particular ASMS method will be discussed and best use cases will be presented.

9:10 Unleashing the Power of Spectral Shift Technology for Ultra-High Throughput Binding Assays

Moran Jerabek-Willemsen, Head of Hit Identification & Profiling, WuXi AppTec/Crelux GmbH

High-throughput screening (HTS) is vital in drug discovery, yet traditional methods like biochemical assays and ASMS face potential limitations. We established a spectral shift-based direct binding assay that enhances precision, sensitivity, and efficiency while reducing sample consumption and turnaround time. This approach has been successfully applied in ultra HTS against targets such as kinase BTK, CDK2, PIK3CA, and transcription factor STAT6. Additionally, we developed a high-throughput method to determine Kinact/Ki for non-reversible interactions, offering superior sensitivity and throughput compared to traditional orthogonal methods, and showcased its application in characterizing covalent fragment binding to BTK.

9:40 Breakout Discussions (In-Person Only)

Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 10: New Technologies Targeting Membrane Proteins

Kris A. Borzilleri, Principal Scientist, Structural Biology & Molecular Sciences, Pfizer Global R&D, Groton Labs

Judith Reeks, PhD, Associate Director, Structural Biology, Astex Pharmaceuticals

In-Person Only BREAKOUT DISCUSSION 11: Hit Identification Strategies

Nathaniel L. Elsen, PhD, Principal Research Scientist, Discovery, AbbVie, Inc.

10:25 Networking Coffee Break

10:50 Discovering Functional Cryptic Allosteric Binding Pockets via a Novel Mass Spectrometry–Based Platform to Screen Cellular Metabolite and Fragment Libraries

Thomas Roddy, PhD, Senior Vice President, Platform Technology, Atavistik Bio

Cellular metabolites control many biological processes through direct interactions with proteins, including allosterically regulating many classes of proteins. We have developed technology using LC/MS-based metabolomics and an endogenous metabolite library to systematically discover functional allosteric pockets. These pockets enable an efficient drug discovery campaign using AI/ML-enabled structure-based drug design. This has been successfully accomplished several times, including for our oncology development candidate, which will be presented.

11:20 Large-Scale Screening of Drug Candidates from Multiple Modalities Using Biophysical Technologies in Early-Stage Drug Discovery

Arusha Acharyya, PhD, Senior Scientist, Mass Spectrometry & Biophysics, Merck & Co. Inc.

A diverse array of biophysical technologies has been pivotal in early-stage drug discovery, particularly the use of assays such as SPR, Fluorescence Spectroscopy, and AS/MS to assess molecular interactions, binding affinities, kinetics, and potential mechanisms of action for identifying potential drug candidates across different modalities. This presentation will highlight the effort to develop and optimize large-scale biophysical assays and industrial workflows to expedite hit validation and accelerate rational drug development.

11:50 First Disclosure of RIP1K Inhibitor Clinical Candidate's Chemical Structure: A 'Multiple Methods' Lead Generation Case Study

Domagoj Vucic, PhD, Principal Fellow, Immunology Discovery, Genentech

Receptor-interacting protein 1 (RIP1) kinase is a key mediator of TNF induced signaling pathways that regulate inflammatory responses, and the kinase activity of RIP1 has been implicated in tissue damage and numerous inflammatory and neurodegenerative diseases. GDC-8264 represents a novel class of RIP1 inhibitors, and it has great potency in cellular and animal inflammatory models, favorable safety, pharmacokinetics (PK), and pharmacodynamics (PD) in healthy volunteers.

12:20 pm Transition to Lunch

12:25 LUNCHEON PRESENTATION: Application of One-Bead-One-Compound (OBOC) DEL in Drug Discovery

Wenji Su, Executive Director, Early Discovery Platform, WuXi AppTec

Recently, solid-phase DEL, also known as one bead one compound (OBOC), has been developed to further expand DEL screening from affinity-based screening into biochemical activity screening. As a new add-on to the comprehensive early discovery platform, we present multiple application case studies of OBOC, including biochemical activity screening and traditional affinity screening. Our study demonstrates that OBOC technology could be used for wide-range of drug discovery scenarios.

12:55 Session Break

CRYO-EM & SPR FOR COMPLEX MEMBRANE PROTEINS

1:45 Chairperson's Remarks

Thomas P. Garner, PhD, Principal Scientist, Biophysics, Genentech, Inc.

1:50 Using CryoEM to Capture Multiple Activation States of an Orphan GPCR

Claire Metrick, PhD, former Senior Scientist, Structural Biology, Biogen

Inaugural

Emerging Technologies for Discovery Chemistry

Covalent Approaches and New Biophysical Tools

Class A GPCRs are small receptors that often lack an extracellular domain. GPCRs mediate physiological functions through ligand binding, and in orphan GPCRs these ligands are unidentified. GPCRs are attractive targets for indications from brain injury to obesity, but structural study has been hindered by their innate qualities. Here we present and compare novel structures of a class A orphan GPCR with bound ligand to inform mechanism and drug discovery.

2:20 Enabling High Throughput Electron Cryo-Microscopy for Structure-Based Design

Judith Reeks, PhD, Associate Director, Structural Biology, Astex Pharmaceuticals

Access to high resolution structural data on protein-ligand complexes is a prerequisite for structure-based drug design. For proteins refractory to X-ray crystallography, high throughput structure determination by cryo-EM has the potential to be transformational for medicinal chemistry. This talk will describe a workflow, from protein production through to high resolution structural data, applied to a biologically important ion channel target in complex with a chemically diverse range of ligands.

2:50 SPR-Microscopy for Detecting GPCR Target Engagement

Kris A. Borzilleri, Principal Scientist, Structural Biology & Molecular Sciences, Pfizer Global R&D, Groton Labs

Measuring direct binding and kinetics to membrane proteins has long been a challenge due to poor behavior of these targets when purified out of their native environments. Surface Plasmon Resonance Microscopy (SPRm), which combines optical microscopy with label-free SPR, allows for detection of binding in the whole cell environment. Using SPRm, we measured binding affinities on several targets that are in excellent agreement with radioligand binding and functional IC50 assays.

3:20 How Assessment of Cellular Target Engagement Accelerates Drug Discovery

PELAGO BIOSCIENCE
The home of CETSA®

Agata Habas, PhD, Project Advisor, Pelago Bioscience

Applications of CETSA in drug discovery:

- Primary screening with CETSA to tackle challenging targets without the need to modify the cell line, target, or the compound.
- Rapid and reliable hit confirmation enables certainty and early confidence in prioritization between your compounds or series.
- Unbiased selectivity profiling to identify liabilities earlier and select candidates with relevant biological efficacy.

3:35 Grand Opening Refreshment Break in the Exhibit Hall with Poster Viewing and Best of Show Voting Begins

PLENARY KEYNOTE SESSION

4:35 Plenary Welcome Remarks from Lead Content Director

Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

4:50 PLENARY KEYNOTE: Applying Diverse Small Molecule Strategies to Difficult Targets: Drugging BTK for (Neuro)Immunology

Christopher J. Helal, PhD, Vice President & Head, Medicinal Chemistry, Biogen

Bruton's Tyrosine Kinase (BTK) plays a central role in certain cancers which has led to the identification and approval of several covalent inhibitors. Despite this progress, challenges exist in identifying BTK inhibitors with improved safety profiles and brain penetration to address both peripheral and central immunological diseases. In this talk we will share application of diverse strategies to inhibit or degrade BTK for optimal efficacy and safety.

5:35 Welcome Reception in the Exhibit Hall with Poster Viewing

6:35 Close of Day

WEDNESDAY, APRIL 16

7:15 am Registration Open and Morning Coffee

COVALENT APPROACHES FOR DRUG DISCOVERY

8:00 Chairperson's Remarks

Phillip Schwartz, PhD, Director, Biophysics, Septerna

8:05 FEATURED PRESENTATION: Unlocking Difficult-to-Drug Targets with Covalent Fragments

Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation

Frontier Medicines unites fragment-based and covalent drug discovery to unlock previously intractable targets. This presentation will describe how we apply Frontier's platform to important biological problems including validating a novel E3 ligase and finding leads against other challenging targets.

9:05 Expanding the Chemical Tractability of the Human Proteome

Christopher G. Parker, PhD, Associate Professor, Chemistry, Scripps Research Institute

In this talk, I will describe our lab's efforts to develop powerful photoaffinity-based chemical proteomic strategies to broadly map ligandable sites on proteins directly in cells, and how this information can be advanced into useful chemical probes for targets that play critical roles in human health and disease.

9:35 Coffee Break in the Exhibit Hall with Poster Awards Announced

10:30 Photo-Affinity Probes for Drug Discovery

Jarrett R. Remsberg, PhD, Senior Scientist I, Platform and Proteomics, Belharra Therapeutics

Belharra Therapeutics applies a novel chemistry-enabled non-covalent probe library and quantitative mass spectrometry to identify chemical probes that selectively bind any pocket, on any protein, in live cells. This next-gen chemoproteomics discovery engine identifies chemical probes that selectively engage diverse protein classes including transcription factors, adaptors, ion channels, and transporters, dramatically increasing the scope of the druggable proteome.

11:00 Histidine and Tyrosine Targeting for Covalent Fragment Discovery

Maurizio Pellecchia, PhD, Professor, Biomedical Sciences Division, University of California, Riverside

The design of covalent drugs targeting residues other than Cys, such as His, or Tyr, is gaining significant traction. I will discuss strategies and opportunities to design covalent ligands targeting those residues using both ligand-first structure-based design or covalent-fragment screening. I will present our successful implementations of both approaches.

11:30 Proteomic and Direct-to-Biology-Based Covalent-Fragment Discovery

Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

We introduce COOKIE-Pro (COvalent Occupancy KInetic Enrichment via Proteomics), a novel method for quantifying covalent inhibitor binding kinetics proteome-wide. The method accurately determines kinact and KI values using a desthiobiotin probe and mass spectrometry. By integrating direct-to-biology synthesis with COOKIE-Pro, we enabled rapid screening of covalent fragments without purification, generating high-confidence hits within days. This approach overcomes limitations of traditional methods and accelerates development of selective covalent therapeutics.

12:00 pm Close of Emerging Technologies Conference

TUESDAY, APRIL 15, 2025, 8:00 AM-3:35 PM | WEDNESDAY, APRIL 16, 2025, 8:00 AM-12:00 PM

The Medicinal Chemistry-Pharmacology Interface: The 3 Independent SARs for New Drug Candidates

Training seminar takes place in-person only

Instructor:

Terrence P. Kenakin, PhD, Professor, Pharmacology, University of North Carolina at Chapel Hill

This training seminar will cover the three independent structure-activity-relationships (SARs) that must be satisfied for new drug success: (1) Primary Target Activity, (2) Pharmacokinetic Profile, and (3) Safety.

