

Department of Medicinal Chemistry 2013 Annual Report



Weaver-Densford Hall

308 Harvard Street Southeast

717 Delaware Building

717 Delaware Street Southeast

Cancer & Cardiovascular Research Building

2231 Sixth Street Southeast

Minneapolis, Minnesota

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Greetings!

The year of 2013 included many accomplishments in the Department of Medicinal Chemistry.

It is my pleasure to report to you that two new tenured faculty members joined the Department this year. Dr. Courtney Aldrich, formerly a member of the Center for Drug Design at the University of Minnesota, joined the Department as an Associate Professor. Dr. Aldrich's area of expertise is designing new antibacterial agents. Dr. Robert Turesky, from the Wadsworth Center, New York State Department of Health, joined the Department and the Masonic Cancer Center as a Professor. His work will focus on toxicology and carcinogenesis. Faculty promotions included Dr. Elizabeth Amin to Associate Professor with tenure, Dr. Eyup Akün was named Research Associate Professor, and Dr. Jon Hawkinson, Director of the ITDD HTS lab, was named Research Professor.

Graduate faculty member Dr. Lisa Peterson and I were selected as 2013 American Chemical Society Fellows and were honored at the ACS national meeting in Indianapolis. I received the Volwiler Research Achievement Award from the American Association of Colleges of Pharmacy (AACCP) during their July annual meeting. I was also voted by my peers in the Academic Health Center to be inducted into the AHC's Academy for Excellence in Health Research for enhancing the research identity of the University of Minnesota, where I join other lifetime honorees including Dr. Phillip Portoghese. Dr. Elizabeth Amin was named Professor of the Year by the PharmD class of 2015, Twin Cities campus, and Professor of the Spring Semester by the 2015 Duluth class. Professor of Fall Semester honors went to Dr. David Ferguson from the 2016 Duluth class, and Dr. Daniel Harki from the 2017 Twin Cities class.

I will serve as the principal investigator to discover pharmaceutical alternatives to existing hormone-based birth control under a new \$8.3 million contract from the National Institutes of Health's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). This project includes co-investigators from the Institute of Therapeutics Discovery and Development (ITDD). The primary goal of our five-year research contract is to develop new non-hormonal male and female birth control drug targets. ITDD will work with collaborators at the Moffitt Cancer Center in Tampa, Florida. This new award is the largest ever received by the College of Pharmacy.

Stephen Hecht became Editor-in-Chief of the ACS journal *Chemical Research in Toxicology* and so stepped down from his associate editor position with the *Journal of Medicinal Chemistry*. Four University of Minnesota faculty serve as editors-in-chief for ACS journals (Georg: *J. Med. Chem.*; Hecht: *Chem. Res. Toxicol.*; Timothy Lodge: *ACS Macro Lett.* and *Macromolecules*; William Tolman: *Inorg. Chem.*) This is the largest number of editors-in-chief from any university in the U.S., covering about 10% of ACS journals.

Faculty members Dan Harki, Stephen Hecht, Lisa Peterson, Natalia Tretyakova, Robert Turesky, Carston Wagner, and Chris Xing moved their labs to the Cancer and Cardiovascular Building (CCRB), which is part of the new Biomedical Research District near the TCF Bank Stadium. The idea of the District is to create synergy and foster interdisciplinary research among faculty by placing them in close proximity to one another.

The 2013 Gisvold lecture "*Molecular Recognition of DNA by Small Molecules: from Discovery to Applications*" was delivered by Dr. Peter Dervan, Bren Professor, Division of Chemistry and Chemical Engineering, California Institute of Technology. Dr. Iwao Ojima, Distinguished Professor, Institute of Chemical Biology and Drug Discovery, SUNY Stony Brook, was chosen to give the Distinguished Speaker Lecture for fall 2013. The title of his lecture was "*New Generation Taxoids and Their Tumor-Targeting Drug Conjugates – Medicinal Chemistry, Chemical Biology, and Preclinical Development.*"

The Department of Medicinal Chemistry received \$6.5 million in research support from external agencies in FY13.

This year we had 50 students in our graduate program. We welcomed four new students to the graduate program this fall and five students graduated. Kari Gabrielse from the Wagner lab, Srikanth Kotapati from the Tretyakova lab, and Yiyun Yu from my lab have moved on to pursue the next step of their research careers. Nick Bleeker from the Xing lab and Kathy Nelson from the Aldrich lab have joined the ITDD research staff. The Department also employs 50 postdoctoral and research associates.

David Huang, a student in my lab, received an AFPE fellowship. Several Harki lab members received awards this year including graduate students Maggie Olson, awarded a Division of Medicinal Chemistry Predoctoral Fellowship for 2013-14, Nicholas Struntz, who received a predoctoral fellowship from the American Heart Association for 2013-2015 and an 18-month Bridging Funds Award from the Graduate School, undergraduate Jacob Edwards received a Department of Chemistry Gleysteen summer research fellowship, and PharmD student Bo Hu received a College of Pharmacy Melendy/Peter's summer research fellowship. John Widen, Harki Lab, and Elbeck Kurbanov, Amin Lab, received Bighley fellowships. Li-Kai Liu, of the Finzel Lab, received a predoctoral fellowship from the American Heart Association for 2014.

In 2013, the Institute for Therapeutics Discovery and Development (ITDD) continued its research projects in the area of drug discovery and development, and services to the scientific community of the University of Minnesota and beyond. Minnelide, an anticancer drug that was developed by ITDD in collaboration with other scientists at the University of Minnesota has entered phase I clinical trials for patients with advanced gastrointestinal tumors.

I hope you share our pride in the Department's accomplishments of 2013 and wish you all the best for the coming year.



Gunda Georg, Department Head

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.

Teaching & Service

Medicinal Chemistry faculty members taught numerous professional and graduate courses in 2013 and were recognized throughout the year for quality teaching and dedication to students.

