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21ST ANNUAL

Drug Discovery Chemistry

Today's Synthetic Molecules for Tomorrow's Therapeutics

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APRIL 13, 2026

- Targeting Transcription Factors & Regulators
- Covalent & Induced Proximity-Based Drugs
- RNA-Modulating Small Molecule Drugs
- Generative AI & Predictive Modeling
- Drug Exposure at the Target

APRIL 14 - 15, 2026

- Degraders & Molecular Glues - Part 1
- Fragment-Based Drug Discovery
- Emerging Technologies for Discovery Chemistry
- AI/ML for Early Drug Discovery - Part 1
- Oral & Macrocyclic Peptides - Part 1

APRIL 15 - 16, 2026

- Degraders & Molecular Glues - Part 2
- Targeting Protein-Protein Interaction
- DNA-Encoded Libraries
- AI/ML for Early Drug Discovery - Part 2
- Oral & Macrocyclic Peptides - Part 2

PLUS! Dinner Short Courses on Monday April 13th & Wednesday April 15th evening

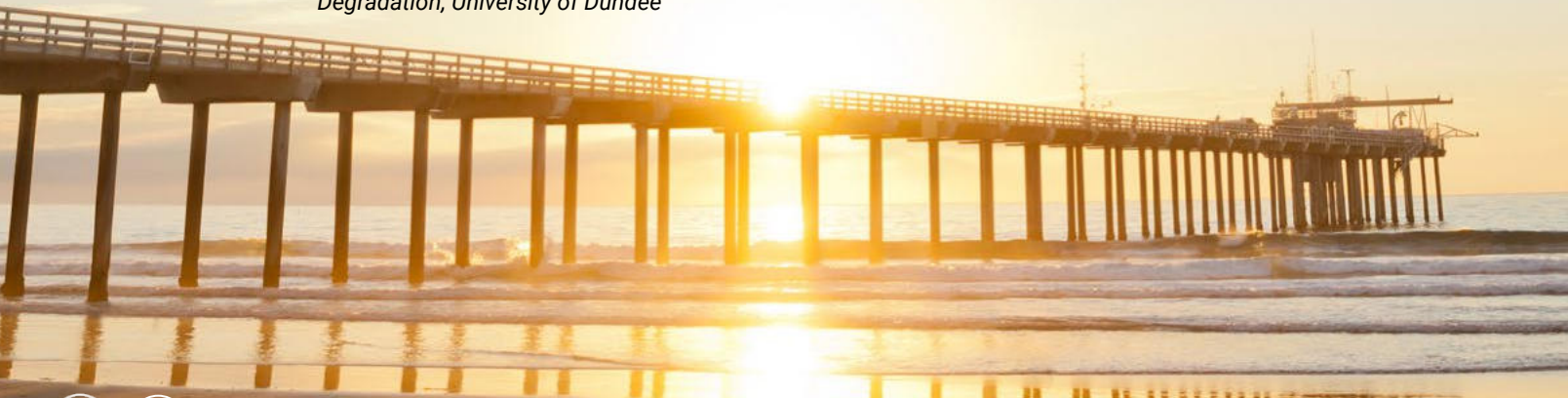
PLENARY KEYNOTES

Charting the Evolution & Future of Targeted Protein Degradation: From Fundamental Mechanisms to Translational Impact

Alessio Ciulli, PhD
Professor, Chemical & Structural Biology and Director of the Centre for Targeted Protein Degradation, University of Dundee

Directed and Random Walks in Chemical Space

Brian K Shoichet, PhD
Professor & Chair, Pharmaceutical Chemistry
University of California San Francisco (UCSF)



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Drug Discovery Chemistry

CONFERENCE-AT-A-GLANCE

APRIL 13 – CONCURRENT SYMPOSIA & TRAINING SEMINAR	APRIL 14-15 – CONCURRENT CONFERENCES	APRIL 15-16 - CONCURRENT CONFERENCES
S1: Targeting Transcription Factors & Regulators	C1A: Degraders & Molecular Glues – Part 1	C1B: Degraders & Molecular Glues – Part 2
S2: Covalent & Induced Proximity-Based Drugs	C2A: Fragment-Based Drug Discovery	C2B: Targeting Protein-Protein Interactions
S3: RNA-Modulating Small Molecule Drugs	C3A: Emerging Technologies for Discovery Chemistry	C3B: DNA-Encoded Libraries
S4: Generative AI & Predictive Modeling	C4A: AI/Machine Learning for Early Drug Discovery – Part 1	C4B: AI/Machine Learning for Early Drug Discovery – Part 2
TS: Drug Exposure at the Target: The Role of ADME and Pharmacokinetics (In-Person Only)	C5A: Oral & Macrocyclic Peptides: Discovery to Development – Part 1	C5B: Oral & Macrocyclic Peptides: Discovery to Development – Part 2

DINNER SHORT COURSES (IN-PERSON ONLY)	
April 13	**April 15**
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: Next-Gen AI Toolkit for Drug Discovery: From LLMs to Multi-Agent System	SC7: DNA-Encoded Libraries in Drug Discovery: Design, Screening, and Lead Development
SC4: From Biophysics to Cellular Target Engagement: Tools for Small Molecule Ligand Identification & Analysis	

PLENARY SESSIONS

Charting the Evolution & Future of Targeted Protein Degradation: From Fundamental Mechanisms to Translational Impact

Alessio Ciulli, PhD

Professor, Chemical & Structural Biology and Director of the Centre for Targeted Protein Degradation, University of Dundee

Directed and Random Walks in Chemical Space

Brian K Shoichet, PhD

Professor & Chair, Pharmaceutical Chemistry, University of California San Francisco (UCSF)

PLENARY PANEL:

Insights from Venture Capitalists

THURSDAY, APRIL 16TH, 12:40 PM

TRACK-HOPPING

At Drug Discovery Chemistry, "track-hopping" is encouraged!

While you curate your personalized agenda, your registration unlocks the entire program. For the best value—and to tailor the experience to your research—choose a Premium registration. You'll get access to all 10 conferences, your pick of 1 symposium or training seminar, 2 short courses, networking events, and 1 year of on-demand access to every session.

SC1-SC4 - MONDAY, APRIL 13 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 first 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 for characterization of PROTACs and glues.

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

Instructors:

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

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

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: Next-Gen AI Toolkit for Drug Discovery: From LLMs to Multi-Agent Systems

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

This short course provides an overview of the next generation of AI toolkits for drug discovery, with a focus on the transition from large language models (LLMs) to multi-agent systems. The session will introduce participants to recent advances in generative and agentic AI and explore how these innovations are reshaping the way researchers approach molecular design, synthesis planning, and knowledge integration. Through a structured presentation of concepts, frameworks, and curated resources, the course will highlight practical avenues by which scientists can apply AI in their own research. Attendees will be introduced to emerging approaches such as agentic workflows, evolving and multi-agent frameworks, and examples of AI-driven discovery pipelines that connect predictive models with generative design.

SC4: From Biophysics to Cellular Target Engagement: Tools for Small Molecule Ligand Identification & Analysis

Instructors:

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

Karanbir Pahil, PhD, Senior Principal Scientist, Affinity Selections & Biophysics, GlaxoSmithKline

Matthew T. Eddy, PhD, Assistant Professor, Chemistry, University of Florida, Gainesville

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

This course covers biophysical and biochemical strategies for discovering small molecules that engage difficult-to-drug protein targets such as protein-protein interactions (PPIs) and G protein-coupled receptors (GPCRs). You'll hear introductions to various technologies, case studies of their applications, and insights on the challenges for which the particular approach is best suited.

SC5-SC7 - WEDNESDAY, APRIL 15 6:15-8:45 PM

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

Instructors:

Prasoon Chaturvedi, PhD, Vice President & Head, DMPK, C4 Therapeutics, 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 Remsberg, PhD, Senior Scientist, Discovery Technologies, Belharra Therapeutics

Angelo Andres, Senior Scientist, Chemical Biology, AstraZeneca

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. Next-generation chemoproteomic technologies such as proximity labeling proteomics (BioID, MicroMap, and MultiMap) and their application to drug discovery will also be discussed. 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: DNA-Encoded Libraries in Drug Discovery: Design, Screening, and Lead Development

Instructors:

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

Ghotas Evindar, PhD, Co-Founder & President, DEL Source; Former DEL Platform Senior Manager, GSK; and Head of Research at Exo Therapeutics and 1859

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

This course provides a comprehensive overview of DNA-Encoded Library (DEL) technology, including library design, synthesis workflows, selection methodologies, data analysis, and hit identification. Participants will learn best practices for constructing and curating DEL collections, along with effective strategies for screening, prioritizing, and advancing hits from DEL campaigns, including emerging DEL applications. The course will also cover interpretation of selection data and the use of AI/ML approaches to accelerate hit-to-lead progression and early-stage drug discovery.

**Premium or Separate Registration Required | Short courses take place in-person only*

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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!

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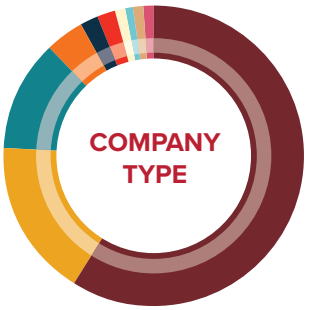

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The Best of Show Awards offer exhibitors of Drug Discovery Chemistry an exclusive opportunity to distinguish and highlight their products, ranging from an innovative application, technology, tool, or solution. The community is invited to identify exceptional innovation in technologies used by life science professionals, voting on the most impactful new products of the year.

Exhibitors are invited to enter your products via the online submission form below. Attendees are encouraged to explore the novel technologies and solutions firsthand in the exhibit hall and vote for the People's Choice Award once the conference has begun. Please note, selection is not based upon level of sponsorship or exhibit participation.

4th Annual

Targeting Transcription Factors & Regulators

Small Molecule and Peptide Drugs to Modulate TF Structure, Function & Interactions

MONDAY, APRIL 13

9:00 am Pre-Conference Training Seminar & Symposium Registration

DISCOVERY OF NOVEL TARGETS & DRUG MODALITIES

1:00 pm Welcome Remarks

1:10 Chairperson's Remarks
Sherry Niessen, PhD, Vice President, Proteomics, Belharra Therapeutics

1:15 FEATURED PRESENTATION: Targeting the Hippo Pathway in Cancers
Anwesha Dey, PhD, Executive Director & Distinguished Scientist, Research Oncology, Genentech Inc.
TEAD transcription factors (TEAD1–4) are key effectors of the Hippo signaling pathway. We investigated mechanisms underlying resistance to the pan-TEAD inhibitor GNE-7883. Our findings reveal that resistance is driven by upregulation of AP-1 transcription factors and reactivation of YAP–TEAD signaling. This study uncovers a key crosstalk between the Hippo and MAPK pathways and suggests that MAPK pathway inhibition could help overcome resistance to TEAD-targeted therapies in Hippo-dependent cancers.

1:45 Native Regulome Profiling for AI-Guided Discovery of Transcription Factor Inhibitors
Alexander Federation, PhD, Co-Founder & CEO, Talus Bioscience
Native regulome profiling captures the complete landscape of chromatin-associated proteins in their natural context, quantifying transcription factors (TFs), cofactors, and chromatin machinery that regulate gene expression. Integrating these proteomic measurements with chemical perturbations and AI-driven modeling reveals how compounds reshape regulatory networks. This systems-level approach enables machine learning–guided discovery of small molecules that functionally modulate TF activity, unlocking new therapeutic opportunities across the previously "undruggable" regulome.

2:15 Development of RTX-117, an Inhibitor of the Integrated Stress Response, for the Treatment of Neurodegenerative Diseases
Sridhar Narayan, PhD, Vice President, ReviR Therapeutics
The cellular integrated stress response (ISR) enables cells to adapt to stressors and return to homeostasis. However, unresolved chronic ISR activation leads to cellular apoptosis and is a hallmark of several neurodegenerative diseases. The ISR pathway signals through transcription factors ATF4, CHOP, GADD34, and ATF5, which determine cellular fate. Here, I describe the discovery and development of RTX-117, an oral, brain-penetrant inhibitor of the ISR currently entering Phase 1 clinical trials.

2:45 Sponsored Presentation *(Opportunity Available)*

3:15 Networking Refreshment Break

3:30 Discovery and Optimization of a First-in-Class p300-Selective Oral Degrader Candidate
Susanta Samajdar, PhD, CSO, Aurigene Discovery Technologies Ltd.
Our p300-selective degrader offers a novel cancer therapy by targeting histone acetyltransferase p300 while sparing CBP, reducing off-target effects like thrombocytopenia. It shows potent antiproliferative activity in p300-dependent hematologic and solid tumors, with favorable oral pharmacokinetics. This precision oncology approach is especially promising in cancers with p300 overexpression or CBP mutations. Data showing how this exquisitely selective molecule identified using Aurigene's proprietary A-PROX platform will be presented.

4:00 Optimization of NRF2 Modulators Targeting the Kelch Domain of KEAP1
Terry Moore, PhD, Associate Professor, Pharmaceutical Sciences, University of Illinois Chicago
We describe efforts to optimize small-molecule NRF2 modulators that disrupt the interaction between NRF2 and the Kelch domain of KEAP1. Structure-guided design and SAR studies have led to improved potency and selectivity, enhancing NRF2 stabilization and downstream antioxidant responses. This work supports the development of therapeutics targeting oxidative stress-related diseases by modulating the KEAP1–NRF2 axis.

4:30 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 Close of Symposium

6:00 Dinner Short Courses*
**Premium Pricing or separate registration required. See Short Courses page for details.*

"The meeting was inspirational, and informative. Meeting researchers from the top performing labs and companies around the world was great."

RUBEN A, PROFESSOR, UC SAN DIEGO

5th Annual

Covalent & Induced Proximity-Based Drugs

Innovative Chemistries and Assays for Studying and Modulating Proximity-Induced Interactions

MONDAY, APRIL 13

9:00 am Pre-Conference Training Seminar & Symposium Registration

LEVERAGING PROXIMITY FOR DRUG DISCOVERY

1:00 pm Welcome Remarks

1:10 Chairperson's Remarks
Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation

1:15 Going beyond Cysteine: Development of Targeted Covalent Inhibitors for Class I Bromodomain-Containing Proteins
William Pomerantz, PhD, Associate Professor, Department of Medicinal Chemistry, University of Minnesota, Twin Cities
Here, I will discuss a new targeted covalent inhibitor approach targeting histone acetyltransferases PCAF/GCN5, and nucleosome remodeling complex members, CECR2 and BPTF. A structure-based design approach has been guided by medicinal chemistry efforts targeting non-conserved nucleophilic amino acids in a flexible loop of the bromodomain binding pocket. Choice of electrophilic designs has imparted selectivity towards these bromodomain-containing proteins, leading to cell-active inhibitors and starting points for designing new proximity-inducing molecules.

