Program and Proceedings for the 20th Annual

PEPTIDE THERAPEUTICS SYMPOSIUM

October 21-22, 2025 | The Scripps Seaside Forum | La Jolla, California

www.peptidetherapeutics.org

20th Annual Peptide Therapeutics Symposium

October 21-22, 2025
The Scripps Seaside Forum
8610 Kennel Way, La Jolla, CA 92037

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20th Annual Peptide Therapeutics Symposium

2025 TRAVEL GRANT AWARDEES

Sebin Abraham, *Texas A&M University*
Samuel Geathers, *Philadelphia College of Osteopathic Medicine*
Jordi Hintzen, *University of Pennsylvania*
Jahnu Saikia, *Vanderbuilt University*
Katherine Truelson, *Boston College*

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20th Annual Peptide Therapeutics Symposium

Dear Colleagues,

The Peptide Therapeutics Foundation and its sponsors welcome you to the beautiful Scripps Seaside Forum for the 20th Annual Peptide Therapeutics Symposium. In our continuing mission to engage colleagues worldwide, the symposium is once again a hybrid format. We have strived to provide you with a program that presents thought provoking discussions of new discoveries and advances in peptide therapeutics and related R&D. Please take full advantage of the networking opportunities and make sure to swing by the symposium sponsor tables.

This year we begin with a Plenary Lecture from Andrew Young, CSO and CMO of i2O Therapeutics, that describes the discovery and unique attributes of Amylin and GLP-1 agonists. Our next Plenary Lecture from Mary Elizabeth Patti, Associate Professor, Harvard Medical School will discuss how the intestine acts as a regulator of systemic glucose metabolism. The second morning session will feature talks from Julie Sutcliffe, Michael Evans and Ali Tavassoli covering the use of integrins for targeted imaging and treatments, novel chemical strategies to target radiotherapies and a platform for HTS of cyclic peptides.

Following lunch, we will continue with lectures from Pep2Tango Therapeutics Inc., Gubra and Novo Nordisk describing novel unimolecular tetra-agonists for use in obesity, next steps for the de novo synthesis of peptides and neurokinin's role in the treatment of cardiometabolic disease. The final session of the day will focus on the use of cutting-edge platforms for the design and discovery of novel peptides with therapeutic potential. We will hear unique perspectives from Simon Bailey, Goran Krilov and Rasmus Leth. We hope you will join us for the Opening Reception and poster viewing that will immediately follow the last session.

Wednesday morning will commence with Plenary Lectures from Kevan Shokat, Professor at UCSF and UC Berkley, Investigator Howard Hughes Medical and Jirong Lu, SVP at Eli Lilly & Company discussing strategies to overcome the undruggable nature of K-Ras and the immunotherapy driven phagocytosis of amyloid plaques. This will be followed by three presentations by Eric Appel, Aktham Aburub and Tyler Grant each focused on different aspects of drug delivery and the development of oral peptides. We finish the day with a panel on this same topic guided by Rumit Maini.

A networking lunch will follow the close of the Symposium and we invite you to join your colleagues and enjoy the view.

The taped presentations will be available online for viewing for 60 days following the close of the meeting.

Sincerely,

Phil Dawson
Chairman of the Board
Peptide Therapeutics Foundation

Adam Mezo
President
Peptide Therapeutics Foundation

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Ferring Ventures Group manages a portfolio of research-driven companies around the globe that are committed to the development of life-changing treatments for life-shortening diseases. Headquartered in Switzerland, Ferring Ventures is privately-owned, and was founded in 2014. Alongside its sister company, Ferring Pharmaceuticals, it forms an integral part of the Ferring Foundation. Ferring Ventures invests heavily in its research infrastructure both in terms of people and technology to enable the discovery of innovative medicines including novel gene and cell therapies, that have the potential to transform the lives of patients. The Ferring Ventures organization is spread across key locations in Europe (St-Prex Switzerland, Hamburg Germany, London UK, Kuopio Finland) and in the US (San Diego). Ferring Ventures San Diego is advancing a pipeline of peptide-based radiopharmaceuticals that builds on the foundations of Ferring Pharmaceuticals, a world leading pharmaceutical company with one of the largest peptide therapeutic portfolios.

PLATINUM SPONSOR

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Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs, but few options. We are dedicated to discovering and developing life-changing treatments for patients with under-addressed neurological, neuroendocrine, and neuropsychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, Parkinson's disease, endometriosis* and uterine fibroids*, as well as over a dozen mid- to late-stage clinical programs in multiple therapeutic areas. For three decades, we have applied our unique insight into neuroscience and the interconnections between brain and body systems to treat complex conditions. We relentlessly pursue medicines to ease the burden of debilitating diseases and disorders, because you deserve brave science. (*in collaboration with AbbVie).

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Novo Nordisk is a global healthcare company with more than 90 years of innovation and leadership in diabetes care. This heritage has given us experience and capabilities that also enable us to help people defeat obesity, haemophilia, growth disorders and other serious chronic diseases. Headquartered in Denmark, Novo Nordisk employs approximately 41,700 people in 77 countries and markets its products in more than 165 countries. Novo Nordisk's B shares are listed on Nasdaq Copenhagen (Novo-B). Its ADRs are listed on the New York Stock Exchange (NVO). For more information, visit novonordisk.com

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PolyPeptide Group AG and its consolidated subsidiaries ("PolyPeptide") is a specialized Contract Development & Manufacturing Organization (CDMO) for peptide- and oligonucleotide-based active pharmaceutical ingredients. By supporting its customers mainly in pharma and biotech, it contributes to the health of millions of patients across the world. PolyPeptide serves a fast-growing market, offering products and services from pre-clinical through to commercial stages. Its broad portfolio reflects the opportunities in drug therapies across areas and with a large exposure to metabolic diseases, including GLP-1. Dating back to 1952, PolyPeptide today runs a global network of six GMP-certified facilities in Europe, the U.S. and India. PolyPeptide's shares (SIX: PPGN) are listed on SIX Swiss Exchange.

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Zealand Pharma A/S is a biotechnology company founded in 1998 and headquartered in Denmark. We aim to tackle some of the greatest healthcare challenges of our time through the discovery, design, and development of innovative peptide-based medicines.

Our scientists have invented more than 10 drug candidates that have advanced into clinical development, of which two have reached the market and several are in mid- to late-stage development. Today, the peptides in our pipeline are targeting obesity, rare diseases, and chronic inflammation.

For more information, visit www.zealandpharma.com

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AmbioPharm is a global peptide CDMO founded in 2005 and headquartered in North Augusta, South Carolina, USA specializing in developing highly efficient manufacturing processes for peptide-based Active Pharmaceutical Ingredients (APIs) at clinical and commercial stages. In our manufacturing facilities in South Carolina, USA and Shanghai, China, we manufacture New Chemical Entities (NCEs) under cGMP for clients worldwide. Both facilities have been inspected multiple times by the FDA as well as other global regulatory bodies with excellent outcomes. Our mission is to accelerate your peptides to patients.

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AsymChem

Asymchem a global CDMO leader, has provided one-stop pharmaceutical solutions for over 25 years. With a strong foundation in small molecule services, it has advanced capabilities in chemical macromolecules, biologics, drug products, clinical research, synthetic biology, and technology transfer. Supported by 9,000+ professionals—45% in R&D—and facilities in China, the U.S., the U.K., and beyond, Asymchem adheres to top-tier cGMP and EHS standards. Trusted by global pharma and biotech leaders, Asymchem delivers high-quality, cost-effective services, reducing time-to-market for therapies and providing client-centric solutions to meet the diverse needs of global drug development.

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Bachem Americas

Bachem is a leading, innovation-driven company specializing in the development and manufacture of peptides and oligonucleotides. With over 50 years of experience and expertise Bachem provides products for research, clinical development and commercial application to pharmaceutical and biotechnology companies worldwide and offers a comprehensive range of services.

Bachem operates internationally with headquarters in Switzerland and locations in Europe, the US and Asia. The company is listed on the SIX Swiss Exchange. For further information, see www.bachem.com

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WuXi TIDES, part of Wuxi AppTec, is a unique Contract Research, Development and Manufacturing platform. WuXi TIDES offers our partners efficient, flexible, and high-quality solutions from discovery through the commercial supply of oligonucleotides, peptides and related synthetic conjugates ("TIDES" drugs).

Website: https://tides.wuxiapptec.com/

Peptide Therapeutics Foundation

Peptide Therapeutics Foundation is a not-for-profit 501C (3), established in 2008 to promote research and development of peptide therapeutics. The Foundation is supported by the following corporate sponsors: Ferring Ventures, Neurocrine Biosciences Inc., Novo Nordisk, Polypeptide, and Zealand Pharma. The Foundation sponsors an annual meeting, Peptide Therapeutics Symposium, which brings together world leaders from academia, the biopharmaceutical industry, CMOs, CROs, and investors interested in all aspects of peptide R&D, including drug discovery, safety and toxicology, clinical development, manufacturing, pharmaceutical development, formulation, drug delivery and regulatory affairs.

20th Annual Peptide Therapeutics Symposium

October 21-22, 2025
The Scripps Seaside Forum
8610 Kennel Way, La Jolla, CA 92037

TUESDAY, OCTOBER 21, 2025

8:00 a.m. - 4:00 p.m.	**Registration Check-in** The Scripps Seaside Forum Lobby
8:00 a.m. - 8:30 a.m.	**Breakfast & Poster Viewing** The Scripps Seaside Forum Lobby
8:30 a.m. - 5:00 p.m.	**20th Annual Peptide Therapeutics Symposium** Samuel H. Scripps Auditorium
8:30 a.m. - 8:35 a.m.	**Opening Remarks** Adam Mezo, Ph.D. *President, Peptide Therapeutics Foundation; Vice President, Research, Peptides and Bioconjugates, Neurocrine Biosciences, Inc.*
8:35 a.m. - 10:05 a.m.	**Plenary Lectures** **Moderator:** David Parks, Ph.D. *President, DGP Scientific Inc.*
8:35 a.m. - 9:20 a.m.	**Discovering Physiology and Novel Utilities of Amylin and GLP-1** Andrew Young, MD, Ph.D. *Chief Scientific and Medical Officer, i20 Therapeutics*
9:20 a.m. - 10:05 a.m.	**The Intestine as a Regulator of Systemic Glucose Metabolism** Mary Elizabeth Patti, MD *Senior Investigator, Adult Endocrinologist, and Director, Hypoglycemia Clinic, Joslin Diabetes Center; Associate Professor of Medicine, Harvard Medical School*
10:05 a.m. - 10:35 a.m.	**Beverage Break & Poster Viewing** The Scripps Seaside Forum Lobby
10:35 a.m. - 12:05 p.m.	**Session I** **Moderator:** Bryan Fuchs, Ph.D. *Head, Ferring Ventures San Diego*
10:35 a.m. - 11:05 a.m.	**αvβ6 Targeted Imaging and Treatment: Bench to Bedside** Julie Sutcliffe, Ph.D. *Professor Internal Medicine, and Biomedical Engineering, University of California Davis*

TUESDAY, OCTOBER 21, 2025 ***(Continued)***

11:05 a.m. - 11:35 a.m.	**Chemical Strategies to Expand the Therapeutic Window for Targeted Radiotherapies** Michael J. Evans, Ph.D. *Professor, Department of Radiology and Biomedical Imaging, University of California San Francisco*
11:35 a.m. - 12:05 p.m.	**Platforms for the Intracellular Generation and High-throughput Screening of Cyclic Peptide Libraries** Ali Tavassoli, Ph.D. *Professor, University of Southhampton, & CSO Curve Therapeutics*
12:05 p.m. - 1:30 p.m.	**Lunch & Poster Viewing** The Scripps Seaside Forum Lawn
1:30 p.m. - 3:00 p.m.	**Session II** **Moderator:** Soumitra Ghosh, Ph.D. *CSO, Pep2Tango Therapeutics Inc.*
1:30 p.m. - 2:00 p.m.	**Discovery of Novel Unimolecular Tetra-agonists for the Treatment of Obesity and Related Disorders** Cristina M Rondinone, Ph.D. *Co-Founder and CEO Pep2Tango Therapeutics Inc.*
2:00 p.m. - 2:30 p.m.	**Next Steps for De Novo Designed Peptide Therapeutics** Jens Christian Nielsen, Ph.D. *Director, Computational Drug Discovery, Gubra*
2:30 p.m. - 3:00 p.m.	**Leveraging New Insights into Neurokinin Biology to Treat Cardiometabolic Disease** Zach Gerhart-Hines, Ph.D. *Associate Professor, Novo Nordisk Foundation Center for Basic Metabolic Research*
3:00 p.m. - 3:30 p.m.	**Beverage Break & Poster Viewing** The Scripps Seaside Forum Lobby
3:30 p.m. - 5:00 p.m.	**Session III** **Moderator:** Ron He, Ph.D. *Sr. Principal Scientist, Neurocrine Biosciences*
3:30 p.m. - 4:00 p.m.	**Macrocyclic Peptide Drug Discovery: Designing for Oral Delivery** Simon Bailey, Ph.D., MBA *Chief Operating Officer and President of R&D Unnatural Products*

20th Annual Peptide Therapeutics Symposium

TUESDAY, OCTOBER 21, 2025 *(Continued)*

4:00 p.m. - 4:30 p.m.

Physics-based Modeling Advances Powering the Design of Cyclic Peptide Therapeutics
Goran Krilov, Ph.D.
Senior Director, Computational Chemistry, Schrödinger

4:30 p.m. - 5:00 p.m.

Computational Chemistry and Deep Learning for Peptide Design
Rasmus Leth, Ph.D.
Lead Scientist, Zealand Pharma

5:00 p.m. - 6:30 p.m.

Opening Reception
The Scripps Seaside Forum Lawn

WEDNESDAY, OCTOBER 22, 2025

8:00 a.m. - 10:00 a.m.

Registration Check-in
The Scripps Seaside Forum Lobby

8:00 a.m. - 8:30 a.m.

Breakfast & Poster Viewing
The Scripps Seaside Forum Lobby

8:30 a.m. - 1:00 p.m.

20th Annual Peptide Therapeutics Symposium
Samuel H. Scripps Auditorium

8:30 a.m. - 8:35 a.m.

