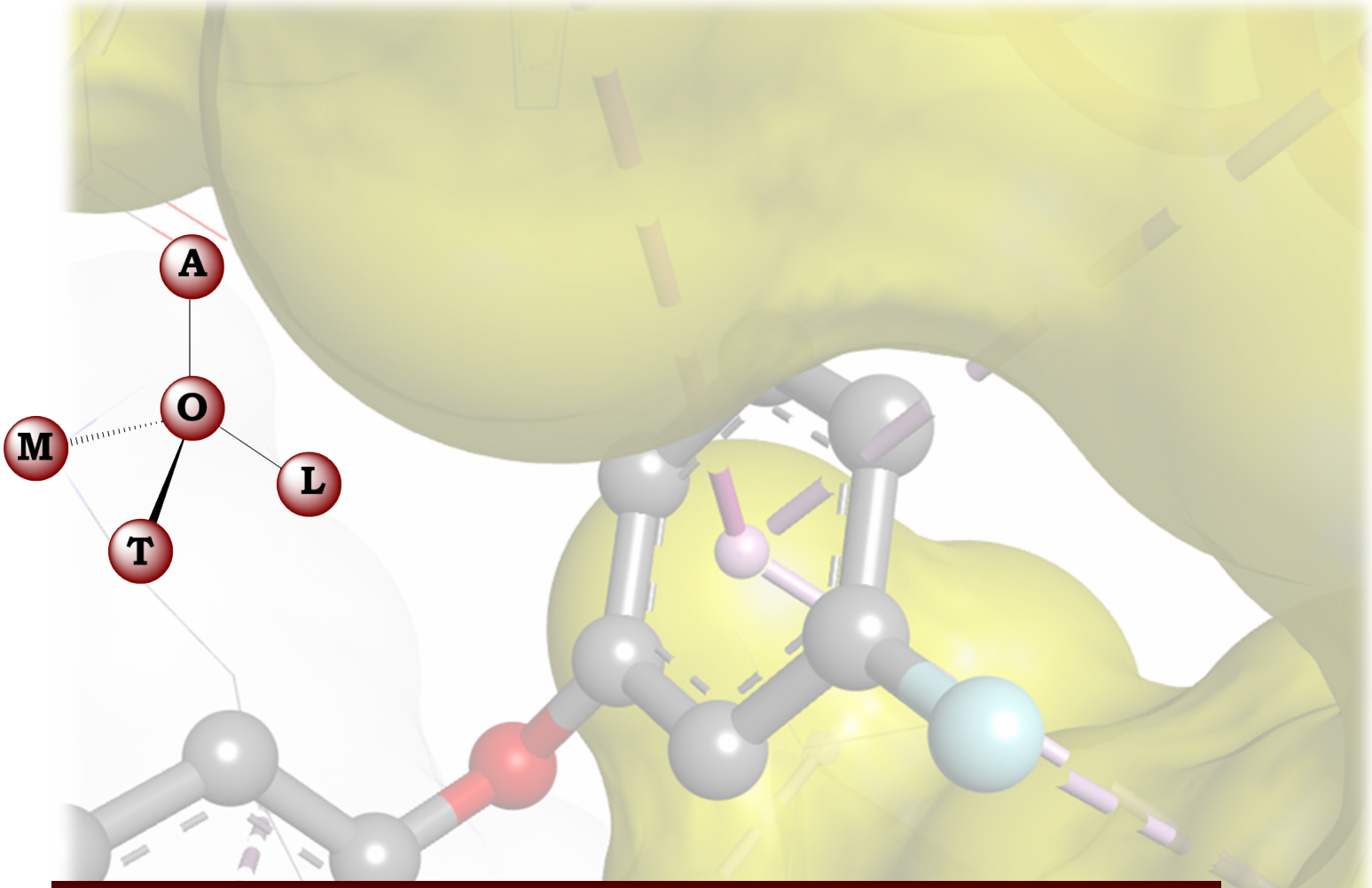


# 50th Annual MALTO Medicinal Chemistry-Pharmacognosy Meeting -in-Miniature

Texas A&M Irma Lerma Rangel
College of Pharmacy
Texas A&M University
May 21-23, 2025, College Station.

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# MALTO 2025
# TEXAS A & M UNIVERSITY, COLLEGE STATION

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Co-Chairs: **Hamed Aly Ismail,** Ph.D.

**Shiqing Xu**, Ph.D.

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**Wenshe Liu**, Ph.D., **Yinan Wei**, Ph.D.

## *Multimedia & Podium Support*

**Ms. Shelby L. Purdy, Mr. Artug Altug, Mr. Steve Leggio**

## *Graduate Student Committee Members*

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**Rajpal Vangala** **Sahel Hajimirzaei** **Khan Huynh**

**Yuqi Zhou**

## *Administration Advisors*

**Ms. Agatha Alonso**
**Ms. Pamela Williams**

# GENERAL PROGRAM " The 50th MALTO "

| Time | Event | Location |
|---|---|---|
| **Wednesday, May 21, 2025,** | | |
| 4:00 pm<br>4:30-6:00 pm | **Registration**<br>**Reception Mixer**<br>**Poster setup** | At TAMU Innovative Learning Classroom Building (ILCB)-Room 207 (Address: 215 Lamar St, College Station, TX) |
| **Thursday, May 22, 2025**<br>At TAMU Innovative Learning Classroom Building (ILCB)-Room 207<br>(Address: 215 Lamar St, College Station, TX 77844) | | |
| 7:30-8:30 am | **Breakfast** | |
| 8:30-9:00 am | **Welcoming Remarks:** Dr. Mansoor Khan<br>*Interim Dean of Rangel College of Pharmacy, Texas A&M University*<br>*Regents & Distinguished Professor of Pharmaceutical Sciences*<br>**MALTO Introduction:** Dr. John Rimoldi / Dr. Dai Lu | |
| 9:00-10:00 am | **PODIUM SESSION 1 (O1-O3)** | |
| 10:00-10:30 am | **Coffee break:**<br>*Conference site, posters available for viewing only* | |
| 10:30-11:30 pm | 36th Annual A. Nelson Voldeng Memorial Lecture<br>**Keynote Speech:** Dr. Kevin Dalby<br>*Professor of Chemical Biology & Medicinal Chemistry, The University of Texas at Austin* | |
| 11:30 -12:10 pm | **PODIUM SESSION 2 (O4-O5)** | |
| 12:10-1:00 pm | **Lunch:** 2nd floor ILCB building, near Room 207 | |
| 1:00-3:00 pm | **POSTER SESSION**<br>**Coffee Break** *(Concurrent with Poster Session)* | |
| 3:00-4:00 pm | AGGIE Lecture: **Keynote Speech:** Dr. Wenshe Liu<br>*Harry E. Bovay, Jr. Endowed Chair and Professor in Chemistry, Texas A&M University* | |
| 4:00-5:00 pm | **PODIUM SESSION 3 (O6-O8)** | |
| 6:00-8:30 pm | **Dinner & Banquet***:*<br>*At Napa Flats Wood-Fired Kitchen: 1727 Texas Ave S, College Station.* | |
| **Friday, May 23, 2025** | | |
| 7:30-8:30 am | **Breakfast** | |
| 8:30-9:30 am | **PODIUM SESSION 4 (O9-O11)** | |
| 9:30-10:00 am | **Coffee break:** 2nd floor ILCB building, near Room 207 | |
| 10:00-11:20 am | **PODIUM SESSION 5 (O12-O15)** | |
| 11:30-12:30 pm | **Lunch:** 2nd floor ILCB building, near Room 207 – (*Pick up your lunch box)* | |
| 11:30-12:30 pm | **MALTO Business Meeting:** *Conference room 224. (MALTO Faculty Only)* | |
| 12:30-1:30 pm | **MALTO Awards Ceremony & Closing Remarks**<br>*- 2025 Robert A. Magarian Podium Presentation Award*<br>*- 2025 Thomas L. Lemke Poster Presentation Award*<br>*- 2025 Ronald F. Borne Postdoctoral Poster Presentation Award* | |
| 1:30 pm | **Adjourn** | |

## WELCOME MESSAGE FROM DEAN KHAN

**Howdy!**

It is my distinct honor and privilege to welcome our guests to the 50th MALTO conference.

I sincerely appreciate your participation in this event, as we come together to discuss the advancements of pharmaceutical research within the professional schools from six southern states.

The topics covered in this conference indicated a multitude of focus areas, including basic science, such as methodology development, to translational research relevant to unmet medical needs. Your presence and contributions will significantly enrich the scientific discussions and the overall experience of the conference. The 50th MALTO meeting features dynamic keynote speakers who are experts in their respective fields. They have each been invited to deliver thought-provoking presentations, engage in robust discussions with the audience, and promote networking and collaboration with the MALTO community. Their insights and perspectives will be of tremendous value to MALTO trainees and scientific professionals.

I am eagerly looking forward to hosting the MALTO community, including professional pharmacy students, graduate students, and postdoctoral fellows, so they may share their latest research discoveries and innovations, particularly in the areas of medicinal chemistry and pharmacognosy. The exchange of knowledge and ideas that will take place during this event is something we will particularly be excited about.

The abstracts presented in this book are meant to foster reflection and inspire conversations on the meaningful contributions that the authors have made. The work and insights are of tremendous value to the advancement of the pharmaceutical discipline, and I am confident that you will find the discoveries shared here vital to your own research and beyond.

Over the next two days, we have packed scientific sessions, featuring keynote speeches, MALTO trainees' presentations, and networking opportunities.

On behalf of the College of Pharmacy and the 2025 MALTO organizing committee, thank you for joining the Texas A&M University Irma Lerma Rangel College of Pharmacy on this endeavor.

**Gig 'em!**
**Mansoor A. Khan, Ph.D.**
Interim Dean
Regents and Distinguished University Professor of Pharmaceutical Sciences
Presidential Impact Fellow

# MALTO MEDICINAL CHEMISTRY AND PHARMACOGNOSY

*A Brief History*

MALTO began with the concept of a miniature medicinal chemistry meeting at which students could have the opportunity to present their research to their peers and mentors. This concept was first put into practice in the early 1960's under the leadership of Drs. Portoghese, Cannon, Smissman, and Bauer at the Universities of Minnesota, Iowa, Kansas, and Illinois, respectively (MIKI). Credit for the concept and the inspiration for our own miniature medicinal chemistry meeting must be given to this group of individuals. For several of us who experienced the excitement and value of such an experience, it was only natural to attempt to bring this same opportunity to our region of the country.

In the spring of 1974, Tom Lemke (University of Houston) called his KU classmate Nelson Voldeng (Nels) at the University of Arkansas to ask what he thought of the idea. Not only did Nels think that the idea would work in our region of the country, but he indicated that he had another transplanted Kansan at Arkansas, Danny Lattin. When the conversation got around to who else might be interested in helping to develop a MIKI clone, Danny suggested Bob Magarian at Oklahoma, who had also experienced MIKI while a post-doc at KU. Thus, a regional medicinal chemistry meeting in the South-Central region of the U.S. was born. By the time of the first meeting (October 2-4, 1974), two other schools had signed on under the leadership of Jay Nematollahi at the University of Texas and Ray Saenz at Northeast Louisiana University.

The first meeting, titled "First Annual Medicinal Chemistry Meeting-in-Miniature", was sponsored by the University of Houston, The Upjohn Company, E.R. Squibb & Sons, Roche Laboratories, and Alcon Eye Research Foundation. Dr. Joe Buckley, Dean at the University of Houston, welcomed the attendees who listened to 17 student and faculty presentations, plus invited presentations from Dr. E. Wenkert of Rice University and Dr. S. Welch from the Chemistry Department at the University of Houston. Dr. Lin Cates suggested a shorter name for the organization and the members voted to call the organization ALTO (Arkansas, Louisiana, Texas, and Oklahoma).

Since football was "king" in Arkansas, Texas and Oklahoma, the decision was made to move the meeting to the spring, rather than risk a scheduling conflict, and Bob Magarian volunteered to host the second meeting in Oklahoma.

The second annual ALTO meeting took place in Norman, Oklahoma, preceded by a mixer with 32 attendees. The largest contingent at the 2nd meeting came from Texas Southern University (8). The meeting saw 13 student and faculty presentations and three invited presentations from faculty at Oklahoma, including Drs. Pushkar Kaul, Alfred Weinheimer, and Francis Schmitz. The highlight of the meeting was a cookout prepared by master chef Magarian and an evening of excitement in downtown

Norman. It should be mentioned that ALTO's expenses for 1975 amounted to $131.64, leaving a balance of $395.00 in the ALTO account.

The 3rd ALTO Medicinal Chemistry & Pharmacognosy Meeting in Miniature took place on May 19-21, 1976, in Monroe, Louisiana, and besides attendance by the four founding schools, representatives and presentations came from Texas Southern University, the University of Mississippi, and Southwestern Oklahoma State College. A total of 24 presentations were given, plus an invited lecture by Dr. W.K. Taylor from Northeast Louisiana University.

The 4th annual meeting returned to Houston, hosted by Texas Southern University. Again, the meeting had participation from Southwestern Oklahoma University and the University of Mississippi. Following the meeting, Mississippi was asked to join ALTO, and they were accepted. Beginning with the 5th annual meeting at Little Rock, the organization took on its present name of MALTO.

MALTO completed its cycle of host institutions following the 6th and 7th annual meetings, which were hosted by the University of Mississippi in 1979 and the University of Texas in 1980. In 1982 MALTO became an IRS 501(c) 3 not for profit Oklahoma Corporation (tax-exempt) with Bob Magarian, President; Ron Borne, Vice President; Tom Lemke, Secretary; and Danny Lattin, Board Member.

Other milestone events in the history of MALTO consisted of the participation and hosting of a meeting by Xavier University in 1986 in New Orleans (13th meeting). In 1988, the organization began the first A. Nelson Voldeng Memorial Lecture. This began at the 15th MALTO meeting, and Dr. Wendel Nelson gave the lecture. Auburn University hosted this meeting. Eighty-two registrants attended the meeting, and it marked the first meeting attended by faculty from the University of Georgia. In 1991, Tom Lemke resigned as secretary/treasurer (1974 - 1991). He has been followed in this office by Bob Sindelar (Mississippi, 1991 - 1995), Michael Crider (Louisiana, Monroe, 1995-2004), E. Kim Fifer (Arkansas, 2004 – 2017) and Dai Lu (Texas A&M, 2018 - present).

The 19th Annual MALTO Meeting hosted by the University of Arkansas was the first meeting at which attendance exceeded 100 registrants.

At the 1993 meeting (20th MALTO), the University of Tennessee participated for the first time. In 1994, Peter Ruenitz, University of Georgia, began attending the meetings. At the 25th Annual MALTO Meeting (1998), poster sessions were used for the first time. Posters became necessary when the number of papers submitted exceeded the time available for podium sessions. (8 posters and 22 presentations). In 1999, an award for the outstanding student podium presentation was established in the name of Robert A Magarian. Similar awards were established in 2003 and 2015 for the outstanding student poster in honor of Dr. Thomas L. Lemke and the outstanding postdoctoral poster in honor of Dr. Ronald F. Borne, respectively.

# A. NELSON VOLDENG MEMORIAL LECTURE

A. Nelson Voldeng was Professor of Medicinal Chemistry at the University of Arkansas, College of Pharmacy from 1964 until lingering illness forced his retirement in 1986. Nelson was born and raised in the south-central Kansas town of Wellington. He earned both his B.S. in Pharmacy (1960) and his Ph.D. in Medicinal Chemistry (1964) at the University of Kansas. His dissertation advisor was the late Dr. Edward E. Smissman. Nelson was well known for his efforts to encourage promising undergraduate pharmacy students to continue their education in graduate studies in the pharmaceutical sciences. Numerous pharmacy students worked with him in his research laboratory and many of these students made presentation at MALTO meetings. Nelson's research interest included the synthesis of novel, broad-spectrum penicillin derivatives and the synthesis of long-acting opiate analgesics derived from pentapeptides.

Nelson was one of the founding organizers of our MALTO organization. Since 1973, when MALTO held its first meeting, Nelson provided energetic leadership and worked tirelessly to help bring the idea of an annual regional medicinal chemistry and pharmacognosy meeting to fruition. Until he died in 1987, Nelson continued to contribute his energies to ensure the successful growth of MALTO.

The MALTO faculty voted unanimously in 1987 to name the annual lecture by a visiting scientist the "A. Nelson Voldeng Memorial Lecture" in recognition of Nelson's invaluable contributions to MALTO. The first A. Nelson Voldeng Memorial Lecture was presented on June 13, 1988, during the 15th Annual MALTO Meeting held at Auburn University. Dr. Wendel L. Nelson, Professor of Medicinal Chemistry at the University Of Washington School Of Pharmacy, who had been a fellow graduate student of Voldeng and a personal friend of long standing, presented this inaugural lecture.

The MALTO faculty designed a special plague commemorating the A. Nelson Voldeng Memorial Lecture. This plaque and an honorarium are presented annually to the visiting scientist lecturer. A copy of the first plaque was presented by MALTO to Nelson's wife, Mrs. Diana Voldeng of Little Rock, Arkansas.

## A. NELSON VOLDENG MEMORIAL LECTURER:

1988 Wendel L. Nelson, University of Washington
1989 Peter Gund, Merck, Sharpe and Dohme Laboratories
1990 Walter Korfmacher, National Center for Toxicological Research
1991 Duane D. Miller, Ohio State University
1992 Corwin Hansch, Pamona College
1993 William H. Pirkle, University of Illinois
1994 J. Andrew McCammon, University of Houston
1995 Robert P. Hanzlik, University of Kansas
1996 James A. Bristol, Parke-Davis Pharmaceuticals
1997 Yvonne Martin, Abbott Laboratories
1998 Gunda Georg, University of Kansas
1999 Michael F. Rafferty, Parke-Davis Pharmaceuticals
2000 Robert C. Anderson, Sphinx Pharmaceuticals, a Division of Eli Lilly & Company
2001 Phillip Crews, University of California at Santa Cruz
2002 David H. Coy, Tulane Medical College
2003 Dennis M. Zimmerman, Eli Lilly and Company
2004 Mitchell S. Steiner, MD, FACS, GTx, Inc.
2005 F. Ivy Carroll, RTI International
2006 Michael Eissenstat, Sequoia Pharmaceuticals
2007 Peter A. Crooks, University of Kentucky
2008 Kenner C. Rice, National Institute on Drug Abuse
2009 Thomas R. Webb, St. Jude Children's Research Hospital
2010 Derek Lowe, Vertex Pharmaceuticals
2011 Harold Kohn, University of North Carolina
2012 James D. McChesney, Arbor Therapeutics, LLC, Ironstone Separations, Inc., Cypress Creek Pharma, Inc.
2013 Thomas E. Prisinzano, Department of Medicinal Chemistry, University of Kansas
2014 Richard E. Lee, St Jude Children's Research Hospital
2015 Alan Kozikowski, University of Illinois at Chicago
2016 Richard A.F. Dickson, Texas Heart Institute
2017 Maria Alvim-Gaston, Eli Lilly and Company
2018 Carol Fierke, Texas A&M University
2019 Jeffrey Aube, The University of North Carolina at Chapel Hill
2022 Douglas Kinghorn, The Ohio State University
2023 Stephen F. Martin, University of Texas at Austin
2024 Pankaj Daga, Neuron23, Inc.

## 36TH ANNUAL A. NELSON VOLDENG MEMORIAL LECTURE

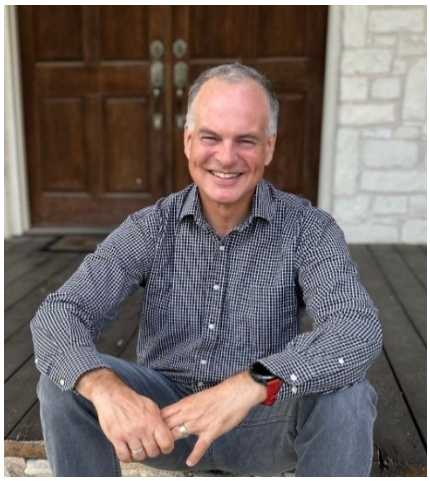
# THE REGULATION OF TRANSLATION ELONGATION: OPPORTUNITIES FOR THERAPEUTIC DEVELOPMENT

**Presenter:**

**Kevin Dalby, Ph.D.**

*Professor of Chemical Biology & Medicinal Chemistry*
*Johnson & Johnson Centennial Professor in Pharmacy*
*The University of Texas at Austin*
Kevin Dalby, Ph.D. | College of Pharmacy

**Biographical Sketch**



Dr. Dalby is the Johnson & Johnson Professor of Pharmacy at UT Austin. He is a distinguished chemist and a recognized expert in protein kinase biochemistry, signaling, and enzymology. He directs the Targeted Therapeutic Drug Discovery & Development Program (TTP). Dr. Dalby's current research is dedicated to developing novel covalent ERK inhibitors to target the ERK pathway, driven by RAS mutations. His work aims to characterize the chemical and allosteric mechanisms involved in this process. Additionally, Dr. Dalby investigates the dysregulation of translation elongation in chronic neurological conditions and various cancers. His studies focus on the phosphorylation of eEF2 on Thr-56, a crucial regulatory mechanism affecting protein synthesis. He has discovered novel regulatory mechanisms of eEF2K, an atypical protein kinase, and is working on therapeutic strategies targeting eEF2K for the treatment of neurodegenerative diseases and malignancies. Since 2011, Dr. Dalby has led TTP, providing specialized resources for cancer drug discovery to Texas institutions. TTP supports preclinical research, high-throughput screening, lead development, and target validation.

## 36TH ANNUAL A. NELSON VOLDENG MEMORIAL LECTURE

**Thursday, May 22, 2025, 10:30 -11:30 am**

## Abstract

Eukaryotic elongation factor 2 kinase (eEF2K) is an atypical, calmodulin-dependent kinase that plays a pivotal role in regulating protein synthesis in response to cellular stress. In this talk, I will present our integrated approach to understanding the structural, biochemical, and cellular mechanisms governing eEF2K activity. Structural studies have revealed key regulatory interactions with calmodulin and defined conformational transitions essential for activation. Complementary kinetic and cellular analyses elucidate how autophosphorylation and signal-dependent regulation modulate eEF2K's function in translational control. Building on these insights, I will outline our strategy for structure-informed drug discovery aimed at selectively targeting eEF2K activity in disease contexts, including cancer and neurological disorders.

## AGGIE Lecture

## SPONSORED BY: VCANBIO CENTER FOR TRANSLATIONAL BIOTECHNOLOGY

### TARGETING YEATS – AN EPIGENETIC READER DOMAIN FOR ANTI-CANCER DRUG DISCOVERY

**Presenter:**

**Wenshe Liu, Ph.D.**

*Harry E. Bovay, Jr. Endowed Chair and Professor in Chemistry Texas A&M University Department of Chemistry, Department of Biochemistry & Biophysics, Department of Molecular & Cellular Medicines,*
*https://artsci.tamu.edu/chemistry/contact/profiles/wenshe-liu.html*

**Biographical Sketch**

Dr. Wenshe Ray Liu is the Harry E. Bovay, Jr. Endowed Chair and Professor in Chemistry at Texas A&M University. He earned his B.S. degree from Peking University in 2000 and his Ph.D. degree from UC-Davis in 2005. He finished a two-year postdoc training at the Scripps Research Institute and started his independent research career in 2007 at Texas A&M University as an Assistant Professor. He was promoted to Associate Professor in 2013 and then Full Professor in 2016. Dr. Liu was the inaugural holder of the Emile & Marta Schweikert Professorship from 2014 to 2018, the Gradipore Chair in Chemistry from 2018 to 2022, and the inaugural holder of the Harry E. Bovay, Jr. Endowed Chair in Chemistry since 2022 at Texas A&M University. The focus of his research is to invent novel chemical biology techniques to study posttranslational modifications of chromatin and build generally applied platforms for the identification of therapeutics for cancer and infectious diseases. His drug discovery research focuses on unnatural phage display-based drug discovery and the development of small molecules and PROTACs as therapeutics. Dr. Liu has received multiple awards, including an NSF CAREER Award, Biomatrick Distinguished Professor Award, and several internal awards from Texas A&M University.

