Oncology

Division Data Summary

Research and Training Details

Number of Faculty	**20**
Number of Joint Appointment Faculty	**4**
Number of Research Fellows	**5**
Number of Research Students	**4**
Number of Support Personnel	**87**
Direct Annual Grant Support	**$2,320,582**
Direct Annual Industry Support	**$61,221**
Peer Reviewed Publications	**35**

Clinical Activities and Training

Number of Clinical Staff	**2**
Number of Clinical Fellows	**6**
Number of Other Students	**14**
Inpatient Encounters	**8,575**
Outpatient Encounters	**6,814**

Division Photo

Row 1: J Perentesis, M O'Brien, C Cost, K Burns
Row 2: C Phillips, M Absalon, B Weiss, R Nagarajan, A Hammil
Row 3: T Hummel, B Mikukawa, J Geller, T Cripe, L Wagner

Significant Publications

Chow LM, Endersby R, Zhu X, Rankin S, Qu C, Zhang J, Broniscer A, Ellison DW, Baker SJ. **Cooperativity within and among Pten, p53, and Rb pathways induces high-grade astrocytoma in adult brain**. *Cancer Cell.* 19(3): 305-16. 2011.

> Mutations in the PTEN, TP53, and RB1 pathways are obligate events in the pathogenesis of human glioblastomas. We induced various combinations of deletions in these tumor suppressors in astrocytes and neural precursors in mature mice, resulting in astrocytomas ranging from grade III to grade IV (glioblastoma). There was selection for mutation of multiple genes within a pathway, shown by somatic amplifications of genes in the PI3K or Rb pathway in tumors in which Pten or Rb deletion was an initiating event. Despite multiple mutations within PI3K and Rb pathways, elevated Mapk activation was not consistent. Gene expression profiling revealed striking similarities to subclasses of human diffuse astrocytoma. Astrocytomas were found within and outside of proliferative niches in the adult brain.

Fouladi M, Park JR, Stewart CF, Gilbertson RJ, Schaiquevich P, Sun J, Reid JM, Ames MM, Speights R, Ingle AM, Zwiebel J, Blaney SM, Adamson PC. **Pediatric phase I trial and pharmacokinetic study of vorinostat: a Children's Oncology Group phase I consortium report**. *J Clin Oncol.* 28(22): 3623-9. 2010.

> The purpose of this study was to determine the maximum-tolerated dose (MTD), dose-limiting toxicities (DLT), and pharmacokinetics of vorinostat administered as a single agent and in combination 13-cis retinoic acid (13cRA) in children with refractory solid tumors; to evaluate the tolerability of the solid tumor MTD in children with refractory leukemias; and to characterize the pharmacokinetics of a vorinostat suspension in children. Vorinostat was administered orally daily starting at 180 mg/m(2)/d with escalations planned in 30%

increments. Pharmacokinetic studies were performed with the initial dose. Acetyl-histone (H3) accumulation was assessed by Western blotting of peripheral blood mononuclear cells (PBMC). Sixty-four patients were enrolled on this multipart trial. In patients with solid tumors, the MTD was 230 mg/m(2)/d with dose-limiting neutropenia, thrombocytopenia, and hypokalemia at 300 mg/m(2)/d. DLTs observed with the combination of 13cRA and vorinostat included thrombocytopenia, neutropenia, anorexia, and hypertriglyceridemia, resulting in a MTD of vorinostat 180 mg/m(2)/d 4 times per week and 13cRA 80 mg/m(2)/dose twice per day, days 1 through 14 every 28 days. Wide interpatient variability was noted in vorinostat disposition, with area under the concentration-time curves at 230 mg/m(2)/d for the capsule (range, 1,415 to 9,291 ng/mL x hr) and oral suspension (range, 1,186 to 4,780 ng/mL x hr). Significant accumulation of acetylated H3 histone in PBMC was observed after administration of vorinostat, particularly at higher doses. One patient with neuroblastoma experienced a complete response to the combination. In children with recurrent solid tumors, vorinostat is well-tolerated at 230 mg/m(2)/d, with a modest dose reduction being required when combining vorinostat with 13cRA. Drug disposition is similar to that observed in adults.

Hummel TR, Jessen WJ, Miller SJ, Kluwe L, Mautner VF, Wallace MR, Lazaro C, Page GP, Worley PF, Aronow BJ, Schorry EK, Ratner N. **Gene expression analysis identifies potential biomarkers of neurofibromatosis type 1 including adrenomedullin**. *Clin Cancer Res.* 16(20): 5048-57. 2010.

Plexiform neurofibromas (pNF) are Schwann cell tumors found in a third of individuals with neurofibromatosis type 1 (NF1). pNF can undergo transformation to malignant peripheral nerve sheath tumors (MPNST). There are no identified serum biomarkers of pNF tumor burden or transformation to MPNST. Serum biomarkers would be useful to verify NF1 diagnosis, monitor tumor burden, and/or detect transformation. We used microarray gene expression analysis to define 92 genes that encode putative secreted proteins in neurofibroma Schwann cells, neurofibromas, and MPNST. We validated differential expression by quantitative reverse transcription-PCR, Western blotting, and ELISA assays in cell conditioned medium and control and NF1 patient sera. Of 13 candidate genes evaluated, only adrenomedullin (ADM) was confirmed as differentially expressed and elevated in serum of NF1 patients. ADM protein concentration was further elevated in serum of a small sampling of NF1 patients with MPNST. MPNST cell conditioned medium, containing ADM and hepatocyte growth factor, stimulated MPNST migration and endothelial cell proliferation. Thus, microarray analysis identifies potential serum biomarkers for disease, and ADM is a serum biomarker of NF1. ADM serum levels do not seem to correlate with the presence of pNFs but may be a biomarker of transformation to MPNST.

Nagarajan R, Kamruzzaman A, Ness KK, Marchese VG, Sklar C, Mertens A, Yasui Y, Robison LL and Marina N. **Twenty years of follow-up of survivors of childhood osteosarcoma: a report from the Childhood Cancer Survivor Study**. *Cancer.* 117(3): 625-34. 2011.

