DEPARTMENT OF MEDICINAL CHEMISTRY

2017 Annual Report

Cancer and Cardiovascular Research Building

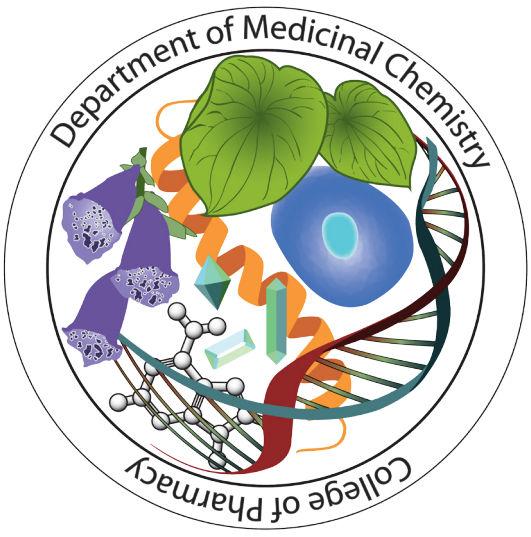
3321 Sixth Street Southeast

717 Delaware Building

717 Delaware Street Southeast

Weaver-Densford Hall

308 Harvard Street Southeast



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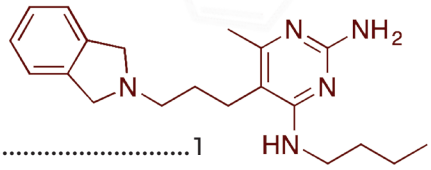
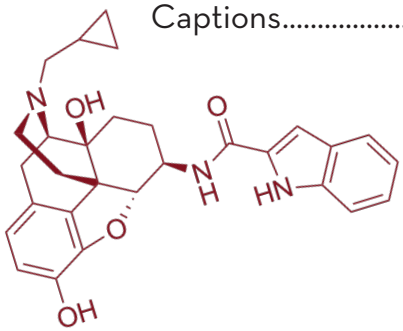




Letter from the Department Head

Dear Friends and Members of the Department:

As I have done in previous years, I want you to share with you some highlights of the year 2017.

This year we had 54 graduate students, 51 postdocs and research staff, 29 PharmD/ undergraduate students and nine visiting scientists from other countries in our Department. As you will note in this report, our students again received many prestigious fellowships and honors.

We continue to do well in garnering grant support from agencies such as the NIH, despite the challenging funding climate. The Department of Medicinal Chemistry and the Institute for Therapeutics Discovery and Development (ITDD) received more than $8.7 million in research support from external agencies in fiscal year 2017. The previous year it was $6.7 million.

The ITDD, funded in 2007 by Professor **Georg** and Dr. **Gurvich** celebrated its 10 year anniversary.

Staff member **Ann Howarth** was awarded a Meritorious Service Award for excellent work in the Department of Medicinal Chemistry and **Mary Crosson** was promoted to Administrative Manager 1.

The Department, under the leadership of Professor **Carston Wagner**, continues to play a leading role in the Chemical Biology Initiative. Professor **Natalia Tretyakova** is leading the Epigenetics Consortium and Professor **Rory Remmel** is involved in the Precision Medicine Initiative that is part of the University of Minnesota Grand Challenges initiative.

I was introduced into the ACS Medicinal Chemistry Division Hall of Fame, joining faculty members Dr. **Portoghese** and Dr. **Vince** in that distinction.

Dr. **Peter Dosa** from the ITDD was promoted to Research Associate Professor.

After a five-year phased retirement, Professor **Yusuf Abul-Hajj** retired June 30, 2017. A faculty member since 1968, Dr. Abul-Hajj has served in many leadership positions, including Head of the Department of Medicinal Chemistry for 21 years.

Dr. **Elizabeth Ambrose** and Dr. **David Ferguson** received College of Pharmacy Teaching Awards.

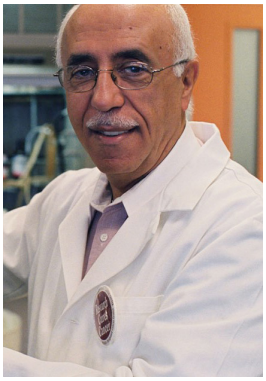
Dr. **Kathryn Nelson**'s, **Michael Walters**,' et al. 2017 article in the *Journal of Medicinal Chemistry* about curcumin was the most read article with 53,665 views online (April 2018).

I hope you will enjoy reading this Annual Report and share in our pride in the Department's accomplishments of 2017.

Gunda I. Georg, Department Head

Dr. Vadim Gurvich

Dean Lynda Welage



Dr. Yusuf Abul-Hajj

Dr. Todd Doran

Mission Statement

The mission of the Department of Medicinal Chemistry is to educate and train scientists of the highest caliber, to provide future pharmacy practitioners with the basis for understanding the relationships between molecular structure and drug action, and to achieve and perpetuate excellence in medicinal chemistry through chemical and biological research for the improvement of human health.

University News

Department of Medicinal Chemistry Head, Dr. **Gunda Georg** is serving on the campus-wide Grand Challenges Research Strategies group, which launched its second phase in 2017. The 2017 phase will focus on establishing grants and collaborative groups to address the challenges of *Assuring Clean Water and Sustainable Ecosystems* and *Fostering Just and Equitable Communities*.

The University of Minnesota joined the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), was created to respond to the accelerating demands of the healthcare industry and will be co-lead by Dr. **Vadim Gurvich**. The coalition is comprised of academic institutions, private companies, and government and nonprofit organizations that will work to advance medical treatment, economic development, and U.S. leadership in the biopharmaceutical industry.

The College of Pharmacy welcomed Dr. Lynda Welage as Dean after Dr. **Marilyn Speedie** stepped down in early 2017. Dr. Welage joins the college from the University of New Mexico, where she held the position of Dean of the College of Pharmacy since 2011. "We are confident that her leadership experience, research accomplishments, and collaborative working style will advance the excellence of the College of Pharmacy—building on the exceptional leadership of Marilyn Speedie," said Provost Karen Hanson in a released statement.

Coming and Going

Dr. **Yusuf Abul-Hajj** retired on June 30. A faculty member since 1968, Dr. Abul-Hajj has served in many leadership positions, including Head of the Department of Medicinal Chemistry for 21 years. Under his leadership, Medicinal Chemistry became one of the top ranked departments in the country and prepared numerous future medicinal chemists. He also served as Senior Editor of the *Journal of Medicinal Chemistry* from 1995 to 2012. For nearly 50 years, Dr. Abul-Hajj conducted groundbreaking research on the development of steroidal agents for the treatment of breast cancer as well as studying the underlying mechanisms involved in the genotoxicity and carcinogenicity of estrogen. In 2012, he co-authored the book, *From Digitalis to Ziagen*, which covers the history of Medicinal Chemistry at the college, including the establishment of the department as well as the leadership role the department and its faculty played in drug development. Dr. Abul-Hajj has received many awards and recognition throughout his career, including the Lawrence and Delores Weaver Medal, and was named a Fellow of both the American Association for the Advancement of Science and the American Chemical Society.

Dr. **Todd Doran** joined the department in July as an Assistant Professor, coming from the Department of Chemistry at the Scripps Research Institute in Florida. His experience includes specialization in diagnostic imaging, immunotherapeutics, organic synthesis, and high-throughput screening. His research focus is based on the exploration of the molecular-level events that underlie neurodegenerative diseases such as Alzheimer's and Parkinson's diseases.

Rita Stodolka joined the department as the National Institute for Pharmaceutical Technology and Education (NIPTE) Executive Office and Administrative Specialist. She joined the University after several years as a independent business consultant.

Erin Warholm-Wohlenhaus and **Megan Jensen** joined the department as Executive Office and Administrative Specialists for Weaver-Densford Hall and 717 Delaware Ave S.E. respectively. Erin brought with her eight years of University experience working at the University of Minnesota Press. Megan held student positions at the University before taking a full-time position in Professional Education at the Carlson School of Business Management. She brought with her five years of full-time experience.

Teaching and Service

Medicinal Chemistry faculty members taught numerous professional and graduate courses in 2017 and were recognized throughout the year for their insightful, balanced approaches to teaching and their dedication and attentiveness to students.

Dr. **Elizabeth Ambrose** was selected as Professor of Fall Semester 2017 by the class of 2019 and Dr. **David Ferguson** was selected by the class of 2021.

Faculty members also contributed to a variety of committees representing service to the Department, the University, the College of Pharmacy, national and professional organizations, and government entities. Additionally, faculty routinely served as peer reviewers for professional journals and as grant reviewers for government panels.

Dr. Elizabeth Ambrose

Dr. David Ferguson

Graduate Courses

- General Principles of Medicinal Chemistry I (MedC8001)
- General Principles of Medicinal Chemistry II (MedC 8002)
- Physical and Mechanistic Organic Chemistry (MedC 8050)
- Medicinal Chemistry Seminar (MedC 8100)
- BioAssays (MedC 8435)
- Molecular Targets of Drug Discovery (MedC 9753)
- Design of Cancer Immunotherapeutics (MedC 8461)
- Research in Medicinal Chemistry (MedC 8900)
- Nucleic Acids (MedC 8413)

Professional Courses

- Medicinal Chemistry Seminar (Phar 6150)
- Becoming a Pharmacist (Phar 6700)
- Integrated Biochemical Sciences (Phar 6702)
- Pharmaceutical Care Skills Lab I (Phar 6710)
- Medicinal Chemistry and Pharmacology of Cardiovascular Agents (Phar 6732)
- Cellular Metabolism and Nutrition (Phar 6734)
- Medicinal Chemistry and Neuropharmacology (Phar 6762)
- Biotechnology Derived Drugs (Phar 6766)
- Infectious Disease (Phar 6768)
- Therapeutics of Herbal and Other Natural Medicinals (Phar 5270)
- Applied Pharmaceutical Care [Chemistry/Mechanism of Oral Antibiotics] (Phar 6716)
- Pharm Care Skills Lab [Chemistry in Action] (Phar 6720)
- Principles of Med Chem [Essential Tools of Med Chem for the Profession] (Phar 6722)
- Principles of Pharmacology [Essential Tools of Pharmacology for the Profession] (Phar 6726)
- Immune System and Infectious Disease [Innate/Adaptive Immunity, Med Micro] (Phar 6724)
- Integrated Endocrinology [Steroids, Hormones and Growth Related Drugs] (Phar 6752)
- Diabetes and Metabolic Syndrome [Anti-diabetics] (Phar 6754)
- Oncology [Cancer Drugs, Mechanism of Action, Resistance] (Phar 6784)
- Drugs of Abuse [Chemistry, Pharmacology] (Phar 6908)

Drs. Georg and Gurvich

Dr. Rolf Hartmann

Dr. Kathryn Nelson

Dr. Michael Walters

Institute for Therapeutics Discovery and Development

The Institute for Therapeutics Discovery and Development (ITDD) continued its research projects in the discovery and advancement of drug design and provided services to the scientific communities of the University of Minnesota, the State of Minnesota, and private industry. The ITDD has continued its efforts towards developing non-hormonal male and female contraceptive agents, led by the ITDD's Director, Dr. **Gunda Georg**. The highly innovative and collaborative program has had continuous multi-million dollar funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) for over a decade.

