RESEARCH TO PATIENT CARE

University of Pittsburgh
School of Pharmacy
MISSION

The School of Pharmacy is committed to improving health through excellence, innovation, and leadership in education of pharmacists and pharmaceutical scientists, in research and scholarship, in care of patients, and in service to our communities.

VALUES

Integrity guides our daily work.
We foster:
Passion, commitment, and diligence;
Creativity and personal growth;
Collaboration and teamwork;
A culture of respect for the individual.
RESEARCH TO
PATIENT CARE

UNIVERSITY OF PITTSBURGH
SCHOOL OF PHARMACY
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Translating research findings to patient care has been a challenge for years. It is such a challenge that the National Institutes of Health (NIH) created Clinical and Translational Science Awards to increase the adoption of research discoveries in patient care. The University of Pittsburgh was among the first 12 universities nationwide to receive the award. The School of Pharmacy figured prominently in the collaboration among the schools of the health sciences in the education, research, and practice endeavors.

The School of Pharmacy is meeting the challenge to bridge the gap between research and patient care. Faculty research spans from identifying new drug targets and molecular modeling to developing and implementing evidence-based guidelines for effective drug therapy. With the exception of drug discovery and pharmacogenetics, this booklet organizes accomplishments by therapeutic area.
Research to Patient Care

Peer-reviewed Research Publications by Type

- Practice Based Research: 22%
- CEDAR: 17%
- Pre-clinical: 39%
- Clinical and Translational: 22%

$14.3 Million Annual Costs FY 2010

- NIH: $1,035,203
- Other Federal: $308,641
- Foundation: $187,737
- Other Funding: $75,685
- Industry: $12,708,698
The School of Pharmacy’s 28 faculty researchers have active grant awards totaling $72.8 million, with $14.3 million allocated to fiscal year 2010. NIH requires that all grant funds are used directly to support the work proposed in the grant application.

The scope of research and practice improvements is apparent in the distribution of the 135 peer-reviewed publications. These manuscripts share with the world the incredible contribution that the research makes to human health and to our understanding of human disease.
The three figures show that each postgraduate program has grown and contributes to the well-being and reputation of the School of Pharmacy and the University of Pittsburgh. The School of Pharmacy has taken to heart the University of Pittsburgh’s goal of increasing the number of PhD graduates as shown in the middle graph to the left.

The increase in the number of postdoctoral fellows parallels the growth in research programs, while the increase in the number of residents reflects a commitment to advance practice that facilitates early adoption of research findings. The School of Pharmacy has created a Mastery of Teaching program that prepares the trainees for academic positions at great universities throughout the world.

Thirty-five faculty members at five UPMC hospitals impact the quality of patient care by providing medication and health-based care, developing models and protocols of care, training future pharmacists, and translating research into care. The impact also spreads through the community with other partners.

The School of Pharmacy is on a remarkable trajectory of achievement.
The Center for Pharmacogenetics, established in 2000, has been a source of pride for the School of Pharmacy and the University of Pittsburgh. The faculty members are known internationally for their research, which has been recognized by significant prizes.

In the ten years since its founding, the Center has become known for the extensive contribution to the field of orphan nuclear receptors, which modify gene expression. In addition, Center faculty members investigate molecular mechanisms and new drug targets including protein degradation controlled by the ubiquitin system and targeted delivery of genetic material.
Pharmacogenetics
Major Accomplishments

FACULTY MEMBER(S):

Received annual NIH grant funding of $3,621,285.

Discovered that UBR2 can mediate genome-wide transcriptional silencing via its E3 activity for ubiquitination of histone H2A.

Established the molecular principles of N-end rule recognition.

Received NIH funding to develop novel formulations for in vivo delivery of radiation mitigators that are developed in the National Institute of Allergy and Infectious Diseases (NIAID) Center for Countermeasures against Radiation at the University of Pittsburgh.

