

# Hematology-Oncology

## **Division Photo**



First Row: B. Lampkin; Second Row: B. DasGupta, R. Nagarajan, E. Mullins, P. Malik, C. Joiner, C. Quinn, C. Tarango, K. Kalinyak, K. Burns, T. Kalfa; Third Row: J. Geller, A. Perumbeti, R. Drissi, L. Wagner, F. Smith, C. Phillips, J. Perentesis, A. Hammill

#### **Division Data Summary**

#### **Research and Training Details**

Number of Faculty	28
Number of Joint Appointment Faculty	5
Number of Research Fellows	7
Number of Research Students	5
Number of Support Personnel	149
Direct Annual Grant Support	\$5,100,417
Direct Annual Industry Support	\$182,957
Peer Reviewed Publications	36
Clinical Activities and Training	
Number of Clinical Fellows	15
Inpatient Encounters	7,192
Outpatient Encounters	11,550

## **Significant Publications**

F. K. Eshun, M. A. Currier, R. A. Gillespie, J. L. Fitzpatrick, W. H. Baird and T. P. Cripe (2010). "VEGF blockade decreases the tumor uptake of systemic oncolytic herpes virus but enhances therapeutic efficacy when given after virotherapy." Gene Ther 17(7): 922-929.

Effective therapies for metastatic sarcomas remain elusive. Oncolytic viruses have shown promise as anticancer agents, but their access to metastatic sites following systemic delivery is low. As systemic delivery of small-molecule chemotherapy is enhanced by previous treatment with antiangiogenic agents because of changes in intravascular-to-tumor interstitial pressure, we sought to determine whether antiangiogenic pretreatment increases the antitumor efficacy of systemic virotherapy by increasing virus uptake into tumor. Virus biodistribution and antitumor effects were monitored in tumor-bearing mice given antihuman vascular endothelial growth factor (VEGF) or antimouse VEGFR2 before or after an intravenous (i.v.) injection of virus. Without pretreatment, the average virus titers in the

tumor samples amplified 1700-fold over 48 h but were undetectable in other organs. After antiangiogenic treatment, average virus titers in the tumor samples were unchanged or in some cases decreased up to 100-fold. Thus, antiangiogenic pretreatment failed to improve the tumor uptake of systemic oncolytic herpes simplex virus (oHSV), in contrast to previously reported enhanced uptake of small molecules. Superior tumor control because of the combined effects of virus and anti-VEGF was seen most dramatically when anti-VEGF was given after virus. Our data suggest that i.v. oHSV can treat distant sites of disease and can be enhanced by antiangiogenic therapy, but only when given in the proper sequence.

T. A. Kalfa, S. Pushkaran, X. Zhang, J. F. Johnson, D. Pan, D. Daria, H. Geiger, J. A. Cancelas, D. A. Williams and Y. Zheng (2010). "Rac1 and Rac2 GTPases are necessary for early erythropoietic expansion in the bone marrow but not in the spleen." Haematologica 95(1): 27-35.

We evaluated the role of Rac1 and Rac2 GTPases in erythropoiesis, demonstrating that these signaling molecules are essential for medullary but not for extramedullary erythropoiesis, implicating different signaling pathways for homeostatic and stress erythropoiesis. In addition, in this manuscript, we have revised a widely adopted protocol of murine erythroid differentiation analysis by flow cytometry after staining for CD71 and Ter119, offering a clear interpretation of the correspondence of the populations identified by flow cytometry to the erythroblast populations identified by morphologic characteristics.

R. Nagarajan, A. Kamruzzaman, K. K. Ness, V. G. Marchese, C. Sklar, A. Mertens, Y. Yutaka, L. L. Robison and N. Marina (2010). "Twenty years of follow-up of survivors of childhood osteosarcoma: a report from the Childhood Cancer Survivor Study (CCSS)." Cancer (in press).

We assessed the long-term outcomes of 733 five-year survivors of childhood osteosarcoma diagnosed from 1970 -1986 to provide a comprehensive evaluation of medical and psychosocial outcomes for survivors enrolled on 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 psycho-social factors. Outcomes of osteosarcoma survivors were compared to generalpopulation statistics, other CCSS survivors, and CCSS siblings. Childhood osteosarcoma survivors in this cohort did relatively well considering their extensive treatment but are at risk to experience chronic medical conditions and adverse health status. Survivors warrant life-long follow-up.

K. A. Steinbrecher, N. A. Horowitz, E. A. Blevins, K. A. Barney, M. A. Shaw, E. Harmel-Laws, F. D. Finkelman, M. J. Flick, M. D. Pinkerton, K. E. Talmage, K. W. Kombrinck, D. P. Witte and J. S. Palumbo (2010). "Colitisassociated cancer is dependent on the interplay between the hemostatic and inflammatory systems and supported by integrin alpha(M)beta(2) engagement of fibrinogen." Cancer Res 70(7): 2634-2643.

A link between colitis and colon cancer is well established, but the mechanisms regulating inflammation in this context are not fully defined. Given substantial evidence that hemostatic system components are powerful modulators of both inflammation and tumor progression, we used gene-targeted mice to directly test the hypothesis that the coagulation factor fibrinogen contributes to colitis-associated colon cancer in mice. This fundamental provisional matrix protein was found to be an important determinant of colon cancer. Fibrinogen deficiency resulted in a dramatic diminution in the number of colonic adenomas formed following azoxymethane/dextran sodium sulfate challenge. More detailed analyses in mice expressing a mutant form of fibrinogen that retains clotting function, but lacks the leukocyte integrin receptor alpha(M)beta(2) binding motif (Fibgamma(390-396A)), revealed that alpha(M)beta(2)-mediated engagement of fibrin(ogen) is mechanistically coupled to local inflammatory processes (e.g., interleukin-6 elaboration) and epithelial alterations that contribute to adenoma formation. Consistent with these findings, the majority of Fibgamma(390-396A) mice developed no discernable adenomas, whereas penetrance was 100% in controls. Furthermore, the adenomas harvested from Fibgamma(390-396A) mice were significantly smaller than those from control mice and less proliferative based on quantitative analyses of mitotic indices, suggesting an additional role for fibrin(ogen) in the growth of established adenomas. These studies show, for the first time, a unique link between fibrin(ogen) and the development of inflammation-driven malignancy. Given the importance of antecedent inflammation in the progression of numerous cancers, these studies suggest that therapies targeting fibrin(ogen)-alpha(M)beta(2) interactions may be useful in preventing and/or treating this important subset of malignancies.

