Pharmaceutical Department

2015

Annual Report

2015 Annual Report
Pharmaceutical Department

Faculty • Full Members: William E. Evans, PharmD; William Greene, PharmD; Mary V. Relling, PharmD (chair); Erin G. Schuetz, PhD; John D. Schuetz, PhD, Clinton F. Stewart, PharmD; Associate Members: James M. Hoffman, PharmD ; Jun J. Yang, PhD

*Left institution in 2015: Associate Members: Sharyn Baker, PharmD, PhD; Alex Sparreboom, PhD

Staff Scientists • Barthelemy Diouf, PhD; Amarjit Chaudhry, PhD; John Lynch, PhD

Laboratory Directors • Alejandro Molinelli, PhD; Kristine R. Crews, PharmD

Fellows • Ju Bao, PhD; Vinay Daryani, PharmD; Christina Drenberg, PhD; Christian Fernandez, PhD; Yu Fukuda, PhD; Yoshihiro Gocho, MD, PhD; Charnise Goodings, PhD; Seth Karol, MD; Elixabet Lopez Lopez, PhD; Robert McCorkle, PhD; Jessica Morgan, PhD; Takaya Moriyama, MD, PhD; Jolieke Van Oosterwijk, PhD; Navjotsingh Pabla, PhD; Yogesh Patel, PhD; Steven Paugh, PhD; Virginia Perez-Andreu, MD, PhD; Aaron Pitre, PhD; Maoxiang Qian, PhD; Laura Ramsey, PhD; Aksana Vasilyeva, PhD; Juwina Wijaya, PhD; Heng Xu, PhD; Hui Zhang, MD, PhD

Residents •, JT Fannin, PharmD; Melissa Quinn, PharmD; Amy Pasternak, PharmD; Clay Daniels, PharmD, PhD

Graduate Students • Chengcheng Liu, Rebecca Quillivan, Nick Keeling, and Ashley Crumby

Overview:

The primary goal of the Pharmaceutical Sciences Department is to improve therapy for children with catastrophic diseases by elucidating the basis for interpatient variability in response to medications. Survival rates for children with cancer, HIV-1 infection, or other serious disease continue to increase, largely through the improved use of medications. Failure of current therapies and unacceptable adverse effects are partly due to less-than optimal medication dosing. Our goal is to elucidate the biological basis of interindividual differences in pharmacologic response, and to translate our findings into improving patient care.

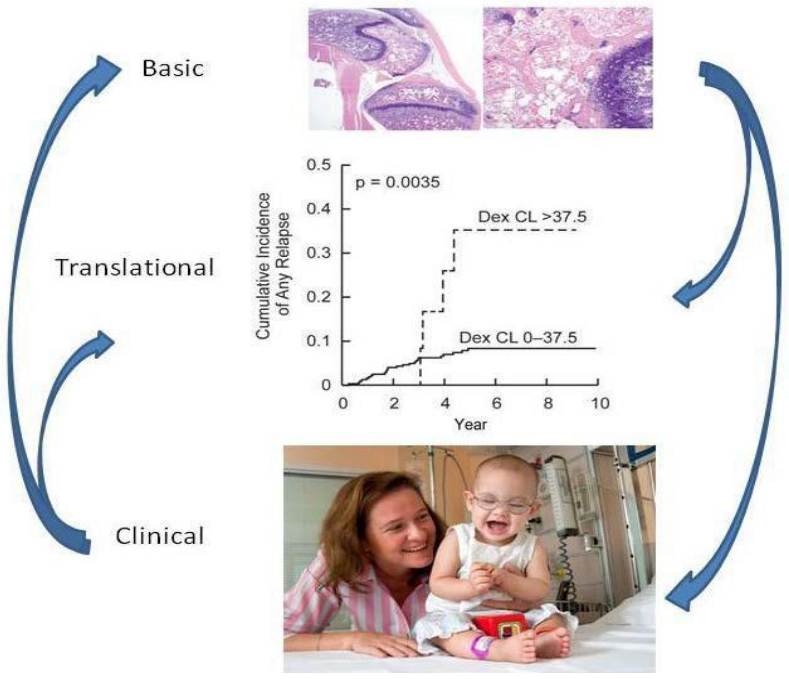

Figure 1. The Pharmaceutical Department encompasses basic, translational and clinical research, and transitions innovative strategies into patient care.

Heterogeneity in the metabolism, transport, elimination, targets, and receptors of many drugs and consequent variability in therapeutic or adverse effects may result from germline genetic differences or genetic alterations in malignant cells. Drug response is also influenced by nongenetic factors (e.g.,drug interactions, host organ function and maturity, disease severity, adherence to therapy).

We develop preclinical models to systematically characterize the determinants of human variation in drug response, and we integrate our work into translational clinical studies (Figure 1). Laboratory work informs clinical studies, and clinical problems drive much of the laboratory work. Faculty members lead and participate in interdisciplinary St. Jude programs and national cooperative research collaborations. Our pharmacogenetic research integrates genome-wide analyses, molecular analyses, functional genomics, pharmacokinetics, and pharmacodynamics to identify genetic determinants of drug effects, with the long- term goal of optimizing therapy for individual patients. The Department comprises both Pharmaceutical Sciences and Pharmaceutical Services, and includes ten faculty members, 15-25 post-doctoral fellows (Figure 2) and residents, 10-20 undergraduate and graduate students, over 45 pharmacists, and over 110 full time staff members working as computing experts, research nurses, technical, laboratory, administrative, and clinical staff. The laboratory faculty members all have NIH-supported programs. The research in the department includes clinical pharmacology, pharmacokinetics, pharmacodynamics, and pharmacogenomics. Pharmaceutical Sciences occupies over 15,000 sq. ft. of contiguous state-of-the-art equipped laboratory and office space, and Pharmaceutical Services occupies over 18,000 square feet of space in the clinical areas of St. Jude. The department hosts weekly research workshops and journal clubs that are open to the entire institution and are widely attended by colleagues outside the department, in addition to multiple laboratory or Services specific meetings, webinars with national and international colleagues, and regular pharmacogenomics meetings.

Figure 2. Post-doctoral fellows 2015-2016 Back row: Chengcheng Liu, Robert McCorkle, Ju Bao, Yogesh Patel, Vinay Daryani, and Seth Karol. Front row: Maxoxiang Qian, Aaron Pitre, Juwina Wijaya, Yu Fukuda, Charnise Goodings, Elixabet Lopez Lopez, Takaya Moriyama, Yoshihiro Gocho, and Hui Zhang.

Details on the rich St. Jude environment for clinical care and for clinical and basic research are available at www.stjude.org.

Pharmaceutical Department faculty, staff, and trainees work closely with each other; with our collaborators in other departments at St. Jude; and with colleagues around the world on basic translational, and clinical research projects and to provide outstanding pharmaceutical care to St. Jude patients.

Faculty:

William E. Evans, PharmD

Research in the Evans lab is focused on the pharmacogenomics of anticancer agents, with an emphasis on childhood acute lymphoblastic leukemia (ALL) (reviewed in Evans and Relling, *Nature* 2004; Pui and Evans, *NEJM* 2006; Paugh et al, *Clin Pharmacol Ther* 2011; Relling and Evans, *Nature* 2015). Several approaches are currently being used to identify genes and genome variations that are important determinants of the disposition and effects of antileukemic agents, including the use of genome wide approaches such as gene expression profiling (mRNA, microRNA) of leukemia cells, genome-wide SNP analyses (germline and somatic) and whole exome/genome sequencing of patient cohorts that have been uniformly treated and evaluated on prospective clinical trials at St. Jude Children's Research Hospital (reviewed in Evans and Relling, *Nature* 2004), or by our collaborators in the COG and in Europe (eg, Princess Maxima Center, Utrecht). Ongoing studies are investigating genes that the lab has linked with resistance to antileukemic agents (Holleman et al, *NEJM* 2004; Lugthart et al, *Cancer Cell* 2005), and genes linked to the disposition (Kager et al, *JCI* 2005; Zaza, *Blood* 2005) or pharmacologic targets (Diouf et al, *JAMA* 2015; Paugh et al, *Nat Genet* 2015) of antileukemic agents as well as the influence of somatic and karyotypic abnormalities on genotype-phenotype concordance (Cheng, *Nature Genetics* 2005; Diouf et al, *Nature Med* 2011). Work in the lab is funded by a long-standing R01 from NCI (CA36401, W. Evans, PI), a project in the Center for Precision Medicine P50 Grant from NIGMS as part of the NIH-funded Pharmacogenetics Research Network (GM115279, M. Relling PI), by a Cancer Center Support grant from NCI (CA21765 S. Baker, PI), and by ALSAC, the fundraising organization for St. Jude Children's Research Hospital. The lab comprises a number of post-doctoral fellows, staff scientists, research technologists, bioinformaticists, computational scientists and students, working with collaborators at St. Jude (including Mary Relling, Ching-Hon Pui, Charles Mullighan, Hiroto Inaba, Kirsten Ness and Jun Yang as major collaborators, plus additional physicians, clinical pharmacists, research nurses and other staff at St. Jude), and with collaborators at other institutions in the US (HudsonAlpha, University of

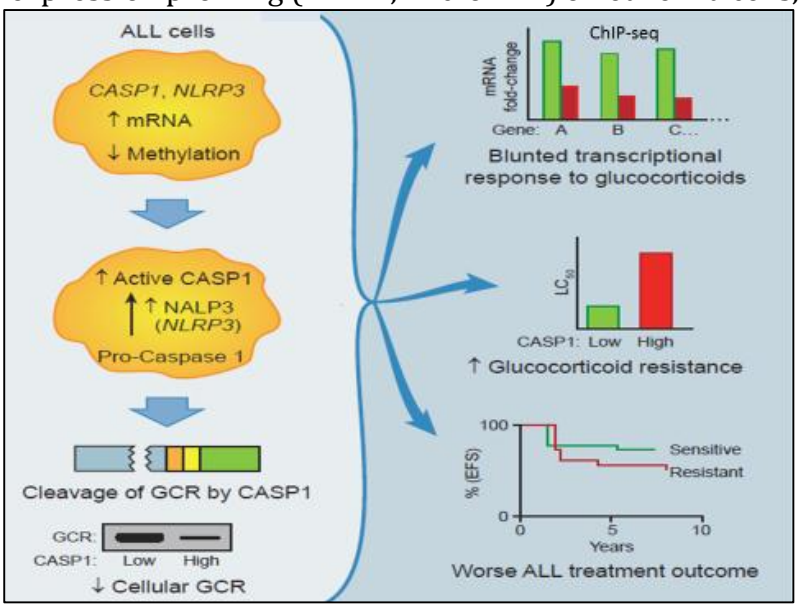

Figure 3: CASP1 causes glucocorticoid resistance via glucocorticoid receptor cleavage
Increased expression of inflammasome components CASP1 and NLRP3 via somatic hypo-methylated promoter regions leads to glucocorticoid receptor cleavage by CASP1. Decreased levels of functional glucocorticoid receptor leads to blunted transcriptional response to glucocorticoids, glucocorticoid resistance in ALL cells and is associated with inferior treatment outcome (see Paugh et al, *Nature Genet* 2015).

Chicago) and Europe (Erasmus University, Princess Maxima Center). The lab's overall goals are to elucidate genomic determinants of toxicity and efficacy of anticancer agents and translate this knowledge into new diagnostics and treatment strategies to optimize the therapy of ALL (Relling and Evans, *Nature* 2015; Dunnenberger et al, *Ann Rev Pharmacol Tox* 2015).