Welcoming Remarks
Phil Dawson, Ph.D.
Chairman of the Board, Peptide Therapeutics Foundation; Professor of Chemistry, Scripps Research

8:35 a.m. - 10:05 a.m.

Plenary Lectures
Moderator: Nick Cox, Ph.D.
Director, Peptide Therapeutics Foundation; Sr. Director of Chemical Biology, Novo Nordisk

8:35 a.m. - 9:20 a.m.

Overcoming the Undruggable Nature of the Most Common Human Oncogene: K-Ras
Kevan Shokat, Ph.D.
Professor, Cellular and Molecular Pharmacology, UC San Francisco; Professor, Department of Chemistry, UC Berkeley; Investigator, Howard Hughes Medical

9:20 a.m. - 10:05 a.m.

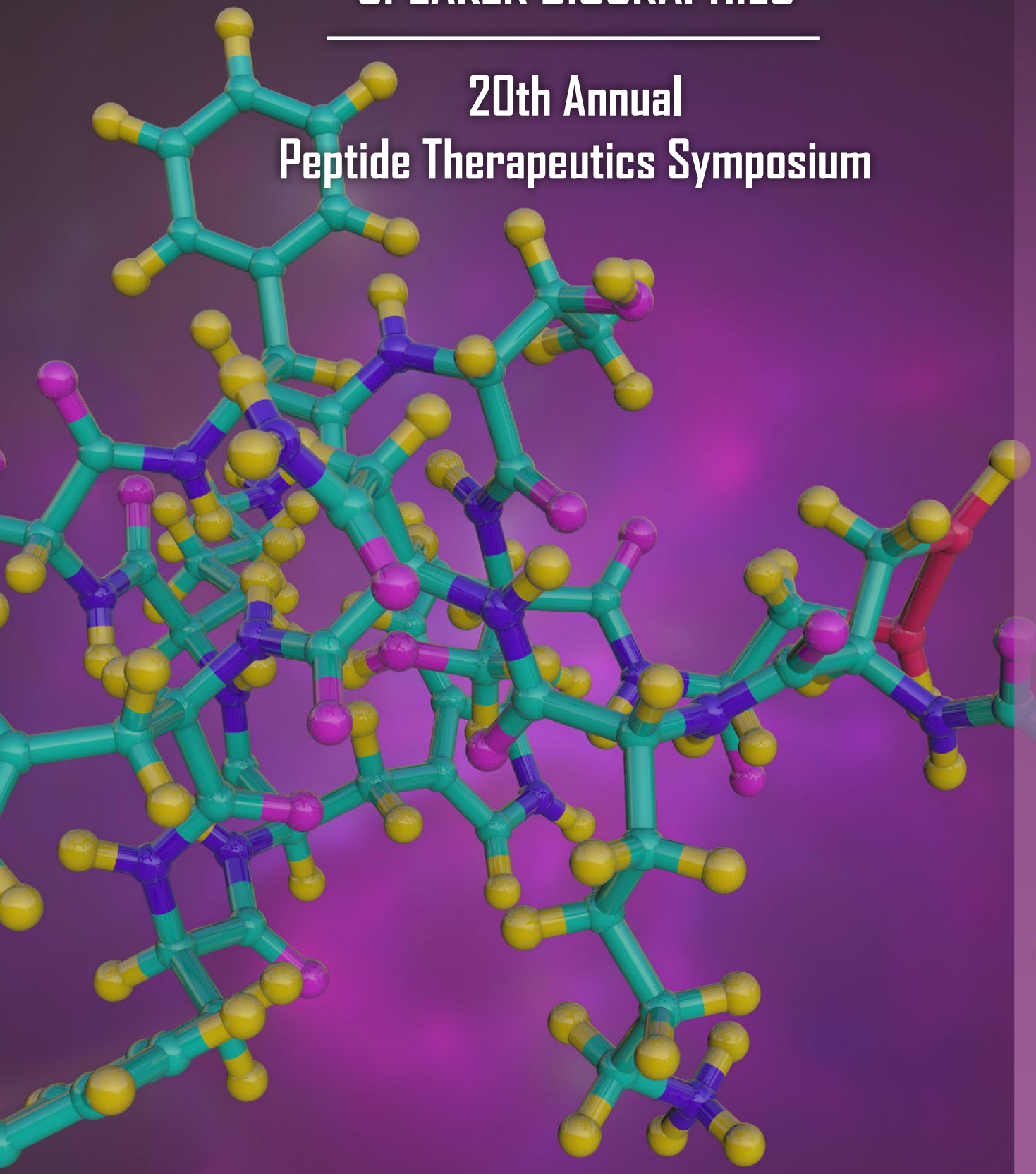
Engaging the Enemy: Mechanistic Insights for Immunotherapy Driven Phagocytosis of Amyloid Plaque and Clinical Translation
Jirong Lu, Ph.D.
Senior Vice President, Biotechnology Research, Eli Lilly & Company

WEDNESDAY, OCTOBER 22, 2025 *(Continued)*

10:05 a.m. - 10:35 a.m.	**Beverage Break & Poster Viewing** The Scripps Seaside Forum Lobby
10:35 a.m. - 12:05 p.m.	**Session IV** **Moderator:** Florence Brunel, Ph.D. *Scientific Director at Novo Nordisk US*
10:35 a.m. -11:05 a.m.	**Dynamic Biomaterials Enabling Innovations in Cell and Drug Delivery** Eric Andrew Appel, Ph.D. *Professor, Stanford University*
11:05 a.m. - 11:35 a.m.	**Enabling Peptides Orally through Peptide Engineering and Formulation** Aktham Aburub, Ph.D. *Vice President-Research Synthetic Molecule Design and Development, Eli Lilly & Company*
11:35 a.m. - 12:05 p.m.	**Overcoming Barriers to Oral Peptide Delivery** Tyler Grant, Ph.D. *Sr. Director Advanced Drug Delivery, Novo Nordisk*
12:05 p.m. - 12:55 p.m.	**Drug Delivery Panel** **Moderator:** Rumit Maini, Ph.D. *Sr. Director & Head of Peptide Discovery, Eli Lilly & Company* Aktham Aburub, Ph.D. *Vice President-Research Synthetic Molecule Design and Development, Eli Lilly & Company* Eric Andrew Appel, Ph.D. *Professor, Stanford University* Simon Bailey, Ph.D., MBA *Chief Operating Officer and President of R&D Unnatural Products* Tyler Grant, Ph.D. *Sr. Director Advanced Drug Delivery, Novo Nordisk*
12:55 p.m. - 1:00 p.m.	**Closing Remarks** Adrienne Day, Ph.D. *Director, Peptide Therapeutics Foundation;* *President, Blue Gum Advisors LLC*
1:00 p.m. - 2:00 p.m.	**Networking Lunch** The Scripps Seaside Forum Lawn

SPEAKER BIOGRAPHIES

20th Annual
Peptide Therapeutics Symposium



Aktham Aburub, Ph.D.
Vice President-Research Synthetic Molecule Design and Development, Eli Lilly & Company
Enabling Peptides Orally Through Peptide Engineering and Formulation
Drug Delivery Panel

Dr. Aburub is Vice President at Eli Lilly & Company with expertise in drug delivery. He has led and contributed to the development, submission and commercialization of multiple products spanning different modalities. Aktham published more than 80 journal articles, book chapters, patents & conference proceedings. He is an adjunct professor at the University of Minnesota and lecturer at the University of Maryland. Aktham received a Ph.D. in pharmaceutical sciences from the University of Iowa and a BSc in Pharmacy from Jordan University of Science and Technology.

Eric Andrew Appel, Ph.D.
Professor, Stanford University
Dynamic Biomaterials Enabling Innovations in Cell and Drug Delivery
Drug Delivery Panel

Eric A. Appel is an Associate Professor of Materials Science & Engineering at Stanford University. He received his BS in Chemistry and MS in Polymer Science from California Polytechnic State University in San Luis Obispo, CA. Eric performed his MS thesis research with Dr. Jim Hedrick and Dr. Robert Miller at the IBM Almaden Research Center in San Jose, CA. He then obtained his Ph.D. in Chemistry with Prof. Oren A. Scherman at the University of Cambridge. Upon graduating from Cambridge, he was awarded a National Research Service Award from the NIBIB and a Wellcome Trust Postdoctoral Fellowship to work with Prof. Robert Langer at MIT. Eric's research at Stanford focuses on the development of biomimetic polymeric materials that can be used as tools to better understand fundamental biological processes and to engineer advanced healthcare solutions. His research has led to 150 publications, over 40 patents, and formed the basis for four start-up companies. He has been awarded young faculty awards from the Hellman Foundation, American Diabetes Association, American Cancer Society, and PhRMA Foundation. Eric received the IUPAC Hanwha-TotalEnergies Young Polymer Scientist Award in 2022, the Society for Biomaterials Young Investigator Award in 2023, and the Biomaterials Science Lectureship Award in 2023. In 2024, he was named a Fellow of the American Institute for Medical & Biological Engineers, and he was recently awarded the Kathryn C. Hach Award for Entrepreneurial Success from the American Chemical Society.

Simon Bailey, Ph.D., MBA
Chief Operating Officer and President of R&D Unnatural Products
Macrocyclic Peptide Drug Discovery: Designing for Oral Delivery
Drug Delivery Panel

Simon is Chief Operating Officer and President of R&D at Unnatural Products (UNP), a macrocyclic peptide drug discovery company. Simon joined UNP in 2024, bringing over 25 years' experience of drug discovery and early development experience in oncology and metabolic disease in big pharma, and public and private biotech companies.

Simon joined UNP from Plexium where he was EVP Drug Discovery and led the company's science and technology groups to identify novel molecular glue protein degrader drugs. Prior positions included SVP, Head of Research for Intercept Pharmaceuticals, leading the company's programs in NASH/MASH from inception through Phase 1. Earlier in his career, Simon was a medicinal chemist at Pfizer, where he led the Diabetes and Oncology Medicinal Chemistry Departments. Simon holds a Ph.D. in synthetic organic chemistry from the University of Manchester and an MBA from UC San Diego's Rady School of Management. He is a 2021 recipient of the American Chemical Society's Hero of Chemistry award for his leadership role in the discovery of Lorbrena™ a macrocyclic inhibitor of mutant ALK kinase for the treatment of NSCLC.

Phil Dawson, Ph.D.
Chairman of the Board, Peptide Therapeutics Foundation;
Professor of Chemistry, Scripps Research
Closing Remarks

Phil Dawson is a Professor in the Department of Chemistry, Scripps Research in La Jolla, CA and former Dean of the Skaggs Graduate School of Chemical and Biological Sciences (2017-2024). He received an A.B. (1992) in Chemistry from Washington University, and Ph.D. (1996) from Scripps Research under the guidance of Steve Kent. After pursuing postdoctoral work at Caltech, he returned to Scripps as an Assistant Professor. He has served as President of the American Peptide Society, the Board of Directors for FASEB and cochaired the 22nd American Peptide Symposium and the GRC on Biology and Chemistry of Peptides. He has published over 200 papers and has been honored with an Alfred P. Sloan Foundation fellowship, the Vincent du Vigneaud Award, the Max Bergmann Kreis Gold Medal, the Zervas Award, the RSC MedImmune Protein and Peptide Science Award, the Akabori Memorial Award from the Japanese Peptide Society, the Cathay Award from the Chinese Peptide Society, the ACS Cope Scholar Award, and the APS Bruce Merrifield Award.

Professor Dawson is a pioneer of chemoselective ligation methods for macromolecule synthesis and modification and has applied these tools broadly to better understand biological systems.

Adrienne Day, Ph.D.
Director, Peptide Therapeutics Foundation; President, Blue Gum Advisors LLC
Closing Remarks

Dr. Day is the President of Blue Gum Advisors LLC, a consulting firm focused on providing fractional C-suite support focused on business development and operations to the life science industry. She is a seasoned business development professional with more than 30 years of experience in the biotechnology and biopharmaceutical industries. Dr. Day has hands-on operational and executive management experience in the non-profit, for-profit and startup environments.

Most recently she was Senior Director of Business Development for Ferring Pharmaceuticals. Prior to that Dr. Day ran a successful consulting practice. She has previously served as Vice President of Business Development at what is now the Sanford Burnham Prebys Medical Discovery Institute, Vice President of Business Development Conforma Therapeutics, Senior Director of Business Development at Molecumetics Ltd., Associate Director of Corporate Development at Ligand Pharmaceuticals. She was Ligand Pharmaceuticals' first Project Manager, and began her biotechnology career at Invitrogen Corporation where she held various positions.

Dr. Day received her B.Sc., B.Sc. Honors, and Ph.D. degrees in Biochemistry from the University of Adelaide, Australia. She completed her postdoctoral training at the University of Southern California and the La Jolla Cancer Research Center.

Michael J. Evans, Ph.D.
Professor, Department of Radiology and Biomedical Imaging, University of California San Francisco
Chemical Strategies to Expand the Therapeutic Window for Targeted Radiotherapies

Michael Evans, Ph.D., is a Professor in Residence in the UCSF Department of Radiology and Biomedical Imaging. He is a chemical biologist with an interest in radiopharmaceutical development for molecular imaging and theranostic applications. Dr. Evans earned a BA in Chemistry from St. Mary's College of Maryland and he obtained his PhD in Organic Chemistry from The Scripps Research Institute (CA) under the supervision of Professor Benjamin Cravatt. This was followed by a postdoctoral fellowship in Molecular Imaging from the Memorial Sloan Kettering Cancer Center in New York under the supervision of Professors Charles Sawyers and Jason Lewis. In 2013, Dr. Evans accepted a faculty position at UCSF. Dr. Evans has published nearly 100 peer-reviewed articles, 40 meeting abstracts, and is a co-inventor on 16 patents pending or issued. He is a scientific co-founder and previously served on the scientific advisory board of ORIC Pharmaceuticals, Inc. He is a co-founder of Therapaint, Honeybear Biosciences, and Inversion Therapeutics. He has been recognized with numerous honors, including a 2013 Young Investigator Award from the Prostate Cancer Foundation, a Pathway to Independence Award (K99/R00) from the National Cancer Institute, a 2017 Research Scholar Award from the American Chemical Society, the 2023 Roger Tsien Award for excellence in chemical biology from the World Molecular Imaging Society, the 2024 Sam Gambhir Trailblazer award from the Society of Nuclear Medicine and Molecular Imaging, and he was a 2020 inductee to the Council of Distinguished Investigators in the Academy of Radiology and Biomedical Imaging Research.