Osteosarcoma survivors have received significant chemotherapy and have undergone substantial surgeries. The authors assessed the long-term outcomes (at 20 years) of 733 5-year survivors of childhood osteosarcoma diagnosed from 1970 to 1986 to provide a comprehensive evaluation of medical and psychosocial outcomes for survivors enrolled in the Childhood Cancer Survivor Study (CCSS). Outcomes evaluated included overall survival, second malignant neoplasms (SMNs), recurrent osteosarcoma, chronic health conditions, health status (general and mental health and functional limitations), and psychosocial factors. Outcomes of osteosarcoma survivors were compared with general-population statistics, other CCSS survivors, and CCSS siblings. The overall survival of children diagnosed with osteosarcoma who survived 5 years at 20 years from original diagnosis was 88.6% (95% confidence interval [CI], 86.6%-90.5%). The cumulative incidence of SMNs at 25 years was 5.4%, with a standardized incidence ratio of 4.79 (95% CI, 3.54-6.33; P<.01). Overall, 86.9% of osteosarcoma survivors experienced at least 1 chronic medical condition, and >50% experienced >/=2 conditions. Compared with survivors of other cancers, osteosarcoma survivors

did not differ in their reported general health status (odds ratio [OR], 0.9; 95% CI, 0.7-1.2), but were more likely to report an adverse health status in at least 1 domain (OR, 1.9; 95% CI, 1.6-2.2), with activity limitations (29.1%) being the most common. Childhood osteosarcoma survivors in this cohort did relatively well, considering their extensive treatment, but are at risk of experiencing chronic medical conditions and adverse health status. Survivors warrant life-long follow-up.

Spence JR, Mayhew CN, Rankin SA, Kuhar MF, Vallance JE, Tolle K, Hoskins EE, Kalinichenko VV, Wells SI, Zorn AM, Shroyer NF, Wells JM. **Directed differentiation of human pluripotent stem cells into intestinal tissue in vitro**. *Nature.* 470(7332): 105-9. 2011.

Studies in embryonic development have guided successful efforts to direct the differentiation of human embryonic and induced pluripotent stem cells (PSCs) into specific organ cell types in vitro. For example, human PSCs have been differentiated into monolayer cultures of liver hepatocytes and pancreatic endocrine cells that have therapeutic efficacy in animal models of liver disease and diabetes, respectively. However, the generation of complex three-dimensional organ tissues in vitro remains a major challenge for translational studies. Here we establish a robust and efficient process to direct the differentiation of human PSCs into intestinal tissue in vitro using a temporal series of growth factor manipulations to mimic embryonic intestinal development. This involved activin-induced definitive endoderm formation, FGF/Wnt-induced posterior endoderm pattering, hindgut specification and morphogenesis, and a pro-intestinal culture system to promote intestinal growth, morphogenesis and cytodifferentiation. The resulting three-dimensional intestinal 'organoids' consisted of a polarized, columnar epithelium that was patterned into villus-like structures and crypt-like proliferative zones that expressed intestinal stem cell markers. The epithelium contained functional enterocytes, as well as goblet, Paneth and enteroendocrine cells. Using this culture system as a model to study human intestinal development, we identified that the combined activity of WNT3A and FGF4 is required for hindgut specification whereas FGF4 alone is sufficient to promote hindgut morphogenesis. Our data indicate that human intestinal stem cells form de novo during development. We also determined that NEUROG3, a pro-endocrine transcription factor that is mutated in enteric anendocrinosis, is both necessary and sufficient for human enteroendocrine cell development in vitro. PSC-derived human intestinal tissue should allow for unprecedented studies of human intestinal development and disease.

Division Collaboration

Behavioral Medicine and Clinical Psychology; Human Genetics; Neurology; Pathology; Physical Medicine and Rehabilitation; Radiology » M. Ernst; L. Bao; T. Smolarek; M. Sutton; R. McMasters; J. Mo; D. Pruitt; M. Gelfand

Leukemia/Lymphoma Program clinical multidisciplinary care (J. Perentesis, M. Absalon, K. Burns, A. Hammill, M. O'Brien, C. Phillips)

Biomedical Informatics; Biostatistics and Epidemiology; Clinical Pharmacology; Pathology; Radiology » B. Aronow; M. Kim; A. Vinks; D. Witte; M. Gelfand; A. Towbin

Scholar Training Program in Pediatric Oncology Developmental Therapeutics and Clinical Pharmacology, funded by the Hyundai Hope on Wheels Foundation (J. Perentesis, M. Fouladi)

Adolescent Medicine; Behavioral Medicine and Clinical Psychology; Biostatistics and Epidemiology; Human Genetics; Neurology; Physical Medicine and Rehabilitation » L. Ayensu-Coker; D. Drotar; M. Kim; S. Knapke; R. Hopkin; M. Sutton; D. Pruitt

Scholar Training Program in Cancer Survivorship, funded by the Hyundai Hope on Wheels Foundation (J. Perentesis, K. Burns, R. Nagarajan)

Surgical Services » R. Azizkhan; G. Tiao

Surgical services for oncology patients; Children's Oncology Group clinical research activities

UC Department of Radiation Oncology » J. Breneman; R. Lavigne

Radiation oncology clinical services for oncology patients; Children's Oncology Group clinical research activities

Human Genetics » L. Bao; T. Smolarek

Genetic services for oncology patients; Children's Oncology Group clinical research activities

Pathology » D. Witte; M. Collins; J. Yin; J. Mo; R. McMasters; L. Miles

Pathology services for oncology patients; Children's Oncology Group clinical research activities

Behavioral Medicine and Clinical Psychology » D. Drotar; A. Pai

Adherence research; "Promoting Treatment Adherence in Adolescent Leukemia" (NIH)

Radiology » M. Gelfand; A. Towbin

Nuclear medicine services for oncology patients; Children's Oncology Group clinical research activities

Endocrinology » S. Rose; M. Rutter

Endocrinology services for oncology patients; Children's Oncology Group and other clinical research activities

Physical Medicine and Rehabilitation » D. Pruitt

Rehabilitation services for oncology patients; Children's Oncology Group and other clinical research activities

Biomedical Informatics; Human Genetics; Developmental and Behavioral Pediatrics; Biostatistics and Epidemiology » B. Aronow; T. Smolarek; D. Schonfeld; M. Kim

Down syndrome leukemia research: etiology and risk factors, pharmacogenetics of therapy and outcomes (J. Perentesis)

Pathology; Radiology; Surgical Services » M. Gelfand; S. Sharp; A. Towbin; J. Yin; T. Maugins

Clinical services for neuroblastoma patients; clinical research related to neuroblastoma (J. Perentesis, B. Weiss)

University of Cincinnati Drug Discovery Center » R.Papoian

Pediatric leukemia, solid tumor, and brain tumor drug discovery screening (J. Perentesis, B. Weiss, M. Absalon, M. O'Brien)

Neurosurgery; Pathology; Radiology » T. Maugins; J. Yin; M. Gelfand; S. Sharp

Neuroblastoma Program: (B. Weiss, R. Nagarajan)

Rayburg M et al. **Langerhans cell histiocytosis in a patient with stage 4 neuroblastoma receiving oral fenretinide**. *Pediatr Blood Cancer.* 53(6): 1111-1113. Dec, 2009.