William Greene, PharmD

I joined Pharmaceutical Sciences as Chief Pharmaceutical Officer in August 2007. I have had a long career as a clinical pharmacy practitioner and leader in development of drug policy in hospital- based practice. My interests have been diverse and are summed up in the goal of developing structures, personnel, policy and practice to accomplish the best possible system to assure optimal outcomes of pharmacotherapy. My interests in Infectious Disease, Pharmacokinetics, Performance Improvement and Medication Safety continue.

As the senior leader of Pharmaceutical Services, it is my goal to assure the best possible design and function of pharmacy services to assure that we achieve the desired outcomes of drug therapy for St. Jude patients. Toward this end, Pharmaceutical Services collaborates closely with other disciplines in providing patient care, and with clinicians and scientists in translational and clinical research, and employs the principles of continuous process improvement in ongoing refinement/improvement of patient-related services. Clinical research in Pharmaceutical Services has focused on collaboration in applying pharmacokinetic, pharmacogenetic, and therapeutic drug monitoring principles to patient care, and in improving the safety of medication use. I currently retain a faculty appointment with the University of Tennessee College of Pharmacy (Professor, Affiliated), and am active in national and state professional organizations (current member of the Board of Directors of Tennessee Pharmacists Association).

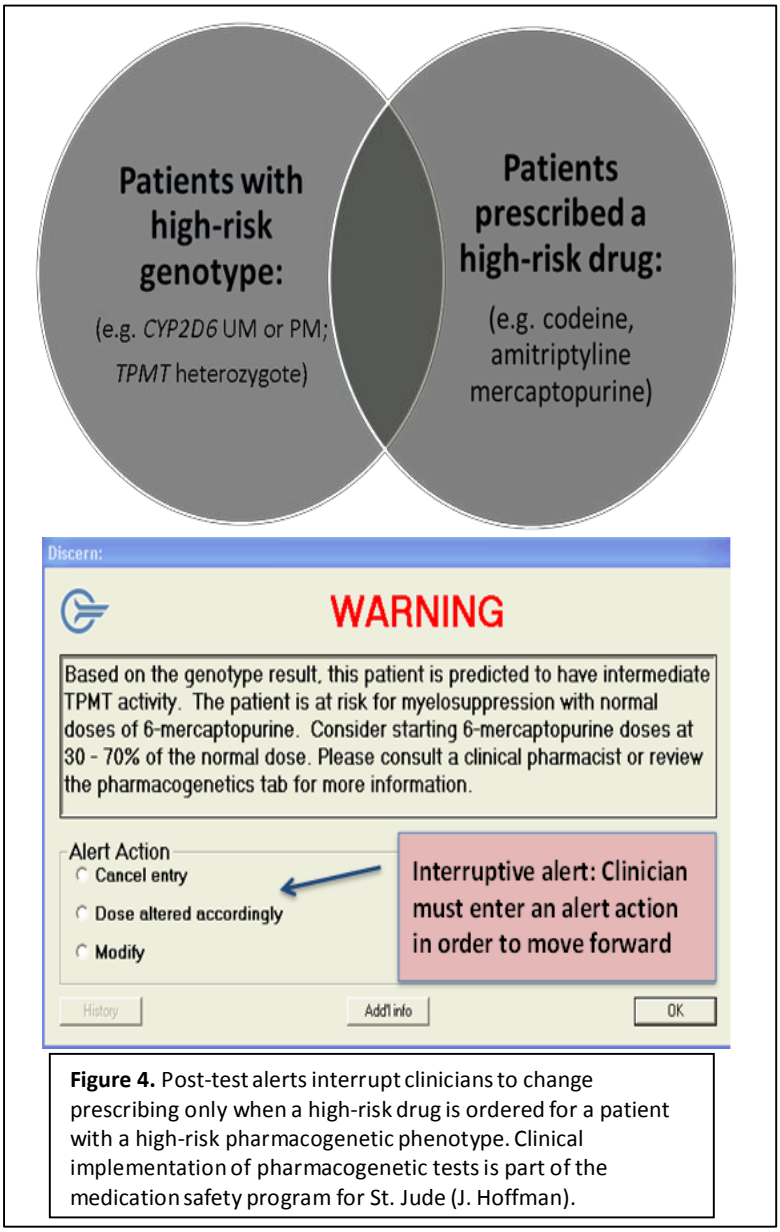

Figure 4. Post-test alerts interrupt clinicians to change prescribing only when a high-risk drug is ordered for a patient with a high-risk pharmacogenetic phenotype. Clinical implementation of pharmacogenetic tests is part of the medication safety program for St. Jude (J. Hoffman).

James Hoffman, PharmD

I joined the Pharmaceutical Department in 2004, and the St. Jude Faculty in 2011. My career has focused on evaluating and improving complex medication use systems, and I currently provide leadership of patient safety activities across St. Jude. Through my role as the hospital's Chief Patient Safety Officer, I am dedicated to postgraduate training by directing specialized residency program in

Medication-Use Safety. My research is focused on patient safety event detection, patient safety culture, and clinical decision support. Our work on patient safety event detection and reporting systems is built on our department's leadership to develop and implement St. Jude's novel electronic event reporting system (EERS) software. EERS is used to report all patient safety events at St. Jude, and this system has resulted in a 20% increase in event reporting. Because a healthy patient safety culture is essential to safe care, we have focused on assessing patient safety culture at St. Jude and devised new tools to measure specific aspects of safety culture in the hospital setting (Petschonek S et al *J Patient Saf 2014* and Burlison JD et al *J Patient Saf 2014*). I also lead a variety of efforts to expand and improve the use of clinical decision support (CDS) in the electronic health record (EHR) Through the PG4KDS protocol, St. Jude is a leader in incorporating pharmacogenetic data and associated CDS into the EHR (Bell et al, JAMIA, 2013) (Figure 4), and I have contributed to this protocol as an investigator since its inception. I have also been actively engaged in the Clinical Pharmacogenetic Implementation Consortium (CPIC) since its inception, and I co-lead the CPIC Informatics Working Group. CPIC has devised vendor agnostic informatics resources for each guideline (Martin et al, Clin Pharmacol Ther 2014), and these resources are being systematically added to all CPIC guidelines.

Mary V. Relling, PharmD

I have been a faculty member in the Pharmaceutical Department at St. Jude since 1988. Since then, the majority of my efforts have been directed to translational research in childhood acute lymphoblastic leukemia (ALL), although I have also maintained clinical involvement at St. Jude and in the Children's Oncology Group (COG). The clinical problems faced by children with ALL drive my research. Much of the work of my laboratory focuses on finding the genetic basis of why patients and their tumor cells differ from one another. We also study how nongenetic factors (e.g., diet and drug interactions, kidney and liver function, and age) affect how patients differ from each other in response to medications. The ALL phenotypes we focus on most include relapse, glucocorticoid induced osteonecrosis (Figure 5) and asparaginase immunogenicity and pharmacodynamics. Our laboratory has a heavy reliance on computational approaches, as we use genome-wide tools to interrogate genetic variability. We also use chemical analyses (e.g. HPLC, LC/MS) to study medication pharmacokinetics, cell culture models,

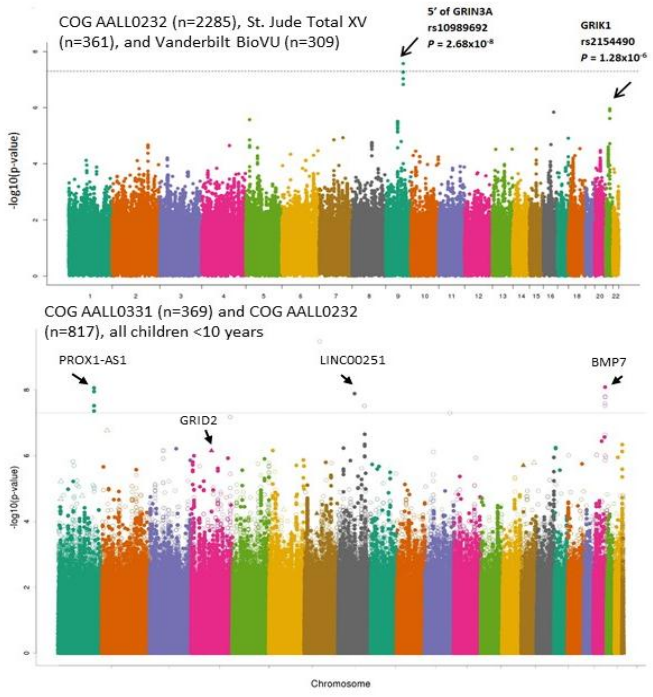

Figure 5. Manhattan plots of inverse log p values for associations of germline SNP variants with risk of osteonecrosis in patients with ALL and in adults without ALL (top panel, Karol et al 2015) and in patients younger than 10 years of age (bottom panel, Karol et al, 2016). Variants in glutamate receptor genes were associated with osteonecrosis in all cohorts.

molecular biologic techniques, murine models, and analysis of clinical outcomes and phenotypes. In 2011, we opened a clinical protocol, PG4KDS, with the goal of using array-based clinical genotyping to implement preemptive pharmacogenetic tests into clinical care for St. Jude patients (Dunnenberger et al 2014, Hoffman et al 2014). We collaborate with many investigators within the department, throughout St. Jude, within the COG, and within the Pharmacogenomics Research Network (PGRN).

Erin G. Schuetz, PhD

I joined the St. Jude Pharmaceutical Sciences Department in 1993. My lab studies cytochromes P450 (CYP), enzymes that metabolize many of the drugs administered to St. Jude patients. The lab identifies genetic determinants explaining variation in hepatic and intestinal CYP activities and, hence, variation in drug efficacy, toxicity and, ultimately, therapeutic outcome. The lab strategically uses both the candidate gene approach and exploits network and pathway analysis tools to illuminate the genetic variation in novel candidate genes affecting the CYP genetic network. The liver system biology/network approach has identified the node genes that, when individually perturbed, co-regulate many genes in the CYP network. My lab then uses deep resequencing of these novel candidate genes, and allelic expression imbalance analysis, to identify the functional and regulatory variants responsible for altering CYP activity and driving changes in the CYP expression network. Standard molecular, cellular and biochemical studies are then used to determine the functional consequence of these variants. Retrospective association studies are performed to determine if functional variants in candidate genes translate to clinical differences in CYP mediated drug clearance.

More recently our studies have focused on how drug transporters in the meningeal barrier layer influence the disposition of drugs administered by intralumbar injection (intrathecally, IT) into the cerebrospinal fluid (CSF). These studies were prompted by our unexpected discovery of high drug transporter expression in the meningeal barrier cells lining the cranial and spinal CSF space.

However, there is a complete lack of understanding on how these transporters influence CSF and CNS drug disposition and drug removal into the systemic circulation, despite the fact that the number of St. Jude patients receiving IT chemotherapy continues to grow. Our studies include determining the disposition of radiolabeled and fluorescent drugs administered IT to mice with and without drug transporters and using confocal immuohistochemistry to determine transporter membrane location in primary mouse leptomeningeal cells.