Received a five-year NIH R01 grant titled “A Novel Role of the Aryl Hydrocarbon Receptor in Hepatic Steatosis.” The goal of this project is to study the role of the aryl hydrocarbon receptor (AhR) in fatty liver disease.

Was appointed director of the Smart Drug Delivery Core in NIAID center.

Was invited by the Advanced Drug Delivery Reviews to guest-edit a theme issue on “Development of novel therapeutic strategies by regulating the nuclear hormone receptors.”
Faculty

Yong Tae Kwon, PhD, Associate Professor
Song Li, MD, PhD, Associate Professor
Yong Li, PhD, Assistant Professor
Takafumi Tasaki, PhD, Research Assistant Professor
Tara Wada, PhD, Instructor
Wen Xie, MD, PhD, Professor

Graduate Students

Jie Gao, MS
Mohammed Ghazwani, BPharm
Chibueze Ihunnah, BS
Mengxi Jiang, BS
Dong Eun Kim, MS
Sung Tae Kim, MS
Shashikanth Sriram, MS
Yifei Zhang, MS

Postdoctoral Fellows

Jee-Young An, PhD
Quiqiong Cheng, PhD
Lihua Jin, PhD
Marina Karikozova, PhD
Ramaling Karuba, PhD
Euna Kim, PhD
Xiaowu Li, PhD
Dariusz Martynowski, PhD
Zhongliang Zheng, PhD
Selected Publications


Reports an important metabolic function of CAR and may establish this “xenobiotic receptor” as a novel therapeutic target for the prevention and treatment of obesity and type 2 diabetes.


UBR2-deficient spermatocytes are profoundly impaired in chromosome-wide transcriptional silencing of genes linked to unsynapsed axes of the X and Y chromosomes. These findings suggest that insufficiency in UBR2-dependent histone ubiquitination triggers a pachytene checkpoint system, providing a new insight into chromatin remodeling and gene expression regulation.


Farnesoid X receptor (FXR) plays an important role in the maintenance of cholesterol and bile acid homeostasis; treatment with an FXR agonist increased expression of DDAH-1 and CAT-1 in both liver and kidney.
Selected Invited Presentations

World Class University Distinguished Lecture Series, Seoul National University, Seoul, South Korea. Yong Tae Kwon. “Regulated proteolysis by the protein N-terminus.” May 26, 2010.


Drug Discovery

The faculty plays a major role in the Drug Discovery Institute of the University of Pittsburgh, which comprises the School of Pharmacy, School of Medicine, and the Department of Chemistry of the School of Arts and Sciences. The School faculty is on the forefront internationally of computational chemistry as they develop in silico methods to facilitate drug design. Pitt is a national leader in the application of multicomponent reaction chemistry in the synthesis of small molecular weight molecules. Recent target systems of interest are MDM2-P53 inhibitors, CB2 (cannabis receptor), and tubulin stabilizers.
Drug Discovery

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Major Accomplishments

FACULTY MEMBER(S):

Received annual NIH grant support of $831,051 in FY10.

Designed, synthesized, and developed small molecule inhibitors of MDM2 binding to P53 with potential as anticancer drugs.

Received additional funds to hire medicinal chemists to work on development of new lead compounds for the Drug Discovery Institute.

Received approval to participate in National Cancer Institute (NCI) chemical biology consortium resulting in NCI contracts for screening and for synthesis.
Faculty

Billy W. Day, PhD, Professor
Alexander S. Doemling, PhD, Professor
Barry I. Gold, PhD, Professor
Chair, Department of Pharmaceutical Sciences
Donna M. Huryn, PhD, Professor
Xiangqun (Sean) Xie, PhD, Professor

Graduate Students

Abdulrahman A. Almehizia, BPharm
Ananda Chowdhury, MS
Yijun Huang, MS
Kareem Khoury, BS
Timothy R. Pouland, BS
Ryan D. Whetstone, MS

Postdoctoral Fellows

Haiping Cao, PhD
Manjori Ganguly, PhD
Vasily Korotchenko, PhD
Ajay Srinivasan, PhD
Kan Wang, PhD
LiRong Wang, PhD
Wei Wang, PhD
Selected Publications

The paper describes the design and synthesis of small molecule scaffolds that block the interaction between MDM2 and p53; the synthesis uses multi-component chemistry.