Each professional pharmacy program class votes to honor their professors for outstanding teaching. This year, PharmD students in the Twin Cities class of 2015 honored **Elizabeth Amin** as their Professor of the Year, while the Duluth class of 2015 named her Professor of Spring Semester. The Twin Cities class of 2016 chose **David Ferguson** and the Duluth class of 2017 named **Dan Harki** their Professors of the Fall Semester.

Faculty also contributed to numerous committees, representing service to the Department, the University, the College of Pharmacy, national and professional organizations, and government agencies. Additionally, faculty served as reviewers for professional journals and as grant reviewers for governmental panels.

Graduate Courses

- Introduction to Drug Design (MEDC 5245)
- Vistas in Medicinal Chemistry Research (MEDC 5495)
- Principles of Medicinal Chemistry I (MEDC 8001)
- Principles of Medicinal Chemistry II (MEDC 8002)
- Recitation in Mechanistic Organic Chemistry (MEDC 8050)
- Medicinal Chemistry Seminar (MEDC 8100)
- Chemistry of Nucleic Acids (MEDC 8413)
- High Throughput Drug Discovery (MEDC 8471)
- Design of Chemotherapeutic Agents (MEDC 8500)
- Advanced Concepts in Drug Design (MEDC 8700)
- Medicinal Chemistry Laboratory Techniques (MEDC 8800)
- Research in Medicinal Chemistry (MEDC 8900)

Professional Courses

- Honors Course: Medicinal Chemistry Seminar (PHAR 6150)
- Biochemistry of Medicinals II (PHAR 6152)
- Medicinal Agents I (PHAR 6154)
- Medicinal Agents II (PHAR 6155)
- Medicinal Agents III (PHAR 6156)
- Human Nutrition & Drug Therapy (PHAR 6157)
- Recombinant DNA-Derived Drugs (PHAR 6158)
- Pharmaceutical Immunology & Biotechnology (PHAR 6159)
- PharmD IV Seminar (PHAR 6182)
- Drugs of Abuse (PHAR 4248/6248)
- Integrated Biochemical Sciences (PHAR 6702)
- Pharmacology I (PHCL 5101)
- Pharmacology II (PHCL 5102)



University News

A new research facility, the Cancer and Cardiovascular Research Building, opened in the Biomedical Discovery District near TCF Bank Stadium. The goal of the district is to create synergy and foster interdisciplinary research among faculty by placing them in close proximity to one another. Medicinal Chemistry faculty members Dan Harki, Stephen Hecht, Lisa Peterson, Natalia Tretyakova, Robert Turesky, Carston Wagner, and Chris Xing moved their labs to CCRB, joining faculty from the Cancer Center, Lillehei Heart Institute, and the Integrative Biology and Physiology program, among others.

ITDD



The Institute for Therapeutics Discovery and Development (ITDD) continued its research projects in the area of drug discovery and development, and provided services to the scientific community of the University of Minnesota and beyond.

ITDD researchers participated in over two dozen external and internal scientific programs and projects with other academic and industrial institutions. The Institute's large NIH-funded contraceptive program was renewed for another

five-year period. ITDD continued its activities within the NCI Chemical Biology Consortium as a designated Center for Chemical Diversity, with the goal to perform translational research in medicinal chemistry for the NCI. Other scientific collaborations continued, including four collaborative scientific projects with Mayo Clinic.

Fifteen peer-reviewed scientific papers were published and several scientific presentations were made at national scientific meetings by ITDD researchers. A half dozen patent applications and invention disclosures were submitted.

A new promising anti-cancer agent, Minnelide™, designed by Institute researchers in collaboration with other University departments, entered clinical trials in August 2013.

J Med Chem

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. **Gunda Georg** is Co-Editor-in-Chief, with Shaomeng Wang at the University of Michigan Comprehensive Cancer Center. **Courtney Aldrich** is a new member of the editorial advisory board and **Carrie Haskell-Luevano** is an associate editor.



Stephen Hecht stepped down from his associate editor position with *J Med Chem* to become editor-in-chief of another ACS journal, *Chemical Research in Toxicology*. Currently, four University of Minnesota faculty serve as editors-in-chief for ACS journals, the largest number of ACS editors-in-chief of any American university.

Comings & Goings

Robert Turesky, from the Wadsworth Center, New York State Department of Health, joined the University of Minnesota Cancer Center with an appointment in the Department of Medicinal Chemistry in June. He brought his postdoc **Byeong Hwa (BH) Yun** and has formed a new research group in the Cancer and Cardiovascular Research Building. Turesky's research investigates metabolism of genotoxicants in the environment and diet, and development of biomarkers of their urinary metabolites and adduction products to DNA and protein. Mass spectrometric methods are employed to measure these biomarkers in collaborative molecular epidemiological studies, which seek to understand the role of hazardous chemicals and inter-individual susceptibilities in the risk of developing cancer.

Courtney Aldrich from the Center for Drug Design has a new affiliation with the department as Associate Professor with tenure. His lab has relocated to Weaver-Densford Hall.

Comings & Goings (continued)

Recent graduates **Nick Bleeker** from the Xing lab and **Kathy Nelson** from the Aldrich lab joined ITDD's research staff. **Mary Smart**, lab manager for ITDD, was accepted to and started her first year in the University's Pharm.D. program. She continues to work part-time as her studies allow.



Joyce Reha, long-time executive secretary for the department, retired in April.

Rachel Rud joined the Weaver-Densford administrative staff in April, having previously worked in Electrical and Computer Engineering. She is a University of Minnesota graduate.

Kelli Pettinelli returned to support ITDD members at 717 Delaware, and **Sarah Sexton** moved to the Cancer and Cardiovascular Research Building.