## Abstract:

In humans, four YEATS domain-containing proteins (ENL, AF9, YEATS2, and YEATS4) bind to histone lysine acetylation in chromatin to take part in transcription elongation and chromatin remodeling. Dysregulation of YEATS proteins has been linked to the onset and progression of various cancers. In mixed-lineage leukemia rearranged leukemias (MLL-r leukemias), a common mechanism is mediated by AF9/ENL either through their reader function or MLL fusions, suggesting a putative therapeutic potential of their inhibition. To selectively engage the lysine acetylation binding site of YEATS for mechanistic inhibition, we used three different approaches for the development of candidate therapeutics, including small molecules, peptides, and proteasome-targeting chimeras (PROTACs). Some of our developed molecules show very high potency and effectively inhibit acute myeloid leukemia progression in an animal model.

# THE ROBERT A. MAGARIAN OUTSTANDING PODIUM PRESENTATION AWARD

Dr. Robert A. Magarian, professor emeritus of medicinal chemistry and vice chair of the Department of Medicinal Chemistry and Pharmaceutics, College of Pharmacy, University of Oklahoma Health Sciences Center, Oklahoma City, OK, retired on June 30, 1996, after 26 years. He had been a professor of medicinal chemistry at the University of Oklahoma since 1978, having served as associate professor from 1970. Prior to joining the faculty at Oklahoma, he was an assistant professor of medicinal chemistry at the St. Louis College of Pharmacy from 1967 to 1970. He was a National Institutes of Health Postdoctoral Fellow under Dr. Edward Smissman in the Department of Medicinal Chemistry, University of Kansas, Lawrence, Kansas, from 1966 to 1967.

Dr. Magarian attended the University of Mississippi, where he earned a B.A. degree in Chemistry and Biology (1956); B.S. in Pharmacy (with highest honors, January 1960; and a Ph.D. in Medicinal Chemistry (August 1966). While an undergraduate in the University of Mississippi School of Pharmacy, he was initiated as a member of the Rho Chi National Honor Society (1959); was the recipient of the Rexall Trophy Award (1959); and in 1960 he received three awards: The Merck Award, the Lehn and Fink Gold Medal Award, and Taylor Medal---the highest honor awarded by the University of Mississippi. He practiced as a pharmacist in Illinois from January 1960 to August 1961.

Dr. Magarian's research was directed at finding pure (non-estrogen) estrogen antagonists, which were effective in treating different breast cancers (hormonal and non-hormonal dependent tumors) in both pre- and postmenopausal females. His approach to investigating pure antiestrogens was multidisciplinary, involving: (1) the design and synthesis of new organic compounds; (2) the pharmacological testing of each compound; (3) testing the compounds in tissue culture assays involving breast cancer cells; (4) the use of single crystal x-ray analysis of each molecule to study its structure; and (5) molecular modeling to assist in the design of new agents.

During his career, Dr. Magarian published many articles, abstracts, review articles, and book chapters in the breast cancer area. He has ten U.S. patents on antiestrogenic and antitumor agents (di- and

triarylcyclopropyl analogs) synthesized and tested in his laboratory by graduate students and postdoctoral fellows. Some of his key publications involve: "Synthesis and Biological Evaluation of a series of Pure Cyclopropyl Antiestrogens," *J. Med. Chem.*; "Influence of Novel Tirarylcyclopropyl Analogues on Human Breast Cancer Cells in Culture," *Anti-Cancer*

*Drugs*; *Anticancer research*; *Breast Cancer & Treatment*; "Synthesis and Enantiomeric Separation of an Antitumor Agent," *Anti-Cancer Drug Design*; *Bioorganic Chemistry*; *Bioorganic and Medicinal Chemistry*; "Molecular Structures and Conformational Studies of Triarlycyclopropyl and related Non-

Steroidal Antiestrogens," *Acta. Cryst*; *J. Med. Chem.*; "The Medicinal Chemistry of Nonsteroidal Antiestrogens: A Review," *Current Medicinal Chemistry*.

Dr. Magarian is listed in Who's Who in America; Who's Who in the Southwest; American Men and Women of Science, Chemistry; The International Who's Who of Intellectuals (Cambridge, England); and Men of Achievement (Cambridge, England). He was an Associate Editor of the international journal, *Current Medicinal Chemistry*. His research was supported by Mead Johnson, National Science Foundation, National Institutes of Health (National Cancer Institute), and the Presbyterian Health Foundation. During his teaching career, Dr. Magarian received numerous teaching awards: the Baldwin Study-Travel Award in 1978 from the University of Oklahoma for teaching excellence, which allowed him to travel to England where he presented two papers at an international chemistry meeting held at Oxford University; the Associated Distinguished Lectureship Award from the University of Oklahoma in 1988; in 1985 the Rho Chi Society's Excellence in Teaching and Research Award; and in 1996, the Rho Chi Society Recognition Award for "Promoting Scholastic Excellence and Imparting Knowledge in Creative and Helpful Ways."

Dr. Magarian is a member of the American Chemical Society, American Association of College of Pharmacy, Sigma Xi, Phi Kappa Phi, Golden Key National Honor Society, and the Kappa Psi Pharmaceutical Fraternity. Dr. Magarian became the Executive Director of The Kappa Psi Pharmaceutical Fraternity, Inc. in January 1980, occupying that position in The Kappa Psi Central Office, College of Pharmacy, University of Oklahoma HSC until June 30, 2000.

Dr. Magarian has been writing fiction since his retirement and has published two medical thrillers: *The Watchman* and *72 Hours,* and a detective thriller titled *You'll Never See Me Again, A Crime to Remember*. He is working on his fourth novel, a detective thriller in which he is bringing back his lead detective, Noah McGraw, and his partner, Holly Roark. For additional information, please visit his website: www.robertamagarian.com.

* * *

MALTO Medicinal Chemistry, OK Inc., became a not-for-profit organization in 1982 with Dr. Magarian as its president.

# PAST RECIPIENTS OF THE ROBERT A MAGARIAN OUTSTANDING STUDENT PODIUM PRESENTATION AWARD

**1999: Robert H. Cichewicz**, "Dimerization of Resveratrol by the Grapevine Pathogen Botrytis cinerea," University of Louisiana at Monroe, Monroe, LA. **Advisor: Dr. Samir A. Kouzi.**

**2000: Valeria N. Rubin**, "Preparation and Selective Estrogen-Like Bone Protective and Cholesterol-Lowering Effect of Hydroxytriarylethylenes Bearing Acidic Side Chains," University of Georgia. **Advisor: Dr. Peter C. Ruenitz**

**2001: Theresa L. Johnson**, "Inhibition of Lactate Dehydrogenase C: The Design Synthesis, and Testing of Ligands as an Approach to Male Contraception," University of Mississippi, **Advisor: Dr. Mitchell A. Avery**

**2002: Kris Virga**, "Structure-Based Design and Synthesis of Pantothenate Kinase Inhibitors," University of Tennessee, **Advisor: Dr. Richard E. Lee**

**2003: Lindsay Odom**, "Alkylation and Cyclization Reactions of Diazoketones: Synthesis of Substituted Azetidines," University of Mississippi, **Advisor: Dr. John M. Rimoldi**

**2004: Kerim Babaolu**, "Crystal Structure of Dihydropteroate Synthase from Bacillus anthracis: Studies into Mechanism and Starting Point for Novel Inhibitor Design," University of Tennessee Health Science Center, **Advisor: Dr. Richard E. Lee**.

**2005: Nakul Telang**, "Design, Synthesis and Biological Evaluation of Isoflavones as Antigiardial Agents," University of Mississippi, **Advisor: Dr. Mitchell Avery.**

**2006: Tarek Mahfouz**, "Computer-aided Inhibitor Discovery of the Botulinum Neurotoxin Serotype A," University of Houston, **Advisor: Dr. James M. Briggs**.

**2007: Kirk Hevener**, "Structure-Guided Virtual Screening Against Dihydropteroate Synthase Utilizing Pharmacophore Filtering and Fragment-based Constraints," University of Tennessee Health Science Center, **Advisor: Dr. Richard E. Lee.**

**2008: Yatan Shukla**, "Novel Pregnane Glycosides from *Hoodia gordonii*," University of Mississippi, **Advisor: Dr. Ikhlas A. Khan.**

**2009: Amir E. Wahba,** "Zinc Mediated Reductive *N*-Alkylation and Amidation of Nitro Arenes with an Application to natural Products," University of Mississippi, **Advisor: Dr. Mark T. Hamann.**

**2010: Sarah Chijkowski**, "The Reaction of the Sesquiterpene Lactone Repin with Various Amine Nucleophiles," University of Mississippi, **Advisor: John M. Rimoldi.**

**2011: Amanda Waters**, "Methodologies for the Structural Assignment of Karlotoxin Polyketides in High-Throughput using Overlaid 2D NMR Techniques," University of Mississippi, **Advisor: Mark T. Hamann.**

**2012: Fathy Behery**, "Tocotrienol Elecrophilic Substitution Products as Breast Cancer Proliferation and Migratio Inhibitory Leads," University of Louisiana, Monroe, **Advisor, Khalid El Sayed.**

**2103: Min Xiao**, "Discovery of 4-Aryl-2-benzoyl-imidazoles as Tubulin Polymerization Inhibitor with Potent Antiproliferative Properties," University of Tennessee, **Advisor: Wei Li.**

**2014: Eric Bow**, "Novel Benzofuran and Benzopyran Scaffolds Targeting the Cannabinoid Receptors," University of Mississippi, University of Mississippi, **Advisor: John M. Rimoldi.**

**2015: Chalada Suebsuwong,** "Structure-Based Design of Potent and Selective DLG-OUT RIPK1 Inhibitors," University of Houston, **Advisor: Greg Cuny.**

**2016: Quinghui Wang**, "Structural Optimization of ABI-231 Targeting the Colchicine Site in Tubulin for Advanced Melanoma," University of Tennessee, **Advisor: Wei Li.**

**2017**: ***Songtao Lin***, "Investigation of 20S(OH)D3 Analogs as Potent VDR Agonists and Anti-Inflammatory Agents," University of Tennessee, ***Advisor: Wei Li.***

**2018**: ***Kinsie Arnst,*** "Targets the colchesine biding site on Tubulin and Overcomes Taxane Resistance" University of Tennessee, ***Advisor: Wei Li.***

**2019**: ***Sahar Alahamdi***, Anti-inflammatroy Effect of Selective CB2 inverse Agonists in Murine and Human Microglial Cells", University of Tennessee, ***Advisor: Bob M. Moore II.***

**2022**: ***Haowen Zhang***, "Optimization and Biological Validation of a Vimentin Binding Peptoid Antagonist in Non-Small Cell Lung Cancer stem Cells", University of Houston, ***Advisor: Gomika Udugamassoriya.***

**2023**: ***Kelli Hartman***, "Novel Tubulin Inhibitors Overcome Paclitaxel Resistant Prostate Cancer and Cross the Blood Brain Barrier to Treat Breast Cancer Brain Metastasis", University of Tennessee Health Science Center, ***Advisor: We Li.***

**2024**: ***Ashton Coker***, "Synthesis and Structure-Activity Relationship Based Design of Human Pantothenate Kinase Inhibitors", St. Jude Children's Research Hospital, ***Advisor: Richard Lee.***

# THE THOMAS L. LEMKE OUTSTANDING POSTER PRESENTATION AWARD

Tomas L. Lemke is Professor of Medicinal Chemistry and Associate Dean at the College of Pharmacy at the University of Houston. He received his B.S. in Pharmacy from the University of Wisconsin (1962) and went on to complete his Ph.D. in Medicinal Chemistry under Dr. Edward E. Smissman in 1966. Dr. Lemke went on to work as a Research Scientist for Upjohn from 1966 to 1970, at which time he joined the faculty at the University of Houston as Assistant Professor of Medicinal Chemistry, was promoted through the ranks, receiving tenure in 1975, then Full Professor in 1984. In 1984, he was honored to spend two years as Visiting Professor at the Institut De Chimie, Université Louis Pasteur, De Strasbourg, in Strasbourg, France, where he worked in the Laboratory of Jean-Marie Lehn, who went on to receive the Nobel Prize in Chemistry.

Dr. Lemke is also a noted author of several well-known books, one being “Review of Organic Functional Groups, Introduction to Medicinal Chemistry,” and he is one of the editors of the textbook “Foye’s Principles of Medicinal Chemistry.”

Most noteworthy of Dr. Lemke’s contributions is the fact that he was one of the founding organizers of our MALTO organization. He, along with Nelson Voldeng, who we also honor every year with the Nelson Voldeng Memorial Lecture, had the vision and, with a lot of hard work, made it happen.

It is therefore very fitting that we, the MALTO community of scholars (faculty and students), show our great appreciation to Dr. Thomas Lemke for a job well done by naming this award in his honor.

# PAST RECIPIENTS OF THE THOMAS L. LEMKE OUTSTANDING STUDENT POSTER PRESENTATION AWARD

**2003: Srinivasan P. Venkatachalan**, "Effect of Urethane on the $5HT3_A$ and $5HT3_{AB}$ Receptor," University of Lousiana, Monroe, **Advisor: Dr. Marvin K Schulte.**

**2005: Wayun Sheng**, "3D High-resolution NMR Characterizatin of Recombiant CB2 Membrane Protein Fragment," University of Houston, **Advisor: Dr. Xiang-Qun (Sean) Xie.**

**2006: Lukasz Kutrzeba**, "In-vitro Studies on Metabolism of Salvinorin A," University of Mississippi, **Advisor: Dr. Jordan K. Zjawiony**.

**2007: Prasanna Sivaprakasam**, "Computational Insights into PfDHFR-TS: Application of 2D,3D-QSAR and Docking Studies to Cycloguanil Derivatives," University of Mississippi, **Advisor: Dr. Robert J Doerksen**.

**2008: Sanju Narayanan**, "Discovery of Highly Selective $\sigma_2$ Antagonist as Anti-cocaine Agent," **Advisor: Dr. Christopher R. McCurdy.**

**2009: Lacey D. Gamblin**, "Synthesis of Thiourea Analogues as Potential Somatostatin Receptor Subtype 4 Agonists" Southern Illinois University, Edwardsville, **Advisor: Dr. A. Michael Crider.**

**2010: Swapnil Kulkarni**, "Studies Towards Total Synthesis of Pseudolaric Acid B," University of Mississippi, **Advisor: Mitchel A. Avery.**

**2011: Horrick Sharma**, "Synthesis, Docking and Biological Studies of Phenanthrene β-Diketo Acids as Novel HIV-1 Integrase Inhibitors," University of Tennessee, **Advisor: John K. Buolamwini.**

**2012: Amanda L. Waters**, "Isolation and Structure Determination of Antifungal Lactone Lipids and Other Secondary Metabolites From Sooty Mold, *Scorias Spongiosa*," University of Mississippi, **Advisor: Mark Hamann.**

**2013: "**An Approach to identifying Potent and Selective DXG-OUT RIP1 Kinase Inhibitors," University of Houston, **Advisor: Gregory D. Cuny**

**2014: Manal A. Nael**, "Targeting Protein Kinase RNA-like Endoplasmic Reticulum Kinase to Manage Alzheimer's Disease," University of Mississippi, **Advisor: Robert J. Doerksen.**

**2015: Jai Shankar K. Yadlapalli,** "Pharmacology, Pharmacokinetics, and Therapeutic Implications of Morphine-6-*O*-Sulfate Sodium in Diabetic Neuropathy," University of Arkansas, **Advisor: Peter A. Crooks.**

**2016: Abu Bakar Siddique**, "Extra-Virgin Olive Oil Based Oleocanthal: A Promising Lead for the Control of C-MET-Dependent Brest Malignancies," Univesity of Louisiana, **Advisor: Khalid El Sayed.**

**2017: Sri Sujana Immadi**, "Application of Hemetsberger-Knittel Reaction in the Synthesis of Indole/Azaindole-2-carboxamides for Development of Allosteric Modulators of Cannabinoid CB1 Receptor, Texas A & M University, **Advisor: Dai Lu.**

**2018**: ***Vikas Mishra***, "Selective CB2 Receptors Agonists as Dual Suppressors for Pain and Cancer Growth" Texas A & M University, ***Advisor: Dai Lu***.

**2019**: ***Achyut Dahal***, "Characterization of HER-2-Targeted Modified Peptidomimetic" University of Louisiana, ***Advisor: Seetharama Jois.***

**2022**: ***Imdadul Khan***, "Discovery of 5α-pregnan-2β,3α-diol-20-one as a NeuroHIVProtective Agent", ***Advisor: Hoang Le***.

**2023**: ***Baharul Islam***, "Discovery of a one-pot method to synthesis α,α-difluoro-β-amino ketones from α-amidosulfones and dilfuoroenolates, University of Mississippi", ***Advisor: David A. Colby.***

**2024**: ***Mostafa Ali Eldeen***, "Chemoenzymatic Synthesis of Glycosylated And Sulfated N-Terminal Pepetides of CCR5", University of Mississippi, ***Advisor: Joshwa Zhu.***

# THE RONALD F. BORNE OUTSTANDING POSTDOCTORAL POSTER PRESENTATION AWARD

Dr. Ronald F. Borne, professor emeritus of medicinal chemistry at the University of Mississippi, School of Pharmacy, retired on June 30, 2006, after 38 years of service to the University. A native of New Orleans, LA, he earned the B.S. degree in chemistry from Loyola University of the South, the M.S. degree in organic chemistry from Tulane University, and the Ph.D. in medicinal chemistry from the University of Kansas (under the tutelage of Professor Matt Mertes). Early in his career, he was employed as a chemist at the Ochsner Research Medical Foundation and as a research chemist at the C. J. Patterson Co. in Kansas City, KS. After earning his doctorate degree he joined Mallinckrodt Chemical Works in St. Louis, MO as a research chemist.

In 1968, he joined the faculty at the University of Mississippi as an assistant professor of medicinal chemistry and began a career of teaching, research, and administration. He was promoted to the rank of associate professor in 1970 and to full professor in 1973. He received the Outstanding Teaching Award for the University in 1972 and the School of Pharmacy Outstanding Teacher Award on six occasions (1982, 1983, 1989, 1993, 1997 and 1988). He was named the State of Mississippi Professor of the Year in 1992 by the National Council for the Advancement and Support of Education. In 1994 Dr. Borne received the Burlington Northern Faculty Achievement Award from the University of Mississippi and the National Rho Chi
Lecture Award. In 1996 he received the Distinguished Pharmacy Educator Award from the American Association of Colleges of Pharmacy.

Dr. Borne's research career and interests primarily involved efforts to elucidate the importance of conformational factors in the actions of agents affecting the central and peripheral nervous systems. In particular: analgetics, anti-arthritics, dopaminergics, cholinergics and adrenergics received considerable attention. Other recent interests included synthesis of novel pharmacotherapeutic agents for the treatment of dependence on cocaine and other substances of abuse as well as the synthesis of new antimalarial agents. In 1988-89 he was awarded an N.I.H. Senior International Fellowship to conduct research in the Department of Pharmacology at the University of Edinburgh Medical School in Edinburgh, Scotland. His

research involved the synthesis of radioligands selective for serotonin 5-HTlA receptors as diagnostic tools for Alzheimer's disease, and the synthesis of analogues of the excitatory amino acids, glutamate and aspartate, to study the etiology of senile dementia disorders. Because of the interdisciplinary nature of his research program, Dr. Borne established collaborative relationships with other researchers and has published with a faculty or staff member in every other department or division in the School of Pharmacy (pharmacology, pharmacognosy, pharmaceutics, pharmacy administration, clinical pharmacy, RIPS, NCNPR, continuing education), including the Pharmacy Library. He has received federal research funding from NIH, NSF, the Department of Education, NASA, the Department of Commerce, CDC and the Department of Defense as well as several industrial research companies. Dr. Borne has published approximately 100 research, drug abuse education and professional publications and book chapters covering a span of six decades and was granted four U.S. patents.

Dr. Borne held several administrative positions in the School of Pharmacy and the University. He served as Chairman of the Department of Medicinal Chemistry (1979-88), Associate Vice Chancellor for Research and Dean of the Graduate School (1985-86), and as Associate Vice Chancellor for Research (1998-2001). In the latter position he was responsible for coordinating all research activities on campus with numerous state and national agencies and coordinated all university-related research activities with the Mississippi Congressional delegations. During this period, extramural funding (external grants and contracts) on the Oxford campus increased from $18.6 million in FY96-97 to $73.6 million in FY00-01. He also established the Laboratory for Applied Drug Design and Synthesis (LADDS) in the Department of Medicinal Chemistry. When he returned to full time teaching and research in 2001 the University established an endowment to establish the Ronald F. Borne Endowed Chair of Medicinal Chemistry. Dr. Borne was also heavily committed to community service through his appointment as Chairman of the City of Oxford Park Commission Board. During this period (1978-1980) the city experienced its greatest growth in park and recreational facilities as exemplified by the construction of a $275,000 Community Activity Center and a $300,000 public swimming pool, the city's first community pool. He was subsequently appointed to serve on the School Board for the City of Oxford Public School System (being the first member of the University Community to be appointed to that Board) and served as a member and as Vice-Chair from 1980-1983. He is a medicinal chemist by education and a writer by avocation. He has written poetry, a play, and has several non-scientific articles and short stories published in the *Ole Miss Review*, *Mississippi Magazine*, and the *Ole Miss Spirit*. He has also written or edited several books, including *The Great College Coaches Cookbook* (Stanley-Clark Publishing Co., 1988) and *Beginnings and Ends* (Nautilus Publishing Co., 2012). His biography of Mississippian Hugh Clegg, *TROUTMOUTH: The two careers of Hugh Clegg*, was published by the University Press of Mississippi in 2015. Dr. Borne passed away unexpectedly on October 18, 2016, while working on a history book, *1936 – A Pivotal Year in American and World History: The Confluence of Sports and Politics*. His insight and contributions to MALTO will be sorely missed.

# PAST RECIPIENTS OF THE RONALD F. BORNE OUTSTANDING POSTDOCTORAL POSTER PRESENTATION AWARD

**2015: Pallavi Rajaputra, "**Far Red Light-Activatable Prodrugs of a Photosensitizer and Anti-Cancer Drug for Effective Tumor Ablation Using Photodynamic Therapy", University of Oklahoma, **Advisor: Youngjae You.**

**2016: Staya Prakash Shukla**, "Homo- and Hetero-Multimerizations of Peptoids to Target Cancer," University of Houston, **Advisor: Gomika Udugamasooriya.**

**2017**: **Moses Bio**, "Targeted Far-Red Light Activatable Prodrugs: Folate Receptor-Targeting, Optical Imaging, and a Combination of Photodynamic Therapy and Site-Specific Chemotherapy", University of Oklahoma, **Advisor: Youngjae You**.

**2018**: **Pankaj Pandey**, "Identification of Potent Natural Product Chemotypes as Cannabinoid Receptor 1 Inverse Agonists Using Protein Structure-Based Virtual Screening", University of Mississippi, **Advisor, Robert J. Doerkse**.

**2019**: **Sampad Jana**, "Use of α-Fluoronitroalkenes as a Synthetic Equivalent for FluoroAlkynes in Cycloaddition Reaction with Organic Azides", University of Mississippi, **Advisor, Sudeshna Roy.**

**2022**: **Vijay Boda**, "Discovery of Selective TRPC3 Antagonists for the Treatment of Neurodegenerative Disease", **Advisor, Wei Li**.