1:45 TRIM7 Inhibition Blocks RTK/RAS Pathway-Driven Tumor-Cell Proliferation Independent of Mutation and Restores Tumor-Intrinsic IFN Responsiveness
George Fromm, Jr., PhD, CSO, Kayak Therapeutics
KT-300 is a first-in-class covalent inhibitor of the E3 ubiquitin ligase TRIM7, a key effector downstream of RTK–KRAS signaling. By blocking hyperactivated TRIM7 in cancers with EGFR, KRAS, BRAF, or MEK alterations, KT-300 induces potent tumor growth inhibition. Kayak's preclinical studies show superior efficacy to KRAS inhibitors and antibodies, with mutation-agnostic activity enabling broad targeting of RTK–KRAS–driven tumors.

2:15 Interrogating the Druggable Proteome with Proximity Pharmacology
Fleur Ferguson, PhD, Assistant Professor of Chemistry and Biochemistry and Assistant Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego
Traditional small molecule drugs target fewer than 3,000 of the 20,000+ human proteins. Induced proximity approaches—PROTACs, molecular glues, and related technologies—expand the druggable proteome by engaging cellular machinery rather than requiring direct inhibition. We developed complementary chemical biology platforms to systematically identify and optimize proximity-inducing compounds. This presentation describes these platforms and their application to discover first-in-class degraders and molecular glues for challenging targets.

2:45 Sponsored Presentation *(Opportunity Available)*

3:15 Networking Refreshment Break

3:30 Rewiring of DNA Repair by Proximity Pharmacology
Michael Erb, PhD, Associate Professor, Department of Chemistry, The Scripps Research Institute
We recently introduced PCIPs (PARP-based chemical inducers of proximity), which rewire chromatin-regulated DNA repair processes by recruiting BET proteins to PARP2. PCIPs are synthetically lethal to homologous recombination (HR)–deficient tumors and show increased toxicity to cancer cells that are resistant to conventional PARP inhibitors, presenting a promising new modality for therapeutic translation. This class of compounds establishes an exciting new framework for probing and controlling DNA repair through proximity pharmacology.

4:00 Rethinking Chromatin Remodeling: Leveraging Induced Proximity to Rewire Transcription
Gabriel Sandoval, PhD, Principal Scientist, Foghorn Therapeutics
The induced proximity landscape has recently exploded with academic and industry groups investigating various biological outcomes of linking two targeted warheads. Here we focus on utilizing bifunctional molecules to specifically modulate transcriptional programs and signaling outcomes mediated by chromatin regulatory complexes. Our efforts reveal compounds which can either activate or repress transcription at specific loci or more broadly across chromatin. This approach suggests a promising path forward for drug discovery.

4:30 FEATURED PRESENTATION: Induced Proximity in Medicine and Biology
Gerald Crabtree, MD, David Korn Professor of Experimental Pathology & Developmental Biology, Stanford University
Chemical inducers of proximity were developed to understand the role of proximity in biology. These studies revealed far-reaching roles of induced proximity that extend to virtually every aspect of cellular function and provided a foundation for the development of therapeutics including molecular glues, degraders, and others. Most recently, we developed a new class of molecules that rewire the fundamental circuitry of cells for therapeutic and/or investigative purposes.

5:15 Close of Symposium

6:00 Dinner Short Courses*
**Premium Pricing or separate registration required. See Short Courses page for details.*

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7th Annual

RNA-Modulating Small Molecule Drugs

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

MONDAY, APRIL 13

9:00 am Pre-Conference Training Seminar & Symposium Registration

TECHNOLOGIES ENABLING RNA TARGETING

1:00 pm Welcome Remarks

1:10 Chairperson's Remarks

Amanda Garner, PhD, Charles Walgree, Jr. Professor and Associate Chair, College of Pharmacy, Department of Medicinal Chemistry, University of Michigan

1:15 Enabling Technologies for Revealing Druggable Paths in RNA Biology

Amanda Garner, PhD, Charles Walgree, Jr. Professor and Associate Chair, College of Pharmacy, Department of Medicinal Chemistry, University of Michigan

RNAs play a paramount role in maintaining human health. Beyond their intermediary role as messenger RNA, RNAs perform diverse cellular functions, including regulating transcription, splicing, and translation. Called to action by discoveries connecting aberrant RNA biology with human diseases, targeting of RNAs with small molecules has arisen to the forefront of drug discovery. This talk will highlight technologies developed by the Garner laboratory for enabling RNA-targeted drug discovery.

1:45 Enhancing Oligonucleotide Screening Efficiency with DNA-Encoded Library Technology

Dillon Flood, PhD, Scientific Director, Elsie Biotechnologies, a GSK company

Elsie Biotechnologies developed an encoded platform to identify potent and safe oligonucleotide drugs. Our platform was used to discover RNase H-activating antisense oligonucleotides (ASOs) against a target. First, encoded oligonucleotide pools were designed to tile the target, exploring every possible ASO sequence along the mRNA and pre-RNA transcript. ASO hits were identified and screened for activity. We are eager to expand the concept for optimization of other properties.

2:15 Integrating AI and Structural Analysis to Accelerate RNA-Targeted Drug Discovery

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

Despite significant advances, discovering RNA-targeted small molecules remains challenging. Here, I will present approaches combining multiple AIs, tailored for different drug discovery stages, with 3D structural analyses. Our AI-augmented iterative screening boosts SAR-tractable hit identification, while structural insights clarify binding modes and guide rational design, improving efficiency, selectivity, and ADMET properties. Supported by accumulated data and quantitative HTS, our approaches drive progess in RNA-targeted small molecule drug discovery.

2:45 Sponsored Presentation *(Opportunity Available)*

3:15 Networking Refreshment Break

NOVEL STRATEGIES FOR RNA MODULATION

3:30 A Structure-Based Approach to Drugging RNA with Small Molecules

Emily Garcia Sega, PhD, Senior Scientist, Medicinal Chemistry, Arrakis Therapeutics

Our mission at Arrakis is to solve very broadly the problem of how to drug RNA with small molecules. This presentation will provide an update on the platform we have built to achieve that mission and provide early data on specific mRNA targets.

4:00 Context-Selective Translation Inhibition as a Novel, rRNA Binding Therapeutic Modality

Lawrence Hamann, PhD, Co-Founder & President & CEO, Interdict Bio

Interdictors are small molecule context-dependent ribosome stallers that inhibit translation of disease-causing genes. We have developed interdictors that potently inhibit the growth of short half-life oncogene-dependent cancers *in vitro* and demonstrate robust efficacy in mice xenograft models at a low oral, well-tolerated dose, as well as interdictors which reduce the synthesis of aggregation-prone neurotoxic proteins. Our lead candidate is undergoing IND-enabling characterization for clinical study in multiple MYC-driven tumor types.

4:30 A Molecular Clamp Targeting the TOE1:Sm Complex Imparts Tunable Regulation of Splicing

Haoxin Li, PhD, Damon Runyon Post-Doctoral Fellow, Laboratory of Dr. Benjamin Cravatt, Scripps Research Institute

snRNAs are required for the structure and function of the spliceosome. Here we report a potent and selective covalent ligand that targets TOE1, a 3' RNA exonuclease, only when bound to the Sm complex. We find that this compound acts as a "molecular clamp", dramatically stabilizing TOE1-Sm complex interactions and triggering the excessive trimming of snRNA 3' termini in cells. Our findings may have therapeutic implications for splicing-related diseases.

4:50 FEATURED PRESENTATION: Targeting RNA Tertiary Structures with Small Molecules: Establishing the Metrics for Specificity

Anna Marie Pyle, PhD, Sterling Professor of Molecular & Cellular & Developmental Biology; Professor of Chemistry; Yale University

By merging medicinal chemistry and RNA biochemistry, one can now create small molecules specifically designed to target individual RNA tertiary structures, such as self-splicing introns and RNAse P RNAs, which represent a proving ground for establishing the "rules" for RNA targeting that can be used in designing drugs against complex human targets, such as primary microRNAs and human UTR motifs.

5:20 Close of Symposium

6:00 Dinner Short Courses*

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

"The conference was exceptionally well-organized... informative and engaging... networking opportunities were invaluable..."

AMY H, ED OF R&D CHEMISTRY, REGENERON

3rd Annual

Generative AI & Predictive Modeling

Accelerating Drug Discovery by Improving Speed, Scale, and Accuracy

MONDAY, APRIL 13

9:00 am Pre-Conference Training Seminar & Symposium Registration

GENERATIVE DRUG DESIGN

1:00 pm Welcome Remarks

1:10 Chairperson's Remarks
Woody Sherman, PhD, Founder and Chief Innovation Officer, Psivant Therapeutics

1:15 AI-Guided Multi-Objective Optimization of Peptides: Balancing Target Affinity & Membrane Permeability
Alan Nafiiev, PhD, CEO & Founder, Receptor.AI
In this talk, we will discuss the development of predictive models to evaluate peptide target binding and passive diffusion across cell membranes. Application of AI-driven multi-objective optimization strategies to enhance both affinity and permeability simultaneously, and case examples demonstrating how these approaches accelerate peptide drug discovery, will also be highlighted.

1:45 Generative Design of Soluble GPCRs: Strengths and Limitations in Drug Discovery
Alexander Taguchi, PhD, Director of Machine Learning, iBio Inc.
Generative AI promises to revolutionize protein engineering, but are these tools genuinely useful for GPCR drug discovery? Here, we challenge generative models to design soluble analogs of GPCRs and evaluate their performance through experimental binding measurements and structural validation. Experimental validation of these soluble GPCR analogs translates to efficient antibody discovery against the native target, while also exposing the current limitations of this technology.

2:15 Boltz: Towards Accurate Biomolecular Modeling and Design
Gabriele Corso, PhD, Co-Founder and CEO, Boltz
Accurately modeling biomolecular interactions is a central challenge in modern biology. Recent advances, such as AlphaFold3 and Boltz-1, have substantially improved our ability to predict biomolecular complex structures. With Boltz-2, we demonstrated the first AI model to approach the performance of free-energy perturbation (FEP) methods in estimating small molecule–protein binding affinity. I will also present our most recent work in the space of structure-based small molecule and protein design.

2:45 Sponsored Presentation *(Opportunity Available)*

3:15 Networking Refreshment Break

LEVERAGING GEN AI FOR DRUG DISCOVERY

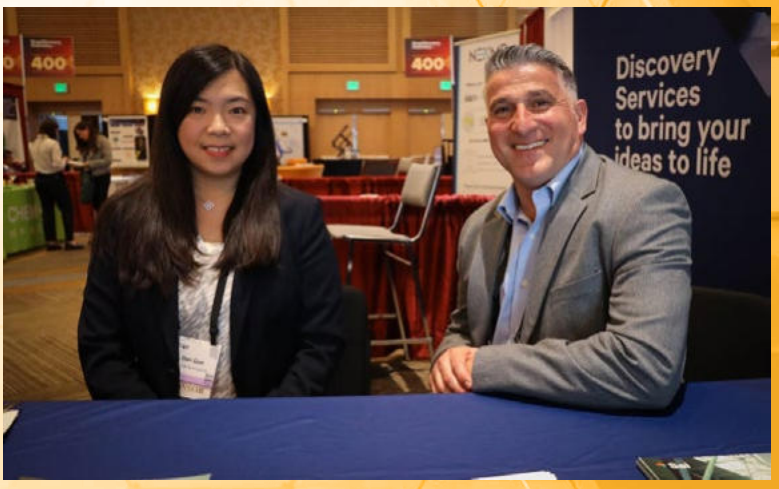
3:30 FEATURED PRESENTATION: From Physics to AI—Capturing Atomic Details and Biologically Relevant Motions in the Era of Generative Drug Discovery
Woody Sherman, PhD, Founder and Chief Innovation Officer, Psivant Therapeutics
AI promises to transform molecular design, yet predictions of molecular recognition and drug properties remain limited. This talk examines the strengths and weaknesses of physics-based and AI approaches in capturing atomic details and biologically relevant motions central to drug discovery. By integrating atomistic simulations, structural biophysics, and AI, we can move beyond interpolation toward predictive models that reveal how proteins move, interact, and respond to ligands in realistic biological contexts.

4:15 OpenBind: Unlocking Protein-Ligand Binding Prediction
Fergus Imrie, PhD, Fellow, Department of Statistics, University of Oxford
Recent advances in protein structure prediction have transformed our ability to model individual proteins, yet predicting the structures and binding affinities of protein-ligand co-complexes remains limited due to a lack of experimental data and current modeling approaches. OpenBind seeks to enable a step-change in protein-ligand modeling by substantially expanding paired structure–affinity measurements. I will discuss this, as well as, advances in computational methods for more accurate and reliable binding prediction.

4:45 Leveraging Multiomics and Multimodal Data for the Discovery of Novel Targets Implicated in Diseases That Disproportionally Affect Women's Health
Petrina Kamya, PhD, Global Head of AI Platforms & Vice President, Insilico Medicine; President, Insilico Medicine Canada

5:15 Close of Symposium

6:00 Dinner Short Courses*
**Premium Pricing or separate registration required. See Short Courses page for details.*



Drug Exposure at the Target:

The Role of ADME and Pharmacokinetics

2026 Training Seminar (In-Person Only)

**Premium Pricing or separate registration required*

Cambridge Healthtech Institute's Training Seminars offer real-life case studies, problems encountered, and solutions applied, along with extensive coverage of the academic theory and background. The training seminar offers a mix of formal lecture and interactive discussions and activities to maximize the learning experience.

INSTRUCTOR: *Erland Stevens, PhD, James G. Martin Professor of Chemistry, Davidson College*

This training seminar describes how pharmacokinetics (PK) affects drug exposure at the intended target. The seminar opens with a foundation of clinical PK including the determination of key PK parameters from Cp-time data. Course materials also cover 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. Various drug modalities (e.g., small molecules, antibodies, and peptides) illustrate the concepts of the course.

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.

SESSION 1

- Determining PK parameters from Cp-time data
- ADME & membrane permeability
- Plasma protein binding & metabolic stability

SESSION 2

- Compartment models & PBPK
- Drug modalities & formulation
- PK/PD models

THIS COURSE IS DESIGNED FOR:

- Scientists and researchers in drug discovery or development who want a stronger grasp of how PK and ADME data impact efficacy and safety.
- Graduate students or postdocs in pharmacology, medicinal chemistry, or pharmaceutical sciences looking to build real-world context around their training.
- Regulatory professionals seeking to better understand how PK data are generated and interpreted.
- Project managers or non-specialists involved in cross-functional teams who need a working knowledge of PK to facilitate communication and strategy.

WHY ATTEND?

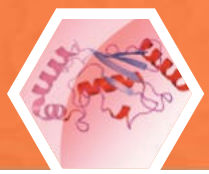
Understanding drug exposure is essential for developing successful therapies. This seminar bridges theoretical PK concepts with practical applications in preclinical and clinical development, helping attendees contribute more effectively to research and decision-making in their organizations.

"Drug Discovery Chemistry was an outstanding experience... The quality of talks, the organization, and the opportunities for meaningful interaction made it a truly valuable event."

DMITRI K, PROFESSOR, UNIVERSITY OF MISSOURI

"Excellent venue to learn about cutting-edge industry research and to network with leading industry scientists."

HETA G, NURIX THERAPEUTICS INC.