John D. Schuetz, PhD

A member of the Pharmaceutical Sciences Department since December 1992, my laboratory focuses on understanding the contribution of ABC transporters to pathological processes and pharmacological response using cell culture model systems as well as gene knockout models (e.g., reviewed *Ann Rev Pharm Tox,* 2006 and 2013). Using these model systems, we have, through collaborative effort with other SJCRH investigators identified one ABC transporter as an important stem cell marker (Zhou et al, *Nat Med,* 2001, Zhou et al, *PNAS*, 2002) that has a prominent role in hematopoietic cell survival under hypoxia (Krishnamurthy et al, *J Biol Chem*, 2004). We extended these studies to establish a knockout mouse which revealed for the first time that the ABC transporter (ABCC4/Mrp4) was important in protecting the brain from penetration of chemotherapeutic agents (Leggas et al, *Mol Cell Biol*, 2004). One could infer from these findings that the therapeutic efficacy of CNS-directed drugs that are Mrp4 substrates may be improved by developing Mrp4 inhibitors. The ABCC4/Mrp4 transporter was first functionally defined by my laboratory (Schuetz et al, *Nat Med*, 1999) and more recently was demonstrated to protect hematopoietic cells from injury due to the widely used immunosuppressive and cancer chemotherapeutic agent 6-mercaptopurine. This finding

allowed us through collaborative efforts within the department (Evans, Relling, E. Schuetz) to identify a defective ABCC4 allele that was prevalent in the Asian population, thus providing an explanation for the anecdotal reports of enhanced sensitivity to the toxic hematopoietic side-effects of 6 mercaptopurine in this population (Krishnamurthy et al, *Cancer Res,* 2008). Further studies suggest ABCC4 has a strong role in modulating platelet function as well as response to anti-platelet drugs (Cheepala, Pitre, et al, *Blood* 2015). Other studies have focused on a mitochondrial and plasma membrane ABC transporter we first characterized (Krishnamurthy et al, *Nature*, 2006; Fukuda et al, *J Biol Chem*, 2011) that protects cells from oxidative stress (Lynch et al, *Cancer Res,* 2009) and appears to have a unique role in regulating other survival responses. Because over a third of ABC transporters contribute to disease processes, our goal has been to understand the role of these genes in pathological conditions, such as our recently described roles for the bile acid transporter, *Abcb11,* in protecting against neonatal respiratory distress (Zhang et al*, Nat Commun, 2015*). From this perspective, we have also been elucidating how select ABC transporters contribute to cancer (medulloblastoma) (Morfouace et al, *Cancer Res*. 2015) and therapeutic response.

Clinton F. Stewart, PharmD

I joined the Pharmaceutical Department at St. Jude in 1991, and since then have focused my research efforts in developmental therapeutics for children with solid malignancies and central nervous system tumors. In the clinic, my research involves the application of state of the art pharmacokinetic (individual and population), pharmacogenetic, and pharmacodynamic approaches to understanding the variability in drug disposition in children with cancer. Little is known about the disposition of anti-cancer agents in infants and young children less than 3 years of age, which often leads to increased risk of morbidity, poor tumor control, and increased incidence of late effects. Thus, we have embarked on a comprehensive series of pharmacokinetic, pharmacogenetic, and pharmacodynamic studies to understand how developmental changes in infants and young children affect the disposition and toxicities of anticancer drugs used in the treatment of infants with malignant brain tumors. Our long-term goal is to determine rational dosing regimens for infants and young children by better understanding the developmental pharmacology of anti-cancer drugs and to apply these regimens to therapy for other childhood malignancies and chronic medical conditions. In addition to the studies we perform at St. Jude, my lab collaborates with investigators within the Pediatric Brain Tumor Consortium and the Children's Oncology Group. Our work in the laboratory is guided by addressing clinically relevant problems encountered in the therapy of children with solid malignancies (e.g., effect of antiangiogenic drugs on cytotoxic drug penetration) or brain tumors (e.g., CNS drug penetration in brain tumors). The studies in the lab are designed to either yield data that can be translated into the design of improved clinical trials or to answer questions generated in the clinic. For example, the treatment of children with primary central nervous system (CNS) tumors continues to be a challenge despite recent advances in technology and diagnostics. A variety of issues unique to pediatric CNS tumors impede development and clinical success of novel therapies and for this reason safe and effective treatments remain elusive. The preclinical approach we use (depicted in the Figure above) employs tumor subgroup-specific models of pediatric CNS

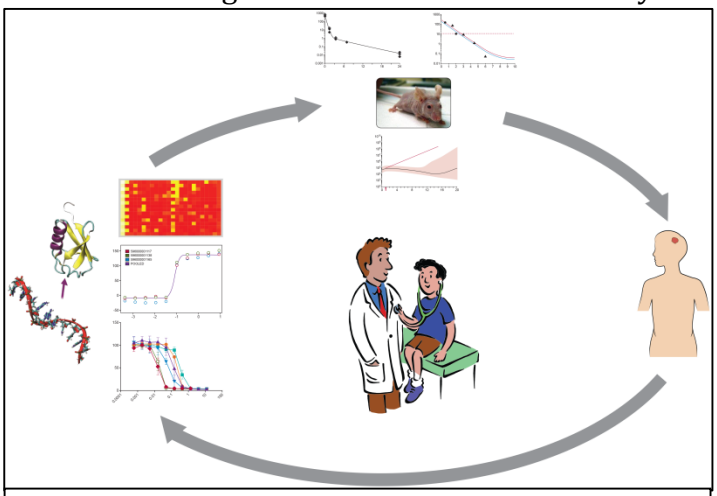

Figure 6. Schematic overview of our approach to using pharmacokinetic modeling and simulation in the identification of new anticancer drugs for treatment of pediatric CNS tumors.

tumors, cerebral microdialysis sampling of tumor extracellular fluid (tECF), and pharmacokinetic modeling and simulation to overcome challenges that currently hinder researchers in this field.

Jun J. Yang, PhD

I joined the St. Jude faculty in 2010 and I am currently an Associate Member in Pharmaceutical Sciences Department. The research focus of my group is pharmacogenomics of treatment outcomes (e.g. relapse) and toxicity in children with childhood acute lymphoblastic leukemia (ALL). Primarily taking a genome-wide approach, we identify genetic variations that contribute to interpatient variability in response to ALL therapy. By doing so, the goals of our research are to elucidate biological pathways dictating response to antileukemic drugs, to identify genetic predictors for drug resistance which can be utilized for treatment individualization, and to develop novel therapeutic agents to overcome drug resistance. Because genetic factors in both host and tumor genome can affect drug response, my lab has focused on characterization of inherited (germline) and acquired (somatic) genetic factors that are associated with treatment response in childhood ALL. We have led the first genome-wide association study to identify germline genetic variations associated with minimal residual disease in response to remission induction therapy in children with ALL (Yang et al, *JAMA,* 2009) and the first genome-wide interrogation of copy number alterations related to ALL relapse (Yang et al, *Blood,* 2008). We are particularly interested in the genetic basis for racial/ethnic differences in ALL treatment outcomes and disease susceptibility, e.g. we recently performed genome-wide studies to characterize ancestry-related genetic variants that (Perez-Andreu et al, *Nat Genet* 2013, *J Clin Oncol* 2012, *J Natl Cancer Inst* 2013) contribute to higher risk of relapse in Hispanic children with ALL (Yang et al, *Nat Genet*, 2011). We are also interested in pharmacogenetics of treatment toxicity, especially thiopurine-related myelosuppression (*J Clin Oncol* 2015, *Nat Genet* 2016). Our group is part of the NIH Pharmacogenomics Research Network (PGRN) and the Center for Precision medicine for Leukemia (CPML).

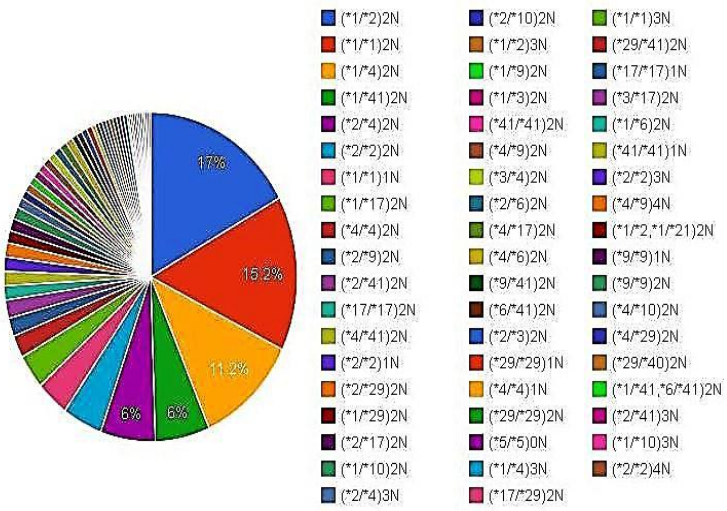

Figure 7. Just for the *CYP2D6* gene, 56 different diplotypes have been observed in the first 499 patients enrolled on the St. Jude clinical protocol, PG4KDS. Each diplotype is translated into a phenotype; high-risk phenotypes drive drug prescribing (Hicks et al 2012).

Pharmaceutical Services

Pharmaceutical Services is led by Dr. William Greene and is staffed by pharmacists, pharmacy technicians, research and administrative staff, and faculty, (see Organization Chart at end) all dedicated to helping patients. St. Jude Pharmaceutical Services is dedicated to providing the best pharmaceutical care required for each child at SJCRH while supporting a collective research endeavor. Our personnel, working with other caregivers in a cutting edge collaborative environment assure the best possible outcomes of drug therapy. Over 110 pharmacists, technicians, and other support personnel are involved in the care of patients and support of clinical research at St. Jude, helping to fulfill our organizational mission to

"advance cures, and means of prevention, for pediatric catastrophic diseases through research and treatment."

Pharmaceutical Services addresses St. Jude patients across the continuum of care – providing services while they are inpatients, in the outpatient clinic, and while in domiciliary facilities or at home. Inpatient services include Clinical Pharmacist collaboration in management of patients of all major clinical patient care groups, including Leukemia/Lymphoma, Solid Tumor, Neuro-Oncology, Bone Marrow Transplant, Hematology, and HIV services. After discharge from the hospital, these patients are seen in outpatient clinics located on campus where pharmacists are directly involved with Caregiver teams. In these settings, pharmacists collaborate in the care of these patients, including the ordering of medications and laboratory tests, the development of clinical treatment protocols, provision of drug therapy and nutritional support consults, and assessment and management of the long-term effects of medication therapy. An on-site infusion center provides medications for outpatients, and is fully staffed by pharmacists. On average, there are approximately 361 patient clinic visits per day, with 103 infusion center encounters, leading to the dispensing of 802 prescriptions or doses per day. An inpatient census of approximately 47 patients per day requires more than 1600 dispensed doses per day. Nutrition support, pharmacokinetic, pharmacogenetic consults, (Figure 7) and routine medication reconciliation at discharge require direct pharmacist involvement in patient care. Patients requiring intravenous therapy while outside the hospital are managed through provision of therapy by the St. Jude Specialty/Home Infusion Pharmacy. This service, initiated in early spring of 2011, was recognized by a Joint Commission surveyor as exhibiting several "best practices" and having no recommendations for improvement during surveys in August of 2011, November 2012, and November 2015. This service is now providing more than 340 doses per day, and is caring for all St. Jude patients in the immediate service region.

At St. Jude, we provide the very best professional environment for pharmacists (Figure 8) – one that supports growth and achievement of professional goals. Clinical Staff Pharmacists work from both centralized and decentralized settings to collaborate with clinical providers in patient care. Clinical Research Pharmacists, Informatics Pharmacists, and pharmacist leaders in medication outcomes and medication safety work to assure optimal system support and design to facilitate the best outcomes of patient care and clinical research. Certified Pharmacy Technicians collaborate with pharmacists to assure excellence in operational functions. A technician career ladder has been developed, and pharmacist developmental pathways provide internal opportunities for professional growth.

Figure 8. Pharmacists are integral members of each of St. Jude's clinical services.

Professional society involvement is encouraged, and resources are dedicated to enhance professional growth. St. Jude pharmacists play an active role in the Children's Oncology Group, American College of Clinical Pharmacy, American Society of Health-System Pharmacy, and many other professional organizations.