Dr. Gunda Georg is also the Principal Investigator of a new National Institutes of Health NICHD U54 Center Grant for the creation of the Contraceptive Discovery, Development, and Behavioral Research Center (2017–2021). In addition to Drs. Gunda Georg, **Leigh Allen**, **Jon Hawkinson**, **Michael Walters**, and **Henry Wong**—all in the ITDD—the Center includes an additional five interdisciplinary groups that are involved in the discovery and development of non-hormonal male contraceptive agents and is investigating ways to improve contraceptive use.

The National Institute for Pharmaceutical Technology and Education (NIPTE), of which Dr. **Vadim Gurvich** is the executive director, was awarded $35 million in funding from the Food and Drug Administration (FDA), to be allocated over a 5-year period. The grant will support a multitude of different projects in the pharmaceutical field from improvements in manufacturing and technology to research and education. "We are very excited about the opportunity to continue this collaboration with the U.S. FDA," explains Dr. Gurvich, who is also the Principal Investigator on the grant. "The funding allows NIPTE faculty to contribute their research expertise, helping the FDA create policies in critical areas such as quality by design of complex pharmaceutical products, characterization of pharmaceutical materials, and formulation strategies like abuse deterrent products to combat opioid abuse. In addition, NIPTE will also address topics such as Quality Metrics and Quality Score Card as tools to improve surveillance and risk-based decisions. This brings our decade-long collaboration with the FDA to the next level, allowing us to make a bigger impact on quality, safety, and affordability of pharmaceutical products."

American Chemical Society Journals

The American Chemical Society (ACS) *Journal of Medicinal Chemistry* is the most-cited journal in medicinal chemistry and ranked as the top primary research journal in impact in its category. Dr. **Gunda Georg** is co-Editor-in-Chief with Shaomeng Wang at the University of Michigan Comprehensive Cancer Center. Dr. **Carrie Haskell-Luevano** serves as an Associate Editor. The journal office is located at the University of Minnesota.

The Philip S. Portoghese *Journal of Medicinal Chemistry*/Division of Medicinal Chemistry Joint Lectureship was awarded to Dr. Rolf Hartmann of the Department of Drug Design and Optimization at the Helmholtz-Institute for Pharmaceutical Research Saarland. The Lectureship is granted each year to individuals who have had a significant impact on medicinal chemistry research and was awarded at the ACS's annual fall meeting in Washington, D.C.

Dr. **Courtney Aldrich** has served as Editor-in-Chief of the *ACS Infectious Diseases* journal since its creation in 2015. The journal highlights the role of chemistry in the multidisciplinary field of infectious disease and published its 36th issue at the end of 2017.

Faculty and Staff Recognition: Awards and Promotions

Drs. **Kathryn Nelson** and **Michael Walters** were co-authors on the *Journal of Medicinal Chemistry*'s most highly-read article, "The Essential Medicinal Chemistry of Curcumin." J Med Chem, January 11, 2017.

Dr. **Gunda Georg** was inducted into the Medicinal Chemistry Hall of Fame at the Fall American Chemical Society Meeting in Washington, D.C. The Hall of Fame recognizes pioneers who have made impactful discoveries in the field of medicinal chemistry. There have been less than 100 inductees in the Hall of Fame since its inception in 1966. Dr. Georg joins Dr. **Philip Portoghese** who was inducted in 1990.

Dr. Georg was also selected as a STEM Research Exemplar. The Research Exemplar Project aims to interview awardees and identify the practices they use to lead and manage their research labs with professionalism and integrity.

Dr. **Yusuf Abul-Hajj** was selected to receive a Citation of Merit from the University of Wisconsin-Madison. Citations of Merit are awarded to individuals who have an outstanding record of contribution to pharmacy and society through research, teaching, or involvement in professional and community organization. Only an honorary degree constitutes a higher University honor than a Citation.

Dr. **Peter Dosa** was promoted to Research Associate Professor in July.

Dr. **Stephen Hecht** was named one of the 2017 Dean's Distinguished Research Lectureship Honorees, which recognizes the best research faculty in the basic and clinical sciences. To be considered, honorees must have the first or last author credits on a publication that has been cited at least 1,000 times by others.

Dr. **Rory Remmel** won the James R. Gillette Drug Metabolism and Disposition Best Paper of 2017 in the Metabolism category for his co-authored paper "CRISPR/Cas9 Genetic Modification of CYP3A5 *3 in HuH-7 Human Hepatocyte Cell Line Leads to Cell Lines with Increased Midazolam and Tacrolimus Metabolism."

Executive Office and Administrative Specialist **Ann Howarth** was awarded a Meritorious Service Award for excellent work in the Department of Medicinal Chemistry in 2016. The award ceremony took place during the 15th Annual College of Pharmacy Employee Day held on June 1 at the Glensheen Mansion in Duluth.

Dr. Peter Dosa

Dr. Stephen Hecht

Dr. Rory Remmel

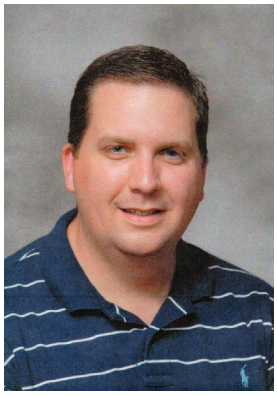
Dr. Courtney Aldrich

Faculty Recognition: In the News

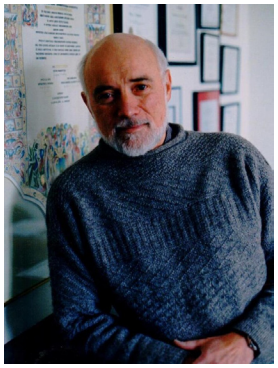
Dr. **Courtney Aldrich** was quoted in the article "'Magic Mushroom' Enzyme Mystery Solved" by *Chemical & Engineering News* discussing recent breakthroughs in identifying enzymes that characterize the psilocybin compound found in "magic mushrooms." As Dr. Aldrich explained in the article, "The new work lays the foundation for developing a fermentation process for production of this powerful psychedelic fungal drug, which has a fascinating history and pharmacology." He is also cited in the similar article by *Gizmodo*, "Scientists Finally Unlock the Recipe for Magic Mushrooms."

Drs. **Michael Walters**, **Gunda Georg**, and **Kathryn Nelson** were featured in multiple news articles to discuss and largely debunk the hyped health potential of curcumin, the most well-known chemical in turmeric. Their analysis suggests that the compound has far fewer potential applications as a pharmaceutical agent than recent literature has led consumers to believe:

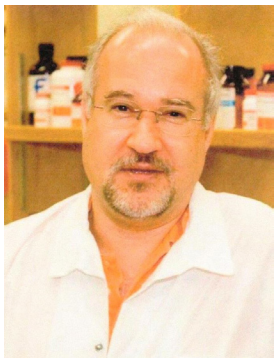
- *Forbes*, "Everybody Needs To Stop With This Turmeric Molecule."
- *Global News, CA*, "The Truth about Turmeric, the So-called Wonder Spice."
- *Health*, "Turmeric May Not Be a Miracle Spice After All."
- *Huffington Post*, "Turmeric May Not Be a Wonder Spice After All."
- *Nature*, "Deceptive Curcumin Offers Cautionary Tale for Chemists."
- *New York Magazine*, "Turmeric Might Not Have Magical Therapeutic Powers After All."
- *Quartz*, "Forget What You've Heard: Turmeric Seems to Have Zero Medicinal Properties."
- *Smithsonian Magazine*, "Turmeric May Be Tasty, But It's Not a Cure-All."
- *Refinery 29*, "Bummer: Turmeric Isn't The Cure-All We All Thought It Was."
- *Time*, "Turmeric May Not Be a Miracle Spice After All."
- *Daily Express*, "Cancer and Alzheimer's Disease: Is THIS Trendy Spice Really a Miracle Cure?"
- *The Washington Post*, "What Should You Make of the Health Claims for Turmeric?"



Dr. Daniel Harki



Dr. Philip Portoghese



Dr. Robert Turesky

Dr. **Daniel Harki** was mentioned in several articles discussing APOBEC, a fundamental antiviral enzyme and mechanism of the human immune system. APOBEC cytidine deaminases were studied extensively by Dr. Harki and implicated as potential sources of mutations in cancer cells. This research will be licensed to the startup ApoGen Biotechnologies, of which Dr. Harki is a co-founder, for its insight into the potential development of new therapeutics agents that could impede cancer mutation and drug resistance.

- *Business Wire*, "Accelerator Corporation Announces $7M Series A Investment in ApoGen Biotechnologies to Develop a New Class of Drugs Targeting Resistance to Cancer Therapy."
- *Minnesota Daily*, "UMN Startup Receives $7 Million to Create Drug for Cancer Treatment."

