

UNIVERSITY OF MINNESOTA

College of Pharmacy

Driven to Discover™

Department of Medicinal Chemistry 2012 Annual Report



717 Delaware Street Southeast
Minneapolis, Minnesota 55414

308 Harvard Street Southeast
Minneapolis, Minnesota 55455

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**Letter
from the
Department
Head**

Greetings! The year of 2012 included many accomplishments in the Department of Medicinal Chemistry.

Research efforts continued with over \$10 million in funding for several new and ongoing projects in cancer, Alzheimer's, epilepsy, contraceptives, opioids, TB, antibiotics, and HIV.

Faculty member Dan Harki received the Hyundai Hope on Wheels Award for targeting childhood brain tumors from Governor Mark Dayton, who declared September 21, 2012 "Hyundai Hope on Wheels" day in Minnesota. The Hyundai grant funds the development of new parthenolide analogues.

Rick Wagner received the 2011-12 College of Pharmacy Excellence in Graduate Education Faculty Award and has been named a Fellow of the American Association for the Advancement of Science. Elizabeth Amin has been approved as a full member in Sigma Xi, and was named Professor of the Semester (Duluth) and Professor of the Year (Twin Cities) by the PharmD class of 2014. Rory Remmel was named Professor of the Year (Twin Cities) from the PharmD class of 2012. The PharmD class of 2016 named David Ferguson Professor of the Fall Semester (Twin Cities). Stephen Hecht was awarded the 2012 Joseph W. Cullen Memorial Award for excellence in tobacco research from the American Society of Prevention Oncology. Associate Administrator Mary Crosson was awarded a 2012 Meritorious Service Award from the College of Pharmacy.

We honored retiring professor Patrick Hanna with a June symposium. Guest speakers included Judy L Bolton, University of Illinois; Adnan Elfarra, University of Wisconsin; Daniel C. Liebler, Vanderbilt University; Rodney F. Minchin, University of Queensland; Edith Sim, University of Oxford; Richard Weinshilboum from Mayo Clinic, and our own Stephen Hecht.

We currently have 45 students enrolled in our graduate program. Nine students joined the Department of Medicinal Chemistry in 2012. Five students graduated with Ph.D. degrees and moved on to postdoctoral positions: David Hermanson (advisor Chris Xing), Aaron Teitelbaum (advisor Rory Remmel), Martin Phillips (advisor Lori Peterson), Michael Peterson (advisor Robert Fecik), and my advisee, Bryant Gay. At the 50th Annual MIKI meeting, held in Iowa, Trinh Doan from my lab took first place in the oral presentations. Amit Gangar from the Wagner lab and Kathy Nelson from the Aldrich lab won two of three poster prizes.

Three of our doctoral students received travel grants to the fall American Chemical Society National Meeting in Philadelphia to present their research. Harki lab member Margaret Olson was one of nine national recipients of the Eli Lilly Travel Award from the Women Chemists Committee of the ACS. From my lab, Trinh Doan received the ACS Division of Medicinal Chemistry travel grant and Wei Li received the Organic Chemistry travel award.

Amit Gangar from the Wagner lab and Tretyakova grad student Srikanth Kotapati received Doctoral Dissertation Fellowships from the University. In addition, Amit was honored as one of the top fifteen of 137 University of Minnesota Dissertation Fellows for 2012-13. Ran Dai from the Finzel lab was awarded a College of Pharmacy Bighley Fellowship award, and Nick Struntz from the Harki lab received a predoctoral fellowship from the American Heart Association.

In the Institute for Therapeutics Discovery & Development, Director Vadim Gurvich was promoted to Research Associate Professor. Dr. Rebecca Cuellar has been promoted to Research Assistant Professor after four years with ITDD. Dr. Derek Hook retired from his position as Director of the High Throughput Screening Laboratory in August and returned to San Diego. We wish him well, and welcome Jon Hawkinson, the new Director of High Throughput Screening and Assay Development. Dr. Hawkinson's previous experience includes Elan Pharmaceuticals and Omneuron, Inc.

I hope you share our pride in the Department's accomplishments of 2012 and wish you all the best for the coming year.



Gunda I. Georg, Professor and Department Head
Department of Medicinal Chemistry

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 and Service

Medicinal Chemistry faculty members taught numerous professional and graduate courses in 2012 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; the following members of our faculty received teaching awards this year.

- The Twin Cities class of 2012 named **Rory Rimmel** their Professor of the Year.
- The classes of 2014 honored **Elizabeth Amin** as their Professor of the Spring Semester (Duluth) and Professor of the Year (Twin Cities).
- **David Ferguson** was chosen Professor of the Fall Semester by the Twin Cities class of 2016.

Faculty also gave of their time 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

- Advanced Methods in Quantitative Drug Analysis (MEDC 5494)
- 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)
- Natural Products Chemistry (MEDC 8420)
- Molecular Targets of Drug Discovery (MEDC 8753)
- Medicinal Chemistry Laboratory Techniques (MEDC 8800)
- Research in Medicinal Chemistry (MEDC 8900)

Professional Courses

- Medical Microbiology and Immunizations (PHAR 6141)
- Honors Course: Medicinal Chemistry Seminar (PHAR 6150)
- Biochemistry of Medicinals I (PHAR 6151)
- Biochemistry of Medicinals II (PHAR 6152)
- Medicinal Agents I (PHAR 6154)
- Medicinal Agents II (PHAR 6155)
- Medicinal Agents III (PHAR 6156)
- Human Nutrition and Drug Therapy (PHAR 6157)
- Recombinant DNA-Derived Drugs (PHAR 6158)
- Pharmaceutical Immunology and Biotechnology (PHAR 6159)
- PharmD IV Seminar (PHAR 6182)
- Pharmacology I (PHCL 5101)
- Pharmacology II (PHCL 5102)