Faculty Recognition

Gunda Georg received the annual Volwiler Research Achievement Award, recognition by her peers as one of the leading researchers in medicinal chemistry with outstanding contributions to the discipline. The award is sponsored by the Abbott Fund and was established as the research prize in academic pharmacy to honor the late Ernest H. Volwiler, former president and research director of Abbott Laboratories. The award consists of a gold medal and a \$12,500 cash prize. Georg was honored during the annual AACP meeting in Chicago in July.

The American Chemical Society named **Gunda Georg** and graduate faculty member **Lisa Peterson** to the class of 2013 ACS Fellows. ACS Fellows are nominated by their peers and selected for their outstanding achievements in and contributions to science and for providing excellent volunteer service to the ACS community. Georg and Peterson were honored at the fall ACS National Meeting in Indianapolis.

Gunda Georg was inducted into the Academy for Excellence in Health Research, the Academic Health Center's highest recognition of excellence in research for faculty that have enhanced the research identity of the University of Minnesota through sustained nationally- and internationally-recognized biomedical or health-related research. Inductees serve a valuable role for the AHC, advising on issues of competitiveness, educational mission and research strategy. Georg is the second Medicinal Chemistry faculty member, along with **Philip Portoghese**, to receive this honor.



Yusuf Abul-Hajj published "From Digitalis to Ziagen," a book covering the history of the Department of Medicinal Chemistry, including the establishment of the department as well as the leadership role the department and its faculty played in drug development. He discussed his book at the Rho Chi Research Day on campus.



Elizabeth Amin was promoted to Associate Professor.

Jon Hawkinson, Director of the Institute for Therapeutics Discovery and Development High Throughput Screening and Assay Development Core, was named Research Professor.

Eyup Akgün, who works with Philip Portoghese, was named Associate Research Professor.

David Ferguson was featured in several HealthTalk stories regarding drug use in sports. He was also quoted in the *Minnesota Daily* article, "Molly Drug Use More Common Than U Think" and in the Tacoma, *Washington News Tribune* story "PED Use Has Led to Suspensions of Six Seahawks under Carroll."

Gunda Georg's research on the male birth control pill was reported in the *Minnesota Daily*, *City Pages*, and *Star Tribune* newspapers, and HealthTalk online. She was quoted in features on Litchfield, Minnesota-based KLFD Radio, and her research with Mayo Clinic molecular biologist Jim Maher was featured in a KARE11 news story.

Faculty Recognition (continued)

Robert Turesky was featured in the HealthTalk story, “Research Q&A: Identifying Cancer’s Source” and in the MedicalXpress.com article, “Advance in Using Biopsy Samples in Understanding Environmental Causes of Cancer.” Turesky and postdoc B.H. Yun reported on an advance in using biopsy samples in understanding environmental causes of cancer at the 246th National Meeting of the American Chemical Society.



Research Activities

Department of Medicinal Chemistry faculty produced 63 publications in more than 25 journals and presented at numerous conferences through oral and poster presentations in 2013.

Robert Turesky was an author of an NIEHS Paper of the Month. The study, “Mutational Signature of Aristolochic Acid Exposure as Revealed by Whole-Exome Sequencing” appeared in the August 7 issue of *Science Translational Medicine*.

Two papers by department researchers were featured on the covers of the publishing journals. **Dan Harki’s** “Small Molecule APOBEC3G DNA Cytosine Deaminase Inhibitors Based on a 4-Amino-1,2,4-triazole-3-thiol Scaffold” was published in *Chem MedChem* volume 8(1) and **Natalia Tretyakova’s** “Capillary HPLC-Accurate Mass MS/MS Quantitation of N7-(2,3,4-trihydroxybut-1-yl)-Guanine Adducts of 1,3-Butadiene in Human Leukocyte DNA” was published in *Chemical Research Toxicology* volume 26(10).

Seminars



The 2013 Ole Gisvold Memorial Seminar was presented by Dr. **Peter B. Dervan**, Bren Professor of Chemistry in the Division of Chemistry and Chemical Engineering at the California Institute of Technology. He presented *Molecular Recognition of DNA by Small Molecules: From Discovery to Application* on October 22.

Many interesting and respected professors and researchers were invited to present seminars in 2013 by the Department of Medicinal Chemistry, the Chemical Biology Initiative (CBI), and the Institute for Therapeutics Discovery and Development (ITDD).

- **Valerie C. Pierre**, Assistant Professor, Department of Chemistry, University of Minnesota. *Imaging Metal-Induced Oxidative Stress: Lanthanides to the Rescue*, February 5.
- **Philip Portoghese**, Professor, Department of Medicinal Chemistry, University of Minnesota. The Philip S. Portoghese Lectureship In Medicinal Chemistry: *Opioid Receptor Heterodimers: Favorable Marriages or Hazardous Liaisons?*, February 12.
- **Patrick Limbach**, Professor, Department of Chemistry, University of Cincinnati. *Studying RNA Editing & Modification Using Mass Spectrometry*, February 18. (CBI)
- **Erin E. Carlson**, Assistant Professor, Department of Chemistry, Indiana University. *Chemical Probes to Explore & Inhibit Bacterial Growth & Pathogenesis*, March 4. (CBI)
- **David S. Lawrence**, Professor, Department of Chemistry, University of North Carolina. *Organic Chemistry at the Edge of Biology: Taming Cell Behavior with Light Responsive Molecules*, March 12.
- **Omid Farokhzad**, Associate Professor, Laboratory of Nanomedicine and Biomaterials, Brigham and Women’s Hospital, Harvard Medical School. *Functionalized Polymeric Nanoparticles for Medical Applications: From Discovery to Clinical Trials*, April 1. (CBI)
- **Sarah E. Reisman**, Assistant Professor, Department of Chemistry, California Institute of Technology. Student-Invited Seminar: *New Methods and Strategies for the Synthesis of Epidithiodiketopiperazine Natural Products*, April 2.