Dr. Harki was also mentioned in a *Twin Cities Business* article discussing his recent patent of a system that uses genetic analysis to quickly and efficiently assess the efficacy of cancer treatment in individuals on a case-by-case basis, "Mayo-U Of M Research On Assessing Anticancer Drug Effectiveness Advances."

Dr. **Gunda Georg** was featured in numerous media outlets this year to discuss her research on developing a male birth control pill, including:

- *Counsel & Heal*, "A Man Needs a Pill: The Race To Find A Male Contraceptive."
- *Bloomberg*, "Why We Can't Have the Male Pill."
- *CNN*, "This is Sex with Lisa Ling."
- *Star Tribune*, "Male Contraceptive Gaining Sex Appeal, Gustavus Survey Finds."

Dr. Gunda Georg was also cited in the Office of the Vice President for Research *Inquiry* article, "Bringing New Drug Therapies to Life" to explain the process of selecting and pursuing promising new areas of pharmaceutical research and development.

Dr. **Philip Portoghese** is mentioned in the *Twin Cities Business* article, "Could A Vaccine End The Opioid Epidemic?" as a member of the research team working to develop a vaccine that could block the effects of opioids and provide an alternative to current treatments which are in and of themselves addictive. The treatment will be filed for application with the U.S. Food and Drug Administration in the near future, which could allow it to enter the human clinical trial phase.

Dr. **Robert Turesky** was quoted in the *Washington Post* article "Evidence Grows Linking Grilled Meat and Cancer, But You Can Lower the Risk" discussing the cancer potential of chemicals that appear in meats that are cooked for a long time or at high temperatures.

Research Activities

Department of Medicinal Chemistry faculty produced 88 publications in more than 40 journals and presented at numerous conferences through oral and poster presentations in 2017.

Dr. **Courtney Aldrich**'s lab is developing new antibiotics for tuberculosis as well as other multidrug resistant bacterial pathogens. In the last year, they have also helped elucidate the mechanistic basis for antimicrobial activity of para-aminosalicylate, the potent synergy of trimethoprim-sulfamethoxazole, and are close to deciphering the mechanism of action of pyrazimamide. Their work integrates medicinal chemistry, enzymology, microbiology, mass spectrometry, and drug metabolism/pharmacokinetics. Current active drug discovery projects are focused on siderophore biosynthesis required for bacterial iron acquisition, biotin metabolism essential for lipid biosynthesis, and menaquinone biosynthesis necessary for bacterial energy metabolism. A new research direction was initiated in 2017 aimed at the design of selective molecules to inhibit production of virulence factors produced by the microbiome. Mechanism-based inhibitors (MBIs) that require enzymatic bioactivation for conversion to a reactive species, which covalently labels the enzyme active site, have captivated the Aldrich group for many years. In 2017, the Aldrich lab developed a general framework for MBI kinetic characterization aimed at rationally improving MBIs. Capping off a productive 2017, the Aldrich group also disclosed diphenyldisiloxane, a new reagent that allows recycling of phosphines in diverse phosphine-dependent reactions, using an elegant series of kinetic and mechanistic studies.

Dr. **Elizabeth Ambrose**'s lab has developed new, small molecules that inhibit the anthrax toxin lethal factor—a secretion from the bacilli that is responsible for anthrax-related mortality. These compounds show promise as anti-bioterror therapeutics that can be used at any stage of anthrax infection. Dr. Ambrose is also working on other anti-terrorism and homeland security-related projects including designing antidotes for the ricin toxin, and engineering enzymes as rapid decontamination solutions against organophosphate nerve agents. Additionally, working in the novel area of geopharmaceuticals, the Ambrose lab has identified key bioactive compounds in Baltic amber for their effects on inflammation, infection, and pain-related pathways.

Drs. Ambrose and **Peter Dosa** have been researching structural modifications to G protein-coupled receptors (GPCRs). They found that by creating even minute structural changes in the GPCRs, functional activity can switch from agonist to antagonist or vice versa. In studying these functional modifications, Drs. Ambrose and Dosa hope to vastly increase the versatility of GPCRs as therapeutic agents.

Dr. **Erin Carlson**'s lab is working to detect, interrupt, and exploit the master regulators of bacterial growth and communication for the identification of new antibiotics. Their research includes the use of mass spectrometry, informatics, and novel separation reagents to explore and interpret the molecular language used by bacteria to respond to environmental cues; the generation of chemical probes and inhibitors for the global profiling and inhibition of histidine kinases - a ubiquitous class of proteins essential for signal transduction in bacteria; exploring multi-protein systems that dictate bacterial growth and division in order to design selective probes for imaging and proteomics with specific focus on the penicillin-binding proteins; and exploring the molecular-level interactions between organisms and nanoparticles to guide the development of environmentally benign nanotechnology.

Dr. **Sunil David**'s lab is working toward discovering new adjuvant compounds that would modify the body's immune response to the Zika virus. Potential adjuvant candidates identified in this study, when added to a Zika vaccine, may stimulate human cells to fight against the virus.

Dr. **Mark Distefano**'s lab is studying protein prenylation, a modification process in eukaryotic cells that controls the activity of a range of proteins and is essential for processes like cell division and the differentiation and development of stem cells. By gaining further insight into the role and function of protein prenylation the lab is able to devise new approaches to the development of therapeutic drugs for cancer, infectious diseases, or Alzheimer's.

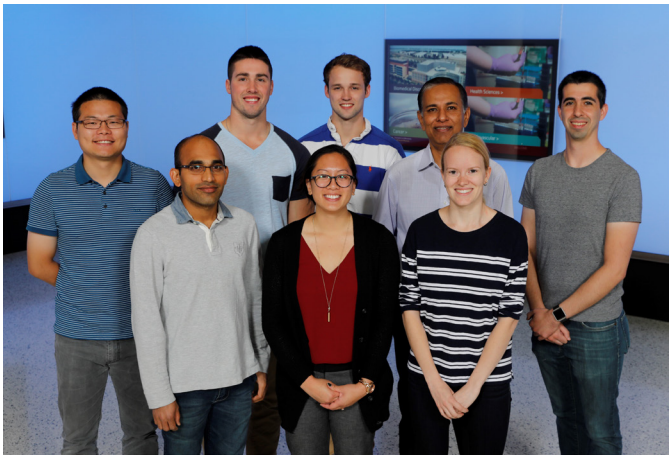
Dr. **Todd Doran** joined the Department in the summer of 2017. The Doran lab is using synthetic organic chemistry to probe neurobiological pathways, and ultimately trying to identify how these pathways contribute to neurodegeneration as we age. Specific processes that have been implicated in neurodegeneration include adaptive immune, redox homeostasis and the misfolded protein responses. Understanding how the biochemistry of the brain changes as we age, will aid in the design and development of early-stage diagnostics and therapeutics that stop or slow the progression of Alzheimer's and Parkinson's diseases.

Aldrich Lab

Ambrose Lab

Dr. Erin Carlson

Dr. Mark Distefano



David Lab

Doran Lab

Finzel Lab

Dr. David Ferguson

Dr. Stephen Hecht

Dr. Thomas Hoye

Dr. Lisa Peterson

Dr. **Barry Finzel**'s lab is conducting research on antagonists of CD44 receptors, which appear on the surfaces of cancer cells and promote metastasis and tumor growth. By interfering with interactions at the cellular level, these novel antagonists have the possibility of application in the treatment of chronic inflammation, cardiovascular disease, and cancer.

Dr. **David Ferguson**'s lab focuses on the application of chemistry to solve problems related to biomolecular structure, function, and activity, especially as it relates to drug design and discovery. His lab pioneered the development of structure-based models for opioid ligand design, described novel catalytic inhibitors of topoisomerase II for use in cancer treatments, and advanced the design of TLR7/8 immunostimulatory agents with cytokine specific attenuation in generating a robust immune response for the design of adjuvants.

Research in Dr. **Daniel Harki**'s laboratory focuses on the medicinal chemistry and chemical biology of small molecules, peptides, and oligonucleotides targeting DNA-interactive enzymes. Areas of particular focus include the development of chemical probes targeting APOBEC DNA cytosine deaminases, the utilization of electrophilic small molecules to target proteins associated with transcriptional initiation, and the development of novel nucleic acid-based probes for applications in modern biotechnology research.

Dr. **Carrie Haskell-Luevano**'s lab is studying agonist and antagonist ligands of the melanocortin pathway - a group of peptide hormones involved in the regulation of satiety, obesity, and energy homeostasis in humans. By understanding how such ligands interact with melanocortin receptors, the lab aims to challenge existing paradigms for ligand design and provide new tools for the development of therapeutics to combat obesity and type II diabetes.

Dr. **Stephen Hecht** is the project leader and Dr. **Natalia Tretyakova** one of the principal investigators on the program project grant "Mechanisms of Ethnic/Racial Differences in Lung Cancer Due to Cigarette Smoking," which examines the differences in susceptibility to lung cancer of smokers from different ethnic/racial groups based on studies of the metabolism of nicotine, 1,3-butadiene, NNK, and related toxicants and carcinogens in cigarette smoke. Dr. Hecht's laboratory is also carrying out studies on the metabolism and DNA binding of carcinogenic tobacco-specific nitrosamines, believed to play an important role in lung and oral cavity cancer in people who use tobacco products. The Hecht laboratory also evaluates toxicant and carcinogen exposure in users of e-cigarettes.

Dr. **Thomas Hoye**'s lab is studying the hexadehydro-Diels-Alder reaction - a novel method for generating highly reactive benzynes. These benzynes can be trapped to create a variety of polycyclic aromatic compounds, which have a number of applications including use in organic light emitting diodes, field-effect transistors, and photovoltaic cells. Alternatively, they can be captured to produce multi heterocyclic compounds having unprecedented structural motifs. Additional activities include the synthesis of sustainable polymers from biorenewable natural products (NPs); NP structure determinations, including lamprey pheromonal compounds; the spontaneous biosynthesis of cytotoxic NPs; and targeted nanoparticle delivery of antitumor agents to cancer stem cells.

