

Pharmaceutical Department

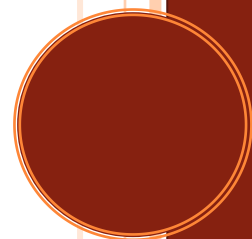
2012 ANNUAL REPORT



St. Jude Children's
Research Hospital

ALSAC • Danny Thomas, Founder

Finding cures. Saving children.



2012 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: Sharyn D. Baker, PharmD, PhD; James Hoffman, PharmD; Alex Sparreboom, PhD; Assistant Member: Jun J. Yang, PhD

Staff Scientists • Barthelemy Diouf, PhD; Ranjit Thirumaran, PharmD, PhD

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

Fellows¹ • Jassada Buaboonnam, PhD; Tamara Chang, MD; Amarjit Chaudhry, PhD; Satish Cheepala, PhD; Christina Drenberg, PhD; Christian Fernandez, PhD; Yu Fukuda, PhD; Kevin Hicks, PharmD, PhD; Cynthia Lancaster, PhD; Shangli Lian, PhD; John A. Lynch, PhD; Joseph McCorkle, PhD; Steven Paugh, PhD; Virginia Perez-Andreu, MD, PhD; Aaron Pitre, PhD; Laura Ramsey, PhD; Jason Sprowl, PhD; Aisha Walker, PhD; Heng Xu, PhD; Aksana Vasilyeva, PhD; Yuanyuan Zhang, PhD; Eric Zimmerman, PhD

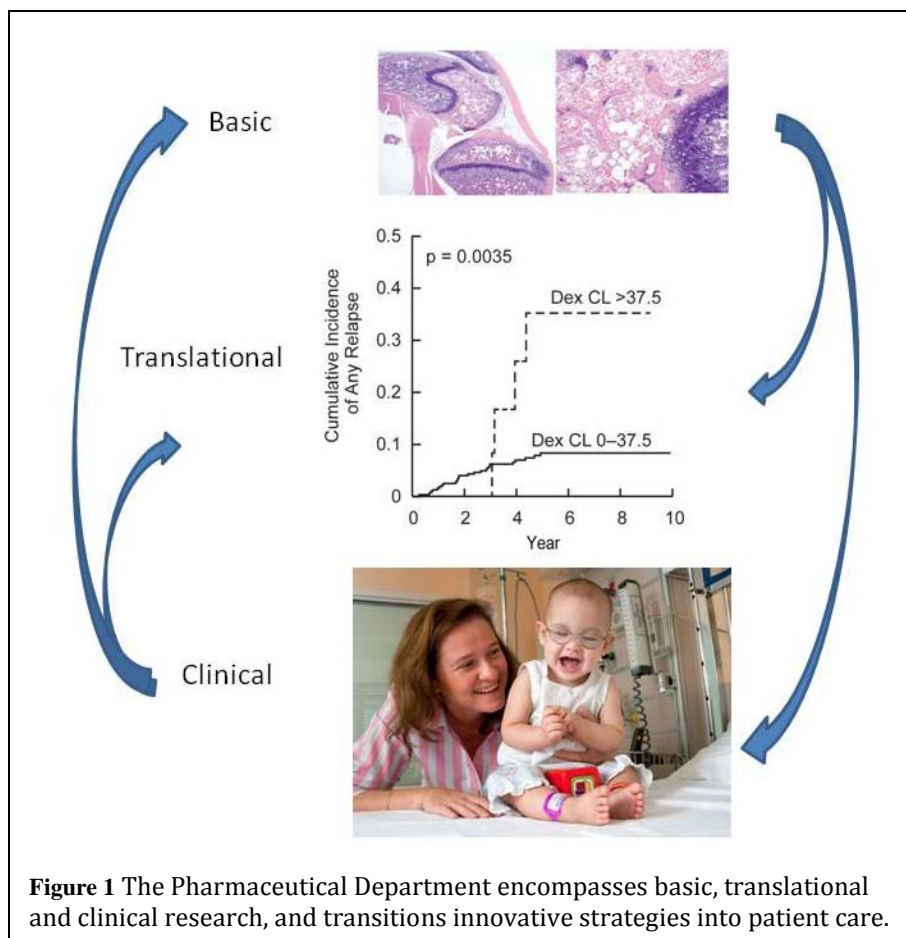
Residents¹ • Gillian Bell, PharmD; Rosemary Call, PharmD; Nathan Gorney, PharmD; Allison Weddington, PharmD