(l) Distinguished Teaching Professor
Rory Rimmel,
Assistant Professor
Elizabeth Amin

(r) Professor David
Ferguson, Director
of Graduate Studies



University News

In 2012, the University welcomed a new senior vice president for academic affairs and provost, **Karen Hanson**. Dr. Hanson received her B.A. in philosophy and mathematics from the University of Minnesota, and her M.A. and Ph.D. from Harvard University. She returns to Minnesota from Indiana, where she was on the faculty of Indiana University, and also served as provost, executive president, and dean.

The College of Pharmacy was ranked third in the nation in 2012 by *U.S. News and World Report*, retaining its position from 2008, the last time peer assessment surveys were tallied. Researchers in the college are known for their expertise in drug design, delivery, therapy and policy. “*This ranking reflects our exceptional work, dedication and high standards our students, faculty and staff of the College of Pharmacy set for themselves and their colleagues,*” said Dean **Marilyn K. Speedie**. The College also ranked eighth among U.S. colleges of pharmacy for all NIH, federal, and non-federal grants received in 2011, the last year data was compiled, with \$12.8 million in funding. According to Dean Speedie, “*Cutting-edge research by world-renown faculty enhances our excellent education program.*”

Institute for Therapeutics Discovery and Development

Research in the areas of drug discovery and development continued in the Institute for Therapeutics Discovery and Development (ITDD), as ITDD faculty and staff provided services to the scientific community of the University of Minnesota and beyond.

ITDD faculty **Vadim Gurvich**, **Gunda Georg**, and **Mike Walters**, as members of the National Institute for Pharmaceutical Technology and Education (NIPTE), began a contract with SAIC-Frederick, Inc. in support of the National Institutes of Health’s Therapeutics for Rare and Neglected Diseases (TRND). TRND’s goal is to close the gap between basic research discovery and testing of new drugs in humans by generating sufficient quality data to support new drug applications to the FDA. “*Developing therapies for rare and neglected diseases is the area where academic research can really make a difference,*” said Gurvich, who is the Associate Director of NIPTE.

Results published in the October 17 issue of the prestigious journal *Science Translational Medicine* describe ongoing research with an injectable chemotherapy designed to target tumor cells. The anti-cancer drug Minnelide™ was developed by ITDD researchers working with University colleagues, and may hold the answer to defeating pancreatic cancer, the most lethal of all cancers. Researchers expect to begin human trials in 2013.

Over the course of the year, ITDD researchers participated in xx external and internal scientific programs and projects, including twelve funded by the NIH and and one collaborative project with the Mayo Clinic. Eight peer-reviewed scientific papers were published and four presentations were made at national meetings by ITDD researchers. In addition, ten patent applications and invention disclosures were submitted.

Journal of Medicinal Chemistry

The *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. Professor **Gunda Georg** is Co-Editor-in-Chief, with Professor Shaomeng Wang at the University of Michigan Comprehensive Cancer Center. Professor **Carrie Haskell-Luevano** and editor emeritus Professor **Philip S. Portoghese** now serve on the journal’s editorial advisory board.

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(l) Provost Karen Hanson

(r) ITDD researchers Associate Professor Vadim Gurvich, Principal Scientist Lev Lis, Assistant Scientist Mary Smart, and Professor Gunda Georg



Faculty & Staff Recognition

Dr. Yusuf Abul-Hajj has retired from journal editorial service. Dr. Stephen Hecht resigned editorial board duties to take on the editor-in-chief role for another ACS journal, *Chemical Research in Toxicology*.

A new book, "*From Digitalis to Ziagen*," is the history of the Department of Medicinal Chemistry at the University of Minnesota. Authored by Professor Yusuf Abul-Hajj and Richard Broderick, the book covers everything from the establishment of the College of Pharmacy and the department to profiles of notable faculty members and the leadership role the department and its faculty played in drug development.

Many department faculty and staff members were honored for their professionalism and achievements over the past year by internal and external organizations.

Dr. Elizabeth Amin was approved as a full member in the University's chapter of Sigma Xi, an international, multidisciplinary research society. Sigma Xi promotes the health of scientific enterprise, honors scientific achievement, and encourages camaraderie and collaboration among scientists in all fields through its programs and activities.

Mary Crosson, Associate Administrator, was nominated by department faculty and colleagues and recognized with a 2012 Meritorious Service Award from the College of Pharmacy.

The annual Volwiler Research Achievement Award was presented to Dr. Gunda Georg. This prestigious prize is sponsored by the Abbott Fund to recognize leading researchers in medicinal chemistry for outstanding contributions to the discipline.

The American Society of Prevention Oncology selected Dr. Stephen Hecht to receive the 2012 Joseph Cullen Memorial Award for excellence in tobacco research.

Dr. Carston (Rick) Wagner, Endowed Chair in Medicinal Chemistry and director of the Chemical Biology Initiative, was named a Fellow of the American Association for the Advancement of Science (AAAS). He was elected in the Section on Pharmaceutical Sciences for distinguished contributions to the field of drug design and delivery, particularly for the design and development of nucleotide prodrugs and chemically assembled protein nanostructures. He joins six other AAAS Fellows from the College of Pharmacy, all also Medicinal Chemistry faculty: Gunda Georg, Patrick Hanna, Rodney Johnson, Philip Portoghese, Tom Shier and Robert Vince.