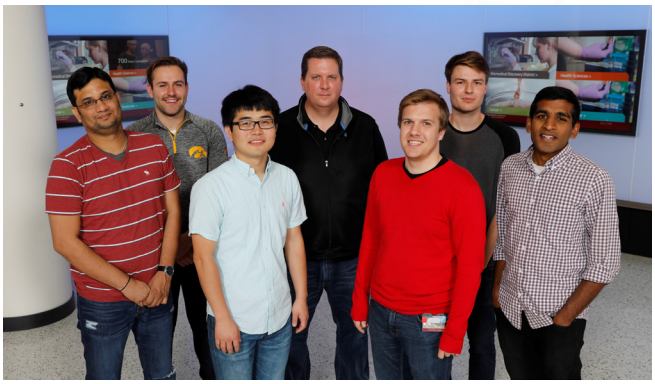
Dr. **Lisa Peterson**'s lab has been studying the prevalence of tobacco-specific carcinogens, their role in the development of DNA adducts and the onset of cancer, and DNA's ability to repair itself after exposure to these carcinogens. Better understanding of these carcinogens and their effects could lead to the identification of biomarkers for increased cancer risk.

Dr. **Valerie Pierre**'s lab exploits coordination and organic chemistry to solve medical and environmental problems. The group uses siderophores—natural products synthesized by bacteria to chelate iron—as a template to design novel chemical probes and imaging agents to rapidly diagnose bacterial infections in vitro and in vivo, and to develop antibiotics with improved efficacy against antimicrobial-resistant bacteria. As part of their environmental efforts, they are designing new complexes, supramolecular receptors and polymeric membranes to remove pollutants and toxic compounds such as phosphates, arsenate and cyanide from surface water.

Dr. **William Pomerantz**'s lab is researching protein-protein interactions (PPIs), utilizing fluorine to tag PPIs to increase their visibility and using NMR to visualize the resulting interactions. Understanding the molecular processes involved in PPIs could allow researchers to develop therapeutic agents to inhibit or facilitate these interactions for the treatment of blood disorders and cancer, and for the improvement of cognitive function. One major thrust of the lab is the current development of two of their lead compounds for inhibiting a class of proteins involved in the epigenetic regulation of breast cancer.

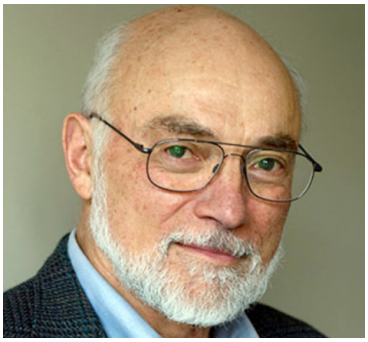
Dr. **Eyup Akgun** and researcher **Mary Lunzer** in Dr. **Philip Portoghese**'s lab continued their research on the development of novel analgesics for the treatment of chronic pain without tolerance or dependence. Collaborative studies with the Medical School revealed that MCC22, a highly potent analgesic, possesses ~1000 times the efficacy of morphine in mice with antibody-induced rheumatoid arthritis. Research also revealed it to be an effective analgesic for neuropathic pain and for homozygous sickle cell diseased mice. It was also discovered that a ligand (BOMI) synthesized by Dr. Akgun, when combined with loperamide, afforded extraordinary potentiation of analgesia tolerance, and this opioid combination has been patented and licensed. A new series of analgesics related to the delta opioid antagonist naltrindole was discovered to selectively target the mu-delta heteromer (MOR-DOR). The lab found that opioid agonism occurs via ligand binding to DOR which allosterically activates MOR without producing tolerance—a feature of interest in the development of potent orally active opioids. In collaboration with Dr. **Haskell-Luevano**, Mary Lunzer continued her studies on the potential of MMG22 to treat type-2 diabetic neuropathy in mice.

Dr. **Rory Remmel**'s lab is studying the genetic risk variants of kidney transplant patients and how those risk factors interact with prescribed medications. In particular, the immunosuppressant medication Tacrolimus is often prescribed following organ transplantation but is also found to have lower levels of metabolization and efficacy in African American recipients. Understanding how drug efficacy and side effects can interact with genetic predispositions will help doctors to personalize treatment and reduced morbidity levels for patients in the future.



Harki Lab

Haskell-Luevano Lab



Dr. Philip Portoghese

Dr. Valerie Pierre

Dr. William Pomerantz

Dr. Rory Remmel

Dr. W. Thomas Shier

Dr. **W. Thomas Shier**'s lab is working to develop innovative drug discovery platforms designed to produce novel antibiotics and anticancer agents. One focus is on fungi that use mycotoxins to target dividing cells in plant root tips as part of the mechanism they use to infect roots from the soil. Known mycotoxins that play this role also kill dividing mammalian cells, so they are a potential source of novel anticancer drugs. Large numbers of fungal isolates of this type are available in the freezers of agricultural scientists, who are happy to collaborate. A second major focus is on developing a genome mining technique based on a proposed mechanism by which Streptomyces species have acquired known antibiotic biosynthetic enzyme gene cassettes. A particular interest in this type of approach is the potential to apply it to produce in quantity scarce marine natural products with drug potential, such as bryostatin. Other studies are focused on novel extremophiles as sources of new antibiotics.

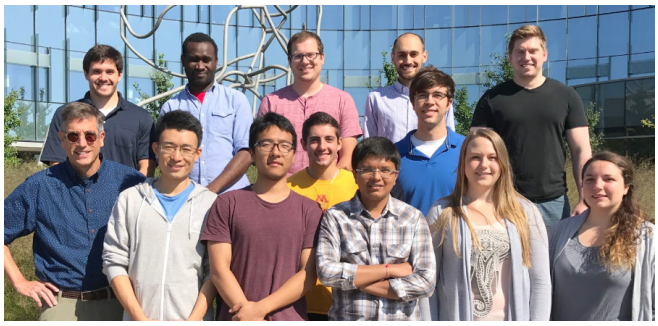
Dr. **Natalia Tretyakova**'s lab is conducting research into DNA-protein cross-links (DPCs), which are helix-distorting DNA lesions that result from exposure to certain anticancer drugs, ionizing radiation, or environmental toxins. These lesions are thought to interfere with DNA-protein interactions like replication and repair due to their bulky, distorted nature. The lab seeks to discover the role that DPCs play in the development of human diseases and cancer. The lab is also researching DNA adduct formation by 1,3-butadiene, an important industrial chemical and known human carcinogen present in automobile exhaust, cigarette smoke, and forest fires. This project focuses on identifying the mechanisms of carcinogenicity and the biological targets of 1,3-butadiene in cells. Additional research includes investigating epigenetic effects of chemical exposures and inflammation. Epigenetics controls the levels of gene expression by reversible modifications of DNA and histone proteins. This process is deregulated in many human diseases, including cancer. The lab is discovering DNA epigenetic marks and their protein readers as potential new targets for drug design.

Tretyakova Lab

Dr. **Robert Turesky**'s lab continues biomarker research into DNA adducts, in which hazardous environmental and dietary chemicals or those sometimes found in chemotherapeutic or antiretroviral drugs can become bound to a segment of DNA and lead to mutation and the onset of cancer. Using liquid chromatography-mass spectrometry, the lab is able to identify and quantify these adducts in a variety of human tissue samples to better understand their formation and to assess the potential toxicity and cancer risk associated with therapeutic drugs and environmental exposures.

Turesky Lab

Dr. **Carston Rick Wagner**'s lab has developed new protein evolution techniques and expanded the understanding and use of Histidine Triad Nucleotide Binding Protein 1 (HINT1). In collaboration with Dr. Ben Hackel's lab, PhD candidate **Cliff Csizmar** published a new method for the evolution and selection of high affinity protein binders, which led to the development of the first low nanomolar fibronectin binders to the cancer antigen EpCAM. In collaboration with Dr. **Finzel**'s lab, PhD candidate **Rachit Shah** and postdoc **Kimberly Maize** mapped the enzyme mechanism trajectory of HINT1 from substrate binding to product release in order to obtain the first crystal structure of a catalytically active histidine-nucleotidylated intermediate. They also developed a set of rules governing HINT1 substrate specificity. Rachit went on to develop the first "fluorescent on" inhibitors for HINT enzymes, thus providing a probe for future drug design and mechanistic studies. In collaboration with Dr. Aldrich's lab, PhD candidate **Aniekan Okon** designed and developed the first anchimerically activatable ProTides, which significantly improve the oral bioavailability of the corresponding nucleotide and improve anti-cancer and anti-viral potency. Unlike current approaches, the new proTide approaches may expand the utility of proTides beyond the liver while still taking advantage of the unique phosphoramidase activity of HINT1.



Wagner Lab

Research Activities: Labs of the ITDD

Dr. **Peter Dosa**'s lab has been developing ATP sensitive potassium channel openers as potential therapeutic agents for the treatment of glaucoma. These compounds have proven effective at lowering intraocular pressure in animal models. Dr. Dosa's lab has also been pursuing a novel approach to preventing the recurrence of *Clostridium difficile* infections. Standard antibiotic-based strategies for the treatment of C. *difficile* infections disrupt indigenous microbiota and commonly fail to eradicate bacterial spores—two key factors that allow recurrence of infection. Dr. Dosa's group has been developing bile acid derivatives designed to inhibit the germination of C. *difficile* spores without disrupting the indigenous microbiota, which should help reduce the chance of a reoccurrence of the infection.

Dr. **Gunda Georg**'s group has furthered their research into the development of a non-hormonal male contraceptive. The lab is looking into several potential approaches, including means of reducing sperm count, preventing sperm from forming in the first place, and inhibiting sperm motility. By creating a safe and reversible birth control for men, the Georg lab hopes to increase the choices families and individuals have over their reproductive options.