Human Genetics; Neurology; Clinical Pharmacology; Radiology; Neurosurgery; Ophthalmology; Orthopaedic Surgery; Physical Medicine and Rehabilitation; Pathology » E. Schorry; R. Hopkin; A. Vinks; A. Towbin; S. Sharp; M. Gelfand; M. Sutton; M. Collins; D. Pruitt; C. West; A. Crawford; K. Crone

Multidisciplinary clinical services for patients with neurofibromatosis; clinical research related to neurofibromatosis, including national clinical trial of mTOR inhibition to treat NF1-related plexiform neurofibromas (B. Weiss, J. Perentesis, T. Hummel)

Experimental Hematology and Cancer Biology; Pathology; University of Cincinnati Department of Cancer and Cell Biology; University of Minnesota » N. Ratner; M. Collins; G. Thomas; S. Kozma; D. Largaespeda

Cincinnati Center of Neurofibromatosis Research (P50) (J. Perentesis, T. Cripe)

Pathology » L. Miles

ACNS0822: a randomized phase II/III study of suberoylanilide hydroxamic acid (SAHA) (IND# 71976) and local irradiation or temozolomide and local irradiation or arsenic trioxide and local irradiation followed by maintenance bevacizumab (IND# 7921) and irinotecan in children with newly diagnosed high-grade glioma (M. Fouladi, R. Drissi)

Human Genetics » X. Qi

Testing SapC nanoparticle for anti-glioma activity in vivo (L. Chow)

Pathology » L. Miles

Characterization of murine brain tumors and collection of pediatric glioma samples (L. Chow)

Obstetrics and Gynecology » L. Ayensu-Coker

Fertility Consultation Service for oncology patients (K. Burns)

Obstetrics and Gynecology; Christ Hospital » L. Ayensu-Coker; S. Lindheim

Cincinnati chapter of the Oncofertility Consortium

UC Department of Cancer and Cell Biology Proteomics Core » K. Greis

Phosphoproteomic analysis of glioblastoma (B. DasGupta)

UC Drug Discovery Center » R. Papoian

Small molecule inhibition of AMP kinase (B. DasGupta)

Developmental Biology » K. Campbell

Understanding the role of AMP kinase in mammalian forebrain development (B. DasGupta)

Pathology » K. Setchell

Analysis of metabolites and nucleotides in the developing brain (B. DasGupta)

Imaging Research Center » D. Lindquist

Proton and phosphorus MRS to examine brain metabolites in the postnatal brain (B. DasGupta)

University of Minnesota » M. Georgieff; I. Tack; R. Rao

Proton spectroscopy detection of metabolic intermediates during early postnatal brain development (B. DasGupta)

University of Minnesota » M. Georgieff; I. Tack; R. Rao

Detection of glycolysis and TCA cycle intermediates from subregions of the developing mouse brain by LC-MS (B. DasGupta)

University of Leuven, Belgium » K. Norga

Understanding AMPK-dependence of AICAR and metformin action in the fly brain (B. DasGupta)

Mayo Clinic » S. Giri

Examining AMPK-dependence of metformim action in mice (B. DasGupta)

Neurology; Ophthalmology; Radiology » D. Rose; C. West; J. Leach

Visual pathway research for children with retinal or optic pathway tumors (J. Geller)

Ophthalmology » J. Augsburger

A pilot study of intravenous topotecan and vincristine in combination with subconjunctival carboplatin for patients with a history of bilateral retinoblastoma and refractory/recurrent intraocular disease (IND# 104,942) (J. Geller)

Human Genetics; Pathology; Surgical Services » N. Leslie; A. Gupta; G. Tiao

Screening children affected by hepatoblastoma for familial adenomatous polyposis (FAP) and a retrospective review of clinical and pathology features of children with hepatoblastoma with or without FAP (J. Geller)

Pathology; Pediatric and Adolescent Gynecology » R. McMasters; L. Ayensu-Coker

Management of ovarian sex-cord stromal tumors (J. Geller)

Human Genetics » N. Leslie

Pediatric Hereditary Cancer Predisposition Clinic (J. Geller)

Surgical Services; Gastroenterology, Hepatology, and Nutrition; Radiology; Pathology » G. Tiao; J. Nathan; M. Leonis; A. Towbin; K. Kukreja; A. Gupta; K. Bove; J. Yin

Liver Tumor Research Group (J. Geller)

Surgical Services; Gastroenterology, Hepatology and Nutrition; Developmental Biology; Radiology; Pathology » J. Nathan; M. Alonso; F. Ryckman; G. Tiao; M. Leonis; J. Bucuvalas; K. Campbell; A. Towbin; K. Kukreja; K. Bove; A. Gupta

Liver transplantation clinical services and clinical research activities for hepatoblatoma patients (J. Geller)

Nephrology; UC Division of Hematology/Oncology » J. Bissler; M. Czyzk-Krzeska; O. Rixe; G. Thomas

UC/CCHMC Renal Tumor Working Group (J. Geller)

Infectious Diseases; Investigational Pharmacy; Radiology; Crusade Labs » B. Connelly; M. Cloughessy; D. Lagory; J. Racadio; A. Towbin; M. Brown; J. Connor

Phase I trial of HSV1716 (T. Cripe)

Infectious Diseases; Investigational Pharmacy; Radiology; Experimental Hematology and Cancer Biology; Jennerex Biotherapeutics » B. Connelly; M. Cloughessy; D. Lagory; J. Racadio; A. Towbin; H. van der Loo; D. Kirn

Phase I trial of JX-594 (T. Cripe)

Pediatric General and Thoracic Surgery; Immunobiology; Molecular Immunology; Pulmonary Medicine; Bioceros » J. Frischer; D. Hildeman; S. Divanovic; E. Janssen; L. Boon

Proangiogenic inflammatory response to oncolytic HSV injection in preclinical models (T. Cripe)

Immunobiology; Molecular Immunology » D. Hildeman; E. Janssen

Role of dendtric cells is sensing oncolytic HSVs in cancer (T. Cripe)

Pathology; The Ohio State University; University of Pittsburgh » M. Collins; A. Chiocca; B. Kaur; J. Gloriosos; W. Goins

Receptor-mediated resistance to oncolytic HSV in neuroblastoma (T. Cripe)