The University also rewarded Dr. Wagner for his contributions to college teaching and research programs with the 2011-12 College of Pharmacy Excellence in Graduate Education Faculty Award.

Dr. Michael Walters is a member of the NIH NINDS Neurological Sciences and Disorders C (NSD-C) Translational Research study section.

Several department faculty were promoted in 2012. Dr. Vadim Gurvich and Dr. Eyup Akgün, were both promoted to Research Associate Professor. Dr. Rebecca Cuellar, former postdoc in the Georg lab, was promoted to Research Assistant Professor.

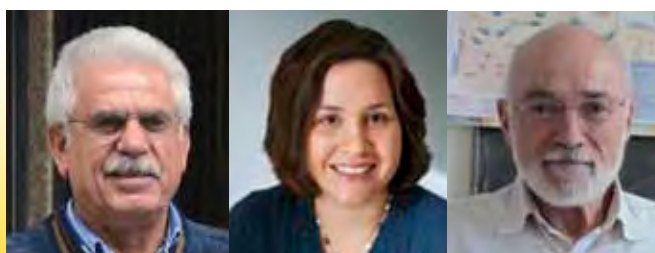
Department faculty were interviewed and featured by the media throughout the year. Faculty David Ferguson, Gunda Georg, and Chengguo Xing were quoted in stories on the news blog *Health Talk*; Philip Portoghese and Robert Vince were featured in *AHC GameChangers* posts.

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(l) cover of Professor Yusuf Abul-Hajj's book

(r) Research Associate Professor Eyup Akgün, Research Assistant Professor Rebecca Cuellar, Professor Philip Portoghese



Dr. Ferguson also discussed synthetic drugs on WCCO radio, and was quoted in “*Law enforcement fighting ‘epidemic’ of heroin use*” on MPR Morning Edition (and their website) on June 19. **Michael Walters** was quoted by *HealthCanal.com* in the January 2 story “*Minnesota Partnership Researchers Close in on Drug to Fight Fungal Infections*” and in the March 29 *Nature* story “*Chemistry’s web of data expands.*” **Gunda Georg** was quoted in the *Science Business eXchange (SciBX)* November 29 article, “*Solving Triptolide.*”

A recent publication by the Georg laboratory on the synthesis of Oximidine II (*Angew. Chem. Int. Ed.* 2011, 50, 7855) was highlighted in the *Organic Chemistry* portal “*C-O Ring Construction*” column dated April 9. *Chemical & Engineering News* featured Dr. Georg in their story, “*Hunt For The Male Contraceptive Pill Continues Despite Decades Of Research.*”

Both *ScienceCodex* and *Science Daily* featured research by Dr. **Robert Vince** on December 3. He and his colleagues in the Center for Drug Design have developed a synthetic compound that, in a mouse model, successfully prevents the neurodegeneration associated with Alzheimer’s disease. Professor Vince and his passion for science are explored in the feature story “*To be a scientist*” on the *UMNews* website.

Vytacera Pharma, Inc. announced they will develop Sulfanegen, a treatment of cyanide poisoning invented by Medicinal Chemistry professors **Robert Vince**, director of the Center for Drug Design (CDD) and emeritus professor **Herbert Nagasawa** with Steve Patterson, CDD associate director.

A Young Scientist Roundtable at the Wayzata Middle School on November 13 featured ITDD Director **Mike Walters**, who presented “*The Art and Science of Molecular Construction*” and answered questions from teens.

Research Activities

Department of Medicinal Chemistry faculty produced 86 publications in more than 50 journals in 2012. In addition, the Department was represented at numerous conferences through oral and poster presentations.

Symposia

The 2012 Taito O. Soine Lecture was presented by Dr. **Robert P. Hanzlik**, Professor of Medicinal Chemistry at the University of Kansas. His October 23 presentation was entitled “*Reactive metabolites cellular targets and beyond.*”

On June 8, the Department of Medicinal Chemistry held a symposium to honor retiring professor **Patrick E. Hanna** for his 43 years of distinguished teaching, research and scholarship in the College of Pharmacy, University of Minnesota. Guest speakers included:

- Dr. **Judy L. Bolton**, Professor and Head, Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago. *Prevention of estrogen carcinogenesis by selective estrogen receptor modulators (SERMs) and botanical dietary supplements.*
- Dr. **Adnan Elfarra**, Professor of Toxicology, Department of Comparative Biosciences, University of Wisconsin, Madison. *Glutathione-dependent bioactivation as a tool for anticancer prodrug design.*
- Dr. **Stephen S. Hecht**, Wallin Land Grant Professor of Cancer Prevention, Masonic Cancer Center, University of Minnesota. *DNA Binding and carcinogenicity of tobacco-specific nitrosamine enantiomers.*



(l) Research Associate Professor
Michael Walters

(r) Professor Thomas Shier,
Professor Carston R. Wagner,
Distinguished Professor Philip
Portoghese, Soine lecturer
Professor Robert Hanzlik,
and Professor Gunda Georg
(clockwise from left)



- Dr. **Daniel C. Liebler**, Professor of Biochemistry and Biomedical Informatics, Ingram Professor of Cancer Research, Professor of Pharmacology, Vanderbilt University. *Understanding damage caused by reactive intermediates: Probes, proteomics and networks.*
- Dr. **Rodney F. Minchin**, Ph.D., Chair, Department of Molecular Pharmacology, University of Queensland. *Nanoparticle unfolding of proteins - Arylamine N-acetyltransferase as a probe.*
- Dr. **Edith Sim**, Dean, Faculty of Science, Engineering and Computing, Kingston University. *Arylamine N-acetyltransferases – from drug metabolism to drug discovery.*
- Dr. **Richard Weinshilboum**, Professor, Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester. *Pharmacogenomics: Beyond biomarkers.*

Seminars

Many interesting and respected professors and researchers were invited to present seminars in 2012 by the Department of Medicinal Chemistry, the Chemical Biology Initiative (CBI), and the Institute for Therapeutics Discovery and Development (ITDD).