Zach Gerhart-Hines, Ph.D.
Associate Professor, Novo Nordisk Foundation Center for Basic Metabolic Research
Leveraging New Insights into Neurokinin Biology to Treat Cardiometabolic Disease

Zach Gerhart-Hines carried out his doctoral studies in mitochondrial biology and skeletal muscle function in the context of metabolic diseases, from 2004 to 2011, at the Johns Hopkins University School of Medicine and Dana-Farber Cancer Institute at Harvard Medical School in the lab of Professor Pere Puigserver, Ph.D. Then from 2011-2014, he conducted postdoctoral research at the University of Pennsylvania in the lab of Dr. Mitch Lazar, M.D., Ph.D., where he continued a focus on obesity and type 2 diabetes through the interrogation of the circadian control of adipose tissue metabolism. In 2014, Zach began his own research group at the Novo Nordisk Foundation Center for Basic Metabolic Research at the University of Copenhagen where his lab broadly interrogates peripheral and central mechanisms of homeostatic control. His ultimate goal is to leverage these discoveries to develop novel pharmacotherapies for the treatment of obesity, type 2 diabetes, and associated diseases. He is a co-founder of Embark Biotech, Embark Laboratories, and Incipiam Pharma, spinouts based on targeting different energy-expending modes-of-action.

Tyler Grant, Ph.D.
Sr Director Advanced Drug Delivery, Novo Nordisk
Overcoming Barriers to Oral Peptide Delivery
Drug Delivery Panel

Dr. Tyler Grant leads the Advanced Drug Delivery department at Novo Nordisk in Boston MA, where he and the team are developing cutting edge drug delivery technologies for a rapidly expanding therapeutic landscape. He conducted his Ph.D. at the University of Oxford where he focused on developing platforms to enable tissue targeting of musculoskeletal tissue. From there, he joined the Langer Lab at MIT as a postdoc where he co-invented several drug delivery platforms, one of which led to the spin-out of Lyndra Therapeutics. There he led scientific translation of the first ever long-acting oral dosage form as head of R&D from preclinical through successful Phase III efficacy study. Dr Grant's core passion is developing drug delivery technologies that increase the precision and efficacy of therapies while making them more affordable and accessible to patients.

Goran Krilov, Ph.D.
Senior Director, Computational Chemistry, Schrödinger
Physics-based Modeling Advances Powering the Design of Cyclic Peptide Therapeutics

Dr. Krilov completed his undergraduate education at Drake University in Des Moines, IA where he obtained two B.S. degrees in Physics and Chemistry. He moved on to Columbia University in New York for his graduate studies where he obtained a Ph.D. in Chemical Physics working with Bruce Berne on dissipative quantum dynamics. For twenty five years, his work has focused on developing and applying cutting-edge computational chemistry techniques to problems in condensed phase dynamics, biophysics and drug discovery. Over the years, Dr. Krilov has worked both in industry, including IBM and Strand Life Sciences, as well as academia where he held an assistant professorship in Chemistry at Boston College. For the past fifteen years Dr. Krilov has been at Schrödinger where he has held various roles, and is currently a Senior Director of Computational Chemistry in the Therapeutics Group. There, he has co-led several drug discovery projects, two of which are presently in clinical development. He has authored over 30 scientific papers and is a co-inventor on a number patents.

Rasmus Leth, Ph.D.
Lead Scientist, Zealand Pharma
Computational Chemistry and Deep Learning for Peptide Design

Rasmus Leth has a diverse background in biotechnology and pharmaceutical sciences, holding a Ph.D. in computational chemistry from the University of Copenhagen's School of Pharmacy. His research focused on using computational methods to study drug metabolism by cytochrome P450.

Previously, Rasmus worked at Optibrium in Cambridge, UK, a company specializing in software that guides successful drug discovery. There, he primarily worked on a metabolism module, developing methods for fast and accurate prediction of cytochrome P450 metabolism using ab-initio calculations.

In 2019, Rasmus started in a consulting position at the biotechnology company Zealand Pharma in Copenhagen to build their computational platform. He currently serves as a lead scientist in the Computational Chemistry team, which is responsible for advancing the company's capabilities in AI, machine learning, simulations, and ab-initio calculations. At present, Rasmus is leading a research project and developing innovative workflows to integrate various computational chemistry methodologies in peptide design.

Jirong Lu, Ph.D.
Senior Vice President, Biotechnology Research, Eli Lilly & Company
Engaging the Enemy: Mechanistic Insights for Immunotherapy Driven Phagocytosis of Amyloid Plaque and Clinical Translation

Dr. Jirong Lu earned a Bachelor of Science Degree in Chemistry from Sichuan University in 1986. She completed her doctoral program at the University of Oregon in 1992 and a postdoctoral fellowship at Washington University in St. Louis in 1997. Dr. Lu then joined Eli Lilly Research Laboratories, where she currently serves as the Senior Vice President in the Biotechnology Discovery Research group and is the San Diego site head.

With extensive training in protein biochemistry and biophysics, Dr. Lu is recognized as a pioneer in advancing multiple molecules for clinical development at Lilly. She is named as the inventor for ixekizumab(Taltz™), remternetug, and most notably, donanemab (Kisunla™). At Lilly, Dr. Lu oversees a team dedicated to discovering and designing protein, peptide, and antibody therapeutics across various therapeutic areas. In 2020, Dr. Lu's team contributed to the discovery of the first monoclonal antibody therapies to treat COVID-19.

Dr. Lu has also played a crucial role in developing biotechnology platforms and cutting-edge technologies to discover and optimize biotherapeutics. This includes platforms to enhance the delivery of proteins and antibodies across the blood-brain barrier, a significant challenge in neurodegeneration research and development. Dr. Lu also led efforts to develop muti-specific antibodies, advance oral biologics and nucleotide delivery systems, and integrate cutting-edge machine learning and AI for biotherapeutic discovery and design. She has made a broad impact on drug discovery and development at Lilly and serves as the Board Chair and member for numerous programs.

Beyond Lilly, Dr. Lu has contributed to the scientific community through numerous publications and patents. In 2024, she was named one of the top 20 Women in Biopharma R&D.

Adam Mezo, Ph.D.
President, Peptide Therapeutics Foundation; Vice President, Research, Peptides and Bioconjugates, Neurocrine Biosciences, Inc.
Opening Remarks

Dr. Adam Mezo has worked in the pharmaceutical industry for over 20 years with a focus on the discovery of novel peptide, small molecule and protein therapeutics. Dr. Adam Mezo is currently Vice President, Research, Peptide Chemistry at Neurocrine Biosciences, Inc in San Diego. In his current role at Neurocrine, he is focused on the discovery of novel peptide therapeutics for a range of unmet medical needs. Prior to this role, he led teams of chemists, biochemists and drug hunters at the Ferring Research Institute, Eli Lilly, Biogen Idec and Syntonix. He has worked in various therapeutics areas, including diabetes, hemophilia, immunology and reproductive and women's health. Although peptides are his focus, he has also led teams in other modalities including small molecules and proteins as projects and priorities dictate. Dr. Mezo has over 50 published manuscripts and conference presentations, along with over 20 issued US patents. He received his undergraduate degree in chemistry from Queen's University (Canada), PhD from the University of British Columbia in organic chemistry and performed postdoctoral work at the Massachusetts Institute of Technology in the field of bioorganic chemistry.

Jens Christian Nielsen, Ph.D.
Director, Computational Drug Discovery, Gubra
Next Steps for De Novo Designed Peptide Therapeutics

Jens Christian Nielsen is the Director of Computational Drug Discovery at Gubra, where he leads efforts at the intersection of experimental assays, software development, and AI-based data analysis. He began his career at Gubra as a bioinformatician focusing on gene expression analysis in metabolic diseases. Over time, he developed a strong interest in drug discovery and peptide pharmaceuticals, leading him to specialize in machine learning applications within the drug discovery process. Jens played a key role in the development of the streaMLine platform, a machine learning-driven peptide drug discovery platform. He has contributed to advancing multiple drug discovery projects toward clinical testing and is the inventor of four patents of therapeutic peptides. Jens holds a Ph.D. in bioinformatics from Chalmers University of Technology.

Mary Elizabeth Patti, MD
Senior Investigator, Adult Endocrinologist, and Director, Hypoglycemia Clinic, Joslin Diabetes Center; Associate Professor of Medicine, Harvard Medical School
The Intestine as a Regulator of Systemic Glucose Metabolism

Dr. Patti is a physician-scientist and adult endocrinologist at Joslin Diabetes Center, Director of the Hypoglycemia Clinic, and Associate Professor of Medicine at Harvard Medical School. NIH-funded laboratory studies focus on identification of molecular and epigenetic mechanisms by which environmental/nutritional factors during early life confer metabolic disease risk in later life and in subsequent generations. Clinical/translational studies focus on the intestine as a mediator of systemic glucose metabolism, and novel approaches to treatment of post-bariatric hypoglycemia. Dr. Patti received her MD from Jefferson Medical College magna cum laude, internal medicine residency at University of Pittsburgh and endocrinology fellowship at Harvard Medical School. Numerous leadership roles include organizer of a diabetes-focused Keystone Symposium, chair of ADA Scientific Sessions Planning Committee, and NIH study section member. She was elected to the American Society of Clinical Investigation, Association of American Physicians, and to Fellowship in both American College of Physicians and Obesity Society.

Cristina M Rondinone, Ph.D.
Co-Founder and CEO Pep2Tango Therapeutics Inc.
Discovery of Novel Unimolecular Tetra-agonists for the Treatment of Obesity and Related Disorders

Senior executive and leader with more than 25 years of experience in the bio pharmaceutical industry with a record of successfully leading teams for the discovery and development of numerous medicines including Rezdiffra, dorzagliatin and bentracimab. Co-Founder and CEO of Pep2Tango Therapeutics Inc., a new biotech company developing superior unimolecular multi-agonist peptides for obesity and related disorders. Member of the Health Council at TECNALIA and former member of the Board of Directors at Axcella (AXLA). Former President of Cellarity Inc. and former Senior Vice President of AstraZeneca (Medimmune), Head of Research and Development of Cardiovascular, Metabolic and Renal Diseases where she led numerous programs that progressed from target identification to late-stage clinical trials. Prior to Astra-Zeneca, she held leadership positions at Hoffmann-La Roche and Abbott Laboratories where she led multiple programs including the discovery of Rezdiffra. Before joining the pharmaceutical industry, she was Associate Professor (Docent) of Molecular Medicine at the University of Gothenburg in Sweden and received her Ph.D. in Biochemistry from the University of Buenos Aires. Her postdoctoral training was at the Laboratory of Cellular and Developmental Biology at NIDDK, National Institutes of Health, USA. Authored more than 80 scientific publications and 10 patents. Inducted as a Member of the Royal Academy of Pharmacy and Biochemistry, Spain.

Kevan Shokat, Ph.D.
Professor, Cellular and Molecular Pharmacology, UC San Francisco; Professor, Department of Chemistry, UC Berkeley; Investigator, Howard Hughes Medical
Overcoming the Undruggable Nature of the Most Common Human Oncogene: K-Ras

Kevan is currently an Investigator of the Howard Hughes Medical Institute, Professor in the Department of Cellular and Molecular Pharmacology at UCSF and a Professor of Chemistry at UC Berkeley. Kevan received his undergraduate degree at Reed College, his PhD at UC Berkeley and did post-doctoral training at Stanford. He was inducted into the National Academy of Sciences (2010), the National Academy of Medicine (2011), and the American Academy of Arts and Sciences (2011). His lab is most well-known for drugging the "undruggable" oncogene K-Ras (G12C) in 2013. K-Ras was the first human oncogene to be discovered in 1982 and remained undrugged until work from the Shokat lab at UCSF. In May of 2021 the drug sotorasib which binds to the pocket identified by Shokat on K-Ras (G12C) was approved for the treatment of lung cancer patients with this mutation. The field of K-Ras drug discovery is expanding quickly to hunt for drugs to target the other K-Ras mutants such as those which drive colon and pancreatic cancers which collectively represent almost 20% of all cancer patients world-wide.

Julie Sutcliffe, Ph.D.
Professor Internal Medicine, and Biomedical Engineering, University of California Davis
αvβ6 Targeted Imaging and Treatment: Bench to Bedside

Dr. Sutcliffe is a Professor of Internal Medicine and Biomedical Engineering at the University of California Davis. She serves as the co-director of the Center for Molecular and Genomic imaging and as the director of radiochemistry. Dr Sutcliffe is the leader of a multidisciplinary translational research team that is recognized nationally for it contributions to the field of Molecular Imaging and Theranostics. Dr Sutcliffe is the Principal investigator of 4 active clinical trials and is the leader of the UC Davis Lustgarten Foundation/ StandupToCancer Pancreatic Cancer Collective Research Team. She is a Fellow of the Society of Nuclear Medicine and Molecular Imaging, a Fellow of the World Molecular Imaging Society and Fellow of the American Institute for Medical and Biological Engineering.

Ali Tavassoli, Ph.D.
Professor, University of Southhampton, & CSO Curve Therapeutics
Platforms for the Intracellular Generation and High-throughput Screening of Cyclic Peptide Libraries

Ali is Professor of Chemical Biology at the University of Southampton (UK), and Chief Scientific Officer of Curve Therapeutics.

Ali leads an interdisciplinary team of scientists whose efforts are focused on the discovery and development of cyclic peptides as novel chemical tools that enable new insight into the role of protein-protein interactions in cells, and as the starting point for new therapeutics.

Ali is a Fellow of the Royal Society of Chemistry (RSC) and served as president of the RSC Chemical Biology Interface Division (2020-2023). Ali is on the editorial board of RSC Chemical Biology, was Chair of the RSC's Chemical Biology and Bioorganic Group (2012-2015), and an elected member of the RSC's Chemistry and Biology Interface Division council (2012-2016). Ali has won several awards, including the EuCheMS medal for European Young Chemist (2008), the RSC Medimmune Protein and peptide Science Award (2017), the European Peptide Society's Leonidas Zervas award (2020), and the RSC Interdisciplinary Prize (2025).