Graduate Students¹ • Jonathan Burlison; Chengcheng Liu; Jessica Morgan; Rachel Scheib
¹during calendar year 2012

Overview:

The primary goal of the Pharmaceutical Sciences Department is to improve therapy for children with catastrophic disease 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. 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



Figure 2. Post-doctoral fellows 2011-2012 Back row: Joseph McCorkle, Heng Xu, David Turner, Amarjit Chaudhry, Eric Zimmerman, Laura Ramsey, John Lynch, Steven Paugh; Front row: Jason Sprowl, Satish Cheepala, Aaron Pitre, Yuanyuan Zhang, Shangli Lian, Yu Fukuda, Christina Drenberg, Virginia Perez-Andreu, Aisha Walker, Christian Fernandez.

students, over 45 pharmacists, and over 106 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.

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

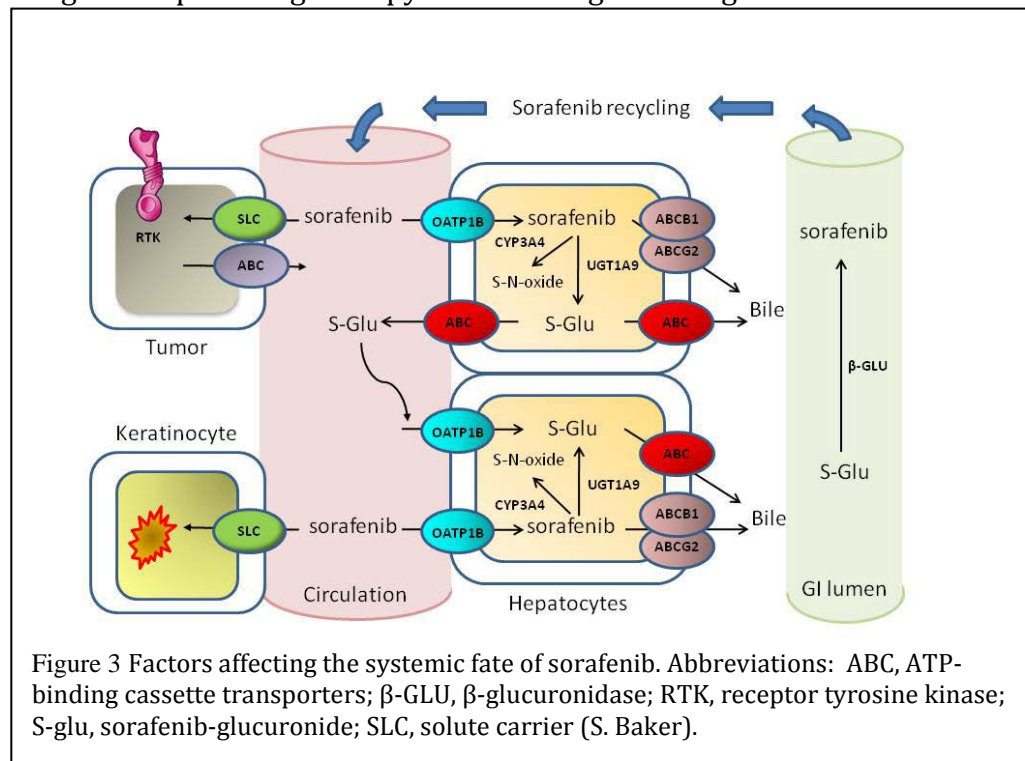
Pharmaceutical Department faculty, staff, and trainees work closely with each other; with our collaborators in other departments at St. Jude; and with colleagues around the world on basic,

translational, and clinical research projects and to provide outstanding pharmaceutical care to St. Jude patients.