- Dr. **Katherine Seley-Radtke**, Professor, Medicinal and Bioorganic Chemistry, University of Maryland, Baltimore County. *Flexibility: A new paradigm for nucleoside drug design*, January 24.
- Dr. **Kamil Ugurbil**, Professor, Radiology/Magnetic Resonance Research Center, University of Minnesota. *Imaging brain function and connectivity with ultrahigh field magnetic resonance*, February 3 (ITDD).
- Dr. **Jim Paulson**, Professor, Department of Chemical Physiology, The Scripps Research Institute. *Siglecs as sensors of self*, February 6 (CBI).
- Dr. **Silvia Balbo**, Research Associate, Masonic Cancer Center, University of Minnesota. *Development of a high-resolution mass spectrometry method for observation and characterization of unknown adducts in human DNA*, February 14.
- Dr. **Alexander Doemling**, Professor, Department of Pharmaceutical Sciences, University of Pittsburgh. *Instant discovery of protein-protein interaction antagonists using anchor query*, February 21.
- Dr. **Gregory Cook**, Professor and Chair, Department of Chemistry and Biochemistry, North Dakota State University. *Following the zinc: An organic chemist's journey from MMPs to HDACs*, March 2 (ITDD).
- Dr. **Sam Gellman**, Professor, Department of Chemistry, University of Wisconsin, Madison. *Mimicry of information-rich protein surfaces with peptidic foldamers*, March 5 (CBI).
- Dr. **Caren L. Meyers**, Assistant Professor, Department of Pharmacology and Molecular Sciences, Johns Hopkins University School of Medicine. *Intracellular delivery of polyphosphonates: The chemistry and biology of bisphosphonamidate prodrugs*, March 6.
- Dr. **Steven Rokita**, Professor, Department of Chemistry and Biochemistry, University of Maryland. *Reversible alkylation of DNA by quinone methide intermediates*, March 20.
- Dr. **Robert Vassar**, Professor, Department of Cell and Molecular Biology, Northwestern University. *BACE1, the Alzheimer's beta-secretase enzyme, in health and disease*, April 9 (CBI).
- Dr. **Sanjay Malhotra**, Head, Laboratory of Synthetic Chemistry. Drug Synthesis and Chemistry Branch, National Cancer Institute. *Podofilox – potential for anti-cancer drugs*, May 3 (ITDD).



(l) Morse-Alumni Distinguished Teaching Professor Patrick Hanna

(r) Stephen Hecht, Medicinal Chemistry Adjunct Professor, and Assistant Professor William Pomerantz, CBI presenter – both faculty in the University's Department of Chemistry



- Dr. Larry Walker, Director, National Center for Natural Products Research, University of Mississippi School of Pharmacy. *Natural products discovery for pharmaceutical and agrichemical applications*, May 11 (ITDD).
- Dr. Zhihao Zhuang, Assistant Professor, Department of Chemistry and Biochemistry, University of Delaware. *Chemical biology of translation synthesis and the regulation by reversible ubiquitylation*, May 14 (CBI).
- Dr. Qisheng Zhang, Assistant Professor, Division of Chemical Biology and Medicinal Chemistry, University of North Carolina. *Chemical tools to monitor and regulate the phosphatidylinositide signaling network*, June 26.
- Dr. Chris Douglas, Assistant Professor, Department of Chemistry, University of Minnesota. *Organic synthesis based on the insertion of transition metals adjacent to carbonyls: Moving beyond C-H activation*, July 20 (ITDD).
- Dr. Douglas S. Johnson, Associate Research Fellow, Pfizer. *Chemical biology with clickable probes: Application to the discovery of FAAH inhibitors and γ -secretase modulators*, September 18.
- Dr. William Pomerantz, Assistant Professor, Department of Chemistry, University of Minnesota. *Organofluorine: the "odd man in" in chemical biology*, September 24 (CBI).
- Dr. Alexei Demchenko, Professor, Chemistry and Biochemistry, University of Missouri, St. Louis. *From chemical glycosylation to expeditious oligosaccharide synthesis*, September 25.
- Dr. Edward B. Skibo, Professor, Department of Chemistry and Biochemistry, Arizona State University. *Design of target-based antitumor agents*, October 2.
- Dr. Stephen V. Frye, Director, Center for Integrative Chemical Biology and Drug Discovery, University of North Carolina, Chapel Hill. *Chemical biology of methyl1 lysine readers*, October 16.
- Dr. Robert P. Hanzlik, Professor, Department of Medicinal Chemistry, University of Kansas. Taito O. Soine Lecture: *Reactive metabolites, cellular targets, and beyond*, October 23.
- Dr. David A. Colby, Assistant Professor, Department of Medicinal Chemistry, Purdue University. *Synthesis and biological evaluation of difluoromethyl ketones synthesized by a trifluoroacetate-release aldol reaction*, November 6.
- Dr. Barry O'Keefe, Head, Protein Chemistry and Molecular Biology Section, Center for Cancer Research. *Antiviral proteins from natural product extracts*, November 9 (ITDD).
- Dr. Edmond J. LaVoie, Professor, Medicinal Chemistry and Chair, Department of Pharmaceutical Chemistry, University of New York, Buffalo. *Macrocyclic G-quadruplex stabilizers as antitumor agents*, November 13.
- Dr. Anna K. Mapp, Professor, Department of Chemistry, University of Michigan. *Regulating transcription with large and small molecules*, November 20.