St. Jude Pharmaceutical Services also collaborates closely with various colleges of pharmacy in providing experiential education to pharmacy students. The department is formally affiliated with the University of Tennessee (UT) College of Pharmacy, but also works with students from other colleges as they request the opportunity. Members of the department hold affiliated faculty appointments with the UT College of Pharmacy. St. Jude pharmacy personnel provide approximately 50 student-months of experience during an academic year and 40 contact hours of classroom training for UT pharmacy students.

Pharmacists are integrated into each of the major clinical services at St. Jude and state-of-the-art distribution and computer support systems assure efficient, effective delivery and use of medications. Pharmacy Information Systems is intimately involved in the maintenance and refinement of a complete electronic medical record with computerized prescriber order entry and clinical decision support. These same personnel lead efforts to identify and implement the best technology to ensure optimal and safe patient outcomes.

Pharmacy Specialty Residencies

Trainees at St. Jude are supported by an institutional Office of Academic Programs, whose goal is to assist our investigators and professional staff to improve the quality of experiences, training, benefits, and support for our undergraduate, graduate, professional and postdoctoral trainees. Over 300 post-doctoral trainees (post-Ph.D, M.D, and Pharm.D.) are at St. Jude, among whom are our PGY2 pharmacy specialty residents. Our PGY2 residencies in Pediatric Oncology, Medication Use Safety, and in Pharmacogenomics are accredited by the American Society of Health System Pharmacists (ASHP). Further details are available on St. Jude's website (www.stjude.org/pharmacyresidency).

Figure 9. St. Jude PGY2 residents 2015-2016 (left to right): JT Fannin, PharmD, Melissa Quinn, PharmD, Amy Pasternak, PharmD, Clay Daniels, PharmD, PhD

Pharmacokinetics Shared Resources

The Pharmacokinetics Shared Resource is part of the NCI-designated Cancer Center, is housed within Pharmaceutical Sciences laboratory space, is directed by Dr. Mary Relling, and provides centralized high-quality, competitively funded, peer-reviewed pharmacokinetic/pharmacodynamics research in both clinical and pre-clinical models at the St. Jude Cancer Center.

Our objectives are to facilitate:
Proper pharmacokinetic study design and implementation
Efficient and proper collection of biological samples for clinical pharmacokinetic and pharmacodynamic studies

Implementation and quality control of sensitive and specific analyses of those samples for anticancer drugs, their metabolites, or other relevant pharmacologic indices
The biomedical modeling of pharmacokinetic and pharmacodynamic data
Services include:
Protocol implementation (development of standard physician orders; building computerized laboratory tests; refining sampling and processing procedures)
Research sample acquisition (centralized receiving, initial processing, storage, and distribution)
Analytical assay implementation and ongoing quality control, biomedical modeling, study design and optimal sampling

Clinical Pharmacokinetics Laboratory

The Clinical Pharmacokinetics Laboratory (CPK lab), located in the Pharmaceutical Department supports St. Jude's mission by providing state of the art therapeutic drug monitoring and pharmacogenetic testing that is interpreted by clinical pharmacists to assure optimal drug dosing. It is directed by Dr. Alejandro Molinelli with translational support from Dr. Kristine Crews.

The Clinical Pharmacokinetics Laboratory is certified as a high complexity laboratory by CLIA and is accredited by the College of American Pathologists. Our staff consists of licensed medical laboratory scientists. Every year the laboratory will process and analyze approximately 8000 clinical specimens and send-out another 300 to reference laboratories. The laboratory's in-house test menu includes multiple high-complexity assays ranging from therapeutic drug determinations (e.g. immunosuppressant, antifungal drugs) to glomerular filtration rate estimation using 99mTc- DTPA. Some of our resources include random access immunochemistry analyzers (e.g. Abbott Architect) and analytical instrumentation (e.g. LC-MS/MS, GC/MS, HPLC). Most of our instruments have bidirectional interfaces with the Cerner Millennium clinical informatics system. The laboratory also handles pharmacogenetic testing for the hospital offering genotyping results that are always accompanied by consults prepared by the clinical pharmacists or residents.

The laboratory staff and pharmacists at St. Jude work closely to provide results in a timely manner. Once a test result is obtained the laboratory scientists alert the pharmacist, who in turn prepares a clinical consult. This close integration of care assures that our patients receive the best treatment while minimizing adverse effects from the drugs. The laboratory staff is also involved in clinical translational science projects, for which tests developed in the research laboratories are validated and incorporated into the CPK lab test menu as needed.

In addition to the samples for clinical testing, the CPK laboratory staff members also process thousands of patient research specimens a year, in support of various St. Jude research protocols, for the Pharmacokinetics Shared Resource.

Pharmaceutical Department Publications 2014-2015

Barr J, Choughule K, Nepal S, Wong T, Chaudhry AS, Joswig-Jones CA, Zientek MA, Strom S, Schuetz EG, Thummel K, Jones JP. Why do most human liver cytosol preparations lack xanthine oxidase activity? Drug Metab Dispos 42(4):695-699, 2014. (PMCID: PMC3965898)

Bhatia S, Landier W, Hageman L, Kim H, Chen Y, Crews KR, Evans WE, Bostrom B, Casillas J, Dickens DS, Maloney KW, Neglia JP, Ravindranath Y, Ritchey AK, Wong FL, Relling MV. Adherence to oral 6 mercaptopurine in African American and Asian children acute lymphoblastic leukemia – A Children's Oncology Group Study. Blood 124(15):2345-2353, 2014. (PMCID: PMC4192748)

Bhatia S, Landier W, Hageman L, Chen Y, Kim H, Sun CL, Kornegay N, Evans WE, Angiolillo AL, Bostrom B, Casillas J, Lew G, Maloney KW, Mascarenhas L, Ritchey AK, Termuhlen AM, Carroll WL, Wong FL, Relling MV. Systemic Exposure to Thiopurines and Risk of Relapse in Children with Acute Lymphoblastic Leukemia: A Children's Oncology Group Study. *JAMA Oncol*. 2015 1(3):287-95. (PMCID: PMC4561178)

Bhojwani D, Sabin ND, Pei D, Yang JJ, Khan RB, Panetta JC, Krull KR, Inaba H, Rubnitz JE, Metzger ML, Howard SC, Ribeiro RC, Cheng C, Reddick WE, Jeha S, Sandlund JT, Evans WE, Pui CH, Relling MV. Methotrexate-induced neurotoxicity and leukoencephalopathy in childhood acute lymphoblastic leukemia. J Clin Oncol 32(9):949-959, 2014. (PMCID: PMC3948096)

Bhojwani D, Darbandi R, Pei D, Ramsey LB, Chemaitilly W, Sandlund JT, Cheng C, Pui CH, Relling MV, Jeha S, Metzger ML. Severe hypertriglyceridemia during therapy for childhood acute lymphoblastic leukemia. Eur J Cancer 50(15):2685-2694, 2014. (PMCID: PMC4180109)

Bhojwani D, Yang JJ, Pui C-H. Biology of Childhood Acute Lymphoblastic Leukemia. Pediatr Clin North Am. 2015 Feb;62(1):47-60. (PMCID: PMC4250840)

Bi W, Kang G, Zhao Y, Cui Y, Yan S, Li Y, Cheng C, Pounds SB, Borowitz MJ, Relling MV, Yang JJ, Liu Z,Pui CH, Hunger SP, Hartford CM, Leung W, Zhang JF. SVSI: Fast and Powerful Set-Valued System Identification Approach to Identifying Rare Variants in Sequencing Studies for Ordered Categorical Traits. Ann Hum Genet. 2015 79(4):294-309. (PMCID: PMC4474746)

Brennan RC, Furman W, Mao S, Wu J, Turner DC, Stewart CF, Santana V, McGregor LM. Phase I dose escalation and pharmacokinetic study of oral gefitinib and irinotecan in children with refractory solid tumors. Cancer Chemotherap Pharmacol 74:1191-1198, 2014. (PMCID: PMC4562671).

Burger H, Den Dekker AT, Segeletz S, Boersma AWM, De Bruijn P, Debiec-Rychter M, Taguchi T, Sleijfer S, Sparreboom A, Mathijssen RH, Wiemer EAC. Intracellular imatinib levels are primarily determined by lysosomal sequestration. Br J Pharmacol 2015 88(3): 477-87 PMID: 26108972

Burlison JD, Scott SD, Browne EK, Thompson SG, Hoffman JM. The second victim experience and support tool validation of an organizational resource for assessing second victim effects and the quality of support resources. J Patient Saf, 2014 [Epub ahead of print] (PMCID: PMC4342309)

Call RJ, Burlison JD, Robertson JJ, Scott JR, Baker DK, Rossi MG, Howard SC, Hoffman JM. Adverse drug event detection in pediatric oncology and hematology patients: using medication triggers to identify patient harm in a specialized pediatric patient population. J Pediatr 2014 165(3): 447-52 (PMCID: PMC4145034)

Caudle KE, Klein TE, Hoffman JM, Müller DJ Whirl-Carrillo M, Gong L, McDonagh EM, Sangkuhl K, Thorn CF, Schwab M, Agúndez JA, Freimuth RR, Huser V, Lee MT, Iwuchukwu OF, Crews KR, Scott SA, Wadelius M, Swen JJ, Tyndale RF, Stein CM, Roden D, Relling MV, Williams MS, Johnson SG. Incorporation of pharmacogenomics into routine clinical practice: the Clinical Pharmacogenetics

Implementation Consortium (CPIC) guideline Development Process. Curr Drug Metab 15(2):209-217, 2014. (PMCID: PMC3977533)

Chaudhry A, Prasad B, Shirasaka Y, Fohner A, Finkelstein D, Fan Y, Wang S, Wu S, Aklillu E, Sim S, Thummel KE and Schuetz EG. The CYP2C19 intron 2 branch point SNP is the ancestral polymorphism contributing to the poor metabolizer phenotype in livers with CYP2C19*35 and CYP2C19*2 alleles. Drug Metab Dispos. 2015 Aug; 43(8):1226-35. (PMCID: PMC4518065)

*Cheepala SB, *Pitre A, Fukuda Y, Takenaka K, Zhang Y, Wang Y, Frase S, Pestina T, Gartner TK, Jackson C, Schuetz JD. The ABCC4 membrane transporter modulates platelet aggregation. Blood. 2015 Nov 12;126(20):2307-19 (PMCID: PMC4643005) *co-first authorship

De Graan AJ, Sparreboom A, De Bruijn P, De Jonge E, Van der Holt B, Wiemer EAC, Verweij J, Mathijssen RH, Van Schaik RH. 4β-Hydroxycholesterol as an endogenous CYP3A marker in cancer patients treated with taxanes. Br J Pharmacol 2015 80(3): 560-8 (PMCID: PMC4574840)

De Wit D, Gelderblom H, Sparreboom A, Den Hartigh J, Den Hollander M, Konig-Quartel JMC, Hessing T, Guchelaar H-J, Van Erp NP. Midazolam as a phenotyping probe to predict sunitinib exposure in patients with cancer. Cancer Chemother Pharmacol 2014 73(1): 87-96 PMID:24149944

Demetz E, Schroll A, Auer K, Heim C, Patsch JR, Eller P, Theurl M, Lener D, Stanzl U, Theurl I, Seifert M, Haschka D, Asshoff M, Sichtl S, Nairz M, Huber E, Stadlinger M, Li X, Pallweber P, Scharnagl H, Stojakovic T, Marz W, Kleber ME, Garlaschelli K, Uboldi P, Catapano AL, Stellaard F, Rudling M, Kuba K, Imai Y, Arita M, Schuetz JD, Pramstaller PP, Tietge U, Trauner M, Norata G, Claudel T, Hicks AA, Weiss G, Tancevski I. The arachidonic acid metabolome as conserved regulator of cholesterol metabolism. Cell Metab 20(5):787-798, 2014. (PMCID: PMC4232508) **Featured in "Research Highlight in Nature Reviews Endocrinology**