Dr. **Vadim Gurvich**'s lab continues work on developing alternative analgesic treatments for moderate to severe pain that will minimize the potential for drug tolerance, dependence, and abuse by targeting opioid receptor heteromers. His lab also received a contract through the National Institute of Drug Abuse for their project "(-)-Phenserine Tartrate Purification, Encapsulation, and Testing Support Services." The project will create a synthetic compound to be used in human clinical research studies for the treatment of Alzheimer's disease within the National Institute on Aging.

Dr. Peter Dosa

Dr. Gunda Georg

Dr. Vadim Gurvich

Dr. Henry Wong

Hawkinson Lab

Walters Lab

Dr. **Jon Hawkinson**'s lab conducts biochemical, biophysical, and cell-based assay development, high-throughput and fragment based screening, structure-activity relationships, and hit characterization for small molecule probe and drug discovery. They collaborate in all therapeutic areas, including CNS (pain, synapse formation, neurofibromatosis), cardiovascular (soluble guanylate cyclase), cancer (Mcm10, FANCM), metabolic disease (steatosis), and contraception (BRDT, TSSK2/6, CDK2, Wee2, RAR). In collaboration with Dr. Portoghese, Dr. Hawkinson leads a drug discovery project to identify a development candidate to treat chronic pain devoid of opioid side effect liability.

Dr. **Michael A. Walters**' lab is studying the development of caspase inhibitors for the potential treatment of cognitive loss in tauopathies. His group is also engaged in the collaborative discovery of therapeutics to treat heart valve calcification, breast cancer, spinocerebellar ataxia, muscular dystrophy, and chronic pain. By working across therapeutic areas to enable drug discovery, his Lead and Probe Discovery Group (LaPD) serves as a nexus of early stage translational science at the University of Minnesota.

Dr **Henry L. Wong**'s lab focuses on the pre-clinical evaluation of the in vivo pharmacology of drug candidates. As Director of the Pharmacology Core in the ITDD, he is involved in the development of translational approaches to drug discovery that include cell-based assays, pharmacokinetic and pharmacodynamic analysis, efficacy in disease models, and non-GLP toxicology. Although Dr. Wong collaborates with investigators with a broad range of expertise, his own research has focused on oncology and inflammatory disease indications with emphasis on novel drugs that target tubulin dynamics.

Dr. Ulrike Holzgrabe

Dr. Rommie Amaro

Seminars

The spring Distinguished Seminar Lecture was given by Dr. Ulrike Holzgrabe, who is the Professor and Chair of Pharmaceutical and Medicinal Chemistry at the University of Würzburg, Germany. Her talk "Small Molecules for the Treatment of Critical Infectious Diseases," took place on August 15. The fall Distinguished Seminar Lecture was given by Dr. Rommie Amaro, who is Associate Professor of Chemistry and Biochemistry at the University of California, San Diego. Her lecture, "Computing Cures: Discovery through the Lens of a Computational Microscope," took place on October 3.

Other seminars in 2017 by the Department of Medicinal Chemistry, the Chemical Biology Initiative (CBI), the Epigenetics Consortium, and the Institute for Therapeutics Discovery and Development (ITDD) included:

January 17	**Ellie Hofer**, Graduate Student in the Wagner Group, "Selective Targeting of BCI-2 for the Treatment of Chronic Lymphocytic Leukemia with BH3 Mimetics"
January 19	Dr. Brian Van Ness, Professor in the Department of Genetics, Cell Biology, and Development at the University of Minnesota, "Targeting the Epigenome in Multiple Myeloma"
January 24	**Dmitri Konorev**, Graduate Student in the Turesky Group, "Proteogenomic Approaches Towards Novel Biomarkers of Colorectal Cancer"
January 31	**Anand Divakaran**, Graduate Student in the Pomerantz Group, "VX-770 (Ivacaftor) and Beyond: The Development of Small Molecules to Treat Cystic Fibrosis"
February 7	**John Schultz**, Graduate Student in the Aldrich Group, "Repurposing Drugs of the Past: Combating Resistance"
February 13	Dr. **Mark Distefano**, Distinguished McKnight Professor and Merck Professor at the University of Minnesota, "Choosing a Postdoctoral Position: A Panel Discussion with Postdocs and Research Advisors"

February 16	Dr. James Kiefer, Senior Scientist, Project Team Lead, and Group Leader at Genentech Inc., "How We Learned to Stop Chelating and Love Histone Demethylases"
February 21	**Amanda Degner**, Graduate Student in the Tretyakova Group, "The Application of Metabolomics and Precision Medicine in Cancer Treatment"
February 27	Clifford Gee, Graduate Student in the Pomerantz Group, "Protein Tetris: Ligand Discovery, Characterization, and Development for BrdT via Protein Observed Fluorine NMR;" and Tory Schaaf, Graduate Student in the Thomas Group, "Novel Fluorescence Tools for the Discovery of Cardiac Calcium Pump Therapeutics"
February 28	**Connor McDermott**, Graduate Student in the Ambrose Group, "From Simple 2D Shapes to Complex 3D Nanostructures: DNA Origami as a Drug Delivery Vehicle"
March 7	**Katherine Schlasner**, Graduate Student in the Haskell-Luevano Group, "CXCR4 Drug Target: Using Chimeric Peptides for Mechanistic Studies"
March 13	Dr. Mary Kay Pflum, Associate Professor in the Department of Chemistry at Wayne State University, "Kinase-catalyzed Labeling: Chemical Approaches to Mapping Cell Signaling Pathways"
March 16	Dr. Timothy Hallstrom, Assistant Professor in the Department of Pediatrics, Div. Blood and Marrow Transplantation at the University of Minnesota, "Epigenetics at the Proliferation/Differentiation Switch in Retinal Progenitor Cells"
March 21	**William McCue**, Graduate Student in the Finzel Group, "Targeting de novo Biosynthesis of Cysteine for Novel Therapeutics of Mycobacterium Tuberculosis"
March 27	Dr. David Vocadlo, Professor in the Department of Chemistry at Simon Fraser University, "Chemical Biology of O-GlcNAc: Enzyme Mechanisms to Chemical Probes"
April 10	Dr. Michael Smanski, Assistant Professor in the Department of Biochemistry, Molecular Biology, and Biophysics at the University of Minnesota, "Harnessing DNA Synthesis and Assembly Technology for Natural Product Discovery and Engineering"
April 11	Dr. Thomas Baillie, Professor of Medicinal Chemistry and Dean Emeritus at the University of Washington, "Targeted Covalent Inhibitors: Evolution of a New Paradigm in Drug Design"
April 18	Dr. Bruce Armitage, Professor of Chemistry and Co-director of CNAST at Carnegie Mellon University, "Targeting G-Quadruplex RNA by Peptide Nucelic Acid Oligomers"
April 20	Dr. Winnie Wan-yee Tang, Associate Professor in the Department of Environmental Health and Engineering at Johns Hopkins University, "Tet1-mediated DNA Hydroxymethylation and Airway Hyperresponsiveness"
April 24	Dr. Katherine J. Franz, Professor and Associate Chair in the Department of Chemistry at Duke University, "Designing Molecules to Mine for Copper along the Host-Pathogen Interface"
April 25	Dr. Arthur Olson, Professor of Molecular Biology and Director of the Molecular Graphics Library at The Scripps Research Institute, "From Structural Modeling to Molecular Therapeutics, an Integrative Perspective"
May 2	**Cody Lensing**, Graduate Student in the Haskell-Luevano Group, *Abul-Hajj/ Hanna Awardee Seminar,* "Bivalent Ligands as Pharmacological Probes for the Melanocortin Receptors: The Bivalent Advantage"
May 16	**Cliff Csizmar**, Graduate Student in the Wagner Group, "Diagnostic and Therapeutic Applications of EpCAM-Targeted Fibronectin"

May 18	Dr. Daumantas Matulis, Professor and Head of the Department of Biothermodynamics and Drug Design at Vilnius University, "Anticancer Drug Design Targeting Carbonic Anhydrase and a Database of Protein-Compound Binding Gibbs Energy, Enthalpy, Entropy, Heat Capacity, and Volume Correlations with the Crystal Structure"
May 30	**Evan Alexander**, Graduate Student in the Aldrich Group, "Targeting Polyketide and Nonribosomal Peptide X and a Database of Protein-Compound Binding Klebsiella Oxytoca for Treating Tuberculosis and Hemorrhagic Colitis"
June 6	**Katlyn Fleming**, Graduate Student in the Haskell-Luevano Group, "Investigation of Melanacortin-4 Receptor Modulators and Screening Strategies"
July 11	**Alex Strom**, Graduate Student in the Wagner Group, "Kinetic and Structural Comparison of HINT1 and HINT2: Two Similar Enzymes with Separate Biological Roles?"
July 18	**Kellan Passow**, Graduate Student in the Harki Group, "Chemical Probes for Modulation of Transcription Factor Signaling"
July 25	**Jenna Fernandez**, Graduate Student in the Tretyakova Group, "Chemical Biology of DNA Methylation and Demethylation"
August 1	**Jiewei Jiang**, Graduate Student in the Georg Group, "Design and Synthesis of Dihydropyrimidine Analogs as BRDT Selective Inhibitors for Male Contraception"
August 8	**Xianghong Guan**, Graduate Student in the Georg Group, "Discovery of Selective Inhibitors and Fluorescence Tools for Testis-Specific Bromodomain (BRDT)"
September 5	**Mark Distefano**, Distinguished McKnight Professor and Merck Professor at the University of Minnesota, "The Chemical Biology Protein Prenylation, the Anchor of Life"
September 19	Dr. Jason Gestwicki, Professor in the Department of Pharmaceutical Chemistry at the University of California, San Francisco, "Targeting Protein-Protein Interactions in the Molecular Chaperone Networks"
September 21	Dr. Chris Faulk, Assistant Professor of Functional Genomics at the University of Minnesota, "Conservation or Flexibility of the Epigenome in Ultraconserved Non-coding Elements by Comparing 60 Species"
September 26	**Jian Tang**, Graduate Student in the Harki Group, "Proteolysis Targeting Chimeras (PROTACs): New Strategy Targeting the Undruggable Proteome"
October 6	Dr. Mark Hixon, Principal at Mark S. Hixon Consulting LLC, "Next Generation Irreversible Inhibitors: From Design to Clinical Development"
October 9	Dr. Kevin G. Rice, Professor in the Department of Pharmaceutical Sciences and Experimental Therapeutics at the University of Iowa, "Bioconjugate Packaging of Oligonucleotides For Systemic Gene Delivery"
October 17	Dr. Eric Olson, Chief Scientific Officer at Syros Pharmaceuticals, "Discovering and Developing Therapies for Cystic Fibrosis That Restore Function to the Defective CFTR Protein"
October 19	**Jenna Fernandez** and **Chris Seiler**, Graduate Students in the Tretyakova Group, "Chemical Biology of DNA Methylation and Demethylation"
October 31	Dr. Jordan Meier, Investigator in the Chemical Biology Laboratory at the National Cancer Institute's Center for Cancer Research, "Neuropeptides and Their Effect on Human Behavioral Disorders"
November 6	Dr. Wenshe Liu, Professor in the Department of Chemistry at Texas A&M University, "Use an Expanded Genetic Code to Study Epigenetic Erasers"