L. M. Wagner, J. P. Perentesis, J. M. Reid, M. M. Ames, S. L. Safgren, M. D. Nelson, Jr., A. M. Ingle, S. M. Blaney and P. C. Adamson (2010). "Phase I trial of two schedules of vincristine, oral irinotecan, and temozolomide (VOIT) for children with relapsed or refractory solid tumors: a Children's Oncology Group phase I consortium study." Pediatr Blood Cancer 54(4): 538-545.

In preclinical models, temozolomide, and vincristine are additive or synergistic with irinotecan. We examined this three-drug combination in children with relapsed solid tumors. Patients received orally administered irinotecan together with temozolomide and vincristine on two different schedules, using cefixime to reduce irinotecan-associated diarrhea. Oral irinotecan was given daily on days 1-5 and 8-12 (Schedule A), or on days 1-5 (Schedule B). Temozolomide was given on days 1-5, with vincristine 1.5 mg/m(2) administered on days 1 and 8 (Schedule A)

or day 1 (Schedule B) in 21-day courses. The 5-day schedule of VOIT was well tolerated and provided SN-38 exposures similar to those achieved with intravenous IRN. Activity on this and prior studies suggests a potential role for VOIT in a spectrum of childhood solid tumors.

## **Division Collaboration**

Collaboration with Gastroenterology, Hepatology and Nutrition

**Collaborating Faculty: K. Steinbrecher** 

Colitis-associated cancer is dependent on the interplay between the hemostatic and inflammatory systems and supported by integrin alpha(M)beta(2) engagement of fibrinogen. Cancer Res. 70(7): 2634-2643. (J. Palumbo) Collaboration with Experimental Hematology and Cancer Biology

Collaborating Faculty: J. Mulloy; J. Cancelas; M.D. Filippi; F. Guo; Y. Zheng GTPases in hematopoiesis and hemopathies. Blood. Feb 4; 115 (5):936-47. (T. Kalfa) Collaboration with Experimental Hematology and Cancer Biology

Collaborating Faculty: Y. Zheng

Altered phosphorylation of cytoskeleton proteins in sickle red blood cells: the role of protein kinase C, Rac GTPases, and reactive oxygen species. Blood Cells Mol Dis. Jun 15;45(1):41-5. (C. Joiner, T. Kalfa) Collaboration with Experimental Hematology and Cancer Biology

Collaborating Faculty: Y. Zheng; D. Pan; H. Geiger; J. Cancelas Rac1 and Rac2 GTPases are necessary for early erythropoietic expansion in the bone marrow but not in the spleen. Haematologica. Jan;95(1):27-35. (T. Kalfa)

Collaboration with Experimental Hematology and Cancer Biology

Collaborating Faculty: P. Malik; D. Pan

Reprogramming erythroid cells for lysosomal enzyme production leads to visceral and CNS cross-correction in mice with Hurler syndrome. Proc Natl Acad Sci USA. 2009 106(47): 19958-19963. (T. Kalfa) Collaboration with Gastroenterology, Hepatology, and Nutrition

Collaborating Faculty: N. Yazigi

Clinical care of children with liver disease and hematologic disorders (T. Kalfa) Collaboration with Radiology

**Collaborating Faculty: R. Fleck** 

Evaluation of children with transfusional hemosiderosis (iron overload) by liver MRI (T. Kalfa) Collaboration with University of Cincinnati Department of Cancer and Cell Biology Proteomics Core

**Collaborating Faculty: K. Greis** 

Phosphoproteomic analysis of glioblastoma (B. DasGupta) Collaboration with University of Cincinnati Drug Discovery Center

**Collaborating Faculty: R. Papoian** 

Small molecule inhibition of AMP kinase (B. DasGupta)

Collaboration with Developmental Biology

**Collaborating Faculty: K. Campbell** 

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

**Collaboration with Pathology** 

**Collaborating Faculty: P. Tang** 

Metabolic profiling of AMPK-inhibited gliomas (B. DasGupta) Collaboration with Radiology; Ophthalmology

Collaborating Faculty: T. Abruzzo; J. Augsburger A pilot study of intra-ophthalmic artery topotecan infusion for patients with retinoblastoma for which ocular enucleation remains the only standard treatment option (J. Geller)

Collaboration with Neurology; Opthalmology; Radiology

Collaborating Faculty: D. Rose; C. West; J. Leach

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

**Collaborating Faculty: 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) Collaboration with Surgical Services; Gastroenterology, Hepatology, and Nutrition; Radiology; Pathology

Collaborating Faculty: J. Nathan; M. Alonso; F. Ryckman; G. Tiao; M. Leonis; J. Bucuvalas; K. Campbell; A. Towbin; K. Kukreja; K. Bove; A. Gupta

Chemotherapy and liver transplantation for unresectable hepatoblastoma: the CCHMC experience (J. Geller, L. Wagner) Collaboration with Human Genetics; Pathology; Surgical Services