Day 1 (AM): SAR 1: Primary Target Activity

- Affinity: What concentrations are needed in the receptor compartment for target binding?
- Efficacy: How do drugs produce cellular response (drugs have many efficacies)? How the combination of signaling effects yields a 'quality' of efficacy to cells.

Day 1 (PM): SAR 1: Primary Target Activity (cont.)

- Efficacy/how biased-signaling causes complex patterns of efficacy (and how can this be manipulated?)
- Allosteric vs. orthosteric interaction of molecules: how allosteric interaction fundamentally differs from orthosteric (same site) interaction
- Kinetics of ligand interaction for *in vivo* target coverage: the importance of *in vivo*-restricted diffusion/ importance of receptor offset rates for target coverage (PK-PD dissociation)/methods to measure kinetics

Day 2 (AM): SAR 2-Pharmacokinetic Profile and SAR 3—Safety

- SAR 2 (ADME): Methods for modification of candidate ADME properties (modification of 'druglike' activity/specific modification of interactions with recognition processes (i.e., hepatic enzymes, transporters)
- SAR 3: Safety: Basic safety issues faced early on (cytotoxicity, hepatotoxicity, hERG, Ames test)/ translation of *in vitro* to *in vivo* activity

Beginning his career as a synthetic chemist, Terry Kenakin received a PhD in Pharmacology at the University of Alberta in Canada. After a postdoctoral fellowship at University College London, UK, he joined Burroughs-Wellcome as an associate scientist for 7 years. From there, he continued working in drug discovery for 25 years first at Glaxo, Inc., then Glaxo Wellcome, and finally as a Director at GlaxoSmithKline Research and Development laboratories at Research Triangle Park, North Carolina, USA. Dr. Kenakin is now a professor in the Department of Pharmacology, University of North Carolina School of Medicine, Chapel Hill. Currently he is engaged in studies aimed at the optimal design of drug activity assays systems, the discovery and testing of allosteric molecules for therapeutic application, and the quantitative modeling of drug effects. In addition, he is Director of the Pharmacology graduate courses at the UNC School of Medicine. He is a member of numerous editorial boards, as well as Editor-in-Chief of the *Journal of Receptors and Signal Transduction.* He has authored numerous articles and has written 10 books on pharmacology.

WEDNESDAY, APRIL 16, 2025, 1:30-5:45 PM | THURSDAY, APRIL 17, 2025, 10:15 AM-5:40 PM

Drug Exposure at the Target: The Role of ADME and Pharmacokinetics

Training seminar takes place in-person only

Instructor:

Erland Stevens, PhD, James G. Martin Professor, Department of Chemistry, Davidson College

This training seminar describes how pharmacokinetics (PK) affects drug exposure at the intended target. It opens with a foundation of clinical PK including the determination of key PK parameters from Cp-time data. It also covers common preclinical ADME assays that allow estimation of a compound's human PK properties. The materials bridge the idea of a compound's PK and its observed pharmacodynamic effects (PD) through coverage of PK/PD modeling.

Session 1

- Drug discovery—typical order of operations
- ADME and key pharmacokinetic parameters
- Modeling Cp-time curves from an IV dose
- Modeling Cp-time curves from an oral dose

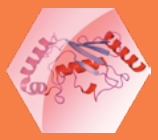
Session 2

- Oral drug space and membrane permeability
- Metabolic stability and intrinsic clearance
- Plasma, PPB, and the free drug hypothesis
- Compartment models

Session 3

- Pre-formulation and formulation
- Preclinical species and PBPK
- Non-small molecule drug modalities PK/PD modeling

Erland Stevens is formally trained as a synthetic organic chemist, with a PhD from the Department of Chemistry at the University of Michigan at Ann Arbor. He specialized in nitrogen heterocycle synthetic methodology. After completing his postdoctoral research at The Scripps Research Institute in La Jolla, CA, he joined the chemistry faculty at Davidson College in Davidson, NC. In addition to teaching organic chemistry, he created an undergraduate medicinal chemistry course and later published a textbook, *Medicinal Chemistry: The Modern Drug Discovery Process*, with Pearson Education. He then created an online medicinal chemistry course, which has been continuously revised and publicly available for approximately 10 years. He subsequently worked with Novartis to create additional online materials that are used with employees for continuing education purposes. He maintains an interest in the computational prediction of pharmacokinetic parameters based on structural features of drug-like structures.



8th Annual

Degraders & Molecular Glues — Part 2

Pursuing Diverse Targets, Exploring New Ligases and Degradation Pathways

WEDNESDAY, APRIL 16

12:00 pm Registration Open

EXPLORING NEW LIGASES

1:30 Welcome Remarks

1:35 Chairperson's Remarks

Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

1:40 Identification of Disulfide Constrained Peptide-Based Binders against Membrane Bound E3 Ubiquitin Ligases

Xinxin Gao, PhD, Principal Scientific Manager, Peptide Therapeutics, Genentech, Inc.

Disulfide constrained peptides (DCPs) show great potential as templates for drug discovery. We developed DCPs binding to membrane-bound E3 ubiquitin ligases. They can be used to develop strategies for targeted protein degradation at the plasma membrane. These DCPs can be produced synthetically or recombinantly, providing great versatility compared with large biologics or small molecules.

2:10 Targeting Tissue-Specific E3 Ligases

Stephen W. Fesik, PhD, Professor of Biochemistry, Pharmacology & Chemistry; Orrin H. Ingram II Chair in Cancer Research, Vanderbilt University

Only a handful of ligands are available for > 600 known E3 ligases. Using fragment-based methods and structure-based design, we have discovered ligands for additional E3 ligases that are tissue specific and are only present in cancer cells but not normal tissue. We are using these ligands to create less toxic PROTACS for cancer therapy.

2:40 Talk Title to be Announced

Sreekanth Rouduri , Vice President and Site Head, Integrated Drug Discovery , Jubilant Biosys Limited

2:55 Rediscovering Potential of Liposome in Advanced Drug Discovery in Oncology

Naoki Yamada, Dir & Head, Marketing & Strategy, FUJIFILM Pharmaceuticals, U.S.A., Inc.

Small molecules are a promising modality for anticancer drugs. The complicated design of advanced small molecules such as Targeted Protein Degrader (TPD) have inherited significant difficulties in biodistribution. The presenter will show how liposomes improve the biodistribution of small molecule drugs and discuss the potential of liposomes to create new value not only in traditional chemotherapy but also in the growing field of molecular targeted therapy and immunotherapy by presenting in-house data.

3:10 Breakout Discussions (In-Person Only)

Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 1: Novel Degradation Modalities, New E3 Ligases and Ligands

Gerald Crabtree, MD, David Korn Professor of Experimental Pathology & Developmental Biology, Stanford University
Daniel Nomura, PhD, Professor of Chemical Biology and Molecular Therapeutics, Department of Chemistry, University of California, Berkeley
Masoud Vedadi, PhD, Senior Scientific Advisor, Drug Discovery, Ontario Institute for Cancer Research

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Structural Insights into DCAF1 Substrate Specificity and Interaction with PROTACs

Masoud Vedadi, PhD, Senior Scientific Advisor, Drug Discovery, Ontario Institute for Cancer Research

Effectiveness of PROTACs necessitates addition of new substrate receptors and E3 ligases to avoid resistance. DCAF1 is a substrate receptor of EDVP and CUL4 E3 ligases with diverse substrate specificity. We will discuss structural insights into a mechanism by which DCAF1 could gain such diverse substrate specificity and describe why it could be a reliable and possibly better alternative to the commonly used E3 substrate receptors for development of PROTACs.

5:15 Proteomics-Enabled E3 Ligase Discovery

Angelo Andres, Senior Scientist, Chemical Biology, AstraZeneca Pharmaceuticals

Generating therapeutic targeting hypothesis for drugging proteins lacking traditional binding pockets is critical for tackling unprecedented targets. We describe a proximity labeling proteomics approach for revealing putative regulatory E3 ligases as a strategy-generating platform by targeting existing complexes via induced proximity. Furthermore, we discuss considerations for deploying this approach and bioinformatics strategies for increased confidence of putative hits.

5:45 Close of Day

5:45 Dinner Short Course Registration

6:15 Dinner Short Course*
SC5: Protein Degraders: An *in vivo* ADME and Safety Perspective

*Premium Pricing or separate registration required. See Short Courses page for details.

THURSDAY, APRIL 17

7:15 am Registration Open

7:45 Breakfast Small Group Discussions: Navigating Career Challenges

Grab a plate and seat (continental breakfast provided by Drug Discovery Chemistry) to talk about career challenges with fellow scientists at your table. This session is being offered in-person only (not recorded).

PLENARY KEYNOTE SESSION

8:30 Plenary Welcome Remarks from Lead Content Director

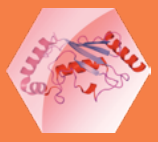
Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

8:40 PLENARY KEYNOTE: Simplifying Synthesis with Radicals

Phil Baran, PhD, Chair & Professor, Department of Chemistry, Scripps Research Institute

Our latest findings on how the use of radical cross-coupling can dramatically simplify the practice of medicinal chemistry will be presented through the invention of reactions that have wide-substrate scope, use ubiquitous starting materials, and are experimentally trivial to conduct.

9:25 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced



8th Annual

Degraders & Molecular Glues — Part 2

Pursuing Diverse Targets, Exploring New Ligases and Degradation Pathways

PROXIMITY & MOLECULAR GLUE STRATEGIES

10:15 Chairperson's Remarks

Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.

10:20 FEATURED PRESENTATION: Rewiring Cancer Drivers to Activate Programmed Cell Death Using Chemical Induced Proximity (CIP)

Gerald Crabtree, MD, David Korn Professor of Experimental Pathology & Developmental Biology, Stanford University

We are developing small molecules (TCIPs or SCIP for Transcriptional/ epigenetic or Signaling Chemical Inducers of Proximity) that rewire mutated cancer drivers to activate powerful and specific pathways of programmed cell death. TCIPs induce proximity of the cancer driver to the promoters of proapoptotic BH3-only genes, rapidly reversing their epigenetic repression and activating cell death. In PDX models they eliminate specific lymphomas without significant toxicity.

10:50 FEATURED PRESENTATION: Reimagining Druggability Using Chemoproteomic Platforms

Daniel Nomura, PhD, Professor of Chemical Biology and Molecular Therapeutics, Department of Chemistry, University of California, Berkeley

One of the greatest challenges that we face in discovering new disease therapies is that most proteins are considered "undruggable," in that most proteins do not possess known binding pockets or "ligandable hotspots" that small-molecules can bind to modulate protein function. Our research group addresses this challenge by advancing and applying chemoproteomic platforms to discover and pharmacologically target unique and novel ligandable hotspots for disease therapy.