Student Recognition

Students in the Department of Medicinal Chemistry are a hard working, talented group. Nine students joined the Department of Medicinal Chemistry in 2012. In addition, visiting scholars from other countries and a student from the Mayo Clinic came to the University to work with department faculty over the year.

Several Medicinal Chemistry students were awarded travel funds by the American Chemical Society to attend the Fall 2012 National Meeting held in Philadelphia. The ACS Division of

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(r) 2012 Medicinal Chemistry incoming class members Cody Lensing, Emily Boldry, Carter Eiden, Andrea Wisniewski (back); Erick Carlson, Jacob Petersburg, Matthew Bockman, Christopher Seiler (front)

Not pictured: Harrison (Trent) West



Medicinal Chemistry awarded a travel grant to **Trinh Doan** from the Georg lab, and fellow Georg lab member **Wei Li** received the ACS Division of Organic Chemistry travel award. **Maggie Olson** from the Harki Lab presented at this meeting as one of nine national recipients of the Eli Lilly Travel Award from the Women Chemists Committee.

The University also rewarded Department of Medicinal Chemistry students with special financial support. **Amit Gangar**, Wagner Lab, and **Srikanth Kotapati**, Tretyakova Lab, received Doctoral Dissertation Fellowships from the Graduate School. This fellowship is intended to enable Ph.D. candidates of particular promise to devote full-time effort to the research and writing of their dissertations, and has been awarded to one or more Medicinal Chemistry students each of the past three years. Ganger was additionally honored in the top fifteen of 137 fellows for 2012, and was selected to present his research on “*Self-assembled nanostructures for the cellular delivery of small molecules, DNA, and proteins for the treatment of cancer*” in a November seminar.

Ran Dai, Finzel Lab member, was awarded a 2012 Bighley Fellowship, intended to support students working with faculty on collaborative and interdisciplinary research. Since its inception in 2010, half of these College of Pharmacy fellowships have been awarded to Medicinal Chemistry students.

Harki Lab member **Nick Struntz** was awarded a two-year, \$52,000 predoctoral fellowship from the American Heart Association for his proposal, “*Development of Photochemically Regulated DNA Decoys to Control NF-kappa-B Activity*.”

Commencement

Shui Li M.S., August..... Advisor: Wagner
Evaluation of Eukaryotic Initiation Factor 4E (eIF4E) Antagonist 4Ei-1 in Mammalian Breast Cancer and Lung Cancer Cells: Chemosensitization with Low Cytotoxicity

David Lee Lampi Hermanson..... Ph.D., August..... Advisor: Xing
Mechanisms of CXL017: Targeting drug resistant cancer

Aaron Matthew Teitelbaum Ph.D., August..... Advisor: Remmel
Pre-clinical drug development of 9-aminoacridines for malignant glioma and meropenem prodrugs for drug-resistant tuberculosis

Martin Blake Phillips Ph.D., September..... Advisor: Peterson
Characterization of the chemical properties of intermediates in furan metabolism.

Michael T. Peterson Ph.D., October..... Advisor: Fecik
Design and synthesis of tubulysin analogs that stabilize and mimic a key acetate important for potent antiproliferative activity against multi-drug resistant cancers

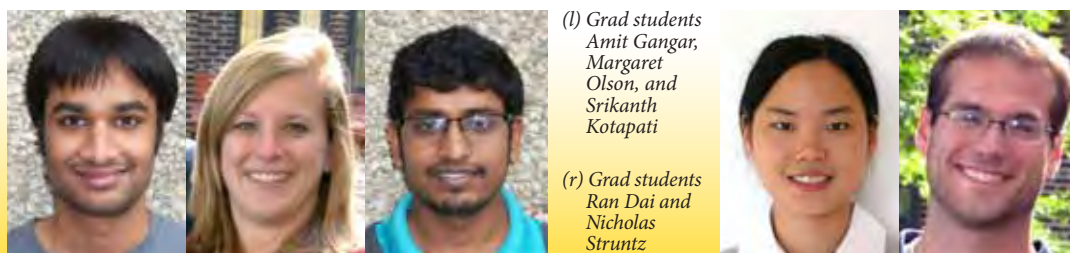
Bryant Charles Gay Ph.D., November..... Advisor: Georg
Cyclic enamines: Synthons for piperidine containing natural products and natural product analogs

Curtis Alan Engelhart M.S., December Advisor: Aldrich
Synthesis and evaluation of conformationally constrained analogues of SAL-AMS, a potent bisubstrate inhibitor of the mycobacterial aryl acid adenylating enzyme MbtA involved in mycobactin biosynthesis

MIKI Meeting 2012

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 graduate students in the departments of Medicinal Chemistry at the Universities of Minnesota, Iowa, Kansas, and Illinois at Chicago.