Faculty:

Sharyn D. Baker, PharmD, PhD

I have been a faculty member in the Pharmaceutical Sciences Department at St. Jude since 2006. The majority of my research efforts have been focused on developmental therapeutics of childhood acute myeloid leukemia (AML). A strong emphasis is placed on principles of clinical pharmacology (pharmacokinetics, pharmacodynamics, pharmacogenetics, drug metabolism, drug transport, drug interactions, adverse drug reactions) during all aspects of drug development with the goal of optimizing therapy with investigational agents in children with cancer. We evaluate



novel agents in combination with standard AML chemotherapeutic agents such as cytarabine to assess for systemic and intracellular pharmacokinetic and pharmacodynamic interactions, define the mechanisms of interaction, and select drug combinations that demonstrate favorable interactions and optimal anti-leukemic activity. In preclinical models,

we are evaluating histone deacetylase inhibitors and spliceosome modulators against high risk M7 AML, and first- and second-generation FLT3 inhibitors against FLT3-ITD-positive AML. Clinically, we are evaluating the multi-kinase inhibitor sorafenib with cytarabine-based drug regimens in children with newly diagnosed FLT3-ITD positive AML and relapsed/refractory AML at St. Jude. The clinical problems observed with sorafenib have driven new research projects in my laboratory including: to identify determinants of sorafenib inter-patient pharmacokinetic variability, to determine the role of drug metabolism in the anti-leukemic activity of sorafenib; to identify mechanisms involved in sorafenib-induced skin toxicity; to identify mechanisms of sorafenib resistance in FLT3-ITD positive cases and identify new agents for FLT3-ITD resistance. Figure 3 demonstrates our integrated approach to understand factors affecting the pharmacokinetics and pharmacodynamics of sorafenib. Recent studies have identified secondary FLT drug-resistant mutations in children with FLT3-ITD-positive AML receiving sorafenib and sunitinib. Next generation sequencing has allowed us to monitor the emergence of low level mutations, which is now guiding our preclinical in vivo studies to identify effective treatment strategies for this disease. We use HPLC and mass spectrometric methods to study drug pharmacokinetics, flow cytometry, multi-plex cytokine and phosphoprotein assays, and genomics to study pharmacodynamics, cell culture models, molecular biologic techniques, murine models,

and analysis of clinical outcomes (toxicity and efficacy). We collaborate with many investigators within the department, throughout St. Jude, and at Johns Hopkins University and Karmanos Cancer Institute.