11:20 Design and rapid synthesis of RIPK-2 degraders using an in-house partial PROTAC library

Gayathri Ramaswamy, PhD, Global Head, Discovery Services, Aurigene Pharmaceutical Services

Inhibition of RIPK2, a Ser/Thr/Tyr kinase has been shown to be therapeutically beneficial for certain types of cancers. However, its degradation through PROTACs or Molecular Glues is not well investigated. We built an in-house partial PROTAC library to rapidly generate PROTACs from selected E3-Ligase ligands, and assessed their solubility, permeability, and stability and RIPK2 degrader activity *in vitro*. We found that the new analogues had improved metabolic stability and demonstrated improved RIPK2 target engagement and potent inhibitory activity *in vitro*.

11:35 Targeting the Hippo Pathway in Cancers

Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.

TEAD transcription factors (TEAD1-4) play a key role in gene regulation but require YAP and TAZ as coactivators. Targeting the lipid pocket of TEAD enables inhibiting the oncogenic activities of the cofactors YAP and TAZ. We demonstrate the use of TEAD inhibitors in Hippo-driven *in vivo* tumor models and these represent a significant advancement towards potent, specific, and effective Hippo-targeting cancer therapies.

12:05 pm PANEL DISCUSSION: Session Speakers Share Feedback on Degradation Approaches for Transcription Factors

Moderator: Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.

12:35 Transition to Lunch

12:40 LUNCHEON PRESENTATION: HIT SYNERGY Platform: Building Successful Molecular Glue Hit ID Campaigns

Dr Stephen Young, VP Hit ID Technologies, Alliance Management, Sygnature Discovery Ltd

HIT SYNERGY is a powerful multi-technology platform for Hit ID which maximise chances to generate high quality hits for today's first in class targets. The presentation will demonstrate a number of methodologies capable of identifying both ligase specific and ligase agnostic degrader molecules. These methods include biophysical assays and cellular imaging assays and open the door to a systematic search for novel chemotypes that can induce biomolecular proximity and provide the starting point for a drug discovery program.

1:10 Dessert Break in the Exhibit Hall: Meet the VCs, Poster Prize Awarded and Book Raffle Winners Announced

1:35pm Poster Winner Announced & Prize Awarded
1:40 pm Book Raffle with Author Signings
(Book Raffle: during exhibit hall breaks until the raffle drawing, enter your name in raffle bins of associated drug discovery books for a chance to win a signed copy of the book. Winners must be present to win).

VENTURE CAPITALIST INSIGHTS

2:00 PLENARY PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation
Panelists:
James Edwards, PhD, Venture Partner, Samsara BioCapital
Seth Lieblich, PhD, Principal, 8VC
Swetha Murali, PhD, Vice President, OMX Ventures
Chris Smith, PhD, CSO Partner Team, Curie.Bio
Rachit Neupane, PhD, Life Sciences Investor, General Catalyst
Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

NOVEL INHIBITORS & DEGRADERS OF TRANSCRIPTION FACTORS

2:50 Chairperson's Remarks

Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation

2:55 Orally Bioavailable Selective SMARCA2 Degraders for Cancer Therapy

Susanta Samajdar, PhD, CSO, Aurigene Discovery Technologies Ltd.

Genetic-silencing studies have established that the oncogenic activity of tumors lacking SMARCA4 is primarily driven by SMARCA2-containing residual SWI/SNF complex, suggesting the importance of inhibiting SMARCA2. Although a few PROTAC degraders have been reported in the literature, they either lack adequate selectivity or oral bioavailability. We identified an exquisitely selective and highly potent orally bioavailable degrader of SMARCA2.

3:25 Biophysical and Structural Characterization of the Molecular Glue-Mediated Interaction of Transcription Factors with Cereblon

Charles Wartchow, PhD, Associate Director, Global Discovery Chemistry, Novartis Institutes for BioMedical Research

Transcription factors are known to bind to cereblon in the presence of molecular glues and some reports implicate interactions with multiple zinc fingers. We present biophysical and structural assessments of the minimal binding domains of IKZF2 and other transcription factors, revealing

that multiple zinc fingers interact with cereblon:glue complexes. In these examples, the binding modes are distinct and may have implications for the design of selective degraders.

3:55 Networking Refreshment Break

4:10 Development of Degrader Antibody Conjugates as Double Precision Anticancer Therapeutics

Jin Wang, PhD, Director, Biochemistry and Molecular Pharmacology, Baylor College of Medicine

Development of Degrader Antibody Conjugates (DACs) represents a novel therapeutic modality combining antibody specificity with targeted protein degradation. Our DAC has a GSPT1 molecular glue as the payload, enabling selective protein degradation in cancer cells. Different linker chemistries were compared for GSPT1 degradation efficiency and cellular potency. This dual-targeting approach demonstrates potent anti-tumor activity with improved therapeutic window compared to traditional ADCs.

4:40 Application of Biophysical Methods for Molecular Glue Discovery and Characterization

Alexandra Frommlet, Scientist, Biochemical and Cellular Pharmacology, Biophysics Group, Genentech Inc.

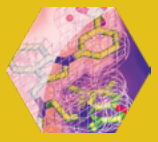
The application of biophysical methods in the discovery of molecular glue degraders will be presented. By leveraging techniques such as Surface Plasmon Resonance and Spectral Shift assays and putting emphasis on ternary complex affinity and kinetic characterization, novel molecular glues to an important oncology target protein have been identified and validated.

5:10 CG-SLENP: From Protein Labeling to PROTAC Therapeutic Opportunities

Xiangshu Xiao, PhD, Professor, Chemical Physiology & Biochemistry, Oregon Health & Science University

PROTACs are an emerging class of therapeutics for many disease areas including oncology. We recently developed a novel chemical genetics-based method to selectively label existing proteins and newly synthesized proteins (CG-SLENP) in living cells. Using this method, we found that existing proteins and newly synthesized proteins have drastically different responses to small molecule inhibitors and PROTACs. We further found that combining PROTACs and small molecule inhibitors show synergistic anticancer activities.

5:40 Close of Conference



18th Annual

Protein-Protein Interactions

Macrocyclic & Small Molecule Drug Leads Against Intracellular Protein Complexes

APRIL 16-17, 2025

WEDNESDAY, APRIL 16

12:00 pm Registration Open

CELL-PERMEABLE MACROCYCLICS FOR PPI TARGETS

1:30 Welcome Remarks

1:35 Chairperson's Remarks
Katerina Leftheris, PhD, formerly Chief Scientific Officer, Vilya Therapeutics

1:40 Macrocyclic Cell-Permeable Peptide Inhibitors of Cyclin A/B RxL: A New Class of Targeted Anti-Cancer Agents
James B. Aggen, PhD, Vice President of Medicinal Chemistry, Circle Pharma
I discuss a permeable-first strategy to evolve a macrocyclic peptide PPI hit into a cell-active lead. It is the first *in vivo* demonstration of cyclin A/B RxL inhibitors as a new class of targeted anti-cancer agents.

2:10 Macrocyclic Peptides Inhibiting Intracellular Protein-Protein Interaction Targets
Christian Heinis, PhD, Associate Professor, Lab of Therapeutic Proteins & Peptides, EPFL Lausanne
We have developed methods for nanoscale chemical synthesis and high-throughput screening of combinatorial libraries of tens of thousands of small, non-polar cyclic peptides that can passively cross membranes. After initial proof-of-concept screens against proteases, we have applied the approach to intracellular protein-protein interaction targets and recently identified cell-active inhibitors.

2:40 Poster Spotlight(s)

3:10 Breakout Discussions (In-Person Only)
Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 2: Emerging Technologies for Addressing PPIs
Rick Ewing, PhD, Vice President and Head of Chemistry, Rapafusyn Pharmaceuticals

In-Person Only BREAKOUT DISCUSSION 3: Biophysical Tools for Targeting PPIs
Elisa Barile, PhD, formerly Associate Director, Head of Biophysics, Takeda, San Diego
Phillip Schwartz, PhD, Director, Biophysics, Septerna

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

INNOVATIVE APPROACHES FOR DIFFICULT TARGETS

4:45 A Platform for Allosteric Drug Discovery Targeting Protein-Protein Interactions: Focus on BCL-2 Family Proteins
Evris Gavathiotis, PhD, Professor, Biochemistry, Albert Einstein College of Medicine
We have developed an integrated computational and experimental methodology to identify allosteric sites and inhibitors of protein-protein interactions, specifically applied to select BCL-2 family proteins. My talk will highlight various structural, biochemical, and cellular methods used to uncover novel allosteric binding sites, providing insights into their functional relevance. I will particularly focus on the discovery of allosteric inhibitors targeting the anti-apoptotic BCL-XL protein, which holds therapeutic potential in modulating apoptosis.

5:15 Targeting the Secretory Translocon (Sec61) to Selectively Eliminate Extracellular Proteins: A New Therapeutic Strategy for Prion Disease
Jennifer Pitzen, PhD, Associate Director, Chemistry, Gate Bioscience
Molecular Gates are small molecules designed to eliminate disease-causing extracellular proteins by targeting their origin inside cells. By binding to the secretory translocon, these drugs create a "gate" that disrupts the protein's journey, leading to its degradation. This novel mechanism offers a new therapeutic approach for diseases that are difficult to treat. We are developing selective, orally administered Molecular Gates that lower prion protein for the treatment of prion disease.

5:45 Close of Day

5:45 Dinner Short Course Registration

6:15 Dinner Short Course*
SC8: Principles of Drug Design: Ligand-Receptor Interactions and More

*Premium Pricing or separate registration required. See Short Courses page for details.

THURSDAY, APRIL 17

7:15 am Registration Open

7:45 Breakfast Small Group Discussions: Navigating Career Challenges
Grab a plate and seat (continental breakfast provided by Drug Discovery Chemistry) to talk about career challenges with fellow scientists at your table. This session is being offered in-person only (not recorded).

PLENARY KEYNOTE SESSION

8:30 Plenary Welcome Remarks from Lead Content Director
Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

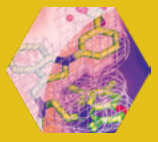
8:40 PLENARY KEYNOTE: Simplifying Synthesis with Radicals
Phil Baran, PhD, Chair & Professor, Department of Chemistry, Scripps Research Institute
Our latest findings on how the use of radical cross-coupling can dramatically simplify the practice of medicinal chemistry will be presented through the invention of reactions that have wide-substrate scope, use ubiquitous starting materials, and are experimentally trivial to conduct.