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The University of Iowa hosted the 50th Annual MIKI meeting and featured Dr. **Heidi Hamm**, Earl W. Sutherland, Jr. Professor and Chair of the Department of Pharmacology, Vanderbilt University Medical Center, who presented the keynote lecture “*Heterotrimeric G protein activation by G-protein-coupled receptors.*”

University of Minnesota graduate students represented the department well. **Trinh Doan** took first place in the oral presentations at meeting, and **Amit Gangar** and **Kathy Nelson** won two of three poster prizes.

New and Departing Members

Jon Hawkinson joined the Institute for Therapeutics Discovery and Development in November as the new Director of the High Throughput Screening and Assay Development Core. He is a former vice president of research and development at Omneuron, Inc., and former senior director in lead discovery and optimization at Elan Pharmaceuticals.

Research professor **Derek Hook** retired from his position as director of the High Throughput Screening Laboratory for the Institute for Therapeutics Discovery and Development. He has returned to his home in San Diego, California.

Jeanine Ferguson, Ph.D., is the current Assistant to Dr. Georg and Administrative Coordinator for the Department of Medicinal Chemistry and the Institute for Therapeutics Discovery and Development. A graduate and long-term employee of the University, Jeanine has spent the last fifteen years working directly to assist faculty, graduate students, and post-docs to secure internal and external support for projects of varying type and scale. She joins us after working for the Deans' offices in CLA and CEHD, on the programmatic level in AHC, and most recently for the Office of the Senior Vice President for System Academic Administration.

The administrative office at 717 Delaware welcomed **Kelli Pettinelli**, Principal Office and Administrative Specialist. Kelli is a University of Minnesota graduate with a bachelors degree in Asian Languages and Literature. She has studied abroad in China and Ecuador and is fluent in Chinese and Spanish. Kelli comes to us from the University of Minnesota China Center.

Faculty

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

Rodney L. Johnson Associate Department Head & Distinguished Professor

David M. Ferguson Director of Graduate Studies & Professor

Yusuf J. Abul-Hajj Professor

Eyup Akgün Research Associate Professor

Elizabeth A. Amin Assistant 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



(l) Graduate students Trinh Doan and Kathy Nelson at the 50th MIKI meeting in Iowa

(r) Retiring Research Professor Derek Hook and new Research Professor Jon Hawkinson, ITDD High Throughput Screening Core



Patrick E. Hanna.....	Morse-Alumni Distinguished Teaching Professor
Daniel A. Harki.....	Assistant Professor
Carrie Haskell-Luevano.....	Professor; Philip Portoghese Endowed Chair; Institute for Translational Neuroscience (ITN) Scholar
Jon Hawkinson.....	Research Professor; Director, ITDD High Throughput Screening & Assay Development Core
Derek J. Hook.....	Research Professor; Director, ITDD High Throughput Screening Core
Herbert T. Nagasawa.....	Professor Emeritus
Philip S. Portoghese.....	Distinguished Professor
Rory P. Rummel.....	Distinguished Teaching Professor
W. Thomas Shier.....	Professor
Marilyn K. Speedie.....	Dean, College of Pharmacy; Professor
E. John Staba.....	Professor Emeritus
Natalia Y. Tretyakova.....	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 & Probe Discovery Core
Henry L. Wong.....	Associate Research Professor; Director, ITDD Pharmacology & Biomarkers Core
Chengguo (Chris) Xing.....	Associate Professor

Adjunct Faculty

Courtney C. Aldrich.....	Associate Professor, Center for Drug Design
Mark D. Distefano.....	Distinguished McKnight Professor; Merck Professor of Chemistry and Medicinal Chemistry, Department of Chemistry
Stephen S. Hecht.....	Professor, Wallin Chair in Cancer Prevention, Masonic Cancer Center
Thomas R. Hoye.....	Merck Professor, Department of Chemistry
Krzysztof W. Pankiewicz....	Research Professor; Associate Director, CDD
Lisa A. Peterson.....	Professor, Division of Environmental Health Sciences

Administrative Staff

Caitlin Boley.....	Principal Office & Administrative Specialist
Laura Burnes.....	Student Office Assistant
Mary Crosson.....	Associate Administrator
Sandy Dewing.....	Associate Administrator, Journal of Medicinal Chemistry
Jeanine Ferguson.....	Assistant to Dr. Gunda Georg
Briana Gray.....	Student Office Assistant
Kelli Pettinelli.....	Principal Office & Administrative Specialist
Joyce Reha.....	Executive Secretary
Sarah Johnson Sexton.....	Executive Office & 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
Amanda Esades.....	Research Associate, Tretyakova Lab
Adrian Fegan.....	Research Associate, Wagner Lab

(r) Amin lab members Elbek Kurbanov, Assistant Professor Elizabeth Amin, Dr. Ting-Lan Chiu, and Xia Zhang



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
 Delshanee Kotandeniya Research Associate, Tretyakova lab
 Sidath Kumarapperuma Research Associate, Wagner Lab
 Jae Chul Lee..... Research Associate, Wagner Lab
 Pablo Leitzman Senior Lab Technician, Xing Lab
 Lev Lis Principal Scientist, Gurvich Lab
 Mary Lunzer..... Scientist, Portoghese Lab
 Brock Matter Scientist, Tretyakova Lab
 Angela Perkins-Harki Research Associate, Harki Lab
 Michael Powers Scientist, Portoghese Lab
 Stephen Schnell..... Scientist, Portoghese Lab
 Anamika Singh Research Associate, Haskell-Luevano Lab
 Rondedrick Sinville Research Associate, Hawkinson Lab
 Mary Smart..... Assistant Scientist, Laboratory 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, Georg lab
 Defeng Tian..... Research Associate, Hawkinson Lab
 Timothy Ward..... Research Associate, Georg Lab