Andrew Young, Ph.D.
Chief Scientific and Medical Officer, i20 Therapeutics
Discovering Physiology and Novel Utilities of Amylin and GLP-1

Intertwined with his medical training and clinical practice, Andrew Young completed higher degrees in thermoregulatory and sensory neurophysiology at the University of Auckland School of Medicine in New Zealand. He taught physiology there until recruited to join an NIH group as a Fogarty Fellow in Phoenix, Arizona where a longitudinal study was examining the metabolic fate of members of the Pima tribe, a group with the world's highest incidence of type 2 diabetes. Following a period as a Max Planck Fellow in Germany, Andrew Young returned to New Zealand to resume teaching and neurophysiologic research.

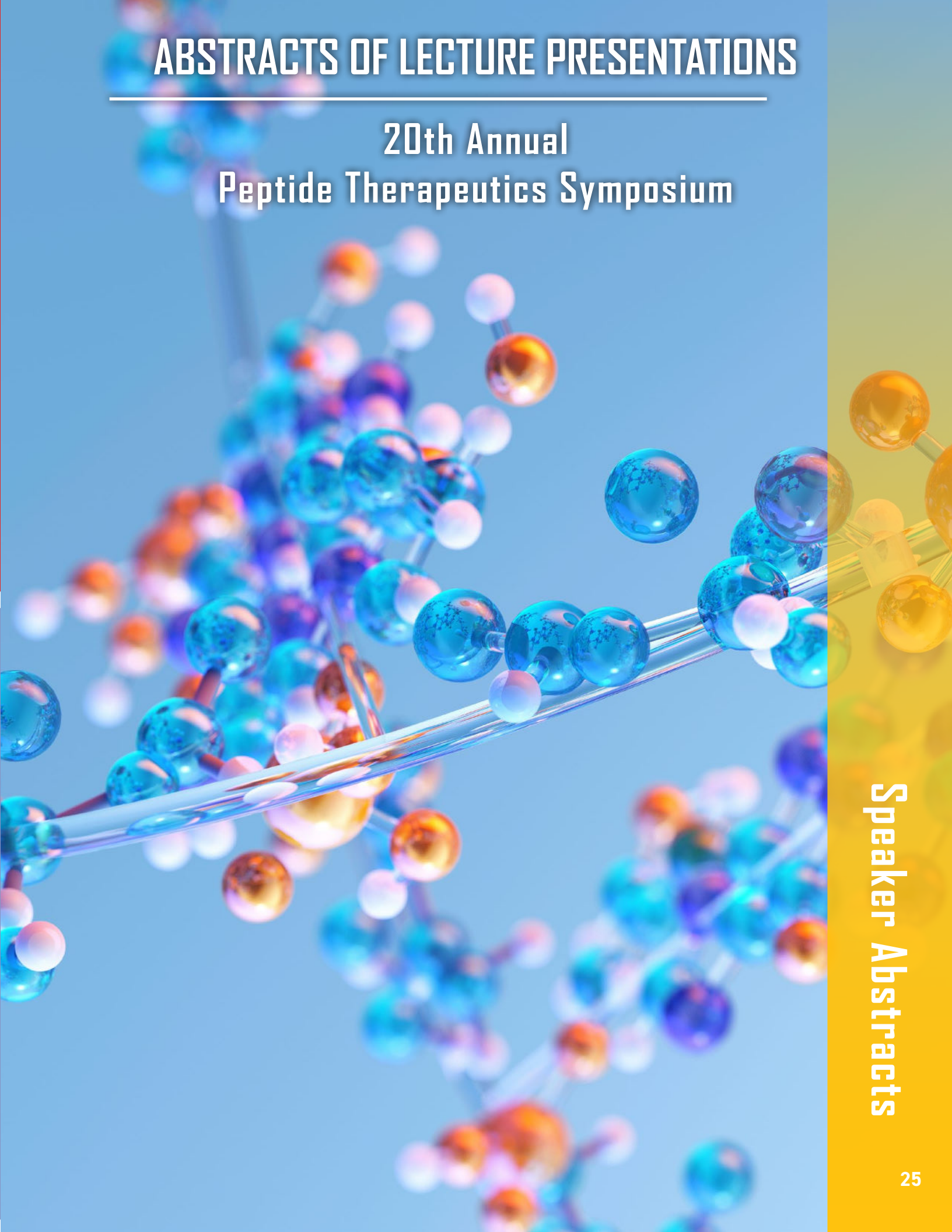
Meanwhile, the Pima work attracted the attention of Garth Cooper, a compatriot and relative who had just discovered what he predicted was a new hormone, which he named amylin. Garth recruited Andrew as the founding physiologist at Amylin Pharmaceuticals in 1989 with a remit to characterize the function of the presumptive hormone amylin. The research group that evolved there comprised peptide chemistry, immunochemistry, pharmacology and physiology. It focused entirely on peptides, initially amylin, then other metabolic peptides including exenatide and PYY, and then regulatory peptides in general. The content of this lecture will spotlight this 15-year period of intense exploration of the biology of amylin, exenatide, and other peptides.
(continued on next page)

Andrew Young left Amylin in 2008 to join GlaxoSmithKline in NC as head of enteroendocrine biology. His primary remit was to identify druggable targets that could be accessed from the lumen of the gut without systemic absorption, therefore posing minimal risk of systemic toxicity. A second remit was to establish the development of highly druggable peptides for the treatment of metabolic diseases. When GSK downsized the NC campus, the peptide development group spun out as Phoundry Pharmaceuticals who were rapidly acquired by Intarcia Therapeutics. Intarcia was a Boston Company with a chronic delivery technology but (apart from exenatide) no pipeline of potent molecules to pair with it (Phoundry had the opposite problem). When Intarcia suffered regulatory misadventure, its molecular assets passed to i2O, a Harvard spinout still in stealth mode, where Andrew is now Chief Scientific and Medical Officer.

Notes

ABSTRACTS OF LECTURE PRESENTATIONS

20th Annual
Peptide Therapeutics Symposium



Speaker Abstracts

Enabling Peptides Orally Through Peptide Engineering and Formulation

Aktham Aburub, Ph.D.
Vice President-Research Synthetic Molecule Design and Development
Eli Lilly & Company

Delivering peptides and biologics orally has been the holy grail of delivery sciences. Combination of poor physicochemical & biopharmaceutical properties as well as harsh gastrointestinal environment being primary challenges resulting in poor oral bioavailability. Despite decades of research both in academic and pharmaceutical industry labs, success has been limited culminating in the approval and launch of two oral peptide products in recent years. Oral bioavailability of either product has not exceeded ~1%. In this presentation, a strategy in which a combination of peptide engineering "designing oral delivery in" and permeation enhancer-based delivery will be shared resulting in 3-5x higher clinical oral bioavailability compared to recent approvals.

Dynamic Biomaterials Enabling Innovations in Cell and Drug Delivery

Eric Andrew Appel, Ph.D.
Professor, Stanford University

Dynamic biomaterials exhibit highly useful properties that are impossible with traditional materials but crucial for a wide variety of emerging applications in biomedicine. These materials typically employ enthalpy-dominated crosslinking interactions that become weaker at elevated temperatures, leading to significant softening. Herein, we will discuss the development of a physical hydrogel platform exploiting dynamic and multivalent interactions between biopolymers and nanoparticles that are strongly entropically driven, providing alternative temperature dependencies than typical for materials of this type. We will discuss the implications of these crosslinking thermodynamics on the observed mechanical properties and discuss the desired mechanical properties for injectability, including viscous flow under shear stress (shear-thinning) and rapid recovery of mechanical properties when the applied stress is relaxed (self-healing). Moreover, the hierarchical construction of these biphasic hydrogels enables innovative approaches to formulation and delivery of a diverse array of compounds over user-defined timeframes ranging from days to months. In one example application, we demonstrate that these unique material characteristics can be leveraged for controlled locoregional exposure of immunomodulatory cargo to greatly enhance anti-cancer immune responses. In another example, we demonstrate that the dynamic structure of these materials can be leveraged for co-delivery of immunostimulatory cytokines and CAR-T cells to improve cancer treatments. Overall, this talk will illustrate our recent efforts exploiting dynamic and multivalent interactions between polymers and nanoparticles to generate injectable hydrogel depot technologies exhibiting properties not previously observed in biomaterials and affording unique opportunities in biomedicine.

Macrocyclic Peptide Drug Discovery: Designing for Oral Delivery

Simon Bailey, Ph.D., MBA
Chief Operating Officer and President of R&D Unnatural Products

Interest in the discovery of peptide therapeutics is enjoying a resurgence, in part because of the medical benefits and commercial success of the GLP-1 agonist class of anti-obesity medicines. Despite the demonstrated success of peptide therapeutics, their application has thus far typically been limited to parenteral administration due to the challenges of designing peptides that can cross the gut, which is an essential component of oral bioavailability.

In recent years, much effort has been applied to devising strategies to enable the oral delivery of peptide drugs. This talk will highlight some of the work done at Unnatural Products, and elsewhere, aimed at developing generalizable approaches for oral delivery of peptide drugs.

Chemical Strategies to Expand the Therapeutic Window for Targeted Radiotherapies

Michael J. Evans, Ph.D.
Professor, Department of Radiology and Biomedical Imaging, University of California San Francisco

The recent FDA approvals (Lutathera, Pluvicto) and the swell of promising experimental agents in clinical trials underscore the surging enthusiasm to investigate radioligand therapy (RLT) as a treatment modality for many cancers. However, the clinical experience shows that tumor responses to RLTs are often transient and/or variable among patients, owing in part to low target expression, short drug residence time in tumor, and sub saturating and infrequent drug dosing. Thus, exploring new strategies beyond ligand/receptor complexes for the tumoral delivery of radioisotopes is a worthwhile goal. We have approached this challenge by developing a new class of radiopharmaceuticals termed "restricted interaction peptides" (RIPs) which are low molecular weight (MW) peptides that are internally cleaved by a tumor endoprotease to unmask a radiolabeled membrane binding peptide. After RIP proteolysis, the membrane binding peptide adopts a helical conformation and immediately attaches to a nearby plasma membranes in the tumor. Using PET, we have found that RIPs deliver more radiation to tumors than RLTs against the same target. Coupling isotope retention in tumors to proteolysis causes catalytic isotope accumulation beyond the stoichiometric limits of a ligand/receptor approach. Also, cancer cells do not have efficient mechanisms to disrupt the peptide/membrane complex, and we have observed that radiolabeled membrane binding peptides can persist in the tumor >96 hours post injection. RIPs, ~ 4 kDa, also clear quickly from serum, as expected. Lastly, RIPs are modular and the internal cleavage site can be readily exchanged to customize the probe to a tumor type of interest. On this basis, we hypothesize that RIPs may be a mutually safe and effective platform for molecularly targeted radiotherapy.

Leveraging New Insights into Neurokinkin Biology to Treat Cardiometabolic Disease

Zach Gerhart-Hines, Ph.D.
Associate Professor, Novo Nordisk Foundation Center for Basic Metabolic Research

Incretin-based therapies have revolutionized the treatment of obesity and diabetes. However, these drugs largely work through appetite suppression that is aversive and is linked to adverse effects including nausea. In this presentation, I will present new data from our group that suggests that activation of the neurokinin receptor 2 (NK2R) holds the potential to address several of the remaining unmet needs with the cardiometabolic space. We have previously shown that long-acting NK2R agonism not only suppresses appetite in a non-aversive manner but also increases energy expenditure independent of the sympathetic nervous system. The combination of appetite control and energy expenditure leads to insulin sensitization and a higher quality weight loss that spares lean mass. Another potential area of differentiation is that GLP-1-based therapies exhibit reduced weight-lowering efficacy in individuals living with both obesity and diabetes. Whereas NK2R activation is significantly more efficacious in diabetic, obese preclinical rodent and primate models. In addition to exploring the mechanistic underpinnings of these features of NK2R activation, we have more recently interrogated the structural basis for receptor selectivity using Cryo-EM and investigated combinatorial opportunities for polypharmaceutical approaches. Collectively, our work suggests that NK2R agonism could impart several unique advantages to the next generation of cardiometabolic therapies.

Overcoming Barriers to Oral Peptide Delivery

Tyler Grant, Ph.D.
Senior Director Advanced Drug Delivery, Novo Nordisk

Oral delivery of peptides remains a key priority within the field of drug delivery as it offers a noninvasive and convenient route of administration preferred by many patients. However, overcoming anatomical and physiological barriers of the gastrointestinal tract remains a major challenge that will require breakthrough technologies to achieve improved bioavailability. Absorption enhancers, nanocarriers, and ingestible devices are just a few of the approaches being pursued by scientists within academia and industry to enhance absorption. This talk will focus on challenges and recent innovations within oral peptide delivery. Moreover, it will highlight an oral PCSK9i program including some key formulation learnings including scientific translation from the bench to clinic.

Physics-based Modeling Advances Powering the Design of Cyclic Peptide Therapeutics

Goran Krilov, Ph.D.
Senior Director, Computational Chemistry, Schrödinger

Macrocyclic peptides (CP) have emerged as promising therapeutic agents with distinct biochemical and pharmacokinetic properties. CPs combine high binding affinity, target specificity, and low toxicity of antibodies, with potential oral bioavailability and cell permeability of small molecules. A key challenge in cyclic peptide drug design is optimizing their pharmacokinetic properties, primarily bioavailability and stability, while retaining the favorable on target potency. Here we describe enhancements to the Schrödinger computational platform facilitating in silico design and high-throughput profiling of CP libraries for hit finding, as well as optimization of potency and permeability for rapid identification of clinically viable orally available agents. In particular, we present an optimized FEP+ protocol for predicting binding potency with accuracy comparable to small molecules; we introduce efficient macrocyclic peptide conformational sampling and docking workflows; and discuss physics-based methods to tackle peptide permeability. Finally, we introduce several CP specific enhancements to LiveDesign for Biologics data integration and design platform.

Computational Chemistry and Deep Learning for Peptide Design

Rasmus Leth, Ph.D.
Lead Scientist, Zealand Pharma

Computational chemistry leverages established theoretical frameworks to develop mathematical models of molecular behavior, utilizing computer assistance for enhanced precision. The advent of methodologies such as AlphaFold, RFdiffusion, and ProteinMPNN, driven by advances in deep learning and neural networks, have significantly impacted this field. At Zealand Pharma, we have created a robust computational chemistry platform incorporating diverse methodologies and tools to guide the design and characterization of novel peptides in our projects. In this presentation, we will demonstrate our use of AlphaFold to characterize our targets and leverage its capabilities for designing novel peptide binders. By employing these methodologies, we illustrate our ability to strategically determine binding sites and create specific selectivity profiles among target homologs.