William E. Evans, PharmD

I have been a member of the St. Jude faculty since 1976. My lab's overarching goals are to elucidate genomic determinants of toxicity and efficacy of anticancer agents and translate this knowledge into new diagnostics and novel treatment strategies to optimize the therapy of childhood acute lymphoblastic leukemia (ALL) (see Evans et al, *Clin Pharm Ther*, 2013; Cheok et al, *Nat Rev Cancer*, 2006). We are currently focused on the pharmacogenomics of anticancer agents, with an emphasis on childhood ALL (reviewed in Evans and Relling, *Science* 1999; Evans and Relling, *Nature*, 2004; Pui and Evans, *NEJM*, 2006; Paugh et al, *Clin Pharm Ther*, 2011). We are using several approaches to identify genes and genome variations that are important determinants of the disposition and effects of antileukemic agents, including the interrogation of candidate genes and genome-wide approaches such as gene expression profiling (mRNA, miRNA) of leukemia cells, genome-wide SNP DNA methylation 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 from the Children's Oncology Group. We are investigating genes that we have linked with resistance to antileukemic agents (Holleman et al, *NEJM*, 2004; Lugthart et al, *Cancer Cell*, 2005), and genes linked to the disposition of antileukemic agents (Kager et al, *JCI*, 2005; Sorich et al, *PLoS Medicine*, 2008), as well as the influence of somatic and karyotypic abnormalities on genotype-phenotype concordance (Cheng et al, *Nat Genet*, 2005; Diouf et al, *Nat Med*, 2011). We deploy a number of genetic and biochemical approaches to pursue mechanisms underlying genome variations that we link to drug-related phenotypes (e.g. drug resistance, toxicity, EFS). We also participate in the St. Jude-Washington University Pediatric Cancer Genome Project (reviewed in Downing et al, *Nat Genet*, 2012). Our work is funded by a long-standing R37 grant from NCI (W. Evans PI), a U01 as part of the NIH-funded Pharmacogenetics Research Network (M. Relling PI), a Cancer Center Support grant from NCI (R. Gilbertson, PI), and by ALSAC, the fundraising organization for St. Jude Children's Research Hospital. Our lab comprises a number of post-doctoral fellows, staff scientists, research technologists, bioinformaticists, computer scientists and students, working with collaborators at St. Jude (including Mary Relling and Ching-Hon Pui 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 and Europe.

William Greene, PharmD

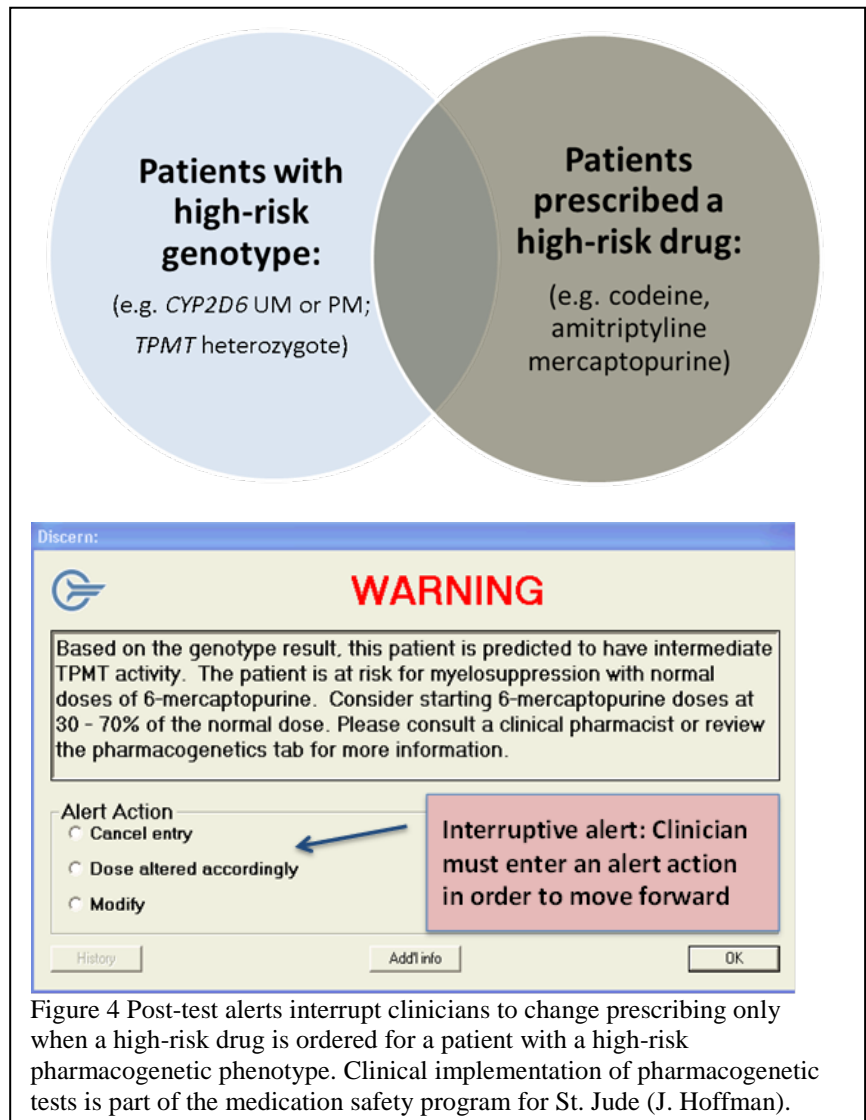
I joined Pharmaceutical Sciences as Chief Pharmaceutical Officer in August 2007. I have had a long career as a clinical pharmacy practitioner and leader in development of drug policy in hospital-based practice. My interests have been diverse, and are summed up in the goal of developing structures, personnel, 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).