A compound was synthesized to place positive charge precisely in the major groove. This modification stabilizes DNA. The results indicate that electrostatic binding may be important in DNA-protein recognition.

The synthesis of a bicyclic β-benzylxoy and β-hydroxy amide library from cyanohydrin ethers was performed using multicomponent reaction. Computational calculations show that these compounds contribute chemical diversity to chemical libraries.
Selected Invited Presentations


18th Annual International Conference on Intelligent Systems for Molecular Biology, Boston, MA. Xiang-Qun (Sean) Xie. “Novel Ligand Classification Algorithm and Application on Modeling Functionality for 5HT1A GPCR Ligands.” July 2010.


Patients in critical care settings present special challenges in drug therapy because of the complexity, criticality, and the rapidly changing nature of their physical condition. Treatments and rapidly changing physical condition affect absorption, distribution, metabolism, and elimination of drugs. School faculty members study the role of drug metabolizing in sequelae of stroke, traumatic brain injury, and myocardial infarction and translate bench research findings to direct patient care. Faculty ensure that patients’ medications are effective and safe, using cost minimization principles in this complex medical environment.
Major Accomplishments

FACULTY MEMBER(S):

Established a Small Molecule and Biomarker Core funded by the Clinical and Translational Science Institute of the University of Pittsburgh.

Received annual NIH funds totaling $563,308 in FY10.

Received a renewal of an R01 as a multiple PI submission for “Determining the Genetic and Biomarker Predictors of DCI and Long Term Outcomes after Subarachnoid Hemorrhage.”

Reduced medication administration errors in the Cardiac Intensive Care Unit by 25 percent by using human patient simulation.

Developed critical care pharmacotherapy education for nurses and physicians in six intensive care units.

Developed the first pharmacy-led multidisciplinary simulation program for the Society of Critical Care Medicine.

Received the NIH KL2 Career Development Award as part of the Clinical Research Scholars Program in the Clinical and Translational Science Institute at the University of Pittsburgh.
Faculty

Neal J. Benedict, PharmD, Assistant Professor
Philip E. Empey, PharmD, PhD, Assistant Professor
Bonnie A. Falcione, PharmD, Assistant Professor
Sandy L. Kane-Gill, PharmD, Associate Professor
Samuel M. Poloyac, PharmD, PhD, Associate Professor
Amy L. Seybert, PharmD, Associate Professor
Interim Chair, Department of Pharmacy and Therapeutics
Pamela L. Smithburger, PharmD, Assistant Professor

Graduate Students

Mark K. Donnelly, BS
Jiangquan (Jocelyn) Zhou, MA

Residents

Ananth M. Anthes, PharmD PGY2 Critical Care Resident
Michael J. Armahizer, PharmD PGY2 Critical Care Resident
Lisa M. Harinstein, PharmD PGY2 Critical Care Resident
Selected Publications


Patients with the rs3783988 TT genotype had > 2.65-times likelihood of better functional outcomes after TBI than individuals harboring a variant allele. Data suggest that the haplotype block represented by rs3783988 in NGB appears to influence recovery after severe TBI.


This comparative effectiveness study shows that continuous sedation with dexmedetomidine results in significantly lower total intensive care unit costs compared with midazolam infusion due to decreased intensive care unit and mechanical ventilation costs.


The clinical use of therapeutic hypothermia has been rapidly expanding due to evidence of neuroprotection. This study provides evidence that midazolam pharmacokinetics are altered in hypothermia and will guide future work to evaluate dose adjustments necessary for optimal use of midazolam.