**2023**: **Ishaq Khan**, "Implications for Clinical Translation: Discovery of Novel VEGFR2 Inhibitor to Potentiate Sorafenib's Antiangiogenic Effects on Hepatocellular Carcinoma", Texas A&M University, **Advisor: Hamed I. Ali**.

**2024**: **Vijay Boda**, "Small Molecules Conjugates with Selective estrogen Receptor bAgonism Promote Anti-Aging Benefits in metabolism and skin Recovery", University of Tennessee, **Advisor, Wei Li**.

# MEETING SCHEDULE

## Wednesday, May 21, 2025

At TAMU Innovative Learning Classroom Building (ILCB)-Room 207

(Address: 215 Lamar St, College Station, TX 77844)

4:00 pm **Registration**

4:30-6:00 pm **Reception Mixer and Poster setup**

## Thursday, May 22, 2025

At TAMU Innovative Learning Classroom Building (ILCB)-Room 207

(Address: 215 Lamar St, College Station, TX 77844)

7.30-8.30 am **Breakfast**

8:30-9.00 am **Welcoming Remarks:** Dr. Mansoor Khan
*Interim Dean of Rangel College of Pharmacy, Texas A&M University*
*Regents & Distinguished Professor of Pharmaceutical Sciences*

**MALTO Introduction:** Dr. John Rimoldi / Dr. Dai Lu

9.00-10.00 am **PODIUM SESSION 1 (O1-O3)**

9.00-9.20 am **O1. COMPUTER-AIDED REPOSITIONING OF KINASE INHIBITORS TO COMBAT ANTIBACTERIAL RESISTANCE**
Eneye D. Ajayi, Mostafa M.A. Aref, Md Emran Hossain, Rokaia Abdulla, Ling Yang, Yinan Wei, Hamed I. Ali*

9.20-9.40 am **O2. DEVELOPMENT OF POTENT COLCHICINE BINDING SITE INHIBITORS FOR THE TREATMENT OF TAXOL-RESISTANT METASTATIC MELANOMA**
Christopher Clark[1,3], Shelby Waddell[4], Carl Womack[2], Meirola Endraws[2], Cole Huddleston[2], Joshua Thammathong[1], Kamil Tanas[1], Beari Jangir[1], Keiluhn Pulis[2], Yang Xie[4], Kevin Bicker[1,3], April Weissmiller[*2,3], Wei Li[*4], and Souvik Banerjee[*1,3]

9.40-10.00 am **O3. PANTOTHENATE KINASE INHIBITORS FOR CANCER**
Ashton Coker[1], Thilina Jayasinghe[1], Chitra Subramanian[2], Rajendra Tangallapally[1], Karen Miller[2], and Richard Lee*[1]

10:00-10:30 am **Coffee break**

Conference site, posters available for viewing only

| | |
|---|---|
| 10:30-11:30 am | 36th Annual A. Nelson Voldeng Memorial Lecture<br>**Keynote Speech: Dr. Kevin Dalby**<br>*Professor of Chemical Biology & Medicinal Chemistry, The University of Texas at Austin* |
| 11:30-12:10 pm | **PODIUM SESSION 2 (O4-O5)** |
| 11:30-11.50 am | **O4. A TRIMERIC PEPTOID THAT SELECTIVELY TARGETS SURFACE PLECTIN IN NON-SMALL-CELL LUNG CANCER STEM CELLS**<br>Charles Owusu Ansah[1], Gomika Udugamasooriya[*,1,2] |
| 11:50-12.10 pm | **O5. ELUCIDATING THE MOLECULAR MECHANISMS OF GATING REGULATION OF N-GLYCOSYLATION ON VOLTAGE-GATED SODIUM CHANNELS**<br>Eslam Elhanafy and Jing Li* |
| 12:10-1:00 pm | **Lunch:** 2nd floor ILCB building, near Room 207 |
| 1:00-3:00 pm | **POSTER SESSION (P1-P19)**<br>**Coffee Break** *(Concurrent with Poster Session)* |
| 3.00-4.00 pm | **AGGIE Lecture:**<br>**Keynote Speech: Dr. Wenshe Liu**<br>*Harry E. Bovay, Jr. Endowed Chair and Professor in Chemistry, Texas A&M University* |
| 4.00-5.00 pm | **PODIUM SESSION 3 (O6-O8)** |
| 4.00-4.20 pm | **O6. PAN-K-RAS INHIBITION VIA 3-DIMENSIONAL (3D) PEPTOIDS FOR LUNG CANCER THERAPY**<br>Eunsun Park[1], Satya Prakash Shukla[1], and D. Gomika Udugamasooriya[*1,2] |
| 4.20-4.40 pm | **O7. DISCOVERY OF BRD9 PEPTIDE INHIBITORS USING A GENETICALLY ENCODED PHAGE DISPLAY SYSTEM**<br>Gopal K. Dubey and Wenshe Ray Liu* |
| 4.40-5.00 pm | **O8. UNEXPECTED PRODUCTS FROM THE SYNTHESIS OF FLUORINATED GLYCOMIMETICS**<br>Dan Mi Huynh[1], Maali D. Alshammari[1], Frank R. Fronczek[2], and David A. Colby[1]* |
| 6:00-8:30 pm | **Dinner & Banquet**:<br>*At Napa Flats Wood-Fired Kitchen: 1727 Texas Ave S, College Station.* |

## Friday, May 23, 2025

At TAMU Innovative Learning Classroom Building (ILCB)-Room 207

(Address: 215 Lamar St, College Station, TX 77844)

7.30-8.30 am **Breakfast**

8:30-9.30 am **PODIUM SESSION 4 (O9-O11)**

8:30-8.50 am **O9. DISCOVERY OF POTENT AND ORALLY BIOAVAILABLE SERCA2 ACTIVATORS FOR THE TREATMENT OF ISCHEMIC STROKE-RELATED BRAIN DAMAGE**
Mir Shahriar Kamal[1], Hao Chen[1], Abdul Majid[2], Djamel Lebeche*[2], Wei Li*[1]

8.50-9.10 am **O10. SYNTHESIS OF NOVEL FLORFENICOL AMINE ANALOGS THAT HIJACK AN INTERNAL RESISTANCE MECHANISM IN MYCOBACTERIUM ABSCESSUS**
Alexander R. Jenner[1,2], Gregory A. Phelps[1,3], Sinem Kurt[4], Shelby M. Anderson[1], Gabriel Papp[1], Robin B. Lee[1], Lucas Boeck[5,6], Bernd Meibohm[7], Andres Obregon-Henao[8], Peter Sander[3,9],
Richard E. Lee[1]

9.10-9.30 am **O11. SB-216, A NEW GENERATION OF TUBULIN INHIBITOR OVERCOMES OSIMERTINIB AND PACLITAXEL RESISTANCE IN DRUG-RESISTANT NON-SMALL-CELL LUNG CANCER**
Sara Sultana[1], Yang Xie, Satyanarayana Pochampally, Duane D. Miller, and Wei Li*

9.30-10.00 am **Coffee break**

2nd floor ILCB building, near Room 207

10:00-11:20 am **PODIUM SESSION 5 (O12-O15)**

10.00-10.20 am **O12. SYNTHESIS OF HEXAFLUOROISOPROPANOLS AS BUILDING BLOCKS FOR FLUORINE-TAGGED MOLECULES**
Meshal A. Alghamdi and David A. Colby*

10.20-10.40 am **O13. BENCH STABLE BORYLTHIANTHRENIUM DICATION ENABLES AZIRIDINYL BORONATE SYNTHESIS VIA METAL-FREE LATE-STAGE AZIRIDINATION**
Veerabhadra R. Vulupala,[1] Disni Gunasekera,[1] Nagarjun R. Mallampudi,[1] Ramy Yousef,[1] Yusif Gyasi,[1] Ramidi Gopal Reddy,[1] and Shiqing Xu[1,2*]

10.40-11.00 am **O14. MECHANISTIC INSIGHTS INTO DISEASE-ASSOCIATED MUTATIONS DISRUPTING FAST INACTIVATION IN VOLTAGE-GATED SODIUM CHANNELS**
Shiva Akhlaghi, Jing Li*

11.00-11.20 am **O15. EVALUATION OF U2AF HOMOLOGY MOTIF (UHM) SPLICING FACTOR INHIBITORS AS A SPLICEOSOME-TARGETED THERAPY IN HEMATOLOGIC MALIGNANCIES**
Amol D. Patil#, Mona Kazemi Sabzvar#, Xinrui Yuan, Daniel M, Collier, and Chao-Yie Yang*

11:20-12:30 pm **Lunch:**

2nd floor ILCB building, near Room 207 – (*Pick up your lunch box)*

12:30-1:30 pm **MALTO Business Meeting:** *Conference room 224. (MALTO Faculty Only)*

12.30-1.30 pm **MALTO Awards Ceremony & Closing Remarks**
- *2025 Robert A. Magarian Podium Presentation Award*
- *2025 Thomas L. Lemke Poster Presentation Award*
- *2025 Ronald F. Borne Postdoctoral Poster Presentation Award*

1.30 pm **Adjourn**

# MALTO 2025 Poster Presentations (P01-P18)

## Thursday, May 22, 2025: 1:00-3:00 pm

### Graduate Students and Postdoctoral Fellow Posters (P1-P18)

**P01** **OPTIMIZATION OF BUCHWALD AMINATION REACTION TO SYNTHESIZE $CB_1$ RECEPTOR ALLOSTERIC LIGANDS FOR NOVEL NON-OPIOID ANALGESICS**

Rajpal Vangala, Zhixing Wu, Pedro Ochoa IV, Priscilla Gracia, Christabel Igwe, Vivian Rios, and Dai Lu*

**P02** **STRUCTURE-GUIDED OPTIMIZATION OF KINASE INHIBITORS FOR ENHANCED BRAIN PENETRATION IN THE TREATMENT OF CNS CANCERS**

Md Emran Hossain, Mostafa M.A Aref, Rokaia Abdulla, Eneye D. Ajayi, Hamed I. Ali*

**P03** **STRUCTURE-BASED DESIGN OF NOVEL COX-2 INHIBITORS THAT UNDERGO ENTEROHEPATIC RECYCLING FOR ENHANCED COLON DISTRIBUTION**

Pooja Atpadkar, Anantha L. Duddupudi, Rashim Singh, Ming Hu, and Gregory D. Cuny

**P04** **DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION OF DUAL-TARGETING TUBULIN/HDAC INHIBITORS AS POTENTIAL ANTICANCER AGENTS**

Zisong Qi,[#] Shelby Waddell,[#] Yang Xie, Hao Chen, Duane D. Miller, and Wei Li*

**P05** **DISCOVERY OF A POTENT c-ABL KINASE INHIBITOR WITH THERAPEUTIC POTENTIAL AGAINST NEUROBLASTOMA**

Zhixing Wu[1], Yang Yu[2], Jianhua Yang[2], Dai Lu*[1]

**P06** **OVERCOMING THE BLOOD-BRAIN BARRIER IN LEUKEMIA THERAPY: DESIGN OF SELECTIVE FLT3 INHIBITORS USING ISOXAZOLINE CHEMISTRY**

Rokaia S. Abdullah, Md Emran Hossain Eneye D. Ajayi, Mostafa M.A. Aref, Hamed I. Ali*

**P07** **STRUCTURE-ACTIVITY RELATIONSHIP AND BINDING MODE ANALYSIS OF A NEW CLASS OF RECEPTOR-INTERACTING PROTEIN KINASE 3 INHIBITORS**

Manu Bala[1], Raghavender Boda[1], Anantha L. Duddupudi[1], Ghada Ali[1], Alexei Degterev[2], Siddharth Balachandran[3], and Gregory D Cuny[1]

**P08** **MULTI-KINASE INHIBITION FOR ADVANCED TREATMENT OF RESISTANT BREAST CANCER**

Mostafa M. A. Aref, Md Emran Hossain, Eneye D. Ajayi, Rokaia Abdullah, Hamed I. Ali*

**P09** **EFFECT OF JARDIANCE TABLET SPLITTING ON SPLITABILITY, WEIGHT VARIATION, ASSAY, AND DISSOLUTION**

Andrew S. Tenpas, Tahir Khuroo, Ziyaur Rahman, Mansoor A. Khan

**P10** **USE MAMMALIAN CELL-BASED ENZYMES FOR THE SYNTHESIS OF O-LINKED GLYCOPEPTIDE**

Nana Yang[1], Ousman Boye, Hailiang Joshua Zhu*

**P11** **BINDING OF BRYOSTATIN-1 WITH THE $C_1C_2B$ DOMAINS OF MUNC13-1**

Netra P. Neupane[1], Sunil Lingaraju[1], Soni Kaundal[2], B.V. Prasad[2] and Joydip Das*[1]

**P12** **FACILE ONE-POT SYNTHESIS OF α-BORYL UREAS TO UNCOVER A POTENT MAIN PROTEASE INHIBITOR**

Yusif I. Gyasi,[†, 1] Satyanarayana Nyalata,[†, 1] Sophea Pa,[1] Disni Gunasekera,[1] Veerabhadra R. Vulupala,[1] Nagarjun R. Mallampudi,[1] and Shiqing Xu*[,1,2]

**P13** **UBIQUITIN AZAPEPTIDE ESTERS as NEXT-GENERATION ACTIVITY-BASED PROBES FOR CYSTEINE ENZYMES IN THE UBIQUITIN SIGNAL PATHWAY**

Saibal Chanda[1], Sandeep Atla[2], Satyanarayana Nyalata[2], Xinlei Sheng[3], Yingming Zhao[3] and Wenshe Ray Liu[1,2]

**P14** **SYNTHESIS AND PRELIMINARY EVALUATION OF NOVEL HETEROCYCLIC COMPOUNDS WITH POTENTIAL ANTICANCER ACTIVITY**

Ahmed Ashraf Elsyyad[1], Shiqing Xu[2] and Sameh Abdelwahed[1]

**P15** **BINDING AFFINITY ANALYSIS OF BIOACTIVE COMPOUNDS AS ACETYLCHOLINESTERASE INHIBITORS IN ALZHEIMER 'S DISEASE MANAGEMENT.**

Caleb Joel Nwaogwugwu[1,2], Chukwudoru Chieme Sunday[3], Sameh, Abdelwahed[1]

**P16** **A STRUCTURE-BASED STRATEGY TO COMBAT ANTI-HER2 RESISTANCE IN HER2-POSITIVE BREAST CANCER**

Wafa Masoud[1], Eneye D. Ajayi[2], Radwan Alnajjar[3], Hamed I. Ali[2*]

**P17** **EXPLORING THE POTENTIAL OF SELECTIVE AGONISTS OF CANNABINOID $CB_2$ RECEPTOR IN TREATMENT OF PANCREATIC CANCER AND PAIN**

Zhixing Wu,[1] Vikas Mishra[1] Sujana Sri Immaldi,[1] Caitlin Scott[2], Deborah Kendall[2], Aron Lichtman[3], Maribel González-García[4], Hua Yang[5], Dai Lu[1]

**P18** **TARGETING KRAS-MUTANT AND CHEMORESISTANT METASTATIC COLORECTAL CANCER**

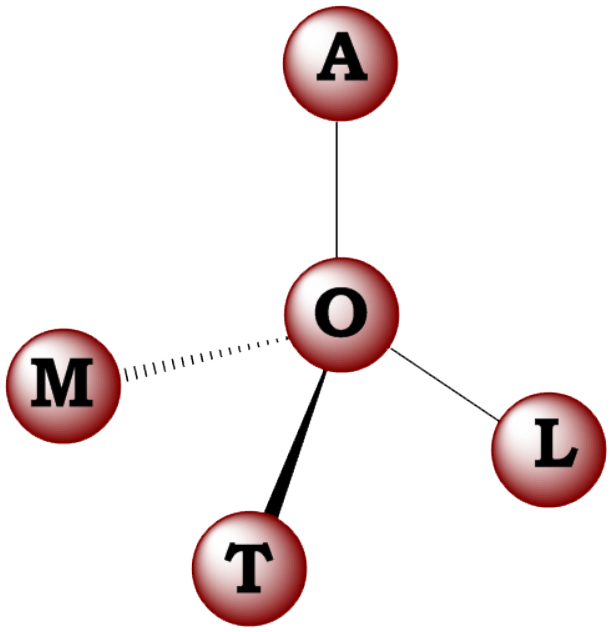
Ashish Tyagi[1], Aniqa Atta[1], Arun K Sharma[2], Chendil Damodaran[1]

**P19** **RATIONAL DESIGN AND SYNTHESIS OF A SELECTIVE 5S-OXA1L INHIBITOR BASED ON SAR FOR TARETED LUNG CANCER TREATMENT**

Wissarut Wijitrmektong[1], Dimosthenis Koinas[1], Junichiro Takaya[2], Haoxin Li[2], Jarret R. Remsberg[2], Verena Albert[2], J.C. Ducom[2], Christopher M. Joslyn[2], Scott C Henderson[2], Kathryn S Spencer[2], Sabrina Barbas[2], Melissa A Dix[2], Kim Masuda[2], Enrique Saez[2], Kenji Sasaki[2], Christopher G. Parker[2], Benjamin F. Cravatt[2], Thomas W. Hanigan[1]

# The 50th Annual MALTO Medicinal Chemistry-Pharmacognosy Meeting-in-Miniature

**May 21-23, 2025**
**Texas A&M University**




# Podium Presentation Abstracts

**(O1- O15)**

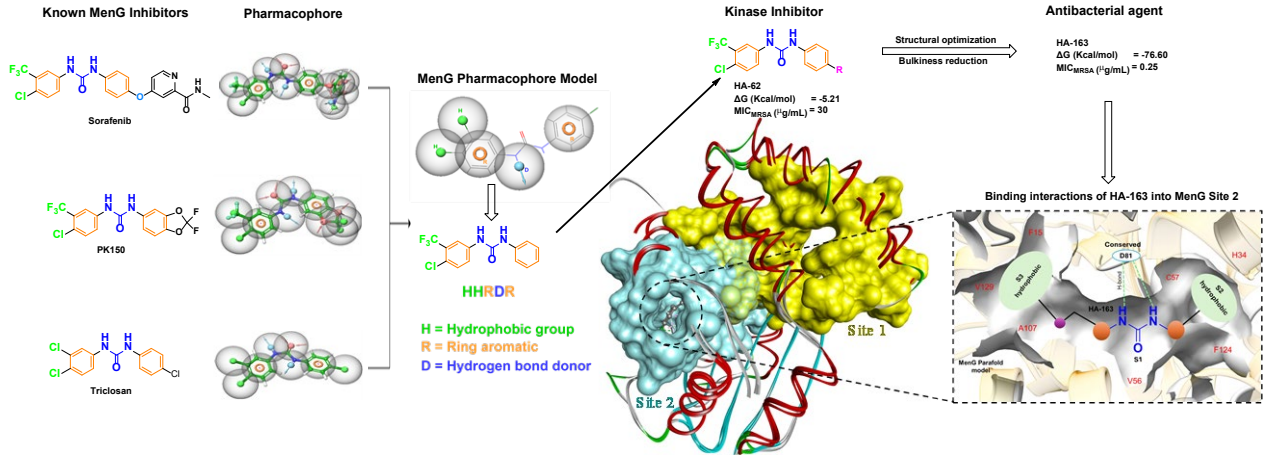
****Accepted for dual (oral + poster) presentations***

## *O1. COMPUTER-AIDED REPOSITIONING OF KINASE INHIBITORS TO COMBAT ANTIBACTERIAL RESISTANCE

**Eneye D. Ajayi, Mostafa M.A. Aref, Md Emran Hossain, Rokaia Abdulla, Ling Yang, Yinan Wei, Hamed I. Ali***

*Department of Pharmaceutical Sciences, Irma Lerma Rangel College of Pharmacy, Texas A&M University, College Station, TX, USA*

Antimicrobial resistance (AMR) is responsible for over 1.2 million deaths annually, potentially exceeding 10 million by 2050. PK150, an antibacterial drug candidate repurposed from sorafenib, inhibits bacterial demethylmenaquinone methyltransferase (MenG), showcasing the antimicrobial potential of kinase inhibitors (KIs). Due to the absence of a crystal structure for MenG, repositioning KIs as MenG-targeting antibacterial agents has been challenging. This study models MenG and analyzes PK150's binding through molecular dynamics (MD) simulations. First, we developed a homology model of MenG and studied the conformational dynamics of both apo and ligand-bound states, revealing critical interactions. Insights from these interactions helped optimize in-house KIs for better binding affinity and antibacterial activity. Notably, we identified a conformational shift in the omega-like loop (residues 106–116) upon ligand binding. Additionally, the diarylurea motif of PK150 forms a crucial hydrogen bond with the conserved D81 residue. Pharmacophoric mapping of known MenG inhibitors indicated that our in-house KI, HA62, contains the essential moieties for binding to MenG. As a result, we simplified the structure to develop HA163. Initial single-strain screening of the optimized compound, HA163, against *methicillin-resistant Staphylococcus aureus* (MRSA) showed a minimum inhibitory concentration (MIC) of 0.25 µg/mL, representing a 100-fold improvement over the parent KI. Further screening against multidrug-resistant strains revealed that HA163 demonstrated potent activity against several strains of *vancomycin-resistant Enterococcus* (VRE), with an MIC of 0.25–0.5 µg/mL, which is about 250 to 500 times more potent than levofloxacin. *In vitro* toxicity assays indicated minimal cytotoxicity of HA163 against normal human cells, suggesting strong bacterial selectivity. This study advances MenG-targeted rational drug design, providing a potential strategy to combat AMR.



## O2. DEVELOPMENT OF POTENT COLCHICINE BINDING SITE INHIBITORS FOR THE TREATMENT OF TAXOL-RESISTANT METASTATIC MELANOMA

**Christopher Clark[1,3], Shelby Waddell[4], Carl Womack[2], Meirola Endraws[2], Cole Huddleston[2], Joshua Thammathong[1], Kamil Tanas[1], Beari Jangir[1], Keiluhn Pulis[2], Yang Xie[4], Kevin Bicker[1,3], April Weissmiller[*2,3], Wei Li[*4], and Souvik Banerjee[*1,3]**

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*[2]Department of Biology, Middle Tennessee State University, Murfreesboro, TN, 37132.*
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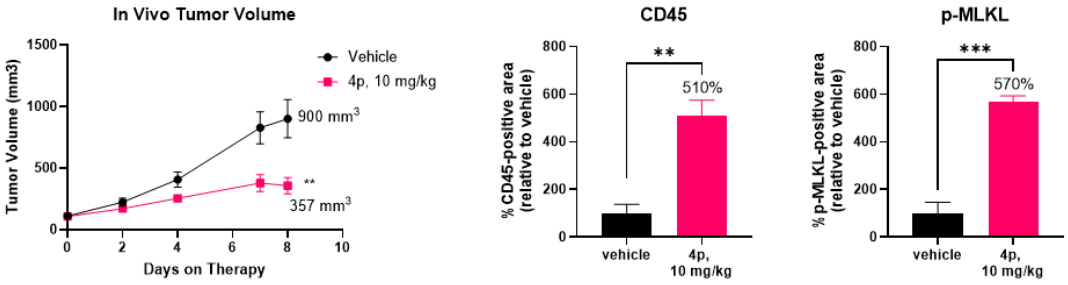
*[4]Department of Pharmaceutical Sciences, College of Pharmacy, University of Tennessee Health Science Center, Memphis, TN, 38163.*

Metastatic melanoma is one of the deadliest types of skin cancer and is responsible for 80% of total deaths from skin cancer. According to the American Cancer Society, patients who have been diagnosed with distant metastasized melanoma only have a 5-year survival rate of 31%. Targeted therapies and paclitaxel are currently used in the clinic for treatment. However, their prolonged usage can lead to resistance and rapid disease progression. Previous literature has indicated that colchicine binding site inhibitors (CBSIs) are promising candidates for the treatment of resistant variants of melanoma. In this study, we designed a new series of CBSIs based on a novel scaffold utilizing molecular modeling and structure-activity-relationship (SAR) studies. Out of the synthesized 22 compounds, we identified our lead compound **4p**, which was confirmed as a CBSI and demonstrated potent antiproliferative activity in the 15-20 nM range against a panel of melanoma cell lines. *In vitro*, compound **4p** arrested cancer cells in the G2/M phase of the cell cycle and inhibited cancer cell behavior such as migration, invasion, and colony-forming ability. The efficacy of compound **4p** was evaluated *in vivo* with a paclitaxel resistant A375 xenograft mouse model. In this model, treatment with compound **4p** led to a moderate inhibition of primary tumor growth. Immunohistochemistry (IHC) and H&E staining showed significant proliferation inhibition, the induction of apoptosis, and most interestingly, immune cell recruitment to the primary tumor. This study was repeated in an immunocompetent mouse model with B16-F10 melanoma cells. In this model, we saw a significant inhibition of tumor growth. IHC and H&E staining of the tumors showed a 500% increase relative to the control for the CD45 leucocyte marker and the necrosis marker phospho-MLKL. This supports our hypothesis that compound **4p** induces tumor cell death through apoptosis and necrosis. Further studies into this effect will be performed with **4p** analogs, such as the recently synthesized compound **M21**.