9:25 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

PPI STABILIZERS/ACTIVATORS/GLUES (NON-DEGRADING)

10:15 Chairperson's Remarks
Michelle Arkin, PhD, Chair and Distinguished Professor, Pharmaceutical Chemistry & Director, Small Molecule Discovery Center, University of California, San Francisco

10:20 Mechanism of Activation by Sub-Stoichiometric Base-Exchange Inhibition of the SARM1 Octameric Complex
Soo Ro, PhD, Senior Scientist I, Biophysics, Genentech Inc.
SARM1 is a highly oligomeric NAD hydrolase implicated in neuronal cell death after injury. Well established small molecules exist that inhibit SARM1 activity, via a base-exchange (BE) mechanism that prevents further hydrolysis. Here, we present extensive MOA characterization of BE dependent SARM1 inhibition via biophysical and biochemical methods, in addition to discovery of unexpected SARM1 activation driven by sub-stoichiometric binding of BE inhibitors.



18th Annual

Protein-Protein Interactions

Macrocyclic & Small Molecule Drug Leads Against Intracellular Protein Complexes

10:50 p97/VCP and High-Throughput Protein Conformation Studies

Chad Altobelli, Graduate Student, Michelle Arkin Laboratory, Chemistry & Chemical Biology, University of California, San Francisco

VCP/p97 is a homohexameric AAA+ ATPase that is directed by more than 30 adaptor proteins to unfold a broad range of cellular targets, mediating their degradation. Our lab seeks to direct biology by developing conformational modulators of VCP that can stabilize interactions with subsets of adaptor proteins that share a conformational preference. To enable this project, we have engineered tools that report on VCP structure using changes in FRET efficiency.

11:20 Sponsored Presentation *(Opportunity Available)*

11:35 Non-Degrading Molecular Glues: Application and Case Studies towards Hard-to-Drug Targets

Rick Ewing, PhD, Vice President and Head of Chemistry, Rapafusyn Pharmaceuticals

A large amount of the proteome remains undrugged. Rapafuysn's platform of non-degrading molecular glues is uniquely positioned to target intracellular proteins and the cytosolic side of transmembrane proteins. RapaGlues takes advantage of the exclusively cytosolic-residing FKBP12 to form ternary complexes with disease-target proteins. The presentation will describe successful hit campaigns for hard to drug targets and the strategy used for optimizing ADME properties to give drug-like molecules.

12:05 pm Targeting the Oncogenic State of RAS with Tri-Complex Inhibitors

Jingwei Yin, PhD, Scientist II Medicinal Chemistry, Discovery Chemistry, Revolution Medicines

We designed a series of tri-complex small molecule inhibitors targeting the GTP-bound, active state of RAS (RAS(ON)). The inhibitors bind non-covalently to abundant intracellular protein, cyclophilin A (CypA) which then selectively engages RAS(ON) and sterically prevents RAS interacting with its downstream effectors. We also describe mutant selective inhibitors that covalently engage RAS(ON) G12C, G13C and G12D respectively. Our RAS(ON) multi-selective inhibitors can also inhibit variants of KRAS, NRAS, and HRAS.

12:35 Enjoy Lunch on Your Own

1:10 Dessert Break in the Exhibit Hall: Meet the VCs, Poster Prize Awarded and Book Raffle Winners Announced

1:35pm Poster Winner Announced & Prize Awarded
1:40 pm Book Raffle with Author Signings
(Book Raffle: during exhibit hall breaks until the raffle drawing, enter your name in raffle bins of associated drug discovery books for a chance to win a signed copy of the book. Winners must be present to win).

VENTURE CAPITALIST INSIGHTS

2:00 PLENARY PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation
Panelists:
James Edwards, PhD, Venture Partner, Samsara BioCapital
Seth Lieblich, PhD, Principal, 8VC
Swetha Murali, PhD, Vice President, OMX Ventures
Chris Smith, PhD, CSO Partner Team, Curie.Bio
Rachit Neupane, PhD, Life Sciences Investor, General Catalyst
Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

DEGRADER APPROACHES FOR KRAS

2:50 Chairperson's Remarks

Heike Wobst, PhD, Director, Pharmacology, Jnana Therapeutics

2:55 KRAS—Degrading the Undruggable

Martin Schmiedel, PhD, Principal Scientist I, Medicinal Chemistry, Boehringer Ingelheim

The KRAS protein, mutated in 20% of human cancers, was long considered undruggable. Recent breakthroughs led to the first KRAS G12C inhibitors, but need still persists for targeting other mutations. In collaboration with the Ciulli group we identified ACBI3, a KRAS degrader with high potency against a variety of KRAS mutations *in vitro* and *in vivo*. These promising preclinical results mark a significant stride towards broad-spectrum KRAS-targeting modalities.

3:25 Discovery and Development of Pan-KRAS Degraders for Cancer Therapy

Murali Ramachandra, PhD, CEO, Aurigene Oncology Ltd.

KRAS mutations are among the most prevalent and challenging targets in cancer. While only the KRAS G12C mutation currently has clinically approved therapies, there is a critical need for effective and durable treatments across all KRAS-driven cancers. We will present our success in identifying a development candidate that degrades all tested KRAS mutants, showcasing its potential as a promising therapeutic strategy for cancer treatment.

3:55 Networking Refreshment Break

COVALENT KRAS INHIBITORS

4:10 Discovery of FMC-376 a Potent Dual Inhibitor of 'ON' and 'OFF' States of KRASG12C Broadly Active in PDX Models of Resistance

Snahel Patel, Vice President, Head, Medicinal & Platform Chemistry, Frontier Medicines Corp.

Once viewed undruggable, frequently mutated oncogene KRAS has led to the recent approval of two $KRAS^{G12C}$ small molecule covalent inhibitors targeting the inactive GDP-bound (OFF) state. Patient benefit has fallen short with these first-generation inhibitors due to innate or acquired resistance driven by upregulation of the activated GTP-bound (ON) state of $KRAS^{G12C}$. We present the discovery of potent dual inhibitor FMC-376 targeting both active and inactive forms of $KRAS^{G12C}$.

4:40 Novel KRAS Inhibitors from Covalent DNA-Encoded Library Screening

Jingjing Xie, PhD, Senior Scientist, Chemistry, Amgen

Covalent inhibition of the KRASG12C oncoprotein has emerged as a promising therapeutic approach for the treatment of NSCLC. A covalent DEL screening was designed to screen approximately 16 million chemically diverse compounds against KRASG12C. The hit identification through this efficient screening followed by structure-based optimization allows for the discovery of a series of structurally novel, potent, and selective covalent inhibitors of KRASG12C with good pharmacokinetic profiles and promising pharmacodynamic effects.

5:10 Tyrosine-Targeted Covalent Fragments for KRAS

Samy O. Meroueh, PhD, Professor, Biochemistry; Member, Cancer Center Drug Discovery Program, University of Illinois Urbana-Champaign

I present my Ras GTPases (mainly Ral and KRAS) work where I used fragment-screening to develop covalent inhibitors that react with tyrosines. A tyrosine-based covalent approach expands the number of KRAS-origin cancers that can be targeted because only 10% of KRAS genes have the G12C mutation. I also discuss our progress with covalent inhibition of Ral GPTase using tyrosine and will present a unique KRAS structure that I recently published.

5:40 Close of Conference

7th Annual

AI/ML for Early Drug Discovery — Part 2

AI/ML for Exploring and Screening Complex Target Biology and Chemical Space

WEDNESDAY, APRIL 16

12:00 pm Registration Open

AI/ML FOR PEPTIDE & ANTIBODY OPTIMIZATION

1:30 Welcome Remarks

1:35 Chairperson's Remarks
Ewa Lis, PhD, Founder & CEO, Koliber Biosciences

1:40 Peptide Hit Discovery and Optimization Using Machine Learning and Small Peptide Arrays
Ewa Lis, PhD, Founder & CEO, Koliber Biosciences
Standard peptide discovery methods like phage and mRNA display face issues like high false positives or costly licensing, limiting therapeutic advances. We introduce a platform merging Koliber's machine learning with RobustDx's peptide arrays, showing that large libraries are unnecessary and hits can be optimized to nanomolar binding affinity. Additionally, we present visualization techniques for binding mode detection and offer insights into the future of ML-driven peptide optimization.

2:10 AlphaBind, a Domain-Specific Model to Predict and Optimize Antibody-Antigen Binding Affinity
Ryan Emerson, PhD, Vice President, Data Science, A Alpha Bio Inc.
We present AlphaBind, a domain-specific model achieving state-of-the-art performance in optimizing antibody affinity using protein language model embeddings and extensive pre-training. We demonstrate affinity optimization for four antibodies with just one round of training data generation per antibody, and we demonstrate the use of a fine-tuned AlphaBind model to guide downstream engineering for biodevelopability and germline reversion for one antibody. AlphaBind weights and code are publicly available.

2:40 Leveraging Predictive ML ADMET Models and Generative Chemistry to Identify Novel Leads in Open-Science Drug Discovery
Speaker to be Announced, MilliporeSigma
In collaboration with the Drugs for Neglected Diseases initiative (DNDi), we used predictive ML ADMET models via the AIDDISON™ software to profile compounds from a lead series in an open-science anti-Chagas drug discovery program. The goal was to identify scaffold hopping opportunities with improved druglike properties to advance this crucial program. Using top-scoring compounds from a multi-parameter ADMET profile, we conducted a pharmacophore search of ultra-large, virtual chemical space and ran generative chemistry calculations to discover promising new leads.

2:55 Cloud databases & screening for virtual drug discovery
Janice Darlington, Scientist, Customer Engagement, Collaborative Drug Discovery Inc
CDD Vault's intuitive, web-based platform has helped scientists centralize and analyze their data over the last 20+ years. Biologists and chemists use it to register entities, track inventory, record experiments and even calculate structure activity relationships. Granting you the agency to standardize and structure your data, to not only eliminate bottlenecks and help you optimize resources, CDD Vault leverages the latest AI machine learning capabilities today. A recently released proprietary AI tool to help you discover lead compounds is amongst the latest offerings brought to you in one seamless intuitive platform. Covering how collaboration works in CDD Vault's ecosystem and how new ideas can be generated in your virtual drug discovery efforts will be the focus of the high level overview of the CDD Vault platform.

3:10 Breakout Discussions (In-Person Only)

Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 4: AI-driven Drug Design, Screening and Optimization
Ruben Abagyan, PhD, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego
Peter Canning, PhD, Principal Scientist, Protein & Structural Sciences, CHARM Therapeutics
Alexander Taguchi, PhD, Director, Machine Learning, Antibody Discovery, iBio, Inc.