James Hoffman, PharmD

I joined the Pharmaceutical Department in 2004, and the St. Jude Faculty in 2011. Through my role as the Medication Outcomes & Safety Officer for St. Jude I lead medication use safety efforts across the hospital, and I am dedicated to postgraduate training by directing a 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 validated tool to evaluate just culture in the hospital setting. 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 (Figure 4), and I have contributed to this protocol as an investigator since its inception.



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, and asparaginase immunogenicity and pharmacodynamics (Figure 5). 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, 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

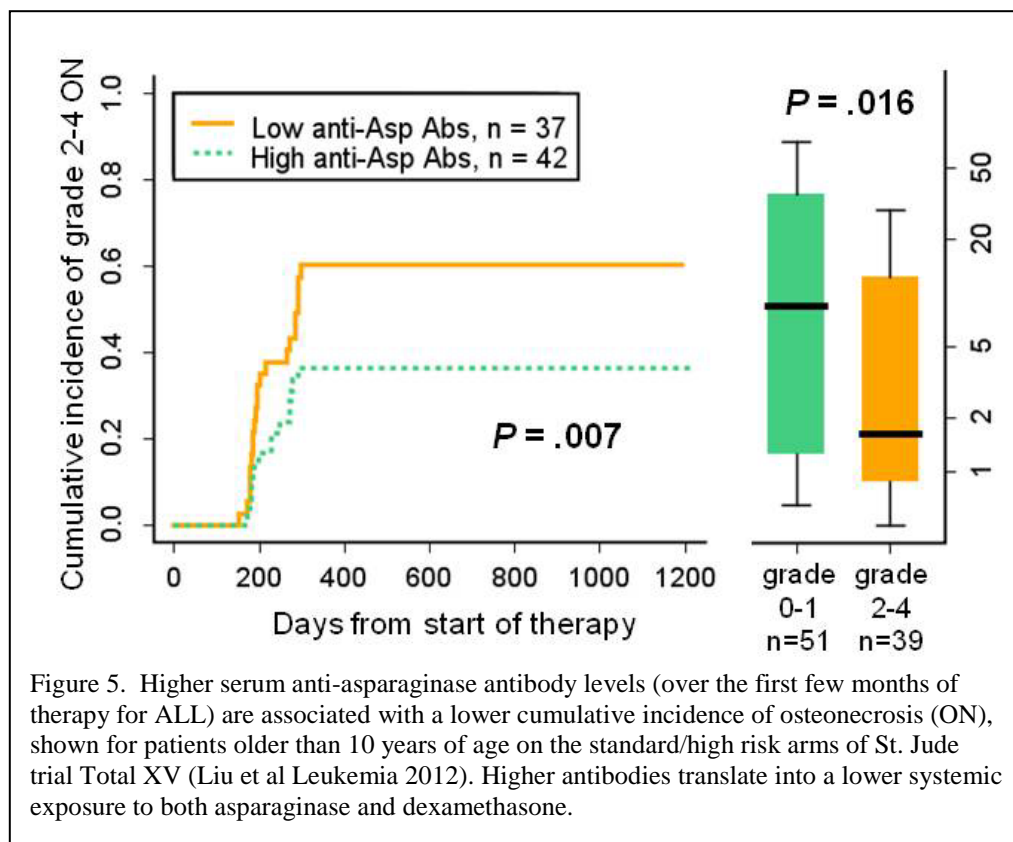


Figure 5. Higher serum anti-asparaginase antibody levels (over the first few months of therapy for ALL) are associated with a lower cumulative incidence of osteonecrosis (ON), shown for patients older than 10 years of age on the standard/high risk arms of St. Jude trial Total XV (Liu et al Leukemia 2012). Higher antibodies translate into a lower systemic exposure to both asparaginase and dexamethasone.

genotyping to implement preemptive pharmacogenetic tests into clinical care for St. Jude patients. 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 immunohistochemistry 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). 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). More recent studies have focused on a mitochondrial 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. From this perspective recent studies have been focused on elucidating how select ABC transporters contribute to leukemogenesis 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. The long-term goal of my lab is to optimize drug therapy for these patients. In addition to the studies we perform at St. Jude, my lab collaborates with investigators within the Children's Oncology Group, the Pediatric Brain Tumor Group, and the New Approaches for Neuroblastoma Therapy consortium. More recently because 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, 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 anti-cancer 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. 