November 7	Dr. Nicholas Levinson, Assistant Professor in the Department of Pharmacology at the University of Minnesota, "Harnessing Conformational Dynamics for Selective Kinase Inhibition"
November 14	Dr. Venkatram Mereddy, Professor in the Department of Pharmacy Practice and Pharmaceutical Sciences and Associate Professor of Biophysics at the University of Minnesota, Duluth, "Simple Organic Chemistry for Complex Cancer Problems"
November 20	Dr. Bryan Dickinson, Assistant Professor in the Department of Chemistry at the University of Chicago, "Chemical Approaches to Probe Signaling by Dynamic Proteome Lipidation,"
November 21	**Joshua Shirley**, Graduate Student in the Carlson Group, "Phage Therapy: A Promising Alternative Treatment for Bacterial Infections"
November 28	**Maxwell Dillenburg**, Graduate Student in the Wagner Group, "Development of G-protein Biased --Opioid Receptor Agonists for Improved Pain Therapies"
December 4	Dr. Amanda Hargrove, Assistant Professor in the Department of Chemistry at Duke University, "Deciphering Patterns in Selective Small Molecule: RNA Interactions"
December 5	**Michael Grillo**, Graduate Student in the Harki Group, "Small Molecule Activation of the Hypoxia-inducible Factor (HIF) Pathway for Treatment of Hypoxia Related Conditions"
December 12	**Scott Brody**, Graduate Student in the Aldrich Group, "Therapeutic Approaches to Treat Cocaine Overdose"
December 14	Dr. Camila Dos Santos, Assistant Professor in the Cold Spring Harbor Laboratory, "Probing the Epigenome to Target Breast Cancer"

Student Recognition

A total of 56 students were enrolled in the graduate program this year. Five students graduated and 10 students joined the department: **Jacob Bouchard**, **Erik Faber**, **Brian Gabet**, **Alexander Hurben**, **Samantha Kennelly**, **Md Abdullah al Noman**, **Jacob Patterson**, **Caitlin Jokipii Krueger**, **Jenna Thomforde**, and **Nan Wang**.

Joseph Buonomo (Aldrich Group) was awarded a 2017-2018 *Doctoral Dissertation Fellowship*. The Fellowship is awarded only to the University's most accomplished PhD candidates making timely progress towards their degrees.

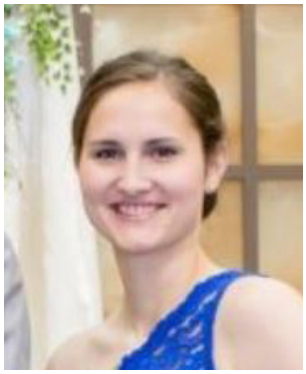
Sydney Schmidt, a junior undergraduate Chemistry major in the Harki lab, received the 2017 *David A. and Merece H. Johnson Scholarship* for outstanding achievement in undergraduate research as well as overall scholastic excellence. This award comes from both the Department of Medicinal Chemistry and the Department of Chemistry.

Alex Strom (Wagner Group) received an *American Foundation of Pharmaceutical (AFPE) Pre-Doctoral Fellowship* based on his research, "Probing a New Target HINT1 for the Management of Chronic Pain through Analgesia and the Reversal of Opioid Tolerance." The fellowship aims to positively impact patient and public health by supporting high performing students who possess the skill and aptitude to become outstanding scientists and leaders in the pharmaceutical industry, academia, and the government/ nonprofit sectors.

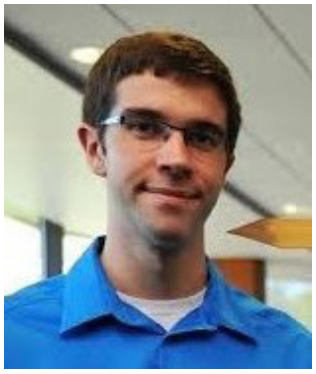
Josh Shirley (Carlson Group) won the *Outstanding TA Award* for 2016–2017 as presented by the College of Pharmacy's Office of Teaching, Learning, and Assessment.

Incoming Class of 2017

Joseph Buonomo



Sydney Schmidt



Alex Strom

Josh Shirley

Katlyn Fleming

Cliff Csizmar

Dmitri Konorev

Dr. Abul-Hajj, Cody Lensing, Dr. Georg, and Dr. Hanna

Katlyn Fleming (Haskell-Luevano Group) and **Cliff Csizmar** (Wagner Group) were both recipients of the *2017-2018 Bighley Graduate Fellowship*. The fellowship was established in 2008 by Dr. Lyle D. Bighley and Sharon Bighley as a way to support graduate students working in the biomedical health sciences. It recognizes excellence in students conducting research in laboratories with an emphasis on collaborative and interdisciplinary work.

Dmitri Konorev (Turesky Group) and **Katlyn Fleming** were both awarded the *2017-2018 Rowell Graduate Fellowship*. This fellowship was established by the family of pharmaceutical industrialist Theodore H. Rowell to support graduate students in the pharmaceutical sciences with an emphasis on drug delivery systems.

Cody Lensing (Haskell-Luevano Group) was selected to receive the 2017 *Abul-Hajj/Hanna Exceptional Graduate Student Award* for his project "Bivalent Ligands as Pharmacological Probes for the Melanocortin Receptors: The Bivalent Advantage."

MIKI Meeting 2017

Held annually since 1963, the MIKI "meeting-in-miniature" is the oldest and most successful regional meeting in medicinal chemistry. Meetings are organized by medicinal chemistry graduate students at the Universities of Minnesota, Iowa, Kansas, and Illinois, and rotate between each location yearly.

The University of Minnesota hosted the 55th Annual MIKI meeting in April, which featured a keynote lecture by Dr. Uttam K. Tambar from UT Southwestern Medical Center titled, "Intersection of Medicinal Chemistry and Reaction Discovery: Selective Inhibitors of Hypoxia Inducible Factor and Catalytic Enantioselective Reactions."

Four graduate students from the department made presentations on behalf of the University of Minnesota:

Cody Lensing	"An In Vitro and In Vivo Investigation of Melanocortin Receptor Homodimers using Bivalent Ligands: A Bivalent Advantage"
Matthew Bockman	"Avoiding Antibiotic Inactivation in Mycobacterium tuberculosis through Strategic Nucleoside Modification"
Chris Seiler	"Epigenetic Effects of Inflammation and Exposure to the Tobacco Carcinogen NNK in the A/J Mouse Model of Smoking-Induced Lung Cancer"
Jacob Petersburg	"EPCAM+ Breast Cancer Treatment Utilizing Prosthetic Antigen Receptors (PARS)"

Degrees Awarded 2017

Jacob Petersburg

Degree: Ph.D.

Advisor: Carston R. Wagner

Thesis Title: Prosthetic Antigen Receptors as a Platform for Solid Tumor Immunotherapy

Rachit Shah

Degree: Ph.D.

Advisor: Dr. Carston R. Wagner

Thesis Title: A New Target for Pain: Development of Tools to Study Human Histidine Triad Nucleotide Binding Proteins

Cody Lensing

Degree: Ph.D.

Advisor: Dr. Carrie Haskell-Luevano

Thesis Title: Bivalent Ligands as Pharmacological Probes for the Melanocortin Receptors: The Bivalent Advantage

Carter Eiden

Degree: Ph.D.

Advisor: Dr. Courtney Aldrich

Thesis Title: Room Temperature Chemoselective Phosphine Oxide Reduction and Mechanism-Based Inhibitors of BioA

John Widen

Degree: Ph.D.