Collaborating Faculty: 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) Collaboration with Pathology; Pediatric and Adolescent Gynecology

Collaborating Faculty: R. McMasters; L. Ayensu-Coker Management of ovarian sex-cord stromal tumors (J. Geller) Collaboration with Human Genetics Collaborating Faculty: N. Leslie Pediatric Hereditary Cancer Predisposition Clinic (J. Geller) Collaboration with Surgical Services; Gastroenterology, Hepatology, and Nutrition; Radiology; Pathology Collaborating Faculty: G. Tiao; J. Nathan; M. Leonis; A. Towbin; K. Kukreja; A. Gupta; K. Bove; J. Yin Liver Tumor Research Group (J. Geller, L. Wagner) Collaboration with Nephrology; University of Cincinnati Division of Hematology/Oncology Collaborating Faculty: J. Bissler; M. Czyzyk-Krzeska; O. Rixe; G. Thomas UC/CCHMC Renal Tumor Working Group (J. Geller) Collaboration with Biomedical Informatics Collaboration Faculty: J. Pestian

Developing a better understanding of a child's needs at end of life: an exploratory study using biologic markers and thought markers (F. Smith)

#### **Collaboration with Biomedical Informatics**

Collaborating Faculty: B. Aronow Modeling AML (F. Smith)

Collaboration with Radiology; Surgical Services; Pathology

Collaborating Faculty: M. Gelfand; T. Laor; F. Ryckman; K. Bove

A welcome surprise: nodular fasciitis presenting as soft tissue sarcoma. *J Ped Hematol Oncol* (in press). (L. Wagner) Collaboration with Surgical Services; Radiology; Pathology; Otolaryngology; University of Cincinnati Department of Radiation Oncology

Collaborating Faculty: R. Dasgupta; M. Gelfand; T. Laor; H. Yin; J. Breneman; R. Elluru Use of sentinel node biopsy for staging parameningeal rhabdomyosarcoma: a case study (B. Weiss, L. Wagner) Collaboration with Bone Marrow Transplantation and Immune Deficiency; Biostatistics and Epidemiology

Collaborating Faculty: S. Jodele; S. Davies; P. Mehta; J. Bleesing; A. Filipovich; M.-O. Kim; C. Liu Chemotherapy and autologous stem cell transplantation in comparison to conventional-dose chemotherapy in pediatric patients with relapsed or refractory Ewing's family tumors (L. Wagner, J. Perentesis) Collaboration with Surgical Services;

#### **Collaborating Faculty: R. Azizkhan**

COG, Surgery services for Oncology patients Collaboration with University of Cincinnati Department of Radiation Oncology

Collaborating Faculty: J. Breneman; R. Lavigne COG; Radiation Oncology clinical services for Hem/Onc patients Collaboration with Human Genetics:

#### **Collaborating Faculty: L. Bao; T. Smolarek**

COG; Genetic services for Hem/Onc patients Collaboration with Pathology

Collaborating Faculty: M. Collins

COG; Pathology services Collaboration with Behavioral Medicine and Clinical Psychology

Collaborating Faculty: D. Drotar; A. Pai

COG; Adherence research Collaboration with Radiology Collaborating Faculty: M. Gelfand

COG; Oncology nuclear medicine services Collaboration with Orthopaedic Surgery

#### **Collaborating Faculty: C. Mehlman**

COG; Brain tumor research and clinical services Collaboration with Experimental Hematology and Cancer Biology

#### Collaborating Faculty: J. Mulloy COG; Leukemia research

Collaboration with Endocrinology

Collaborating Faculty: S. Rose; M. Rutter COG; FA research, neuro-oncology research, endocrinology services as part of clinic Collaboration with University of Cincinnati Department of Cancer and Cell Biology

Collaborating Faculty: G. Thomas; R. Papoian COG; Drug development

#### **Collaboration with Surgical Services**

**Collaborating Faculty: G. Tiao** 

COG; Cancer surgery Collaboration with Clinical Pharmacology

Collaborating Faculty: A. Vinks

COG; Developmental therapeutics research; neurofibromatosis clinical research; new fellowship program in developmental therapeutics

**Collaboration with Anesthesia** 

Collaborating Faculty: N. Weidner COG; Palliative care and pain management Collaboration with Physical Medicine and Rehabilitation

**Collaborating Faculty: D. Pruit** 

Neuro-oncology clinic

Collaboration with Surgical Services; Orthopaedic Surgery; Radiology; Pathology

Collaborating Faculty: R. Dasgupta; J. Sorger; M. Gelfand; S. Sharp; T. Laor; G. Tiao; D. von Allmen; H. Yin Sentinel lymph node biopsy in pediatric oncology patients (L. Wagner, T. Cripe, R. Nagarajan) Collaboration with Pathology: Developmental Biology

Collaborating Faculty: L. Miles; M. Nakafuku

Telomerase: a therapeutic target in pediatric brain tumors (R. Drissi, M. Fouladi, T. Cripe) **Collaboration with Pathology** 

**Collaborating Faculty: L. Miles** 

A pilot study of bevacizumab-based therapy in patients with newly diagnosed high-grade gliomas and diffuse intrinsic pontine gliomas (R. Drissi, M. Fouladi)

Collaboration with Pathology

**Collaborating Faculty: L. Miles** 

Biological characteristics of pediatric high-grade gliomas (R. Drissi, M. Fouladi) Collaboration with Pathology

**Collaborating Faculty: L. Miles** 

Children's Oncology Group 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 gliomas (R. Drissi, M. Fouladi)

**Collaboration with Human Genetics** 

**Collaborating Faculty: K. Zhang** 

Genetic diagnostic services for hematology patients (C. Joiner) Collaboration with Experimental Hematology and Cancer Biology