In-Person Only BREAKOUT DISCUSSION 5: How Successful are AI/ML Approaches in Drug Development Today?
Bryce Allen, PhD, Co-Founder & CEO, Differentiated Therapeutics
Ryan Emerson, PhD, Vice President, Data Science, A Alpha Bio Inc.
Leif Eriksson, PhD, Professor, Chemistry & Molecular Biology, University of Gothenburg

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Generative Protein Design for Overcoming Immune Tolerance in Antibody Discovery
Alexander Taguchi, PhD, Director, Machine Learning, Antibody Discovery, iBio, Inc.
Immunizations for antibody discovery are often unproductive when the antigen exhibits high sequence homology with the host. We overcome this immune tolerance problem with a generative protein design platform, enhancing the immune response against the antigen of interest. Using this approach, we showcase how this technology can generate antibodies against various targets including Activin E, a 97% homologous human target that has remained intractable to traditional methods.

5:15 PANEL DISCUSSION: Session Speakers Discuss the Future of AI/ML-Driven Peptide/Antibody Design and Optimization
Moderator: Ewa Lis, PhD, Founder & CEO, Koliber Biosciences

5:45 Close of Day

5:45 Dinner Short Course Registration

6:15 Dinner Short Course*
SC7: AI Applications in Drug Development: Strategies for Innovation and Integration

*Premium Pricing or separate registration required. See Short Courses page for details.

THURSDAY, APRIL 17

7:15 am Registration Open

7:45 Breakfast Small Group Discussions: Navigating Career Challenges
Grab a plate and seat (continental breakfast provided by Drug Discovery Chemistry) to talk about career challenges with fellow scientists at your table. This session is being offered in-person only (not recorded).

PLENARY KEYNOTE SESSION

8:30 Plenary Welcome Remarks from Lead Content Director
Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

7th Annual

AI/ML for Early Drug Discovery — Part 2

AI/ML for Exploring and Screening Complex Target Biology and Chemical Space

8:40 PLENARY KEYNOTE: Simplifying Synthesis with Radicals

Phil Baran, PhD, Chair & Professor, Department of Chemistry, Scripps Research Institute

Our latest findings on how the use of radical cross-coupling can dramatically simplify the practice of medicinal chemistry will be presented through the invention of reactions that have wide-substrate scope, use ubiquitous starting materials, and are experimentally trivial to conduct.

9:25 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

AI-BASED SCREENING FOR TARGETS & LEADS

10:15 Chairperson's Remarks

Ruben Abagyan, PhD, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego

10:20 Ultrafast Screening and Optimization in Allosteric Pockets with 3D/AI-CPU/GPU Pipeline: Flavivirus Proteases and More

Ruben Abagyan, PhD, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego

Finding the first potent and selective inhibitors against a transient, allosteric, or protein-protein interaction pocket is a challenge requiring multiple levels of data, tools, profile definitions, and ultra large screens combined with *in silico* compound optimization. We present a cloud-based CPU/GPU pipeline designed for that purpose and its application for identifying drug candidates among multibillion compounds. Examples with anti-cancer targets and inhibitors of anti-flaviviral proteases are presented.

10:50 Novel AI-Based Methods for Ultra-Large and Ultra-Fast Virtual Screening in Drug Discovery

Leif Eriksson, PhD, Professor, Chemistry & Molecular Biology, University of Gothenburg

The druglike chemical space of available molecular databases contains ~10^{10} molecules, and grows faster than traditional screening approaches can handle. We present benchmarked methods that circumvent conformational sampling, enabling ultra-large and ultra-fast screening, including a novel AI-based scoring function, generative AI, and scaffold optimization. We also report on a data-driven molecular descriptor model using Neural Machine Translation, for effectively predicting protonation states, performing similarity searches, and generating molecular derivatives.

11:20 Supercharge computational drug discovery with AI-powered serverless high-performance computing (HPC)

Fengbo Ren, CEO, Computer Science & Engineering, Fovus Corp

Fovus is an AI-powered, serverless high-performance computing (HPC) platform delivering intelligent, scalable, and cost-efficient supercomputing power at the computational scientists' fingertips. Fovus uses AI to optimize HPC strategies and orchestrates cloud logistics, making cloud HPC a no-brainer and ensuring sustained time-cost optimality for computational drug discovery amid quickly evolving cloud infrastructure. By accelerating time-to-insights and optimizing cloud costs, Fovus helps Biotech clients accelerate Design-Make-Test-Analyze (DMTA) cycles and discover more with less. Join this talk to learn how Fovus can supercharge your computational drug discovery with case studies and GROMACS/AlphaFold 3 benchmarking results.

11:35 AI-Driven Virtual Screening and Polypharmacology Analysis

Sita Sirisha Madugula, PhD, Postdoctoral Research Associate, Center for Nanophase Materials Sciences, Oak Ridge National Laboratory

Our research demonstrates the potential of AI and machine learning in drug repurposing, specifically for tuberculosis (TB). Through unsupervised learning and polypharmacology approaches, we identified FDA-approved drugs with potential for repurposing by analyzing molecular descriptors and multi-target interactions. These methods offer efficient pathways to explore chemical and biological spaces, providing new insights into drug efficacy and paving the way for therapeutic solutions in infectious and non-infectious diseases.

12:05 pm PANEL DISCUSSION: Session Speakers Discuss Strategies for Exploring Chemical and Biological Spaces Using AI/ML Tools

Moderator: Ruben Abagyan, PhD, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego

12:35 Transition to Lunch

12:40 LUNCHEON PRESENTATION: Beyond Hit ID: Transforming DEL Data Complexity into Powerful Drug Discovery Solutions

Erin Davis, CTO, X-Chem, Inc.

DNA-encoded libraries (DELs) have transformed drug discovery, enabling novel modulator identification across diverse targets. However, DEL data complexity requires high-quality signal-to-noise for AI/ML to extract meaningful insights. This talk explores how X-Chem's 15 years of DEL data and bespoke ML approaches enhance hit selection and structure-function mapping, unlocking new opportunities in drug discovery through real-world case studies.

1:10 Dessert Break in the Exhibit Hall: Meet the VCs, Poster Prize Awarded and Book Raffle Winners Announced

1:35pm Poster Winner Announced & Prize Awarded
1:40 pm Book Raffle with Author Signings
(Book Raffle: during exhibit hall breaks until the raffle drawing, enter your name in raffle bins of associated drug discovery books for a chance to win a signed copy of the book. Winners must be present to win).

VENTURE CAPITALIST INSIGHTS

2:00 PLENARY PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation
Panelists:
James Edwards, PhD, Venture Partner, Samsara BioCapital
Seth Lieblich, PhD, Principal, 8VC
Swetha Murali, PhD, Vice President, OMX Ventures
Chris Smith, PhD, CSO Partner Team, Curie.Bio
Rachit Neupane, PhD, Life Sciences Investor, General Catalyst
Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

CHALLENGES INTEGRATING DIVERSE DATA

2:50 Chairperson's Remarks

2:55 Harmonizing Diverse Data Types and Sources for Drug Discovery and Machine Learning

Peter Canning, PhD, Principal Scientist, Protein & Structural Sciences, CHARM Therapeutics

DragonFold is CHARM therapeutics' state-of-the-art co-folding platform for prediction of ligand-bound protein structures. Evidence has shown that the functional performance of many ML models improves with target-specific training data. We have established a platform to collect and organize various internal and external data sources to inform drug discovery projects and train ML models for improved output confidence.

3:25 AI Methods to Integrate Multi-Modal Omics, Spatial, and Single-Cell Profiling to Identify Mechanisms and Potential Therapeutic Opportunities

Arvind Rao, PhD, Associate Professor, Department of Computational Medicine and Bioinformatics, University of Michigan

Spatial profiling technologies coupled with scRNAseq enable a multi-factorial, multi-modal characterization of the tissue microenvironment. Objective scoring methods inspired by recent advances in statistics and ML can aid the interpretation of these datasets, as well as their integration with companion data like bulk and single-cell genomics. I will discuss analysis paradigms from ML that can be used to integrate and prioritize gene regulatory programs (and therapeutic candidates) underlying oncogenesis.

3:55 Networking Refreshment Break

MACHINE-LEARNING & DNA-ENCODED LIBRARY TECHNOLOGY

4:10 Machine Learning for 3D-Aware Molecular Representations in DEL

Angelina Heyler, Data Scientist, Encoded Libraries, GSK

DNA-encoded libraries (DELs) enable screening billions of ligands against protein targets of interest. To select hits for off-DNA evaluation, quantitative structure-activity relationship (QSAR) modeling is frequently used to find structural features that contribute to enrichment. However, current QSAR typically relies on 2D molecular representations. We leverage machine learning to learn 3D molecular representations for application in hit selection.

4:40 Ligandability of WDR-Containing Proteins Using DEL Then ML

Peter J. Brown, PhD, Chemical Probes, University of North Carolina at Chapel Hill

Target class–focused drug discovery has a strong track record in pharmaceutical research, yet public domain data indicate that many protein families remain unliganded. Here we present a systematic approach to scale up the discovery and characterization of small molecule ligands for the WD40 repeat (WDR) protein family using DNA-encoded chemical library selection followed by machine learning (DEL-ML). Our campaign yielded first-in-class ligands for 7 of the 16 WDR domains screened.

5:10 DELs in Medicinal Chemist's Toolbox: Applications beyond Hit Discovery

Kirill Novikov, PhD, Principal Scientist, High Throughput Chemistry, insitro

We employ targeted second-generation DELs for efficient exploration of chemical space surrounding hit structures. By employing affinity-based electrophoretic separations, we can rank DEL members, facilitating early structure-activity relationship (SAR) hypothesis formation and machine-learning model training to refine predictive accuracy in this chemical environment.

5:40 Close of Conference

7th Annual

DNA-Encoded Libraries

Expanding Chemical Space for Small Molecule-Based Drug Discovery

WEDNESDAY, APRIL 16

12:00 pm Registration Open

DNA-ENCODED LIBRARIES (DEL) & MOLECULAR DEGRADER DISCOVERY

1:30 Welcome Remarks

1:35 Chairperson's Remarks

Christopher B. Phelps, PhD, Vice President and Head, Early Discovery, Nurix Therapeutics, Inc.

1:40 Phenotypic DEL in Droplets for TPD and Beyond

Ken Yamada, PhD, Associate Director, Global Discovery Chemistry, Novartis BioMedical Research

This talk will describe microfluidics-enabled cellular phenotypic DEL workflow—MicDrop. We will introduce cellular DEL screen in droplets, followed by results from a cellular protein degradation screen with a validation library, as well as another set of screens with a prospective library. Our results show the benefits of bead replicates and how this new paradigm of DEL screen can accelerate the field of molecular glue discovery for TPD and beyond.