Advisor: Dr. Daniel Harki

Thesis Title: Design of Cysteine Reactive Probes for Targeting Transcription Factors

Directory

Faculty

Gunda I. Georg	Department Head and Professor; Director, Institute for Therapeutics Discovery and Development (ITDD); Robert Vince Endowed Chair; McKnight Presidential Chair
Rodney L. Johnson	Associate Department Head; Distinguished Professor
David M. Ferguson	Professor
Yusuf J. Abul-Hajj	Professor
Eyup Akgün	Research Associate Professor
Courtney C. Aldrich	Associate Professor
Elizabeth A. Ambrose	Associate Professor
Rebecca A. Cuellar	Research Assistant Professor
Sunil David	Bennett Professor
Todd Doran	Assistant Professor
Peter I. Dosa	Research Associate Professor; Director, ITDD Medicinal Chemistry Core
Earl W. Dunham	Associate Professor
Barry C. Finzel	Professor
Vadim J. Gurvich	Research Associate Professor; Associate Director, ITDD; Director, ITDD Chemical Process Development Core
Patrick E. Hanna	Professor Emeritus
Daniel A. Harki	Associate Professor
Carrie Haskell-Luevano	Professor; Philip S. Portoghese Endowed Chair in Chemical Neuroscience; Institute for Translational Neuroscience Scholar
Jon Hawkinson	Research Professor; Director, ITDD High-Throughput Screening and Assay Development Core
Sidath C. Kumarapperuma	Research Assistant Professor
Herbert T. Nagasawa	Professor Emeritus
Philip S. Portoghese	Distinguished Professor
Rory P. Remmel	Distinguished Teaching Professor
W. Thomas Shier	Professor
Marilyn K. Speedie	Dean Emeritus, College of Pharmacy; Professor
Natalia Y. Tretyakova	Professor
Robert Turesky	Professor
Carston R. (Rick) Wagner	Professor; Endowed Chair in Medicinal Chemistry
Michael A. Walters	Research Associate Professor; Director, ITDD Lead and Probe Discovery Core
Henry L. Wong	Research Associate Professor; Director, ITDD Pharmacology and Biomarker Core

Adjunct Faculty

Erin Carlson	Associate Professor of Chemistry
Mark D. Distefano	Distinguished McKnight Professor and Merck Professor, Department of Chemistry

Stephen S. Hecht	Professor, Wallin Chair in Cancer Prevention, Masonic Cancer Center
Thomas R. Hoye	Professor and Merck Professor, Department of Chemistry
Lisa Peterson	Professor of Environmental Sciences
Valérie C. Pierre	Associate Professor of Chemistry
William C. Pomerantz	Assistant Professor of Chemistry

Administrative Staff

Clarissa Ache Cabello	Student Office Assistant
Leigh Allen	Assistant to the Department Head
Caitlin Boley	Executive Operations Student Services Specialist
Lorri Chapman	Project Manager, REACH
Mary Crosson	Administrative Manager
Sandy Dewing	Associate Administrator, Journal of Medicinal Chemistry
Ann Howarth	Executive Office and Administrative Specialist
Megan Jensen	Executive Office and Administrative Specialist
Ali Niesen	Executive Accounts Specialist
Leah Peck	Executive Office and Administrative Specialist
Mary Quarnstrom	Student Office Assistant
Anna Sisombat	Executive Accounts Specialist to Dr. Sunil David
Rita Stodolka	Executive Administrative Specialist, NIPTE
Katie Torguson	Student Office Assistant
Erin Warholm-Wohlenhaus	Executive Office and Administrative Specialist
Amy Xiong	Student Office Assistant

Research Staff

Danielle Adank	Junior Scientist, Haskell-Luevano Lab
Alex Ayoub	Research Specialist, Harki Lab
Michael Brush	Research Professional, David Lab
Narsihmulu Cheryala	Principal Scientist, Georg Lab
Matthew Cuellar	Principal Scientist, Walters Lab
Ziyou Cui	Research Scientist, Turesky Lab
Andrew Goode	Scientist, Gurvich Lab
Alex Hendricks	Senior Laboratory Technician, Wagner Lab
Collin Gustafson	Research Professional, David Lab
Katie Henning	Assistant Scientist, Haskell-Luevano Lab
Justin Hill	Research Professional, David Lab
Sudhakar Jakkaraj	Senior Principal Scientist, Georg Lab
Kristen John	Assistant Scientist, Hawkinson Lab
Sesha Krishnamachari	Senior Scientist, Turesky Lab
Peter Larson	Senior Lab Technician, Ferguson Lab
Morgan LeNaour	Research Associate, Walters Lab
Lev Lis	Senior Principal Scientist, Gurvich Lab
Mary Lunzer	Scientist, Portoghese Lab
Deepti Mudaliar	Assistant Scientist, Hawkinson Lab

Tahmina Naqvi	Assistant Scientist, Hawkinson Lab
Kathryn Nelson	Principal Scientist, Walters Lab
Michael Powers	Scientist, Portoghese Lab
Henry Schares	Scientist, Harki Lab
Stephen Schnell	Scientist, Portoghese Lab
Jonathan Solberg	Assistant Scientist, Hawkinson Lab
Jessica Strasser	Assistant Scientist, Walters Lab
Shameem Sultana Syeda	Principal Scientist, Georg Lab
Defeng Tian	Principal Scientist, Hawkinson Lab
Kathryn Trautman	Research Professional, David Lab
Teng Wang	Principal Scientist, Gurvich Lab
Timothy Ward	Principal Scientist, Georg Lab
Stacey Wilber	Scientist, Haskell-Luevano Lab
Lihua Yao	Assistant Scientist, Turesky Lab
Byeong Hwa (BH) Yun	Research Associate, Turesky Lab

Postdocs, Fellows, and Visiting Scholars

Mohamed Abou-Karam	Shier Lab
Sana Aslam	Shier Lab
Janardhan Banothu	David Lab
Samina Bashir	Shier Lab
Mallesh Beesu	David Lab
Madjda Bellamri	Turesky Lab
Surendra Dawadi	Aldrich Lab
Skye Doering	Haskell-Luevano Lab
Ruben Eckermann	Harki Lab
Mark Ericson	Haskell-Luevano Lab
Will Fiers	Aldrich Lab
Kate Guo	Turesky Lab
Leila Hejazi	Turesky Lab
Kwon Ho Hong	Georg Lab
Ziwei Hu	David Lab
Yu Jiao	Georg Lab
Sadaf Kayani	Shier Lab
Carolyn Kingsley	Hawkinson
Lakmal Kotelawala	Wagner Lab
Yupeng Li	David Lab
Shuai Lu	Georg Lab
Guru Swamy Madugundu	Tretyakova Lab
Soma Maitra	Georg Lab
Kimberly Maize	Finzel Lab
Ramkumar Moorthy	Harki Lab
Said Muhammad	Shier Lab
Ali Nakhi	Dosa Lab
Balaji Pathakumari	David Lab

Suresh Pujari	Tretyakova Lab
Gurpreet Singh	Walters Lab
Kristen Stoltz	Dosa Lab
Benjamin Walker	Tretyakova Lab
Yi Wang	Turesky Lab
Mu Yang	Doran Lab
Fang Yu	Georg Lab
Shun Xiao	Turesky Lab
Pei-Liang Zhao	Georg Lab

Graduate Students

Evan Alexander	Advisor: Aldrich
Matthew Bockman	Advisor: Aldrich
Emily Boldry	Advisor: Tretyakova
Jacob Bouchard	Advisor: Doran
Scott Brody	Advisor: Aldrich
Joseph Buonomo	Advisor: Aldrich
Katelyn Capistrant	Advisor: Finzel
Erick Carlson	Advisor: Georg
Malcolm Cole	Advisor: Aldrich
Sara Coulup	Advisor: Georg
Cliff Csizmar	Advisor: Wagner
Amanda Degner	Advisor: Tretyakova
Maxwell Dillenburg	Advisor: Wagner
Anand Divakaran	Advisor: Pomerantz
Carter Eiden	Advisor: Aldrich
Eric Faber	Advisor: Georg
Jenna Fernandez	Advisor: Tretyakova
Conrad Fihn	Advisor: Carlson
Katlyn Fleming	Advisor: Haskell-Luevano
Brian Gabet	Advisor: Georg
Michael Grillo	Advisor: Harki
Arnold Groehler	Advisor: Tretyakova
Xianghong Guan	Advisor: Georg
Qiyuan Han	Advisor: Tretyakova
Trihn (Amy) Holth	Advisor: Georg
Alexander Hurben	Advisor: Doran
Shaofei Ji (Chem	Advisor: Tretyakova
Jiewei Jiang	Advisor: Georg
Caitlin Jokipii Krueger	Advisor: Tretyakova
Samantha Kennelly	Advisor: Harki
Ozgun Kilic	Advisor: Wagner
Zoe Koerperich	Advisor: Haskell-Luevano
Dmitri Konorev	Advisor: Turesky
Jillian Kyzer	Advisor: Georg
Cody Lensing	Advisor: Haskell-Luevano

Ellie Mews	Advisor: Wagner
William (Bill) McCue	Advisor: Finzel
Connor McDermott	Advisor: Ambrose
Md Abdullah al Noman	Advisor: Georg
Aniekan Okon	Advisor: Wagner
Daeyoon Park	Advisor: Tretyakova
Kellan Passow	Advisor: Harki
Jacob Patterson	Advisor: Doran
Jacob Petersburg	Advisor: Wagner
Chris Richards (Pharmacology	Advisor: Harki
Alex Salyer	Advisor: David
Garrett Schey	Advisor: Distefano
Katherine Schlasner	Advisor: Haskell-Luevano
John Schultz	Advisor: Aldrich
Christopher Seiler	Advisor: Tretyakova
Rachit M. Shah	Advisor: Wagner
Josh Shirley	Advisor: Carlson
Alexander Strom	Advisor: Wagner
Jian Tang	Advisor: Harki
Jenna Thomforde	Advisor: Tretyakova
Nan Wang	Advisor: Georg
Harrison Trent West	Advisor: Wagner
Andrea Wisniewski	Advisor: Georg
Yu Zhu	Advisor: Tretyakova

Undergraduate Research Assistants and Summer Scholars

Christian Adams	Remmel
Joseph Ahenkorah	Aldrich
Medinat Akindele	Tretyakova
Jordan Baur	Harki
Harrison Berg	Ferguson
Hannah Boman	Tretyakova
David Cullen	Harki
Dillon Diering	Georg
Emina Dzafic	Tretyakova
Mitch Fuller	Aldrich
Travis Hammerstad	Aldrich
Ryan Harding	Remmel
Alex Hendricks	Wagner
Justin Hill	David
Mitch Hoverman	Remmel
Xiang Li	Shier
Greg Mannino	Aldrich
Alex McCracken	Shier

Dominic Najjar	Tretyakova
Vivian Nguyen	Tretyakova
Thomas Perry	Wagner
Ton-Hy Pha	Doran
Caitlin Puro	Harki
Logan Roessler	Georg
Sydney Schmidt	Harki
Hannah Skopec	Harki
Zaid Temrikar	Shier
Angie Tran	Aldrich
Lensa Toka	Tretyakova
Paul Trisko	Tretyakova
Kathleen Wang	Aldrich
Lauren Warmka	Ambrose
Henok Yared	Ferguson
Andrew Zhou	Wagner

Ways to Give

Private support of our activities is important to maintain the quality of our program and the continuation of the mission of the department. Even small contributions accumulate over time and can have a significant impact.