#### **Collaborating Faculty: P. Malik**

Comprehensive Sickle Cell Center; Gene transfer into hematopoietic stem cells. (A. Perumbeti, C. Joiner)

Collaboration with University of Cincinnati Division of Hematology/Oncology

Collaborating Faculty: R. Franco; G. Atweh

Comprehensive Sickle Cell Center; Sickle cell pathophysiology, fetal hemoglobin induction (C. Joiner)

#### Collaboration with University of Cincinnati Division of Endocrinology

**Collaborating Faculty: R. Cohen** 

Comprehensive Sickle Cell Center; Red blood cell survival and hemoglobin glycosylation (C. Joiner) Collaboration with Experimental Hematology and Cancer Biology; Bone Marrow Transplantation and Immune Deficiency

#### Collaborating Faculty: P. Malik; S. Davies

Comprehensive Sickle Cell Center; Gene transfer therapy in sickle cell diseases (A. Perumbeti, K. Kalinyak, C. Joiner)

#### **Collaboration with Developmental Biology**

**Collaborating Faculty: J. Degen** 

Hemophilia and Thrombophilia Program; Role of coagulation programs in cancer metastasis (J. Palumbo)

#### **Collaboration with Experimental Hematology and Cancer Biology**

#### **Collaborating Faculty: J. Degen**

Hemophilia and Thrombophilia Program; Role of prothrombin in inflammation. *Blood.* 2009 ;113(3):696-704. (E. Mullins)

Collaboration with Clinical Pharmacology; Experimental Hematology and Cancer Biology Collaborating Faculty: A. Vinks; P. Malik

Comprehensive Sickle Cell Center; Zileuton therapy for sickle cell disease (K. Kalinyak, C. Joiner) Collaboration with Experimental Hematology and Cancer Biology; Pulmonary Medicine

Collaborating Faculty: P. Malik; W. Hardie; M. Ednick

Comprehensive Sickle Cell Center; Multidisciplinary clinic for sickle cell patients, inflammation in sickle cell disease (K. Kalinyak, C. Joiner)

Collaboration with Experimental Hematology and Cancer Biology; Cardiology; Pulmonary Medicine; Radiology

Collaborating Faculty: P. Malik; J. Towbin; W. Gottleibson; C. Kerschmar; R. Fleck

Comprehensive Sickle Cell Center; Cardiovascular complications of sickle cell disease (K. Kalinyak, C Joiner)

## Collaboration with Experimental Hematology and Cancer Biology

#### **Collaborating Faculty: Y. Zheng**

Comprehensive Sickle Cell Center; signaling pathways in red blood cells

Blood Cells Mol Dis. 2010 Jun 15;45(1):41-5 (T. Kalfa)

## **Collaboration with Anesthesia**

**Collaborating Faculty: D. Kurth** 

Hematology Program; Clinical evaluation of transcutaneous hemoglobin analysis. (K. Kalinyak, C. Joiner)

## Collaboration with Radiology

Collaborating Faculty: A. Towbin Hematology Program; Clinical evaluation of sickle cell patients

Am J Hematol. 2010 Mar;85(3):182-4. (K. Kalinyak, C. Joiner)

## **Collaboration with Sports Medicine**

Collaborating Faculty: J. Divine

Comprehensive Sickle Cell Center; Evaluation and counseling of athletes for sickle cell trait (C. Joiner) Collaboration with University of Cincinnati Division of General Internal Medicine

**Collaborating Faculty: T. Diers** 

Comprehensive Sickle Cell Center; Transition of sickle cell patients to adult care (K. Kalinyak, C. Joiner) Collaboration with Pathology; Surgical Services; Radiology

Collaborating Faculty: M. Gelfand; S. Sharp; A. Towbin; H. Yin; T. Maugins

Neuroblastoma Program clinical services and clinical research

Langerhans cell histiocytosis in a patient with stage 4 neuroblastoma receiving oral fenretinide. *Pediatr Blood Cancer* 53(6): 1111-1113. (R. Nagarajan, B. Weiss)

Collaboration with Human Genetics; Radiology; Clinical Pharmacology; Neurology

Collaborating Faculty: E. Schorry; M. Gelfand; S. Sharp; A. Towbin; A. Vinks; M. Sutton

Neurofibromatosis Program clinical services and clinical research; National clinical trial of mTOR inhibition to treat NF1-related plexiform neurofibromas (B. Weiss)

#### Collaboration with Thoracic and Fetal Surgery; Biomedical Informatics

Collaborating Faculty: T. Crombleholme: B. Aronow

Development of a midkine-regulated oncolytic Herpes virus

Molecular engineering and validation of an oncolvtic herpes simplex virus type 1 transcriptionally targeted to midkinepositive tumors. J Gene Med 12(7): 613-623. (T. Cripe)

#### Collaboration with Experimental Hematology and Cancer Biology; Pathology

Collaborating Faculty: N. Ratner; J. Cancelas; M. Collins EYA4 in MPNST

Inhibition of eyes absent homolog 4 expression induces malignant peripheral nerve sheath tumor necrosis. Oncogene 29(3): 368-379. (T. Cripe)

Collaboration with Immunobiology

**Collaborating Faculty: D. Hildeman** Regulatory T cells in oncolytic HSV virotherapy (T. Cripe) **Collaboration with Allergy and Immunology** 

**Collaborating Faculty: M. Rothenberg** 

Coordinate interaction between IL-13 and epithelial differentiation cluster genes in eosinophilic esophagitis. J Immunol 184: 4033-4041. (S. Wells)

Collaboration with Developmental Biology; Gastroenterology, Hepatology, and Nutrition