The Ohio State University » A. Chiocca; B. Kaur

Oncolytic HSV enhanced by chondroitinase transgene expression (T. Cripe)

Experimental Hematology and Cancer Biology; Biostatistics and Epidemiology; Radiology; Washington University in St. Louis; Harvard University; University of California, San Francisco; House Research Institute; National Institutes of Health » N. Ratner; J. Wu; M. Kim; D. Lindquist; D. Gutmann; K. Cichowski; K. Shannon; M. Giovannini; A. McClatchey; E. Dombi

Children's Tumor Foundation Neurofibromatosis Preclinical Consortium (T. Cripe)

University of Bologna, Italy » I. Orienti

A novel carbon-based polymer micelle as cancer therapy (T. Cripe)

University of New South Wales, Australia » P. Gunning

Preclinical antitumor efficacy of novel tropomyosin isoform inhibitors (T. Cripe)

General and Thoracic Surgery; Biomedical Informatics » T. Crombleholme; B. Aronow

Development of a midkine-regulated oncolytic Herpes virus (T. Cripe)

Experimental Hematology and Cancer Biology; Pathology » N. Ratner; J. Cancelas; M. Collins

EYA4 in MPNST (T. Cripe)

Immunobiology » D. Hildeman

Regulatory T cells in oncolytic HSV virotherapy (T. Cripe)

Surgical Services; Otolaryngology; Dermatology; Radiology; Pathology; Cardiology; Gastroenterology, Hepatology and Nutrition; Urology; Endocrinology; Orthopaedics; Neurology; Pulmonary Medicine; Ophthalmology; Pain Management and Palliative Care; Human Genetics » R. Azizkhan; A. Dasgupta; R. Elluru; A. Lucky; M. Patel; T. Abruzzo; W. Ball; A Zbojniewicz; K. Crone; A. Gupta; P. Eghtesday; K. Goldchneider; R. Hirsch; R. Hopkin; A. Kaul; P. Reddy; M. Rutter; J. Sorger; M. Sutton; R. Wood; K. Yakuboff; J. Taylor; M. Yang; M. Seid

Hemangioma and Vascular Malformation Center, clinical services and clinical research, including a clinical trial of rapamycin for complicated vascular anomalies, a vascular tumor registry, and a vascular anomaly tissue repository (D. Adams, A. Hammill)

Gastroenterology, Hepatology and Nutrition; Radiology; Nephrology; Cardiology; Pathology » N. Yazigi; A. Brody; J. Goebel; R. Spicer; K. Uzark; D. Witte

Post-Transplant Lymphoproliferative Disease Working Group (M. Absalon)

Faculty Members

John Perentesis, MD, FAAP, Professor

Deb Kleisinger Endowed Chair of Novel Cancer Treatments
Executive Co-Director, Cancer and Blood Diseases Institute
Director, Division of Oncology
Director, Leukemia/Lymphoma Program
Cincinnati Children's Principal Investigator, Children's Oncology Group (COG)
Cincinnati Children's Principal Investigator, National Cancer Institute Pediatric Phase I Consortium

Research Interests New anticancer drug development; molecular oncogenesis and pharmacogenetics in high risk leukemia, lymphoma and pediatric cancers

Michael Absalon, MD, PhD, Assistant Professor

Director, Medical Education Program
Associate Director, Leukemia/Lymphoma Program

Research Interests New therapeutics; relapsed leukemia and lymphoma, post-transplant lymphoproliferative disease, T-cell lymphoma

Denise M. Adams, MD, Professor

Medical Director, Comprehensive Hemangiomas and Vascular Malformation Clinic
Director, Hematology/Oncology Fellowship Program

Research Interests Angiogenesis, endothelial cell proliferation, vascular anomalies, mTOR inhibition as a therapeutic approach to complex vascular anomalies

Karen Burns, MD, Assistant Professor

Clinical Director, Cancer Survivor Center

Research Interests Childhood cancer survival; fertility preservation and outcomes; adolescent and young adult outcomes and quality of life

Lionel Chow, MD, Assistant Professor

Research Interests Molecular genetics of pediatric high-grade glioma, animal models of brain tumors, translational therapeutics for gliomas

Timothy Cripe, MD, PhD, Professor

Research Director, Musculoskeletal Tumor Program
Co-Medical Director, Office for Clinical and Translational Research
Director of Pilot and Collaborative Studies, Center for Clinical and Translational Science and Training
Research Interests Mechanistic, preclinical, and clinical studies of oncolytic virotherapy, antiangiogenesis, and signal transduction inhibitors for sarcomas, neuroblastoma and other pediatric solid tumors

Biplab Dasgupta, PhD, Assistant Professor
Research Interests Brain development, energy metabolism, brain cancer

Rachid Drissi, MD, Assistant Professor
Research Interests Replicative senescence, telomere disruption signaling to DNA damage pathways

Maryam Fouladi, MD, FRCP, Professor
Medical Director, Neuro-Oncology Program
Cincinnati Children's Principal Investigator, Collaborative Ependymoma Research Network (CERN)
Research Interests Novel drug development for the treatment of children with recurrent or poor prognosis brain tumors

James I. Geller, MD, Associate Professor
Medical Director, Kidney and Liver Tumors Program
Co-Medical Director, Retinoblastoma Program
Research Interests Developmental therapeutics for pediatric solid tumors, especially liver and kidney tumors and retinoblastoma

Adrienne Hammill, MD, Assistant Professor
Research Interests New approaches to the assessment and treatment of hemangiomas and vascular malformations

Trent Hummel, MD, Instructor
Research Interests New therapeutics in neuro-oncology; diffuse intrinsic pontine glioma, neurofibromatosis type 1 and 2 related tumors, biomarker development

Beatrice Lampkin, MD, Professor Emerita
Research Interests Blood and bone marrow morphology and the significance thereof in relationship to patients' case histories

Benjamin Mizukawa, MD, Instructor
Research Interests Pediatric leukemia and lymphoma; role of small Rho GTPases in leukemogenesis and leukemic stem cell biology and their potential as therapeutic targets in acute myeloid leukemia

Rajaram Nagarajan, MD, Assistant Professor
Outpatient and Inpatient Clinical Director
Director of Cancer Control and Outcomes Research, Cancer Survivor Center
Research Interests Bone tumors; functional and quality of life outcomes following cancer therapy

Maureen O'Brien, MD, Assistant Professor
Associate Director, Leukemia/Lymphoma Program
Research Interests High-risk acute lymphoblastic leukemia; novel therapies for relapsed leukemia and lymphoma; complications of leukemia therapy