Seminars (continued)

- **Kate Carroll**, Associate Professor, Department of Chemistry, The Scripps Institute, Florida Campus. *Painting the Cysteine Chapel: New Tools to Probe Oxidation Biology*, April 15. (CBI)
- **Amit Kalgutkar**, Research Fellow, Pfizer. *Metabolism-Guided Drug Design*, April 16.
- **Nouri Neamati**, Associate Professor, Department of Pharmacology and Pharmaceutical Sciences, University of Southern California. *Navigating Chemical Space for Discovery of Novel Anticancer Drugs*, April 23.
- **Richard DiMarchi**, Professor, Department of Chemistry, Indiana University. *Novel Drug Treatment for Metabolic Disease: From Gut Hormones to Polypharmacy*, April 30.
- **Mei Hong**, Professor, Department of Chemistry, Iowa State University. *Structure & Mechanism of the Influenza M2 Proton Channel Studied by Solid-State NMR*, May 7.
- **Hinh Ly**, Associate Professor, Virology Veterinary Biosciences, and **Yuying Liang**, Associate Professor, Veterinary Biosciences, University of Minnesota. *Host-Pathogen Interactions in Human Lassa & Influenza Virus Infections*, June 7. (ITDD)
- **James Inglese**, Investigator, National Center for Advancing Translational Sciences (NCATS). *Case Studies in Gateway Translational Research and the Curious Curse of the Firefly*, July 9.



- **Iwao Ojima**, Distinguished Professor, Institute of Chemical Biology and Drug Discovery, Stony Brook University. Distinguished Lectureship: *New Generation Taxoids and Their Tumor-Targeting Drug Conjugates – Medicinal Chemistry, Chemical Biology, Cancer Cell Biology & Preclinical Development*, September 17.
- **Frank M. LaFerla**, Chancellor's Professor, Department of Neurology and Behavior, University of California, Irvine. *Stem Cell Therapy for Alzheimer's Disease: Overcoming Translational Issues & New Models*, September 23. (CBI)
- **Paramjit Arora**, Professor, Chemistry, New York University. *Plucking the High Hanging Fruit: A Systematic Approach for Targeting Protein-Protein Interactions*, September 24.
- **Orlando Schärer**, Professor, Pharmacological Sciences and Chemistry, Stony Brook University. *Regulation of Nuclease Activity in Human Repair Pathways: from Molecular Mechanisms to Cancer Therapy & Inherited Human Disorders*, October 1.
- **Elfi Kraka**, Professor, Chemistry, Southern Methodist University. *Learning from Nature-Excursions into Computer Assisted Drug Design*, October 8.
- **Will Pomerantz**, Assistant Professor, Chemistry, University of Minnesota. *Teflon Proteins for Protein-Protein Interaction Ligand Discovery*, October 15.
- **Dionicio R. Siegel**, Assistant Professor, Department of Chemistry and Biochemistry, University of Texas, Austin. *Natural Product Synthesis – an Enabling Tool in the Discovery of New Approaches to Small Molecule-Mediated Neuronal Regeneration*, October 21. (CBI)
- **Bill J. Gurley**, Professor, Pharmaceutical Sciences, University of Arkansas for Medical Sciences. *Can I Take This with My Prozac? An Introduction to Herb-Drug Interactions*, October 29.
- **Laurie Fink**, Science Programs Director, Science Museum of Minnesota; **Mary Beth Henderson**, Vice President of Regulatory Affairs, RCRI, Inc.; **Will Pomerantz**, Assistant Professor, University of Minnesota; **James Wollack**, Assistant Professor, St. Catherine University. Panel Discussion: *What will do I do when I complete my Ph.D.?*, November 4. (CBI)
- **Patrick Woster**, Professor, Medicinal Chemistry and Pharmacognosy, Ohio State University. *Strategies for the Discovery of Small-Molecule Epigenetic Modulators*, November 5.
- **James Bradner**, Assistant Professor, SCCP Drug Discovery and Biomedical Sciences, Medical University of South Carolina. *Chemical Modulation of Chromatin Structure*, November 6.
- **E. James Petersson**, Assistant Professor, Department of Chemistry, University of Pennsylvania. *Thioamides: Minimalist Chromophores for Monitoring Protein Folding & Stability*, November 18. (CBI)
- **James Fuchs**, Assistant Professor, Medicinal Chemistry and Pharmacognosy, Ohio State University. *Disruption of the IL-6/JAK/STAT Signaling Pathway with Natural Product Analogues*, November 19.
- **Jeffrey Aubé**, Professor, Medicinal Chemistry, University of Kansas. *Chemical Probes for Cancer and Neuroscience*, December 17.



Student Recognition



Graduate students in the Department of Medicinal Chemistry are a hard working, talented group.

Four students joined the Department of Medicinal Chemistry in 2013: **Joseph Buonomo**, **Denise Casemore**, **Sara Coulup**, and **Ozgun Kilic**. In addition, visiting scholars from other countries and a graduate student from Mayo Clinic came to the University to work with department faculty.

David Huang (Georg lab) was selected for an American Foundation for Pharmaceutical Education fellowship. The AFPE Fellowship is intended to encourage outstanding pre-doctoral students to continue their studies to earn the Ph.D. **Elbek Kurbanov** (Amin lab) and **John Widen** (Harki lab) were selected to receive Bighley Graduate Fellowships for 2013-14. **Margaret Olson** (Harki lab) was a recipient of a prestigious Division of Medicinal Chemistry Predoctoral Fellowships for 2013-14.

Undergraduate **Jacob Edwards** received a Department of Chemistry Heisig/Gleysteen Summer Undergraduate Research Fellowship. Pharm.D. student **Bo Hu** received a College of Pharmacy Melendy/Peters' Summer Research Scholarship. Both students are members of the Harki lab. Undergraduate **Ryan Harding** was awarded an Undergraduate Research Scholarship and worked in the Rimmel Lab in the summer.