Collaborating Faculty: J. Wells: N. Shrover

Directed differentiation of human pluripotent stem cells into intestinal tissue in culture. Nature. In review. (S. Wells) Collaboration with Pathology; University of Cincinnati Department of Cancer and Cell Biology

Collaborating Faculty: K. Wikenheiser-Brokamp; S. Waltz

The human DEK oncogene stimulates invasion and cancer stem cell potential in breast cancer by modifying beta catenin signaling. Cancer Research. Submitted. (S. Wells)

The CHEK2\*1100delC Mutation Increases Susceptibility to Ron-Induced Mammary Tumorigenesis in Mice. Cancer Letters. In Press. (S. Wells)

Collaboration with Experimental Hematology and Cancer Biology; Nephrology and Hypertension; University of Cincinnati Department of Molecular Genetics; Shriner's Hospital

Collaborating Faculty: P. Andreassen: P. Stambrook: J. Bissler: G. Babcock

The human DEK oncogene regulates the DNA damage sensor kinases ATM and DNA-PK. Oncogene. Submitted. (S. Wells, R. Drissi)

Collaboration with Biomedical Informatics; Developmental Biology; Asthma Research; Adolescent Medicine Collaborating Faculty: B. Aronow; R. Hedge; M. Butsch Kovacic; J. Kahn

Insights from the transcriptional profiling of human papillomavirus infection and associated carcinogenesis. *Research Signposts.* In: Yoshida K (ed). Molecular Biology of DNA Tumor Virus Gene Products: 169-196 (S. Wells) **Collaboration with University of Pittsburgh** 

Collaborating Faculty: S. Duensing; A. Duensing; S. Khan

HPV-16 E7 attenuates DNA damage checkpoint control by increasing the proteolytic turnover of claspin. Cancer Research, 69: 7022-7029. (S. Wells)

Collaboration with Bone Marrow Transplantation and Immune Deficiency

Collaborating Faculty: S. Davies; P. Mehta

HPV infection and associated malignancies in Fanconi Anemia patients. IRB protocol ID2008-1331 (S. Wells) Collaboration with University of Cincinnati Department of Otolaryngology– Head and Neck Surgery

Collaborating Faculty: K. Wilson; Y. Patil; K. Casper An investigation of molecular markers associated with clinical outcomes in head and neck cancers: collection and chart review protocol. IRB protocol ID2009-270 (S. Wells)

Collaboration with Surgery; Otolaryngology; Dermatology; Radiology; Pathology; Cardiology; Gastroenterology, Hepatology and Nutrition: Urology; Endocrinology; Orthopedics; Neurology; Pulmonary Medicine: Opthalmology: Pain Management: Human Genetics

Collaborating Faculty: R. Azizkhan; A. Dasgupta; R. Elluru; A. Lucky; M. Patel; T. Abruzzo; W. Ball; A.

Zbojniewicz; K. Crone; A. Gupta; P. Eghtešady; K. Goldschneider; Ř. Hirsch; Ř. 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)

Collaboration with Gastroenterology, Hepatology and Nutrition; Radiology; Nephrology; Cardiology; Pathology

Collaborating Faculty: N. Yazigi; A. Brody; J. Goebel; R. Spicer; K. Uzark; D. Witte Post-Transplant Lymphoproliferative Disease Working Group (M. Absalon)

### **Faculty Members**

**Franklin O. Smith, MD,** Professor ; Marjory J. Johnson Endowed Chair; Director, Hematology/Oncology; Director, Hematology/Oncology Fellowship Program

Research Interests: Acute myeloid leukemia

Michael Absalon, MD, PhD, Assistant Professor Clinical Research Interests: New therapeutics; ataxia telangiectasia; DNA damage response mechanisms

**Denise M. Adams, MD,** Associate Professor Clinical ; Inpatient Clinical Director; Medical Director of Comprehensive Hemangiomas and Vascular Malformation Clinic;

Research Interests: Research in angiogenesis, endothelial cell proliferation, vascular anomalies.

Jacob Bleesing, MD, PhD, Associate Professor Clinical

**Research Interests:** Clinical Investigation of Primary Immunodeficiency Disorders, with emphasis on disorders of immunodysregulation and B-cell disorders

Karen Burns, MD, Assistant Professor Clinical Research Interests: Outcomes following cancer therapy and outcomes following bone sarcomas

**Timothy Cripe, MD, PhD,** Professor ; *Director, Musculoskeletal Tumor Comprehensive Clinic; Director, Translational Research Trials Office* 

**Research Interests:** Transcriptional regulation; genetic perturbations in cancer; gene therapy of cancer; gene transfer; transcriptional targeting; antiangiogenesis; viral oncolysis; viral oncogenesis

**Stella M. Davies, MBBS, PhD, MRCP,** Professor ; *Jacob G. Schmidlapp Endowed Chair; Director, Blood and Marrow Transplant Program* 

#### Rachid Drissi, PhD, Assistant Professor

Research Interests: Examine telomere disruption signaling to DNA damage pathway

# **Alexandra Filipovich, MD,** Professor ; Ralph J. Stolle Chair in Clinical Immunology; Director, Immunodeficiency and Histiocytosis Program; Medical Director, Diagnostic Laboratory

Research Interests: Immunoreconstitution Following Pediatric Stem Cell Transplantation

- Maryam Fouladi, MD, FRCP, Associate Professor Clinical; *Director, Neuro-Oncology Program* Research Interests: Developing novel drugs for the treatment of children with recurrent or poor prognosis brain tumors
- James I. Geller, MD, Assistant Professor Clinical

**Research Interests:** Solid and brain tumors, with a specific interest in new drug development. Leads renal, liver and retinoblastoma initiative