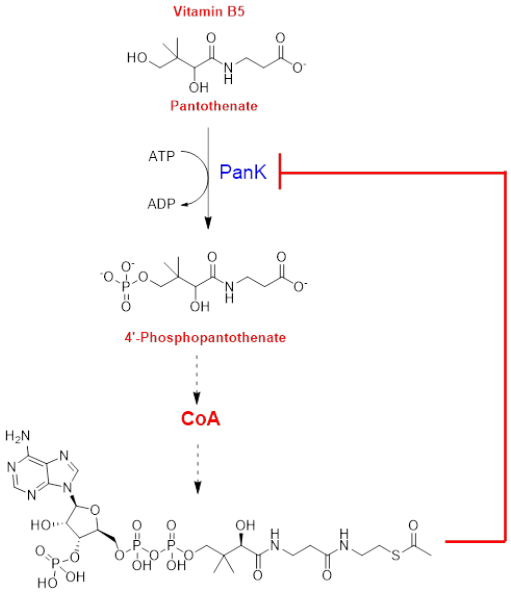
## O3. PANTOTHENATE KINASE INHIBITORS FOR CANCER

**Ashton Coker[1], Thilina Jayasinghe[1], Chitra Subramanian[2], Rajendra Tangallapally[1], Karen Miller[2], and Richard Lee*[1]**

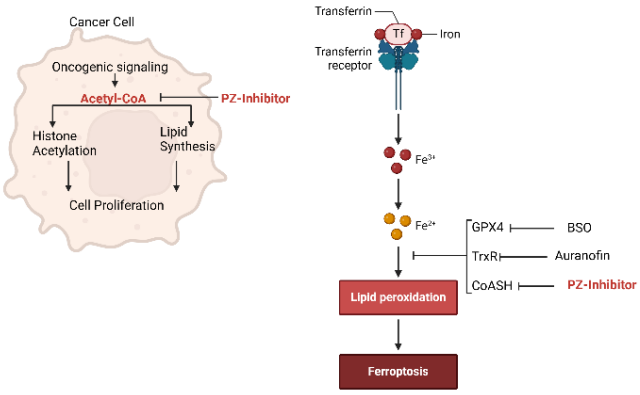
*[1]Department of Chemical Biology and Therapeutics, St. Jude Children's Research Hospital, Memphis, TN.*
*[2]Department of Host-Microbe Interactions, St. Jude Children's Research Hospital, Memphis, TN.*

Coenzyme-A (CoA) and its acylated derivatives, Acyl-CoAs (AcCoA), are important cofactors for many cellular metabolic and regulatory processes, such as the citric acid cycle, lipid synthesis, and histone acetylation. Dysregulation of cellular CoA levels has previously been observed in various diseases like neurodegeneration, acidemia, and cancer. Pantothenate kinase (PANK) is the rate-limiting enzymatic step in the CoA biosynthetic pathway and offers a target for small molecules. Our prior work focused on the discovery of small-molecule PANK activators that elevate cellular CoA levels. Here, we describe our efforts to design pantothenate competitive inhibitors that decrease cellular CoA levels by having pan PANK isoform inhibition using structure-guided design efforts. The work produced ultrapotent (pM) pan isoform inhibitors by introducing a new hydrogen bonding interaction with ATP. These inhibitors cease CoA biosynthesis within C3A cells and were evaluated as anti-cancer agents. Compounds such as lead PZ-5414 were also shown to demonstrate synergy in combination with histone acetyltransferase and bromodomain inhibitors. These compounds offer a novel approach to blocking cancer cell proliferation and metabolism that may aid in overcoming acquired resistance to histone acetyltransferase inhibitors.

**CoA Biosynthetic Pathway**




**Hypothesis of PZ-inhibitor uses in cancer**



## *O4. A TRIMERIC PEPTOID THAT SELECTIVELY TARGETS SURFACE PLECTIN IN NON-SMALL-CELL LUNG CANCER STEM CELLS

**Charles Owusu Ansah[1], Gomika Udugamasooriya*[,1,2]**

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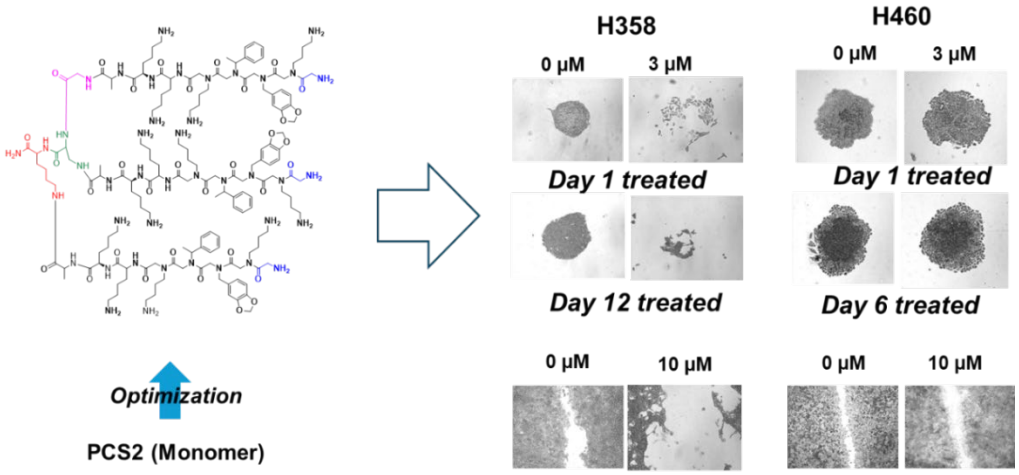
*[2]Department of Cancer System Imaging, MD Anderson Cancer Center, Houston, TX*

Cancer stem cells (CSCs) represent a critical therapeutic challenge due to their inherent resistance to conventional treatments, self-renewal capacity, and metastatic potential. These characteristics underscore the necessity for developing targeted approaches against CSCs to improve patient outcomes. In our previous work, we identified peptoid-PCS2, which selectively binds to a CSC subpopulation in non-small cell lung cancer (NSCLC) through interaction with plectin. While plectin typically functions as a cytoskeletal protein, it translocates to the outer cell membrane in CSCs, termed surface-translocated plectin (STP), where it plays a pivotal role in cell invasion, proliferation, and metastasis. Through systematic structure-activity relationship studies and optimization of multimeric architecture, we developed PCS2T3.9, a trimeric peptoid. PCS2T3.9 demonstrated significant cytotoxic activity against high plectin-expressing H358 cells of ~14-fold while exhibiting markedly reduced efficacy against H460 cells with low plectin expression. Notably, PCS2T3.9 had no activity on normal bronchial epithelial HBEC-3KT cells, indicating exceptional selectivity for CSCs. Further functional studies revealed that PCS2T3.9 effectively suppressed colony formation and cell migration, establishing *in vitro* hallmarks of cancer stemnes, —specifically in H358 cells but not in H460 cells. These findings establish a strong correlation between elevated plectin expression, cancer stemness characteristics, and susceptibility to PCS2T3.9. The highly selective antagonistic effects of PCS2T3.9 against STP-enriched CSCs offer a significant therapeutic advantage by potentially minimizing off-target effects on normal tissues, positioning this compound as a promising candidate for targeted NSCLC therapy.

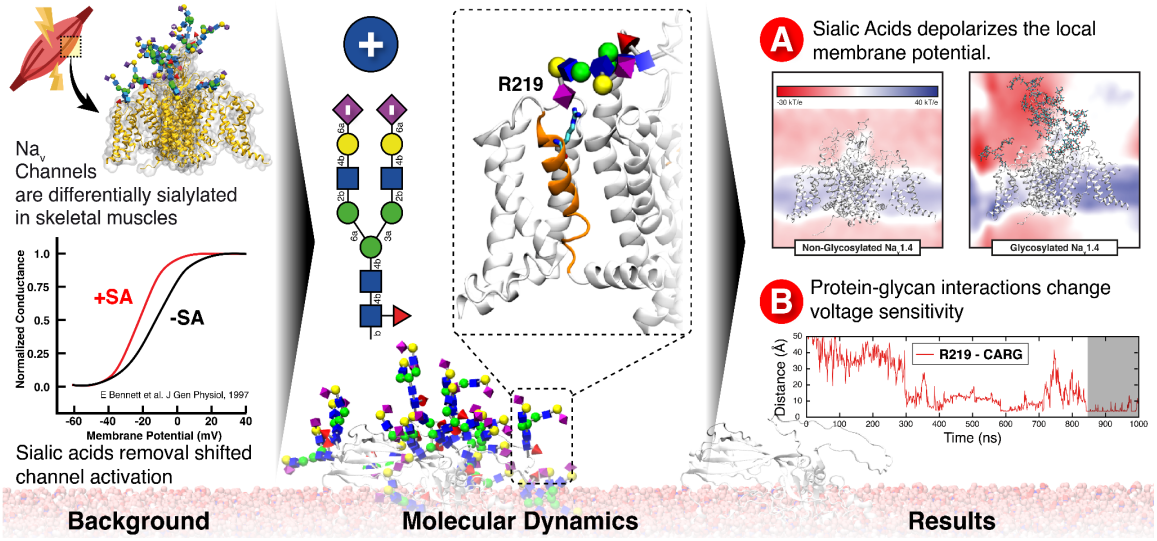


## O5. ELUCIDATING THE MOLECULAR MECHANISMS OF GATING REGULATION OF N-GLYCOSYLATION ON VOLTAGE-GATED SODIUM CHANNELS

**Eslam Elhanafy and Jing Li***

*Department of Biomolecular Sciences, School of Pharmacy, University of Mississippi, USA.*

Voltage-gated sodium channels (VGSCs) are essential for the initiation and propagation of action potentials in excitable cells. VGSCs are differentially sialylated in muscle and heart cells, a phenomenon thought to contribute to the distinctive electrical signaling properties of these two cell types. In this study, we used molecular dynamics (MD) simulations to investigate how glycans alter ion channels, both structurally and dynamically. We investigated the impact of differential sialylation on the structure and function of VGSCs. Using the cryo-EM structure of human $Na_v1.4$, we constructed a model of the glycosylated channel within the lipid bilayer. N-glycosylation sites were targeted, with the chosen glycans representing the most abundant forms identified in previous glycomic profiling analyses of $Na_v$ channels. Multiple 1-microsecond MD simulations of the $Na_v1.4$ channel were conducted to compare simulations with and without sialylated glycans. Comparative simulations between glycosylated and non-glycosylated systems revealed that sialic acids generate pronounced negative electrostatic potentials at the extracellular side of the channel, leading to local depolarization of the membrane potential. These negative charge centers were concentrated near the voltage-sensing domain (VSD) residues, including R219 gating charge. Notably, our analysis uncovered persistent, long-range electrostatic interactions between sialylated glycans and positively charged residues, which may stabilize activated VSD states and shift the voltage dependence of channel opening. These results provide mechanistic insights into how protein-glycan interactions fine-tune voltage sensitivity and may help explain disease-associated phenotypes arising from glycosylation site mutations in $Na_v$ isoforms. Together, this study highlights a novel role of sialylated glycans in regulating $Na_v$ channel function and suggests new directions for investigating glycosylation in channelopathies.



## *O6. PAN-K-RAS INHIBITION VIA 3-DIMENSIONAL (3D) PEPTOIDS FOR LUNG CANCER THERAPY

**Eunsun Park[1], Satya Prakash Shukla[1], and D. Gomika Udugamasooriya*[1,2]**

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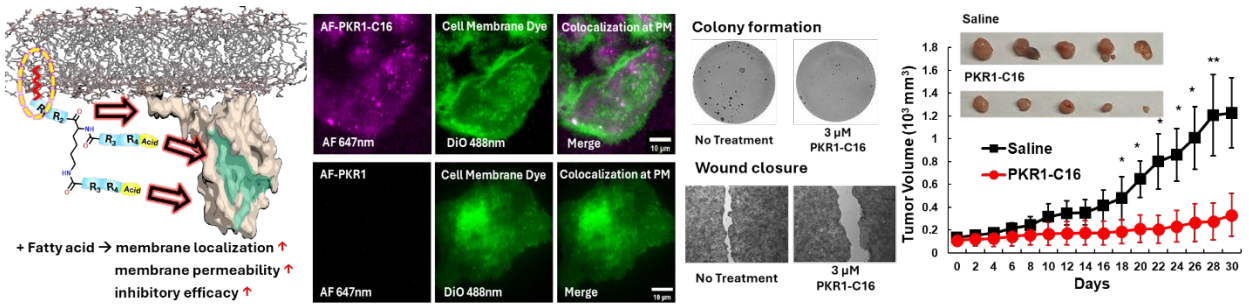
[2]*Department of Cancer System Image, MD Anderson Cancer Center, Houston, TX*

K-Ras is one of the most common oncogenes found across various cancer types, making it an attractive target for pan-K-Ras inhibitors to overcome drug resistance caused by tumor heterogeneity. However, conventional drug types have had limited success targeting K-Ras, which has long been considered "undruggable" due to its large binding surface without deep binding pockets and having strong GDP/GTP affinity. To address these challenges, we developed branched 3D peptoids potentially covering multiple sites on K-Ras. We identified a 'hit' peptoid, **PKR1**, targeting K-Ras G12V via on-bead screening of a 144,500 3D-peptoid library. We observed **PKR1** binds both GDP- and GTP-bound K-Ras G12V with $K_d$ values of 607 nM and 438 nM, respectively, whereas its unbranched (**PKR1.M**) and sequence-scrambled (**PKR1.S**) derivatives showed no binding, suggesting a potential multi-site binding effect of the parent compound.

We further enhanced 3D peptoid interaction with K-Ras by conjugating a fatty acid (**C4** to **C18**) to facilitate membrane anchoring at the K-Ras localization site. **PKR1-C16** incorporating palmitic acid (**C16**) demonstrated the best pan-inhibitory activity across multiple KRAS mutants (G12V, G12C, and Q61H) and WT cancer cell lines, with $IC_{50}$ values ranging from 3.0 to 9.4 μM, but not on normal HBEC3-KT cells. TIRF microscopy using AF647-labeled **PKR1-C16** revealed strong membrane colocalization, whereas the parent **PKR1** showed no detectable membrane association. Additional *in vitro* assays, including clonogenicity, wound healing, and time-course MTS, confirmed dose-dependent inhibition of cancer cell proliferation, survival, and migration. In the H441 xenograft model, **PKR1-C16** effectively reduced tumor growth *in vivo* with no observable weight loss, indicating minimal toxicity.

Overall, we designed a unique 3D-peptoid compound, **PKR1,** for the difficult-to-target KRAS oncoprotein, including the development of **PKR1** derivatives with enhanced efficacy through fatty acid conjugation. These findings highlight the therapeutic potential of developing pan-K-Ras drug candidates across various cancer types.



## *O7. DISCOVERY OF BRD9 PEPTIDE INHIBITORS USING A GENETICALLY ENCODED PHAGE DISPLAY SYSTEM

**Gopal K. Dubey and Wenshe Ray Liu***

*Drug Discovery Center, Department of Chemistry, Texas A&M University, College Station, TX, USA*

Acetylation is the most dynamic protein translational modification, often associated with increased DNA accessibility and transcription. These acetylated histones recruit transcription and remodeling factors, and their deregulation could result in aberrant expression of survival and growth-promoting genes. Recognition of acetylated lysine is principally mediated by bromodomains (BRDs). Recent studies have shown that BRD9 is preferentially used by cancers that harbor SMARCB1 abnormalities, such as malignant rhabdoid tumors and sarcomas. BRD9 is an essential component of the SWI/SNF chromatin remodeling complex and a critical target required in acute myeloid leukemia. As the biological function of BRD9 in tumorigenesis becomes clear, the bromodomain of BRD9 has become a new hot target for effective tumor treatment.

BRD9 has a different architecture than other bromodomains. Due to the larger hydrophobic cavity of BRD9, it can recognize longer propionyl and butyryl marks on lysine. Thus, $N^{\varepsilon}$-butyryl-lysine (BuK) can selectively bind to BRD9. Our group specializes in the amber suppression-based noncanonical amino acid (ncAA) mutagenesis technique. Herein Fig. 1), we propose to extend this technique using phage-displayed ncAA-containing peptide libraries to identify high-affinity and highly selective BRD9 inhibitors.

Phage display is a technique for rapid screening of potential ligands. It is facilitated through the creation of a genetic fusion between a randomized peptide sequence and pIII, a phage coat protein. This direct link between genotype and phenotype allows for peptide screening. We utilized the Phage-assisted, Active Site-Directed Ligand Evolution approach to target BRD9. To identify the binders, we chose 7mer phagemid library, which generates $1.5x10^{10}$ randomized possible peptides displayed on PIII of bacteriophages. The peptides screened were tested for binding using Bio-Layer Interferometry and inhibition by Alpha Screen assay. Based on SARs second-generation focused selection was done to screen for more potent peptides. Studies resulted in the identification of BRD9 binders with increased specificity and affinity. The estimated $IC_{50}$ for the peptide was 0.74 µM and $K_d$ was determined to be 0.53 µM. Second generation selection peptide inhibits protein with $IC_{50}$ 0.54 µM and $K_d$ value 0.104 µM. Selected peptides successfully bind and inhibit BRD9, and we aim to further optimize their cellular target engagement and on-target effects.

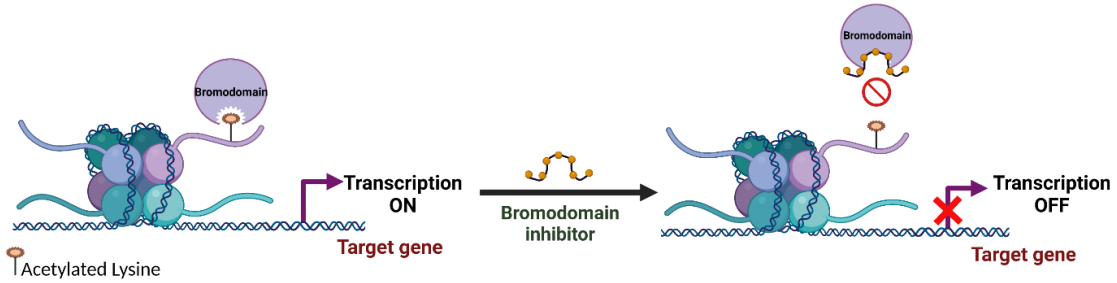



**Fig 1.** *Schematic representation of the bromodomain 9 peptide inhibitor turning off the transcription process.*

## O8. UNEXPECTED PRODUCTS FROM THE SYNTHESIS OF FLUORINATED GLYCOMIMETICS

**Dan Mi Huynh[1], Maali D. Alshammari[1], Frank R. Fronczek[2], and David A. Colby[1]***

[1] *Department of Biomolecular Science, Division of Medicinal Chemistry, School of Pharmacy, The University of Mississippi, Oxford, MS.*
[2] *Department of Chemistry, Louisiana State University, Baton Rouge, LA.*

Glycosylated compounds display valuable biological activity for drug discovery, such as immune modulation, neuroprotection, and anti-inflammation. However, O-glycosidic linkages are often rapidly hydrolyzed by metabolic enzymes, which limits the potential use of glycosylated compounds. Therefore, our design was the replacement of the O-glycosidic linkage with a difluoromethylene ($CF_2$-) group to enhance the stability of the glycosylated compounds. To test this hypothesis, we sought to synthesize a simplified scaffold of a $CF_2$-glycoside using two different approaches with difluoroenolates: 1) addition of radical enolates to dihydropyrans and 2) nucleophilic addition of enolates to lactones. We did not obtain the expected product in either approach, but instead, we observed surprising results that had not been previously reported in the literature. First, the formation of a radical difluoroenolate using copper led to the creation of a trifluoromethyl ketone rather than addition across the dihydropyran. We explored the scope of the process with different structural variants on the difluoroenolate. Second, the addition of a difluoroenolate to a lactone did not occur, but rather an umpolung addition of the lactone to the difluoroketone was observed. We further determined the scope of both these processes and characterized these unexpected compounds by NMR spectroscopy and X-ray crystallography. Although we did not create the simplified derivatives of $CF_2$-glycosides using literature precedents, our findings led to the discovery of new synthetic methods for producing trifluoromethyl ketones and difluoroalcohols through unexpected umpolung reactivity. In future studies, we aim to investigate further the radical-mediated process using a photoredox catalyst, because few methods are available in the existing scientific literature to assemble these valuable targets for medicinal chemistry.