DeWire M, Fouladi M, Turner DC, Wetmore C, Hawkins C, Jacobs C, Yuan Y, Liu D, Goldman S, Fisher P, Rytting M, Bouffet E, Kahkoo Y, Hwang E, Foreman N, Stewart CF, Gilbert MR, Gilbertson R, Gajjar A. An open-label, two-stage, Phase II study of bevacizumab and lapatinib in children with recurrent or refractory ependymoma: a Collaborative Ependymoma Network Study (CERN). J Neurooncol 2015 123(1):85-91. (PMID: 25859842). PMC in Process

Dering C, König IR, Ramsey LB, Relling MV, Yang W, Ziegler A. A comprehensive evaluation of collapsing methods using simulated and real data: excellent annotation of functionality and large sample sizes required. Front Genet 5:323, 2014. eCollection 2014 (PMCID: PMC4164031)

Diouf B, Crews KR, Lew G, Pei D, Cheng C, Bao J, Zheng JJ, Yang W, Fan Y, Wheeler HE, Wing C, Delaney SM, Komatsu M, Paugh SW, McCorkle JR, Li X, Winick NJ, Carroll WL, Loh ML, Hunger SP, Devidas M, Pui C-H, Dolan ME, Relling MV, Evans WE. Association of an inherited genetic variant with vincristine-related peripheral neuropathy in children with acute lymphoblastic leukemia. JAMA 2015 313(8): 815-23 (PMCID: PMC4377066)

Drenberg CD, Paugh SW, Pounds S, Shi L, Orwick SJ, Li L, Hu S, Gibson A, Ribeiro R, Rubnitz J, Sparreboom A, Baker SD. Inherited variation in OATP1B1 is associated with treatment outcome in acute myeloid leukemia. Clin Pharmacol Ther, 2015. [Epub ahead of print] (PMID: 26663398)

Dunnenberger HM, Crews KR, Hoffman JM, Caudle KE, Broeckel U, Howard SC, Hunkler RJ, Klein TE, Evans WE, Relling MV. Preemptive clinical pharmacogenetics implementation: current programs in five United States medical centers. Annu Rev Pharmacol Toxicol, 2014 55: 89-106 (PMCID: PMC4607278)

Edelmann, M.N., V.M. Daryani, M.W. Bishop, W. Liu, T.M. Brinkman, C.F. Stewart, D.A. Mulrooney, C. Kimberg, K.K. Ness, Y.T. Cheung, D.K. Srivastava, L.L. Robison, M.M. Hudson, and K.R. Krull. Neurocognitive and Patient-Reported Outcomes in Adult Survivors of Childhood Osteosarcoma. JAMA Oncol, 2015: p. 1-8. [Epub ahead of print] (PMID: 26583357)

Fernandez CA, Stewart E, Panetta JC, Wilkinson MR, Morrison AR, Finkelman FD, Sandlund JT, Pui CH, Jeha S, Relling MV, Campbell PK. Successful challenges using native E. coli asparaginase after hypersensitivity reactions to PEGylated E. coli asparaginase. Cancer Chemother Pharmacol 73(6):1307-1313, 2014. (PMCID: PMC4137479)

Fernandez CA, Smith C, Yang W, Date M, Bashford D, Larsen E, Bowman WP, Liu C, Ramsey LB, Chang T, Turner V, Loh ML, Raetz EA, Winick NJ, Hunger SP, Carroll WL, Onengut-Gumuscu S, Chen WM, Concannon P, Rich SS, Scheet P, Jeha S, Pui CH, Evans WE, Devidas M, Relling MV. *HLA-DRB1**07:01 is associated with a higher risk of asparaginase allergies. Blood 124(8): 1266-1276, 2014. (PMCID: PMC4141516)

Fernandez CA, Smith C, Yang W, Mullighan CG, Qu C, Larsen E, Bowman WP, Liu C, Ramsey LB, Chang TY, Karol SE, Loh ML, Raetz EA, Winick N, Hunger SP, Carroll WL, Jeha S, Pui CH, Evans WE, Devidas M, and Relling MV. Genome-wide analysis links NFATC2 with asparaginase hypersensitivity. *Blood.* 2015 126(1):69-75. (PMCID: PMC4492197)

Fernandez CA, Smith C, Karol SE, Ramsey LB, Liu C, Pui CH, Jeha S, Evans WE, Finkelman FD, Relling MV. Effect of premedications in a murine model of asparaginase hypersensitivity.J Pharmacol Exp Ther. 2015 352(3):541-51 (PMCID: PMC4352598)

Goldspiel BR; DeChristoforo R; Hoffman JM; Preventing chemotherapy errors: Updating guidelines to meet new challenges. Am J Health Syst Pharm. 2015 72 (8):668-669 PMID:25825190 PMC in Process

Goldspiel B, Hoffman JM, Griffith NL, Goodin S, DeChristoforo R, Montello CM, Chase JL, Bartel S, Patel JT. ASHP Guidelines on Preventing Medication Errors with Chemotherapy and Biotherapy. Am J Health Syst Pharm. 2015 72 (8):e6-e35. PMID:25825193 PMC in Process

Gottardo NG, Hansford JR, McGlade JP, Alvaro F, Ashley DM, Bailey S, Baker DL, Bourdeaut F, Cho YJ, Clay Mr, Clifford SC, Cohn RJ, Cole CH, Dallas PB, Downie P, Doz F, Ellison DW, Endersby R, Fisher PG, Hassall T, Heath JA, Hil HL, Jones DT, Junckerstorff R, Kellie S, Kool M, Kotecha RS, Lichter P, Laughton SJ, Lee S, McCowage G, Northcott PA, Olson JM, Packer RJ, Packer RJ, Pfister SM, Pietsch T, Pizer B, Pomeroy SL, Remke M, Robinson GW, Rutkowski S, Schoep T, Schoep T, Shelat AA, Stewart CF, Sullivan M, Taylor MD, Wainwright B, Walwyn T, Weiss WA Williamson D, Gajjar A. Medulloblastoma Down Under 2013: a report from the third annual meeting of the International Medulloblastoma Working Group. Acta Neuropathol 127:189-201, 2014. (PMCID: PMC3895219).

Guo, J., J.O. Glass, M.B. McCarville, B.L. Shulkin, V.M. Daryani, C.F. Stewart, J. Wu, S. Mao, J.R. Dwek, L.M. Fayad, J.E. Madewell, F. Navid, N.C. Daw, and W.E. Reddick. Assessing vascular effects of adding

bevacizumab to neoadjuvant chemotherapy in osteosarcoma using DCE-MRI. Br J Cancer, 2015. 113(9): p. 1282-8. (PMID: 26461056) PMC in Process

Gurney JG, Bass JK, Onar-Thomas A, Huang J, Chintagumpala M, Bouffet E, Hassall T, Gururangan S, Heath JA, Kellie S, Cohn R, Fisher MJ, Panadiker AP, Merchant TE, Srinivasan A, Wetmore C, Qaddoumi I, Stewart CF, Armstrong GT, Broniscer A, Gajjar. Evaluation of amifostine for protection for protection against cisplatin-induced serious hearing loss in children treated for average-risk or high-risk medulloblastoma. Neuro Oncol 16(6):848-855, 2014. (PMCID: PMC4022215)

Hartke PL, Vermeulen LC, Hoffman JM, Shah ND, Doloresco F, Suda KJ, Matusiak LM, Hunkler RJ, Schumock GT. Accuracy of annual prescription drug expenditure forecasts in AJHP. Am J Health Syst Pharm. Oct. 2015 72 (19):1642-1648. (PMCID:PMC4576353)

Hicks JK, Crews KR, Flynn P, Haidar CE, Daniels CC, Yang W, Panetta JC, Pei D, Scott JR, Molinelli AR, Broeckel U, Bhojwani D, Evans WE, Relling MV. Voriconazole plasma concentrations in immunocompromised pediatric patients vary by *CYP2C19* diplotypes. Pharmacogenomics 15(8):1065-1078, 2014. (PMCID: PMC415556)

Hoffman JM, Haidar CE, Wilkinson MR, Crews KR, Baker DK, Kornegay NM, Yang W, Pui CH, Reiss UM, Gaur AH, Howard SC, Evans WE, Broeckel U, Relling MV. PG4KDS: A model for the clinical implementation of pre-emptive pharmacogenetics. Am J Med Genet C Semin Med Genet 166(1):45-55, 2014. (PMCID: PMC4056586) **Winner of the 2015 ASHP Foundation Literature Award for Innovation in Pharmacy Practice**

Hoffman LM, Fouladi M, Olson J, Daryani VM, Stewart CF, Wetmore C, Kocak M, Onar-Thomas A, Wagner L, Gururangan S, Packer RJ, Blaney SM, Gajjar A, Kun LE, Boyett JM, Gilbertson RJ. Phase I trial of weekly MK-0752 in children with refractory central nervous system malignancies: a pediatric brain tumor consortium study. Childs Nerv Syst. 2015 Aug;31(8):1283-9. (PMCID: PMC4681692).
Hu S, Mathijssen RH, de Bruijn P, Baker SD, Sparreboom A. Inhibition of OATP1B1 by tyrosine kinase inhibitors: in vitro-in vivo correlations. Br J Cancer 110:894-898, 2014. (PMCID: PMC 3929889)

Jacus MO, Throm SL, Turner DC, Patel YT, Freeman BB 3rd, Morfouace M, Boulos N, Stewart CF. Deriving therapies for children with primary CNS tumors using pharmacokinetic modeling and simulation of cerebral microdialysis data. Eur J Pharm Sci. 57:41-7, 2014. (PMCID: PMC4004667).

Jacus MO, Rahija R, Davis A, Throm SL, Stewart CF. An observational evaluation of mice during cerebral microdialysis procedures used in pediatric brain tumor research. J Am Assoc Lab Anim Sci. 2015 May;54(3):304-10. (PMCID: PMC4460944).