Moreover, we have pinpointed several challenges in designing novel peptide binders, including issues of solubility, stability, and fibrillation. We will discuss strategies to address these challenges, featuring complementary computational approaches. These include molecular simulations to understand dynamics, machine learning to analyze peptide characteristic data, and quantum chemistry calculations to improve the predictive performance of our models. Our work illustrates the synergistic potential of integrating computational chemistry and deep learning techniques in peptide design.

Engaging the Enemy: Mechanistic Insights for Immunotherapy Driven Phagocytosis of Amyloid Plaque and Clinical Translation

Jirong Lu, Ph.D.
Senor Vice President, Biotechnology Research, Eli Lilly & Company

Alzheimer's disease (AD) is a progressive neurodegenerative disorder affecting millions of individuals worldwide. It is characterized by cognitive decline, memory loss, and behavioral changes, resulting in challenges for patients, caregivers, and healthcare systems. The development of effective therapeutic strategies for AD is recognized as a high priority, given the potential to address issues associated with the disease.

Antibody therapeutics have been identified as a potential approach for treating Alzheimer's disease by targeting the accumulation of amyloid plaques, which are a hallmark of the condition. Recent clinical trials indicate that certain amyloid-beta (A) antibodies may reduce amyloid plaques and slow cognitive decline in patients with early-stage AD.

Donanemab is a humanized IgG1 monoclonal antibody developed to bind selectively to amyloid plaques and facilitate -amyloid plaque clearance. This presentation examines the mechanistic aspects of immunotherapy-driven phagocytosis of amyloid plaque and its relevance to clinical practice, focusing on the association between amyloid plaques, local toxicity, and neuropil changes. It covers the design of donanemab for selective engagement of amyloid plaques and the translational findings from studies in transgenic mice to clinical application. The process from initial hypothesis to the launch of donanemab is outlined, along with ongoing research and development efforts in Alzheimer's disease. The presentation also addresses future directions in disease-modifying therapy.

Next Steps for De Novo Designed Peptide Therapeutics

Jens Christian Nielsen, Ph.D.
Director, Computational Drug Discovery, Gubra

Peptides are broadly recognized for their effectiveness in treating metabolic disorders such as obesity. From a drug discovery perspective, peptides offer attractive properties such as high receptor potency and selectivity, as well as a potential for long circulating half-life. Traditionally, the development of peptide-based drugs has been based on endogenous hormones; however, this approach is not applicable to targets without an identified native peptide ligand.

To address this challenge, we have developed an AI-based computational pipeline for the de novo design of peptide binders. This pipeline allows for specification of hotspot residues on the target protein and generates peptide sequences by maximizing hotspot proximity and employing structural metrics from AlphaFold2 [1] and proteinMPNN [2]. The predicted peptide binders show high structural diversity and virtually no sequence similarity to known sequences.

We experimentally validated our AI-based strategy by synthesizing and functionally characterizing 190 de novo designed peptides targeting the active site of a G protein-coupled receptor (GPCR). Functional assays revealed receptor activity for 74% of these peptides, with the most potent hits exhibiting an IC_{50} of 34 nM (antagonist) and an EC_{50} of 3.2 µM (agonist). Subsequently, we optimized these de novo hits through deep mutational scans and machine learning (ML)-guided structure-activity relationship (SAR) analyses [3], and identified several mutations that increased potency. *(continued on next page)*

In summary, this study experimentally validates an AI-based pipeline for the de novo design of peptide therapeutics and demonstrates the application of ML-guided optimization to enhance drug properties. The results serve as proof of concept for the integration of AI methodologies in peptide drug discovery, enabling the development of novel therapeutics towards previously undruggable targets in a cost-effective and time-efficient manner.

References:
[1] J. Jumper et al., Highly accurate protein structure prediction with AlphaFold. Nature 596, 583–589 (2021). DOI: 10.1038/s41586-021-03819-2
[2] J. Dauparas et al., Robust deep learning–based protein sequence design using ProteinMPNN. Science 378, 49-56 (2022). DOI: 10.1126/science.add2187
[3] J. C. Nielsen et al., Machine-learning-guided peptide drug discovery: Development of GLP-1 receptor agonists with improved drug properties. J. Med. Chem., 67 (14), 11814–11826 (2024). DOI: 10.1021/acs.jmedchem.4c00417

The Intestine as a Regulator of Systemic Glucose Metabolism

Mary Elizabeth Patti, MD
Senior Investigator, Adult Endocrinologist, and Director, Hypoglycemia Clinic, Joslin Diabetes Center; Associate Professor of Medicine, Harvard Medical School

As an endocrinologist, I care for individuals with both diabetes and hypoglycemia. In translational studies arising from the clinical challenges facing these patients, we have identified clinical profiles, metabolic responses, and pancreatic pathology in patients with hypoglycemia following bariatric surgery. In this session, I will describe recent findings from these studies demonstrating multiple mechanisms by which the intestine can dramatically modulate systemic glucose metabolism, including increases in gut-derived incretin hormone secretion, plasma levels of bile acids, and insulin-independent glucose disposal. Patients with post-bariatric hypoglycemia have elevations in FGF19, suggesting that the BA-FXR-FGF15/19 pathway may uniquely contribute to hypoglycemia in this population. Recent novel informatics approaches have uncovered protein and metabolite mediators of both diabetes remission and hypoglycemia after bariatric surgery, including the serotonin pathway and bile acid metabolism. These findings support novel approaches engaging the intestine as a therapeutic target for both diabetes and hypoglycemia.

Discovery of Novel Unimolecular Tetra-agonists for the Treatment of Obesity and Related Disorders

Cristina M. Rondinone, Ph.D.
Co-Founder and CEO Pep2Tango Therapeutics Inc.

The prevalence of obesity and associated co-morbidities necessitates innovative approaches for safe and efficacious therapies. We describe the discovery and characterization of a novel unimolecular long-acting peptide agonist for GLP-1, GIP, Amylin and Calcitonin Receptors and assessed its efficacy against the dual GIPR/GLP-1R agonist, Tirzepatide. Multiple metabolic endpoints were examined, including acute food intake and calcium regulation effects in lean rats, acute glucose-lowering effects in lean mice, and its chronic effects in diet induced obesity (DIO) rats compared to Tirzepatide. Chronic studies in DIO rats revealed significant reduction in cumulative food intake and body weight, driven by decreases in fat mass without loss of muscle mass, unlike that seen with Tirzepatide. The tetra-agonist peptide demonstrated robust efficacy for glucose and plasma lipid lowering, insulin sensitization and liver benefits, outperforming Tirzepatide at equivalent doses.

Conclusion: Unimolecular tetra-agonist peptides offer superior outcomes for weight loss, glycemic control, insulin sensitization, and liver health compared to Tirzepatide. These findings underscore the promise of such poly-pharmacological agents to tackle the complex challenges associated with obesity-related metabolic disorders.

Overcoming the Undruggable Nature of the Most Common Human Oncogene: K-Ras

Kevan Shokat, Ph.D.
Professor, Cellular and Molecular Pharmacology, UC San Francisco; Professor, Department of Chemistry, UC Berkeley; Investigator, Howard Hughes Medical

Somatic mutations in the small GTPase K-Ras are responsible for approximately 30% of human cancers and are generally associated with poor response to standard therapies. The mutations in K-Ras were identified in the early 1980's but it took almost four decades for the first drugs targeting the protein to be approved. The long delay was a result of the apparent lack of a drug binding pocket on K-Ras despite detailed structural and biochemical characterization of the protein, leading to it being referred to as "undruggable." This view changed when a chemical strategy based on targeting the K-Ras (G12C) mutant common in lung cancer was successful in identifying a druggable pocket in 2013. This finding led eight years later to the approval of two new medicines for patients with K-Ras (G12C) lung cancer, sotorasib and adagrasib. One current challenge in K-Ras drug development is development of agents to inhibit the more frequent K-Ras (G12D) and K-Ras (G12V) versions found in colon and pancreatic cancer. The other challenge is drug resistance which is faced by all targeted cancer therapies including the new K-Ras (G12C) directed drugs. In this lecture I will provide a perspective on challenges and opportunities of newly developed K-Ras targeting drugs.

αvβ6 Targeted Imaging and Treatment: Bench to Bedside

Julie Sutcliffe, Ph.D.
Professor Internal Medicine, and Biomedical Engineering, University of California Davis

Dr. Sutcliffe and her team have identified the integrin αvβ6 as a clinically relevant target and as such have focused significant efforts to develop, optimize and translate high affinity peptides that target αvβ6 for both imaging and treatment. The integrin αvβ6 is an epithelial-specific cell surface receptor that is undetectable in healthy adult epithelium but is significantly upregulated in a wide range of epithelial derived cancers. This receptor is often localized to the invasive front and infiltrating edges of tumors and plays a key role in invasion and metastasis and its expression is often associated with poor prognosis. Dr. Sutcliffe and her team believe that there is a much-needed opportunity to utilize αvβ6 for both diagnostic and therapeutic measures, the clinical impact of αvβ6-targeted molecular imaging is immediate for a broad spectrum of diseases, and αvβ6-tareted therapy holds potential to break through barriers in the treatment of some of the most lethal malignancies facing clinicians today. During her presentation Dr. Sutcliffe will describe some of her teams efforts during their 20 year journey to translate peptides from the bench to the bedside.

Platforms for the Intracellular Generation and High-throughput Screening of Cyclic Peptide Libraries

Ali Tavassoli, Ph.D.
Professor, University of Southhampton, & CSO Curve Therapeutics

Microcycles are head-to-tail cyclic hexapeptides that hold much promise in drug discovery against the most challenging targets. Here, we will detail several platforms for the preparation of genetically encoded Microcycle libraries in cells and in microfluidic droplets. These libraries have been interfaced with a number of high-throughput assays for the direct identification of functional inhibitors of various protein-protein and protein-DNA interactions, including several first in class compounds. The presentation will include examples in which Microcycle hits from these screens have been scaffold-hopped into small molecules as a first step towards clinical candidates.

Discovering Physiology and Novel Utilities of Amylin and GLP-1

Andrew Young, MD, Ph.D.
Chief Scientific and Medical Officer, i20 Therapeutics

It is now 20 years since Amylin Pharmaceuticals received, only 43 days apart, FDA approvals of the first amylin agonist, pramlintide, and the first glucagon-like peptide-1 (GLP-1) agonist, exenatide.

This near-synchrony was adventitious; the amylin development path had taken 16 years while the GLP-1 path was only half of that. The difference was that the normal physiology of amylin, and thereby, its clinical utility, was largely unknown. The spectrum of biologic actions was different between preclinical species and the rodent-to-human translation was misleading; the first 3 of 4 clinical programs testing therapeutic hypotheses were resounding failures.

It was only after 7 years of animal and human physiological experimentation that the natural role of amylin became clear. That path, and amylin's role in the integrated control of nutrient flux, will be discussed. Amylin agonism became the clearest example of a new mode of antidiabetic effect, controlling the rate of appearance of glucose (Ra) and other nutrients in the plasma. This was in contrast to enhancing the disappearance of nutrient from plasma, an insulin-mediated effect, that had been the mainstay of diabetes therapy for over 80 years. Also discussed will be the pharmaceutic challenges in bringing an amylin agonist to the market.

The path for development of exenatide, the first GLP-1, was quite different. By the time Amylin acquired the rights in 1996, the action of GLP-1 to stimulate insulin secretion had been known for a decade. The glucose-dependence of this effect contrasted with the glucose-independence of sulfonylurea drugs and insulin itself, each of which carried a risk of potentially lethal hypoglycemia. This promise of safety generated considerable pharmaceutical interest, but by 1996 no practical GLP-1 had been developed. The issue was rapid degradation by peptidases. How exenatide from the Gila monster solved the problem will be discussed.

The biomedical community still regarded GLP-1 agonism through an insulin-centric prism and viewed its potential as confined to type 2 diabetes. But insulin, stimulating storage of nutrients, is not an effective treatment for obesity. Scientists at Amylin Pharmaceuticals, armed with a compendium of bioassays developed to functionally characterize amylin the hormone, used exenatide to uncover novel GLP-1 actions in a wide array of organ systems. It was with exenatide, for example, that GLP-1 associated weight loss was first observed in animals and in humans. Characterization of actions beyond metabolic control, for example in cardiorenal, enteroendocrine and behavioral systems, enabled prediction (then) of utilities that have emerged only recently as GLP-1 therapies gain wider public use. Some of these "unanticipated" utilities will be discussed.

Finally, I will attempt some predictions of where the field of "Metabolic Peptides", including combinations thereof, may be moving.