Ralph A Gruppo, MD, Professor Clinical ; *Director, Hemophilia Thrombosis Center* Research Interests: Coagulation; hemophilia; thrombosis

#### Richard E. Harris, MD, Professor Clinical Research Interests: Transplantation for children with bone marrow failure syndromes and aplastic anemia

#### Trent Hummel, MD, Instructor Clinical

#### Sonata Jodele, MD, Assistant Professor Clinical

**Research Interests:** Phase I clinical trials; new anticancer drug development; stem cell transplantation; high risk pediatric malignancies; childhood neuroblastoma

Clinton H. Joiner, MD, PhD, Professor ; Interim Director, Hematology Program Research Interests: Sickle cell disease and other hemoglobinopathies

#### Theodosia Kalfa, MD, PhD, Assistant Professor

Research Interests: study of erythropoiesis and red blood cell structural membrane biology

Karen Ann Kalinyak, MD, Professor Clinical ; Hematology Clinical Director

Research Interests: Hematology; bone marrow failure; sickle cell anemia; hemoglobinopathy

Beatrice Lampkin, MD, Professor Emerita ; Jacob G. Schmidlapp Endowed Chair

Thomas Leemhuis, PhD, Associate Professor

Rebecca Marsh, MD, Instructor Clinical

Parinda Mehta, MD, Assistant Professor Research Interests: Blood and Marrow Transplant, Fanconi anemia, Pharmacogenetics and Pharmacokinetics

Eric Mullins, MD, Instructor Clinical

Rajaram Nagarajan, MD, Assistant Professor Clinical Research Interests: Outcomes following cancer therapy and outcomes following bone sarcomas

- Joseph S. Palumbo, MD, Research Assistant Professor Research Interests: Interactions between the hemostatic system and innate immunity effecting tumor progression
- John Perentesis, MD, Professor ; Deb Kleisinger Endowed Chair and Professor of Pediatrics; Director, Oncology Program Research Interests: Recombinant cancer therapeutics and molecular mechanisms for drug action
- Janos Sumegi, MD, PhD, Professor Research Interests: Lymphoproliferative disease, Hemphagocytic Lymphohisstiocytosis, Usher syndrom

Lars Wagner, MD, Associate Professor Clinical Research Interests: Treatment of neuroblastoma, sarcomas, and brain tumors

#### Brian D. Weiss, MD, Assistant Professor Clinical

**Research Interests:** Targeted Agents for Neurofibromatosis Type 1-Related Malignancies (including plexiform neurofibromas, optic pathway gliomas, and Juvenile Myelomonocytic Leukemia)

#### Susanne Wells, PhD, Associate Professor

Research Interests: Papillomavirus biology, molecular mechanisms of cellular growth and senescence

## **Joint Appointment Faculty Members**

- Michael Jordan, MD, Assistant Professor Immunobiology Regulation of the immune response; immunotherapy of cancer
- Mi-Ok Kim, PhD, Assistant Professor Center for Epidemiology and Biostatistics
- Punam Malik, MD, Associate Professor Experimental Hematology and Cancer Biology
- Ahna Pai, PhD, Assistant Professor Adherence Psychology
- Sualius Sumanas, PhD, Assistant Professor Developmental Biology
- Mary Sutton, MD, Assistant Professor Neurology

## **Clinical Staff Members**

- Sarita Joshi, MBBS, MD
- Ernest Lawhorn, MD
- Anna Pesok, MD
- Philip Roehrs, MD
- Gregory Wallace, DO

## Trainees

- Kathleen Dorris, MD, PL-IV, Children's Memorial Hospital, Northwestern University
- Teresa Finke, MD, PL-IV, IU School of Medicine Combined Medicine & Pediatrics

- Sarah Fitzgerald, MD, PL-IV, Rainbow Babies & Children's Hospital/University of Cleveland
- Alex George, MD, PhD, PL-IV, Cincinnati Childrens Hospital Medical Center
- Adrienne Hammill, MD, PhD, PL-V, Cincinnati Children's Hospital Medical Center
- Theodore Johnson, MD, PhD, PL-V, Medical College of Georgia
- Sabine Mellor-Heineke, MD, PL-VI, Staedtisches Klinikum Braunschweig
- Benjamin Mizukawa, MD, PL-V, Cincinnati Children's Hospital Medical Center
- Kasiani Myers, MD, PL-V, Cincinnati Children's Hospital Medical Center
- · Ajay Perumbeti, MD, PL-VII, Upstate Medical University
- Christine Phillips, MD, PL-VI, Children's Memorial Hospital Chicago
- Jennifer Pope, MD, PL-IV, Medical College of Wisconsin
- Melissa Rayburg, MD, PL-VI, University of Texas Health Science Center

## **Significant Accomplishments**

#### Zeroing in on mTOR

Our Oncology program continues its expansion as one of the nation's leading centers for new drug and advanced therapy development for children and young adults with cancer.

Basic research from the laboratories of Nancy Ratner, PhD, and George Thomas, PhD, has demonstrated a key role for altered signaling in mTOR and growth factor pathways in pediatric cancers and neurofibromatosis-driven tumors. In an integrated translational clinical research initiative, Maryam Fouladi, MD, MSc, is leading the first pediatric study combining the mTOR-targeting drug temsirolimus with the insulin-like growth factor-targeting antibody IMC-A12 for children with relapsed cancers.

In addition, Brian Weiss, MD, is leading a national clinical trial of the mTOR inhibitor sirolimus for the treatment of tumors associated with neurofibromatosis type 1 (NF1). Occurring once in every 3,500 births, NF1 is a common, progressive inherited disorder characterized by diverse cutaneous, neurological, skeletal, and potentially life-threatening neoplastic manifestations with no standard drug therapy available. The trial employs novel individually-guided dosing using real-time drug concentration measurements in combination with a Bayesian population model-based target optimization approach developed by Sander Vinks, PharmD, PhD, FCP, of the Division of Clinical Pharmacology. Vinks is a leading authority on the pharmacokinetics of sirolimus in children. The trial also includes pharmacogenetic analyses from the laboratory of John Perentesis, MD, FAAP.