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. Although many resources are available to us for these studies, our laboratory has particular expertise in chromatography (LC MS/MS), microdialysis, molecular biology techniques, and pharmacokinetic modeling (including physiologically-based pharmacokinetic modeling).

Alex Sparreboom, PhD

I have been an associate member in the Department of Pharmaceutical Sciences at St. Jude since 2006. During the last 4-5 years, my laboratory has studied mechanisms by which anticancer agents accumulate in organs involved in drug elimination, such as the kidney and liver, and how that transport process impacts on interindividual variability in drug response. We focus

specifically on three classes of specialized, membrane-localized solute carriers, namely the organic cation transporters (OCT) (Figure 6), organic anion transporters (OAT), and organic anion transporting polypeptides (OATP), and how these carriers affect the disposition, organ-specific toxicity and antitumor efficacy of various clinically important cancer drugs, such as platinum-containing chemotherapeutics and tyrosine-kinase inhibitors. We use cell-culture model systems, conditional gene knock-out/knock-in mouse models, and clinical phenotype/genotype analyses to enhance understanding of interactions between cancer drugs and uptake carriers of interest. We actively

collaborate with multiple investigators at St. Jude, Erasmus University, Johns Hopkins University, Muenster University, Penn State College of Medicine, and University Hospital San Raffaele.

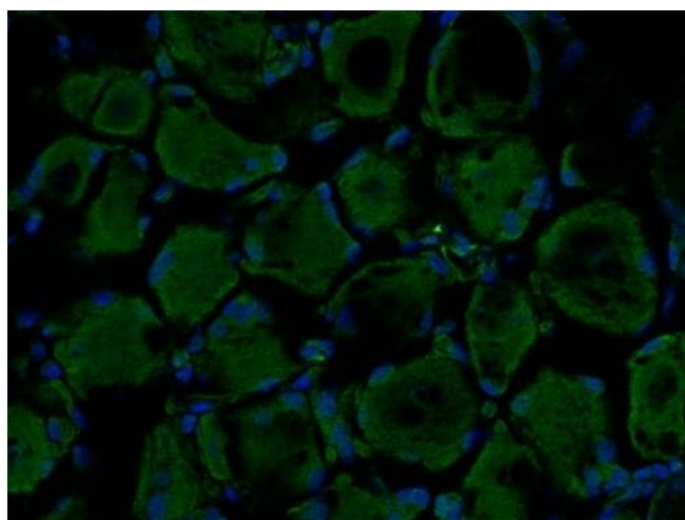


Figure 6 Detection of the transporter Oct2 by immunohistochemistry in dorsal root ganglia of mice. Green, Oct2; Blue, DAPI. (A. Sparreboom)