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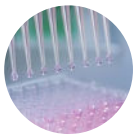

Peptide Class
- Constrained peptides
- Sulfide/bicyclic peptides
- MCP libraries
- Conjugation chemistry
- Bio-orthogonal chemistry

Peptide Therapeutics
- Peptide drug conjugates
- Oligo-peptides
- Oral peptides
- ADC-Linkers and Payloads (HPAPI)

End to End peptide integrated drug discovery with integration of Biology
Scale up synthesis of active peptides and impurity synthesis

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ABSTRACTS POSTER PRESENTATIONS

20th Annual
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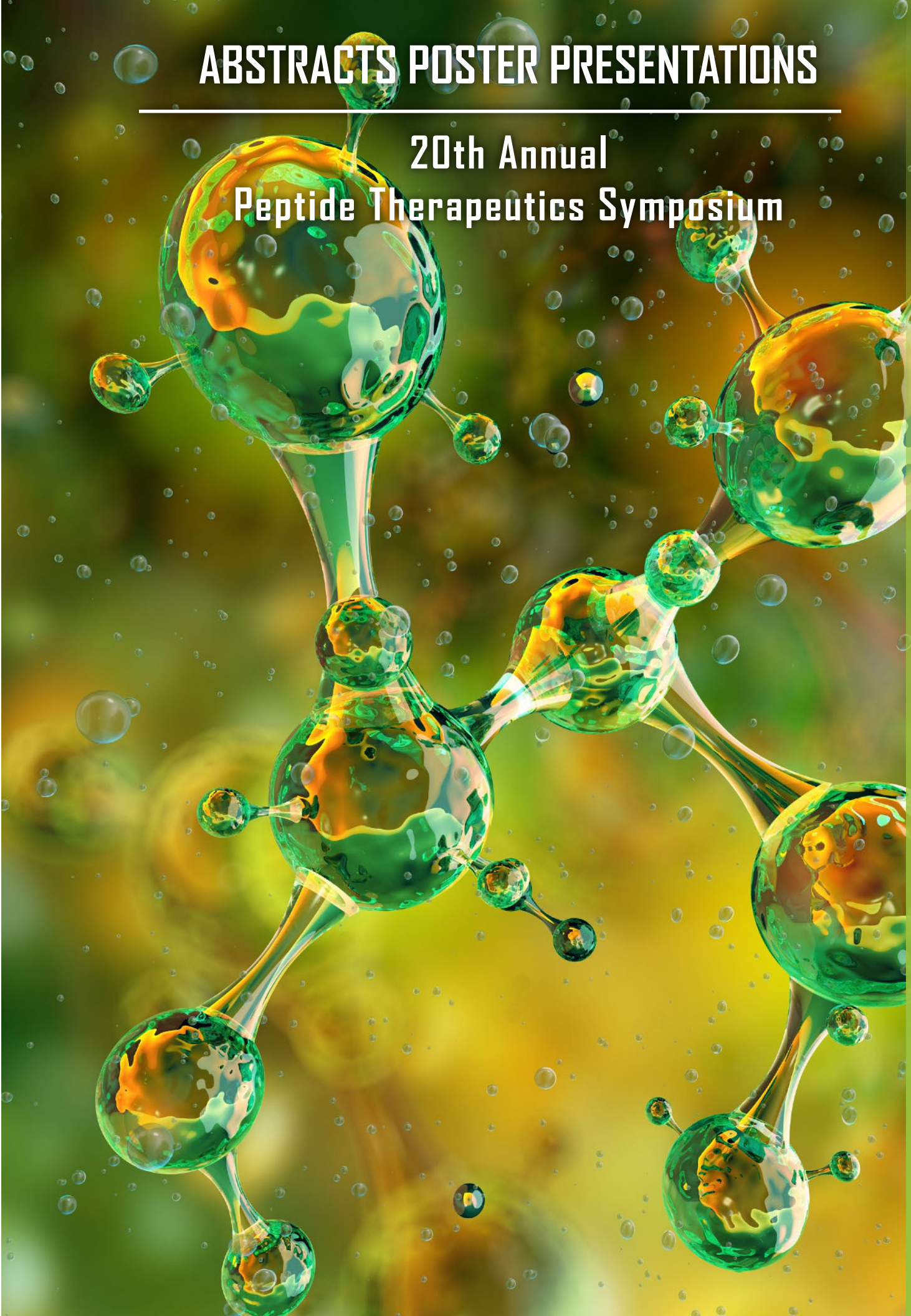

P01 | Molecular Loops, Targeted Hits: Phage Display Unleashes the Power of Macrocyclic Peptides for Next-Generation Precision Therapeutics

Sebin Abraham
Texas A&M University

Oncogenic mutations in small GTPases play a pivotal role in malignant transformation through persistent activation of intracellular signaling networks. A recurrent somatic mutation, G17V, has been identified in a significant fraction of angioimmunoblastic T-cell lymphoma (AITL) cases, where it promotes aberrant T-cell receptor (TCR) signaling by stabilizing its interaction with the guanine nucleotide exchange factor Vav1. This interaction enhances Vav1 phosphorylation at Y174 by Src kinase, driving pathological T-cell activation and proliferation. Given the structural rigidity and paucity of druggable pockets in GTPases, targeting this interface with small molecules remains highly challenging.

Conventional approaches such as small-molecule inhibitors or monoclonal antibodies are poorly suited to address intracellular GTPase-mediated interactions due to their lack of membrane permeability, limited surface complementarity, and difficulty engaging shallow or transient protein-protein interfaces. In contrast, macrocyclic peptides offer an emerging class of therapeutic agents that combine favorable features of both small molecules and biologics. Their constrained structure enhances proteolytic stability and conformational rigidity, while their tunable surface chemistry enables high-affinity binding to challenging targets. In the context of GTPase-driven malignancies, macrocyclic peptides represent a compelling modality for selectively disrupting oncogenic signaling complexes that have eluded conventional drug development.

Following four rounds of iterative biopanning against purified, biotinylated G17V protein, we identified several candidate binders using both 10-mer and 12-mer cyclic peptide libraries. An initial top candidate, RhoA3, exhibited low micromolar affinity and partial disruption of the G17V-Vav1 interaction. To improve affinity and maintain high library diversity, we employed a regioselective cyanobenzothiazole condensation reaction with an N-terminal cysteine and the chloroacetamide reaction with an internal cysteine to generate a 12-mer cyclic library with ~1010 unique variants. This approach yielded several high-affinity binders, among which the macrocyclic peptide Z1 emerged as a lead candidate. Biolayer interferometry revealed that Z1 binds G17V with nanomolar affinity (KD 134nM), and Alpha Screen assays demonstrated functional disruption of the G17V-Vav1 interaction with an IC50 of 2. 8μM. Molecular dynamics simulations of the macrocyclic peptide with RhoA G17V reveal stable binding pocket interactions that disrupts its association with the GEF Vav1, with alanine scanning confirming the key residues identified through structural modeling.

These findings establish a proof-of-concept for targeting intracellular GTPase-mediated protein–protein interactions using macrocyclic peptides. Z1 represents the first reported macrocyclic inhibitor with nanomolar affinity and in vitro functional activity against the oncogenic G17V–Vav1 complex. Ongoing work focuses on improving cellular delivery, evaluating downstream signaling inhibition in T-cell models, and assessing the therapeutic potential of Z1 analogs in preclinical systems. This platform holds promise for expanding the druggable proteome in lymphoid malignancies and other GTPase-driven diseases.

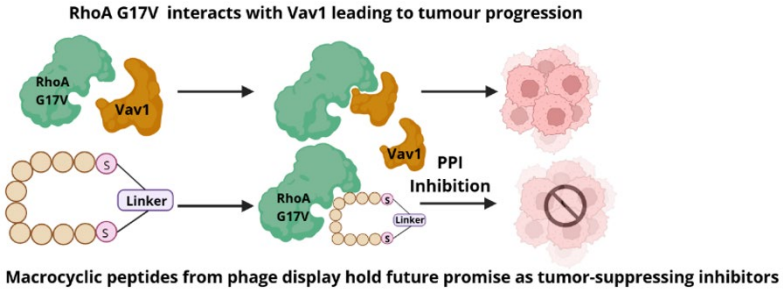

Figure 1: Macrocyclic peptides from phage display as potential tumor-suppressing PPI inhibitors

P02 | Targeted Degradation of Pin1 by Protein Destabilizing Compounds

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[2] Department of Biochemistry, College of Natural and Agricultural Sciences, University of California Riverside, 900 University Avenue, Riverside, CA 92521, USA

The concept of targeted protein degradation (TPD) is at the forefront of modern drug discovery, which aims to eliminate disease-causing proteins using specific molecules. In this context, we explored the design of small covalent peptidomimetics as protein degraders. These molecules are based on sections of ligands that induce protein destabilization, thereby facilitating the cellular breakdown of the target protein. Our studies present covalent agents targeting Pin1, a cis-trans prolyl isomerase that plays a crucial role in tumorigenesis. Our design strategy entailed iterative optimizations of agents for potency and Pin1 destabilization in vitro. Biophysical and cellular studies suggest that the agents act like molecular crowbars, displacing protein-stabilizing interactions that open the structure for recognition by the ubiquitin-proteasome degradation machinery. This approach resulted in a series of potent and effective Pin1 degraders with potential applications in target validation and in therapeutic development. We propose that our design strategy can identify molecular degraders without engineering bifunctional agents that artificially create interactions between a disease-causing protein and a ubiquitin ligase.

P03 | Beyond Cysteine Covalent Platform: Targeting Histidine, Lysine, and Tyrosine

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In recent years, the FDA has approved several oncology drugs, including Osimertinib and Ibrutinib, with Amgen's Lumakras being a notable addition as a first-in-class irreversible agent for treating KRAS G12C mutations. These drugs use an acrylamide warhead for selective reactions with cysteine residues, but the rarity of cysteine significantly limits the range of potential targets for drug development. Armida Labs, a start-up spun out from the University of California, Riverside, aims to enhance existing medicines through covalent modifications, thereby unlocking new therapeutic possibilities. Armida Labs is pioneering the targeting of lysine, tyrosine, and histidine residues, expanding the druggable target space beyond the traditional cysteine-centric approach. This innovative strategy allows us to address previously "undruggable" targets and oncogenic mutations and develop a more versatile drug portfolio. Armida Labs platform employs both ligand- and electrophile-first approaches, both of which rely on the introduction of a stable aryl-fluorosulfate warhead that selectively and efficiently reacts with lysine, histidine, and tyrosine residues. A successful example of this platform is the peptido-mimetic agent we called CovaLys, a pioneering first-in-class covalent pan-IAP (Inhibitor of Apoptosis Protein) inhibitor. CovaLys covalently inhibits IAP proteins XIAP, cIAP1, and cIAP2 by irreversibly binding to a conserved lysine residue present in all three proteins. It is highly stable, cell-permeable, and orally bioavailable, demonstrating effectiveness in reducing tumor growth in a 3D culture of breast cancer cells. CovaLys represents a pioneering leap in covalent drug design, anticipated as the first-in-human Lysine covalent fluorosulfate drug.

P04 | Leader-Independent C-Terminal Macrocyclization of GLP-1 Like Peptides by a Radical SAM Maturase

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Ribosomally synthesized and post-translationally modified peptides (RiPPs) represent a growing class of natural products. Ribosomally produced RiPP precursors are posttranslatioanlly modified by RiPP maturases, also encoded in proximity of the genomically encoded substrate, into bioactive natural products. This maturation process is often thought to depend on an N-terminal leader sequence within the precursor peptide, which engages a complementary RiPP-recognition element (RRE) in the enzyme. In this study, we examined PapB, a radical S-adenosyl-L-methionine (rSAM) RiPP maturase responsible for forming thio(seleno)-ether crosslinks and uncovered that it can dispenses with the leader sequence of the substrate, establishing authentic leader-independent activity. To demonstrate the translational utility of this feature, we applied PapB to three glucagon-like peptide (GLP) pathway agonist analogues, producing C-terminal cyclic architectures. In all cases, the enzyme completely converted the linear precursors into thioether-linked macrocycles. These findings position PapB as a broadly applicable biocatalyst for late-stage peptide macrocyclization, enabling direct access to conformationally restricted therapeutic candidates without the requirement for leader sequences.

P05 | A Pilot Study: Toxicological Assessment of Myristic Acid-Trans-Activator of Transcription Dual Conjugation of Protein Kinase C Epsilon Peptide Inhibitor Cargo is Safe Thirty Times Beyond the Target Dose

Samuel Geathers[1], Kerry-Anne Perkins[2], Juliet Melnik[1], Sunit Singh[1], Arjun Nair[2], Qian Chen[1], Robert Barsotti[1], Lindon Young[1,2]
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Background
Protein kinase C epsilon (PKCε) signaling is known to activate uncoupled endothelial nitric oxide synthase (eNOS) via phosphorylation at serine 1177, leading to reactive oxygen species (ROS) generation upon restoration of blood flow to previously ischemic myocardium or inhibiting nitric oxide (NO) release in coupled eNOS. PKCε inhibits ROS production from mitochondrial ATP-dependent potassium channels during reperfusion following ischemia also.

Objectives
We hypothesize that inhibiting NO release via eNOS with cell permeable PKCε peptide inhibitor will result in cardiovascular shock in our first ever toxicology assessment of this novel cell permeable PKCε peptide inhibitor. We also predict that PKCε peptide inhibitor given at reperfusion will attenuate ROS induced infarct size in ex-vivo rat hearts subjected to myocardial global ischemia-reperfusion injury (IRI) compared to scrambled peptide controls.

Methods
In vivo toxicology study: Cell permeable PKCε inhibitor peptide (EAVSLKPT) was conjugated with Myristic Acid (Myr) and Trans-Activator of Transcription (Tat) (N-Myr-Tat-CC-EAVSLKPT[PKCε-]. Male Sprague-Dawley (SD) rats (275g to 325g) were given a dose range of (0.2mg/kg [target dose, ~ 1μM in serum] to 10mg/kg of Myr-Tat-PKCε- that was dissolved in sterile normal 0.9% saline and administered intravenously via a jugular vein port. *(continued on next page)*

Ex-vivo myocardial global I(30min)RI(50min) study: At the onset of reperfusion, Myr-Tat-PKCε- or scrambled control peptide (N-Myr-Tat-CC-LSETKPAV; Myr-Tat-PKCε-scram). Myr-Tat-PKCε-scram (1 μM) were dissolved in normal saline and further diluted in Krebs' buffer. Isolated perfused rat hearts were perfused at a constant pressure of 80mm of Hg, bubbled with 95% oxygen/5% carbon dioxide and maintained at 37 degrees Celsius throughout the 15min baseline, 30min global ischemia and 50min reperfusion. Data were analyzed via student's t-test.

Results
In vivo: Myr-Tat-PKCε- (n=10 total, n=1 per dose) demonstrated safety from 0.2 mg/kg to 6mg/kg). 10mg/kg rat dosing died instantly whereas, 8mg/kg dose survived until the following day before succumbing to cardiogenic shock. Ex vivo: Myr-Tat-PKCε- showed significant reduction in infarct size (Myr-Tat-PKCε-: 4.2±0.52%; n=3 compared to Myr-Tat-PKCε-scram (22.7±4.6%, n=3; $p<0.05$).

Conclusion
Addition of Myr-Tat-PKCε- is safe up to at least 30x the target dose before cardiogenic shock ensues. Ex vivo rat hearts IRI corroborated our earlier data (Nair et al., 2024) and reduced infarct size when given at the beginning of reperfusion. The data suggests coronary revascularization post-myocardial infarction (MI) exhibits robust cardio-protection and may reduce incident - heart failure after MI.