Jacus, M.O., V.M. Daryani, K.E. Harstead, Y.T. Patel, S.L. Throm, and C.F. Stewart. Pharmacokinetic Properties of Anticancer Agents for the Treatment of Central Nervous System Tumors: Update of the Literature. Clin Pharmacokinet. 2015 Aug 21. [Epub ahead of print] (PMID: 26293618)

Jin D, Ni TT, Sun J, Wan H, Amack J, Yu G, Fleming J, Chiang C, Li W, Papierniak A, Cheepala S, Conseil G, Cole S, Zhou B, Drummond I, Schuetz JD, Malicki J, Zhong T. Prostaglandin signaling regulates ciliogenesis by modulating intraflagellar transport. Nat Cell Biol 16(9):841-851, 2014. (PMCID: PMC4154319) **Featured in News and Views in Nature Cell Biology**

Jones CL, Bhatla T, Blum R, Wang J, Paugh SW, Wen X, Bourgeois W, Bitterman DS, Raetz EA, Morrison DJ, Teachey DT, Evans WE, Garabedian MJ, Carroll WL. Loss of TBL1XR1 disrupts glucocorticoid receptor recruitment to chromatin and results in glucocorticoid resistance in a B-lymphoblastic leukemia model. J Biol Chem 289(30):20502-20515, 2014. (PMCID: PMC4110265)

Kalman LV, Agúndez JA, Appell ML, Black JL, Bell GC, Boukouvala S, Bruckner C, Bruford E, Bruckner C, Caudle K, Coulthard S, Daly AK, Del Tredici AL, den Dunnen JT, Drozda K, Everts R, Flockhart D, Freimuth R, Gaedigk A, Hachad H, Hartshorne T, Ingelman-Sundberg M, Klein TE, Lauschke VM, Maglott DR, McLeod HL, McMillin GA, Meyer UA, Müller DJ, Nickerson DA, Oetting WS, Pacanowski M, Pratt VM, Relling MV, Roberts A, Rubinstein WS, Sangkuhl K, Schwab M, Scott SA, Sim SC, Thirumaran RK, Toji LH, Tyndale R, van Schaik RH, Whirl-Carrillo M, Yeo KJ, Zanger UM. Pharmacogenetic Allele Nomenclature: International Workgroup Recommendations for Test Result Reporting. Clin Pharmacol Ther. 2015 Oct 19. [Epub ahead of print] Review. PMID: 26479518

Kang G, Bi W, Zhao Y, Zhang J-F, Yang JJ, Xu H, Loh ML, Hunger SP, Relling MV, Pounds S, Cheng C. A new system identification approach to identifying genetic variants in sequencing studies for a binary phenotype. Hum Hered 78(2):104-116, 2014. (PMCID: PMC4270367)

Kang G, Liu W, Cheng C, Wilson CL, Neale G, Yang JJ, Ness KK, Robison LL, Hudson MM, Srivastava DK. Evaluation of a two-step iterative resampling procedure for internal validation of genome-wide association studies**.** J Hum Genet. 2015 Dec;60 (12):729-38. (Epub ahead of print) (PMID: 26377241, PMCID n/a)

Karol SE, Yang W, Van Driest SL, Chang TY, Kaste S, Bowton E, Basford M, Bastarache L, Roden DM, Denny JC, Larsen E, Winick N, Carroll WL, Cheng C, Pei D, Fernandez CA, Liu C, Smith C, Loh ML, Raetz EA, Hunger SP, Scheet P, Jeha S, Pui CH, Evans WE, Devidas M, Mattano LA Jr, Relling MV. Genetics of glucocorticoid-associated osteonecrosis in children with acute lymphoblastic leukemia. *Blood.* 2015 126(15): 1770-6. (PMCID: PMC4600016)

Karol SE, Mattano LA Jr, Yang W, Maloney KW, Smith C, Liu C, Ramsey LB, Fernandez CA, Chang TY, Neale G, Cheng C, Mardis E, Fulton R, Scheet P, San Lucas FA, Larsen EC, Loh ML, Raetz EA, Hunger SP, Devidas M, Relling MV. Genetic risk factors for the development of osteonecrosis in children under age 10 treated for acute lymphoblastic leukemia. Blood. 2016 [in press] PMID: 26590194

Kaste SC, Qi A, Smith K, Surprise H, Lovorn E, Boyett J, Ferry RJ Jr, Relling MV, Shurtleff SA, Pui CH, Carbone L, Hudson MM, Ness KK. Calcium and cholecalciferol supplementation provides no added benefit to nutritional counseling to improve bone mineral density in survivors of childhood acute lymphoblastic leukemia (ALL). Pediatr Blood Cancer, 2014 61(5): 885-93 (PMCID: PMC4160024)

Kaste SC , Pei D, Cheng C, Neel MD, Bowman WP, Ribeiro RC, Metzger ML, Bhojwani D, Inaba H, Campbell P, Rubnitz J, Jeha S, Sandlund JT, Downing J, Relling MV, Pui C-H, Howard SC. Utility of early screening magnetic resonance imaging for extensive hip osteonecrosis in pediatric patients treated with glucocorticoids. J Clin Oncol, 2015 33(6): 610-5 (PMCID: PMC4322260)

Kieran MW, Chi S, Goldman S, Onar-Thomas A, Poussaint TY, Vajapeyam S, Fahey F, Wu S, Turner DC, Stewart CF, Moses M, Packer RJ, Jakacki R, Banerjee A, Boyett JM, Fouladi M, Kun L. A phase I trial and PK study of cediranib (AZD2171), an orally bioavailable pan-VEGFR inhibitor, in children with recurrent or refractory primary CNS tumors. Childs Nerv Syst. 2015 Sep;31(9):1433-45 (PMCID: PMC4561207).

Korf BR, Berry AB, Limson M, Marian AJ, Murray MF, O'Rourke PP, Passamani ER, Relling MV, Tooker J, Tsongalis GJ, Rodriguez LL. Framework for development of physician competencies in genomic medicine: report of the Competencies Working Group of the Inter-Society Coordinating Committee for Physician Education in Genomics. Genet Med, 2014 April. 16(11): 804-9 (PMID:24763287)

Lamba JK, Pounds S, Cao X, Crews KR, Cogle CR, Bhise N, Raimondi SC, Downing JR, Baker SD, Ribeiro RC, Rubnitz JE. Clinical significance of in vivo cytarabine-induced gene expression signature in AML. Leuk Lymphoma. 2015 Oct 16:1-12. (PMID: 26366682)

Li-Harms X, Milasta S, Lynch J, Wright C, Joshi A, Iyengar R, Neale G, Wang X, Wang Y-D, Prolla T, Thompson JE, Opferman J, Green DR, Schuetz JD, Kundu, M. Mito-protective autophagy is impaired in erythroid cells of aged mtDNA-mutator mice. Blood. 2015 Jan 1;125(1):162-74. (PMCID:PMC4281825)

Lu C, Zhang J, Nagahawatte P, Easton J, Lee S, Liu Z, Ding L, Wyczalkowski MA, Valentine M, Navid F, Mulder H, Tatevossian RG, Dalton J, Davenport J, Yin Z, Edmonson M, Rusch M, Wu G, Li Y, Parker M, Hedlund E, Shurtleff S, Raimondi S, Bhavin V, Donald Y, Mardis ER, Wilson RK, Evans WE, Ellison DW, Pounds S, Dyer M, Downing JR, Pappo A, Bahrami A. The Genomic Landscape of Childhood and Adolescent Melanoma. J Invest Dermatol. 2015 135(3): 816-23 (PMCID: PMC4340976)

Ma X, Edmonson M, Yergeau D, Muzny D, Hampton OA, Rusch M, Song G, Easton J, Harvey RC, Wheeler DA, Ma J, Doddapaneni H, Vadodaria B, Wu G, Nagahawatte P, Carroll WL, Chen I-M, Gastier Foster JM, Relling MV, Smith MA, Devidas M, Guidry Auvil JM, Downing JR, Loh ML, Willman CL, Gerhard DL, Mullighan CG*, Hunger SP* and Zhang J*. Rise and Fall of Subclones from Diagnosis to Relapse in Pediatric B-progenitor Acute Lymphoblastic Leukemia. Nat Commun 2015 6:6604 (PMCID:PMC4377644)

Manolio TA, Abramowicz M, Al-Mulla F, Anderson W, Balling R, Berger AC, Bleyl S, Chakravarti A, Chantratita W, Chisholm RL, W Dissanayake VH, Dunn M, Dzau VJ, Han BG, Hubbard T, Kolbe A, Korf B, Kubo M, Lasko P, Leego E, Mahasirimongkol S, Majumdar PP, Matthijs G, McLeod HL, Metspalu A, Meulien P, Miyano S, Naparstek Y, O'Rourke PP, Patrinos GP, Rehm HL, Relling MV, Rennert G, Rodriguez LL, Roden DM, Shuldiner AR, Sinha S, Tan P, Ulfendahl M, Ward R, Williams MS, L Wong JE, Green ED, Ginsburg GS. Global implementation of genomic medicine: We are not alone. Sci Transl Med. 2015 7(290):290ps13. Review. PMC in Process

Martin MA, Hoffman JM, Freimuth RR, Klein TE, Dong BJ, Pirmohamed M, Hicks JK, Wilkinson MR, Haas DW, Kroetz DL. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for HLA-B genotype and abacavir dosing: 2014 update. Clin Pharmacol Ther 95(5):499-500, 2014. (PMCID: PMC3994233)

Mathijssen, R.H., A. Sparreboom, and J. Verweij. Determining the optimal dose in the development of anticancer agents. Nat Rev Clin Oncol, 2014. 11(5): p. 272-81. (PMID: 24663127)

McDaniel RB, Burlison JD, Baker DK, Hasan M, Robertson JJ, Hartford C, Howard SC, Sablauer A, Hoffman JM. Alert dwell time: introduction of a measure to evaluate interruptive clinical decision support alerts. J Am Med Inform Assoc. 2015 [Epub ahead of print] (PMID:26499101)

Moon C, Zhang W, Ren A, Arora K, Sinha C, Yarlagadda S, Woodrooffe K, Schuetz JD, Valasani KR, de Jonge HR, Shanmukhappa SK, Shata MT, Buddington RK, Parthasarathi K, Naren AP. Compartmentalized Accumulation of cAMP near Complexes of Multidrug Resistance Protein 4 (MRP4) and Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Contributes to Drug-induced Diarrhea. J Biol Chem. 2015 May 1;290(18):11246-57 (PMCID:PMC4416832)

Morfouace M, Shelat A, Jacus M, Freeman BB 3rd, Robinson S, Turner D, Zindy F, Wang Y-D, Finkelstein D, Bihannic L, Puget S, Ayrault O, Li X-N, Olson JM, Robinson GW, Guy RK, Stewart CF, Gajjar A, Roussel MF. Pemetrexed and gemcitabine as combination therapy for the treatment of group 3 medulloblastoma. Cancer Cell 25(4):516-529, 2014. (PMCID: PMC3994669).

Morfouace M, Cheepala S, Jackson S, Albert YP, Kawauchi D, Shelat A, Fukuda Y, Sorrentino B, Schuetz JD* and Roussel MF*. (*co-corresponding authors) ABCG2 transporter expression impacts Group3 Medulloblastoma response to chemotherapy. Cancer Res. 2015 Sep 15; 75(18):3879-89 (PMCID: PMC4573843)

Morfouace, M., B. Nimmervoll, N. Boulos, Y.T. Patel, A. Shelat, B.B. Freeman, 3rd, G.W. Robinson, K. Wright, A. Gajjar, C.F. Stewart, R.J. Gilbertson, and M.F. Roussel. Preclinical studies of 5-fluoro-2'-deoxycytidine and tetrahydrouridine in pediatric brain tumors. J Neurooncol. 2015 Oct 30. (PMID: 26518542)

Morgan JA, Lynch J, Panetta JC, Wang Y, Frase S, Bao J, Zhang J, Opferman JT, Janke L, Green DM, Chemaitilly W, and Schuetz JD. Apoptosome activation, an important molecular instigator in 6-mercaptopurine induced Leydig cell death. Sci Rep. 2015 Nov 5:16488. (PMCID: PMC4649703)

Moriyama T, Relling MV, and Yang JJ. Inherited Genetic Variation in Childhood Acute Lymphoblastic Leukemia. Blood 2015 125(26):3988-95 (PMCID: PMC4481591)

Moriyama T, Metzger ML, Wu G, Nishii R, Qian M, Devidas M, Yang W, Cheng C, Cao X, Quinn E, Raimondi S, Gastier-Foster JM, Raetz E, Larsen E, Martin PL, Bowman WP, Winick N, Komada Y, Wang S, Edmonson M, Xu H, Mardis E, Fulton R, Pui CH, Mullighan C, Evans WE, Zhang J, Hunger SP, Relling MV, Nichols KE, Loh ML, Yang JJ. Germline genetic variation in ETV6 and risk of childhood acute lymphoblastic leukaemia: a systematic genetic study. Lancet Oncol. 2015 16(16): 1659-66 (PMCID: PMC4684709)