Christine Phillips, MD, Instructor
Research Interests Developmental therapeutics for acute myeloid leukemia; pharmacogenomics of cytarabine and other chemotherapeutic agents

Lars Wagner, MD, Associate Professor
Medical Director, Musculoskeletal Tumor Program

Cincinnati Children's Principal Investigator, Sarcoma Alliance for Research Through Collaboration (SARC)
Research Interests Developmental therapeutics for neuroblastoma, sarcomas, and brain tumors

Brian D. Weiss, MD, Associate Professor
Associate Director for Safety and Compliance, Cancer and Blood Diseases Institute
Medical Director, Neuroblastoma Program
Cincinnati Children's Principal Investigator, New Approaches to Neuroblastoma Therapy Consortium (NANT)
Research Interests Targeted agents for neurofibromatosis type 1-related malignancies (including plexiform neurofibromas, optic pathway gliomas, and juvenile myelomonocytic leukemia); chemotherapy safety

Susanne Wells, MD, Associate Professor
Director, Epithelial Carcinogenesis and Stem Cell Program
Research Interests Epithelial malignancies, human papillomavirus biology and new targets of the HPV E6/E7 oncogenes, the role of epithelial stem cells in carcinogenesis

Joint Appointment Faculty Members

Mi-Ok Kim, PhD, Associate Professor
Center for Epidemiology and Biostatistics

Ahna Pai, PhD, Assistant Professor
Adherence Psychology

Saulius Sumanas, PhD, Assistant Professor
Developmental Biology

Mary Sutton, MD, Associate Professor
Neurology

Clinical Staff Members

- Carina Braeutigam, MD
- Vasudha Narayanaswamy, MD

Trainees

- Michael Bishop, MD, PL-V, Children's Mercy Hospital, Kansas City
- Kathleen Dorris, MD, PL-VI, Children's Memorial Hospital, Northwestern University
- Sarah Fitzgerald, MD, PL-VI, Rainbow Babies & Children's Hospital/University of Cleveland
- Dawn Pinchasik, MD, PL-IV, Children's Hospital of Pittsburgh
- Jennifer Pope, MD, PL-VI, Medical College of Wisconsin
- Jennifer Williams, MD, PL-IV, T.C. Thompson Children's Hospital/University of Tennessee

Significant Accomplishments

Study of Sirolimus for Complex Vascular Anomalies

Complex vascular malformations can be difficult to treat with surgery and cause disfigurement, chronic pain and organ dysfunction with significant morbidity and mortality. Oncologist Denise Adams, MD, medical director of the Hemangioma and Vascular Malformation Center (HVMC), has developed an investigator-initiated phase 2 study to assess the safety and efficacy of the mTOR inhibitor sirolimus. This study, supported by an FDA Orphan Products Grant, represents the first prospective clinical trial of a new medical

therapy for these conditions. Adams is an internationally recognized authority on vascular anomalies, and the HVMC is an internationally recognized referral center and a model of collaboration among the Cancer and Blood Diseases Institute, the Department of Surgery and the Division of Developmental Biology. Adams has also helped to lead development of a robust and growing interdisciplinary working group on vascular biology whose research is guiding the development of future clinical trials.

Targeted Drug Discovery and Personalized Therapies

Despite advances in cure rates with chemotherapy, many children continue to relapse with fatal cancers or suffer severe complications from current therapies. The Division of Oncology is a national leader in the development of drugs and use of personalized genomics for better therapies for pediatric cancers.

The division is home to a leading national center for research in the development of anticancer therapies targeting tumor growth factor signaling pathways in combination with synergistic inhibition of the mTOR growth regulation pathway. Projects in tumors associated with neurofibromatosis (led by Brian Weiss, MD) and in pediatric brain tumors, sarcomas, neuroblastoma and other malignancies (led by Maryam Fouladi, MD, MSc) continue with research to identify molecular markers predictive of response. Early results of this innovative clinical translational work were presented by Fouladi at the national American Society of Clinical Oncology annual meeting. Lars Wagner, MD, is extending the team's research in this area with his leadership of a new phase 2 clinical trial of IMC-A12 and temsirolimus (CCI-779) for children and adolescents with relapsed cancers.

A new initiative this year focuses on epigenetic therapies – specifically targeting chromatin structure and pathologic gene and micro-RNA expression to kill or "mature" malignant cells. At the 2010 American Society for Hematology national meeting, Christine Phillips, MD, presented work from the division demonstrating that complete remissions could be achieved in children with highly treatment-resistant forms of acute myeloid leukemia using decitabine. This work has provided the foundation for a new research study that Phillips is developing combining a related drug, azacytidine, with a chromatin-targeting drug, vorinostat. In parallel work, Trent Hummel, MD, is leading a phase 1 study investigating vorinostat with the conventional chemotherapy drug temozolomide for the treatment of relapsed or refractory brain or spinal tumors.

Understanding the biology of cancer stem cells and using new drugs to target these pathways are a key new area of research for the division. The laboratory of Timothy Cripe, MD, PhD, is funded to find new ways to identify and develop better therapies against neuroblastoma stem cells. James Geller, MD, is leading a phase 1 clinical trial of the small molecule c-Met inhibitor ARQ-197 in children with relapsed malignancies. Signaling through c-Met, also known as the hepatocyte growth factor, is prominent in normal stem cells but not normal tissues. However, c-Met is dysregulated in many types of human malignancies, including cancers of the kidney, liver and brain. In parallel work, Fouladi is leading a phase 1 study of the AKT inhibitor MK2206 in recurrent or refractory solid tumors and leukemias, as well as a Pediatric Brain Tumor Consortium phase 1 study of the Notch inhibitor MK0751. Notch signaling is a key regulator of viability and numbers of normal and malignant stem cells, and targeting this pathway holds particular promise for brain tumor therapy. Rachid Drissi, PhD, is leading important new research efforts to understand the role of telomerase in malignant stem cells in pediatric cancers, particularly brain tumors. He also is leading correlative biology studies for a Children's Oncology Group study, the first national phase 1 trial of a telomerase inhibitor in children with solid tumors.

The division has recently established a new Scholar Training Program in Cancer Developmental Therapeutics

and obtained competitive funding through the Hyundai Hope on Wheels Foundation. We recruited our first scholar, Carrye Cost, MD, who will receive intensive mentoring in advanced clinical oncology, pharmacology and pharmacogenetics, cancer biology and new drug development. This program is integrated with other initiatives in drug discovery and pre-clinical drug development in partnership with the Division of Experimental Hematology and Cancer Biology and the University of Cincinnati's Drug Discovery Center. Closely related efforts in tumor signature profiling are also under way in Division of Oncology laboratories for real-time mutational analysis of patient tumor samples so that patients with high-risk disease can be guided to the most appropriate experimental targeted therapies based on the specific signaling pathways active in their cancers.