Postdocs, Fellows, and Visiting Scholars

Daniel Abate-Pella..... Harki Lab
 Mohamed Abou-Karam Shier Lab
 Sahib Alam Visiting Scholar, Shier Lab
 Karina Bora de Oliviera Visiting Research Scholar, Wagner Lab
 Dennis Brown Fecik Lab
 Matthew Cuellar Wagner Lab
 Jignesh Doshi Portoghese Lab
 Sandra Eichler..... Visiting Research Scholar, Georg Lab
 Teshome Gherezghiher Tretyakova Lab
 Aridoss Gopalakrishnan..... Xing Lab
 Sophie Huang..... Haskell-Luevano Lab
 Dong-Jin Hwang..... Johnson Lab
 Kenneth Johnson Finzel Lab
 Aaron Kempema..... Harki Lab
 Nigam Kumar..... Wagner Lab



(l) Fecik lab members Yang Li, Will Fiers, Michael Peterson, and Associate Professor Robert Fecik

Morgan Le Naour Portoghese Lab
 Matthew Metcalf..... Portoghese Lab
 Anja Meissner Rimmel Lab
 Sreekanth Narayanapillai.... Xing Lab
 Wahab Okunowo..... Visiting Resarch Assistant Professor, Shier Lab
 Charles Schiaffo Ferguson Lab
 Jeffrey Vanvoorst..... Finzel 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
 Erick Carlson Advisor: Georg
 Jameson Dahlin (Mayo)..... Advisor: Walters
 Ran Dai Advisor: Finzel
 Trinh Doan Advisor: Georg
 Skye Doering..... Advisor: Haskell-Luevano
 Carter Eiden Advisor: Aldrich
 Curtis Engelhart Advisor: Aldrich
 William Fiers..... Advisor: Fecik
 Kari Gabrielse Schuett Advisor: Wagner
 Amit Gangar..... Advisor: Wagner
 Bryant Gay..... Advisor: Georg
 Arnold Groehler IV..... Advisor: Tretyakova
 David Hermanson Advisor: Xing
 Kwon Ho (John) Hong..... Advisor: Georg
 Mitch Hoverman (MicroEng) Advisor: Rimmel
 David Huang Advisor: Georg
 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
 Shui Li Advisor: Wagner
 Wei Li (Chem) Advisor: Georg
 Yang Li Advisor: Fecik
 Jing Liu..... Advisor: Wagner
 Li-Kai Liu..... Advisor: Finzel
 Kimberly Maize Advisor: Finzel

(r) Shier Lab members
 Dr. Wahab Okunowo,
 Professor W. Thomas
 Shier, and Dr. Sahib
 Alam



Kathryn Nelson..... Advisor: Aldrich
 Aniekan Okon..... Advisor: Wagner
 Margaret Olson..... Advisor: Harki
 Jacob Petersburg Advisor: Wagner
 Michael Peterson Advisor: Fecik
 Hao Pham (Chem) Advisor: Haskell-Luevano
 Martin Phillips..... Advisor: Peterson
 Adwait Ranade..... Advisor: Georg
 Dewakar Sangaraju..... Advisor: Tretyakova
 Christopher Seiler Advisor: Tretyakova
 Rachit Shah..... Advisor: Wagner
 Jingjing Shen Advisor: Wagner
 Nicholas Struntz Advisor: Harki
 Jonathan Tan Advisor: Tretyakova
 Aaron Teitelbaum..... Advisor: Rimmel
 Sreedhar Tummalapalli..... Advisor: Georg
 Dan Wang..... Advisor: Harki
 (Harrison) Trent West..... Advisor: Wagner
 Susith Wickramaratne (Chem) Advisor: Tretyakova
 John Widen Advisor: Harki
 Andrea Wisnieski..... Advisor: Georg
 Yiyun Yu (Chem)..... Advisor: Georg
 Adam Zarth..... Advisor: Hecht
 Xia Zhang..... Advisor: Amin
 Bo Zhou Advisor: Xing

Undergraduate Research Assistants and Summer Scholars

Danyang ChenWagner Lab
University of Minnesota Undergraduate Research Opportunities Program
 Hanna EricksonTretyakova Lab
 Amanda Esades.....Tretyakova Lab
 Amy Grant.....Tretyakova Lab
 Torie GroverHarki Lab
 Ryan HardingRimmel Lab
 Mohamed HatabShier Lab
 Edward HigginsShier Lab
 Peter HuynhWagner Lab
University of Minnesota Undergraduate Research Opportunities Program
 James LloydTretyakova Lab
 Ezra MenonHarki Lab
 Dan Murphy.....Tretyakova Lab
 Bryan Murray.....Fecik Lab
 Wanqi OoiTretyakova Lab
University of Minnesota Undergraduate Research Opportunities Program
 Katelyn PalmatierWagner Lab
University of Minnesota Undergraduate Research Opportunities Program

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(1) Tretyakova lab members
 Susith Wickramaratne,
 Emily Boldry, Dr. Jung-
 Eun Yeo (back); Dewakar
 Sangaraju, Arnold
 Groehler IV, Professor
 Natalia Tretyakova, and
 Dr. Teshome Gherezghiher
 (front)

Rebecca Pulk.....Walters Lab
 Amanda Reigel.....Tretyakova Lab
 Heedo ShinTretyakova Lab
 Eva Skellie.....Harki Lab
 B.J. Valente.....Tretyakova Lab
 Tram VoHarki Lab
University of Minnesota Undergraduate Research Opportunities Program
 Shuo YanTretyakova 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:

- 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
- Rimmel 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 will 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 exceeded \$6.6 million for fiscal year 2012.