9th Annual

Degraders & Molecular Glues - Part 1

Design & Optimization of Novel PROTACs, Glues, and Proximity Inducers

TUESDAY, APRIL 14

7:00 am Registration Open & Morning Coffee

STRUCTURE-FUNCTION CHARACTERIZATION

8:00 Welcome Remarks

8:05 Chairperson's Remarks

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

8:10 Understanding the Selectivity of the Molecular Glue-Induced Interactions of Zinc Finger-Based Transcription Factors with Cereblon

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

We present assessments of the minimal binding domains of transcription factors IKZF2, WIZ, and counter target SALL4, revealing that each of these proteins interacts with cereblon:glue complexes in a unique manner. In addition, we explore the known binding mode of GSPT1, which interacts with cereblon through a G-loop, and contrast that with the unique binding mode of TBK1, a kinase involved in innate immunity.

8:40 A Cryptic Interfacial Pocket Uncovered in Full CRL4^{CRBN}–IKZF3 Ubiquitylation Complex Enhances IMiD Efficacy

Lei Liu, PhD, Professor, Department of Chemistry, Tsinghua University

We present cryo-EM structures of eight imide drugs (IMiDs) in complex with the full CUL4–RBX1–DDB1–CRBN ubiquitylation complex, which together form active ubiquitylation assemblies with the neosubstrate IKZF3. Four "next-generation" IMiDs interact with an unanticipated cryptic gluing-driven interfacial (GDI) pocket in the non-degron zinc finger 3 (ZF3) domain of IKZF3—an interaction likely explaining their superior efficacy and neosubstrate selectivity. This GDI pocket provides new structure-guided avenues to refine IMiDs.

9:10 Proteomics-Guided Molecular Glue Drug Discovery

NEOsphere BIOTECHNOLOGIES

Patrick Zanon, Sr Research Scientist, NEOsphere Biotechnologies GmbH

Rational and systematic approaches are key to identifying molecular glue degraders that target disease-relevant proteins, a crucial step in unlocking the full potential of targeted protein degradation.
In this presentation, we'll demonstrate how high-throughput proteomic screening quickly identifies innovative degraders and disease-relevant targets. We'll showcase how proteome-wide assessments of SAR, degrader selectivity, potency, kinetics, and efficacy in native cells drive lead optimization. Additionally, we'll highlight how global ubiquitinomics and high-throughput interactomics reveal compound-induced ubiquitination and ternary complex formation, mechanistically validating degraders and providing critical insights for 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 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.

10:25 Networking Coffee Break

10:50 Abbapolin PLK1 Degraders in Prostate Cancer

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

Inhibition of PLK1 may be key to overcoming resistance to androgen-blocking treatments that result in Castration Resistant Prostate Cancer (CRPC) providing new therapeutic options. Using the REPLACE strategy, we found compounds that bind tightly to PLK1 and induce its degradation Through our hit-to-lead conversion studies we have identified an abbapolin degrader with potent on target cellular engagement of PLK1, good oral pharmacokinetics. and antitumor efficacy in prostate xenografts.

11:20 Discovery of Molecular Glues and Novel E3 Ligase Ligands through Function-Based DEL Screening

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

Monovalent, Lipinski-compliant molecular glue-class protein degraders are highly prized but there are few reliable methods for their discovery. In this talk, we describe the establishment of an *in vitro* assay that allows DNA-encoded libraries of bead-displayed small molecules to be screened for the ability to trigger the poly-Ubiquitylation of a co-immobilized target protein by Ubiquitin ligases.

11:50 Higher Throughput Proteomics Screening for Degrader Target Identification and Selectivity Profiling

Anthony Iannetta, PhD, Senior Scientist, Discovery Sciences, AstraZeneca

Proteomics can be an invaluable tool in drug discovery, as it can provide target agnostic information on drug-induced, proteome-wide abundance changes, but a disadvantage is its throughput. To combat this, we developed a workflow in 384-well plates, combining this with faster data acquisition to achieve higher throughput proteomics. We applied this platform in the TPD space to screen compound libraries for hit identification and profile leads to understand off-target selectivity.

12:20 pm Transition to Lunch

12:25 Luncheon Presentation to be Announced

SYGNATURE DISCOVERY

12:55 Session Break

DEGRADERS FOR ONCOLOGY TARGETS

1:45 Chairperson's Remarks

Silvia Escudero, PhD, Principal Scientist, Foghorn Therapeutics

1:50 Identification of First-in-Class Selective ARID1B Degraders

Silvia Escudero, PhD, Principal Scientist, Foghorn Therapeutics

We report the identification and optimization of first-in-class selective ARID1B degraders that drive targeted protein degradation. Using our platform and structure-based design, we developed VHL- and CRBN-based molecules that induce robust ARID1B degradation via the ubiquitin-proteasome system. These compounds demonstrate on-mechanism activity, high selectivity, and downstream gene modulation. Our work lays the foundation for ARID1B degradation as a promising strategy to exploit synthetic lethality in ARID1A mutant cancers.

2:20 The Discovery of an Orally Bioavailable RIPTAC for the Treatment of Breast Cancer

Matthew Perry, PhD, Director, Medicinal Chemistry, Halda Therapeutics Inc.

Estrogen receptor (ER)-targeted RIPTACs selectively inactivate BRD4 in ER+ breast cancer, including post-CDK4/6i resistance settings. These agents show potent *in vitro* anti-proliferative activity across ER wild-type and mutant models, strong *in vivo* efficacy in CDX and PDX models, and lack endometrial agonism. RIPTACs offer a promising, tumor-selective therapeutic approach with broad applicability in metastatic breast cancer and anticipated Phase 1 start in early 2026.

2:50 Interrogating Cancer Drivers Using Targeted Protein Degradation

Behnam Nabet, PhD, Assistant Professor, Human Biology Division, Fred Hutchinson Cancer Center

Targeted protein degradation is transforming how we probe and manipulate the proteome. My talk will showcase how we leverage degradation-based technologies including the dTAG platform to interrogate oncoproteins, mRNA translation factors, and kinases that drive aggressive viral-driven and solid tumor cancers. These studies demonstrate how precise, rapid protein degradation accelerates target validation, reveals functional insights, and expands the druggable proteome.

3:20 Presentation to be Announced

Selvita

9th Annual

Degraders & Molecular Glues - Part 1

Design & Optimization of Novel PROTACs, Glues, and Proximity Inducers

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

4:45 Charting the Evolution & Future of Targeted Protein Degradation: From Fundamental Mechanisms to Translational Impact
Alessio Ciulli, PhD, Professor, Chemical & Structural Biology and Director of the Centre for Targeted Protein Degradation, University of Dundee
I will be reflecting on the evolution of the TPD field, from early design principles to today's landscape of PROTACs and molecular glues. Latest advances from the Ciulli Lab in mechanistic understanding and chemical biology of degraders ternary complexes will be showcased. I will also highlight collaborative academic-industry consortia tackling grand challenges with undruggable targets in paediatric cancers and neurodegenerative diseases, charting the next-generation of proximity-based therapeutics.

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

6:30 Close of Day

WEDNESDAY, APRIL 15

7:15 am Registration and Morning Coffee

SPOTLIGHT SESSION: NEW STRATEGIES FOR NDUCING PROXIMITY

8:00 Chairperson's Remarks
Behnam Nabet, PhD, Assistant Professor, Human Biology Division, Fred Hutchinson Cancer Center

8:05 Linking Cancer Drivers to Programmed Cell Death
Sai Gourisankar, PhD, NCI K99/R00 Postdoctoral Fellow, Laboratory of Dr. Nathanael Gray, Stanford Cancer Institute
A principle in the development of cancer therapeutics is that robust and selective death of the malignant cell is critical. I will present an approach that leverages chemically-induced proximity to rewire oncogenes to activate apoptosis in a lineage-specific manner, using molecules termed transcriptional/epigenetic chemical inducers of proximity (TCIPs). These small molecules redirect epigenetic regulators to selectively activate cell death genes silenced by cancer drivers such as BCL6 in lymphoma.

8:25 Reprogramming the Extracellular Space for Targeted Protein Degradation and Drug Delivery
Fangzhu Zhao, PhD, Postdoctoral Fellow, Laboratory of Dr. Jim Wells, Pharmaceutical Chemistry, University of California San Francisco
Antibody-based degraders offer new ways to manipulate the extracellular proteome for therapy. Here, we developed degrader–drug conjugates that hybridize eTPD and ADC for efficient lysosomal delivery and potent cytotoxic payload release. We further designed a new class of degrader that recruits membrane proteases to remove surface targets via induced extracellular shedding. Together, these modalities expand the mechanisms and therapeutic scope of extracellular targeted protein degradation.

8:45 Bridged Proteolysis Targeting Chimera (PROTAC) Enables Degradation of Undruggable Targets
Yue Zhong, PhD, Post-Doctoral Fellow, Laboratory of Dr. Jian Jin, Pharmacological Sciences & Oncological Sciences, Icahn School of Medicine at Mount Sinai
Proteolysis Targeting Chimeras (PROTACs) have revolutionized targeted protein degradation but remain limited to ligandable proteins. We present a bridged PROTAC platform that leverages small-molecule binders of a target protein's druggable binding partner to enable degradation of previously undruggable proteins. Using this approach, we developed the first-in-class cyclin D1 degrader, which achieves potent, selective, and rapid cyclin D1 degradation accompanied by robust antiproliferative activity across multiple cancer models.

9:05 Discovery and Chemical Optimization of Molecular Glues
Stephen Hinshaw, PhD, Senior Research Scientist, Laboratory of Dr. Nathanael Gray, Stanford Cancer Institute
Small molecules that activate or rewire cellular biochemical pathways can be powerful therapeutic agents. Many such small molecules induce cooperative protein-protein binding that trigger unexpected biochemical outcomes. We have used multiple discovery approaches, along with high-resolution structures, to identify and develop molecular glues with these properties. I will discuss two new molecular glue compounds that rewire cell signaling and have cancer therapeutic activities *in vivo*.

9:25 Session Speakers Address Experimental Bottlenecks

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

AI-ENABLED DEGRADER DESIGN & OPTIMIZATION

10:30 Building a Computational Platform to Design Molecular Glues for Any Protein-Protein Interaction
Christopher Tame, PhD, Co-Founder & CEO, Ternary Therapeutics
Ternary Therapeutics has developed a computational design platform for molecular glues of any protein-protein interaction. This platform has been applied to discover novel molecular glue degraders, activators, and non-degrading inhibitors, which the company is progressing through their drug-discovery pipeline. This presentation will focus on the design and validation of the computational platform.

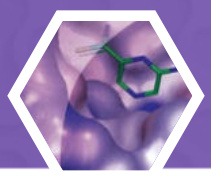
11:00 Prediction of Molecular Glues for Challenging Targets in Oncology
Bryce Allen, PhD, Co-Founder & CEO, Differentiated Therapeutics

11:30 Prediction of Oral Bioavailability of CRBN-Based PROTACs across Various 2D and 3D Descriptors
Tong Li, PhD, Principal Scientist, In Silico Discovery, Johnson & Johnson
Oral bioavailability of TPDs, especially larger sized bifunctional molecules (i.e. PROTAC), is one of the most challenging properties to be optimized. In this study, a comprehensive *in vivo* data set for CRBN-based PROTACs was collected from public domain and 2D/3D descriptors were developed to establish predictive models for oral bioavailability prediction. We address the different behavior of predictive models on different types of animal models, like mouse and rat models.

12:00 pm Enjoy Lunch on Your Own

1:00 Dessert Break with Navigating Chemistry Careers Breakout Tables
Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

1:30 Close of Degraders & Molecular Glues – Part 1 Conference



21st Annual

Fragment-Based Drug Discovery

Small-Molecule Fragments for Generating New Therapeutic Lead Molecules

TUESDAY, APRIL 14

7:00 am Registration Open & Morning Coffee

FRAGMENT APPROACHES FOR DIFFICULT TARGETS

8:00 Welcome Remarks

8:05 Chairperson's Remarks

Elisa Barile, PhD, Executive Director, Biophysics & Chemical Biology, Eli Lilly & Company

8:10 Fragment-Based Discovery Establishes Ligandability of the Transcription Factor MITF

Jürgen Hinrichs, PhD, Senior Principal Scientist, GDC Oncology, Novartis Biomedical Research

The basic helix-loop-helix leucine zipper (bHLH-LZ) transcription factor MITF is a melanoma oncogene, but considered undruggable as direct targeting is unprecedented. We have identified fragments binding to the DNA binding domain of MITF and optimized them to sub-micromolar ligands by fragment merging. Detailed structural and biophysical validation will be presented. NMR studies and MD simulations indicate that the interconversion of kinked and straight helices is slowed down by compound binding.

8:40 FBDD Case Study on eIF4F-mRNA Complex: Lessons Learned

Chiara R. Valenzano, PhD, Associate Director, Molecular Science, Astex Pharmaceuticals

To find anticancer agents, we applied NMR and x-ray crystallographic fragment screening to discover a novel binding site on eIF4E, part of the mRNA translation initiation complex. I present how we used structure-guided design paired with targeted protein degradation and genetic rescue approaches to develop and functionally characterize our fragment hits. I will include lessons learned.

9:10 Sponsored Presentation *(Opportunity Available)*

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 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.

10:25 Networking Coffee Break

10:50 Hit ID and Optimization Using ^{19}F-NMR and SPR Techniques with an Orphan GPCR

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

Developing "binding first" methods to identify chemical matter for GPCRs is an emerging need in drug discovery, especially when targeting an orphan GPCR, where functional activity has not yet been determined. Development of new solubilization techniques for GPCRs has helped to overcome some of the challenges we face when trying to work with detergent solubilized targets. Using 19F-NMR and SPR, we identified and optimized fragment binders for an orphan GPCR.

11:20 NMR-Based Fragment Approaches for G Protein-Coupled Receptors

Matthew T. Eddy, PhD, Assistant Professor, Chemistry, University of Florida, Gainesville

Small molecules are vital for studying and therapeutically targeting membrane proteins, but conventional screening often requires labeled ligands or purified proteins and misses weak binders. We demonstrate a high-resolution magic angle spinning (HRMAS) NMR approach using unpurified membranes containing the A2A adenosine receptor. Using STD-NMR, we rapidly detected and characterized novel fragment binders, revealing distinct binding poses and establishing HRMAS NMR as a useful tool for fragment-based drug discovery.

11:50 Applying FAST NMR to Drug Discovery: A FBDD Case Study

Julien Orts, PhD, (or former lab member), Associate Professor, Pharmaceutical Sciences, University of Vienna

We highlight our progress in targeting proteins with fragment-based approaches when well-diffracting crystals of the protein–ligand complex may be difficult to obtain. We rely on liquid-state NMR for structure determination of these complexes. This strategy opens new avenues for truly quantitative, structure-guided drug design.