#### Killing cancer cells with viruses

Major progress also has been achieved this year in testing the use of genetically engineered viruses to infect and kill cancer cells as a new type of cancer therapy. Preclinical studies led by Timothy Cripe, MD, PhD, showed that a mutated form of herpes simplex virus infects and kills many types of childhood cancer cells and causes tumor shrinkage in human xenograft cancers grown in mice without causing a herpes infection.

We have begun enrolling patients with solid tumors into a Phase I clinical trial of this potential therapy. We also have received approval to open a second virus trial using a vaccinia-based vector, and have a third trial open through the Children's Oncology Group Phase I Consortium that uses a Seneca Valley virus. We are the only pediatric hospital with all three of these studies open to patients.

#### Research progress in colon cancer, sickle cell disease

In April 2010, a research team led by Joseph Palumbo, MD, published an important paper in *Cancer Research* demonstrating the role of fibrinogen interaction with a specific leukocyte receptor in the development of colitis-associated colon cancer.

In August 2009, Clinton Joiner, MD, PhD, collaborated with researchers at Yale University to identify the phosphorylation sites that regulate a membrane cation transporter important in the pathology of sickle cell disease and other disorders. This finding, published in the journal *Cell*, is a first step in developing therapies that can mitigate the abnormal transporter regulation characteristic of sickle red blood cells.

#### **New Faculty**

Two new faculty members also were recruited to the Hematology program in 2010. Charles Quinn, MD, formerly of Texas Children's Hospital, will lead clinical research efforts for our Hematology program. And Cristina Tarango, MD, will

be involved in clinical care for hematology patients. Tarango also comes from Texas Children's, where she completed her fellowship in Hematology/Oncology.

## **Division Publications**

1. :

# Grants, Contracts, and Industry Agreements

rant and Contract Awards	Д	Annual Direct / Project Period Direct
Adams, D		
Phase II Study of Rapamycin for C Food and Drug Administration	omplicated Vascular Anomalie	s IND Exempt
R01 FD 003712	09/25/09 - 07/31/13	\$255,080 / \$1,016,782
Severity Scale and Quality of Life I The Trustees of Indiana University (N		giomas
RC1 AR 058767	09/29/09 - 08/31/10	\$667 / \$667
Cripe, T		
Oncolytic HSV Therapy in Immuno National Institutes of Health	competent Sarcoma Models	
R01 CA 114004	07/06/06 - 05/31/11	\$172,353 / \$866,912
Virotherapy for Neuroblastoma Ste National Institutes of Health	m Cells	
R21 CA 133663	08/01/08 - 07/31/10	\$135,000 / \$247,500
Cincinnati NF1 Preclinical Testing The Children's Tumor Foundation	Center	
	12/01/07 - 06/30/11	\$216,365 / \$664,730
A Phase I Dose Escalation Study C Non-Central Nervous System Solid Solving Kid's Cancer	Of Intratumoral Herpes Simplex	Virus-1 Mutant HSV 1716 in Patients with
-	12/31/09 - 12/30/10	\$39,051 / \$39,051
Finding The Best Herpes Virus To Children's Cancer Research Coalition		oma
	04/01/10 - 03/31/11	\$15,000 / \$15,000
Cincinnati Center for Clinical and T University of Cincinnati (National Insti		ing - Pilot funding
UL1 RR 026314	04/03/09 - 03/31/14	\$25,502 / \$126,246
Cincinnati Center for Neurofibroma National Institutes of Health	tosis Research - Core B	
P50 NS 057531	09/15/08 - 06/30/13	\$105,284 / \$502,625
DasGupta, B		
Inhibition of Pediatric Brainstem G Cancer Free Kids	lioma by Genetic Inhibition of A	AMP Kinase
	06/01/10 - 05/31/11	\$20,000 / \$20,000
Drissi, R		
Decreasing Side Effects of Radiation Cancer Free Kids	on Therapy for Cancer	
	06/01/09 - 05/31/11	\$36,000 / \$36,000
Telomerase: A Therapeutic Target Matthew Larson Pediatric Brain Tumo		
	04/01/10 - 03/31/11	\$75,000 / \$75,000