MIKI Meeting 2013

Held annually since 1963, the MIKI "meeting-in-miniature" is the oldest and most successful regional meeting in medicinal chemistry. Rotating meetings are organized by medicinal chemistry graduate students at the Universities of Minnesota, Iowa, Kansas, and Illinois at Chicago. The 2013 planning committee included students **Kathryn Nelson** (Aldrich lab), **Ran Dai** (Finzel lab), and **Adam Zarth** (Hecht lab).

The University of Minnesota hosted the 51st Annual MIKI meeting, which featured Dr. **Marvin J. Miller**, George and Winifred Clark Professor, Department of Chemistry and Biochemistry at the University of Notre Dame, who presented the keynote lecture *Organic Chemistry and Utilizing Microbial Iron Assimilation Processes for the Development of New Antibiotics*.

University of Minnesota graduate students represented the department well. The schedule of presenters included **Amit Gangar** (Wagner lab), **Kathryn Nelson** (Aldrich lab), **Yi-Yun Yu** (Georg lab), and **Srikanth Kotapati** (Tretyakova lab).

Commencement

Timothy E. Andrews M.S., September Advisor: Harki
Enhancing the Potency and Water Solubility of the Sesquiterpene Lactone Parthenolide.

Nicholas P. Bleeker M.S., September Advisor: Xing
Advancing a Novel Chemotype for the Treatment of Multidrug-Resistant Cancer.

Dan Wang M.S., April Advisor: Harki
Synthesis and Evaluation of Parthenolide Analogues: Chemical Probes and Therapeutic Agents.

Adam R. Benoit Ph.D., December Advisor: Ferguson
Synthesis and Evaluation of Acridine and Acridone Based Compound as anti-Cancer and Anti-Bacterial Agents.

Kari Ann L. Gabrielse Ph.D., August Advisor: Wagner
Chemically Self-Assembled Antibody Nanorings: A Multifaceted Approach to Anti-Cancer Therapeutics Using Techniques Including Drug Delivery, Bispecific Targeting, and T Cell Surface Modification.

Yi-Yun Yu Ph.D., August Advisor: Georg
Innate C-H Functionalization of Cyclic Enaminones.



Commencement (continued)

Srikanth Kotapati..... Ph.D., October Advisor: Tretyakova
Mass Spectrometry-Based Analysis of Urinary Metabolites of 1,3-Butadiene (BD) in Humans and Influence of BD-DNA Adducts on DNA Replication.

Rahul R. Lad..... Ph.D., February
 Advisor: Sturla
Chemical and Biomolecular Structures in Recognition of DNA Modification.

Kathryn Marie Nelson..... Ph.D., June Advisor: Aldrich
Synthesis and Evaluation of Transvalencin Analogues and Adenylation Inhibitors as Antitubercular Agents and Chemical Probes.



Faculty

Gunda I. Georg Department Head and Professor; Director, Institute for Therapeutics Discovery and Development (ITDD); Robert Vince Endowed Chair and McKnight Chair

Rodney L. Johnson Associate Department Head and Distinguished Professor

David M. Ferguson Director of Graduate Studies and Professor

Yusuf J. Abul-Hajj Professor

Eyup Akgün Research Associate Professor

Courtney C. Aldrich Associate Professor

Elizabeth A. Amin Associate Professor

Rebecca A. Cuellar Research Assistant Professor

Peter I. Dosa Research Assistant Professor; Director, ITDD Medicinal Chemistry Core

Earl W. Dunham Associate Professor

Robert A. Fecik 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 Assistant 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

Herbert T. Nagasawa Professor Emeritus

Philip S. Portoghese Distinguished Professor

Rory P. R Emmel Distinguished Teaching Professor

W. Thomas Shier Professor

Marilyn K. Speedie Dean, College of Pharmacy; Professor



Faculty (continued)

Shana Sturla.....	Professor, ETH Zurich
Natalia Y. Tretyakova.....	Professor
Robert Turesky.....	Professor
Robert Vince	Professor; Director, Center for Drug Design (CDD)
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.....	Associate Research Professor; Director, ITDD Pharmacology and Biomarkers Core
Chengguo (Chris) Xing	Associate Professor

Adjunct Faculty

Mark D. Distefano	Distinguished McKnight Professor, Department of Chemistry
Stephen S. Hecht	Professor, Wallin Chair in Cancer Prevention, Masonic Cancer Center
Thomas R. Hoye.....	Distinguished Teaching Professor, Department of Chemistry
Lisa A. Peterson	Professor, Division of Environmental Health Sciences

Administrative Staff

Caitlin Boley.....	Executive Operations Student Services Specialist
Laura Burnes	Student Office Assistant
Geneva Cole	Student Office Assistant
Mary Crosson.....	Associate Administrator
Sandy Dewing	Associate Administrator, Journal of Medicinal Chemistry
Jeanine Ferguson	Assistant to Dr. Gunda Georg
Kelli Pettinelli.....	Principal Office and Administrative Specialist
Rachel Rud.....	Principal Office and Administrative Specialist
Sarah Johnson Sexton	Executive Office and Administrative Specialist

Research Staff

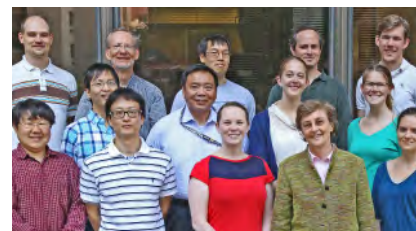
Ramappa Chakrasali	Research Associate, Georg Lab
Ting-Lan Chiu	Research Associate, Amin Lab
Teresa De la Mora-Rey.....	Research Associate, Finzel Lab
Rawle Francis	Research Associate, Hawkinson Lab
Subhashree Francis.....	Research Associate, Walters Lab
Katie Freeman	Assistant Scientist, Haskell-Luevano Lab
Joe Hexum	Junior Scientist, Harki Lab
Xin Huang	Research Associate, Xing Lab
Sudhakar Jakkaraj.....	Research Associate, Georg Lab