P06 | mRNA display: Revolutionizing Drug Discovery

Yongjin Gong, Liling Zeng, Chenguang Gong, Lynn Zhang
PeptiFinder Biotech

mRNA display is a powerful in vitro selection and directed evolution technique that enables the screening of trillions of peptide variants for desired functions in a single experiment. Compared to other display technologies, such as phage display, mRNA display offers distinct advantages, including ultra-high-diversity libraries, in vitro selection, and the ability to incorporate noncanonical amino acids. As a result, mRNA display has become the leading display technique for discovering novel (macrocyclic) peptide binders with antibody-like affinities and even potential oral bioavailability.

PeptiFinder Biotech is the pioneering company specializing in mRNA display technology, providing cutting-edge services to the pharmaceutical industry. PeptiFinder mRNA display platform offers various libraries (linear, monocyclic, and bicyclic peptides) with ultra-high- diversity (up to 10^15), which can be readily screened against almost any biological target of interest (7-8 weeks) with a remarkable success rate (>95%). Furthermore, by incorporating unnatural amino acids into macrocyclic peptide libraries, PeptiFinder mRNA display platform can generate peptide hits with enhanced physiochemical properties and optimized pharmacokinetics, streamlining the process of optimizing lead compounds into clinical candidates and accelerating drug discovery timelines for clients. PeptiFinder also offers customer library service tailored to specific client needs.

Furthermore, PeptiFinder provides additional services including macrocyclic peptide DEL screening, ELISA/SPR hit confirmation, and peptide synthesis.

P07 | Assessment of BAK Inhibition for Therapeutic Applications

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In neurodegenerative diseases such as Alzheimer's, the cytochrome c-dependent apoptosis pathway plays a crucial role in neuronal cell death. BAK, a pro-apoptotic protein of the BCL- 2 family, permeabilizes the mitochondrial outer membrane when activated, leading to the release of cytochrome c and the initiation of apoptosis. The activation of BAK begins when BH3-only proteins bind to its hydrophobic groove, exposing the BH3 region. This exposure drives BAK's dimerization, oligomerization, and the formation of pores in the mitochondrial membrane. In the context of Alzheimer's disease, amyloid-β oligomers can directly interact with BAK, causing neuronal cell death even in the absence of upstream signals. Furthermore, research has shown that the ablation of BAX, another pro-apoptotic protein similar to BAK, reduces amyloid-β-induced neuronal cell death. This suggests that BAK may also significantly contribute to neuronal death in Alzheimer's disease. For this reason, our project aims to identify and evaluate peptide sequences that selectively target BAK's hydrophobic groove to prevent the conformational changes required for BAK's induced pore formation and apoptosis. We synthesized several peptidomimetics, based on known BAK- binding peptides, such as BH3 domains, and other reported peptide sequences. Their affinity for BAK in vitro was analyzed using various biophysical techniques, such as NMR, TSA, and ITC. Moreover, we envision investigating the biological effects of BAK inhibition in neuronal cell lines and other BAK-expressing cells, such as cancer cells.

P08 | Internally Quenched Fluorescent Peptides Provide Insights into Underexplored and Reversible Post-Translational Modifications

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Department of Physiology, University of California San Franscisco, San Francisco, CA, USA

Post-translational modifications (PTMs) are essential regulators of cellular processes, influencing gene expression, protein stability, and protein-protein interactions.1 Among these, lysine and arginine modifications such as acetylation, methylation, citrullination and other acylation variants are key players in epigenetic regulation.2,3 However, the development of assay systems that can adapt to a wide range of PTMs remains a challenge. Here, we present a generalized fluorescent turn-on platform that utilizes simple peptide substrates to study the installation and removal of a diverse set of lysine and arginine PTMs, with a focus on epigenetically relevant ones (Fig. 1).4 In addition to synthetic installation of native post-translationally modified residues in peptides, we employed thialysine and thiaarginine analogs to mimic modified lysine and arginine residues, enabling facile introduction of functional PTM mimetics using simple cysteine chemistry.5,6 We utilize the cleavage of peptidyl lysine and arginine bonds by trypsin, which are only removed when these residues are in their unmodified state (Fig. 1). Conversely, in their post-translationally modified state, the peptides remain intact leading to internal fluorescent quenching, making the system adaptable to studies of both writer and eraser enzymes (Fig. 1).

Model PTMs that have been studied are removal of lysine acetylation, lactylation and β-hydroxybutyrylation by SIRT3 and HDAC2, removal of methylated lysine variants by KDM3A and KDM4A as well as arginine citrullination by PAD4, highlighting the versatility of this approach. Additionally, we studied the removal of the novel methylacetylation PTM on lysine by both HDACs and KDMs.7 Additionally, we have investigated the installation of acyllysine modifications by HDACs as a new paradigm in PTM biology.8,9 By integrating modularity and fluorogenic detection, this system provides an accessible, flexible, efficient, and adaptable tool for PTM

studies. Its broad applicability offers significant potential for exploring enzymatic mechanisms, PTM crosstalk, and protein regulation across diverse biological contexts.

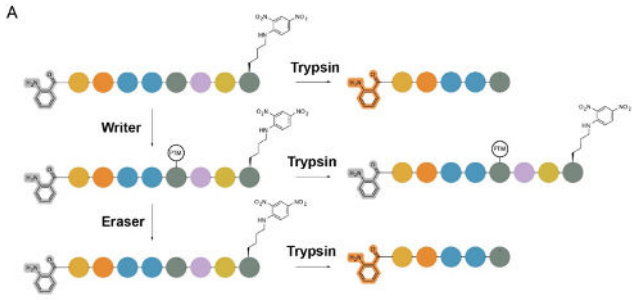

Figure 1: Overview of the internally quenched fluorescent system to study installation and removal of PTMS.

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P09 | Targeting Adipogenesis and Sacropenia: Dual Benefits of Regenotide in Obesity Treatment

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Background
Although GLP-1 receptor agonists are widely used for obesity treatment, their use has raised concerns about loss of skeletal muscle mass and function. In addition, combination therapies that address obesity-associated comorbidities such as metabolic dysfunction–associated steatohepatitis (MASH) remain underdeveloped.

Methods
19–amino-acid synthetic peptide, Regenotide, and evaluated its mechanism of action and therapeutic efficacy. Studies were performed in adipose-derived stem cells (ASCs) and a high-fat diet (HFD)–induced obesity mouse model. Single-cell RNA sequencing (scRNA-seq) was used to delineate mechanisms relative to existing anti-obesity agents.

Results
Regenotide significantly reduced the expression of adipogenesis-related genes (C/EBPα, PPARγ, and aP2) as well as adiponectin and leptin, accompanied by decreased lipid accumulation. In HFD-fed mice, subcutaneous Regenotide markedly suppressed adipose tissue expansion. Notably, Regenotide mitigated muscle atrophy, suggesting a protective effect against sarcopenia during obesity management. Furthermore, compared with a GLP-1 receptor agonist, Regenotide more effectively alleviated hepatic dysfunction by reducing hepatic lipid deposition and inflammatory responses.

Conclusion
Regenotide exerts potent anti-obesity effects by suppressing adipogenesis, limiting adipose expansion, and improving hepatic function, while concurrently preserving skeletal muscle. This dual action distinguishes Regenotide from current GLP-1 receptor agonists and highlights it as a promising therapeutic candidate for obesity and related complications, including MASH. Further preclinical and clinical validation is warranted to confirm translational applicability.

This research was supported by the grant from Osong Medical Innovation foundation funded by Chungcheongbuk-do and Cheongju City.

P10 | Antioxidative and Anti-Atopic Dermatitis Effects of Peptides Derived from Hydrolyzed *Sebastes schlegelii* Tail By-Products

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Atopic dermatitis (AD) is a chronic inflammatory skin disorder associated with significant morbidity, including pruritus, recurrent skin lesions, and immune dysregulation. This study aimed to investigate the antioxidative and anti-AD effects of peptides derived from hydrolyzed Sebastes schlegelii (Korea rockfish) tail by-products. Hydrolysates were prepared using various enzymes, including Alcalase, Flavourzyme, Neutrase, and Protamex. Among them, Protamex hydrolysates demonstrated the highest ABTS radical scavenging activity with an RC50 value of 69.69 ± 0.41 μg/mL. Peptides were further isolated from the Protamex hydrolysate using dialysis, fast protein liquid chromatography (FPLC), and high-performance liquid chromatography (HPLC). The most active peptide, STPO-B-II, exhibited a single peak and was identified as a sequence of Glu-Leu-Ala-Lys-Thr-Trp-His-Asp-Met-Lys, designated as MP003. In vivo experiments were conducted using a 2,4-dinitrochlorbenzene (DNCB)-induced AD model in NC/Nga mice. The isolated peptide, MP003, showed significantly reduced AD symptoms, including erythema, lichenification, and collagen deposition. Additionally, MP003 decreased epidermal and dermal thickness, eosinophil, and mast cell infiltration and downregulated the expression of pro-inflammatory cytokines IL-1β, IL-6, and IgE in serum and skin tissues. These findings suggest that peptides derived from Sebastes schlegelii tail by-products may serve as potential therapeutic agents for AD.

Keywords: Sebastes schlegelii tail by-products; atopic dermatitis; peptides; STAT3; antioxidant

P11 | N-Terminal Sequence Redesign of ExP5 to Modulate G-Protein Signal Bias

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GLP-1 receptor (GLP-1R) agonists are central to the treatment of type 2 diabetes mellitus (T2DM) and obesity and are currently under investigation to address additional metabolic and neurological disorders. “Biased” agonists, ligands that preferentially activate G protein signaling over β-arrestin recruitment, are particularly attractive therapeutic targets as they could reduce GLP-1R desensitization while maintaining potency.

Our discovery of ExP5, a biased GLP-1R agonist identified via high-throughput screening, demonstrated that ligands with N-terminal sequences entirely unrelated to that of the Exendin-4 parent can maintain receptor affinity while introducing ligand bias. Additional structural studies revealed potential intermolecular interactions between the N-terminal region of ExP5 and GLP-1R, which motivated further investigation of a structure–activity relationship underlying signal bias.

In this work, we conducted a detailed investigation of the N-terminal region of ExP5 to optimize both affinity and signaling bias. An alanine scan revealed positions amenable to modification, notably residue 5. Substitutions at other positions, including with non-natural amino acids, were introduced to probe and refine electrostatic interactions with the receptor. The geometry and length of the flexible linker connecting the N-terminal extension to the core sequence were also evaluated. Guided by these insights, a new series of engineered ExP5 analogues was designed and synthesized.

Several analogues exhibited enhanced GLP-1R affinity and a reinforced bias toward Gs-mediated cAMP signalling with reduced β-arrestin recruitment. Ultimately, these findings demonstrate that rationally-guided N-terminal sequence mutagenesis of GLP-1R agonists can modulate signal bias. This class of G-protein biased agonists could offer advantages over non-biased agonists in a therapeutic context, specifically through inhibition of side effects or generation of more “tailored” clinical outcomes.

P12 | Forced Degradation Study of Peptides

Susan Li, Ph.D.
Asymchem

Peptides are a-amino acid polymers composed of 40 or fewer amino acids. Therapeutic peptides are less immunogenic and offering greater safety, selectivity and specificity. By understanding the degradation behavior of peptides, safer and more effective peptide drugs can be designed. Degradation studies are conducted including a selection of stress conditions, degradation products formed, and different peptide degradation mechanisms. Case study on the degradation profile of existing peptide drugs is presented as well.

P13 | Peptide Hit Discovery and Optimization Using Machine Learning and Small Peptide Arrays

Ewa Lis, Ph.D., Koliber[1], Chris Diehnelt, Ph.D.[2]
[1] *Koliber Biosciences Inc.*
[2] *Robust Diagnostics LLC*

Peptide discovery methods like phage display and mRNA display have become standard tools for identifying peptide hits, yet they come with significant challenges. Phage display often produces inconsistent results and a high rate of false positives, necessitating substantial validation efforts. While mRNA display can yield potent hits with the inclusion of unnatural amino acids, it entails high licensing costs and suffers from non-uniform clone amplification. Additionally, hits identified by these methods are frequently hyperoptimized during selection, making it challenging to modify them for developability (stability, solubility, permeability) without compromising potency. These issues constrain the discovery of novel peptide therapeutics. 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.

P14 | Automated Liquid-Phase Peptide Synthesis for Efficient Peptide Manufacturing

Andy Miles, Adrian Amador
Snapdragon Chemistry

Liquid-phase peptide synthesis (LPPS) offers a scalable and cost-effective alternative to traditional solid-phase methods, especially for large-scale production. By enabling solution-phase chemistry with streamlined workups and solvent recycling, LPPS reduces raw material costs and improves environmental sustainability. In this work, we demonstrate the development and execution of an automated LPPS process, designed for efficient coupling, deprotection, and phase separation with minimal manual intervention. The system achieves high conversion and purity across multiple steps, showcasing the viability of automation for consistent and scalable peptide manufacturing. Our approach lays the groundwork for broader adoption of automated LPPS in both clinical and commercial settings.

P15 | Deciphering Peptide Formulations with no-D NMR

Jessie Ochoa
Genentech

Cyclic peptides have long been recognized as multifaceted molecules with intriguing behaviors in solution. For many high-concentration drug substances, apparent aqueous solubility may not accurately reflect their true characteristics. Understanding a compound's propensity to self-assemble or aggregate in solution is crucial for its success. For example, the bioactivity of daptomycin is closely tied to its ability to aggregate. While some compounds display seemingly unlimited solubility in water, others exhibit unusual behaviors, such as reduced solubility at lower concentrations.

Traditional NMR analysis often requires the use of deuterated solvents and formulations different from the native formulation, as well as extensive sample preparation. By applying water suppression techniques to non-deuterated (no-D) NMR, drug formulations can be analyzed without modification, providing a clearer picture of the solution-state behavior of peptides.

To design better therapeutics, it is essential to fully understand how peptides behave in their native solution states. No-D NMR offers a unique and unprecedented perspective on peptide solutions, enabling insights that are inaccessible through other techniques. This work demonstrates the application of no-D NMR towards several drug formulations and what insights might be gained from this analysis.