Adverse drug reactions increase mortality, hospital length of stay, and health care costs, particularly in the critically ill. This review presents evidence for a genetic predisposition to adverse drug reactions in the intensive care unit, focusing on gene variants producing alterations in drug pharmacokinetics and pharmacodynamics and the medication involved.
Selected Invited Presentations


The School of Pharmacy has a distinguished tradition of supporting organ transplantation. Starting in the mid-1980s with cyclosporin, and subsequently tacrolimus, faculty members developed the dosage formulations and designed effective regimens to prevent organ rejection. Research on antifungal and other agents complements the immunosuppressive care of patients and improves patient outcomes. Faculty members have bridged laboratory science and clinical care, increasing the impact of research on patient outcomes.
Transplantation
Major Accomplishments

FACULTY MEMBER(S):

Received annual NIH grant support of $301,595 during FY10.


Received the Poster of Distinction Award for “Treprostinil ameliorates ischemia-reperfusion injury after rat orthotopic liver transplant” at the American Transplant Congress in May 2010.

Received FDA approval for an investigational new drug for the clinical trial to evaluate Treprostinil for use in ischemia reperfusion injury.

Received $128,000 in grant support from the FDA.
Faculty

Heather J. Johnson, PharmD, Assistant Professor
Kristine S. Schonder, PharmD, Assistant Professor
Michael A. Shullo, PharmD, Assistant Professor
Raman Venkataramanan, PhD, Professor

Graduate Students

Jennifer J. Bonner, PharmD
Nisanne S. Ghonem, PharmD
Kelong Han, BS
Jeremiah D. Momper, PharmD
Mohammed S. Shawfequah, PharmD, MS
Selected Publications


Found a fixed dosing regimen of voriconazole results in a highly variable exposure of voriconazole in liver transplant patients. Variability is related to liver function and presence of deficient CYP2C19*2 alleles. Given that trough voriconazole concentration is a good measure of drug exposure (AUC), the voriconazole dose can be individualized based on trough concentration measurements in liver transplant patients.


Systematic review of adverse effects and minimization strategies for pediatric immunosuppression.


Induction therapy with C-1H (Alemtuzumab) after cardiac transplant results in a similar 12-month survival, but a greater freedom from rejection despite lower calcineurin levels and without the use of steroids.


Transplant recipients who receive intravenous azithromycin and/or ceftriaxone concomitantly with tacrolimus therapy should be monitored closely for the duration of the antibiotic administration to minimize affects of drug interaction.
Selected Invited Presentations


International Congress of Therapeutic Drug Monitoring and Clinical Toxicology, Montreal, Canada. Raman Venkataramanan. “Pediatric (liver and small bowel) and adult small transplant patients—Pharmacokinetics of immunosuppressive drugs.” October 3, 2009.
Faculty members affect the treatment of neonates and adults through the consultative practice and through groundbreaking research. Through the UPMC Antibiotic Stewardship Program, anti-infective agent utility is preserved through evidence-based use of anti-infective agents.

Faculty lead research programs that evaluate new combination medication therapy for infections, that investigate stimulating the immune system to help defeat RSV virus in newborn and young infants (Children's Hospital of Pittsburgh of UPMC), and that develop delivery systems to prevent the spread of HIV/AIDS in women (Magee-Womens Hospital of UPMC).
Infectious Diseases
Major Accomplishments

FACULTY MEMBER(S):

Received $4,415,898 in grant support from NIH during FY10.

Received an $11.8 million five-year grant as co-principal investigator from NIAID at NIH for the development of a combination film HIV prevention product.

Reduced mortality rates among solid organ transplant recipients infected with extensively drug-resistant Acinetobacter baumannii by designing a combination drug therapy.

Collaborated to internally validate an automated susceptibility system known as Biomic®, which provides MICs for cultured organism. This system allows direct pharmacodynamic-based dosage determination for individual patients.

Created a rectal-specific product that contains the antiviral tenofovir for HIV prevention. It will be the first rectal-specific microbicide to be evaluated in a clinical trial.