Jun J. Yang, PhD

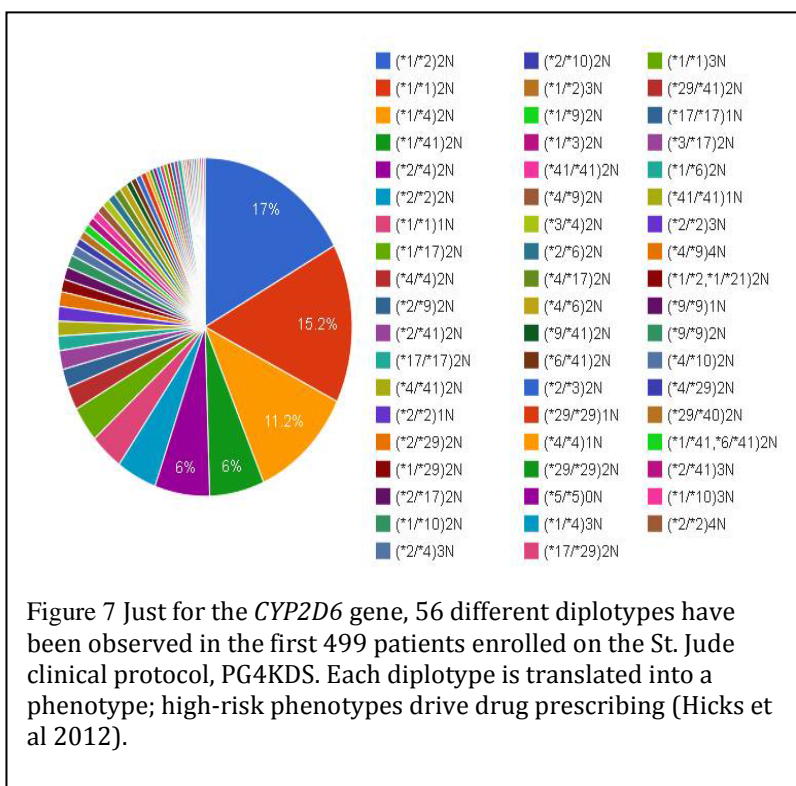
I joined the St. Jude faculty in 2010 as an Assistant Member in Pharmaceutical Sciences, and the research focus of my group is pharmacogenomics of treatment outcomes (e.g. relapse) of childhood acute lymphoblastic leukemia (ALL). Primarily taking a genome-wide approach, we identify genetic variations 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, e.g. we recently performed genome-wide studies to characterize ancestry-related genetic variants that contribute to higher risk of relapse in Hispanic children with ALL (Yang et al, *Nat Genet*, 2011). Our group is part of the NIH Pharmacogenomics Research Network (PGRN) and the Pharmacogenomics of Anticancer Agents Research in Children project (PAAR4Kids).

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, 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. This activity results in dispensing activity of over



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 and November 2012. 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. 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 residency in Pediatric Oncology is accredited by the American Society of Health System Pharmacists (ASHP). Our PGY2 residencies in Medication Use Safety and in Pharmacogenomics (a position that is integrated into the activity of NIH's Pharmacogenomics Research Network (PGRN)), have expanded training opportunities. These latter 2 residencies are both in Candidate status with the Commission on Credentialing at ASHP. Further details are available on St. Jude's website (www.stjude.org/pharmacyresidency).



Figure 9 St. Jude PGY2 residents 2012-2013 (left to right): Gillian Bell, PharmD, Rosemary Call, PharmD, Allison Weddington, PharmD, and Nathan Gorney, PharmD.

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. Sharyn Baker, and provides centralized high-quality, competitively funded, peer-reviewed pharmacokinetic/pharmacodynamic 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 ^{99m}Tc -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 2011-2012

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