2:10 A "Low Tech" Platform for Activity-Based Screens of DNA-Encoded Libraries & Applications to Molecular Glue Discovery

Thomas Kodadek, PhD, Professor, Department of Chemistry, University of Florida, Scripps Biomedical Research

There is considerable interest in the development of platforms for screening DNA-encoded libraries (DELs) functionally, that is for agonists or antagonists of a given process. The only existing methods require specialized microfluidics infrastructure. We present here a "low tech" platform that allows one-bead-one-compound DELs to be screened for compounds capable of mediating various post-translational modifications, including poly-Ubiquitylation, of a protein of interest.

2:40 DEL Platforms at HitGen: New Developments and Applications to Small Molecule Drug Discovery

HITGEN

Alex Shaginian, PhD, MBA, VP of BD and Chemical Sciences, HitGen Inc.

DNA-Encoded Library (DEL) technology presents a disruptive hit identification platform that can vastly expedite the course of early-stage small molecule drug discovery. HitGen is a world and market leader in the development and practice of the DEL technology and has over 500 DEL clients worldwide. A comprehensive overview of HitGen's key DEL platforms, some novel on-DNA chemistries recently developed by HitGen with applications to construction of new libraries, and several representative DEL screening success stories will be presented.

3:10 Breakout Discussions (In-Person Only)

Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 6: Incorporating Machine Learning into DEL Campaigns

Jeff A. Messer, Director, Analytics, Encoded Libraries Technology, GlaxoSmithKline

In-Person Only BREAKOUT DISCUSSION 7: DEL Screening Technology

Ching-Hsuan Tsai, PhD, Executive Director, Structure Therapeutics

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Talk Title to be Announced

Kerem Ozboya, PhD, Scientist, Medicinal Chemistry, Nurix Therapeutics Inc

5:15 Bridging the DEL Divide: A Cross-Pharma Library Building Consortium

Sylvie K. Sakata, PhD, Executive Director & Head, External Research Solutions, Pfizer Inc.

I will give an overview about the recently created DEL Consortium and present the advantages and learnings it provides on pre-competitive collaboration in the pharma industry.

5:45 Close of Day

5:45 Dinner Short Course Registration

6:15 Dinner Short Course*

SC9: DNA-Encoded Libraries

*Premium Pricing or separate registration required. See Short Courses page for details.

THURSDAY, APRIL 17

7:15 am Registration Open

7:45 Breakfast Small Group Discussions: Navigating Career Challenges

Grab a plate and seat (continental breakfast provided by Drug Discovery Chemistry) to talk about career challenges with fellow scientists at your table. This session is being offered in-person only (not recorded).

PLENARY KEYNOTE SESSION

8:30 Plenary Welcome Remarks from Lead Content Director

Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

8:40 PLENARY KEYNOTE: Simplifying Synthesis with Radicals

Phil Baran, PhD, Chair & Professor, Department of Chemistry, Scripps Research Institute

Our latest findings on how the use of radical cross-coupling can dramatically simplify the practice of medicinal chemistry will be presented through the invention of reactions that have wide-substrate scope, use ubiquitous starting materials, and are experimentally trivial to conduct.

9:25 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

DNA-ENCODED LIBRARY INNOVATIONS

10:15 Chairperson's Remarks

Carol Mulrooney, PhD, Investigator, Cheminformatics, GlaxoSmithKline

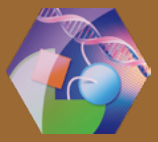
10:20 Activity-Based DEL at the Limit of Detection

Brian M. Paegel, PhD, Professor, Pharmaceuticals Sciences, University of California, Irvine

I will discuss our progress toward further miniaturizing and automating the split-and-pool synthesis of solid-phase DELs and a new microfluidics-free approach to activity-based and cellular DEL screening.

10:50 On-DNA Binder Confirmation: Increasing Confidence in DEL Hits

Karli Holman, PhD, Investigator (Encoded Technologies Lead Discovery Chemistry), GSK



7th Annual

DNA-Encoded Libraries

Expanding Chemical Space for Small Molecule-Based Drug Discovery

DEL hits have traditionally been evaluated via off-DNA resynthesis and biological testing. This approach can be time- and resource-intensive, limiting the number of putative hits selected for follow-up, and hits often fail to confirm off-DNA. On-DNA hit resynthesis increases throughput and emulates the original library synthesis, enabling identification of side product binders. Here we share GSK's application of on-DNA binder confirmation to evaluate and expand hits from DEL screens.

11:20 Poster Spotlight(s)

11:35 Enhancing Lead Discovery Using Target-Focused DNA-Encoded Chemical Libraries

Srinivas Chamakuri, PhD, Assistant Professor, Pathology & Immunology, Baylor College of Medicine

DNA-Encoded Chemistry Technology is a cost-effective, rapidly advancing platform designed to identify drug-like molecules with high-affinity binding to target proteins. Instead of constructing DELs aimed at broadly modulating various targets, our approach initiates with a specific target in mind, creating a smaller, tailored DEL to enhance precision. This targeted library design improves the quality and possibility of positive hits by leveraging structural and binding insights specific to the target protein.

12:05 pm Case Studies Comparing Screening Small vs. Large DNA-Encoded Libraries

Timothy L. Foley, PhD, Senior Principal Scientist & Lab Head, DNA Encoded Library Selection & Pharmacology, Pfizer Global R&D Groton Labs

I will present a platform-science based 'lessons learned' talk from two case studies of screening 'small' and 'big' DEL libraries. The presentation emphasizes the importance of library size and chemical diversity.

12:35 Enjoy Lunch on Your Own

1:10 Dessert Break in the Exhibit Hall: Meet the VCs, Poster Prize Awarded and Book Raffle Winners Announced

1:35pm Poster Winner Announced & Prize Awarded
1:40 pm Book Raffle with Author Signings
(Book Raffle: during exhibit hall breaks until the raffle drawing, enter your name in raffle bins of associated drug discovery books for a chance to win a signed copy of the book. Winners must be present to win).

VENTURE CAPITALIST INSIGHTS

2:00 PLENARY PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation
Panelists:
James Edwards, PhD, Venture Partner, Samsara BioCapital
Seth Lieblich, PhD, Principal, 8VC
Swetha Murali, PhD, Vice President, OMX Ventures
Chris Smith, PhD, CSO Partner Team, Curie.Bio
Rachit Neupane, PhD, Life Sciences Investor, General Catalyst
Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

DEL-ORIGIN COMPOUNDS

2:50 Chairperson's Remarks

Jack D. Scott, PhD, Director, Discovery Chemistry, Merck & Co.

2:55 From DNA-Encoded Library Screening to AM-9747: An MTA-Cooperative PRMT5 Inhibitor with Potent Oral *in vivo* Efficacy

Ian Sarvary, PhD, Principal Scientist, Chemistry, Amgen

MTAP-deleted cancers accumulate of MTA, partially inhibits PRMT5, creating a vulnerability. We identified AM-9959, a side product of DEL91, bound to the PRMT5:MEP50+MTA complex, forming an inhibitory ternary complex. Subsequent optimization of AM-9959 led to AM-9747. AM-9747 selectively inhibited PRMT5 dimethylation, thereby reducing viability in MTAP-deleted cells. AM-9747 was well tolerated and effectively inhibited arginine dimethylation and tumor growth in MTAP-deleted tumors without impacting the growth of MTAP-WT tumors.

3:25 Evaluating the Reliability of DNA-Encoded Library Data: Using PARP Enzymes as Model System

Raphael Franzini, PhD, Assistant Professor, Medicinal Chemistry, University of Utah

DNA-encoded libraries (DELs) not only offer developable hits but provide insights into molecule-target interactions. However, the reliability of DEL data for predicting active compounds remains uncertain. Using a focused DEL and poly(ADP-ribose) polymerases as models, we found that while hits are mostly active, false negatives are prevalent, likely because of constraints caused by DNA attachment. This presentation outlines the implications for computational methods relying on DEL data for activity prediction.

3:55 Networking Refreshment Break

MACHINE-LEARNING & DNA-ENCODED LIBRARY TECHNOLOGY

4:10 Machine Learning for 3D-Aware Molecular Representations in DEL

Angelina Heyler, Data Scientist, Encoded Libraries, GSK

DNA-encoded libraries (DELs) enable screening billions of ligands against protein targets of interest. To select hits for off-DNA evaluation, quantitative structure-activity relationship (QSAR) modeling is frequently used to find structural features that contribute to enrichment. However, current QSAR typically relies on 2D molecular representations. We leverage machine learning to learn 3D molecular representations for application in hit selection.

4:40 Ligandability of WDR-Containing Proteins Using DEL Then ML

Peter J. Brown, PhD, Chemical Probes, University of North Carolina at Chapel Hill

Target class–focused drug discovery has a strong track record in pharmaceutical research, yet public domain data indicate that many protein families remain unliganded. Here we present a systematic approach to scale up the discovery and characterization of small molecule ligands for the WD40 repeat (WDR) protein family using DNA-encoded chemical library selection followed by machine learning (DEL-ML). Our campaign yielded first-in-class ligands for 7 of the 16 WDR domains screened.

5:10 DELs in Medicinal Chemist's Toolbox: Applications beyond Hit Discovery

Kirill Novikov, PhD, Principal Scientist, High Throughput Chemistry, insitro

We employ targeted second-generation DELs for efficient exploration of chemical space surrounding hit structures. By employing affinity-based electrophoretic separations, we can rank DEL members, facilitating early structure-activity relationship (SAR) hypothesis formation and machine-learning model training to refine predictive accuracy in this chemical environment.

5:40 Close of Conference

3rd Annual

Drugging Transcription Factors & Regulators

Small Molecules to Pursue TFs, Chromatin Remodelers, Epigenetic Regulators, Co-Factors

WEDNESDAY, APRIL 16

12:00 pm Registration Open

CHEMOPROTEOMICS STRATEGIES FOR TARGETING TRANSCRIPTION

1:30 Welcome Remarks

1:35 Chairperson's Remarks
Alexander Federation, PhD, Co-Founder & CEO, Talus Bioscience

1:40 Chemoproteomic Strategies for Developing Transcription Factor Modulators
Andrew Wang, PhD, Director of Platform, Belharra Therapeutics
Targets such as transcription factors are often challenging to study in recombinant or biochemical settings as they require native cellular localization, PTMs, and complexation to fold and function properly. Applying our proprietary chemoproteomics platform, Belharra has enabled ligand discovery campaigns in live cells which have uncovered tractable ligands for TFs important in disease pathology. Several examples of these ligand discovery and development efforts will be discussed.