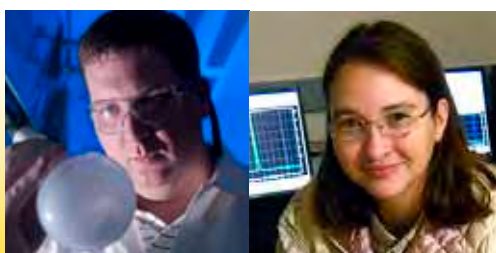
Some grants of special significance include a UO1 grant of \$4.7 million over five years for Dr. Gunda Georg's project "Drug Discovery & Synthesis of Contraceptive Agents." Phil Portoghese was awarded \$2.7 million over five years by the National Institute on Drug Abuse for "Ligands that target opioid-chemokine and opioid-mGluR5 heteromer" research. Department faculty Rory Rimmel and Michael Walters were awarded Engebretson Drug Design and Development grants from the College of Pharmacy. Rimmel is also co-investigator on a new \$1.9 million grant from NIH for the project "Maternal outcomes and neurodevelopment effects of anti-epileptic drugs." Dr. Chengguo Xing received an RO1 grant for more than \$1.5 million over five years for his research into "Mechanisms of anticancer agents selective against drug resistant leukemia."

Other ongoing projects and grants newly funded in 2012 are listed below with their primary investigator.

- Administration of the National Institute for Pharmaceutic Technology and Education Vadim Gurvich
- An anticancer agent selective against drug resistant AML Chengguo Xing

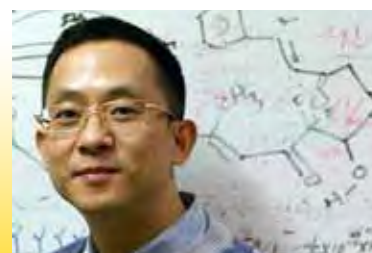


- An NF- κ B inhibitor as a post-carcinogen lung cancer chemopreventive agent Chengguo Xing
- Anthrax toxin lethal factor inhibition study Elizabeth Amin
- APOBEC transfection enhancer technology Daniel Harki
- Beyond parthenolide: Next generation molecules targeting AML cancer stem cells Daniel Harki
- Chemical Biology Consortium Gunda Georg
- Critical interactions of APOBEC3s Daniel Harki
- Defensins as melanocortin ligands Carrie Haskell-Luevano
- Developing a post-carcinogen lung cancer chemopreventive Chengguo Xing
- Development of anti-DUX4 therapies for FSHD Michael Walters
- Development of novel therapeutics for glaucoma Peter Dosa
- Development of small molecule inhibitors of the AAA ATPase p97 Gunda Georg
- Development of VUM4P1 as a novel approach to treatment of Parkinson's disease Vadim Gurvich
- 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
- High-Throughput meso-scale discovery of new frataxin enhancers Derek Hook
- HTS of natural product extract libraries for apoptosis inducers Michael Walters
- HTS of natural product extract libraries for NX106-107-052-0 Gunda Georg
- Identification and optimization of small molecule inhibitors of the histone acetyltransferase Rtt109 Michael Walters
- Integration of paclitaxel into nanorings for treatment of prostate cancer Carston R. Wagner
- Ligands that target opioid-chemokine and opioid-mGlu5 heteromers Philip Portoghese
- Mechanisms of anticancer agents selective against drug resistant leukemia ... Chengguo Xing
- Mechanisms of prostate cancer prevention by Korean Angelica Chengguo Xing
- Melanocortin selective ligands Carrie Haskell-Luevano
- Meropenem prodrugs for the treatment of tuberculosis Rory Rimmel
- Multivalent vaccine for opiate addiction Philip Portoghese
- Nikkomycin Z treatment of early coccidioid pneumonia: Phase II clinical trial Vadim Gurvich
- Possible approaches for parenteral delivery of Fluorocox Vadim Gurvich
- Pro-Leu-Gly-NH₂ and dopamine receptor modulation study Rodney Johnson
- Role of DNA deamination in breast cancer Daniel Harki
- Selective nonpeptide opioid ligands Philip Portoghese
- Self-assembling immunotherapeutic nanorings Carston R. Wagner
- Sequence distribution of tobacco carcinogen-DNA adducts Natalia Tretyakova
- Small molecule inhibitors of PKA: A therapeutic strategy for SCA 1 Michael Walters
- Structural basis of specificity in affinity-labeled polyketide synthase didomains Robert Fecik
- Taming the mutator: Developing small molecules to stabilize the Daniel Harki
genome of cancer cells



(l) Assistant Professor
Daniel Harki,
Professor Carrie
Haskell-Luevano

(r) Associate Professor
Chengguo Xing



- Targeting cancer stem cells with parthenolide-functionalized gold nanoparticles Daniel Harki
- Targeting childhood brain tumors with parthenolide analogues Daniel Harki

Publications

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(l) Wagner lab members Lei Zhang, Katelyn Palmatier, Kari Gabrielse, Karina Bora de Oliveira, Jingjing Shen (back); Jing Liu, Rachit Shah, Dr. Sidath Kumarappruma, Amit Gangar, Professor Carston R. Wagner, Aniekon Okon

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