Opportunities for giving include:

- Abul-Hajj-Hanna Exceptional Graduate Student Award in Medicinal Chemistry
- Dr. Lyle and Sharon Bighley College of Pharmacy Pharmaceutical Development Fund
- Medicinal Chemistry Alumni Graduate Student Fellowship
- MIKI Meeting Fund
- Ole Gisvold Fellowship in Medicinal Chemistry
- Philip S. Portoghese Fellowship in Medicinal Chemistry
- Philip S. Portoghese Lectures in Medicinal Chemistry
- Remmel and Zimmerman Fellowship in Drug Metabolism and Pharmacokinetics
- Rick Wagner Fellowship
- Yusuf J. Abul-Hajj Fellowship in Medicinal Chemistry
- Rodney L. Johnson Medicinal Chemistry Fellowship
- Medicinal Chemistry/Pharmacognosy Fund Quasi

Our Development Director Robert Busch will work with you and answer any questions that you might have. He can be reached by e-mail, busch110@umn.edu, or phone (1-866-437-0012).

Research Grants

(-)-Phenserine Tartrate Clinical Material Storage and Certificate of Analysis Evaluation Support Services ..... Vadim Gurvich
A Pharmacological Screen for Inactivating Antagonists ..... Peter Dosa
Administration of the National Institute for Pharmaceutical Technology and Education ..... Vadim Gurvich
Anti-Cancer CSANs Development ..... Carston Wagner
APOBEC3 Structural Studies ..... Daniel Harki
Biacore S200 Surface Plasmon Resonance Instrument ..... Jon Hawkinson
Cell-cycle Regulatory Kinases as Targets for Male Contraceptive Project ..... Gunda Georg
Chemical Interrogation of Human DNA Cytosine Deaminases ..... Daniel Harki
Chemical Mechanisms of Toxicology ..... Natalia Tretyakova
Chemical Toxicology of the People, for the People and by the People ..... Natalia Tretyakova
Chemoproteomics Profiling Of Parthenolide in Human Glioblastoma ..... Daniel Harki
Critical Path Manufacturing Sector Research Initiative ..... Vadim Gurvich
CRO Support for NCATS Drug Substance Development and Manufacture ..... Vadim Gurvich
Defensins as Melanocortin Ligands ..... Carrie Haskell-Luevano
Design and Synthesis of Stabilized Pironetin Analogs for the Treatment of Resistant Ovarian Cancers ..... Sara Coulup
Development of (-)-Phenserine Tartrate for Clinical Use ..... Vadim Gurvich
Development of a Fluorescence Polarization DNA Displacement Assay and Its Utilization for the Discovery of APOBEC3B Ligands ..... Daniel Harki
Development of Gut-restricted Bile Acid Analogs Inhibitory to C. diff ..... Peter Dosa
Development of NIPTE Industrial Training Program ..... Vadim Gurvich
Development of Safer Soluble Guanylate Cyclase (sGC) Activators to Treat Aortic Valve Calcification ..... Michael Walters
Development of Zika Virus-specific Serodiagnostic Immunoassays and Evaluation of Zika Virus Env-derived Antigens for Subunit Vaccines ..... Sunil David
DNA Cross-Linking By Diepoxybutane ..... Natalia Tretyakova
DNA Protein Cross-Links: Cellular Effects and Repair Mechanisms ..... Natalia Tretyakova
Drug Discovery and Synthesis of Contraceptive Agents ..... Gunda Georg
Engineering Reversible Cell-Cell Interactions with Chemically Self-Assembled CARs ..... Cliff Csizmar
Enzymatic Protein Labeling ..... Carston Wagner
Establishment, Colonization, Toxin Production and Development of the Charcoal Rot Fungus, Macrophomina Phaseolina on Soybean During the Disease Life Cycle: Basic Biology ..... W. Thomas Shier
FANCM High Throughput Screening Aim 1A2 ..... Gunda Georg
Inhibiting Prostate Cancer Cell Motility ..... Vadim Gurvich
Inhibitors of Na,K-ATPase Alpha4 as Male Contraceptives ..... Gunda Georg
Maintenance and Operation of a Medicinal Chemistry Facility ..... Gunda Georg
Mechanism of Soybean Root Infection by Macrophomina Phaseolina ..... W. Thomas Shier
Melanocortin Selective Ligands ..... Carrie Haskell-Luevano
Menaquinone Biosynthesis: A Drug Target in Gram-Positive Bacteria ..... Courtney Aldrich
MMG22, a Potent Analgesic for Chronic Inflammatory Pain Associated with Metastatic/Primary Bone Cancer ..... Philip Portoghese
Molecular Probes of AGRP for Drug Discovery ..... Mark Ericson
Novel Melanocortin Receptor Probe Discovery ..... Carrie Haskell-Luevano

Novel Therapeutic Agents for the Treatment of Glaucoma ..... Peter Dosa
Optimization of a Novel Compound That Enhances the
Activity of Beta-lactams Against Gram+ Bacteria ..... Courtney Aldrich
Precision Medicine Of Aromatase Inhibitors In
Post-menopausal Women With ER+ Breast Cancer ..... Michael Walters
Preclinical Development of Myosolvins, a New Class of Medicine for Asthma ..... Vadim Gurvich
Probing a New Target HINT1 for the Management of Chronic Pain
through Analgesia and the Reversal of Opioid Tolerance ..... Alex Strom
Regenerating New Drug Leads for Schistosomasis ..... Peter Dosa
Scaffold Discovery for Caspase-2 by Fragment Screening ..... Michael Walters
Small Molecule GPR10 Antagonists for the Treatment of Uterine Fibroids ..... Gunda Georg
Smoking-Induced Epigenetic Changes in the Lung: Role of DNA Demethylation ..... Natalia Tretyakova
Stopping Enzyme-Catalyzed Ovarian Cancer Evolution ..... Daniel Harki
Structurally Blinded Synthesis Research Agreement ..... Michael Walters
Synthesis and Metabolic Evaluation of Stabilized Pironetin Analogs as
Novel Microtubule Inhibitors for the Treatment of Ovarian Cancer ..... Sara Coulup
The Structural Basis for Nonribosomal Peptide Biosynthesis ..... Courtney Aldrich
Toward a Mechanism-Based Approach to Treating Atrial Fibrillation ..... Vadim Gurvich
WEE2 Inhibitors as Highly Specific, Non-hormonal Agents to
Block Fertilization for On-demand Contraception ..... Vadim Gurvich

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Captions

Page 7. **Aldrich Lab**: [Back Row] Scott Brody, John Schultz, Evan Alexander, Courtney Aldrich, Malcolm Cole, [Front Row] Joseph Buonomo, Surendra Dawadi, Kathleen Wang; **Ambrose Lab**: Elizabeth Ambrose, Connor McDermott; **David Lab**: [Back Row] Ziwei Hu, Michael Brush, Collin Gustafson, Sunil David, Alex Salyer, [Front Row] Janardhan Banothu, Anna Sisombat, Kathryn Trautman.

Page 8. **Doran Lab**: Jacob Patterson, Maggie Schreiner, Jacob Bouchard, Todd Doran, Alexander Hurben, Mu Yang; **Finzel Lab**: Katelyn Capistrant, Barry Finzel, Bill McCue.

Page 9. **Harki Lab**: [Back Row] Henry Schares, Daniel Harki, Michael Grillo, [Front Row] Ramkumar Moorthy, Jian Tang, Kellan Passow, Anand Divakaran; **Haskell-Luevano Lab**: Zoe Koerperich, Mark Ericson, Katlyn Fleming, Katie Schlasner, Stacey Wilbur.

Page 10. **Tretyakova Lab**: [Back Row] Chris Seiler, Amanda Degner, Arnold Groehler IV, [Front Row] Suresh Pujari, Natalia Tretyakova, Jenna Fernandez; **Turesky Lab**: [Back Row] Hyeong Hwa Yun, Dmitri Konorev, Sesha Krishnamachari [Front Row] Lihua Yao, Madjda Bellamri, Robert Turesky, Jingshu Guo, Haoqing Chen; **Wagner Lab**: [Back Row] Trent West, Aniekan Okon, Max Dillenburg, Cliff Csizmar, Jake Petersburg, [Middle Row] Rick Wagner, Thomas Perry III, Alex Strom, [Front Row] Yaio Wang, Rachit Shaw, Ellie Mews, Ozgun Kilic.

Page 11. **ITDD**: [Back Row] John (Kwon) Hong, Matthew Cuellar, Erik Faber, Yu Jiao, Jiewei Jiang, Leigh Allen, Jonathan Solberg, Kathryn Nelson, [Middle Row] Soma Maitra, Carolyn Kingsley, Jon Hawkinson, Michael Walters, Andi Wisniewski, Jessica Strasser; [Front Row] Rebecca Cuellar, Gunda Georg, Jillian Kyser, Megan Jensen, Mary Crosson.

Page 12. **Hawkinson Lab**: Carolyn Kingsley, Jon Hawkinson, Jonathan Solberg, Deepti Mudaliar; **Walters Lab**: Matthew Cuellar, Michael Walters, Jessica Strasser, Kathryn Nelson.

Page 15. **Incoming Class of 2017**: [Back Row] Caitlin Jokipii Krueger, Jacob Patterson, Barry Finzel, Jacob Bouchard, Erik Faber, Jenna Thomforde, [Front Row] Samantha Kennelly, Gunda Georg, Nan Wang, Md Abdullah al Noman, Alexander Hurben.

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