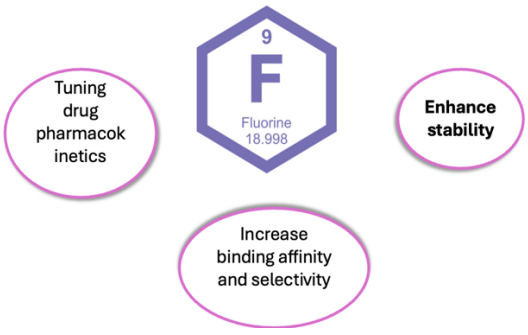



*Figure 1. Role of Fluorine in Medicinal Chemistry*

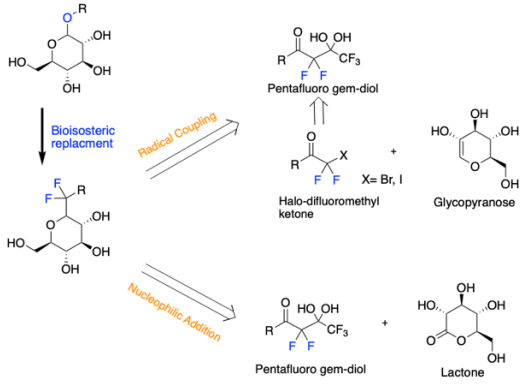


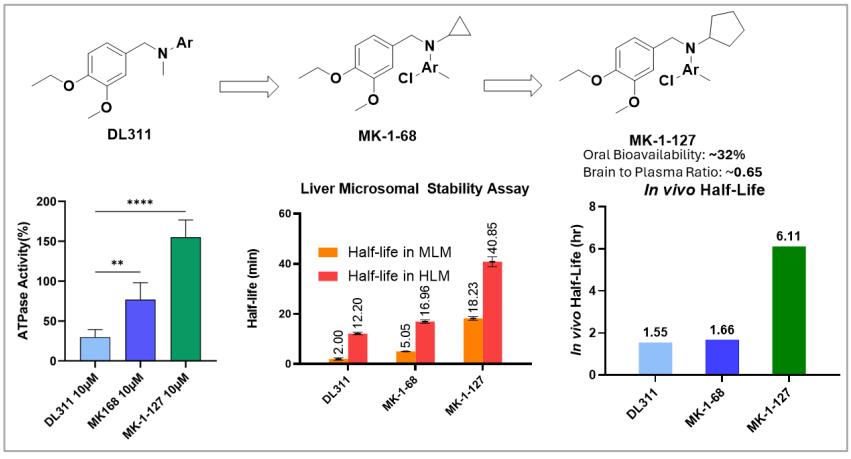

*Figure 2. Designed Synthesis Strategy to Test the Hypothesis.*

## O9. DISCOVERY OF POTENT AND ORALLY BIOAVAILABLE SERCA2 ACTIVATORS FOR THE TREATMENT OF ISCHEMIC STROKE-RELATED BRAIN DAMAGE

**Mir Shahriar Kamal[1], Hao Chen[1], Abdul Majid[2], Djamel Lebeche*[2], Wei Li*[1]**

[1]*Department of Pharmaceutical Sciences, College of Pharmacy, the University of Tennessee Health Science Center, Memphis, TN.*
[2]*Department of Physiology, College of Medicine, the University of Tennessee Health Science Center, Memphis, TN.*

Ischemic stroke (IS) results from the ischemic condition of the brain due to the occlusion of vessel(s) supplying blood to the brain, leading to long-term disability and death. It affects about 700,000 people annually in the USA alone, and the only options available to treat ischemic stroke patients are thrombolytics, blood thinners, and invasive surgery, necessitating the discovery of new therapeutic options. One key feature of ischemic stroke-related brain damage is the elevation of cytosolic calcium concentration in neurons, causing neuronal death. Although many channels and transporters are involved in the regulation of cytosolic calcium ion concentration, the Sarcoplasmic/Endoplasmic Reticulum Calcium ATPase (SERCA) pump is of major importance. SERCA is a calcium transporter located on the Sarcoplasmic reticulum (SR) and Endoplasmic reticulum (ER) membranes that transports calcium ions from the cytosol into these calcium storage organelles. Dysfunctional SERCA activity can result in an increased cytosolic calcium concentration, leading to the damage of cellular organelles and eventual cell death, while potentiating SERCA function has beneficial effects on cell survival. Studies have revealed that activation of SERCA2 b, the brain isoform of SERCA2, with small-molecule activators can be an important strategy to improve ischemic stroke outcomes. By screening a large chemical library, DL311 has been discovered as a potent SERCA2 activator. Although this hit has promising activity, it is not metabolically stable. With our medicinal chemistry-guided optimization strategies utilizing computational modelling, organic synthesis and efficient *in vitro* and *in vivo* assays, we have developed MK-1-127, a SERCA2 activator that has improved activity, potency, metabolic stability over the DL311 hit, as well as adequate oral bioavailability and blood-brain-barrier permeation, laying out the foundation for the development of SERCA2 activators as a therapeutic option for the treatment of ischemic stroke-related brain damage.

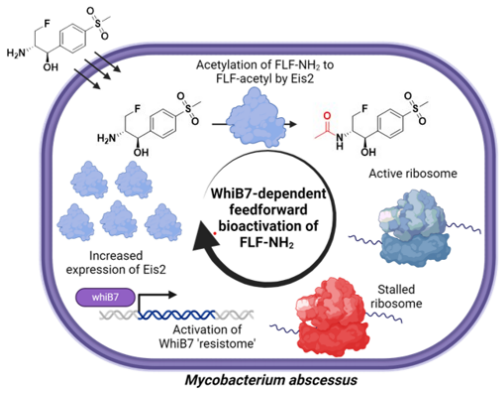


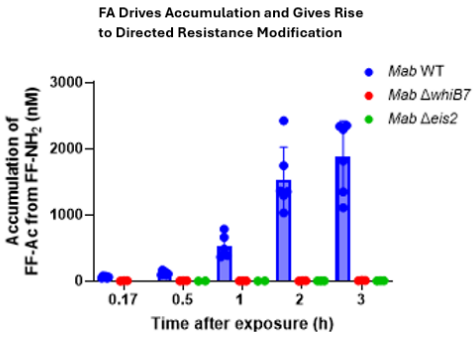
## O10. SYNTHESIS OF NOVEL FLORFENICOL AMINE ANALOGS THAT HIJACK AN INTERNAL RESISTANCE MECHANISM IN MYCOBACTERIUM ABSCESSUS

**Alexander R. Jenner[1,2], Gregory A. Phelps[1,3], Sinem Kurt[4], Shelby M. Anderson[1], Gabriel Papp[1], Robin B. Lee[1], Lucas Boeck[5,6], Bernd Meibohm[7], Andres Obregon-Henao[8], Peter Sander[3,9], Richard E. Lee[1]**

*[1]Department of Chemical Biology and Therapeutics, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA, [2]Department of Pharmaceutical Sciences, University of Tennessee Health Science Center, Memphis, TN, 38163, USA, [3]Graduate School of Biomedical Sciences, St. Jude Children's Research Hospital, Memphis TN, 38103, USA, [4]Institute of Medical Microbiology, University of Zurich, Gloriastrasse 28/30, CH-8006, Zurich, Switzerland, [5]Department of Biomedicine, University of Basel, Basel, Switzerland, [6]Pulmonary Medicine, University Hospital Basel, Switzerland, [7]Department of Pharmaceutical Sciences, University of Tennessee Health Science Center, Memphis, TN, 38105, USA, [8]NTM Center, Mycobacteria Research Laboratory, Department of Microbiology, Immunology, and Pathology, Colorado State University, Fort Collins, CO, 80523, USA, [9]National Reference Center for Mycobacteria, Gloriastrasse 28/30, CH-8006 Zurich, Switzerland.*

Mycobacterium abscessus (Mab), a rapidly emerging nontuberculous mycobacterium (NTM), poses a significant global health challenge due to its high intrinsic resistance and poor treatment outcomes. Current therapies depend on prolonged multi-drug regimens lasting over 12 months, which demonstrate limited efficacy and notable toxicity. In this study, we investigated florfenicol amine (FA), a derivative of florfenicol, as a potential therapeutic agent against Mab. Our preliminary findings suggest that FA paradoxically activates the WhiB7 resistance regulator, resulting in N-acetyltransferase-mediated acetylation that enhances antimicrobial activity. This bioactivation mechanism circumvents the mitochondrial toxicity associated with the phenicol class of antibiotics while preserving potent ribosomal inhibition. This presentation will cover a medicinal chemistry campaign utilizing structure-based drug design to identify FA analogs with improved activity that maintain the novel mechanism of action. Synthetic extension of the para-substituted position of the FA analogs with aromatic substituted groups enhances potency and preserves the biological mechanism. Developing these analogs presented several synthetic challenges. Many routes were explored to identify suitable and scalable synthesis, and issues such as racemization and chemical instability under reaction conditions required strategic resolution. This work introduces an innovative strategy for antibiotic development by exploiting, rather than evading, bacterial resistance mechanisms. Understanding and leveraging intrinsic resistance pathways in Mab could pave the way for pathogen-specific therapeutics and provide a promising alternative to ineffective, toxic treatment regimens.



## O11. SB-216, A NEW GENERATION OF TUBULIN INHIBITOR OVERCOMES OSIMERTINIB AND PACLITAXEL RESISTANCE IN DRUG-RESISTANT NON-SMALL-CELL LUNG CANCER

**Sara Sultana[1], Yang Xie, Satyanarayana Pochampally, Duane D. Miller, and Wei Li***

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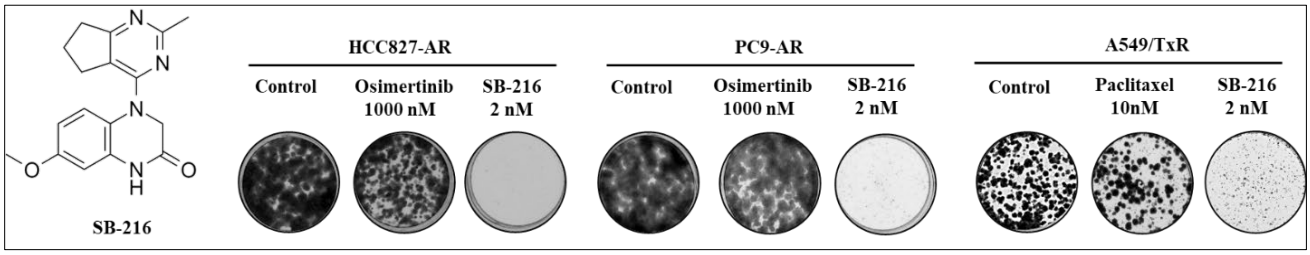
Lung cancer is the most prevalent cancer type, accounting for 12.4% of all cancer diagnoses and 18.7% of global cancer-related deaths. The current available treatment options are chemotherapy, targeted therapy, immunotherapy, or a combination regimen, depending on the disease stage and metastasis level. Among the first-line treatment options for non-small cell lung cancer (NSCLC), paclitaxel and osimertinib, a 3rd generation EGFR-TKI, are widely used. However, the emergence of resistance to these drugs has become a major issue, resulting in loss of long-term efficacy, poor treatment outcomes, and disease progression. We previously reported SB-216, a new generation tubulin inhibitor targeting the colchicine binding site, that shows potent preclinical efficacy in various tumor models. In this study, we demonstrate that SB-216 effectively overcomes the acquired resistance to both osimertinib and paclitaxel in NSCLC. SB-216 maintains potent cytotoxicity in osimertinib-resistant HCC827 and PC9 cell lines (HCC827/AR, PC9/AR) as well as paclitaxel-resistant A549 (A549/TxR) cell line with $IC_{50}$ values in the low nanomolar range (1-4 nM). *In vitro* assays reveal that SB-216 significantly suppresses colony formation, cancer cell migration, and disrupts microtubule formation in these resistant cell lines dose dependently. Furthermore, SB-216 induces cell cycle arrest at G2/M phase and triggers cancer cell apoptosis in a dose-dependent manner. Collectively, these findings highlight the potential of SB-216 as a promising anti-cancer candidate for overcoming resistance to frontline treatments in NSCLC.



## O12. SYNTHESIS OF HEXAFLUOROISOPROPANOLS AS BUILDING BLOCKS FOR FLUORINE-TAGGED MOLECULES

**Meshal A. Alghamdi and David A. Colby***

*Division of Medicinal Chemistry, Department of BioMolecular Sciences, University of Mississippi, University, Mississippi 38677, United States.*

Fluorinated organic molecules have significant potential in medicinal chemistry and drug discovery. Therefore, more than 20% of all FDA-approved drugs contain at least one fluorine atom. A current goal of research is the discovery of new types of fluorinated functional groups to expand chemical space, but methods to create these targets are limited, especially in the case of high levels of fluorination. Among the new functional groups displaying high levels of fluorination, the hexafluoroisopropanol group is attracting interest in drug development as clinical candidates with this group are now being evaluated. The hexafluoroisopropanol group combines high levels of fluorination with an adjacent alcohol, which produces a unique hydrogen bond donor without any nucleophilicity. Despite the current interest, there are few methods to install a hexafluoroisopropanol group in the literature, and the scope of starting materials that participate in such reactions is not well explored. The known reactions use hexafluoroacetone trihydrate to introduce a hexafluoroisopropanol group into molecules; however, water is present in this method, which is typically avoided in organic synthesis. The Colby reagent is an anhydrous form of hexafluoroacetone hydrate but has only been used in trifluoromethylations. Although the Colby reagent has not been investigated for its ability to install of hexafluoroisopropanol group, we hypothesize that this reagent can be used in the synthesis of derivatives of hexafluoroisopropanol from anilines and other substrates for the preparation of drug-like molecules. We adapted a procedure from the literature for the Colby reagent for installing hexafluoroisopropanol. The optimal conditions were identified by employing $^{19}$F-NMR for the determination of yield. Thus far, we have isolated products in reproducible yields with high regioselectivity, as illustrated in *Figure 1*. We are currently testing different substrates to expand the scope of the reaction and the use of hexafluoroisopropanols in drug discovery. We have also identified that using this anhydrous reagent, Lewis acids are now compatible with the process. These advances will be discussed for the creation of new building blocks for drug design and fluorine-tagging molecular structures.

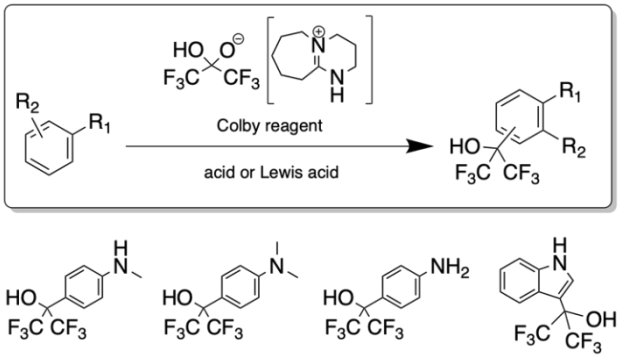



*Figure 1: The general synthetic scheme and isolated derivatives.*

## *O13. BENCH-STABLE BORYL THIANTHRENIUM DICATION ENABLES AZIRIDINYL BORONATE SYNTHESIS VIA METAL-FREE LATE-STAGE AZIRIDINATION

Veerabhadra R. Vulupala,[1] Disni Gunasekera,[1] Nagarjun R. Mallampudi,[1] Ramy Yousef,[1] Yusif Gyasi,[1] Ramidi Gopal Reddy,[1] and Shiqing Xu[1,2*]

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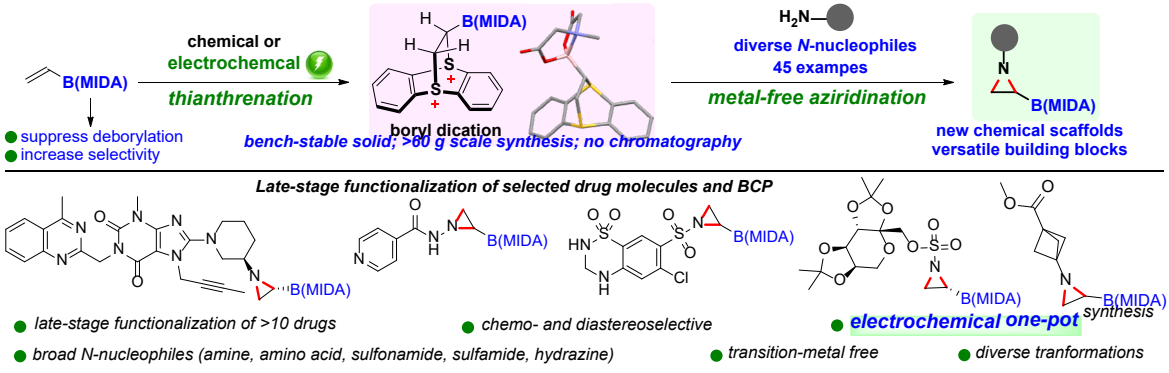
[2]*Department of Pharmaceutical Sciences, Irma Lerma Rangel College of Pharmacy, Texas A&M University, College Station, Texas 77843, United States*

Organoboron compounds are highly versatile building blocks in modern organic synthesis due to their broad applicability in diverse transformations. More recently, these compounds have gained significant attention in chemical biology and drug discovery for their unique chemical properties. A distinguishing feature of boron is its vacant p orbital, which facilitates reversible interactions with biological nucleophiles such as hydroxyl and amine groups in enzyme residues, carbohydrates, and nucleic acids to form anionic $sp^3$-hybridized complexes. This dynamic binding capability, combined with the hydrogen-bonding potential of boronic acids, makes boron an exceptionally versatile and underexplored element in drug design and bioconjugation, as evidenced by the success of several FDA-approved drugs. In this work, we report the first synthesis of bench-stable boryl thianthrenium dicationic compound through chemical or electrochemical thianthrenation of vinyl MIDA boronate. Notably, the MIDA boryl group plays a crucial role in thianthrenation, suppressing undesired deborylation and promoting exclusive mono-adduct formation via a formal [4+2] cycloaddition pathway. This unique boryl thianthrenium dication enables a transition-metal-free, chemo- and diastereoselective synthesis of aziridinyl boronates, utilizing a broad range of nitrogen nucleophiles. The method demonstrates generality, practicality, and functional group tolerance, as evidenced by its application to diverse substrates, including the late-stage modification of several drug molecules. The strategic significance of this approach is further highlighted through electrochemical one-pot protocol and multiple downstream transformations of aziridinyl boronates, offering new opportunities for synthetically challenging boron-containing drug-like scaffolds.

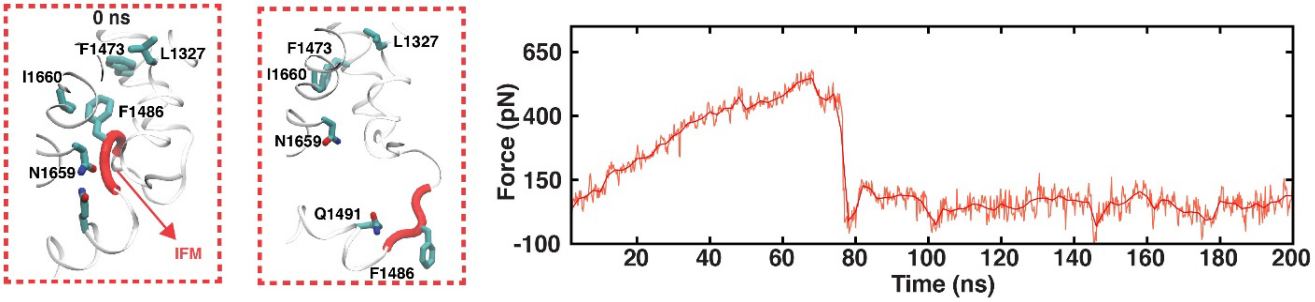


## O14. MECHANISTIC INSIGHTS INTO DISEASE-ASSOCIATED MUTATIONS DISRUPTING FAST INACTIVATION IN VOLTAGE-GATED SODIUM CHANNELS

**Shiva Akhlaghi, Jing Li***

*Department of Biomolecular Sciences, School of Pharmacy, University of Mississippi*

Fast inactivation of Nav (voltage-gated sodium) channels regulates the electrical hyperexcitability in nerve and muscle cells by inducing a transition into a non-conductive state. The IFM (Isoleucine–Phenylalanine–Methionine) motif, situated in the intercellular DIII-DIV (Domain III–Domain IV) linker, acts as an "inactivation gate" by allosterically blocking the intracellular opening of Nav channels. Apart from this IFM motif, several Nav variants have been identified that disrupt fast inactivation and are associated with diseases like long QT syndrome (LQTS) and epilepsy. However, the molecular mechanisms behind these variant effects are still largely unknown. To elucidate these mechanisms, we conducted constant-velocity steered molecular dynamics (CV-SMD) simulations to characterize the unbinding of the IFM motif toward the open state. The force-time profiles from CV-SMDs allow us to determine the major barrier for this unbinding process. A contact analysis was performed for all residues in the vicinity of the DIII-DIV linker to screen important interactions for the IFM binding for fast inactivation. This investigation shows that breaking several interactions located in the upstream (USM) and downstream (DSM) regions of the IFM is linked to the peak unbinding force, highlighting their importance for fast inactivation. Based on this observation, three residues are involved in multiple interactions and are disease-associated; we conducted CV-SMD simulations on the missense mutations (F1473C, N1659I, and E1773K) to validate their structural effects on fast inactivation. These three mutations facilitate IFM unbinding relative to the WT (wild type), resulting in a significant reduction in the required force, with N1659I exhibiting the most distinct effect. E1773K exhibits variable behavior, reducing the force when the salt bridge (D1484-K1773) is present; otherwise, it remains unchanged compared to WT. The following MD simulations reveal that successful IFM rebinding in the WT is driven by persistent distal-side hydrogen bonding, whereas disruption of key anchors in the N1659I mutant destabilizes the binding interface, impairs IFM motif return, and likely contributes to defective fast inactivation. This insight provides molecular explanations for these disease-linked mutations and helps predict their impact on phenotypes related to fast inactivation in voltage-gated sodium channels.



## O15. EVALUATION OF U2AF HOMOLOGY MOTIF (UHM) SPLICING FACTOR INHIBITORS AS A SPLICEOSOME-TARGETED THERAPY IN HEMATOLOGIC MALIGNANCIES

**Amol D. Patil[#], Mona Kazemi Sabzvar[#], Xinrui Yuan, Daniel M, Collier, and Chao-Yie Yang***

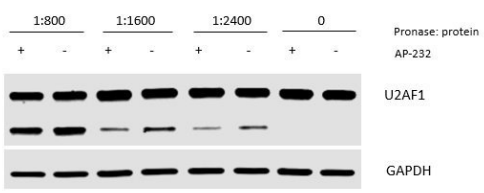
*Departments of Pharmaceutical Sciences, College of Pharmacy, University of Tennessee Health Science Center, Memphis, TN 38163, USA.*

[#] *Contributed equally to this work.*

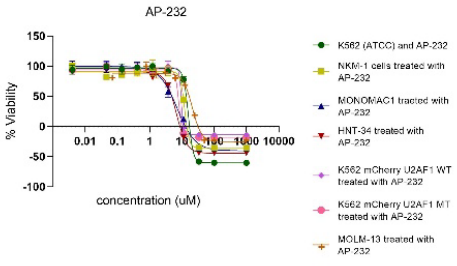
Recurrent hotspot mutations in splicing factors such as SF3B1, SRSF2, U2AF1, and ZRSR2—key regulators of 3' splice site recognition in RNA splicing —have been identified in myelodysplastic neoplasms, other myeloid malignancies, and, to a lesser extent, solid tumors. Malignant cells harboring these mutations exhibit heightened sensitivity to splicing modulators, as the splicing machinery in these cells is defective and vulnerable to additional insults. This also aligns with the observation that these mutations are typically heterozygous and mutually exclusive. However, no FDA-approved therapies are currently available to target these mutant proteins in cancer cells. Given the aging population, where age is a major risk factor for hematologic cancers (especially myelodysplastic neoplasms), developing targeted therapies to treat cancer cells with acquired defective splicing factors is crucial.

U2AF Homology Motif (UHM)-containing splicing factors including U2AF1, U2AF2, RBM39, PUF60, and SPF45 interact with (UHM-Ligand Motif) (ULM)-containing proteins to regulate 3' splice site recognition throughout the splicing process. We propose that disrupting UHM-ULM interactions using a small molecule inhibitor could serve as a novel strategy to target cancer cells with defective spliceosome function, particularly those harboring splicing factor mutations.

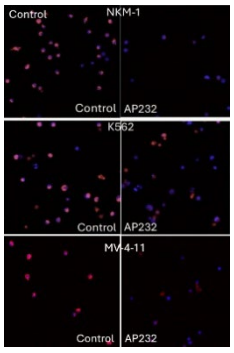
Our findings reveal insight into how this compound not only targets splicing factors but also affects lysosomal function, revealing new therapeutic possibilities.