2:10 Redirecting the Pioneering Function of FOXA1 with Covalent Small Molecules
Michael Won, PhD, Postdoctoral Associate, Laboratory of Dr. Benjamin Cravatt, Department of Chemistry, The Scripps Research Institute
Pioneer transcription factors (TFs) bind to and open closed chromatin, facilitating engagement by other regulatory factors involved in gene activation or repression. We present the chemical proteomic discovery of covalent small molecules that stereoselectively and site-specifically engage the pioneer TF, FOXA1. These compounds rapidly remodel FOXA1 interactions with chromatin in prostate cancer cell and create corresponding changes in chromatin accessibility through relaxing the DNA-binding preferences of FOXA1.

2:40 Accelerating Novel Target Hit Discovery with 1536-Well Plate Cell-Based HTS and HTC Direct to Biology Platform
药明康德 WuXi AppTec
Weihui Guo, Head of High Throughput Screen, WuXi AppTec
This study focuses on the utilization of a fully integrated 1536-well plate cell-based high-throughput screening (HTS) and HTC Direct to Biology (D2B) platform to accelerate novel target hit discovery. By screening 620K diversity libraries, we aim to identify novel hits targeting transcription factors. The adoption of the 1536-well format significantly enhances screening throughput, allowing for the rapid evaluation of large compound libraries against selected novel targets. The D2B platform streamlines the transition from hit identification to biological validation, providing real-time data integration and minimizing lead optimization time.

3:10 Breakout Discussions (In-Person Only)
Breakout Discussions are informal, moderated discussions, allowing participants to exchange ideas and experiences and develop future collaborations around a focused topic. Each breakout will be led by a facilitator/s who keeps the discussion on track and the group engaged. Please visit the Breakout Discussions page on the conference website for a complete listing of topics and descriptions. Breakout Discussions are offered in-person only.

In-Person Only BREAKOUT DISCUSSION 8: Leveraging Covalent Chemistries, Chemoproteomics Tools for Transcription Factors and Undruggable Targets
Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.
Alexander Federation, PhD, Co-Founder & CEO, Talus Bioscience

3:55 Refreshment Break in the Exhibit Hall with Poster Viewing

4:45 Small-Molecule Covalent Stabilization and Inhibition of TEAD•YAP1 Transcription Factor Activity in Cancer Cells
Samy O. Meroueh, PhD, Professor, Biochemistry; Member, Cancer Center Drug Discovery Program, University of Illinois Urbana-Champaign
Here we report acrylamide small molecules that form a covalent bond with a conserved cysteine at the TEAD palmitate pocket. Binding studies showed profound stabilization of TEADs by the small molecules, and co-crystal structures reveal that the compounds mimic the binding mode of palmitate. In mammalian cells, the compounds stabilize the TEAD• YAP1 interaction yet reduce TEAD and YAP1 protein levels and inhibit TEAD transcription factor activity.

5:15 AI-Guided Discovery of Covalent Inhibitors for Intrinsically Disordered Transcription Factors
Alexander Federation, PhD, Co-Founder & CEO, Talus Bioscience
Strategian, a deep tensor factorization model built on Talus Bio's TF-Scan platform, enables discovery of TF-targeted therapeutics by predicting compound effects on TF activity across billions of drug-like molecules. Predicted TF inhibitors are confirmed in TF-Scan, which profiles compound-TF interactions in a native context. The model prioritizes candidates by potency and selectivity, followed by triage in TF-Scan. We identified novel scaffolds for STAT3, and direct inhibitors of IRF5.

5:45 Close of Day

5:45 Dinner Short Course Registration

6:15 Dinner Short Course*
SC6: Chemical Biology for Covalent Drug Discovery, Phenotypic Screening, and Target Deconvolution

*Premium Pricing or separate registration required. See Short Courses page for details.

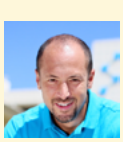
THURSDAY, APRIL 17

7:15 am Registration Open

7:45 Breakfast Small Group Discussions: Navigating Career Challenges
Grab a plate and seat (continental breakfast provided by Drug Discovery Chemistry) to talk about career challenges with fellow scientists at your table. This session is being offered in-person only (not recorded).

PLENARY KEYNOTE SESSION

8:30 Plenary Welcome Remarks from Lead Content Director
Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute



8:40 PLENARY KEYNOTE: Simplifying Synthesis with Radicals
Phil Baran, PhD, Chair & Professor, Department of Chemistry, Scripps Research Institute
Our latest findings on how the use of radical cross-coupling can dramatically simplify the practice of medicinal chemistry will be presented through the invention of reactions that have wide-substrate scope, use ubiquitous starting materials, and are experimentally trivial to conduct.

9:25 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

3rd Annual

Drugging Transcription Factors & Regulators

Small Molecules to Pursue TFs, Chromatin Remodelers, Epigenetic Regulators, Co-Factors

PROXIMITY & MOLECULAR GLUE STRATEGIES

10:15 Chairperson's Remarks

Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.

10:20 FEATURED PRESENTATION: Rewiring Cancer Drivers to Activate Programmed Cell Death Using Chemical Induced Proximity (CIP)

Gerald Crabtree, MD, David Korn Professor of Experimental Pathology & Developmental Biology, Stanford University

We are developing small molecules (TCIPs or SCIP for Transcriptional/epigenetic or Signaling Chemical Inducers of Proximity) that rewire mutated cancer drivers to activate powerful and specific pathways of programmed cell death. TCIPs induce proximity of the cancer driver to the promoters of proapoptotic BH3-only genes, rapidly reversing their epigenetic repression and activating cell death. In PDX models they eliminate specific lymphomas without significant toxicity.

10:50 FEATURED PRESENTATION: Reimagining Druggability Using Chemoproteomic Platforms

Daniel Nomura, PhD, Professor of Chemical Biology and Molecular Therapeutics, Department of Chemistry, University of California, Berkeley

One of the greatest challenges that we face in discovering new disease therapies is that most proteins are considered "undruggable," in that most proteins do not possess known binding pockets or "ligandable hotspots" that small-molecules can bind to modulate protein function. Our research group addresses this challenge by advancing and applying chemoproteomic platforms to discover and pharmacologically target unique and novel ligandable hotspots for disease therapy.

11:20 Design and rapid synthesis of RIPK-2 degraders using an in-house partial PROTAC library

Gayathri Ramaswamy, PhD, Global Head, Discovery Services, Aurigene Pharmaceutical Services

Inhibition of RIPK2, a Ser/Thr/Tyr kinase has been shown to be therapeutically beneficial for certain types of cancers. However, its degradation through PROTACs or Molecular Glues is not well investigated. We built an in-house partial PROTAC library to rapidly generate PROTACs from selected E3-Ligase ligands, and assessed their solubility, permeability, and stability and RIPK2 degrader activity *in vitro*. We found that the new analogues had improved metabolic stability and demonstrated improved RIPK2 target engagement and potent inhibitory activity *in vitro*.

11:35 Targeting the Hippo Pathway in Cancers

Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.

TEAD transcription factors (TEAD1-4) play a key role in gene regulation but require YAP and TAZ as coactivators. Targeting the lipid pocket of TEAD enables inhibiting the oncogenic activities of the cofactors YAP and TAZ. We demonstrate the use of TEAD inhibitors in Hippo-driven *in vivo* tumor models and these represent a significant advancement towards potent, specific, and effective Hippo-targeting cancer therapies.

12:05 pm PANEL DISCUSSION: Session Speakers Share Feedback on Degradation Approaches for Transcription Factors

Moderator: Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.

12:35 Transition to Lunch

12:40 Finding druggable transcription factors: a data-driven journey from identification to small-molecule synthesis

Eric Gilbert, Consultant, Life Sciences, Elsevier Inc

Finding druggable targets that directly or indirectly modulate Transcription Factors can be a challenge. Once target and candidate small molecule lead compounds have been identified, further challenges can be finding a viable synthetic route and to assess potential off-target effects. We present methods and high-quality data sources that can facilitate the drug discovery journey.

1:10 Dessert Break in the Exhibit Hall: Meet the VCs, Poster Prize Awarded and Book Raffle Winners Announced

1:35pm Poster Winner Announced & Prize Awarded
1:40 pm Book Raffle with Author Signings
(Book Raffle: during exhibit hall breaks until the raffle drawing, enter your name in raffle bins of associated drug discovery books for a chance to win a signed copy of the book. Winners must be present to win).

VENTURE CAPITALIST INSIGHTS

2:00 PLENARY PANEL DISCUSSION: Venture Capitalist Insights into Trends in Drug Discovery

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation
Panelists:
James Edwards, PhD, Venture Partner, Samsara BioCapital
Seth Lieblich, PhD, Principal, 8VC
Swetha Murali, PhD, Vice President, OMX Ventures
Chris Smith, PhD, CSO Partner Team, Curie.Bio
Rachit Neupane, PhD, Life Sciences Investor, General Catalyst
Wendy Young, PhD, Scientific Advisor; Board Director & Former Senior Vice President, Small Molecule Drug Discovery, Genentech

NOVEL INHIBITORS & DEGRADERS OF TRANSCRIPTION FACTORS

2:50 Chairperson's Remarks

Daniel A. Erlanson, PhD, Chief Innovation Officer, Innovation and Discovery, Frontier Medicines Corporation

2:55 Orally Bioavailable Selective SMARCA2 Degraders for Cancer Therapy

Susanta Samajdar, PhD, CSO, Aurigene Discovery Technologies Ltd.

Genetic-silencing studies have established that the oncogenic activity of tumors lacking SMARCA4 is primarily driven by SMARCA2-containing residual SWI/SNF complex, suggesting the importance of inhibiting SMARCA2. Although a few PROTAC degraders have been reported in the literature, they either lack adequate selectivity or oral bioavailability. We identified an exquisitely selective and highly potent orally bioavailable degrader of SMARCA2.

3:25 Biophysical and Structural Characterization of the Molecular Glue-Mediated Interaction of Transcription Factors with Cereblon

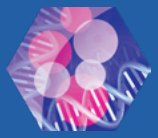
Charles Wartchow, PhD, Associate Director, Global Discovery Chemistry, Novartis Institutes for BioMedical Research

Transcription factors are known to bind to cereblon in the presence of molecular glues and some reports implicate interactions with multiple zinc fingers. We present biophysical and structural assessments of the minimal binding domains of IKZF2 and other transcription factors, revealing that multiple zinc fingers interact with cereblon:glue complexes. In these examples, the binding modes are distinct and may have implications for the design of selective degraders.