12:20 pm Transition to Lunch

12:25 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:55 Session Break

INNOVATIVE FRAGMENT-ASSISTED DRUG DISCOVERY

1:45 Chairperson's Remarks

Jennifer D. Venable, PhD, Senior Director, Discovery Chemistry Site Head, Janssen La Jolla

1:50 Mapping Protein-Protein Interaction Surfaces by Photoactivable Molecular Fragments

Gyorgy Keseru, PhD, Professor, Medicinal Chemistry, Research Centre for Natural Sciences (RCNS), Hungary

Binding sites available at protein-protein interfaces were mapped by a screening concept that combines evolutionary optimized fragment pharmacophores with the use of photoaffinty handles that enables high hit rates by LC-MS detection. Screening our library against challenging targets such as the small GTPase KRASG12D, the transcription factor STAT5B and the E3ligase FBXW7 we have discovered tractable binding sites that were characterized by MS-based peptide mapping, structural studies, and modeling.

2:20 Bead-Displayed Libraries for Fragment Discovery and Growth

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

The fragment-based drug discovery (FBDD) process begins with the identification of low affinity, low molecular weight protein-binding fragments. Subsequently, these fragments are elaborated and/or joined (if they recognize adjacent pockets on the target) to derive higher affinity leads. In this lecture, we describe a multi-step, FBDD-like workflow for the discovery of protein-binding macrocycles using bead-displayed libraries and a novel function-based screening platform.

2:50 DNA-Encoded Libraries for Linker Optimization in FBDD

Jörg Scheuermann, PhD, Professor, Department of Chemistry & Applied Biosciences, ETH Zurich

DNA-encoded libraries, in the setup of Encoded Self-Assembing Chemical (ESAC) libraries, featuring the stable self-assembly of two DNA-encoded sub-libraries of fragments, allow for the identification of pairs of simultaneously binding fragments. In a second step, the most efficient linkage of individual fragment pairs will be obtained by selections of a second, DNA-encoded library of linkers (Linker-DEL), displaying the respective fragment pair.

3:20 Sponsored Presentation *(Opportunity Available)*

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

21st Annual

Fragment-Based Drug Discovery

Small-Molecule Fragments for Generating New Therapeutic Lead Molecules

PLENARY KEYNOTE SESSION

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

4:45 Charting the Evolution & Future of Targeted Protein Degradation: From Fundamental Mechanisms to Translational Impact
Alessio Ciulli, PhD, Professor, Chemical & Structural Biology and Director of the Centre for Targeted Protein Degradation, University of Dundee

I will be reflecting on the evolution of the TPD field, from early design principles to today's landscape of PROTACs and molecular glues. Latest advances from the Ciulli Lab in mechanistic understanding and chemical biology of degraders ternary complexes will be showcased. I will also highlight collaborative academic-industry consortia tackling grand challenges with undruggable targets in paediatric cancers and neurodegenerative diseases, charting the next-generation of proximity-based therapeutics.

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

6:30 Close of Day

WEDNESDAY, APRIL 15

7:15 am Registration and Morning Coffee

COVALENT FRAGMENTS

8:00 Chairperson's Remarks
Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation

8:05 Combining Covalent Fragment Screening, HTP Co-Crystallization, and Direct-to-Biology
Shuai Chen, PhD, Senior Scientist, Medicinal Chemistry, Roche R&D Center (China) Ltd.

A case study shown here is screening with ASC protein, a critical adapter protein in inflammasome activation, making it a promising target for autoimmune disorders. With its PYD and CARD domains providing potential PPI interfaces for drug design, our strategy targets ASC inhibition by disrupting poly-filament formation through covalent binding at Cys173 on its CARD domain. The comprehensive efforts from primary screening, hit validation to fragment-to-lead expansion will be presented.

8:35 FEATURED PRESENTATION: Chemoproteomic Approaches to Shed Light on Functional and Therapeutically Relevant Proteoforms
Keriann Backus, PhD, Associate Professor, Biological Chemistry, University of California, Los Angeles (UCLA)

Cysteine is a unique amino acid, distinguished by its nucleophilicity and sensitivity to oxidative modifications. Therefore, cysteine-reactive molecules have emerged as high value tools for functional biology and drug development applications, and there is widespread interest in the discovery of new ligandable (potentially druggable) and redox sensitive cysteine residues. I will discuss our ongoing efforts cysteine and redox proteomic approaches to define the functional proteoforms targeted by electrophilic compounds.

9:05 Discovery and Structure-Based Rational Design of Novel Reversible and Covalent Inhibitors of a DNA Repair Protein
Nicolas Bocquet, PhD, Director Biochemistry, Biochemistry, FoRx Therapeutics AG

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

DEL & FRAGMENTS FOR COVALENT APPLICATIONS

10:30 Integrating DEL with FBDD for Reversible and Covalent Inhibitor Discovery
Xiaojie Bruce Lu, PhD, Professor & Principal Investigator, Chemical Biology Research Center, Chinese Academy of Sciences

DNA encoded focused library is a powerful technology for the hit to lead optimization of the specific therapeutic target. The integration between FBDD and DNA encoded libraries(DEL) could provide an efficient way to design the focused DEL based on the privileged fragments of corresponding targets identified by diverse screening methods. This lecture will disclose the detailed examples to integrate DEL with FBDD for reversible and covalent inhibitors discovery.

11:00 PANEL DISCUSSION: The Convergance of DNA-Encoded Libraries and Fragment-Based Approaches
Moderator: Jörg Scheuermann, PhD, Professor, Department of Chemistry & Applied Biosciences, ETH Zurich

12:00 pm Enjoy Lunch on Your Own

1:00 Dessert Break with Navigating Chemistry Careers Breakout Tables

Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

1:30 Close of Fragment-Based Drug Discovery Conference

2nd Annual

Emerging Technologies for Discovery Chemistry

Covalent Approaches and New Biophysical Tools

TUESDAY, APRIL 14

7:00 am Registration Open & Morning Coffee

INNOVATIONS FOR SMALL MOLECULE LEAD GENERATION

8:00 Welcome Remarks

8:05 Chairperson's Remarks

Phillip Schwartz, PhD, Director, Biophysics, Septerna

8:10 FEATURED PRESENTATION: Making Your Hits Your Early Leads: Innovative SPR Applications

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

We exploit high-throughput surface plasmon resonance (SPR)-based target array technology to complete fragment screens over wild-type kinases and selected mutants. We generate lead-like compounds directly from screens using computational fragment generation strategies informed by full physics simulations and machine learning-guided design. This integrated approach accelerates fragment-to-lead optimization, dramatically improving efficient progression from hits-to-lead compounds compared to traditional fragment screening approaches, enabling rapid identification and optimization of leads.

8:40 Comparing Biophysical Approaches for Lead Generation: Case Studies from Difficult Targets

Sarathy Karunan Partha, PhD, Principal Research Scientist, AbbVie Inc.

9:10 Talk Title to be Announced

James Vasta, Sr Research Scientist, R&D, Promega Corp

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 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.

10:25 Networking Coffee Break

10:50 Limitations of Small Molecule and Genetic Screening in Phenotypic Drug Discovery

Fabien Vincent, PhD, Consultant; formerly Pharmacology Lab Head, Pfizer Inc.

My presentation surfaces the weaknesses and blind spots of both small molecule and genetic screening. I offer mitigation strategies, when available, to address existing limitations and propose a framework to decide upon how best to apply each approach.

11:20 CHD4 Inhibitor Discovery: Applications FRET-Based Cell-Target Engagement Assays

Kyle M. Miller, PhD, Professor, Winship Cancer Institute, Emory University School of Medicine

CHD4 (NuRD chromatin remodeling complex) regulates transcription and DNA repair, with overexpression correlating with poor prognosis in Glioblastoma. We identify a first-in-class small molecule CHD4i, CH41, that covalently engages CHD4 chromodomain cystines, stabilizing CHD4 on chromatin and disrupting DNA damage/transcription functions resulting in radiation and temozolomide-sensitive cancer cells. MICRO-TAG cellular target-engagement led discovery and validation stages, confirming intracellular CHD4 binding and stabilization. These findings establish CH41 as a selective CHD4i.

11:50 Applying Protein Dynamics and Single-Molecule FRET Analysis to Improving GPCR Ligand Efficiency

Susruta Majumdar, PhD, Professor, Anesthesiology, Washington University School of Medicine

G-protein coupled receptors (GPCRs) represent one-third of all FDA approved therapeutics. Structure based design of partial agonists represents a challenge for the GPCR field. Using natural products medicinal chemistry, single molecule biophysics, pharmacology and structural biology we have identified an allosteric subpocket in the orthosteric site of the mu opioid receptor that acts as an efficacy regulator. Findings could pave way for a new class of safer analgesics.

12:20 pm Transition to Lunch

12:25 Luncheon Presentation to be Announced

12:55 Session Break

BIOPHYSICAL APPROACHES FOR DIFFICULT TARGETS

1:45 Chairperson's Remarks

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

1:50 Tackling Hit ID in GPCR Drug Discovery with an Enhanced Toolbox Including Biophysical Approaches

Alison Heick Varghese, Principal Scientist, Pfizer Inc.

GPCRs present unique challenges to drug discovery due to their low expression, complexity, and poor stability. Detergent extraction from their native environment is commonplace but can prohibit basic biochemical characterization and render false positives in downstream screening campaigns. To address this problem, we have implemented membrane mimics to generate detergent free GPCRs to facilitate their characterization, enable Hit ID screening campaigns and validation follow-up.

2:20 Binding What Matters: Biophysics for Elusive Interactions

Karanbir Pahil, PhD, Senior Principal Scientist, Affinity Selections & Biophysics, GlaxoSmithKline

Validating molecular interactions remains a central challenge in drug discovery, especially for targets with elusive or transient binding profiles. This talk explores biophysical strategies to confirm hits, drawing from recent work on on-DNA binder confirmation and mechanistic triage. Drawing from recent case studies and mechanistic insights, we explore how tailored assays and orthogonal approaches can increase confidence in hit follow-up and accelerate lead optimization.

2:50 Generative Phosphoproteomics for Rational Drug Design

David Proia, PhD, Senior Vice President, Biology and Drug Discovery, Acrivon Therapeutics

3:20 Zero-Click QSAR and Deep Learning Models Embedded in Chemically Aware Workflows

James White, PhD — Collaborative Communications, CDD Vault

CDD Vault introduces zero-click automated QSAR modeling, a fully hands-off AutoML feature that continuously trains, evaluates, and deploys data models using large-scale benchmarking and cross-validation. Users can also run deep-learning similarity searches, identify novel bioisosteres, and perform 3D protein folding/docking. These AI tools integrate directly into CDD Vault's chemically aware registration, search, and analysis to transform multidisciplinary data into accelerated drug discovery.

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

4:45 Charting the Evolution & Future of Targeted Protein Degradation: From Fundamental Mechanisms to Translational Impact

Alessio Ciulli, PhD, Professor, Chemical & Structural Biology and Director of the Centre for Targeted Protein Degradation, University of Dundee

2nd Annual

Emerging Technologies for Discovery Chemistry

Covalent Approaches and New Biophysical Tools

I will be reflecting on the evolution of the TPD field, from early design principles to today's landscape of PROTACs and molecular glues. Latest advances from the Ciulli Lab in mechanistic understanding and chemical biology of degraders ternary complexes will be showcased. I will also highlight collaborative academic-industry consortia tackling grand challenges with undruggable targets in paediatric cancers and neurodegenerative diseases, charting the next-generation of proximity-based therapeutics.

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

6:30 Close of Day

WEDNESDAY, APRIL 15

7:15 am Registration and Morning Coffee

COVALENT FRAGMENTS

8:00 Chairperson's Remarks

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

8:05 Combining Covalent Fragment Screening, HTP Co-Crystallization, and Direct-to-Biology

Shuai Chen, PhD, Senior Scientist, Medicinal Chemistry, Roche R&D Center (China) Ltd.

A case study shown here is screening with ASC protein, a critical adapter protein in inflammasome activation, making it a promising target for autoimmune disorders. With its PYD and CARD domains providing potential PPI interfaces for drug design, our strategy targets ASC inhibition by disrupting poly-filament formation through covalent binding at Cys173 on its CARD domain. The comprehensive efforts from primary screening, hit validation to fragment-to-lead expansion will be presented.

8:35 FEATURED PRESENTATION: Chemoproteomic Approaches to Shed Light on Functional and Therapeutically Relevant Proteoforms

Keriann Backus, PhD, Associate Professor, Biological Chemistry, University of California, Los Angeles (UCLA)

Cysteine is a unique amino acid, distinguished by its nucleophilicity and sensitivity to oxidative modifications. Therefore, cysteine-reactive molecules have emerged as high value tools for functional biology and drug development applications, and there is widespread interest in the discovery of new ligandable (potentially druggable) and redox sensitive cysteine residues. I will discuss our ongoing efforts cysteine and redox proteomic approaches to define the functional proteoforms targeted by electrophilic compounds.

9:05 Discovery and Structure-Based Rational Design of Novel Reversible and Covalent Inhibitors of a DNA Repair Protein

Nicolas Bocquet, PhD, Director Biochemistry, Biochemistry, FoRx Therapeutics AG

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

DIRECT-TO-BIOLOGY (D2B) & SMALL MOLECULE LEAD GENERATION INCLUDING DEGRADERS

10:30 Direct-to-Biology Applications to Lead Generation

Jack Sadowsky, PhD, Co-Founder & Vice President Discovery Chemistry, Kimia Therapeutics

By removing the synthesis bottleneck associated with traditional hit-to-lead optimization, high-throughput synthesis and direct-to-biology (D2B) screening accelerates the discovery of drug candidates with first-in-class structures and mechanisms. Building on the success of D2B implemented at Carmot Therapeutics, we present Kimia's ATLAS platform, a next-generation D2B and direct-to-ADME (D2A) platform that integrates multiple chemistries and machine learning to guide the search for novel drugs, exemplifying the approach with several case studies.

11:00 Direct-to-Biology Enabled Molecular Glue Discovery

Daniel Blair, PhD, Assistant Member, St. Jude's Children Research Hospital

Molecular glues modulate protein proximity, yet have resisted function-first screening. Here, we present a direct-to-biology approach which can distinguish glues from non-glues. Using high-throughput synthesis and affinity-selection mass spectrometry, we can identify a molecular glue from within 20,000 reaction mixtures. Orthogonal assays confirm gluing behavior. Our results outline a roadmap for *de novo* glue discovery via kinetic profiling of unpurified small molecules against protein pairs.

11:30 PANEL DISCUSSION: Applying D2B to Molecular Glue Discovery

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

12:00 pm Enjoy Lunch on Your Own

1:00 Dessert Break with Navigating Chemistry Careers Breakout Tables

Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

1:30 Close of Emerging Technologies for Discovery Chemistry Conference

8th Annual

AI/Machine Learning for Early Drug Discovery - Part 1

AI-Driven Design and Optimization of Small Molecule, Peptide, and Antibody Drugs

TUESDAY, APRIL 14

7:00 am Registration Open & Morning Coffee

IMPACT OF AI/ML IN EARLY DRUG DISCOVERY

8:00 Welcome Remarks

8:05 Chairperson's Remarks
Anthony Bradley, D.Phil, Assistant Professor, Department of Chemistry, University of Liverpool

8:10 Sharpening the Axe: What in Drug Discovery Does AI Get Wrong (and How to Fix It)
Anthony Bradley, D.Phil, Assistant Professor, Department of Chemistry, University of Liverpool
Better tools? Better drugs. This talk makes the case for verification over generation: prioritize decisions that raise quality and cut the true cost center—LO. We propose active learning + automation, prospective time-split/top-k metrics, and stopping rules to make fewer, better molecules. We outline systems to benchmark these ideas prospectively so teams can convert AI progress into measurable cycle-time gains without eroding clinical success.