Drug Affinity Responsive Target Stability (DARTS) assay representing direct binding of AP-232 compound to U2AF1 splicing factor




Cell viability assay for a spectrum of blood cancer cells




Lysosomal tracking of AP-232 compound

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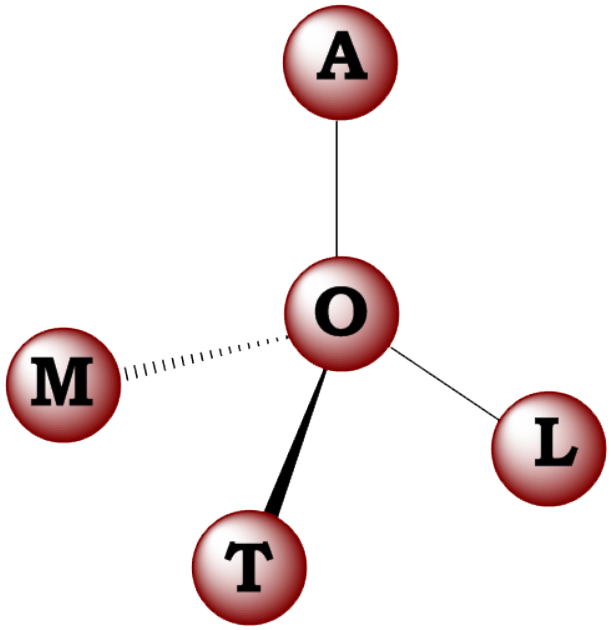



# Poster Presentation Abstracts

**Graduate Students & Postdoctoral Fellow Posters**

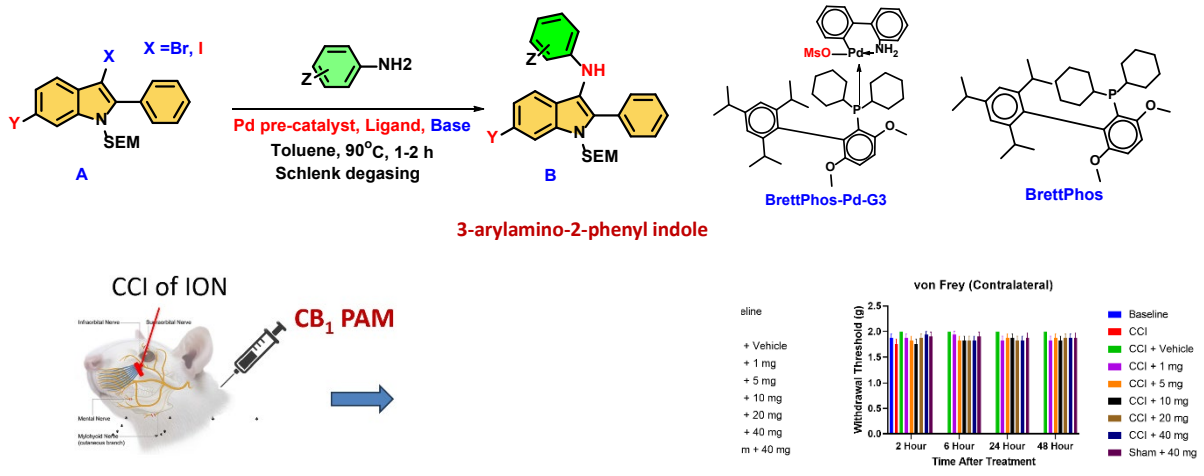
**(P1-P19)**

## P1. OPTIMIZATION OF BUCHWALD AMINATION REACTION TO SYNTHESIZE $CB_1$ RECEPTOR ALLOSTERIC LIGANDS FOR NOVEL NON-OPIOID ANALGESICS

**Rajpal Vangala, Zhixing Wu, Pedro Ochoa IV, Priscilla Gracia, Christabel Igwe, Vivian Rios, and Dai Lu***

*Department of Pharmaceutical Sciences, Rangel College of Pharmacy, Texas A&M Health Science Center, Kingsville, TX.*

A novel class of positive allosteric modulators (PAMs) of the cannabinoid $CB_1$ receptor, namely 3-arylamino-2-aryl indoles, was recently identified in our laboratory. Representative compounds, including PTDP-131 and PTDP-947, demonstrated potent analgesic efficacy without eliciting typical cannabimimetic side effects or addictive liabilities. The synthetic route to this scaffold involves initial formation of the indole core via a Sonogashira coupling, followed by a Buchwald-Hartwig amination at the C-3 position of the indole ring to install the arylamino substituent. This transformation is crucial for accessing the 3-arylamino-2-aryl indole framework. Given the complex interplay among variables in the Buchwald-Hartwig amination, such as the choice of aryl halide, palladium pre-catalyst, phosphine ligand, base, and solvent, each component was systematically evaluated to optimize reaction efficiency. Toluene was selected as the reaction solvent due to its ability to effectively solubilize the desired amination product. A comprehensive optimization campaign was conducted, evaluating over 12 Pd pre-catalysts in combination with various biphenylphosphine ligands. Both strong (*t*-BuONa) and weak ($Cs_2CO_3$) bases were screened. Among the tested conditions, the use of BrettPhos-Pd-G3 pre-catalyst in the presence of *t*-BuONa and BrettPhos ligand provided the highest yield, achieving up to 93% conversion to the desired product. This optimized Buchwald-Hartwig amination protocol enabled the efficient synthesis of a key intermediate, 3-arylamino-2-phenyl indole, thereby facilitating the development of this novel class of $CB_1$ PAMs as promising non-addictive analgesic agents.



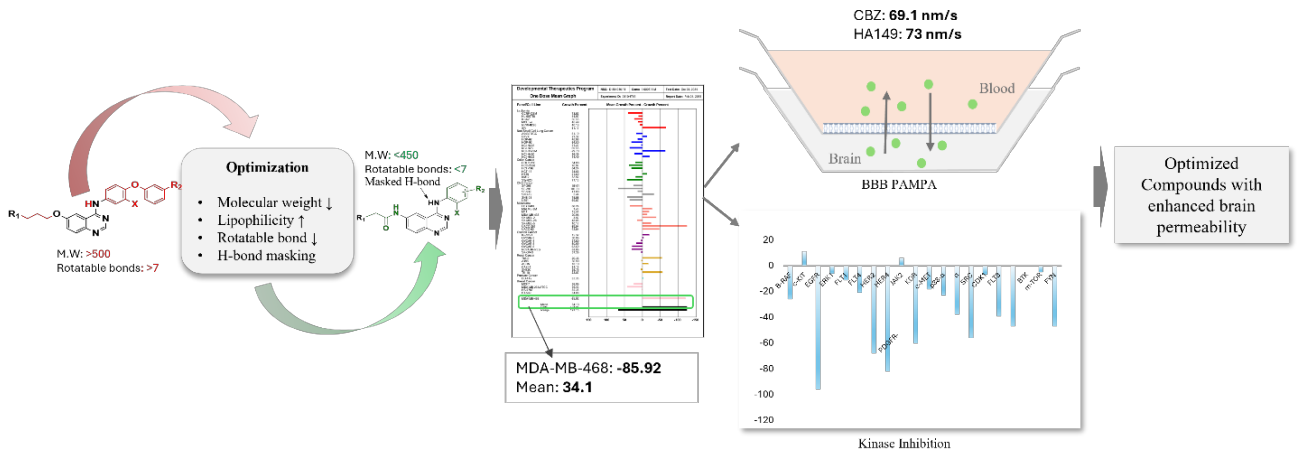

Pain suppression of $CB_1$ PAM

## P2. STRUCTURE-GUIDED OPTIMIZATION OF KINASE INHIBITORS FOR ENHANCED BRAIN PENETRATION IN THE TREATMENT OF CNS CANCERS

**Md Emran Hossain, Mostafa M.A Aref, Rokaia Abdulla, Eneye D. Ajayi, Hamed I. Ali***

*Department of Pharmaceutical Sciences, Irma Lerma Rangel College of Pharmacy, Texas A&M University, College Station, TX, USA*

Despite significant advances in targeted cancer therapy, brain metastasis and other types of brain malignancies continue to present challenges. The therapeutic efficacy of conventional targeted therapies, including kinase inhibitors, remains underutilized due to inadequate brain penetration. This study centers on the rational design, synthesis, and optimization of quinazoline-based kinase inhibitors with improved BBB permeability and potent anti-tumor activity. The study commenced by selecting the most potent compounds from an in-house library of kinase inhibitors. Structural optimization was focused on reducing molecular weight, increasing lipophilicity, minimizing the number of rotatable bonds, etc., to enhance their brain permeability. Artificial intelligence and machine learning algorithms were employed to predict the BBB penetration while maintaining optimal interaction with the target kinases. The top-ranked compounds were synthesized and evaluated for brain permeability by Parallel Artificial Membrane Permeability (PAMPA) assay. Subsequent in vitro studies were carried out to assess their kinase inhibition and antiproliferative effects. The optimized compounds demonstrated enhanced brain permeability in the BBB-PAMPA assay. Notably, compound HA149 achieved a mean permeability of 73 nm/s, surpassing the reference compound carbamazepine (69 nm/s). HA149, HA153, and HA157 exhibited the most potent antiproliferative activity among the tested molecules. MDA-MB-468 breast cancer cell lines displayed the highest sensitivity to these compounds. In vitro kinase screening revealed several candidate compounds significantly inhibiting key oncogenic kinases, including HER2, KDR, and Src. Through CAAD, synthesis, and in vitro studies, we identified lead compounds with strong metabolic stability, selective cytotoxicity toward HER2-positive and TNBC cells, and improved CNS permeability confirmed by PAMPA assay.



## P3. STRUCTURE-BASED DESIGN OF NOVEL COX-2 INHIBITORS THAT UNDERGO ENTEROHEPATIC RECYCLING FOR ENHANCED COLON DISTRIBUTION

**Pooja Atpadkar, Anantha L. Duddupudi, Rashim Singh, Ming Hu, and Gregory D. Cuny**

*Department of Pharmacological and Pharmaceutical Sciences, College of Pharmacy, the University of Houston, TX*

Familial Adenomatous Polyposis (FAP) is a hereditary condition caused by mutations in the APC gene, leading to numerous colorectal polyps and a high risk of early-onset colorectal cancer. The condition is driven by abnormal cell growth and loss of tumor suppression. Tumor progression, cell proliferation, survival, and angiogenesis are enhanced by **Prostaglandin E2 (PGE2)**. Since PGE2 synthesis is mediated by the cyclooxygenase (COX-2) enzyme, selective COX-2 inhibitors can be potentially used to suppress polyp growth. Although effective, long-term use of COX-2 inhibitors has been associated with cardiovascular risks, including heart attacks and strokes. To overcome this, a novel class of **locally bioavailable COX-2 inhibitors (LBD-based COXIBs)** is being developed. These compounds undergo glucuronidation in the liver and are recycled to the colon via **enterohepatic recirculation**, concentrating their effects locally while reducing systemic toxicity. The lead compound LBD-01 (6a1) exhibited a >100-fold colon-to-plasma concentration ratio and low systemic exposure (F < 1%) compared to celecoxib, a well-known COX-2 inhibitor; however, suboptimal free drug levels in colonocytes underscore the need to enhance COX-2 inhibitory efficacy while simultaneously improving liver glucuronidation. This is being addressed through structure-based modifications in two key regions of LBD-01(**Fig.1**): Region 1, aimed at enhancing COX-2 inhibitory activity, and Region 2, designed to facilitate glucuronidation for improved colon-targeting. The current study presents structure–activity relationship (SAR) and molecular docking analyses of LBD-based COXIBs. SAR analysis highlights the critical role of the phenolic group in facilitating glucuronidation and enhancing aqueous solubility. One of the analogues, PA-6a1-08, exhibited moderate COX-2 inhibitory activity and demonstrated a binding mode comparable to that of celecoxib (**Fig.2**). Additionally, docking studies with the UGT1A9 isoenzyme revealed favorable positioning of the phenol (**Fig.3**), supporting its potential for efficient liver glucuronidation and colon-targeting.

*Acknowledgements:* NIH (K12TR004522 to RS) and CPRIT (RP240401 to MH and GDC).

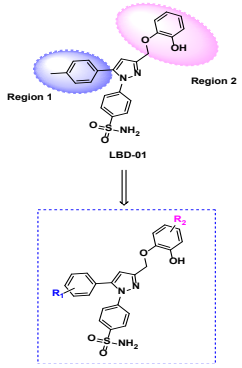



**Fig 1**: SAR Analysis

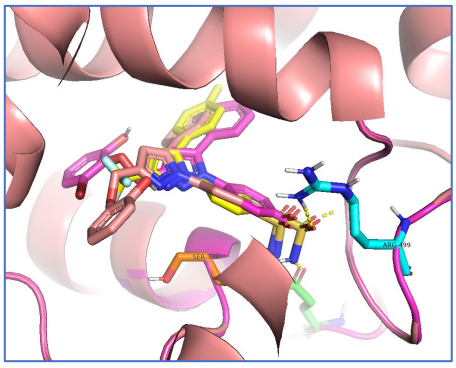


**Fig 2**: Overlay of the celecoxib•mCOX-2 co-crystal structure (PDB: 3LN1) with docked LBD-01 (6a1) and PA-6a1-08.

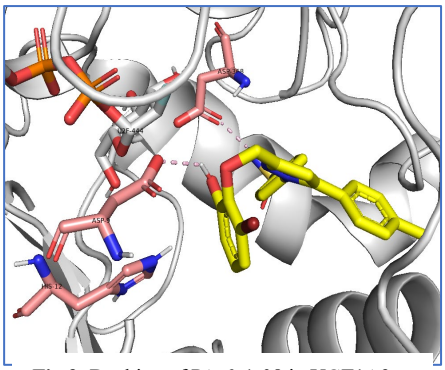


**Fig 3**: Docking of PA-6a1-08 in UGT1A9.

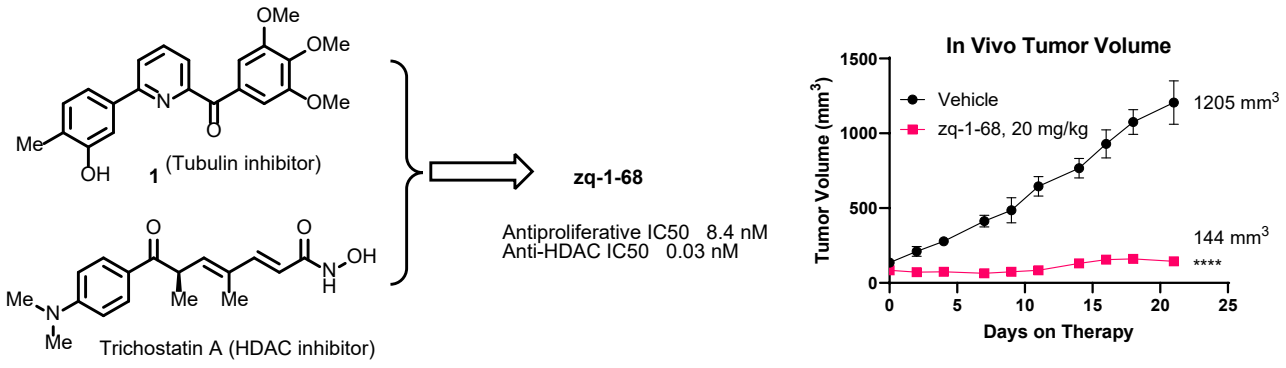
## P4. DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION OF DUAL-TARGETING TUBULIN/HDAC INHIBITORS AS POTENTIAL ANTICANCER AGENTS

**Zisong Qi,[#] Shelby Waddell,[#] Yang Xie, Hao Chen, Duane D. Miller, and Wei Li***

*Department of Pharmaceutical Sciences, College of Pharmacy, the University of Tennessee Health Science Center, Memphis, TN.*

[#] *Contributed equally to this work.*

Cancer, as one of the leading causes of death worldwide, is complicated, involving multiple signaling pathways and factors. Chemotherapy is one of the most common treatments for patients. Tubulin-targeted chemotherapeutics is an important class of drugs by disrupting the microtubule dynamics. In parallel, histone deacetylases (HDACs) play a key role in regulating gene expression by modifying histones and various non-histone proteins, including tubulin. HDAC inhibitors (HDACi) are designed to prevent the deacetylation of histone or non-histone proteins. However, single-target drugs suffer from drug resistance or off-target effects. To address these issues, dual-target design strategies have emerged as a promising solution. We recently discovered the small molecule (6-(3-hydroxy-4-methylphenyl) pyridin-2-yl) (3,4,5-trimethoxyphenyl) methanone (**1**) as a new tubulin inhibitor targeting the colchicine-binding site with high anticancer activities. In this study, we designed and synthesized novel dual tubulin/HDAC inhibitors based on **1**, among which **zq-1-68** was proved to be the most potent antiproliferative activity ($IC_{50}$ values in the range of 3.1 – 10.3 nM) in various cancer models with strong affinity for the colchicine binding site and HDAC activity. The preliminary results indicated that **zq-1-68** is more selective toward HDAC8 and HDAC6 than other isoforms. **Zq-1-68** effectively inhibits primary tumor growth in an *in vivo* patient-derived xenograft (PDX) model. Our findings show that **zq-1-68** represents a novel, promising tubulin/HDAC dual inhibitor, deserving further investigation as a potential anticancer agent for metastatic castration-resistant prostate cancer.



## P5. DISCOVERY OF A POTENT c-ABL KINASE INHIBITOR WITH THERAPEUTIC POTENTIAL AGAINST NEUROBLASTOMA

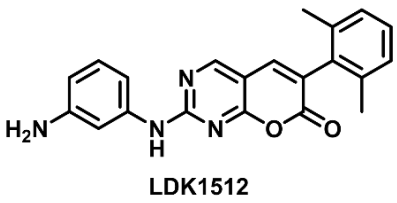
**Zhixing Wu[1], Yang Yu[2], Jianhua Yang[2], Dai Lu*[1]**

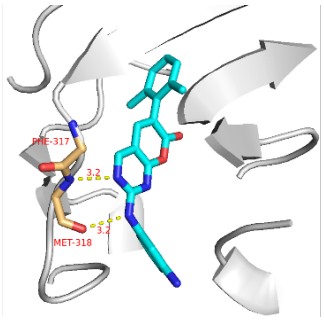
*[1]Department of Pharmaceutical Sciences, College of Pharmacy, Texas A&M University Health Science Center, Kingsville, TX.*
*[2]School of Medicine and Health Sciences, George Washington University and Children's National Hospital, Washington, DC.*

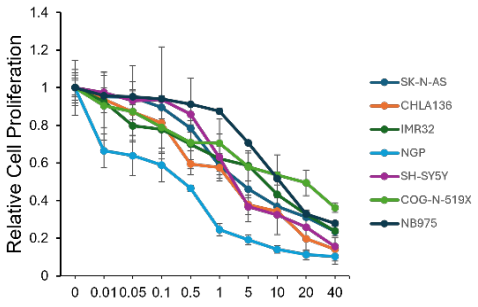
Neuroblastoma is the most prevalent extracranial solid tumor in children and accounts for over 15% of pediatric cancer-related mortality. Despite the therapeutic advances in recent decades, the prognosis for patients with high-risk neuroblastoma remains unfavorable. The three-year overall survival rate for these patients hovers around 70%, underscoring the urgent need for more effective and less toxic therapeutic approaches. Developing novel targeted therapies represents a promising avenue to address this critical unmet clinical need.

The non-receptor tyrosine kinase c-Abl, encoded by the ABL1 gene, plays an important role in regulating cell proliferation, survival, and migration in mammalian cells. Research has indicated that imatinib upregulates the CDK inhibitor $P27^{KIP1}$ in neuroblastoma cells due to c-Abl inhibition. Another study demonstrated that bosutinib has potent anti-tumor efficacy in neuroblastoma by inhibiting the activities of Src, c-Abl, and the downstream signaling pathways both in vitro and in vivo. These results suggest c-Abl is a potential therapeutic target in neuroblastoma and that potent and selective c-Abl inhibitors may be promising therapeutic modalities for treating neuroblastoma patients.

We recently discovered a small molecule 2-((3-aminophenyl) amino)-6-(2,6-dimethylphenyl)-7*H*-pyrano[2,3-*d*] pyrimidin-7-one (LDK1512) as a potent c-Abl kinase inhibitor with an $IC_{50}$ of 1.3 nM in enzymatic test. Computational modeling suggested that LDK1512 can perfectly fit into the ATP binding pocket of c-Abl (PDB:1M52), forming two hydrogen bonds with the main chain of Met318 in the hinge region. A cell antiproliferation study indicated LDK1512 suppressed the growth of a panel of neuroblastoma cell lines, with $IC_{50}$ values ranging from low micromolar to single-digit nanomolar concentrations. Therefore, the potent c-Abl kinase inhibitor LDK1512 shows promise as a novel therapeutic strategy for the treatment of neuroblastoma.



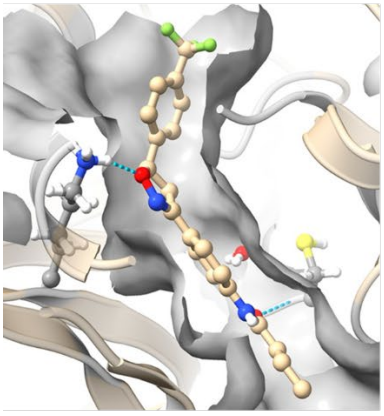



## P6. OVERCOMING THE BLOOD-BRAIN BARRIER IN LEUKEMIA THERAPY: DESIGN OF SELECTIVE FLT3 INHIBITORS USING ISOXAZOLINE CHEMISTRY

**Rokaia S. Abdullah, Md Emran Hossain Eneye D. Ajayi, Mostafa M.A. Aref, Hamed I. Ali***

*Department of Pharmaceutical Sciences, Irma Lerma Rangel College of Pharmacy, Texas A&M University, College Station, TX, USA*

The treatment of acute myeloid leukemia (AML) with central nervous system (CNS) involvement remains a major clinical challenge due to the restrictive nature of the blood-brain barrier (BBB). FLT3 is a validated therapeutic target in AML; however, most FLT3 inhibitors show poor brain penetration, limiting their effectiveness in CNS-complicated cases. To address this, we designed and synthesized novel isoxazoline-based FLT3 inhibitors with improved BBB permeability, enabling their potential use in treating CNS-involved leukemia. A rational drug design strategy was employed to develop a series of isoxazoline derivatives. In silico predictions using Swiss ADME (BOILED-Egg model) were used to assess BBB permeability. Compounds were synthesized and characterized by $^{1}$H NMR, $^{13}$C NMR, $^{13}$C DEPT, HRMS, and FTIR spectroscopy. Biological evaluation included *in vitro* permeability assessment using the PAMP assay and FLT3 kinase inhibition profiling. The lead compound HA-198 exhibited selective FLT3 inhibition and demonstrated a permeability coefficient (Pe =2.37 nm/s). Structural modifications enhanced both selectivity and pharmacokinetic properties. Swiss ADME predictions supported experimental findings, and the synthesized compounds showed promising profiles for CNS delivery. In conclusion, this study introduces a novel class of isoxazoline-based FLT3 inhibitors with dual advantages: potent antileukemic activity and enhanced BBB permeability. These findings support the potential of these compounds as candidates for treating AML with CNS involvement, addressing both pharmacodynamic and pharmacokinetic challenges.