3:55 Networking Refreshment Break

4:05 Chairperson's Remarks

Marina Nelen, PhD, VP & Head, Drug Discovery, Foghorn Therapeutics



3rd Annual

Drugging Transcription Factors & Regulators

Small Molecules to Pursue TFs, Chromatin Remodelers, Epigenetic Regulators, Co-Factors

4:10 Development of a Dual SMARCA2/4 Inhibitor

Shawn Schiller, Director, Medicinal Chemistry, Foghorn Therapeutics

BRM (SMARCA2) and BRG1 (SMARCA4) are mutually exclusive ATPase subunits of the mSWI/SNF (BAF) chromatin remodeling complex. BAF is an attractive therapeutic target because of its role in transcription, and mutations in the subunits of BAF are common in cancer and neurological disorders. Herein, we report the discovery of FHD-286, as a potent allosteric inhibitor of the dual ATPase subunits that is being evaluated in Phase 1 clinical trials.

4:40 Reinforced Dynamics Platform Empowers the Discovery of Novel Inhibitors and Degraders of Transcription Factor c-Myc

Dongdong Li, PhD, Director, Medicinal Chemistry, DP Technology

Dongdong Wang, PhD, Co-President, Drug Discovery, DP Technology

By utilizing the RiDYMO platform, followed by experimental validation, we have identified novel small-molecule inhibitors that directly target c-Myc. The hit compound DP390 directly binds to the c-Myc (evidenced by SPR/FP/STD-NMR), effectively disrupting the interaction between c-Myc and Max, promoting the instability and degradation of c-Myc protein, and affecting downstream transcriptional functions. The degraders designed based on optimized small molecules exhibit nanomolar potency in cells and also directly target c-Myc.

5:10 Cell Penetrating Nano-Antibody, SBT-100, Inhibits Transcription Factor STAT3 for Therapeutic Response

Sunanda Singh, Founder & CEO & President, Singh Biotechnology LLC

SBT-100 is approximately 15kD VHH derived nano-antibody which crosses the cell membrane and blood brain barrier (BBB) in less than 15 minutes *in vivo*. It binds to the transcription factor STAT3 (signal transducer activator of transcription 3) and inhibits its function. SBT-100 inhibits STAT3's phosphorylation (i.e., activation), translocation to the nucleus, and binding to its DNA promoter. It is effective at inhibiting human cancer growth *in vitro* and *in vivo*.

5:40 Close of Conference

HOTEL & TRAVEL

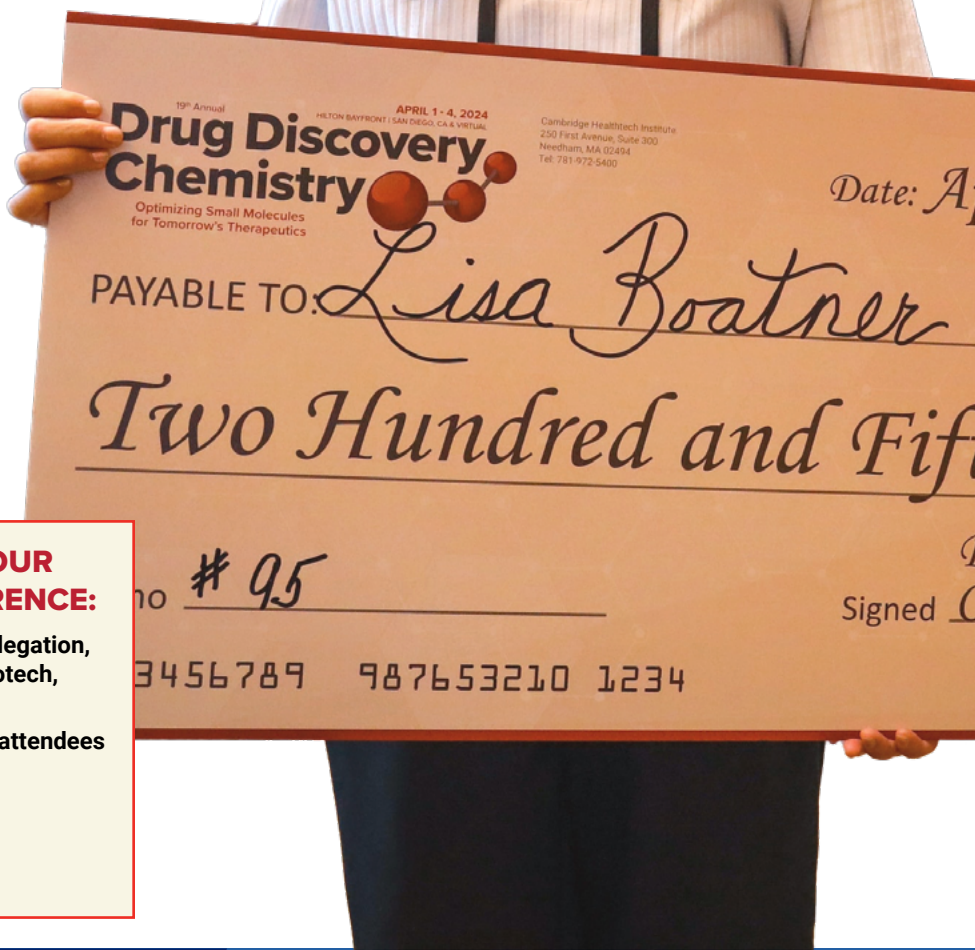
Conference Venue and Host Hotel:
Hilton San Diego Bayfront
1 Park Boulevard
San Diego, CA 92101

Discounted Room Rate: $320
Discounted Room Rate Cut-off Date: March 18, 2025

Visit the Travel page of DrugDiscoveryChemistry.com to make your hotel reservations and for additional information

PRESENT YOUR RESEARCH POSTER AT DRUG DISCOVERY CHEMISTRY

Cambridge Healthtech Institute encourages attendees to gain further exposure by presenting their work in the poster sessions. To secure an onsite poster board and/or ensure your poster is included in the conference materials, your full submission must be received, and your registration paid in full by **March 7, 2025.**



REASONS YOU SHOULD PRESENT YOUR RESEARCH POSTER AT THIS CONFERENCE:

- **Your research will be seen by our international delegation, representing leaders from top pharmaceutical, biotech, academic and government institutions**
- **Discuss your research and collaborate with other attendees**
- **Your poster presentation will be published in our conference materials**
- **Automatically entered in the Poster Competition**
- **Receive $50 off your registration**

Cambridge Healthtech Institute is Proud to Support and Recognize

THE SCIENTISTS OF TOMORROW

Full-time graduate students and PhD candidates presenting a poster are now encouraged to apply for a Student Fellowship. Spaces are limited! Please see website for details.

Pricing and Registration Information

CONFERENCE PRICING	Commercial	Academic, Government, Hospital-Affiliated
PREMIUM CONFERENCE PRICING *BEST VALUE* (Includes access to ALL conferences, in-person short courses, and symposia Monday - Thursday. Plus, On-Demand access for one year.)		
Advance Rate Until March 14, 2025	$3399	$2099
Registrations After March 14, 2025	$3499	$2199
STANDARD CONFERENCE PRICING (Includes access to TWO conferences. Plus, On-Demand access for one year. Excludes short courses and symposia.)		
Advance Rate Until March 14, 2025	$2799	$1299
Registrations After March 14, 2025	$2999	$1399
BASIC CONFERENCE PRICING (Includes access to ONE conference. Plus, On-Demand access for one year. Excludes short courses and symposia.)		
Advance Rate Until March 14, 2025	$2099	$999
Registrations After March 14, 2025	$2199	$1099
SHORT COURSE PRICING (In-person only) April 14 & 16		
1 Short Course	$699	$399
2 Short Courses	$999	$599
MINI SYMPOSIUM ONLY PRICING April 14		
1 Mini Symposium	$999	$599

CONFERENCE DISCOUNTS

WANT TO REGISTER BY PHONE? Contact our Registration department at 781-972-5400 or Toll-free in the US 888-999-6288.

GROUP DISCOUNTS: Have your colleagues or entire team attend! Purchase a full price registration and participants from the same organization will receive a 20% discount when registering through the Group Registration page. For more information on group discounts, contact Uma Patel at 781-972-5447 or upatel@healthtech.com.

ALUMNI DISCOUNT: Cambridge Healthtech Institute 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.

POSTER DISCOUNT ($50 Off) Poster materials are due by **March 7, 2025**. Once your registration has been fully processed, we will send an email containing a unique link and instructions for submitting your abstract and other materials. If you do not receive your link within 5 business days, please contact jring@healthtech.com. CHI reserves the right to publish your poster content in various marketing materials and products.

APRIL 14 – CONCURRENT SYMPOSIA	APRIL 15-16 – CONCURRENT CONFERENCES	APRIL 16-17 - CONCURRENT CONFERENCES
S1: Degraders & Molecular Glues: Beyond Oncology	C1A: Degraders & Molecular Glues – Part 1	C1B: Degraders & Molecular Glues – Part 2
S2: Covalent & Induced Proximity-Based Therapies	C2A: Fragment-Based Drug Discovery	C2B: Protein-Protein Interactions
S3: Generative AI & Predictive Modeling	C3A: AI/Machine Learning for Early Drug Discovery – Part 1	C3B: AI/Machine Learning for Early Drug Discovery – Part 2
S4: Drug Discovery in Women's Health	C4A: GLP1 & Oral Peptides	C4B: DNA-Encoded Libraries
S5: RNA-Modulating Small Molecule Drugs	C5A: Emerging Technologies for Discovery Chemistry	C5B: Drugging Transcription Factors & Regulators
	TS6A: The Medicinal Chemistry-Pharmacology Interface: The 3 Independent SARs for New Drug Candidates (In-Person Only)	TS6B: Drug Exposure at the Target: The Role of ADME and Pharmacokinetics (In-Person Only)

SHORT COURSES (IN-PERSON ONLY)	
April 14	**April 16**
SC1: Protein Degraders: A Beyond Rule of Five Space and *in vitro* ADME Perspective	SC5: Protein Degraders: An *in vivo* ADME and Safety Perspective
SC2: Fragment-Based Drug Design: Advancing Tools and Technologies	SC6: Chemical Biology for Covalent Drug Discovery, Phenotypic Screening, and Target Deconvolution
SC3: Fundamentals of Generative AI for Drug Discovery	SC7: AI Applications in Drug Development: Strategies for Innovation and Integration
SC4: Detecting Target Engagement: Technology Innovations	SC8: Principles of Drug Design: Ligand-Receptor Interactions and More
	SC9: DNA-Encoded Libraries

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!

Please refer to the Registration Code below:

Cambridge HEALTHTECH Institute
A Division of Cambridge Innovation Institute

250 First Avenue, Suite 300
Needham, MA 02494
Healthtech.com
Fax: 781-972-5425