Kristen John.....	Assistant Scientist, Hawkinson Lab
Alvin Kalinda.....	Research Associate, Aldrich Lab
Delshanee Kotandeniya.....	Research Associate, Tretyakova lab
Sidath Kumarapperuma	Research Associate, Wagner Lab
Pablo Leitzman	Senior Lab Technician, Xing Lab
Lev Lis.....	Principal Scientist, Gurvich Lab

Research Staff (continued)

Mary Lunzer.....	Scientist, Portoghese Lab
Brock Matter.....	Scientist, Tretyakova Lab
Angela Perkins.....	Research Associate, Harki Lab
Michael Powers.....	Scientist, Portoghese Lab
Anja Rubenstein.....	Research Associate, Aldrich Lab
Ce Shi.....	Research Associate, Aldrich Lab
Stephen Schnell.....	Scientist, Portoghese Lab
Anamika Singh.....	Research Associate, Haskell-Luevano Lab
Rondedrick Sinville.....	Research Associate, Hawkinson Lab
Mary Smart.....	Assistant Scientist/Lab Manager, Gurvich Lab
Branden Smeester.....	Junior Scientist, Haskell-Luevano Lab
Jonathan Solberg.....	Assistant Scientist, Hawkinson Lab
Jessica Strasser.....	Assistant Scientist, Walters Lab
Shameem Sultana Syeda.....	Research Associate, Georg Lab
Srinivasa Tala.....	Research Associate, Haskell-Luevano Lab
Marina Tanasova.....	Research Associate, Sturla/Georg lab
Defeng Tian.....	Research Associate, Hawkinson Lab
Timothy Ward.....	Research Associate, Georg Lab

**Postdocs, Fellows, & Visiting Scholars**

Mohamed Abou-Karam.....	Shier Lab
Sahib Alam.....	Visiting Scholar, Shier Lab
Karina Bora de Oliviera.....	Visiting Research Scholar, Wagner Lab
Jignesh Doshi.....	Portoghese Lab
Benjamin Duckworth.....	Aldrich Lab
Teshome Gherezghiher.....	Tretyakova Lab
Aridoss Gopalakrishnan.....	Xing Lab
Liang Guo.....	Visiting Scholar, Xing Lab
Dong-Jin Hwang.....	Johnson Lab



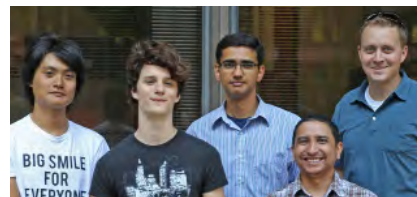
Kenneth Johnson.....	Finzel Lab
Harneet Kaur.....	Aldrich Lab
Shuhei Kawmura.....	Visiting Scholar, Aldrich Lab
Aaron Kempema.....	Harki Lab
Nigam Kumar.....	Wagner Lab
Morgan Le Naour.....	Walters Lab
Matthew Metcalf.....	Portoghese Lab
Anja Meissner.....	Rommel Lab
Sreekanth Narayanapillai.....	Xing Lab
Wahab Okunowo.....	Visiting Research Assistant Professor, Shier Lab
Manohar Puppala.....	Xing Lab
Charles Schiaffo.....	Ferguson Lab
Jeffrey Vanvoorst.....	Finzel Lab
Kishore Viswanathan.....	Aldrich Lab
Jung-Eun Yeo.....	Tretyakova Lab
Xingxin Yu.....	Xing Lab
Chunlin Zhuang.....	Visiting Scholar, Xing Lab

Graduate Students

Timothy Andrews..... Advisor: Harki
 Adam Benoit..... Advisor: Ferguson
 Nicholas Bleeker Advisor: Xing
 Matthew Bockman Advisor: Harki
 Emily Boldry Advisor: Tretyakova
 Joseph Buonomo..... Advisor: Aldrich
 Erick Carlson..... Advisor: Georg
 Denise Casemore Advisor: Xing
 Sarah Coulup..... Advisor: Georg
 Jameson Dahlin (Mayo)..... Advisor: Walters
 Ran Dai Advisor: Finzel



Skye Doering Advisor: Haskell-Luevano
 Carter Eiden..... Advisor: Aldrich
 William Fiers Advisor: Fecik
 Kari Gabrielse Advisor: Wagner
 Amit Gangar Advisor: Wagner
 Arnold Groehler IV Advisor: Tretyakova
 Trinh (Amy) Holth..... Advisor: Georg
 Kwon Ho (John) Hong..... Advisor: Georg
 David Huang Advisor: Georg
 Ozgun Kilic..... Advisor: Wagner
 Yong Wook Kim (Chem)..... Advisor: Georg
 Srikanth Kotapati..... Advisor: Tretyakova
 Elbek Kurbanov Advisor: Amin
 Jillian Kyzer..... Advisor: Georg
 Rahul Lad..... Advisor: Sturla
 Cody Lensing Advisor: Haskell-Luevano
 Wei Li (Chem)..... Advisor: Georg
 Yang Li..... Advisor: Fecik
 Jing Liu Advisor: Wagner
 Li-Kai Liu Advisor: Finzel
 Kimberly Maize..... Advisor: Finzel
 Kathryn Nelson Advisor: Aldrich
 Aniekan Okon..... Advisor: Wagner
 Margaret Olson Advisor: Harki
 Jacob Petersburg..... Advisor: Wagner
 Hao Pham (Chem) Advisor: Haskell-Luevano
 Adwait Ranade Advisor: Georg
 Dewakar Sangaraju Advisor: Tretyakova
 Christopher Seiler..... Advisor: Tretyakova
 Rachit Shah..... Advisor: Wagner
 Jingjing Shen Advisor: Wagner
 Nicholas Struntz..... Advisor: Harki
 Sreedhar Tummalapalli..... Advisor: Georg
 Dan Wang Advisor: Harki
 Harrison (Trent) West..... Advisor: Wagner
 Susith Wickramaratne (Chem) Advisor: Tretyakova