Organized and hosted the International Microbicides Meeting in Pittsburgh attended by more than 1000 scientists from around the world.
Faculty

Kerry M. Empey, PharmD, PhD, Assistant Professor
CTSI KL2 Scholar
Brian A. Potoski, PharmD, Associate Professor
Associate Director, Antibiotic Management Service
Lisa C. Rohan, PhD, Associate Professor
Director, Microbicide Clinical Trial Network
Core Laboratory

Resident

Monica J. Dorobisz, PharmD, PGY2 Infectious Diseases Resident

Graduate Students

Ayman Akil, BS
Lindsay M. Ferguson, PharmD
Tiantian Gong, MS
Minlu Hu, BS

Postdoctoral Fellows

Hrushikesh Agashe, PhD
Rama Mallpeeddi, PhD
Wei Zhang, PhD
Selected Publications


Demonstrated safety and potential efficacy of tenofovir using in vitro model systems designed to quickly evaluate delivery systems for HIV-1 microbicides.


Demonstrated PSC-RANTES can readily be encapsulated into a PLGA nanoparticle drug delivery system, retain its anti-HIV-1 activity, and deliver PSC-RANTES to the target tissue. This is crucial for the success of this drug candidate as a topical microbicide product.


KPC-producing organisms are typically resistant to multiple classes of antibiotics and infections and are associated with high mortality rates. KPC-producing *K. pneumoniae, Escherichia coli,* and *Serratia marcescens* were sequentially identified in a patient who underwent small bowel transplantation. Molecular typing and plasmid analysis suggested that the KPC gene was acquired by *E. coli.*


Respiratory syncytial virus (RSV) is the most frequent cause of infant viral death worldwide, yet there is no vaccine or effective therapy available. This review summarizes the role of palivizumab, the only available prevention option for RSV, and investigates advances made in both RSV vaccine development and treatment strategies.
Selected Invited Presentations


Faculty members conduct basic research on cognition and are leaders in the study of the etiology of substance abuse disorder. Faculty have designed, implemented, and evaluated improvements in patient medication therapy with our partner institution for mental health, Western Psychiatric Institute and Clinic (WPIC) of UPMC.
Major Accomplishments

FACULTY MEMBER(S):

Received $2,957,689 in NIH grant awards during FY10.

Demonstrated that GPR30 (a novel estrogen receptor) is an important regulator of basal forebrain cholinergic neurons.

Reported that cholinesterase inhibitors, which are used to treat Alzheimer’s disease, can enhance beneficial effects of estrogen therapy on cognitive performance in aged rats and in rats with selective cholinergic lesions.

Led the program to engage pharmacists in discharge planning at WPIC for more than 1000 patients and facilitated access to medications for those patients. This patient-centered program has reduced WPIC readmission rates and increased rates of attending first outpatient appointment.

Partnered with the RAND Corporation to translate health promotion research into practice by investigating the impact of a hospital-wide smoking ban on prescribing trends for nicotine replacement.

Gained approval for a collaborative practice pharmacist direct-patient care agreement for pharmacists to offer effective treatments for nicotine dependence both during the hospitalization and upon discharge.
Faculty

Kim C. Coley, PharmD, Professor
Tanya J. Fabian, PharmD, PhD, Assistant Professor
Ulrike L. Feske, PhD, Assistant Professor
Robert B. Gibbs, PhD, Professor
Levent Kirisci, PhD, Professor
Galina P. Kirillova, PhD, Assistant Professor
Ty A. Ridenour, PhD, Assistant Professor
Ralph E. Tarter, PhD, Professor
Michael M. Vanyukov, PhD, Professor

Graduate Students

Rebecca E. Hammond, BS
Diana N. Pinchevsky, PharmD
Selected Publications


The paper shows that alpha-blockers, non-benzodiazepine sleep aids, benzodiazepines, H2 – blockers, lithium, antipsychotics, atypical antidepressants, and anticonvulsants were associated with higher rates of falls.


This paper proposes that cholinergic-enhancing drugs, used in combination with an appropriate estrogen-containing drug regimen, may be a viable therapeutic strategy for use in older postmenopausal women with early evidence of mild cognitive decline.