8:40 The Invisible Pathways of Innovation: AI and Automation in the New Enterprise Boom
Jose Duca, PhD, Global Head Computer Aided Drug Discovery, Global Discovery Chemistry, Novartis Institutes for Biomedical Research Inc.

9:10 Presentation to be Announced DeepOrigin

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 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.

10:25 Networking Coffee Break

10:50 PANEL DISCUSSION: Closing the Loop: Real-Time Learning with Design, Make, and Test
Moderator: Anthony Bradley, D.Phil, Assistant Professor, Department of Chemistry, University of Liverpool
This panel explores the emergence of true closed-loop discovery, where AI models continuously learn from experimental feedback across design, make, and test cycles. Experts will discuss how automation, active learning, and data integration are reshaping discovery workflows—improving decision quality and iteration speed. We'll highlight successes, persistent bottlenecks, and the next steps toward building scalable, self-improving systems that bridge computation and experimentation in real-world drug discovery.

Panelists:
Jacob Berlin, PhD, Founder & CEO, Terray Therapeutics
Jose Duca, PhD, Global Head Computer Aided Drug Discovery, Global Discovery Chemistry, Novartis Institutes for Biomedical Research Inc.
Ashwini Ghogare, PhD, MBA, GenAI Leader, Start-ups, Life Sciences & Healthcare, Amazon Web Services
Janet Paulsen, PhD, Senior Alliance Manager, Drug Discovery, NVIDIA Corp.
Woody Sherman, PhD, Founder and Chief Innovation Officer, Psivant Therapeutics

12:20 pm Transition to Lunch

12:25 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:55 Session Break

AI-DRIVEN DRUG DESIGN & OPTIMIZATION

1:45 Chairperson's Remarks
Simona Cotesta, PhD, Executive Director Medicinal Chemistry, Novartis Biomedical Research

1:50 Built at the Intersection: Chemistry First, AI-Native *de novo* Small-Molecule Discovery and Development
Narbe Mardirossian, PhD, CTO, Terray Therapeutics

2:20 AI-Driven Discovery of IAM1363: A Next-Generation HER2 Inhibitor with Superior Brain Penetrance and a Unique Type II Binding Mode
Shawn Wright, PhD, Research Scientist II, Iambic Therapeutics Inc.
Using Iambic's AI–driven platform, we developed next-generation HER2 inhibitors with exceptional selectivity, broad mutant coverage, and robust brain penetrance, now under evaluation in a Phase 1/1b clinical trial. IAM1363 represents the first reported Type II HER2 tyrosine kinase inhibitor, binding HER2 in a DFG-out conformation. This program was powered by AI technologies, including PropANE and NeuralPLexer, integrated with high-throughput parallel synthesis and screening to accelerate design and optimization.

2:50 GenAI Applied to Chemical Optimization: Real-World Examples from RNA-Small-Molecule Drug Discovery
Rabia Khan, PhD, MBA, CEO, Serna Bio
Serna Bio is redefining what's possible in drug discovery by opening up RNA as a tractable target class for small-molecule therapeutics. Using proprietary datasets and multiple machine-learning architectures, Serna Bio's GenAI engine has outperformed benchmark models in RNA-relevant chemical space. Combined with multi-parametric optimization functions, our platform can rapidly reduce the time to DC nomination.

3:20 Zero-Click QSAR and Deep Learning Models Embedded in Chemically Aware Workflows CDD VAULT Complexity Simplified
James White, PhD — Collaborative Communications, CDD Vault
CDD Vault introduces zero-click automated QSAR modeling, a fully hands-off AutoML feature that continuously trains, evaluates, and deploys data models using large-scale benchmarking and cross-validation. Users can also run deep-learning similarity searches, identify novel bioisosteres, and perform 3D protein folding/docking. These AI tools integrate directly into CDD Vault's chemically aware registration, search, and analysis to transform multidisciplinary data into accelerated drug discovery.

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

PLENARY KEYNOTE SESSION

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

4:45 Charting the Evolution & Future of Targeted Protein Degradation: From Fundamental Mechanisms to Translational Impact
Alessio Ciulli, PhD, Professor, Chemical & Structural Biology and Director of the Centre for Targeted Protein Degradation, University of Dundee
I will be reflecting on the evolution of the TPD field, from early design principles to today's landscape of PROTACs and molecular glues. Latest advances from the Ciulli Lab in mechanistic understanding and chemical biology of degraders ternary complexes will be showcased. I will also highlight collaborative academic-industry consortia tackling grand challenges with undruggable targets in paediatric cancers and neurodegenerative diseases, charting the next-generation of proximity-based therapeutics.

8th Annual

AI/Machine Learning for Early Drug Discovery - Part 1

AI-Driven Design and Optimization of Small Molecule, Peptide, and Antibody Drugs

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

6:30 Close of Day

WEDNESDAY, APRIL 15

7:15 am Registration and Morning Coffee

AI-BASED SCREENING FOR HIT IDENTIFICATION

8:00 Chairperson's Remarks
Christopher Tame, PhD, Co-Founder & CEO, Ternary Therapeutics

8:05 Recurrent Trends in Successful Computational Hit Finding Workflows from Five CACHE Challenges
Matthieu Schapira, PhD, Principal Investigator, Structural Genomics Consortium; Professor, Pharmacology & Toxicology, University of Toronto
CACHE challenges are prospective hit finding exercises where commercial compounds selected for a pre-defined target protein by computational chemistry and AI experts around the world are tested experimentally. With five challenges completed and two ongoing, patterns are emerging from successful computational workflows, including active learning cycles where virtual screening data generated with physics based methods are iteratively used to train and refine machine learning models.

8:35 The Proof Is in the Pudding: Utility of Co-Folding Models in Fragment-Based Drug Discovery
Marcel Verdonk, PhD, Senior Director, Computational Chemistry & Informatics, Astex Pharmaceuticals
We assess the performance of co-folding methods on fragment screening tasks in varying degrees of difficulty, including their ability to identify fragment binding sites, separate fragment hits from misses, and predict fragment binding modes. We evaluate the utility of these models during the hit-to-lead stages in terms of their ability to predict binding modes and, critically, induced fit. As a benchmark, we use the most comprehensive in-house fragment-based drug-discovery dataset.

9:05 Sponsored Presentation *(Opportunity Available)*

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

AI-ENABLED DEGRADER DESIGN & OPTIMIZATION

10:30 Building a Computational Platform to Design Molecular Glues for Any Protein-Protein Interaction
Christopher Tame, PhD, Co-Founder & CEO, Ternary Therapeutics
Ternary Therapeutics has developed a computational design platform for molecular glues of any protein-protein interaction. This platform has been applied to discover novel molecular glue degraders, activators, and non-degrading inhibitors, which the company is progressing through their drug-discovery pipeline. This presentation will focus on the design and validation of the computational platform.

11:00 Prediction of Molecular Glues for Challenging Targets in Oncology
Bryce Allen, PhD, Co-Founder & CEO, Differentiated Therapeutics

11:30 Prediction of Oral Bioavailability of CRBN-Based PROTACs across Various 2D and 3D Descriptors
Tong Li, PhD, Principal Scientist, In Silico Discovery, Johnson & Johnson
Oral bioavailability of TPDs, especially larger sized bifunctional molecules (i.e. PROTAC), is one of the most challenging properties to be optimized. In this study, a comprehensive *in vivo* data set for CRBN-based PROTACs was collected from public domain and 2D/3D descriptors were developed to establish predictive models for oral bioavailability prediction. We address the different behavior of predictive models on different types of animal models, like mouse and rat models.

12:00 pm Enjoy Lunch on Your Own

1:00 Dessert Break with Navigating Chemistry Careers Breakout Tables
Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

1:30 Close of AI/Machine Learning for Early Drug Discovery – Part 1 Conference

14th Annual

Oral & Macrocyclic Peptides: Discovery to Development - Part 1

Expanding the Frontier of Peptide Therapeutics

TUESDAY, APRIL 14

7:00 am Registration Open & Morning Coffee

ORAL PEPTIDES: CASE STUDIES

8:00 Welcome Remarks

8:05 Chairperson's Remarks

Emel Adaligil, PhD, Executive Director, Chemical Biology and Peptide Macrocycles, Eli Lilly and Company

8:10 Strategic Design of Orally Bioavailable Cyclic Peptide Inhibitors

Atsushi Ohta, PhD, Head of Modality Technology Department, Chugai Pharmaceutical Co., Ltd.

Macrocyclic peptides are promising scaffolds for inhibiting protein-protein interactions. Here, we report a methodology for creating a cell-permeable and orally bioavailable peptide drug by identifying important factors for better drug-likeness and developing library technologies affording highly N-alkylated cyclic peptides. Several examples, including the latest findings, will be featured in this presentation.

8:40 Orally Bioavailable Cyclin A/B RxL Inhibitors: Optimization of a Novel Class of Macrocyclic Peptides to Target E2F High and G1–S-Checkpoint Compromised Cancers

Nathan Dupper, PhD, Scientist II, Organic Chemistry, Circle Pharma Inc.

Cyclins A/B orchestrate key activities throughout the cell cycle. Many substrates and regulators are recruited to the hydrophobic patch on Cyclins A/B through the interaction of their RxL-motif. This session will describe the development of macrocyclic peptide cyclin A/B RxL inhibitors which demonstrate tumor regression in CDX models of small-cell lung cancer via oral dosing. We are currently evaluating Cyclin A/B inhibition in a Phase 1 clinical trial (NCT06577987).

9:10 Sponsored Presentation *(Opportunity Available)*

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 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.

10:25 Networking Coffee Break

10:50 Discovery of Novel Oral Cyclic Peptide PCSK9 Inhibitor SG-6001

Chester Chenguang Yuan, PhD, CoFounder & CSO, Sungening Biosciences

Orally bioavailable cyclic peptides represent a promising class of therapeutic agents, offering significant potential to address unmet medical needs across various disease areas. This presentation highlights the discovery and preclinical development of novel orally active cyclic peptide inhibitors targeting PCSK9 for the treatment of hypercholesterolemia. We will present and discuss preclinical data on SG6001, a preclinical compound identified by Sungening, demonstrating its promise as an effective oral PCSK9 inhibitor.

11:20 Next-Generation Macrocyclic Peptide Drugs: Designing Oral Agents for Difficult-to-Drug Targets

Simon Bailey, PhD, MBA, COO and President, R&D, Unnatural Products, Inc.

Interest in the discovery of peptide drugs is enjoying a resurgence, driven by the GLP-1 agonist class of anti-obesity medicines. Despite the demonstrated benefits of peptide therapeutics, developing oral drugs in this class has proved challenging, due to the difficulty of designing peptides that can cross the gut membrane. This talk will highlight work done at Unnatural Products aimed at developing generalizable approaches for oral delivery of peptide drugs.

11:50 Novel Macrocyclic KIF18A Inhibitors for Treatment of Chromosomally Unstable Tumors: Discovery and Preclinical Characterization

Murali Ramachandra, PhD, CEO, Aurigene Oncology Ltd.

Chromosomal instability (CIN) drives tumor progression and therapy resistance. KIF18A, a kinesin motor protein, maintains spindle integrity during mitosis, and its inhibition selectively kills CIN-high tumor cells while sparing normal cells. Using cryo-EM–guided design, we developed potent, selective macrocyclic KIF18A inhibitors with strong ATPase inhibition, anti-proliferative activity in CIN-high ovarian cancer cells, favorable ADMET and oral bioavailability, and significant *in vivo* efficacy, supporting their advancement as selective anti-CIN therapeutics.

12:20 pm Transition to Lunch

12:25 Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:55 Session Break

PEPTIDE DESIGN INNOVATIONS

1:45 Chairperson's Remarks

Robert D. Mazzola, PhD, Director & Principal Scientist, Chemical Research, Merck & Co.

1:50 Rational Design of Peptide Therapeutics

Krishna Kumar, PhD, Robinson Professor of Chemistry, Tufts University

Peptide hormones offer a versatile platform for engineering next-generation therapeutics. We present a rational design strategy that integrates structural insight, receptor pharmacology, and iterative optimization to tune potency, selectivity, and stability. By systematically combining modular sequence elements, we generate multifunctional peptide constructs that engage complementary pathways, highlighting general principles for translating natural signaling scaffolds into clinically promising metabolic drug leads.

2:20 *De novo* Design of D-Peptide Ligands

Rameshwar Kadam, PhD, Senior Scientist II, Structural & Protein Sciences, Johnson & Johnson Innovative Medicine

D-peptides exhibit superior stability and reduced immunogenicity compared to L-peptides, yet their discovery has been constrained by traditional screening approaches. We present a computational framework for *de novo* design of D-peptides that accurately targets epitopes without requiring synthesis of D-enantiomeric proteins. This strategy enables efficient development of stable, nonimmunogenic peptide therapeutics, offering broad applicability and the potential to accelerate drug discovery across diverse biological targets.

2:50 A New Biocompatible Peptide Cyclization: Development and Application

Tianxiong Mi, PhD, Senior Scientist, Discovery Chemistry, Merck & Co.

Macrocyclic peptides are a compelling modality for disrupting protein-protein interactions. Beyond thioether formation and CuAAC, novel biocompatible cyclization methods are being developed to broaden the synthetic toolbox for macrocycle construction in both singleton and library formats. This presentation highlights our efforts to initiate new ring-closing chemistry and its integration into macrocyclic DNA-encoded library (DEL) platform for hit discovery.

3:20 Sponsored Presentation *(Opportunity Available)*

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

Oral & Macrocyclic Peptides: Discovery to Development - Part 1

Expanding the Frontier of Peptide Therapeutics

PLENARY KEYNOTE SESSION

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

4:45 Charting the Evolution & Future of Targeted Protein Degradation: From Fundamental Mechanisms to Translational Impact
Alessio Ciulli, PhD, Professor, Chemical & Structural Biology and Director of the Centre for Targeted Protein Degradation, University of Dundee
I will be reflecting on the evolution of the TPD field, from early design principles to today's landscape of PROTACs and molecular glues. Latest advances from the Ciulli Lab in mechanistic understanding and chemical biology of degraders ternary complexes will be showcased. I will also highlight collaborative academic-industry consortia tackling grand challenges with undruggable targets in paediatric cancers and neurodegenerative diseases, charting the next-generation of proximity-based therapeutics.