National Leadership in Research Consortia

Cincinnati Children's faculty continue to provide critical leadership in national clinical research efforts focused on pediatric cancers. John Perentesis, MD, director of the Division of Oncology, was elected to the executive committee of the Children's Oncology Group (COG), for which he also serves as chairman of the Acute Myeloid Leukemia Relapse Committee and vice chairman of the Adolescent and Young Adult Cancer Steering Committee. In addition, he serves on the Investigational Drug Steering Committee of the National Cancer Institute's Cancer Therapy Evaluation Program, for which he chairs the Signal Transduction Agents Task Force, and the national steering committee of the NCI-funded Pediatric Developmental Therapeutics/Phase I Consortium.

Maryam Fouladi, MD, MSc, medical director of the Neuro-Oncology Program, chairs the CNS Tumor New Agents/Relapse Committee for the Children's Oncology Group, for which she also serves on the CNS Tumor Committee; she is a member of the national steering committee for the Collaborative Ependymoma Research Network (CERN). Brian Weiss, MD, leads a national COG pilot study of the targeted radiopharmaceutical 131I-MIBG in high-risk neuroblastoma as well as a national phase 2 study of sirolimus in neurofibromatosis type 1-related plexiform neurofibromas through the Neurofibromatosis Consortium.

Division Publications

1. Adams DM. **Special considerations in vascular anomalies: hematologic management**. *Clin Plast Surg*. 2011; 38:153-60.
2. Bagatell R, London WB, Wagner LM, Voss SD, Stewart CF, Maris JM, Kretschmar C, Cohn SL. **Phase II study of irinotecan and temozolomide in children with relapsed or refractory neuroblastoma: a Children's Oncology Group study**. *J Clin Oncol*. 2011; 29:208-13.
3. Bai F, Tagen M, Colotta C, Miller L, Fouladi M, Stewart CF. **Determination of the gamma-secretase inhibitor MK-0752 in human plasma by online extraction and electrospray tandem mass spectrometry (HTLC-ESI-MS/MS)**. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2010; 878:2348-52.
4. Browne AW, Leddon JL, Currier MA, Williams JP, Frischer JS, Collins MH, Ahn CH, Cripe TP. **Cancer screening by systemic administration of a gene delivery vector encoding tumor-selective secretable biomarker expression**. *PLoS One*. 2011; 6:e19530.
5. Chow LM, Endersby R, Zhu X, Rankin S, Qu C, Zhang J, Broniscer A, Ellison DW, Baker SJ. **Cooperativity within and among Pten, p53, and Rb pathways induces high-grade astrocytoma in adult brain**. *Cancer Cell*. 2011; 19:305-16.
6. Cripe TP. **Ewing sarcoma: an eponym window to history**. *Sarcoma*. 2011; 2011:457532.
7. Dmitrieva N, Yu L, Viapiano M, Cripe TP, Chiocca EA, Glorioso JC, Kaur B. **Chondroitinase ABC I-mediated enhancement of oncolytic virus spread and antitumor efficacy**. *Clin Cancer Res*. 2011;

17:1362-72.

8. Drolet BA, Chamlin SL, Garzon MC, Adams D, Baselga E, Haggstrom AN, Holland KE, Horii KA, Juern A, Lucky AW, Mancini AJ, McCuaig C, Metry DW, Morel KD, Newell BD, Nopper AJ, Powell J, Frieden IJ. **Prospective study of spinal anomalies in children with infantile hemangiomas of the lumbosacral skin**. *J Pediatr*. 2010; 157:789-94.
9. Duffy KJ, Runge-Samuelson C, Bayer ML, Friedland D, Sulman C, Chun R, Kerschner JE, Metry D, Adams D, Drolet BA. **Association of hearing loss with PHACE syndrome**. *Arch Dermatol*. 2010; 146:1391-6.
10. Eshun FK, Currier MA, Gillespie RA, Fitzpatrick JL, Baird WH, Cripe TP. **VEGF blockade decreases the tumor uptake of systemic oncolytic herpes virus but enhances therapeutic efficacy when given after virotherapy**. *Gene Ther*. 2010; 17:922-9.
11. Fernandez C, Geller JI, Ehrlich PF, Hill DA, Kalapurakal JA, Grundy PE, Dome JS. **Renal tumors**. *Principles and practice of pediatric oncology.* Philadelphia: Lippincott Williams & Wilkins; 2011: 861-885. .
12. Fernandez KS, Baum R, Fung B, Yeager N, Leonis MA, Wagner LM, Tiao G, Ross ME. **Chemoresistant hepatoblastoma in a patient with mosaic trisomy 18 treated with orthotopic liver transplantation**. *Pediatr Blood Cancer*. 2011; 56:498-500.
13. Fouladi M, Park JR, Stewart CF, Gilbertson RJ, Schaiquevich P, Sun J, Reid JM, Ames MM, Speights R, Ingle AM, Zwiebel J, Blaney SM, Adamson PC. **Pediatric phase I trial and pharmacokinetic study of vorinostat: a Children's Oncology Group phase I consortium report**. *J Clin Oncol*. 2010; 28:3623-9.
14. Fouladi M, Stewart CF, Blaney SM, Onar-Thomas A, Schaiquevich P, Packer RJ, Gajjar A, Kun LE, Boyett JM, Gilbertson RJ. **Phase I trial of lapatinib in children with refractory CNS malignancies: a Pediatric Brain Tumor Consortium study**. *J Clin Oncol*. 2010; 28:4221-7.
15. Geller JI, Dome JS. **Molecularly targeted therapy for Wilms' tumor**. *Molecularly targeted therapy for childhood cancer.* New York: Springer Science+Business Media, LLC; 2010: 401-24. .
16. Gibson B, Perentesis J, Alonzo TA, Kasper GJL. **Treatment of Acute Myeloid Leukemia**. *Childhood leukemia : a practical handbook.* New York: Springer; 2010: 121-160. .
17. Haas-Kogan DA, Banerjee A, Poussaint TY, Kocak M, Prados MD, Geyer JR, Fouladi M, Broniscer A, Minturn JE, Pollack IF, Packer RJ, Boyett JM, Kun LE. **Phase II trial of tipifarnib and radiation in children with newly diagnosed diffuse intrinsic pontine gliomas**. *Neuro Oncol*. 2011; 13:298-306.
18. Hammill AM, Conner J, Cripe TP. **Oncolytic virotherapy reaches adolescence**. *Pediatr Blood Cancer*. 2010; 55:1253-63.
19. Hummel T, Anyane-Yeboa A, Mo J, Towbin A, Weiss B. **Response of NF1-related plexiform neurofibroma to high-dose carboplatin**. *Pediatr Blood Cancer*. 2011; 56:488-90.
20. Hummel TR, Jessen WJ, Miller SJ, Kluwe L, Mautner VF, Wallace MR, Lazaro C, Page GP, Worley PF, Aronow BJ, Schorry EK, Ratner N. **Gene expression analysis identifies potential biomarkers of neurofibromatosis type 1 including adrenomedullin**. *Clin Cancer Res*. 2010; 16:5048-57.
21. Lavado A, Lagutin OV, Chow LM, Baker SJ, Oliver G. **Prox1 is required for granule cell maturation and intermediate progenitor maintenance during brain neurogenesis**. *PLoS Biol*. 2010; 8.
22. Liu C, Cripe TP, Kim MO. **Statistical issues in longitudinal data analysis for treatment efficacy studies in the biomedical sciences**. *Mol Ther*. 2010; 18:1724-30.
23. Maldonado AR, Klanke C, Jegga AG, Aronow BJ, Mahller YY, Cripe TP, Crombleholme TM. **Molecular engineering and validation of an oncolytic herpes simplex virus type 1 transcriptionally targeted to midkine-positive tumors**. *J Gene Med*. 2010; 12:613-23.
24. Meyer SE, Peace BE, Bahassi el M, Kavanaugh GM, Wagh PK, Robbins SB, Yin M, Wells SI, Zinser GM, Stambrook PJ, Waltz SE. **Chk2*1100delC Acts in synergy with the Ron receptor tyrosine kinase to accelerate mammary tumorigenesis in mice**. *Cancer Lett*. 2010; 296:186-93.