Mullighan CG, Jeha S, Pei D, Payne-Turner D, Coustan-Smith E, Roberts KG, Waanders E, Choi JK, Ma X, Raimondi SC, Fan Y, Yang W, Song G, Yang JJ, Inaba H, Downing JR, Leung WH, Bowman WP, Relling MV, Evans WE, Zhang J, Campana D, Pui CH. Outcome of children with hypodiploid ALL treated with risk-directed therapy based on MRD levels. Blood. 2015 126(26): 2896-9 PMC in Process

Murphy AJ, Sarrezy V, Wang N, Bijl N, Abramowicz S, Welch CB, Schuetz JD, Yuan-Charvet L. Deficiency of ATP binding cassette transporter B6 in Megakaryocyte progenitors accelerates atheroschlerosis in mice. Arterioscler Thromb Vasc Biol 34(4):751-758, 2014. (PMID: 24504733; PMCID: N/A)

Nies AT, Schaeffeler E, van der Kuip H, Cascorbi I, Bruhn O, Kneba M, Pott C, Hofmann U, Volk C, Hu S, Baker SD, Sparreboom A, Ruth P, Koepsell H, Schwab M. Cellular uptake of imatinib into leukemic cells is independent of human Organic Cation Transporter 1 (OCT1). Clin Cancer Res 20:985-994, 2014. (PMCID: PMC3932302)

Nieuweboer AJ, Hu S, Gui C, Hagenbuch B, Ghobadi Moghaddam-Helmantel IM, Gibson AA, De Bruijn P, Mathijssen RH, Sparreboom A. Influence of drug formulation on OATP1B2-mediated transport of paclitaxel. Cancer Res, 2014 74(11):3137-45 (PMCID: PMC4161133)

Nieuweboer, A.J., E.S. de Morree, A.J. de Graan, A. Sparreboom, R. de Wit, and R.H. Mathijssen. Inter-patient variability in docetaxel pharmacokinetics: A review. Cancer Treat Rev, 2015. 41(7): p. 605-13. (PMID: 25980322)

Nieuweboer, A.J., M. Smid, A.M. de Graan, S. Elbouazzaoui, P. de Bruijn, F.A. Eskens, P. Hamberg, J.W. Martens, A. Sparreboom, R. de Wit, R.H. van Schaik, and R.H. Mathijssen. Role of genetic variation in docetaxel-induced neutropenia and pharmacokinetics. Pharmacogenomics J. 2015. (PMID: 26345519)

Nikanjam M, Stewart CF, Takimoto CH, Synold TW, Beaty O, Fouladi M, Capparelli EV. Population pharmacokinetic analysis of oxaliplatin in adults and children identifies important covariates for dosing. Cancer Chemotherap Pharmacol 75:495-503, 2015. (PMCID: PMC4344382).

Pabla, N., A.A. Gibson, M. Buege, S.S. Ong, L. Li, S. Hu, G. Du, J.A. Sprowl, A. Vasilyeva, L.J. Janke, E. Schlatter, T. Chen, G. Ciarimboli, and A. Sparreboom. Mitigation of acute kidney injury by cell-cycle inhibitors that suppress both CDK4/6 and OCT2 functions. Proc Natl Acad Sci U S A, 2015. 112(16): p. 5231-6. (PMCID: PMC4413320)

Pabla, N. and A. Sparreboom. CCR 20th anniversary commentary: BMS-247550-microtubule stabilization as successful targeted therapy. Clin Cancer Res, 2015. 21(6): p. 1237-9. (PMCID: PMC4362690)

Packer RJ, Rood BR, Turner DC, Stewart CF, Fisher M, Smith C, Young-Pouissant T, Goldman S, Lulla R, Banerjee A, Pollack I, Kun L, Boyett JM, Onar-Thomas A, Wu S, Fouladi M. Phase I and pharmacokinetic trial of PTC299 in pediatric patients with refractory or recurrent central nervous system tumors: a PBTC study. J Neurooncol 121(1):217-224, 2015. (PMCID: PMC4330963)

Patel Y, Jacus M, Boulos N, Dapper J, David A, Vuppala P, Freeman III B, Mohankumar K, Throm S, Gilbertson R, Stewart CF. Preclinical examination of clofarabine in pediatric ependymoma: intratumoral concentrations insufficient to warrant further study. Cancer Chemotherap Pharmacol 2015 75:897-906. (PMCID: PMC4420645)

Paugh SW, Bonten, EJ, Savic D, Ramsey LB, Thierfelder WE, Gurung P, Malireddi RK, Actis M, Mayasundari A, Min J, Coss DR, Laudermilk LT, Panetta JC, McCorkle JR, FanY, Crews KR, Stocco G, Wilkinson MR, Ferreira AM, Cheng C, Yang W, Karol SE, Fernandez CA, Diouf B, Smith C, Hicks JK, Zanut A, Giordanengo A, Crona D, Bianchi JJ, Holmfeldt L, Mullighan CG, den Boer ML, Pieters R, Jeha S, Dunwell TL, Latif F, Bhojwani D, Carroll WL, Pui CH, Myers RM, Guy RK, Kanneganti TD, Relling MV, Evans WE. NALP3 inflammasome up-regulation and CASP1 cleavage of the glucocorticoid receptor causes glucocorticoid resistance in leukemia cells. *Nat Genet.* 2015 47(6):607-14. (PMCID: PMC4449308)

Perez-Andreu V, Roberts KG, Xu H, Smith C, Zhang H, Yang W, Harvey RC, Payne-Turner D, Devidas M, Cheng IM, Carroll WL, Heerema NA, Carroll AJ, Raetz EA, Gastier-Foster JM, Marcucci G, Bloomfield CD, Mrózek K, Kohlschmidt J, Stock W, Kornblau SM, Konopleva M, Paietta E, Rowe JM, Luger SM,

Tallman MS, Dean M, Burchard EG, Torgerson DG, Yue F, Wang Y, Pui CH, Jeha S, Relling MV, Evans WE, Gerhard DS, Loh ML, Willman CL, Hunger SP, Mullighan CG, Yang JJ. A genome-wide association study of susceptibility to acute lymphoblastic leukemia in adolescents and young adults. Blood. 2014 125(4): 680-6 (PMCID: PMC4304112)

Phelps, M.A. and A. Sparreboom. Irinotecan pharmacogenetics: a finished puzzle? J Clin Oncol, 2014. 32(22): p. 2287-9. (PMID: 24958823)

Phelps, M.A. and A. Sparreboom. A snapshot of challenges and solutions in cancer drug development and therapy. Clin Pharmacol Ther, 2014. 95(4): p. 341-6. (PMID: 24646480)

Pui C-H, Yang JJ, Hunger SP, Pieters R, Schrappe M, Biondi A, Vora A, Baruchel A, Silverman LB, Schmiegelow K, Escherich G, Horibe K, Benoit Y CM, Izraeli S, Yeoh AEJ, Liang D-C, Downing J, Evans WE, Relling MV, Mullighan CG. Childhood acute lymphoblastic leukemia: progress through collaboration. J Clin Oncol 2015 33(27): 2938-48 (PMCID: PMC4567699)

Pui CH, Pei D, Campana D, Cheng C, Sandlund JT, Bowman WP, Hudson MM, Ribeiro RC, Raimondi SC, Jeha S, Howard SC, Bhojwani D, Inaba H, Rubnitz JE, Metzger ML, Gruber TA, Coustan-Smith E, Downing JR, Leung WH, Relling MV, Evans WE. A revised definition for cure of childhood acute lymphoblastic leukemia. Leukemia. 2014 28(12): 2336-43 (PMCID: PMC4214904)

Pui CH, Pei D, Coustan-Smith E, Jeha S, Cheng C, Bowman WP, Sandlund JT, Ribeiro RC, Rubnitz JE, Inaba H, Bhojwani D, Gruber TA, Leung WH, Downing JR, Evans WE, Relling MV, Campana D. Clinical utility of sequential minimal residual disease measurements in the context of risk-based therapy in childhood acute lymphoblastic leukaemia: a prospective study. *Lancet Oncol.* 2015 16(4):465-74. (PMCID: PMC4612585)

Ramsey LB, Janke LJ, Edick MJ, Cheng C, Williams RT, Sherr CJ, Evans WE , Relling MV. Host thiopurine methyltransferase status affects mercaptopurine antileukemic effectiveness in a murine model. Pharmacogenet Genomics 24(5):263-271, 2014. (PMCID: PMC4019208)

Ramsey LB, Janke LJ, Payton MA, Cai X, Paugh SW, Karol SE, Kamdem LK, Cheng C, Williams RT, Jeha S, Pui CH, Evans WE, Relling MV. Antileukemic Efficacy of Continuous vs Discontinuous Dexamethasone in Murine Models of Acute Lymphoblastic Leukemia. *PLoS One*. 2015 10(8):e0135134. (PMCID: PMC4529108)

Relling MV, McDonagh EM, Chang T, Caudle KE, McLeod HL, Haidar CE, Klein T, Luzzatto L. clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for rasburicase therapy in the context of G6PD deficiency genotype. Clin Pharmacol Ther 96(2):169-174, 2014. (PMCID: PMC4111801)

Relling MV and Evans WE: Pharmacogenomics in the Clinic. *Nature*, 2015. 526(7573): 343-50 (PMID: 26469045) PMC in Process

Roberts KG, Li Y, Payne-Turner D, Harvey RC, Yang YL, Pei D, McCastlain K, Ding L, Lu C, Song G, Ma J, Becksfort J, Rusch M, Chen SC, Easton J, Cheng J, Boggs K, Santiago-Morales N, Iacobucci I, Fulton RS, Wen J, Valentine M, Cheng C, Paugh SW, Devidas M, Chen IM, Reshmi S, Smith A, Hedlund E, Gupta P, Nagahawatte P, Wu G, Chen X, Yergeau D, Vadodaria B, Mulder H, Winick NJ, Larsen EC, Carroll WL, Heerema NA, Carroll AJ, Grayson G, Tasian SK, Moore AS, Keller F, Frei-Jones M, Whitlock JA, Raetz

EA, White DL, Hughes TP, Guidry Auvil JM, Smith MA, Marcucci G, Bloomfield CD, Mrózek K, Kohlschmidt J, Stock W, Kornblau SM, Konopleva M, Paietta E, Pui CH, Jeha S, Relling MV, Evans WE, Gerhard DS, Gastier-Foster JM, Mardis E, Wilson RK, Loh ML, Downing JR, Hunger SP, Willman CL, Zhang J, Mullighan CG. Targetable kinase activating lesions in ph-like acute lymphoblastic leukemia. N Engl J Med 371(11):1005-1015, 2014. (PMCID: PMC4191900)

Roberts KG, Pei D, Campana D, Payne-Turner D, Li Y, Cheng C, Sandlund JT, Jeha S, Easton J, Becksfort J, Zhang J, Coustan-Smith E, Raimondi SC, Leung WH, Relling MV, Evans WE, Downing JR, Mullighan CG, Pui CH. Outcomes of children with *BCR-ABL1*-like acute lymphoblastic leukemia treated with risk-directed therapy based on the levels of minimal residual disease. J Clin Oncol, 2014 Jul 21. [Epub ahead of print] (PMCID: PMC4162497)

Roberts MS, Turner DC, Broniscer A, Stewart CF. Determination of crizotinib in human and mouse plasma by liquid chromatography electrospray ionization tandem mass spectrometry (LC-ESI-MS/MS). J Chromatography B 960C:151-157, 2014. (PMCID: PMC4062842)

Robinson GW, Orr BA, Wu G, Gururangan S, Lin T, Qaddoumi I, Packer R, Goldman S, Prados M, Desjardins A, Chintagumpala M, Takebe N, Kaste SC, Rusch M, Allen SJ, Onar-Thomas A, Stewart CF, Fouladi M, Boyett JM, Gilbertson RJ, Curran T, Ellison DW, Gajjar A. Vismodegib exerts targeted efficacy against recurrent SHH-subgroup medulloblastoma: results from phase II pediatric brain tumor consortium studies – PBTC-025B and PBTC-032. J Clin Oncol. 2015 Aug 20;33(24):2646-54. (PMCID: PMC4534527).