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

6:30 Close of Day

WEDNESDAY, APRIL 15

7:15 am Registration and Morning Coffee

LIBRARIES FOR MACROCYCLIC PEPTIDE DRUG DISCOVERY

8:00 Chairperson's Remarks
Charles Johannes, PhD, Founder, President, and Chief Scientist, EPOC Scientific LLC; Vice President, Peptide Drug Hunting Consortium

8:05 Pure-DEL: DNA-Encoded Libraries to Discover Small Macrocyclic Peptides with Drug Potential
Jörg Scheuermann, PhD, Professor, Department of Chemistry & Applied Biosciences, ETH Zurich
Pure-DEL technologies features the solid phase-based synthesis of ultra-large libraries of highly-pure and chemically diverse DNA-encoded small macrocyclic peptides with drug-like properties. Pure-DELs can be screened at once in affinity-based selections and I will present the results of Pure-DEL selections for a variety of "undruggable" targets.

8:35 Integrating mRNA Display and DNA-Encoded Libraries for Cyclic Peptide Drug Discovery
Xiaojie Bruce Lu, PhD, Professor & Principal Investigator, Chemical Biology Research Center, Chinese Academy of Sciences
DNA encoded cyclic peptide library is a powerful platform for cyclic peptides identification and optimization for biological interesting therapeutic targets with the advantage for the inclusion of thousands of unnatural amino acids and diverse cyclization methods for the library construction. The integration between mRNA Display and DNA Encoded Libraries could effectively accelerate the cyclic peptide drug development by speeding up the hit (generated by the mRNA display) to lead optimization.

9:05 Oral Peptide Inhibitors of IL-1b for Atherosclerotic Cardiovascular Disease
Christopher Plummer, PhD, Senior Director, Discovery Chemistry, Merck & Co
An oral therapy to treat the inflammatory components of cardiovascular disease would meet a significant unmet need for CVD patients at high risk for major adverse cardiovascular events. mRNA-display was leveraged to generate a macrocyclic peptide inhibitor of IL-1b as a starting point for molecular optimization. Structure-based drug design and informatics were utilized to progress this hit toward suitable candidates for oral pk and *in vivo* PK/PD studies.

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

PEPTIDE THERAPEUTICS: DEVELOPMENT CHALLENGES

10:30 Innovations in Peptide Chemistry to Enable Discovery of an Oral, Unimolecular GLP-1 and Amylin Receptor Agonist
Thomas E. Nielsen, PhD, Corporate Vice President, Drug Product Research, Novo Nordisk AS
Recombinant expression can efficiently and sustainably produce high-volume active pharmaceutical ingredients. However, this approach can also pose challenges to peptide drug design if a range of extensive post-recombinant chemistry is required to preserve drug-like properties. Here, we present innovations in peptide chemistry to convert recombinantly expressed peptides into biologically active C-terminal a-amides, as well as key medicinal chemistry efforts, in the discovery of an oral, unimolecular GLP-1 and amylin agonist.

11:00 PANEL DISCUSSION: Current and Future Directions of Peptide Therapeutics
Moderator: Katerina Leftheris, PhD, formerly CSO, Vilya Therapeutics
- How important is oral bioavailability
- Impact of GLP1 innovations
- Formulation advances

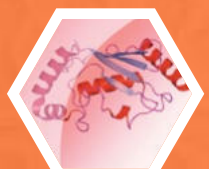
12:00 pm Enjoy Lunch on Your Own

1:00 Dessert Break with Navigating Chemistry Careers Breakout Tables
Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

1:30 Close of Oral & Macrocyclic Peptides Part 1 Conference

"Very good and relevant content covering recent innovations and trends in DD. The organizers are very experienced and understand the drug discovery audience needs very well mostly through making direct and long-lasting connections."

ANASTASIA V, VP, VILYA



9th Annual

Degraders & Molecular Glues - Part 2

Pursuing Challenging Drug Targets, Exploring New Ligases and Degradation Pathways

WEDNESDAY, APRIL 15

12:00 pm Registration Open

1:00 Dessert Break in the Exhibit Hall with Navigating Chemistry Careers Breakout Tables

Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

EMERGING MODALITIES FOR DEGRADATION

1:30 Welcome Remarks

1:35 Chairperson's Remarks

Dominic J. Reynolds, PhD, CSO, R&D, Remix Therapeutics

1:40 FEATURED PRESENTATION: Development of Degrader-Antibody Conjugates (DACs)

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

While protein degraders are typically more potent and efficacious than traditional small-molecules, there are significant barriers for their successful development, including more pronounced toxicities against normal tissues for many protein targets and sub-optimal pharmacokinetics. Degrader-antibody conjugates (DACs) have emerged as a new therapeutic modality with advantages of antibody-drug conjugates (ADCs) and protein degraders. I will present development of degrader-antibody conjugates (DACs) targeting transcriptional factors for the treatment of human cancers.

2:10 Next-Generation Antibody Degraders: Design Principles for Tissue-Specific Receptor Degradation and ADC Payload Delivery

Felipe de Sousa e Melo, PhD, Director, Large Molecule Modality, Induced Proximity Platform, Amgen

We engineered bispecific antibody degraders to achieve tissue-restricted degradation of cell-surface receptor targets. These molecules drive receptor internalization and lysosomal clearance while minimizing toxicity and enhancing specificity. They can also be adapted into next-generation ADCs to deliver potent, selective efficacy. This versatile platform integrates cell surface receptor degradation with payload delivery, advancing safer and more effective antibody-based degraders.

2:40 Sponsored Presentation *(Opportunity Available)*

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Strategies to Drug RNA-Protein Complexes with Small Molecules

Dominic J. Reynolds, PhD, CSO, R&D, Remix Therapeutics

REM-422, a first-in-class mRNA Degrader of the MYB Oncogene, is being developed by Remix Therapeutics for the treatment of ACC and AML/HR-MDS. The REMaster platform identifies compounds that address undruggable, high unmet medical-need targets. These next-generation drug discovery programs are enabled by a suite of biophysical assays and expand the scope of pharmacologically tractable splice modulator modalities.

4:30 From Membranes to Lysosomes: Rewriting Protein Fate with Small-Molecule LYMTACs

Dhanusha Nalawansha, PhD, Senior Scientist, Induced Proximity Platform, Amgen Inc.

LYMTACs are heterobifunctional small molecules that harness lysosomal membrane proteins (LMPs) to relocalize and degrade otherwise undruggable membrane proteins. We demonstrate that oncogenic KRASG12D signaling can be effectively inhibited by LYMTACs, which act through both target relocalization and degradation. Extending this approach across diverse targets and LMPs, we establish LYMTACs as a versatile small molecule-based platform for targeted lysosomal degradation of challenging membrane proteins, expanding therapeutic possibilities.

5:00 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 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.

5:45 Close of Day

6:15 Dinner Short Courses*

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

THURSDAY, APRIL 16

7:30 am Registration and Morning Coffee

PLENARY KEYNOTE SESSION

8:15 Plenary Welcome Remarks from Lead Content Director

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

8:25 Directed and Random Walks in Chemical Space

Brian K Shoichet, PhD, Professor & Chair, Pharmaceutical Chemistry, University of California San Francisco (UCSF)

Docking libraries have rapidly expanded from three million to over a trillion molecules. We compare billion vs. million molecule library docking on the same targets, demonstrating that as the libraries grow so too do hit-rates and affinities. I consider how and if new ML methods separate true from false positives. How good are our subsequent ligand optimization strategies versus what we might expect against a random background? (surprisingly unimpressive).

9:10 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

MOLECULAR GLUES FOR NOVEL TARGETS

10:00 Chairperson's Remarks

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

10:05 Molecular Glue Degraders Overcome Target-Engaging Limits of Traditional Inhibitors

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

Roughly 75% of disease targets are considered difficult-to-drug or insufficiently drugged. Molecular glue degraders provide an unique approach to engage these targets. I will use case studies from Degron's internal pipeline programs to illustrate the power of molecular glue degraders to overcome such challenges and even illuminate novel target biology in disease treatment.

10:35 FEATURED PRESENTATION: Modulation of Cancer-Specific Interactomes via Chemical Switches and Molecular Glues

Arvin Dar, PhD, Professor, Chemical Biology, Memorial Sloan Kettering Cancer Center

9th Annual

Degraders & Molecular Glues - Part 2

Pursuing Challenging Drug Targets, Exploring New Ligases and Degradation Pathways

Chemically-induced proximity of bimolecular complexes is a powerful modality to rewire signal transduction networks. Most extensively studied in the context of protein degradation, its full scope and potential for novel targets and pharmacological mechanisms has yet to be realized. I will discuss structure-based strategies to advance it in several complementary areas, including an approach to overcome drug resistance and as a mechanism to achieve ultra-selective modulators of kinase targets.

11:05 Sponsored Presentation *(Opportunity Available)*

11:20 Protein Relocalization Using Covalent Molecular Glues

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

We discovered a covalent GSTP1 inhibitor that functions as a molecular glue via a ligand-induced protein tethering (LIPT) mechanism. Electrophilic modification of GSTP1 induces reversible disulfide-dependent protein–protein interactions enriched in nuclear and splicing factors. LIPT relocalizes splicing factors, altering lipid metabolism and suppressing proliferation in LIPT-sensitive cancer cells. These findings highlight covalent molecular glues as a strategy to modulate neo-PPIs and cancer metabolism.

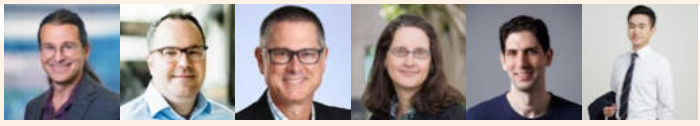
11:50 Transition to Lunch

12:00 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:30 Transition to VC Panel

INSIGHTS FROM VENTURE CAPITALISTS

12:40 PANEL DISCUSSION: VC Insights on Drug-Discovery Trends



Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation
Panelists:
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Sarah Hymowitz, PhD, Partner, The Column Group
Jamie Kasuboski, PhD, Partner, Luma Group
Ken Lin, CEO & Founder, ABIES Capital

1:30 Dessert Break with Meet the VC Panelists and Poster Awards

GLUE DISCOVERY & OPTIMIZATION

2:10 Chairperson's Remarks

Maria Soloveychik, PhD, Co-Founder & CEO, SyntheX

2:15 Transforming Molecular Glue Discovery with an Empirical, Cell-Based, Discovery Platform

Maria Soloveychik, PhD, Co-Founder & CEO, SyntheX

ToRNeDO is an empirical, cell-based platform that revolutionizes molecular glue discovery by eliminating reliance on serendipitous discoveries. ToRNeDO enables functional selection of molecular glues that use specific target/ligase pairs. The system is used to map novel degrons for rational glue design. Using this platform, we discovered highly selective molecular glues against previously untargeted effectors and E3s, demonstrating ToRNeDO's potential to unlock new therapeutic strategies through systematic, directed molecular glue development.

2:45 Leveraging High-Throughput Proteomics and AI to Accelerate Molecular-Glue Discovery

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

Key topics of discussion include the power of high-throughput proteomics for unbiased discovery of novel neosubstrates, the application of AlphaFold-like algorithms to predict ternary complex structures, and the use of direct-to-biology strategies to expand the chemical space. These integrated approaches are paving the way for the next generation of molecular glue therapeutics.

3:15 An Industry Case Study in Mechanistic PK/PD Modeling of Covalent Degraders: Interspecies Differences, Long-Acting Injectables, and the Four Pillars

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

3:45 Networking Refreshment Break

DEL FOR TARGETED PROTEIN DEGRADATION

4:00 Phenotypic DEL in Droplets for TPD and Beyond

Mihaljo Todorovic, PhD, Principal Scientist II, Medicinal Chemistry, Novartis Institutes of 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.

4:30 Picowell DEL Screening Enables the Discovery of Cereblon Modulator PLX-66140, a Potent and Selective CDK2 Degrader for CCNE1-Amplified Cancers

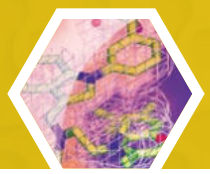
Jean-Francois Brazeau, PhD, Director, Medicinal Chemistry, Plexium Inc.

Herein, we report the discovery of PLX-66140, a potent CDK2 cereblon-based degrader. Using Plexium's picowell DEL screening platform, we identified multiple CDK2 degrader hits. Medicinal chemistry optimization resulted in the identification of a selective and orally bioavailable drug development candidate. Oral administration of PLX-66140 in tumor-bearing mice demonstrated robust target degradation and enhanced anti-tumor activity over ATP-competitive inhibitors in multiple CCNE1-amplified mouse xenograft models at well tolerated doses.

5:00 DEL-Origin Compounds Progressing in Clinical Trials

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

5:30 Close of Conference



19th Annual

Targeting Protein-Protein Interactions

Medicinal Chemistry Progress against Intractable Targets

WEDNESDAY, APRIL 15

12:00 pm Registration Open

1:00 Dessert Break in the Exhibit Hall with Navigating Chemistry Careers Breakout Tables

Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

PROTEIN-PROTEIN INTERACTIONS (PPIs) AS DRUG TARGETS

1:30 Welcome Remarks

1:35 Chairperson's Remarks

Heike Wobst, PhD, Director, Pharmacology, Jnana Therapeutics

1:40 FEATURED PRESENTATION: Cutting and Gluing: Manipulating Protein-Protein Interactions Guided by Biophysical Insight

Mela Mulvihill, PhD, Director and Distinguished Scientist, Biochemical & Cellular Pharmacology, Genentech, Inc.

Protein-protein interactions (PPIs) are fundamental to biology and disease, making them attractive therapeutic targets. Small molecule (SM) drugs have major benefits such as permeability and bioavailability, but developing SMs against PPI surfaces is challenging. Recent advances in modalities such as peptides and molecular glues have improved the ability to manipulate PPIs, enabling both inhibition and induction. This presentation features case studies demonstrating compound-induced PPI mechanisms and their elucidation using biophysics.

2:10 Photocatalytic Proximity Proteomics for Mechanistic Understanding of PPIs

Jordan Mattheisen, PhD, Postdoctoral Fellow, Chemical Biology, AstraZeneca

Protein-protein interactions govern cellular signaling and drug responses. Photocatalytic proximity labeling uses light-activated iridium or xanthene photocatalysts linked to targeting modalities to generate reactive species that tag proximal proteins, enabling high-resolution mapping of protein neighborhoods in living cells by MS proteomics. This talk will discuss the approach used to validate small-molecule target engagement, elucidate protein degrader mechanisms, and reveal previously hidden disease-relevant interactions, accelerating discovery of next-generation therapeutics.

2:40 Sponsored Presentation *(Opportunity Available)*

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Discovery of a Selective Covalent Inhibitor of Werner Syndrome Helicase (WRN), MOMA-341: Chemically Distinct and Potent

Momar Toure, PhD, Director, Medicinal Chemistry, MOMA Therapeutics

MOMA-341 is a distinct, potent and selective clinical stage covalent inhibitor of WRN. Covalent series optimization was based on refinement of covalent warhead trajectory, compound rigidity, and improvement of binding affinity to drive high kinact/KI. Further refinement of potency and ADME properties, guided by in vivo target occupancy prediction, led to the discovery of MOMA-341, which demonstrates robust tumor regression in mouse xenograft models and is in clinical development.