25. Mizukawa B, George A, Pushkaran S, Weckbach L, Kalinyak K, Heubi JE, Kalfa TA. **Cooperating G6PD mutations associated with severe neonatal hyperbilirubinemia and cholestasis**. *Pediatr Blood Cancer*. 2011; 56:840-2.
26. Nagarajan R, Kamruzzaman A, Ness KK, Marchese VG, Sklar C, Mertens A, Yasui Y, Robison LL, Marina N. **Twenty years of follow-up of survivors of childhood osteosarcoma: a report from the Childhood Cancer Survivor Study**. *Cancer*. 2011; 117:625-34.
27. Phillips CL, Gerbing R, Alonzo T, Perentesis JP, Harley IT, Meshinchi S, Bhatla D, Radloff G, Davies SM. **MDM2 polymorphism increases susceptibility to childhood acute myeloid leukemia: a report from the Children's Oncology Group**. *Pediatr Blood Cancer*. 2010; 55:248-53.
28. Pressey JG, Wright JM, Geller JI, Joseph DB, Pressey CS, Kelly DR. **Sirolimus therapy for fibromatosis and multifocal renal cell carcinoma in a child with tuberous sclerosis complex**. *Pediatr Blood Cancer*. 2010; 54:1035-7.
29. Sanchez-Pinto LN, Laskin BL, Jodele S, Hummel TR, Yin HJ, Goebel J. **BK virus nephropathy in a pediatric autologous stem-cell transplant recipient**. *Pediatr Blood Cancer*. 2011; 56:495-7.
30. Spence JR, Mayhew CN, Rankin SA, Kuhar MF, Vallance JE, Tolle K, Hoskins EE, Kalinichenko VV, Wells SI, Zorn AM, Shroyer NF, Wells JM. **Directed differentiation of human pluripotent stem cells into intestinal tissue in vitro**. *Nature*. 2011; 470:105-9.
31. Spicakova T, O'Brien MM, Duran GE, Sweet-Cordero A, Sikic BI. **Expression and silencing of the microtubule-associated protein Tau in breast cancer cells**. *Mol Cancer Ther*. 2010; 9:2970-81.
32. Wagner L. **Camptothecin-based regimens for treatment of ewing sarcoma: past studies and future directions**. *Sarcoma*. 2011; 2011:957957.
33. Wagner LM, Gelfand MJ, Laor T, Ryckman FC, Al-Ghawi H, Bove KE. **A welcome surprise: nodular fasciitis presenting as soft tissue sarcoma**. *J Pediatr Hematol Oncol*. 2011; 33:316-9.
34. Wald AI, Hoskins EE, Wells SI, Ferris RL, Khan SA. **Alteration of microRNA profiles in squamous cell carcinoma of the head and neck cell lines by human papillomavirus**. *Head Neck*. 2011; 33:504-12.
35. Woodard P, Carpenter PA, Davies SM, Gross TG, He W, Zhang MJ, Horn BN, Margolis DA, Perentesis JP, Sanders JE, Schultz KR, Seber A, Woods WG, Eapen M. **Unrelated donor bone marrow transplantation for myelodysplastic syndrome in children**. *Biol Blood Marrow Transplant*. 2011; 17:723-8.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct / Project Period Direct
ADAMS, D		
Phase II Study of Rapamycin for Complicated Vascular Anomalies		
Food and Drug Administration		
R01 FD 003712	09/25/09-07/31/13	$246,510
Severity Scale and Quality of Life Instrument for Infantile Hemangiomas		
National Institutes of Health(Indiana Univ - Purdue Univ @ Indianapolis)		
RC1 AR 058767	09/29/09-08/31/11	$667
CHOW, L		
Establishment of a Pre-Clinical Model for Pediatric Glioblastoma		
The Cure Starts Now Foundation		
	10/01/10-09/30/11	$35,000
CRIPE, T		
Phase I Study of HSV1716 in Pediatric Non-CNS Solid Tumors		
Food and Drug Administration		

R01 FD 003717 09/01/10-08/31/13 $153,320

Preclinical Efficacy Studies of TR100 in Pediatric Cancer
Oncology Children's Foundation
07/01/10-06/30/11 $59,973

The Role of Dendritic Cells in Oncolytic Virotherapy for Rhabdomyosarcoma
Joanna McAfee Childhood Cancer Fdn. Inc.
01/01/11-12/31/11 $5,000

Cincinnati NF1 Preclinical Testing Center
The Children's Tumor Foundation
12/01/07-06/30/11 $216,365