Salloum-Asfar S, Teruel-Montoya R, Arroyo AB, García-Barberá N, Chaudhry A, Schuetz E, Luengo-Gil G, Vicente V, González-Conejero R, Martínez C. Regulation of coagulation factor XI expression by microRNAs in the human liver. PLoS One. 2014 Nov 7; 9(11). (PMCID: PMC4224396)

Schuetz JD**, Swaan PW, Tweedie DJ. The role of transporters in toxicity and disease. Drug Metab Dispos 42(4):541-545, 2014. (PMCID: PMC3965901) **corresponding author

Schully SD, Lam TK, Dotson WD, Chang CQ, Aronson N, Birkeland ML, Brewster SJ, Boccia S, Buchanan AH, Calonge N, Calzone K, Djulbegovic B, Goddard KA, Klein RD, Klein TE, Lau J, Long R, Lyman GH, Morgan RL, Palmer CG, Relling MV, Rubinstein WS, Swen JJ, Terry SF, Williams MS, Khoury MJ. Evidence synthesis and guideline development in genomic medicine: current status and future prospects. Genet Med, 2015 17(1): 63-7 (PMCID: PMC4272332)

Schumock GT, Li EC, Suda KJ, Matusiak LM, Hunkler RJ, Vermeulen LC, Hoffman JM. National trends in prescription drug expenditures and projections for 2014. Am J Health Syst Pharm 71(6):482-499 2014. PMID: 24589540. PMC: N/A

Scott JR, Zhou Y, Cheng C, Ward DA, Swanson HD, Molinelli AR, Stewart CF, Navid F, Jeha S, Relling MV, Crews KR. Comparable efficacy with varying dosages of glucarpidase in pediatric oncology patients. Pediatr Blood Cancer. 2015 62(9):1518-22. PMID: 25631103 PMC in Process

Shirasaka Y, Chaudhry AS, McDonald M, Prasad B, Wong T, Calamia JC, Fohner A, Thornton TA, Isoherranen N, Unadkat JD, Rettie AE, Schuetz EG, Thummel KE. Interindividual variability of CYP2C19-catalyzed drug metabolism due to differences in gene diplotypes and cytochrome P450 oxidoreductase content. Pharmacogenomics J. 2015 Sep 1. (epub ahead of print) PMID: 2632359 PMC in Process

Sinha C, Ren A, Arora K, Moon CS, Yarlagadda S, Woodrooffe K, Lin S, Schuetz JD, Ziady AG, Naren AP. PKA and actin play critical roles as downstream effectors in MRP4-mediated regulation of fibroblast migration. Cell Signal. 2015 Jul;27(7):1345-55. (PMCID: PMC4437852)

Sparreboom, A. and R.H. Mathijssen. Hepatic uptake transporters and docetaxel disposition in mice-letter. Clin Cancer Res, 2014. 20(15): p. 4167. (PMCID: PMC4127641)

Sprowl JA, Lancaster CS, Pabla N, Hu S, Hermann E, Kosloske A, Gibson AA, Zeeh D, Li L, Schlatter E, Janke L, Ciarimboli G, Sparreboom A. Cisplatin-induced renal injury is independently mediated by OCT2 and p53. Clin Cancer Res, 2014 20(15): 4026-35 (PMCID: PMC4119572)

Sprowl, J.A. and A. Sparreboom. Uptake carriers and oncology drug safety. Drug Metab Dispos, 2014. 42(4): p. 611-22. (PMCID: PMC3965905)

Stewart CF, Tagen M, Schwartzberg LS, Blakely LJ, Tauer KW, Smiley LM. Phase I dosage finding and pharmacokinetic study of intravenous topotecan and oral erlotinib in adults with refractory solid tumors. Cancer Chemother Pharmacol 73(3):561-568, 2014. (PMCID: PMC3965853)

Tong WH, Pieters R, Kaspers GJ, Te Loo DM, Bierings MB, van den Bos C, Kollen WJ, Hop WC, Lanvers-Kaminsky C, Relling MV, Tissing WJ, van der Sluis IM. A prospective study on drug monitoring of PEGasparaginase and Erwinia asparaginase and asparaginase antibodies in pediatric acute lymphoblastic leukemia. Blood 123(13):2026-2033, 2014. (PMCID: PMC3968389)

Turner DC, Navid F, Daw NC, Mao S, Wu J, Santana VM, Neel M, Rao B, Willert JR, Loeb DM, Harstead KE, Throm SL, Freeman BB III, Stewart CF. Population pharmacokinetics of bevacizumab in children with osteosarcoma: implications for dosing. Clin Cancer Res 20:1-10, 2014. (PMCID: PMC4024352)

Touchette DR, Doloresco F, Suda KJ, Perez A, Turner S, Jalundhwala Y, Tangonan MC, Hoffman JM. Economic evaluations of clinical pharmacy services: 2006-2010. Pharmacotherapy 2014 Mar 19. doi:10.1002/phar.1414. (PMID: 24644086. PMC: N/A)

Vasilyeva A, Durmus S, Li L, Wagenaar E, Hu S,1 Gibson AA, Mani S, Sparreboom A, Baker SD, Schinkel AH. Hepatocellular shuttling and recirculation of sorafenib-glucuronide is dependent on Abcc2, Abcc3, and Oatp1a/1b. Cancer Res. 2015 Jul 1;75(13):2729-36 (PMCID: PMC4490028).

Vilgelm AE, Pawlikowski JS, Liu Y, Hawkins OE, Davis TA, Smith J, Weller KP, Horton LW, McClain CM, Ayers GD, Turner DC, Essaka DC, Stewart CF, Sosman JA, Kelley MC, Ecsedy JA, Johnston JN, Richmond A. Mdm2 and Aurora A inhibitors synergize to block melanoma growth by driving apoptosis and immune clearance of tumor cells. Cancer Research 75:181-93, 2015. (PMCID: PMC4286469).

Wang X, Liu W, Sun CL, Armenian SH, Hakonarson H, Hageman L, Ding Y, Landier W, Blanco JG, Chen L, Quiñones A, Ferguson D, Winick N, Ginsberg JP, Keller F, Neglia JP, Desai S, Sklar CA, Castellino SM, Cherrick I, Dreyer ZE, Hudson MM, Robison LL, Yasui Y, Relling MV, Bhatia S. Hyaluronan Synthase 3 Variant and anthracycline-related cardiomyopathy: a report from the Children's Oncology Group. J Clin Oncol 32(7):647-653, 2014. (PMCID: PMC3927733)

Wang Z, Wong T, Hashizume T, Dickmann LZ, Scian M, Koszewski NJ, Goff JP, Horst RL, Chaudhry AS, Schuetz EG, Thummel KE. Human UGT1A4 and UGT1A3 conjugate 25-hydroxyvitamin D3:

metabolite structure, kinetics, inducibility and interindividual variability. Endocrinology 155(6):2052-2063, 2014. (PMCID: PMC4020929)

Wilson CL, Liu L, Yang JJ, Kang G, Ojha RP, Neale G, Srivastava DK, Gurney JG, Hudson MM, Robison LL, Ness KK. Genetic and clinical factors associated with obesity among adult survivors of childhood cancer: A report from the St. Jude Lifetime cohort. Cancer 2015 [Epub ahead of print] (PMCID: PMC4641835)

Wright KD, Panetta JC, Onar-Thomas A, Reddick WE, Patay Z, Qaddoumi I, Broniscer A, Robinson G, Boop FA, Klimo P, Ward D, Gajjar A, Stewart CF. Delayed methotrexate excretion in infants and young children with primary central nervous system tumors and postoperative fluid collections. Cancer Chemother Pharmacol 75:27-35, 2015. (PMCID: PMC4282603)

Wright, K.D., V.M. Daryani, D.C. Turner, A. Onar-Thomas, N. Boulos, B.A. Orr, R.J. Gilbertson, C.F. Stewart, and A. Gajjar, Phase I study of 5-fluorouracil in children and young adults with recurrent ependymoma. Neuro Oncol, 2015. 17(12): p. 1620-7. (PMCID: PMC4633933)

Xu H, Zhang H, Yang W, Yadav R, Morrison AC, Qian M, Devidas M, Liu Y, Perez-Andreu V, Zhao X, Gastier-Foster JM, Lupo PJ, Neale G, Raetz E, Larsen E, Bowman WP, Carroll WL, Winick N, Williams R, Hansen T, Holm JC, Mardis E, Fulton R, Pui CH, Zhang J, Mullighan CG, Evans WE, Hunger SP, Gupta R, Schmiegelow K, Loh ML, Relling MV, Yang JJ. Inherited coding variants at the CDKN2A locus influence susceptibility to acute lymphoblastic leukaemia in children. Nat Commun. 2015 Jun 24; 6:7553. (PMCID: PMC4544058)

Xu H, Robinson GW, Huang J, Lim JY, Zhang H, Bass JK, Broniscer A2, Chintagumpala M, Bartels U, Gururangan S, Hassall T, Fisher M, Cohn R, Yamashita T, Teitz T, Zuo J, Onar-Thomas A, Gajjar A, Stewart CF, Yang JJ. Common variants in ACYP2 influence susceptibility to cisplatin-induced hearing loss. Nat Genet. 2015 Mar; 47 (3):263-6. (PMCID: PMC4358157)

Yang JJ, Landier W, Yang W, Liu C, Hageman L, Cheng C, Pei D, Chen Y, Crews KR, Kornegay NM, Wong FL, Evans WE, Pui C-H, Bhatia S, Relling MV. Inherited *NUDT15* variant is a genetic determinant of mercaptopurine intolerance in children with acute lymphoblastic leukemia. J Clin Oncol 2015. 33(11): 1235-42 (PMCID: PMC4375304)

Yasuda K, Cline C, Lin YS, Scheib R, Ganguly S, Thirumaran R, Chaudhry AS, Kim RB, Schuetz EG. In Vivo Imaging of Human MDR1 Transcription in the Brain and Spine of MDR1-Luciferase Reporter Mice. Drug Metab Dispos. 2015 Nov;43(11):1646-54. (PMCID: PMC4613952)

Zhang Y, Li F, Wang Y, Fang Z, Frank M, Calabrese C, Krausz KW, Neale G, Frase S, Vogel P, Rock CO, Gonzalez FJ and Schuetz JD. Maternal bile acid transporter deficiency promotes neonatal demise. Nat Commun. 2015 Sep 29; 6:8186. doi: 10.1038/ncomms9186. (PMCID: PMC4598356). **2015 Selected to Faculty 1000 Must Read.**

Zimmerman, E.I., A.A. Gibson, S. Hu, A. Vasilyeva, S.J. Orwick, G. Du, G.P. Mascara, S.S. Ong, T. Chen, P. Vogel, H. Inaba, M.L. Maitland, A. Sparreboom, and S.D. Baker. Multikinase Inhibitors Induce Cutaneous Toxicity through OAT6-Mediated Uptake and MAP3K7-Driven Cell Death. Cancer Res, 2015. 76(1):117-26 PMID:26677977 PMC in Process