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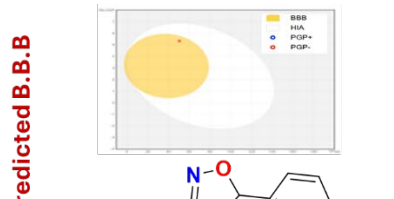



Predicted B.B.B

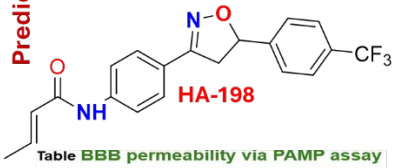
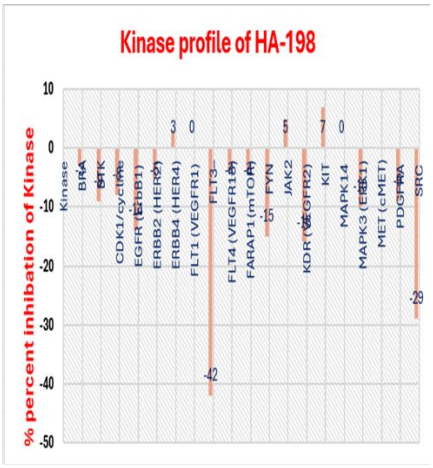



Table BBB permeability via PAMP assay

Calculated B.B.B

| Compound ID | Nadolol | Carbamazine | HA-198 |
|---|---|---|---|
| Test Concentration (μM) | 10.0 | 10.0 | 10.0 |
| Incubation Time (hour) | 4 | 4 | 4 |
| Mean Pe (nm/s) | 0.00206 | 67.1 | 2.37 |
| Mean %Solution Recovery | 99.1 | 100.4 | 55.3 |




**FLT3 inhibitor+ BBB penetration=Novel CNS-Target AML Therapy**

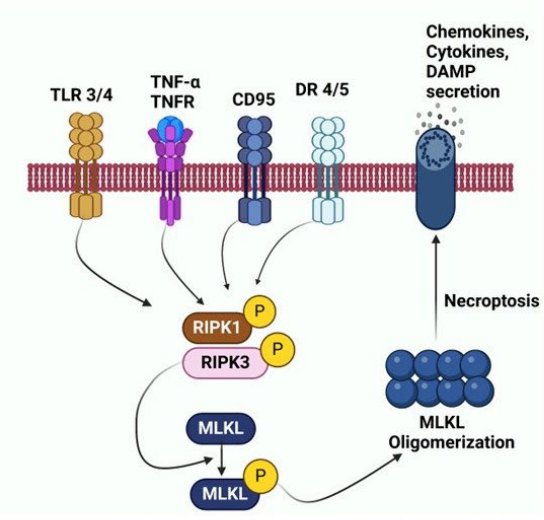
## P7. STRUCTURE-ACTIVITY RELATIONSHIP AND BINDING MODE ANALYSIS OF A NEW CLASS OF RECEPTOR-INTERACTING PROTEIN KINASE 3 INHIBITORS

**Manu Bala[1], Raghavender Boda[1], Anantha L. Duddupudi[1], Ghada Ali[1], Alexei Degterev[2], Siddharth Balachandran[3], and Gregory D Cuny[1]**

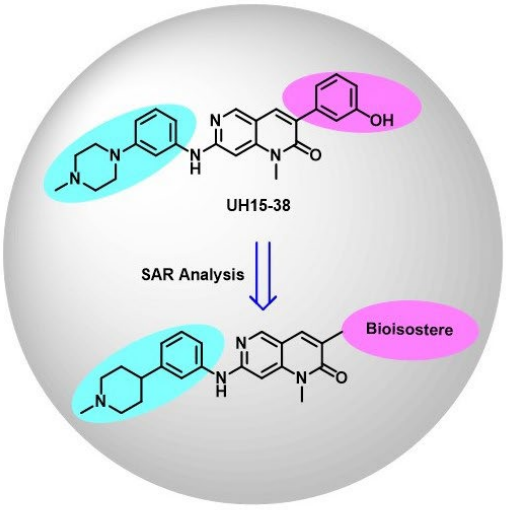
*[1]Department of Pharmacological and Pharmaceutical Sciences, College of Pharmacy, University of Houston, Houston, TX.*
*[2]Department of Developmental, Molecular & Chemical Biology, Tufts University School of Medicine, Boston, MA;*
*[3]Center for Immunology, Fox Chase Cancer Center, Philadelphia, PA.*

Necroptosis is a programmed cell death triggered by death receptors when apoptosis fails. It has been linked to numerous diseases, such as cancers, liver diseases, cardiovascular diseases, neurodegenerative disorders, pancreatic diseases, lung diseases, and kidney diseases. Necroptosis is highly dependent on the protein receptor-interacting protein kinase 3 (RIPK3) and its substrate mixed lineage kinase domain-like (MLKL) pseudo-kinase, the fundamental players of the necroptotic pathway. Activated RIPK3 leads to MLKL phosphorylation, which results in MLKL oligomerization and translocation to the plasma membrane, triggering cell rupture and release of chemokines, cytokines, and damage-associated molecular patterns (DAMPs).

Our previous studies identified UH15-38 as a potent inhibitor of RIPK3-mediated necroptosis (e.g., TNF-induced cell death in FADD-deficient JK cells), with an $IC_{50}$ of 205 nM. Herein, we report a structure–activity relationship (SAR) and binding mode analysis of UH15-38 and its analogs. Substitution of the phenol ring with a bioisostere and incorporating a piperidine moiety at the 3- or 4-positions of the solvent-exposed phenyl ring resulted in MB-2-03 that demonstrated significantly enhanced RIPK3 inhibitory activity ($IC_{50}$ of 49 nM). Molecular docking studies of the optimized compound MB-2-03 demonstrated a strong binding affinity to the DFG-in active conformation of RIPK3, consistent with the binding mode of the lead compound UH15-38.



Molecular Mechanism of Necroptosis



## P8. MULTI-KINASE INHIBITION FOR ADVANCED TREATMENT OF RESISTANT BREAST CANCER

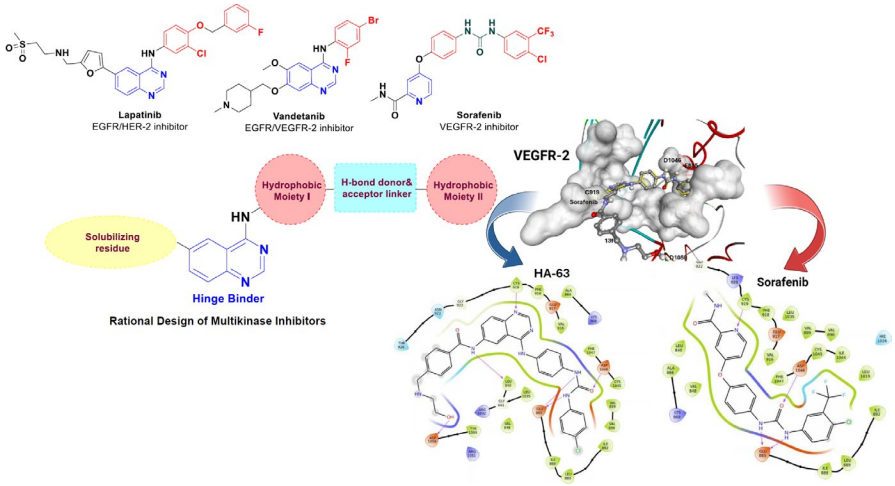
**Mostafa M. A. Aref, Md Emran Hossain, Eneye D. Ajayi, Rokaia Abdullah, Hamed I. Ali***

*Department of Pharmaceutical Sciences, Irma Lerma Rangel School of Pharmacy, Texas A&M University, College Station, TX, USA.*

Tyrosine kinases (TKs) are central mediators in breast cancer progression, playing pivotal roles in cell proliferation, survival, and metastasis. The dysregulation and overexpression of these kinases are hallmark features in resistant breast cancer subtypes. By targeting multiple oncogenic kinases simultaneously, multikinase inhibitors represent a promising therapeutic approach. The 4-substituted quinazoline core has emerged as a privileged scaffold in the design of TK inhibitors due to its favorable pharmacokinetic profile and high binding affinity.

We aimed to rationally design multitargeted kinase inhibitors capable of overcoming resistance mechanisms in aggressive breast cancers. Special emphasis was placed on inhibiting HER2 and angiogenic kinases such as VEGFR2 (KDR) and FLT3, which are integral to tumor growth and vascularization. To develop quinazoline-based small-molecule inhibitors, a structure-based drug design strategy was adopted. Key pharmacophoric features common to known multitarget TK inhibitors were incorporated. The synthesized compounds were subjected to in vitro kinase profiling, metabolic stability testing, and cytotoxicity assays in HER2-positive and triple-negative breast cancer (TNBC) cell lines. Several novel analogs were synthesized and evaluated. Notably, compound **HA-63** inhibited 8 out of 23 tested kinases, including HER2, KDR, FLT3, FLT4, Kit, PDGFR, EGFR, and FLT1. **HA-66** exhibited the most potent HER2 inhibition ($IC_{50}$ = 17.5 µM), while **HA-73** showed superior VEGFR inhibition ($IC_{50}$ = 1.3 µM). Metabolic and cellular assays confirmed the selectivity and potency of these compounds. Compounds **HA-153** and **HA-157** demonstrated selective cytotoxicity toward breast cancer cells, especially TNBC. **HA-157** exhibited potent Multikinase inhibition, with 96% EGFR, 68% HER2, 82% HER4, and 60% KDR at 10 µM.

This study introduces novel quinazoline-based multitarget inhibitors with promising therapeutic potential for resistant breast cancer, particularly TNBC. Compound **HA-157** emerges as a strong candidate for further lead optimization.

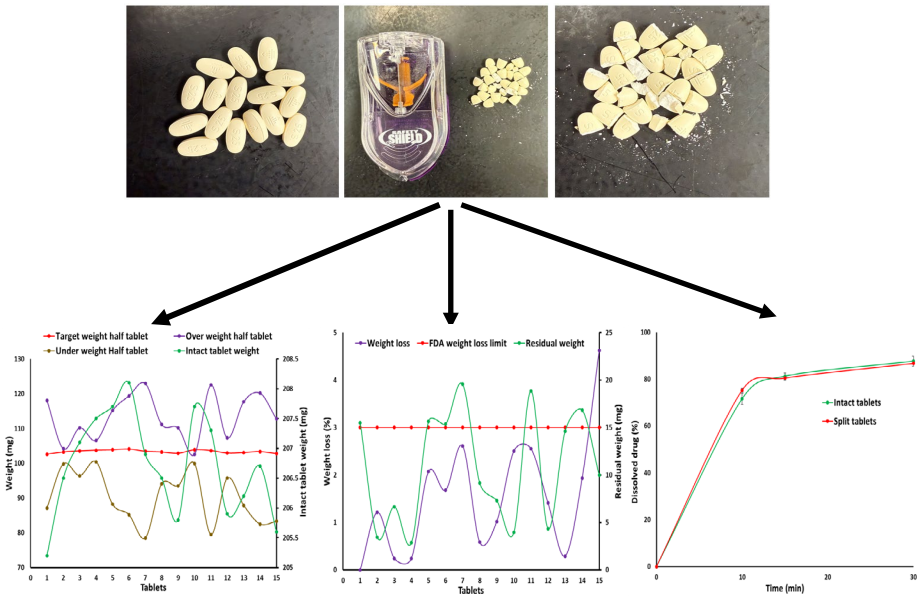


## P9. EFFECT OF JARDIANCE TABLET SPLITTING ON SPLITABILITY, WEIGHT VARIATION, ASSAY, AND DISSOLUTION

**Andrew S. Tenpas, Tahir Khuroo, Ziyaur Rahman, Mansoor A. Khan**

*Irma Lerma Rangel College of Pharmacy, Texas A&M Health Science Center, Texas A&M University, College Station, TX 77843, USA*

To save money on prescription drugs, consumers are often encouraged to split tablets. One such drug is empagliflozin (*Jardiance*), a popular medication for type 2 diabetes mellitus, chronic kidney disease, and heart failure. Due to their unscored and film-coated structure, the manufacturer warns that Jardiance tablets "*should be taken whole and should not be cut or divided*." Despite this warning, the practice commonly occurs. Both the U.S. Food and Drug Administration (FDA) and the United States Pharmacopeia (USP) have established quality requirements for tablet splitting, including weight variation, weight loss during splitting, friability, content uniformity, assay, and dissolution. In this study, we evaluated those characteristics in fifteen intact and thirty split tablets of Jardiance. Weight variation, content uniformity, and assay followed USP standards, while dissolution was performed using the USP Apparatus 2 Method. Content uniformity, assay, and dissolution samples were analyzed by ultra-high liquid chromatography. Our analytical results were mixed. First, split tablets failed to meet the 3% weight loss and weight variation limits stipulated by the FDA. Second, the friability (or tendency to break) of intact and split tablets met the 1% limit established by the USP. Third, both split and unsplit tablets met the USP's 85-115% content uniformity limit. Finally, both tablet types met FDA dissolution requirements. Though our weight loss and variation findings underscore how patients may struggle with splitting Jardiance tablets and receiving consistent doses, the real-world clinical or therapeutic implications of inconsistent tablet splitting remain unclear.



## P10. USE MAMMALIAN CELL-BASED ENZYMES FOR THE SYNTHESIS OF O-LINKED GLYCOPEPTIDE

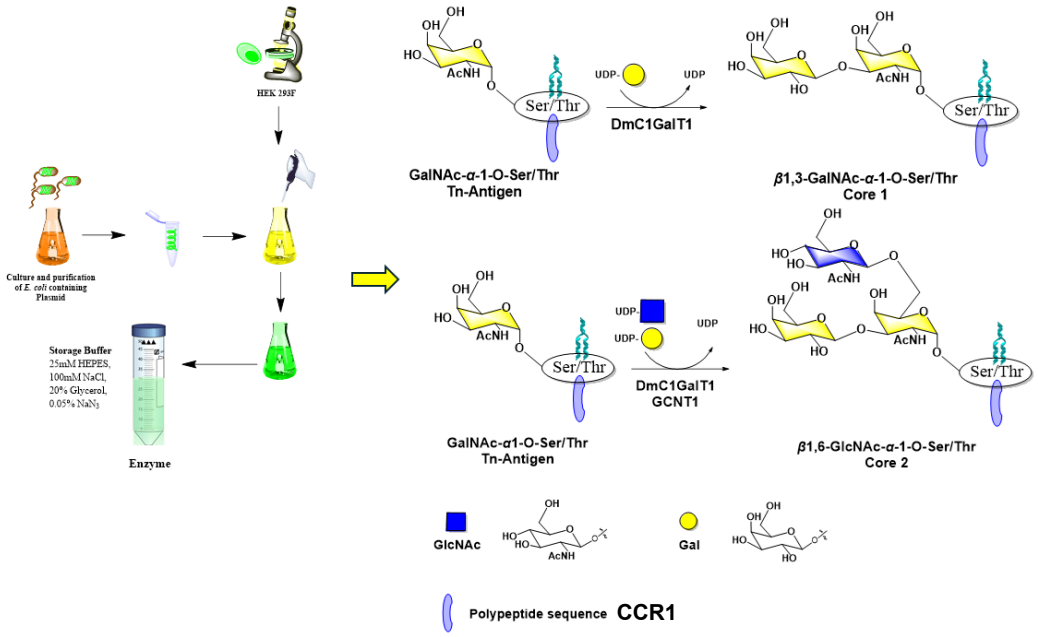
**Nana Yang[1], Ousman Boye, Hailiang Joshua Zhu***

*Department of BioMolecular Sciences, School of Pharmacy, The University of Mississippi*

Carbohydrates play a pivotal role in biology, extensively participating in critical biological processes such as energy metabolism, cellular structure assembly, signal transduction, and immune regulation. In particular, **O-glycosylation** commonly initiates with **N-acetylgalactosamine (GalNAc)**, which forms the **Tn antigen (GalNAc-*α*-1-O-Ser/Thr)** as a scaffold for glycan elongation. In normal cells, the Tn antigen can be further modified into complex structures like **Core 1** and **Core 2 glycans**, which are essential for physiological functions including intercellular signaling and immune modulation.

The biosynthesis of glycopeptides is mediated by specific **glycosyltransferases**. For instance, **DmC1GalT1** catalyzes the formation of a ***β*1,3-glycosidic bond** between UDP-Gal and glycopeptide substrates, while **GCNT1** mediates the linkage of UDP-GlcNAc to glycopeptides via a ***β*1,6-glycosidic bond**. Thus, investigating glycopeptide synthesis holds significant scientific value.

Our research group has successfully synthesized part of the **CCR1** sequence and achieved high-level expression of **DmC1GalT1** and **GCNT1** in HEK293F cells, with confirmed enzymatic activity. In future studies, we aim to complete the synthesis of **CCR1** glycopeptides and their derivatives and to investigate the biological activity of site-specific threonine-linked glycopeptides at different sequence positions to further elucidate their functional roles.



## P11. BINDING OF BRYOSTATIN-1 WITH THE $C_1C_2B$ DOMAINS OF MUNC13-1

**Netra P. Neupane[1], Sunil Lingaraju[1], Soni Kaundal[2], B.V. Prasad[2] and Joydip Das*[1]**

*[1]Department of Pharmacological and Pharmaceutical Sciences, College of Pharmacy, University of Houston, Houston, TX 77204.*
*[2]Verna and Marrs McLean Department of Biochemistry and Molecular Pharmacology, Baylor College of Medicine, Houston, TX 77030.*

Munc13-1 is a presynaptic active-zone protein essential for priming synaptic vesicles and enhancing neurotransmitter release in the brain. Munc13-1's role has been implicated in several neurodegenerative diseases. Munc13-1 contains a regulatory $C_1$ domain where the activators, diacylglycerol and phorbol ester, bind. The $C_2B$ domain of Munc13-1 has a unique $Ca^{2+}$ binding site constituted by an amphipathic α-helix. During the activation of Munc13-1, both $C_1$ and $C_2B$ domains bind to the plasma membrane. Bryostatin-1 activates Munc13-1 by binding to its regulatory $C_1$ domain. Recent preclinical studies on Alzheimer's disease suggested that bryostatin-1 could enhance neurotransmitter release. We hypothesized that bryostatin-1's neuroprotective effects are through its interaction with Munc13 1. The objective of this study is to understand how bryostatin-1 binds to the $C_1C_2B$ domains of Munc13-1 and activates it.

Bryostatin-1 was docked into the $C_1C_2B$ system, and a molecular dynamics (MD) simulation was performed by building a natural lipid membrane system. To measure binding affinity C1-C2B-MBP fusion protein was expressed in *E. coli* by cloning the Munc13-1 gene into the pET-28a (+)-TEV vector, purified using affinity and size exclusion chromatographic techniques, and characterized by SDS-PAGE. The MBP tag was cleaved using TEV protease to obtain pure C1-$C_2B$ protein.

Bryostatin 1 interacts with the C1 domain by forming three hydrogen bonds with Ala591, Thr575, Ile590, and Trp588, forming hydrophobic interactions. The $Ca^{2+}$ holding loop of the $C_2B$ domain was highly involved in interacting with the plasma membrane. The protein expression was optimized with a yield of 2 mg/L.

We have identified bryostatin 1 binding residues in Munc13-1 and purified the $C_1C_2B$ protein for functional and structural studies. This study expounds the role of $C_1$ and $C_2B$ domain residues in bryostatin-1-induced activation mechanisms that may lead us to develop therapeutics for neurodegenerative disorders in the future.

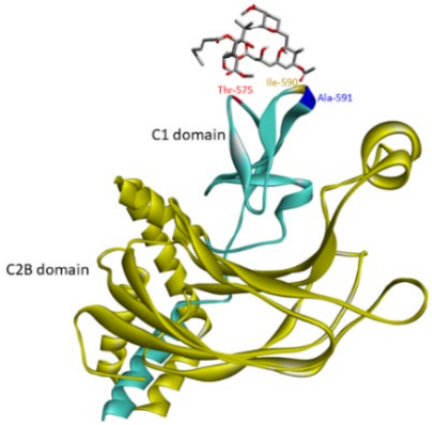


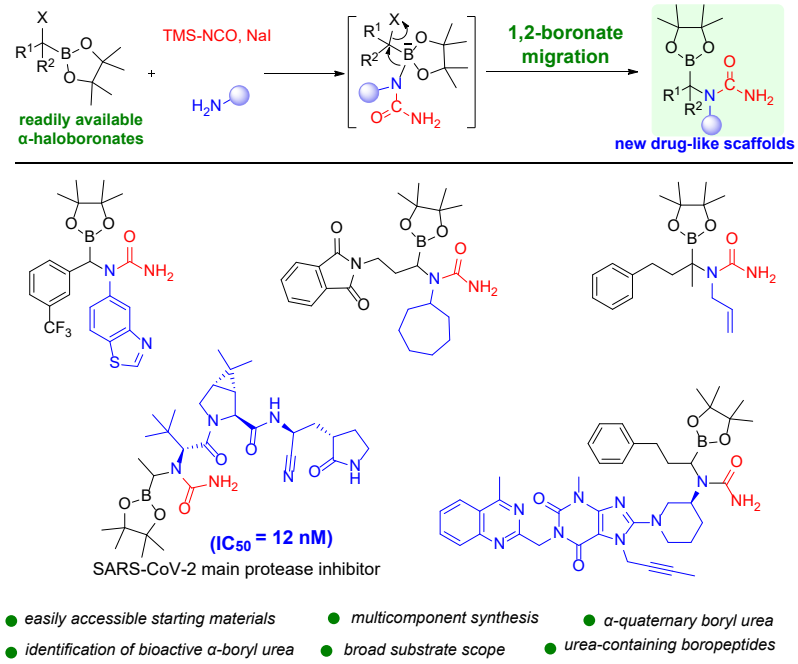

*Fig. 1 Bryostatin-1 interaction with $C_1C_2B$ domains of Munc13-1*

## P12. FACILE ONE-POT SYNTHESIS OF α-BORYL UREAS TO UNCOVER A POTENT MAIN PROTEASE INHIBITOR

Yusif I. Gyasi,[†, 1] Satyanarayana Nyalata,[†, 1] Sophea Pa,[1] Disni Gunasekera,[1] Veerabhadra R. Vulupala,[1] Nagarjun R. Mallampudi,[1] and Shiqing Xu*[,1,2]

[1]*Department of Chemistry, Texas A&M University, College Station, Texas 77843, United States*
[2]*Department of Pharmaceutical Sciences, Irma Lerma Rangel College of Pharmacy, Texas A&M University, College Station, Texas 77843, United States*

The development of efficient synthetic methods for α-boryl ureas is of significant interest due to their potential as drug-like scaffolds in medicinal chemistry. This study presents a multicomponent synthesis of α-boryl ureas from widely available α-haloboronates. The method leverages *in situ* generation of nucleophilic urea intermediates through the reaction of trimethylsilyl isocyanate, sodium iodide, and diverse amines, facilitating the formation of α-boryl ureas via 1,2-boronate migration under mild conditions. The broad substrate scope and functional group tolerance of this protocol enable the synthesis of diverse α-boryl ureas, including biologically relevant molecules and late-stage pharmaceutical derivatives. To showcase the potential of this methodology in drug discovery, an α-boryl urea analog of nirmatrelvir, a SARS-CoV-2 main protease inhibitor, was synthesized, demonstrating enhanced potency ($IC_{50}$ = 12 nM) compared to nirmatrelvir. This work not only offers a streamlined, direct approach for the preparation of synthetically challenging α-boryl ureas with broad structural diversity but also underscores the importance of α-boryl ureas as valuable scaffolds for the development of new therapeutics.