Graduate Students (continued)

John Widen.....	Advisor: Harki
Andrea Wisniewski	Advisor: Georg
Yi-Yun Yu (Chem).....	Advisor: Georg
Adam Zarth.....	Advisor: Hecht
Xia Zhang	Advisor: Amin
Bo Zhou	Advisor: Xing



Undergraduate Research Assistants & Summer Scholars

Ruby Boateng	Tretyakova Lab
Tenley Brown.....	Harki Lab
Charlie Buhler	Tretyakova Lab
Tho (Miranda) Chieu	Tretyakova Lab
Jacob Edwards	Harki Lab
Hanna Erickson	Tretyakova Lab
Amanda Esades.....	Tretyakova Lab
Torie Grover	Harki Lab
Ryan Harding	Rommel Lab
Mohamed Hatab	Shier Lab
Edward Higgins.....	Shier Lab
Mitch Hooverman	Rommel Lab
Bo Hu (Pharm.D.)	Harki Lab
Peter Huynh.....	Wagner Lab
Jared Koch.....	Tretyakova Lab
Ezra Menon	Harki Lab
Jessica Nickelson.....	Harki Lab
Eva Skellie	Harki Lab
Tram Vo.....	Harki Lab

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 add up over time and can have a significant impact.

Giving opportunities include:

- Abul-Hajj–Hanna Exceptional Graduate Student Award in Medicinal Chemistry
- 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
- Rommel and Zimmerman Fellowship in Drug Metabolism and Pharmacokinetics
- Robert Vince Graduate Student Fellowships
- Taito O. Soine Lectures in Medicinal Chemistry
- Yusuf J. Abul-Hajj Fellowship in Medicinal Chemistry

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

Awards to the Department of Medicinal Chemistry and Institute for Therapeutics Discovery and Development from the National Institutes of Health and other sources again exceeded \$6.6 million for calendar year 2013.

For the past several years, overall NIH funding in all areas of research has declined. In spite of this reduction and an increasingly competitive marketplace, faculty with the College of Pharmacy have received an increased amount of NIH funding in recent years.

Gunda Georg will lead a team of researchers from the Institute for Therapeutics Discovery and Development (ITDD) and collaborators at the Moffitt Cancer Center in Tampa, Florida, working to further birth control research conducted at the University of Minnesota, University of Kansas, and elsewhere thanks to a new \$8.3 million contract awarded by the National Institutes of Health's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). The primary goal of the five-year research contract is to both develop new non-hormonal male and female birth control drug targets and expand on existing targets.

Peter Dosa received a \$775,577 grant from the Minnesota Partnership for Biotechnology and Medical Genomics for his project, "Novel Therapeutic Agents for the Treatment of Glaucoma." Michael Fautsch from the Mayo Clinic is co-investigator on the grant.

Natalia Tretyakova received a \$32,000 grant-in-aid to fund her project "DNA-Protein Crosslinks in the Etiology of Heart Disease." **Dan Harki** received a \$23,000 Engebretson/Bighley Drug Design and Development Grant for his project, "Discovery of APOBEC3B Small Molecule Inhibitors."

Other ongoing projects and grants newly funded in 2013 are listed below with their primary investigator.

- Administration of the National Institute for Pharmaceutical Technology and Education..... Vadim Gurvich
- Anthrax toxin lethal factor inhibition study..... Elizabeth Amin
- Antitubercular Bir A Inhibitors..... Courtney Aldrich
- Beyond parthenolide: Next generation molecules targeting AML cancer stem cells..... Daniel Harki
- Chemical Biology Consortium..... Gunda Georg
- Critical interactions of APOBEC3s..... Daniel Harki
- Defensins as melanocortin ligands..... Carrie Haskell-Luevano
- Design of antibacterial agents that target Biotin Met..... Courtney Aldrich
- Design of antituberculosis agents that target Sidephor..... Courtney Aldrich
- Developing a post-carcinogen lung cancer chemopreventive..... Chengguo Xing
- Development of anti-DUX4 therapies for FSHD..... Michael Walters
- Development of antibodies for the detection of Topoisomerase I and II DNA complexes..... Daniel Harki
- Development of Novel p16INK4a Mimetics as Anticancer The..... Rory Rimmel
- Development of Photochemically Regulated DNA Decoys to Control NFkB Activity..... Dan Harki/Nicholas Struntz
- Development of small molecule inhibitors of the AAA ATPase p97..... Gunda Georg
- Development of small molecule inhibitors of the breast cancer oncoprotein APOBEC3B..... Daniel Harki/Margaret Olson
- DNA cross-linking by diepoxybutane..... Natalia Tretyakova
- Drug discovery and synthesis of contraceptive agents..... Gunda Georg
- Elucidating the cellular targets of parthenolide – A promising anti-atherosclerosis natural product..... Daniel Harki
- Endogenous G-protein coupled receptor antagonists..... Carrie Haskell-Luevano
- 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
- Formulation development and manufacturing of propofol hemisuccinate..... Vadim Gurvich

Research Grants (continued)