4:30 A Review of Frequent Hitters/Promiscuous Compounds in FDA-Approved Libraries Used for Drug Repurposing

Jonathan B. Baell, PhD, Chief Scientific Officer, Manas AI

The allure of testing compound libraries comprising clinically-used drugs is compelling: your screening hit is already FDA-approved and hence can be repurposed to serve your new target along with its associated indication to progress straight into patients. Not only is thinking flawed, but, as we now describe, we have identified with statistical proof the more concerning phenomenon that widely used drug repurposing libraries are disproportionately populated by promiscuous compound.

5:00 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 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.

5:45 Close of Day

6:15 Dinner Short Courses*

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

THURSDAY, APRIL 16

7:30 am Registration and Morning Coffee

PLENARY KEYNOTE SESSION

8:15 Plenary Welcome Remarks from Lead Content Director

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

8:25 Directed and Random Walks in Chemical Space

Brian K Shoichet, PhD, Professor & Chair, Pharmaceutical Chemistry, University of California San Francisco (UCSF)

Docking libraries have rapidly expanded from three million to over a trillion molecules. We compare billion vs. million molecule library docking on the same targets, demonstrating that as the libraries grow so too do hit-rates and affinities. I consider how and if new ML methods separate true from false positives. How good are our subsequent ligand optimization strategies versus what we might expect against a random background? (surprisingly unimpressive).

9:10 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

STABILIZERS OF PPIs: NON-DEGRADING GLUES

10:00 Chairperson's Remarks

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

10:05 RIPTAC "Hold-and-Kill" Approach for Cancer Targets: Prostate Cancer Clinical Candidate HLD-0915

Kyle J. Eastman, PhD, Vice President, Chemistry, Halda Therapeutics Inc.

Phase 1 clinical candidate HLD-0915, a Regulated Induced Proximity Targeting Chimera (RIPTAC) Therapeutic, is a heterobifunctional small molecule that leverages full-length AR expression in tumor cells to form a cooperative trimeric complex with AR and BRD4, resulting in BRD4 loss of function in mCRPC cells and a potent antitumor effect. HLD-0915 activity requires only presence, not driver status, of FL-AR and retains activity in models of anti-androgen therapy resistance settings.

10:35 14-3-3 Molecular Stabilization of Parkinson's Disease Target LRRK2

Christian Ottmann, PhD, Founder CTO, Ambagon Therapeutics

14-3-3s are regulatory proteins for LRRK2. Upon phosphorylation-dependent binding of 14-3-3 to LRRK2, kinase activity and propensity for oligomerization and aggregation of LRRK2 are reduced. We are developing molecular glues that bind to the interface of LRRK2 and 14-3-3, stabilize the inhibitory binding of 14-3-3

to LRRK2 and counteract the above-mentioned PD-related LRRK2 activities. We present the protein crystallography-guided optimization of these cooperative 14-3-3 molecular glues toward cell active compounds.

11:05 Sponsored Presentation *(Opportunity Available)*

11:20 Disruption of PPIs by Non Degrading Molecular Glues—A Survey of Ternary X-Ray Crystal Structures

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

This presentation will highlight the RapaGlue platform, a novel non-degrading macrocyclic molecular glue modality for modulating hard-to-drug targets. We will present new ternary X-ray structures of TRADD and TRAF2 revealing unique PPI-disrupting binding modes. Analysis of the RapaGlue DNA-encoded library will demonstrate diverse binding across transcription factors, GSTP1, TRADD, and TRAF2. We will also discuss integrated AI/ML design and structural data guiding SAR strategies to enhance binding and drug-like properties.

11:50 Transition to Lunch

12:00 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:30 Transition to VC Panel

INSIGHTS FROM VENTURE CAPITALISTS

12:40 PANEL DISCUSSION: VC Insights on Drug-Discovery Trends

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation
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1:30 Dessert Break with Meet the VC Panelists and Poster Awards

TARGETING NEURODEGENERATION OR CANCER PROTEIN COMPLEXES

2:10 Chairperson's Remarks

Simona Cotesta, PhD, Executive Director Medicinal Chemistry, Novartis Biomedical Research

2:15 Targeting Tau in Neurodegenerative Disease Models: Applying Orthogonal Biophysical Approaches for PPI-Based Drug Discovery

Shaun McLoughlin, PhD, Principal Scientist I, High Throughput Screening, AbbVie Inc

Tauopathies are characterized by the formation of tau protein-based neurofibrillary tangles which impede neuronal function. Here, we sought to identify new targets to address tauopathies, through a phenotypic screen using a cellular model of tau-aggregate clearance. An optimized analogue derived from this effort induced aggregate clearance in multiple models of hTauP301L aggregation at nanomolar concentrations. Chemoproteomic studies implicated protein disulfide isomerase 1 (P4HB), as a candidate target.

2:45 New Modalities, Including Degraders, for Neurodegenerative PPI Targets

Nur Kocaturk, PhD, Post Doctoral Fellow, Center for Targeted Protein Degradation, University of Dundee

The use of small molecule induced proximity to understand and potentially treat neurodegenerative diseases holds significant potential. Targeted Protein Degraders are having growing clinical impact with examples of CNS-active Proteolysis Targeting Chimeras entering Phase1 trials. Nevertheless, paths to prospectively identify and profile such molecules for CNS application remains underexplored. I will discuss how we approach the discovery of CNS-compliant chemical space for induced proximity modalities and our key learnings.

3:15 What can we Learn for Future Drugs?: Analyzing Dose Regimen, Pharmacokinetics and Safety of Recently Approved Small Molecule Oral Drugs

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

An analysis 104 small molecule oral drugs approved by the FDA from 2020-2024 was conducted on approved dose, human pharmacokinetics, safety and DDIs. This analysis highlights several successful drugs with properties that may be considered outside the range of typical drugs, such as high dose, high clearance or low oral bioavailability. These insights may help scientists to understand which risks may be acceptable to developing small molecule drugs.

3:45 Networking Refreshment Break

4:00 Adventures in Aspartate: Covalent Targeting of KRAS G12D

Veronika Ehmke, PhD, Senior Principal Scientist, Global Discovery Chemistry, Oncology, Novartis Biomedical Research Basel

Efforts for covalent targeting non-cysteine mutants like KRASG12D have been hampered by the lack of suitable electrophiles. The development of ß-lactone warheads has enabled structure-guided design and optimization of covalent aspartate-reactive inhibitors. X-ray crystallography and quantum chemical calculations of transition-state barrier heights have been employed to establish structure-activity and -stability correlations with the goal of broadening the use of aspartate covalency and substituted ß-lactones as chemoselective electrophiles in medicinal chemistry.

4:30 Targeting Oncogenic RAS^{G12D}(ON) and RAS^{G12V}(ON) with Tri-Complex Inhibitors

Mark Tye, PhD, Scientist II Medicinal Chemist, Discovery Chemistry, Revolution Medicines

We developed a platform of RAS(ON) tri-complex inhibitors that bind cyclophilin A (CYPA). The resulting binary complex engages RAS(ON), forming a tri-complex that sterically inhibits RAS interaction with its downstream effectors. We generated multiple RAS(ON) mutant-selective and multi-selective inhibitors. We will discuss the G12D- and G12V-selective inhibitors zoldonrasib (RMC-9805) and RMC-5127, respectively. These inhibitors suppress RAS pathway signaling and induce tumor regressions in KRAS mutant human xenograft models in mice.

5:00 Presentation to be Announced

5:30 Close of Conference

WEDNESDAY, APRIL 15

12:00 pm Registration Open

1:00 Dessert Break in the Exhibit Hall with Navigating Chemistry Careers Breakout Tables
Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

DNA-ENCODED LIBRARY (DEL) INNOVATIONS AND TRENDS

1:30 Welcome Remarks

1:35 Chairperson's Remarks
Carol Mulrooney, PhD, Investigator, Cheminformatics, GlaxoSmithKline

1:40 FEATURED PRESENTATION: Beyond Boundaries—Driving DEL Innovation across Targets and Technologies
Timothy L. Foley, PhD, Senior Principal Scientist & Lab Head, DNA Encoded Library Selection & Pharmacology, Pfizer Global R&D Groton Labs

2:10 DEL-Based Identification of PTPN22 Modulators: Inhibitors, Activators, and Degraders from Distinct Allosteric Sites
Henry Korman, PhD, Senior Scientist II, Global Medicinal Chemistry, AbbVie Inc.

2:40 Sponsored Presentation *(Opportunity Available)*

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Activity- and Cell-Based Screening Technology across Encoded Library Modalities
Brian M. Paegel, PhD, Professor, Pharmaceuticals Sciences, University of California, Irvine
Encoded library technologies—mRNA display, DEL, SELEX—have become increasingly important components of the early-discovery toolkit as targets become more complex. These technologies operate via affinity selection to identify ligands, which may or may not be functional. Given that binding is a prelude to function, we are developing technology to interface affinity-selection output (binders) scalably with activity-based and cellular screening for these various modalities.

4:30 Meta-Analysis of Recent Trends in DNA-Encoded Library Hits and Computational Approaches
Raphael Franzini, PhD, Assistant Professor, Medicinal Chemistry, University of Utah
There is a rapidly growing number of successful applications of DNA-encoded libraries for the discovery of bioactive molecules in pharmaceutical development. Recently, the integration of DNA-encoded libraries with machine learning and computational methods has gained traction, aiming to predict the activity of commercially available compounds. This presentation will highlight ongoing developments and provide a meta-analysis of recent reports, identifying the current state of capabilities and limitations.

5:00 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 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.

5:45 Close of Day

6:15 Dinner Short Courses*
**Premium Pricing or separate registration required. See Short Courses page for details.*

THURSDAY, APRIL 16

7:30 am Registration and Morning Coffee

PLENARY KEYNOTE SESSION

8:15 Plenary Welcome Remarks from Lead Content Director
Anjani Shah, PhD, Senior Conference Director, Cambridge Healthtech Institute

8:25 Directed and Random Walks in Chemical Space
Brian K Shoichet, PhD, Professor & Chair, Pharmaceutical Chemistry, University of California San Francisco (UCSF)
Docking libraries have rapidly expanded from three million to over a trillion molecules. We compare billion vs. million molecule library docking on the same targets, demonstrating that as the libraries grow so too do hit-rates and affinities. I consider how and if new ML methods separate true from false positives. How good are our subsequent ligand optimization strategies versus what we might expect against a random background? (surprisingly unimpressive).

9:10 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

DEL APPROACHES FOR G-PROTEIN-COUPLED RECEPTORS

10:00 Chairperson's Remarks
Christopher B. Phelps, PhD, Vice President and Head, Early Discovery, Nurix Therapeutics, Inc.

10:05 Exploring GPCR Allostery Using High-Throughput DEL Screening
Evan O'Brien, PhD, Assistant Professor, Biophysics & Biophysical Chemistry, The Johns Hopkins University School of Medicine
G-protein-coupled receptors (GPCRs) have an extremely complex allosteric landscape. This complexity plays a key role in determining their multifaceted signaling outcomes. In order to properly exploit this complexity, new ligands are needed. DNA-encoded chemical libraries (DELs) have proven to be a valuable tool for discovery of such novel GPCR allosteric modulators that can both teach us about GPCR allostery and serve as powerful lead molecules for pain and overdose.

10:35 Enabling DNA-Encoded Libraries for the Discovery of Small-Molecule Modulators of Obesity-Related Peptide-Binding GPCRs
Ching-Hsuan Tsai, PhD, Executive Director, Structure Therapeutics
GPCRs present unique challenges to drug discovery due to their low expression, structural complexity, and limited stability. I will describe how Structure Therapeutics integrates reagent and tool compound generation with biophysical and biochemical characterization to enable DEL screening and identify novel small-molecule starting points for obesity-related GPCR targets.

11:05 Sponsored Presentation *(Opportunity Available)*

11:20 Encoding Both Chemicals and Assays with DNA for Applications in Medicinal Chemistry
Casey J. Krusemark, PhD, Associate Professor, Medicinal Chemistry & Molecular Pharmacology, Purdue University
The commonly used assay for DNA-encoded chemical libraries (DELs) is a simple affinity selection with an immobilized protein on a bead. We present alternative approaches for discovery to improve selection results using bromodomains as a test-bed target group. We also present the use of DNA-linked compounds

as assay probes and their application in assaying conventional compound collections and one-bead-one-compound (OBOC) libraries in high-throughput screening (HTS).

11:50 Transition to Lunch

12:00 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:30 Transition to VC Panel

INSIGHTS FROM VENTURE CAPITALISTS

12:40 PANEL DISCUSSION: VC Insights on Drug-Discovery Trends

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1:30 Dessert Break with Meet the VC Panelists and Poster Awards

FROM HIT-TO-LEAD: DEL APPLICATIONS

2:10 Chairperson's Remarks
Ken Yamada, PhD, Associate Director, Global Discovery Chemistry, Novartis BioMedical Research

2:15 Biophysical Methods for Encoded Oligonucleotide Hit Qualification and Development
Rajeev Chorghade, PhD, Principal Scientist, Biophysics, GlaxoSmithKline

2:45 Applying DEL Technology for Lead Generation across Diverse Targets: Case Studies
Benjamin Brennecke, PhD, Scientist, DELT Platform, Small Molecule Research Lead Discovery, F. Hoffmann-La Roche Ltd.
The DELT platform is a central hit identification methodology at Roche. We utilize property-driven building block selection and innovative library design to generate attractive chemical starting points for drug discovery programs. In this talk, I will discuss how we leverage the implementation of novel strategies and new modalities to enable our DELT platform having a sustainable impact on Roche's small-molecule discovery pipeline.

3:15 Presentation to be Announced

3:45 Networking Refreshment Break

DEL FOR TARGETED PROTEIN DEGRADATION

4:00 Phenotypic DEL in Droplets for TPD and Beyond
Mihaljo Todorovic, PhD, Principal Scientist II, Medicinal Chemistry, Novartis Institutes of 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.

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Jean-Francois Brazeau, PhD, Director, Medicinal Chemistry, Plexium Inc.
Herein, we report the discovery of PLX-66140, a potent CDK2 cereblon-based degrader. Using Plexium's picowell DEL screening platform, we identified multiple CDK2 degrader hits. Medicinal chemistry optimization resulted in the identification of a selective and orally bioavailable drug development candidate. Oral administration of PLX-66140 in tumor-bearing mice demonstrated robust target degradation and enhanced anti-tumor activity over ATP-competitive inhibitors in multiple CCNE1-amplified mouse xenograft models at well tolerated doses.

5:00 DEL-Origin Compounds Progressing in Clinical Trials
Christopher B. Phelps, PhD, Vice President and Head, Early Discovery, Nurix Therapeutics, Inc.

5:30 Close of Conference

"The beauty of Drug Discovery Chemistry conferences is the even when clinical stage compounds and clinical results are presented, the talks never lose the science; the presentations stay married to the underlying chemistry.

MARK P., CYCLENIUM

8th Annual

AI/Machine Learning for Early Drug Discovery - Part 2

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

WEDNESDAY, APRIL 15

12:00 pm Registration Open

1:00 Dessert Break in the Exhibit Hall with Navigating Chemistry Careers Breakout Tables

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SPOTLIGHT SESSION: WHERE CAN AI/ML MAKE A DIFFERENCE?