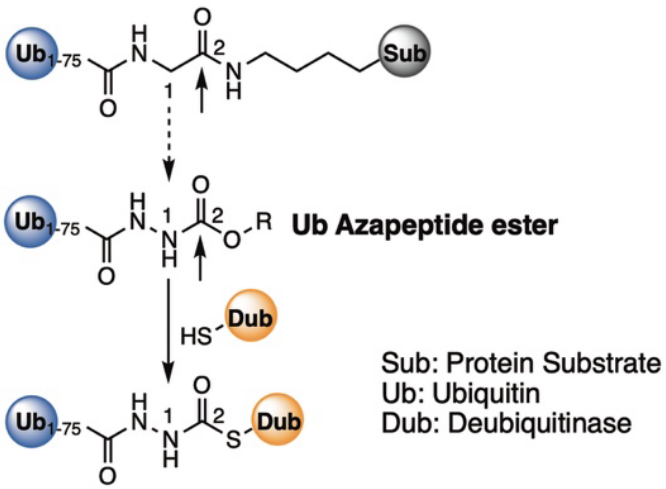


## P13. UBIQUITIN AZAPEPTIDE ESTERS AS NEXT-GENERATION ACTIVITY-BASED PROBES FOR CYSTEINE ENZYMES IN THE UBIQUITIN SIGNAL PATHWAY

**Saibal Chanda[1], Sandeep Atla[2], Satyanarayana Nyalata[2], Xinlei Sheng[3], Yingming Zhao[3] and Wenshe Ray Liu[1,2]**

*[1]Department of Biochemistry and Biophysics, Texas A&M University, College Station, TX 77843,*
*[2]Texas A&M Drug Discovery Center and Department of Chemistry, Texas A&M University, College Station, TX 77843,*
*[3]Ben May Department of Cancer Research, The University of Chicago, IL 60637*

Ubiquitination is a pivotal cellular process that controls protein homeostasis and regulates numerous biological functions. Its pathway operates through a cascade of enzyme reactions involving ubiquitin-activating (E1), ubiquitin-conjugating (E2), and ubiquitin-ligating (E3) enzymes and deubiquitinases (DUBs), many of which are cysteine enzymes. Activity-based ubiquitin probes were previously developed for profiling these enzymes. However, most conventional probes do not mimic natural enzyme−substrate interactions and involve chemical mechanisms different from enzyme catalysis. Their uses potentially affect the comprehensiveness of enzyme profiling results. The current study introduces a novel class of activity-based ubiquitin probes, ubiquitin azapeptide esters, designed to overcome these limitations. These probes incorporate an azaglycine ester at the ubiquitin *C*-terminus. They structurally mimic a ubiquitinated protein substrate and react with a cysteine enzyme via a mechanism like enzyme catalysis. It was demonstrated that ubiquitin azapeptide esters are reactive toward a large variety of DUBs and several tested E1, E2, and E3 enzymes as well. Compared to a conventional probe, ubiquitin propargylamine, ubiquitin azapeptide esters generally provide superior labeling and profiling of active cysteine enzymes in the ubiquitination/deubiquitination cascade in both HEK293T cells and mouse tissue lysates. Activity-based protein profiling using these probes in mouse tissue lysates also revealed distinct patterns of labeled enzymes, confirming their potential in understanding the unique roles of these enzymes in different tissues.



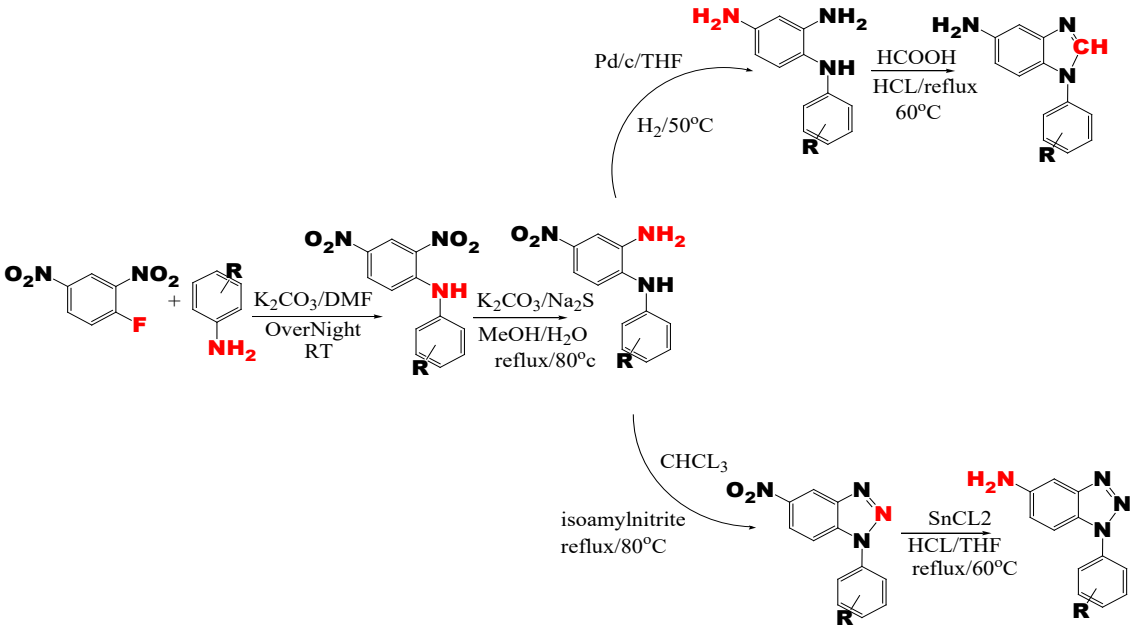
## P14. SYNTHESIS AND PRELIMINARY EVALUATION OF NOVEL HETEROCYCLIC COMPOUNDS WITH POTENTIAL ANTICANCER ACTIVITY

**Ahmed Ashraf Elsyyad[1], Shiqing Xu[2] and Sameh Abdelwahed[1]**

*[1]Department of Chemistry, College of Arts and Sciences, Prairie View A & M University, TX.*
*[2]Department of Chemistry, College of Arts and Sciences, Texas A & M University, TX.*

We have developed an efficient synthetic route to a novel class of benzimidazole and benzotriazole derivatives from aniline precursors, achieving excellent yields (80–90%) with structures confirmed by NMR spectroscopy. Based on their unique heterocyclic architectures and structural analogs known for anticancer properties, these compounds are strongly anticipated to exhibit activity against cancer cell lines.

Current efforts are focused on comprehensive biological screening to validate their therapeutic potential. Due to the proprietary nature of this research, detailed mechanistic targets and screening data are reserved for future disclosure.

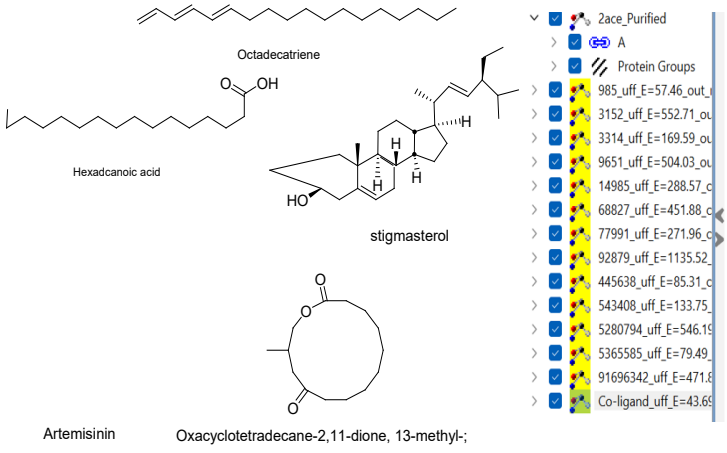


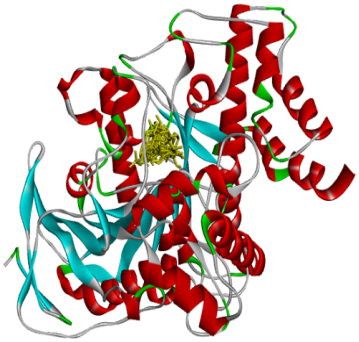
## P15. BINDING AFFINITY ANALYSIS OF BIOACTIVE COMPOUNDS AS ACETYLCHOLINESTERASE INHIBITORS IN ALZHEIMER 'S DISEASE MANAGEMENT.

**Caleb Joel Nwaogwugwu[1,2], Chukwudoru Chieme Sunday[3], Sameh, Abdelwahed[1]**

[1]*Department of Chemistry, College of Arts and Sciences, Prairie View A & M University, TX*
[2]*Abia State University, Uturu, Abia State, Nigeria.*
[3]*Federal University of Technology, Owerri, Imo State, Nigeria.*

This study aimed to evaluate the binding affinities and molecular interactions of selected bioactive compounds originally derived from medicinal plants with the acetylcholinesterase enzyme (PDB ID: 2ACE), to identify promising candidates for Alzheimer's disease therapy.
Molecular docking techniques were employed to investigate the interactions of selected anticholinesterase compounds with the active site of acetylcholinesterase. Binding energies and key molecular interactions were analyzed to determine their inhibitory potential.
Among the compounds assessed, artemisinin demonstrated the strongest binding affinity (-9.2 kcal/mol), engaging key residues Phe330 and Trp84 through van der Waals, pi-alkyl, and pi-sigma interactions. Oxacyclotetradecane-2, 11-dione, 13-methyl- and alpha-tocopherol followed with binding affinities of -8.8 kcal/mol and -8.3 kcal/mol, respectively. Galantamine, used as a reference drug, displayed a binding affinity of -8.2 kcal/mol, confirming the docking protocol's reliability. Other compounds, including hexadecenoic acid (-6.6 kcal/mol), hexadecanoic acid (-6.5 kcal/mol), and E-11, Z-13-octadecatriene (-6.3 kcal/mol), showed moderate interactions, while stigmasterol exhibited the weakest affinity (-1.9 kcal/mol), suggesting limited inhibitory activity.
The findings highlight artemisinin, oxacyclotetradecane-2,11-dione, and alpha-tocopherol bioactive compounds derived from medicinal plants as promising acetylcholinesterase inhibitors. These compounds warrant further investigation as potential therapeutic agents in the management of Alzheimer's disease.



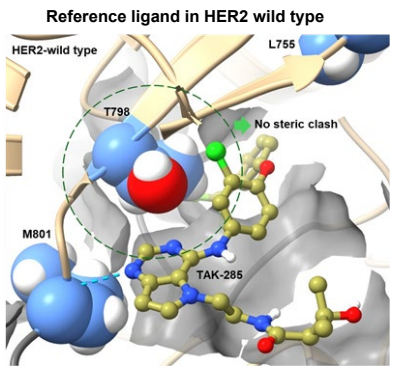
**Bound Ligands to the Active site**

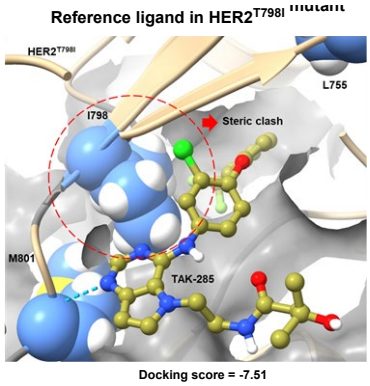
## P16. A STRUCTURE-BASED STRATEGY TO COMBAT ANTI-HER2 RESISTANCE IN HER2-POSITIVE BREAST CANCER

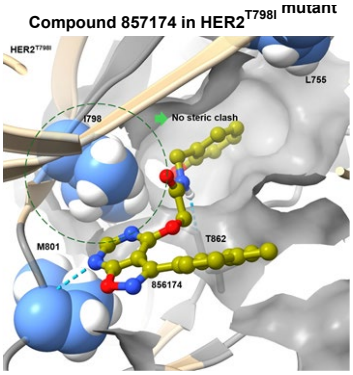
**Wafa Masoud[1], Eneye D. Ajayi[2], Radwan Alnajjar[3], Hamed I. Ali[2*]**

*[1]Department of Pharmaceutical Sciences, PharmD Program, School of Health and Medical Science, Libyan International University, Benghazi, Libya*
*[2]Department of Pharmaceutical Sciences, Irma Lerma Rangel College of Pharmacy, Texas A&M University, College Station, TX, USA*
*[3]CADD Unit, Faculty of Pharmacy, Libyan International University, Benghazi, Libya*

Mutations in the HER2 gene play a significant role in the resistance to HER2-targeted therapies across various cancers, particularly breast cancer (BC). These mutations disrupt the regulation of HER2, rendering it unresponsive to drugs such as Lapatinib. Specific mutations, including T798I, T987M, and L755S within the HER2 kinase domain, create steric hindrance that obstructs the binding of inhibitors. This study aimed to design novel analogs of Lapatinib that could effectively bind to the $HER2^{T798(M)I}$ and $HER2^{L755S}$ mutants, thereby reducing resistance to HER2-targeted therapies in HER2-positive BC. We conducted a virtual screening of 1.6 million compounds against these HER2 mutants using Glide scoring functions (HTVS, SP, and XP) within the Schrödinger software suite. The top-scoring compounds were then analyzed for crucial protein-ligand interactions and assessed for binding stability through molecular dynamics simulation (MDS). The pharmacokinetic properties of the selected compounds were further evaluated using Swiss ADME. Among the ten screened compounds, several displayed superior binding potentials to $HER2^{T798I}$ compared to the reference drug. The most promising candidate, Compound 856174, achieved a high docking score of -9.921 kcal/mol and formed crucial hydrogen bonds with key residues (THR 862, MET 801). Additionally, Compound 856174 complex with the $HER2^{T798I}$ mutant exhibited high stability when subjected to a 300 ns molecular dynamics simulation. Data from Swiss ADME indicated that Compound 856174 possesses moderate solubility, high gastrointestinal absorption, and low hepatotoxicity. It is classified as non-toxic (Class VI, $LD_{50}$ > 5000 mg/kg). This study identified Compound 856174 as a potential candidate for overcoming resistance to anti-HER2 therapies by inhibiting $HER2^{T798I}$. Ongoing in silico studies aim to identify additional potential inhibitors targeting $HER2^{L755S}$ and $HER2^{T798M}$ mutants. Further in vitro and in vivo studies will be performed to validate these findings.



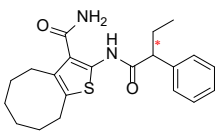
## P17. EXPLORING THE POTENTIAL OF SELECTIVE AGONISTS OF CANNABINOID $CB_2$ RECEPTOR IN TREATMENT OF PANCREATIC CANCER AND PAIN

**Zhixing Wu,[1] Vikas Mishra[1] Sujana Sri Immaldi,[1] Caitlin Scott[2], Deborah Kendall[2], Aron Lichtman[3], Maribel González-García[4], Hua Yang[5], Dai Lu[1]**

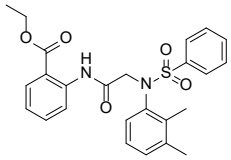
*[1]Department of Pharmaceutical Sciences, Rangel College of Pharmacy, Texas A&M Health Science Center, Kingsville, TX. [2]Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut, Storrs, Connecticut. [3]School of Medicine, Virginia Commonwealth University, [4]Chemistry Department, Texas A&M University at Kingsville, [5]MD Anderson Cancer Center*

The cannabinoid $CB_2$ receptor is one of the two primary G-protein-coupled receptors (GPCRs) in the endocannabinoid system (ECS). This complex cell-signaling network is key in regulating various physiological processes, including immune response, inflammation, pain, and tissue repair. Unlike the $CB_1$ receptor, which is predominantly found in the central nervous system and is responsible for the psychoactive effects of cannabinoids, the $CB_2$ receptor is primarily expressed in peripheral tissues, especially within the immune system, including the spleen, tonsils, and immune cells such as macrophages and B cells. $CB_2$ receptor plays a significant role in the modulation of pain, particularly in the context of inflammation and neuropathic pain**.** $CB_2$ receptor is **e**xpressed in pancreatic tissue, and its expression is often higher in pancreatic cancer cells compared to normal pancreatic cells. These triggered our interest in the potential of targeting $CB_2$ receptors for pancreatic cancer treatment and pain management in cancer patients.

In collaboration with industry partners, a compound library (~2,000 compounds) was screened, and two highly selective $CB_2$ agonists (*i.e.,* BDN053042 and CSC053411) were identified. We carried out a preliminary SAR investigation and explored the concept of using $CB_2$ receptor selective agonists for dual applications, including suppression of pain and pancreatic cancer, and found that $CB_2$ selective ligands can suppress chemotherapeutic-induced neuropathic pain and promote the apoptosis of pancreatic cancer cells.




BDN053042

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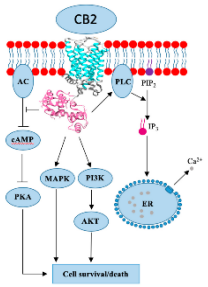
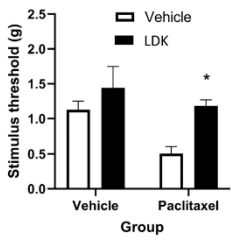
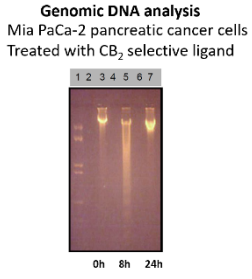



$CB_2$ selective ligand LDK suppressed neuropathic pain induced by paclitaxel.



## P18. TARGETING KRAS-MUTANT AND CHEMORESISTANT METASTATIC COLORECTAL CANCER

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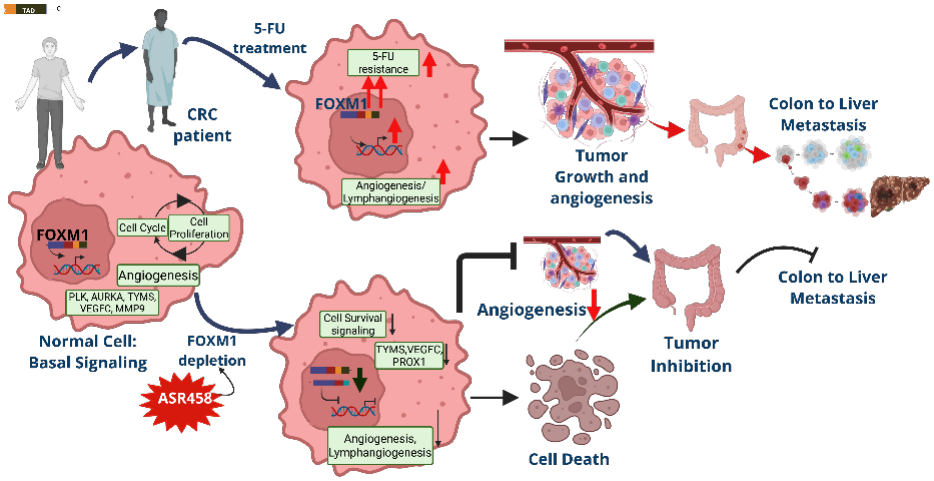
Colorectal cancer (CRC) is a leading cause of mortality in the United States. mCRC poses a critical clinical challenge due to its poor long-term outcomes and limited therapeutic responsiveness, particularly among patients harboring KRAS mutations. KRAS-mutant tumors, which comprise nearly 50% of all CRC cases, are intrinsically resistant to anti-EGFR therapies. Standard treatment regimens, including 5-fluorouracil (5-FU) in combination with the anti-angiogenic agent bevacizumab, offer modest progression-free survival benefits. FOXM1 (Forkhead Box M1) has emerged as a master regulator of both chemoresistance and lymphatic metastasis in several solid tumors, including colorectal cancer. Consequently, we have identified novel inhibitors, ASR458 and SAC53, which effectively inhibit FOXM1 expression and significantly reduce growth in metastatic CRC and 5FUR-CRC cell lines and tumors. In this study, we conducted cell viability assays in metastatic CRC, 5FU-resistant CRC, and normal colon epithelial cells, followed by Western blotting, immunohistochemistry, FACS analysis, and xenograft studies.

Our results show that FOXM1 expression is markedly elevated in patients with metastatic CRC compared to primary tumors. Notably, treatment with 5FU induced the expression of FOXM1 in mCRC cell lines. Our newly identified small molecules, ASR458 and SAC53, inhibited the growth of HCT-116 and HCT-5FUR at nanomolar concentrations without causing significant toxicity to normal colon epithelial cells. Their efficacy surpassed the currently available FOXM1 inhibitor, FDI-6, which requires μM concentrations to inhibit the growth of the 5FUR cell line. Western blot analysis corroborated that treating ASR458 and SAC53 led to a downregulation of FOXM1 expression, and in silico analysis suggested that ASR458 may directly bind to FOXM1. Moreover, ASR458 demonstrated the ability to inhibit tumor growth in mCRC xenograft models, while further studies on SAC53's efficacy are underway.

In conclusion, the suppression of FOXM1 in 5FUR-CRC suggests a promising therapeutic potential for overcoming chemoresistance in colorectal cancer.



## P19. RATIONAL DESIGN AND SYNTHESIS OF A SELECTIVE 5S-OXA1L INHIBITOR BASED ON SAR FOR TARETED LUNG CANCER TREATMENT

**Wissarut Wijitrmektong[1], Dimosthenis Koinas[1], Junichiro Takaya[2], Haoxin Li[2], Jarret R. Remsberg[2], Verena Albert[2], J.C. Ducom[2], Christopher M. Joslyn[2], Scott C Henderson[2], Kathryn S Spencer[2], Sabrina Barbas[2], Melissa A Dix[2], Kim Masuda[2], Enrique Saez[2], Kenji Sasaki[2], Christopher G. Parker[2], Benjamin F. Cravatt[2], Thomas W. Hanigan[1]**

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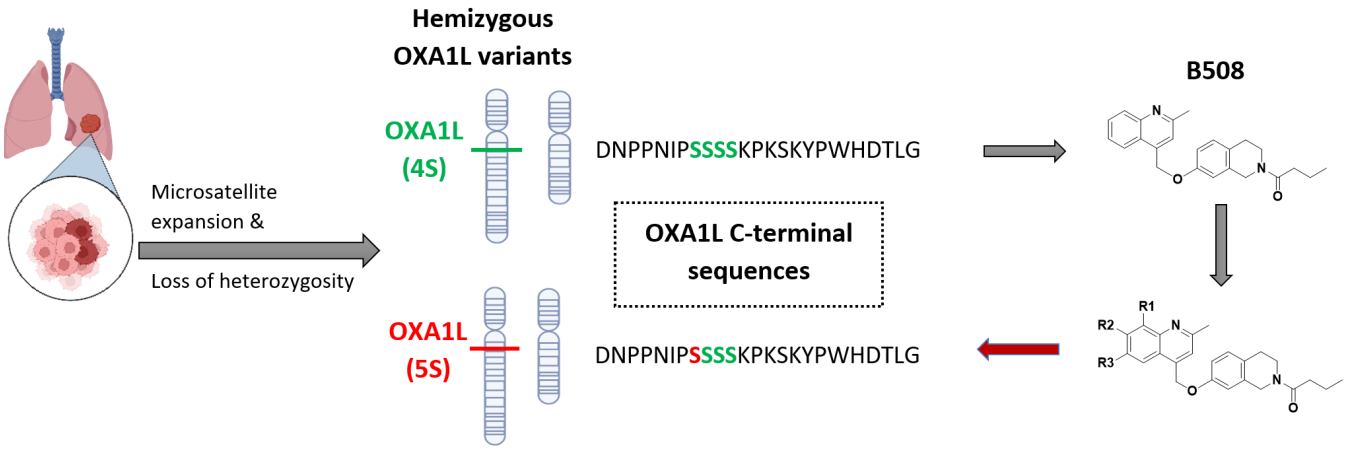
Mutations in cancer cells often lead to resistance against various chemotherapies, but also present opportunities to develop novel therapeutic strategies. OXA1L, a mitochondrion inner membrane insertase, is an essential enzyme navigating nascent subunit peptides of oxidative phosphorylation (OXPHOS) complexes (e.g., complex IV) into the mitochondria inner membrane. Notably, OXA1L is polymorphic in 30% in humans and its loss-of-function mutation underlies certain lethal recessive disorders, highlighting its critical role in cancer therapy. In non-small cell lung cancers, OXA1L frequently undergoes co-occurring collateral loss of heterozygosity with the oncogene NKX2-1 on the chr14q, leading to two hemizygous variants that differ in the number of tandem serine repeats (4S and 5S) at the C-terminal tail. Our previous study discovered a hit compound, B508, and its fully functionalized version, called B819, potently inhibiting a non-small cell lung cancer (NSCLC) H460 cell line by targeting the 4S-OXA1L variant ($GC_{50}$ = 34 and 50 nM, respectively). This study will use a SAR-guided strategy to synthesize a compound that selectively inhibits the 5S-OXA1L variant by exploiting the extra serine to study the treatment outcome compared to B508 and initiate a new modality of targeted cancer treatment based on mismatch repair deficiency (dMMR).



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