- Hit Triage ChemistryGunda Georg
- Identification and optimization of small molecule inhibitors of the histone acetyltransferase Rtt109Michael Walters
- Inhibitors of Na,K-ATPase alpha4 as male contraceptivesGunda Georg
- Ligands that target opioid-chemokine and opioid-mGlu5 heteromersPhilip Portoghese
- Maintenance and operation of a medicinal chemistry facilityGunda Georg
- Mechanisms of anticancer agents selective against drug resistant leukemiaChengguo Xing
- Mechanisms of ethnic/racial differences in lung cancerNatalia Tretyakova
- Mechanisms of prostate cancer prevention by Korean AngelicaChengguo Xing
- Melanocortin selective ligandsCarrie Haskell-Luevano
- Meropenem prodrugs for the treatment of tuberculosis.....Rory Rimmel
- Novel therapeutic agents for the treatment of glaucomaPeter Dosa
- Possible approaches for parenteral delivery of Fluorocox.....Vadim Gurvich
- Production of human MUC17 (CRD1-L-CRD2) recombinant proteinJon Hawkinson
- Role of DNA deamination in breast cancerDaniel Harki
- Sequence distribution of tobacco carcinogen-DNA adductsNatalia Tretyakova
- SERCA activators for a breakthrough in Diabetes therapy.....Courtney Aldrich
- Structural basis of specificity in affinity-labeled polyketide synthase didomainsRobert Fecik
- Structures of peptide synthetases and related enzymes.....Courtney Aldrich
- The Development of Pironetin as an Ovarian Cancer Chemo.....Gunda Georg/David Huang
- Targeting childhood brain tumors with parthenolide analoguesDaniel Harki
- Translational technology pilotPeter Dosa

Publications

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3. **Akgün, E.**; Javed, M.I.; Lunzer, M.M.; Smeester, B.A.; Beitz, A.J.; **Portoghese, P.S.** Ligands that Interact with Putative MOR-mGluR5 Heteromer Produce Potent Antinociception in Mice with Inflammatory Pain. *Proc. Natl. Acad. Sci. USA*, 110(28), 11595-11599.
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5. Bancos, I.; Bida, J.P.; Tian, D.; Bundrick, M.; John, K.; Holte, M.N.; Her, Y.F.; Evans, D.; Saenz, D.T.; Poeschla, E.M.; Hook, D.; **Georg, G.**; Maher, L.J. High-throughput Screening for Growth Inhibitors using a Yeast Model of Familial Paraganglioma. *PLOS ONE*, 8(2), e56827.
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34. Li, S.; Jia, Y.; Jacobson, B.; McCauley, J.; Kratzke, R.; Bitterman, P.E.; **Wagner, C.R.** Treatment of Breast and Lung Cancer Cells with an N-7 Benzyl Guanosine Monophosphate Tryptamine Phosphoramidate Pronucleotide (4Ei-1) Results in Chemosensitization to Gemcitabine and Induced eIF4E Proteasomal Degradation. *Mol. Pharmaceutics*, 10(2), 523-531.
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36. Martin, M.P.; Olesen, S.H.; **Georg, G.I.**; Schönbrunn, E. Cyclin-Dependent Kinase Inhibitor Dinaciclib Interacts with the Acetyl-Lysine Recognition Site of Bromodomains. *ACS Chem. Biol.*, 8(11), 2360-2365.
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46. Sangaraju, D.; Villalta, P.; Goggin, M.; Agunsoye, M.O.; Campbell, C.; **Tretyakova, N.** Capillary HPLC-Accurate Mass MS/MS Quantitation of N7-(2,3,4-trihydroxybut-1-yl)-Guanine Adducts of 1,3-Butadiene in Human Leukocyte DNA. *Chem. Res. Toxicol.*, 26(10), 1486-1497. Featured on the cover.
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53. Teitelbaum, A.M.; Meissner, A.; Harding, R.A.; Wong, C.A.; **Aldrich, C.C.**; **Rommel, R.P.** Synthesis, pH-Dependent and Plasma Stability of Meropenem Prodrugs for Potential Use Against Drug-Resistant Tuberculosis. *Bioorg. Med. Chem.*, 21(17), 5605-5617.
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Photo Captions

- cover Cancer & Cardiovascular Research Building, opened June 2013
- p. 1 Fall 2013 Department of Medicinal Chemistry faculty, staff, and students
- p. 2 top ITDD researchers L. Lis, G. Georg, V. Gurvich, M. Smart
bottom J Med Chem editors G. Georg, S. Hecht, S. Wang
- p. 3 top G. Georg, J. Reha, S. Dewing @ Reha's retirement
middle P. Portoghese, G. Georg @ AHC Academy of Excellence award ceremony
bottom R. Johnson, E. Amin @ Amin promotion celebration
- p. 4 top R. Turesky (from HealthTalk feature)
bottom P.B. Dervan, Gisvold Lecturer
- p. 5 top I. Ojima, Distinguished Lecturer
bottom D.R. Siegel, Chemical Biology Colloquium speaker
- p. 6 top New graduate students J. Buonomo, D. Casemore, S. Coulup, O. Kilic
bottom Parents of Y. Yu, Y. Yu, G. Georg @ fall graduation 2013
- p. 7 top back: C. Wagner, N. Tretyakova, M. Speedie, D. Ferguson, C. Aldrich, D. Harki; front: D. Hermanson, S. Kotapati, A. Benoit, K. Nelson, K. Gabrielse @ spring graduation 2013
bottom Fall 2013 Department of Medicinal Chemistry & ITDD Faculty
- p. 8 J. Hawkinson lab members: R. Sinville, J. Hawkinson, D. Tian, J. Solberg, K. Johns, R. Francis
- p. 9 top Fall 2013 ITDD faculty, staff, and students
bottom M. Walters lab members: K. Nelson, M. Walters, J. Strasser, S. Francis, J. Dahlin, M. LeNaour
- p. 10 top C. Aldrich lab members: S. Kawamura, C. Eiden, K. Viswanathan, S. Dawadi, B. Duckworth
middle C. Haskell-Luevano lab members, back: S. Doering, M. Ericson, S. Tala, B. Smeester; front: C. Lensing, K. Freeman, A. Singh, C. Haskell-Luevano
bottom B. Finzel lab members: K. Maize, B. Finzel, L.-K. Liu
- p. 11 top D. Harki lab members, back: S. Breunig, J. Nickelson, T. Brown, A. Perkins, J. Edwards, M. Olson; front: D. Harki, E. Skellie, C. Richards, A. Kempema, J. Widen, J. Hexum, B. Hu.

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