1:30 Welcome Remarks

1:35 Chairperson's Remarks
Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.

1:40 Drug Hunter's Guide to the AI/ML Galaxy
Tudor Oprea, MD, PhD, CEO, Expert Systems, Inc.
We will briefly discuss the difference between machine learning (ML) and artificial intelligence (AI). While scientific aspects are often highlighted, economics are rarely discussed. Reliable ML models in early drug discovery allow us to be wrong more often, as long as we use active learning. Agentic AI models, combined with ML, are shifting the probability of success from companies with "the most data" to those with "the most GPUs."

2:10 Data to Enable AI Drug Discovery: Where Can AI Move the Needle?
John Overington, PhD, Chief Data Officer, Drug Hunter Inc.
It's clear that the application of AI in drug discovery needs data, and based upon historically available data there have been profound advances in parts of the drug discovery process using AI/ML—ranging from ligand-receptor docking and virtual screening; federated learning; genomics, genetics, and 'omics data integration and analysis; and via the application and tuning of LLMs to scientific use cases. However, there are many operational challenges ahead.

2:40 Sponsored Presentation *(Opportunity Available)*

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Where is the AI in Drug Discovery, and Where Should it be Instead?
Abraham Heifets, PhD, Former Co-Founder & Former CEO, Atomwise Inc.
Despite intense interest, it is safe to say that AI has not been as quickly embraced in drug discovery. Why not? Where have we seen successes so far, what would it take to deliver true transformative value? I'll share my answers to these questions, based on my perspective of co-founding one of the first AI-for-pharma startups, and offer suggestions to where new entrepreneurs can find opportunities in the current landscape.

4:30 Q&A with Session Speakers

5:00 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 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.

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THURSDAY, APRIL 16

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8:25 Directed and Random Walks in Chemical Space
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Docking libraries have rapidly expanded from three million to over a trillion molecules. We compare billion vs. million molecule library docking on the same targets, demonstrating that as the libraries grow so too do hit-rates and affinities. I consider how and if new ML methods separate true from false positives. How good are our subsequent ligand optimization strategies versus what we might expect against a random background? (surprisingly unimpressive).

9:10 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

EXPLORING CHEMICAL SPACE USING AI/ML SCREENING

10:00 Chairperson's Remarks
Ruben Abagyan, PhD, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego

10:05 Drug Discovery with Fast and Accurate Docking and ML/AI Tools in Multiple Chemical Spaces
Ruben Abagyan, PhD, Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego
Rapid expansion of high-resolution data in 3D and molecular activity space led to new methods and a large variety of 3D/ML/AI predictive models of thousands of activities. A pipeline of target definition, defining its chemical and 3D state, search of synthesizable chemicals in giga-/tera-spaces, and re-ranking the top compounds by a complex profile is presented. Several projects illustrate the process that led to drug candidates in clinical trials.

10:35 Transparent Trillion-Scale Docking with ChemSTEP
Olivier Mailhot, PhD, Assistant Professor, Faculty of Pharmacy, Institute for Research in Immunology and Cancer, Université de Montréal
Make-on-demand libraries are so large that brute-force docking can't keep up. ChemSTEP is a simple, transparent way to explore huge libraries to only dock what's worth docking, recovering most top virtual hits at a fraction of the compute. Instead of black-box AI/ML, ChemSTEP uses familiar chemical-similarity logic, yet delivers over 2,000-fold acceleration and equivalent-to-superior performance compared to AI/ML. We'll show results from docking a 1-trillion library against model targets.

11:05 Sponsored Presentation *(Opportunity Available)*

11:20 Optimization Algorithms for Chemical Systems and Processes
Gaurav Chopra, PhD, Professor, Department of Chemistry, Purdue University

11:50 Transition to Lunch

12:00 pm Luncheon Presentation *(Sponsorship Opportunity Available)* **or Enjoy Lunch on Your Own**

12:30 Transition to VC Panel

8th Annual

AI/Machine Learning for Early Drug Discovery - Part 2

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

INSIGHTS FROM VENTURE CAPITALISTS

12:40 PANEL DISCUSSION: VC Insights on Drug-Discovery Trends

Moderator: Daniel A. Erlanson, PhD, Chief Innovation Officer, Frontier Medicines Corporation
Panelists:
Chris De Savi, PhD, CSO Partner, Curie Bio
James Edwards, PhD, Venture Partner, Samsara BioCapital
Sarah Hymowitz, PhD, Partner, The Column Group
Jamie Kasuboski, PhD, Partner, Luma Group
Ken Lin, CEO & Founder, ABIES Capital

1:30 Dessert Break with Meet the VC Panelists and Poster Awards

PURSUING DIFFICULT TARGETS USING AI/ML

2:10 Chairperson's Remarks
Gaurav Chopra, PhD, Professor, Department of Chemistry, Purdue University

2:15 Generating Synthetic Binding Landscapes to Support Modeling, Pre-training, and Undruggable Target Discovery
Amy He, PhD, Computational Chemist, Drug Design, Topos Bio
Co-folding and docking are powerful tools for predicting receptor-ligand structures, but both struggle when the receptor presents a weak/fuzzy binding context, such as intrinsically disordered regions (IDRs). We show that rapid, large-scale blind docking with an enhanced search algorithm can generate synthetic binding landscapes that (i) improve modeling and show reasonable agreement with experimental data in these challenging systems and (ii) help guide small-molecule discovery for traditionally "undruggable" targets.

2:45 FEATURED PRESENTATION: Finding Goldilocks: How AI-Powered Covalent Drug Discovery Removes the "Un" from "Undruggable"
Johannes C. Hermann, PhD, CTO, Frontier Medicines
Covalent drug discovery has recently experienced a renaissance, especially for "hard to drug" targets. Combining AI with other technologies such as chemoproteomics and quantum mechanics is key to efficiently discovering drugs against these so-called undruggables. The Frontier™ platform has been custom-built to integrate these technologies, thus enabling us to drug the majority of the human proteome.

3:45 Networking Refreshment Break

AI & PEPTIDE DESIGN

4:00 FEATURED PRESENTATION: AI-Based Peptide Macrocycle Design
Gaurav Bhardwaj, PhD, Assistant Professor, Medicinal Chemistry, University of Washington
Designing peptides that are simultaneously optimized for multiple drug-like properties, such as target binding, oral bioavailability, and metabolic stability, remains very challenging with traditional methods. I will discuss our recent work on developing AI-enabled peptide design methods (AfCycDesign, RFpeptides, and more) and applying them to custom design high-affinity macrocyclic binders and orally bioavailable peptides. Together, these new tools provide opportunities for highly accurate and robust design of functionally relevant peptides.

4:30 Peptide Hit Discovery and Optimization Using Machine Learning and Small Peptide Arrays
Ewa Lis, PhD, Founder & CEO, Koliber Biosciences
In this presentation, we introduce how Koliber's machine-learning technology, integrated with Robust Diagnostics' peptide-array technology, overcomes these limitations. We demonstrate that large libraries are unnecessary, as Koliber's machine learning can optimize initial hits to achieve improved binding affinity. We also present visualization techniques for detecting binding modes, offering new insights into peptide-array applications for therapeutic peptide discovery.

5:00 Machine Learning Applied to Oral and Macrocyclic Peptide Design
Hans Melo, PhD, Co-Founder & CEO, Menten AI
Cyclic peptides have long been considered attractive as a drug modality due to their medium size and combining the advantages of small molecules and biologics. However, membrane permeability remains a significant challenge. Recently, physics-based Generative AI has emerged as a promising technology to design cyclic peptides with specific properties in mind. Here we focus on applying this method to design *de novo* cyclic peptides with drug-like oral bioavailability.

5:30 Close of Conference

"The talks and topics were the best that I've been a part of from 20 years of going to conferences.

CHARLES W., NOVARTIS

Inaugural

Oral & Macrocyclic Peptides: Discovery to Development - Part 2

Expanding the Frontier of Peptide Therapeutics

WEDNESDAY, APRIL 15

12:00 pm Registration Open

1:00 Dessert Break in the Exhibit Hall with Navigating Chemistry Careers Breakout Tables

Enjoy a dessert break in the Exhibit Hall! Network with our sponsors and exhibitors or join a moderated roundtable to talk about career challenges with fellow scientists. The discussions are offered in-person only and will not be recorded.

CELL PERMEABLE MACROCYCLIC PEPTIDES

1:30 Welcome Remarks

1:35 Chairperson's Remarks

Katerina Leftheris, PhD, formerly CSO, Vilya Therapeutics

1:40 Wrangling Property Space in Encoded Macrocyclic Libraries: Towards Potent *and* Permeable Hits

Scott Lokey, PhD, Professor, Chemistry and Biochemistry, University of California, Santa Cruz

We have been investigating the membrane permeability of large cyclic peptide scaffold model systems. In our efforts to apply insights gained from these systems to find macrocycles that are both permeable and bioactive, we have designed large macrocyclic libraries with enhanced permeability. We now report lead compounds from these libraries selected against two intracellular proteins, their permeabilities, as well as their biochemical and cellular activities.

2:10 Discovery of a New Class of Cell-Permeable Macrocycles

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

The development of macrocyclic peptides (MPs) able to access intracellular protein targets is of keen interest. Here we describe new types of MPs in which the ring is closed through formation of a moiety in which a permanent positive charged is embedded within a hydrophobic heterocyclic ring system. We show that this strategy increases the passive membrane permeability of any MP, often dramatically.

2:40 Sponsored Presentation *(Opportunity Available)*

3:10 Refreshment Break in the Exhibit Hall with Poster Viewing

4:00 Permeation Screening of DNA-Encoded Macrocyclic Peptides

Juan Hu, PhD, Assistant Professor, Chemistry & Biochemistry, San Diego State University

Macrocyclic peptides promise access to intracellular "undruggable" targets but suffer poor permeability. We developed a microfluidic, liposome-based permeation screen using click chemistry and a 19.6K-member thioether-cyclized DNA-encoded macrocycle library. Using DOPC liposomes, we identified, resynthesized, and plate-validated permeant hits, demonstrating scalable, permeability-driven selection. Next, we'll diversify scaffolds and deploy bacterial and mammalian-derived membranes to better mimic barriers, sharpening structure–permeability insight in the bRo5 space and enabling predictive PK modeling.

4:30 Advances in Peptidic Conjugates with Limited Permeability: Strategies to Enhance and Validate Cellular Uptake

Jakob Fuhrmann, PhD, Senior Principal Scientist, Peptide Therapeutics, Genentech, Inc.

Peptidic conjugates offer a promising strategy for targeting intracellular proteins, yet limited cell permeability remains a major barrier. This work introduces strategies to enhance and validate the cellular uptake of moderately permeable peptides. By integrating an innovative assay system with structure–permeability design principles beyond PAMPA, MDCK, and Caco-2 models, the study provides insights to advance peptide-based modalities for intracellular drug discovery.

5:00 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 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.

5:45 Close of Day

6:15 Dinner Short Courses*

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

THURSDAY, APRIL 16

7:30 am Registration and Morning Coffee

PLENARY KEYNOTE SESSION

8:15 Plenary Welcome Remarks from Lead Content Director

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

8:25 Directed and Random Walks in Chemical Space

Brian K Shoichet, PhD, Professor & Chair, Pharmaceutical Chemistry, University of California San Francisco (UCSF)

Docking libraries have rapidly expanded from three million to over a trillion molecules. We compare billion vs. million molecule library docking on the same targets, demonstrating that as the libraries grow so too do hit-rates and affinities. I consider how and if new ML methods separate true from false positives. How good are our subsequent ligand optimization strategies versus what we might expect against a random background? (surprisingly unimpressive).

9:10 Coffee Break in the Exhibit Hall with Poster Viewing and Best of Show Awards Announced

PEPTIDE RADIOLIGANDS

10:00 Chairperson's Remarks

Bryan C. Fuchs, PhD, Senior Director & Research Therapeutic Area Head, GI & Liver Disease, Ferring Research Institute

10:05 Presentation to be Announced

10:35 Constrained Peptide Radioligands

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

I present a targeted delivery approach based on conjugating peptide ligands of the EphA2 receptor to chemotherapeutic drugs. This strategy selectively delivers cytotoxic agents or radioligands to cancer cells, while sparing normal cells. In mice xenograft models, this approach increases the therapeutic window of chemotherapy by increasing efficacy while reducing side effects. We are applying this conjugation approach to first line cancer chemotherapeutic agents such as taxol, gemcitabine, and others.

11:05 Sponsored Presentation *(Opportunity Available)*

11:20 A Macrocyclic Radioligand

Keykavous Parang, PhD, Professor, Biomedical and Pharmaceutical Sciences, Chapman University

Cyclic peptide conjugation is a powerful method for re-engineering classic chemotherapeutics to achieve higher efficacy and reduced side effects. I present our work on conjugating a cyclic peptide, [(WR)4WK]ßA, to epirubicin. The resulting conjugate was tested across multiple cancer cell lines, including triple-negative breast cancer and multidrug-resistant uterine sarcoma, with heart cells serving as a control for toxicity. The conjugate showed enhanced tumor uptake and potency while significantly reducing cardiotoxicity.

Inaugural

Oral & Macrocyclic Peptides: Discovery to Development - Part 2

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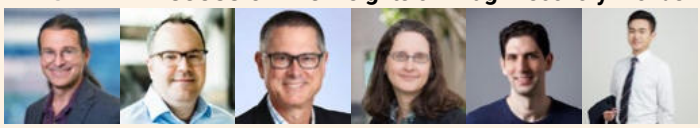

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MACROCYCLIC DESIGN STRATEGIES

2:10 Chairperson's Remarks

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

2:15 Designing Oral (and Permeable!) Peptides

Emel Adaligil, PhD, Executive Director, Chemical Biology and Peptide Macrocycles, Eli Lilly and Company

Although there are several examples of macrocyclic peptides showing that they are promising drug candidates to inhibit protein-protein interactions, developing orally available macrocyclic peptides are still a challenge. Developing oral macrocyclic peptides is a two-step process that is required to be optimized simultaneously due to their complex 3D solution conformations: optimization of affinity/activity and oral bioavailability. This talk reviews how to utilize mRNA display platform to develop oral macrocyclic peptides.

2:45 Membrane-Permeable Cyclic Peptides against Intracellular Targets and for Oral Delivery

Christian Heinis, PhD, Associate Professor, Lab of Therapeutic Proteins & Peptides, EPFL Lausanne

My lab is working on the long-standing goal of developing cell membrane–permeable peptides for modulating intracellular targets and for oral delivery. We have developed nanoscale synthesis methods to generate and screen tens of thousands of sub-kDa synthetic peptides. My talk will highlight this platform and examples of successful ligand discovery, including membrane-permeable protein-protein inhibitors (unpublished) and orally available cyclic peptides.

3:15 AI-Driven Macrocycle Design

Patrick J. Salveson, PhD, Co-Founder and CTO, Vilya Therapeutics

3:45 Networking Refreshment Break

AI & PEPTIDE DESIGN

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