The Transmissible Liability Index (TLI) and Non-Transmissible Liability Index (NTLI) together predicted with 70 percent and 75 percent accuracy cannabis-use disorder manifest by age 19 and age 22.
Selected Invited Presentations


Faculty are educating and training students and practitioners; they are testing and evaluating models for interacting with patients and for collaborating with members of health care teams. The overall goal is to improve medication therapy and its outcomes for community-dwelling patients, including the homeless, the working poor, and the underinsured. Faculty members conduct research and care for patients in collaboration with UPMC physician practices and ambulatory clinics and a number of community partners.
Care for Community-Dwelling Patients

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Major Accomplishments

FACULTY MEMBER(S):

Received grant support totaling $908,648 in FY10, including $562,000 from Public Health Service.

Created pharmacist-managed clinical service at the Birmingham Free Clinic for patients with diabetes, hypertension, or dyslipidemia.

Evaluated the impact of pharmacists in family physician practices operating as medical homes in partnership with UPMC Health Plan and UPMC St. Margaret.

Hosted the HRSA Collaborative Regional Meeting, “Enhancing Diabetes Care through an Interprofessional Approach to Performance Improvement.”

Developed the Pennsylvania Pharmaceutical Care Network; worked collaboratively with the Pennsylvania Pharmacists Association.

Administered a total of 3004 seasonal influenza vaccines and 532 H1N1 influenza vaccines through the “Pharmacist-Provided Vaccine Program.”

Created SMaRT (Screening brief intervention and referral to treatment Medical education And Residency Training) which is providing innovative blended curricula to 750 residents to develop knowledge and clinical skills in brief screening for alcohol and drugs use.

Demonstrated that medication therapy management pharmacists who foster therapeutic alliance between themselves and their patients can improve medication adherence in collaboration with Kerr Drug, a regional chain headquartered in North Carolina.

Trained 300 pharmacists in 118 pharmacies to screen patients for risk of non-adherence to medications to provide 2- to 5-minute brief interventions in collaboration with the Pharmacy Quality Alliance, Highmark, RiteAid, and CECity.
Care for Community-Dwelling Patients

Faculty

Sharon E. Connor, PharmD, Assistant Professor
Director, Grace Lamsam Pharmacy Program for the Underserved
Scott R. Drab, PharmD, Assistant Professor
Deanne L. Hall, PharmD, Assistant Professor
Lauren J. Jonkman, PharmD, Instructor
Melissa S. McGivney, PharmD, Associate Professor
Karen S. Pater, PharmD, Assistant Professor
Janice L. Pringle, PhD, Research Associate Professor
Director, Program Evaluation and Research Unit

Residents

Shara E. Elrod, PharmD, PGY2 Ambulatory Care Specialty Resident
Mindy E. Kozminski, PharmD, PGY1 Community Practice Resident
Brooke E. Lowry, PharmD, PGY1 Community Practice Resident
Shannon M. McLaughlin, PharmD, PGY1 Community Practice Resident
Selected Publications


Survey instruments showed significant differences in perceived patient safety climate among hospitals, respondents, and departments. The differences in responses suggest that such instruments may be useful to identify and reinforce aspects of safety, culture, and organizational characteristics that may need to be targeted to improve patient safety outcomes.


Established a guide on how pharmacists and physicians can develop collaborative working relationships based on findings from established physician-pharmacist dyads.


A previously identified barrier to the universal provision of MTM is the lack of physician understanding of pharmacist-provided MTM. Through qualitative methodology, physician perceptions of MTM were identified in addition to perceived barriers and benefits to collaborating with pharmacists to provide MTM. These findings have been incorporated into practice and education models.


This qualitative research sought to identify effective strategies for marketing pharmacist-provided medication therapy management (MTM) services to patients in a self-insured employer setting. Strategies identified included emphasizing patient benefits (personal medication record), and using patient-friendly language such as “medication check-up” when marketing the service. This work has been cited in other peer-reviewed publications.
Selected Invited Presentations


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