Cincinnati Center for Clinical and Translational Sciences and Training (Pilot/Collaborative Studies)
National Institutes of Health(University of Cincinnati)
UL1 RR 026314 04/03/09-03/31/14 $27,761

Cincinnati Center for Neurofibromatosis Research (Project B)
National Institutes of Health
P50 NS 057531 09/15/08-0$6/30/13 $105,859

DASGUPTA, B

Inhibition of Pediatric Glioma Growth by Genetic Inhibition of AMP Kinase
CancerFree Kids Pediatric Cancer Research Alliance
06/01/2011-05/31/2012 $30,000

DORRIS, K

Molecular Epidemiology in Children's Environmental Health
National Institutes of Health(University of Cincinnati)
T32 ES 010957 10/01/10-09/30/12 $37,377

DRISSI, R

Telomerase: A Therapeutic Target in Pediatric Tumors
The Cure Starts Now Foundation
09/01/10-08/31/11 $75,000

Correlative Biology Studies in the First Phase I Trial of a Telomerase Inhibitor in Children with Recurrent Solid Tumors
CancerFree Kids Pediatric Cancer Research Alliance
6/01/11-05/31/12 $10,000

FOULADI, M

Phase I Study of MK2206, an AKT Inhibitor, in Children with Recurrent Solid Tumors or Leukemias
CancerFree Kids Pediatric Cancer Research Alliance
06/01/2011-05/31/2012 $10,000

Children's Oncology Group Chair's Grant
National Institutes of Health (Children's Oncology Group)
U10 CA 98543 3/01/11-2/29/12 $12,500

CERN Clinical Trials Network-Per Patient
Univ of Texas M.D. Anderson Cancer Center
07/01/09-05/13/12 $9,702

Pediatric Brain Tumor Consortium
National Institutes of Health (St. Jude Children's Research Hospital)
U01 CA 098543 04/01/08-03/31/12 $2,880

Pediatric Brain Tumor Consortium - per patient
National Institutes of Health (St. Jude Children's Research Hospital)
U01CA098543 04/01/08-03/31/12 $8,990

HUMMEL, T

COG Phase I Agreement
National Institutes of Health(National Childhood Cancer Foundation)
U01 CA 097452 02/01/10-07/31/11 $15,532

IRWIN, M

Developing a National Model: Cincinnati Children's School Intervention Program
The Jeff Gordon Foundation
01/01/11-12/31/11 $15,000

LEDDON, J

The Role of Dendritic Cells in Oncolytic Virotherapy
CancerFree Kids Pediatric Cancer Research Alliance
06/01/11-05/31/12 $30,000

MARMER, D

Pilot Study to Assess Minimal Residual Disease in Ewing Sarcoma
CancerFree Kids Pediatric Cancer Research Alliance
06/01/11-05/31/12 $10,000

MIZUKAWA, B

Characterization of Rac GTPases inacute myeloid leukemia (AML) and their potential as therpeutic targets
National Institutes of Health(Yale University School of Medicine)
K12 HD 000850 07/01/08-08/31/10 $17,708

ORIENTI, I

Development of RC-16 as a New Cancer Therapy
CancerFree Kids Pediatric Cancer Research Alliance
06/01/11-05/31/12 $30,000

PERENTESIS, J

The Children's Oncology Group Chair Grant
National Institutes of Health(Children's Oncology Group)
U10 CA 098543 03/01/08-02/28/13 $30,083

The Children's Oncology Group Chair Grant- Per Patient
National Institutes of Health(Children's Oncology Group)
U10 CA 098543 03/01/08-02/28/13 $156,398

Children's Oncology Group Phase I
National Institutes of Health(Children's Oncology Group)
U01 CA 097452 08/01/02-07/31/12 $23,222

Children's Oncology Group Phase I - Per Patient
National Institutes of Health(Children's Oncology Group)
U01 CA 097452 08/01/02-07/31/12 $70,203

Children's Oncology Group New Publication Committee
National Institutes of Health(Children's Oncology Group)
U01 CA 97542 09/01/06-07/31/12 $25,363

Cincinnati Children's Hyundai Scholar in Childhood Cancer Drug Development
Hyundai Hope on Wheels
10/01/10-09/31/11 $100,000

Cincinnati Center for Neurofibromatosis Research (Project 1)
National Institutes of Health
P50 NS 057531 09/15/08-06/30/13 $296,849

POPE, J

Analysis of Antioxident Polymorphisms in Patients with Down Syndrome and CML
St. Baldrick's Foundation
07/01/10-06/30/12 $68,209

Analysis of Antioxidant Polymorphisms in Patients with Down Syndrome and CML
Hyundai Hope on Wheels
07/01/10-06/30/11 $50,000

PRIVETTE-VINNEDGE, L

The Role of DEK in Breast Cancer Development and Therapy
National Institutes of Health
F32 CA 139931 09/15/09-09/14/11 $50,474

WAGNER, L

NAB-PACLITAXEL and SPARC in Pediatric Sarcoma
CancerFree Kids Pediatric Cancer Research Alliance
06/01/11-05/31/12 $15,000

WANG, P-Y

Virotherapy on Primary Neuroblastoma Cells
Alex's Lemonade Stand Foundation
07/01/10-06/30/12 $40,000

WEISS, B

Neurofibromatosis Consortium (STOPN - Protocol 102 mTOR)
Department of Defense Army(University of Alabama-Birmingham)
07/01/10-06/30/11 $19,373

Children's Oncology Group Chairs Grant
National Institutes of Health (Children's Oncology Group)
U10 CA 098543 03/01/11-02/29/12 $12,500

WELLS, S

Fanconi Anemia and HPV Transformation
National Institutes of Health
R01 CA 102357 09/30/09-08/31/14 $197,767

Current Year Direct **$2,320,582**

Industry Contracts

CRIPE, T

Crusade Laboratories Limited $8,163
Jennerex Biotherapeutics $6,582

FOULADI, M

Genetech $15,400

GELLER, J

ArQule, Inc $1,277

OBRIEN, M

Novartis Pharmaceuticals $11,935

PERENTESIS, J

CHLA - NANT $10,795

WAGNER, M

Sarcoma Alliance for Res through Collabo $7,069

Current Year Direct Receipts **$61,221**

Funded Collaborative Efforts

CRIPE, T

Cincinnati Center for Clinical and Translational Scienes and Training
National Institutes of Health

Heubi, J	04/01/09-03/31/14	6%

PERENTESIS, J

Promoting Treatment Adherence in Adolescent Leukemia
National Institutes of Health

Drotar, D	09/28/07-07/31/12	3%

Total **$2,381,803**