P16 | Modification of a Cyclic Peptide Inhibitor to Covalently Target KRAS Histidine Residues

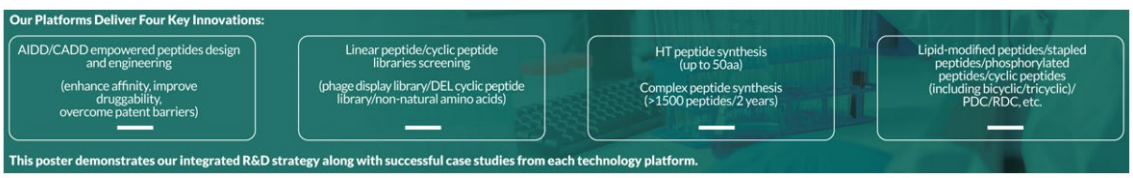
Anne Marie Prentiss
UC Riverside

KRAS is the most frequently mutated oncogene, playing a critical role in cell signaling and stimulating pathways such as Raf/MEK/ERK, PI3K-PKB/Akt, and RAL (Ras□Like) that are integral to cell growth, division, maturation, and death. KRAS has previously been considered undruggable, but with recent advancements in identification of the switch-II pocket, opportunities for development of both reversible and irreversible inhibitors have become possible. Currently, there are two FDA-approved drugs for KRAS that target the KRAS G12C mutation covalently via an acrylamide warhead. Notably, there are no covalent compounds in clinic that target KRAS residues other than C12 and D12, and there are no clinical candidates for KRAS G12V, Q61K, or Q61H, which leaves a large unmet need for novel therapies toward these mutations. In recent years, apart from the use of acrylamide-based compounds for the covalent targeting of cysteine residues, sulfonyl-fluorides (-SO2F) and aryl-fluorosulfates (-OSO2F) have been explored for the covalent targeting of lysine, histidine, and tyrosine residues.18 In this project, we are exploring the structure- based targeting of KRAS through the covalent modification of peptides that target the KRAS G12D mutation.

P17 | Innovative Approaches to Peptide Drug Development From Screening to PCC

Yue Qian, Bing Xia, Xinyu Deng, Justin Cui, Fang Fang, Weiji Li, Liyan Fang, Deqian Sun, Yanxia Yang, Yi Qu, Yinghong Gao
Viva Bioech

Peptide drugs are reshaping the global pharmaceutical landscape at an unprecedented pace, with the market projected to exceed USD 100 billion within the next five years and become one of the fastest-growing engines in biopharma. To meet the rising demand for high-quality peptide therapeutics, Viva Biotech has established a comprehensive R&D approach that integrates core technology platforms, including peptide screening, peptide conjugation, AIDD/CADD, peptide synthesis, bioassays, and pharmacological evaluation. This end-to-end workflow spans from early screening to confirmation of preclinical candidates (PCCs), enabling efficient and targeted advancement of peptide drug development.



P18 | Optimized Albumin-piggybacking Strategy Enhances Ultra-short Peptide Delivery and Bioavailability in a PTOA Mouse Model

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LSKL, an ultra-short peptide derived from the Latent Associated Peptide domain, effectively inhibits TSP1-mediated TGF activation, making it a promising therapeutic candidate for ischemic injury, hypertrophic scarring, and fibrosis. However, its rapid systemic clearance limits its clinical utility. To overcome this, we developed an albumin piggybacking strategy by conjugating LSKL to octadecanedioic acid (C18 diacid) via an oligoethylene glycol (OEG) linker, preserving peptide functionality with minimal cytotoxicity. To further enhance bioavailability and reduce aggregation, we designed and evaluated three linker variants: (1) direct conjugation, (2) γ-glutamic acid, and (3) γ-glutamic acid with two OEG units. Bio-Layer Interferometry and Size-Exclusion FPLC identified the optimal C-terminal branching site as Peptide-OEG-OEG-γGlu-C18 diacid, which exhibited strong albumin binding. These lipid-modified peptide variants demonstrated improved pharmacokinetics after subcutaneous injection (t□/□ = 52h) and enhanced biodistribution to injury sites in a post-traumatic osteoarthritis (PTOA) mouse model. Our findings present a viable strategy for optimizing the pharmacokinetics and therapeutic efficacy of short peptides, offering potential advancements in regenerative medicine.

P19 | DNA-Encoded Libraries and Display Technologies Empower Early Discovery of Peptide Drugs and Peptide-Based Delivery Tools

Rhys Taylor
WuXi AppTec

Peptide therapeutic discovery is experiencing a resurgence, particularly for challenging, historically “undruggable” targets. WuXi AppTec is leading the way in this field with innovative technologies and platforms. Traditional phage display, while cost-effective and providing substantial library diversity, is limited by its reliance on only the 20 natural amino acids, resulting in restricted chemical diversity. In response, we have developed our mRNA display capabilities, which surpasses phage display in robustness with macrocycles up to 15 amino acids long. Additionally, our peptide DNA-encoded library (DEL) service provides an alternative approach, leveraging unnatural amino acids to generate hundreds of billions of linear and cyclic peptide-like molecules. These DEL macrocycles offer broader chemical diversity and improved physicochemical properties compared to traditional peptide libraries, with smaller ring sizes (6-9 amino acids) and innovative cyclization strategies, including the ‘click’ reaction. Conversely, we have also designed focused peptide-DEL libraries based on an initial phage or mRNA-Display screen with up to 4 sites to include any of our 1400+ validated natural and unnatural amino acids. In our poster we demonstrate the effectiveness of our technologies for discovering peptides including the discovery of i) a 9 nM cyclic inhibitor of the MDM2-p53 interaction, ii) potential tumor cell-specific peptide ligands that are being explored for targeted delivery of payloads via oligonucleotides or radioisotopes, iii) Significantly improved affinity from Display to DEL cyclic peptides.

P20 | Enabling the Rational Computational Design of Peptide Therapeutics with Physics-based Affinity Prediction Methods

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Compared with small molecules and antibodies, peptides are increasingly seen as occupying a "Goldilocks zone" in drug discovery, combining the precision of antibodies with the flexibility and scalability of small molecules. Their larger size, greater flexibility, and more complex structural topologies, however, make them notoriously difficult to model with conventional computer-aided drug design tools. In particular, Free Energy Perturbation (FEP), a gold-standard in silico potency assay for small molecules, often falls short for peptides. In this work, we present two complementary computational strategies designed to overcome these barriers: **PepFEP**, an FEP method that enables accurate relative binding affinity predictions for peptides that differ in local structural changes such as side-chain composition, and **PepACES**, an enhanced sampling-based conformational analysis approach that can be used to rank binding affinities of structurally diverse peptides based on preferred bioactive conformations observed in solution and protein-bound states. Both approaches are powered by **PepFF**, a hybrid peptide-specific force field that uses the AMBER protein force field for standard protein residues and incorporates the GAFF2 small molecule force field along with the AMBER protein force field for peptides that contain non-standard residues and linkers. Through case studies involving diverse protein-peptide systems, we demonstrate how these methods deliver predictive accuracy and practical guidance for peptide-based drug design. Together, PepFEP and PepACES offer a physics-based toolkit that enables the rational computational design of peptide therapeutics.clinical outcomes.

P21 | Structure-Guided Design of IGF1R-Specific Antagonist Therapeutics Using Viral Insulin-like Peptides

Katherine Truelson, Sofia Pansini, Emrah Altindis
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The insulin/IGF-1 signaling axis regulates cell metabolism and growth, and its dysregulation is implicated in several diseases, including cancer. Elevated IGF-1 levels and IGF1R overexpression drive tumor proliferation, survival, and therapy resistance. While IGF1R is a promising oncology target, selective inhibition remains challenging due to structural homology with the insulin receptor (IR). Existing IGF1R inhibitors lack specificity and cause hyperglycemia by inhibiting IR signaling. Our lab recently identified viral insulin/IGF1-like peptides (VILPs), a novel protein family encoded by Iridoviridae viruses, sharing ~30–50% identity with human insulin and IGF-1. Chemically synthesized VILPs bind both IR and IGF1R, with most acting as agonists. Remarkably, VILPs from Mandarin fish ranavirus (MFRV) and Lymphocystis disease virus-1 (LCDV1) function as natural IGF1R-selective antagonists, sparing the IR.
Preliminary studies using chimeric VILPs demonstrate that the LCDV1-VILP C-domain and a Gly8>Ser substitution in the B-domain convert IGF-1 into an IGF1R antagonist; reversing these changes abolishes antagonism. To further define structural features driving antagonism, we are engineering IGF-1/MFRV-VILP chimeras and mutating five conserved residues shared among antagonistic VILPs. Candidate peptides will be screened in IGF1R-overexpressing murine embryonic fibroblasts to assess effects on receptor autophosphorylation and Akt/Erk signaling. Promising hits will advance to recombinant production and detailed analysis of IGF1R versus IR selectivity. *(continued on next page)*

This platform provides a rational path to designing next-generation IGF1R antagonists with minimal IR cross-reactivity, addressing a critical limitation of current therapies and offering a novel therapeutic avenue for IGF1R-driven diseases.

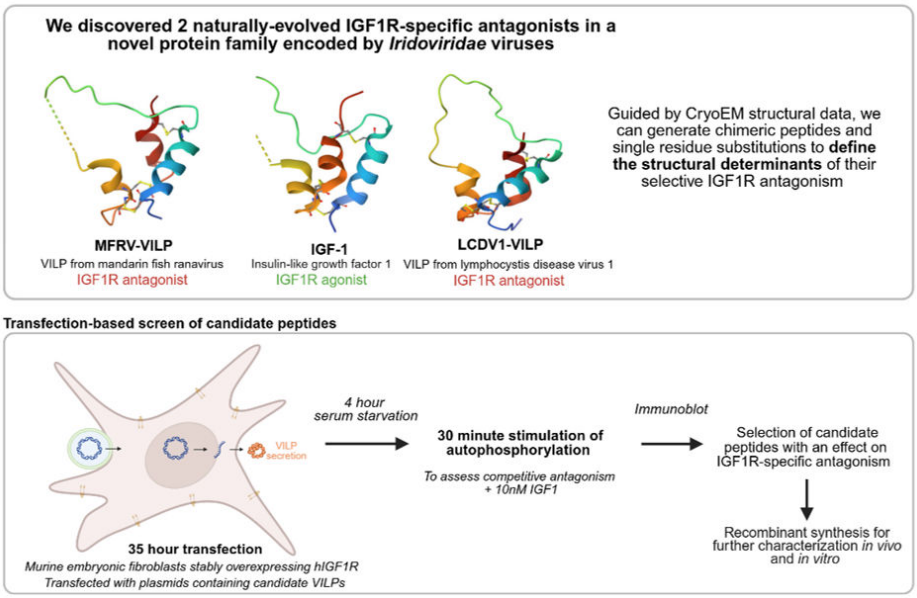

Figure 1. Understanding the structural determinants of selective IGF1R antagonism by MFRV- and LCDV1-VILPs, members of a novel class of insulin/IGF1 peptide hormones.

P22 | Lipid Depot Formulations Transform Short-acting Peptides into Long-acting Medications

Maria Sörhede Winzell and Markus Johnsson
Camurus AB, R&D, Lund, Sweden

Many peptide therapeutics are sensitive to degradation resulting in short duration and frequent dosing schedules for patients. By use of depot technology this can be improved, and short-acting peptides can be turned into weekly or monthly long-acting medicines. A lipid-based liquid crystalline depot formulation offers an approach for sustained release of a variety of molecules. The drug is mixed with natural lipid components and biocompatible solvents into a liquid formulation, which upon contact with water in the subcutaneous tissue, turns into a gel-like highly viscous liquid crystalline matrix. The composition can be tuned to avoid initial burst release, and deliver an extended drug release profile, from weeks to months. The lipid depot is biodegradable in the tissue and resolves completely over time.

The lipid depot technology has been validated in multiple clinical trials as well as in approved products. Small molecules peptides and peptides have demonstrated extended-release profiles, in non-clinical and clinical studies. Octreotide, a peptide with eight amino acids, is a somatostatin receptor ligand with a plasma half-life of less than 2 hours. Formulation of octreotide into a lipid depot allows for a once monthly dosing using a pre-filled pen delivery device with convenient patient self-administration. Native glucagon-like peptide 1 (GLP-1), a 30 amino acid peptide with a half-life of 2 min, formulated in a lipid depot demonstrated an extended-release profile for one week in mini-pigs.

The lipid depot technology opens a path for sensitive molecules with short half-life to be transformed into long-acting and convenient drugs to patients.

Notes

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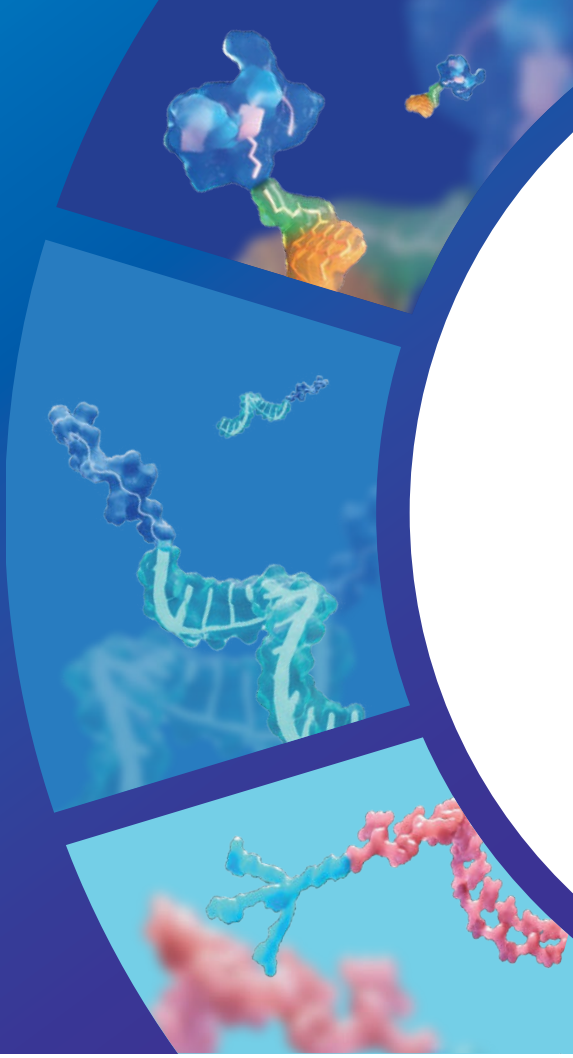

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