	on 09/01/09 - 08/31/10	\$50,000 / \$50,000
Childrenia Oncology Crown D		\$50,0007 \$50,000
Children's Oncology Group P Children's Oncology Group (Na		
U01 CA 097452	06/01/09 - 05/31/11	\$93,498 / \$93,498
Pediatric Brain Tumor Conso St. Jude Research Hospital (Na		
U01 CA 081457	04/01/08 - 03/31/11	\$4,000 / \$44,967
Pediatric Brain Tumor Conso St. Jude Research Hospital (Na	tional Institutes of Health)	
U01 CA 081457	04/01/08 - 03/31/11	\$1,386 / \$2,772
eller, J A Pilot Trial of Catheter Assis Cancer Free Kids	sted Delivery of Intra-Ophthalmic Artery Chemoth 05/01/10 - 04/30/11	nerapy in Retinoblastoma \$40,000 / \$40,000
Childron's Openlagy Group (		\$40,0007 \$40,000
Children's Oncology Group C Children's Oncology Group (Na		
U10 CA 098543	09/01/09 - 08/31/11	\$13,911 / \$13,911
Hemophilia And Thrombosis Hemophilia Foundation of Mich Hemophilia Prevention Netwo	igan (Cascade Hemophilia Consortium) 06/01/03 - 05/31/11	\$77,835 / \$317,293
	igan (Centers for Disease Control and Prevention)	
U01 DD 000203	10/01/97 - 09/30/10	\$21,000 / \$76,77
U01 DD 000203 Hemophilia Comprehensive C	- · · ,	ders
U01 DD 000203 Hemophilia Comprehensive C Hemophilia Foundation of Mich 5H30MC0015 ummel, T COG Phase I Agreement #199	10/01/97 - 09/30/10 Care & Prevention Core Center for Bleeding Disor igan (Maternal and Child Heath Bureau) 10/01/97 - 05/31/11	ders \$14,500 / \$153,190
U01 DD 000203 <b>Hemophilia Comprehensive C</b> Hemophilia Foundation of Mich 5H30MC0015 <b>ummel, T</b> <b>COG Phase I Agreement #199</b> National Childhood Cancer Fou U01 CA 097452	10/01/97 - 09/30/10 Care & Prevention Core Center for Bleeding Disor igan (Maternal and Child Heath Bureau) 10/01/97 - 05/31/11 286 ndation (National Institutes of Health)	
U01 DD 000203 Hemophilia Comprehensive C Hemophilia Foundation of Mich 5H30MC0015 ummel, T COG Phase I Agreement #199 National Childhood Cancer Fou U01 CA 097452 Diner, C Cincinnati Sickle Cell Project	10/01/97 - 09/30/10 Care & Prevention Core Center for Bleeding Disor igan (Maternal and Child Heath Bureau) 10/01/97 - 05/31/11 286 ndation (National Institutes of Health) 02/01/10 - 07/31/11	ders \$14,500 / \$153,190
U01 DD 000203 Hemophilia Comprehensive C Hemophilia Foundation of Mich 5H30MC0015 ummel, T COG Phase I Agreement #199 National Childhood Cancer Fou U01 CA 097452 Diner, C Cincinnati Sickle Cell Project Ohio Department of Health (He 03130011SK0411 Comprehensive Sickle Cell Co National Institutes of Health	10/01/97 - 09/30/10 Care & Prevention Core Center for Bleeding Disor igan (Maternal and Child Heath Bureau) 10/01/97 - 05/31/11 286 ndation (National Institutes of Health) 02/01/10 - 07/31/11 alth Resources & Services Administration) 07/01/09 - 06/30/10 enter	ders \$14,500 / \$153,190 \$11,417 / \$11,41 \$117,363 / \$117,363
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U01 DD 000203 Hemophilia Comprehensive C Hemophilia Foundation of Mich 5H30MC0015 ummel, T COG Phase I Agreement #199 National Childhood Cancer Fou U01 CA 097452 Diner, C Cincinnati Sickle Cell Project Ohio Department of Health (He 03130011SK0411 Comprehensive Sickle Cell Co National Institutes of Health	10/01/97 - 09/30/10 Care & Prevention Core Center for Bleeding Disor igan (Maternal and Child Heath Bureau) 10/01/97 - 05/31/11 286 ndation (National Institutes of Health) 02/01/10 - 07/31/11 alth Resources & Services Administration) 07/01/09 - 06/30/10 enter	ders \$14,500 / \$153,190 \$11,417 / \$11,41 \$117,363 / \$117,363
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U01 DD 000203 Hemophilia Comprehensive C Hemophilia Foundation of Mich 5H30MC0015 ummel, T COG Phase I Agreement #199 National Childhood Cancer Fou U01 CA 097452 oiner, C Cincinnati Sickle Cell Project Ohio Department of Health (He 03130011SK0411 Comprehensive Sickle Cell CA National Institutes of Health U54 HL 070871 Mitchell, M Joiner, C	10/01/97 - 09/30/10 Care & Prevention Core Center for Bleeding Disor igan (Maternal and Child Heath Bureau) 10/01/97 - 05/31/11 286 ndation (National Institutes of Health) 02/01/10 - 07/31/11 alth Resources & Services Administration) 07/01/09 - 06/30/10 enter 04/01/08 - 03/31/12 Project 3 Project 4	ders \$14,500 / \$153,19 \$11,417 / \$11,41 \$117,363 / \$117,36 \$1,003,125 / \$3,096,54 108,644 314,760
U01 DD 000203 Hemophilia Comprehensive C Hemophilia Foundation of Mich 5H30MC0015 ummel, T COG Phase I Agreement #199 National Childhood Cancer Fou U01 CA 097452 oiner, C Cincinnati Sickle Cell Project Ohio Department of Health (He 03130011SK0411 Comprehensive Sickle Cell Co National Institutes of Health U54 HL 070871 Mitchell, M Joiner, C Malik, P	10/01/97 - 09/30/10 Care & Prevention Core Center for Bleeding Disor igan (Maternal and Child Heath Bureau) 10/01/97 - 05/31/11 286 ndation (National Institutes of Health) 02/01/10 - 07/31/11 alth Resources & Services Administration) 07/01/09 - 06/30/10 enter 04/01/08 - 03/31/12 Project 3 Project 4 Project 5	ders \$14,500 / \$153,19 \$11,417 / \$11,41 \$117,363 / \$117,363 \$1,003,125 / \$3,096,54 108,644 314,760 371,040

New England Research Institutes (Nationa	al Institutes of Health)	
U10HL083721	03/01/09 - 02/28/11	\$3,465 / \$3,465
Sickle Cell Disease CTN- IMPROVE		
New England Research Institutes (Nationa		
U10HL083721	03/01/09 - 02/28/11	\$1,925 / \$1,925
Calfa, T		
Rac1 and Rac2 Guanosine Triphosphat	tases in Erythroid Function and Diffe	erentiation
National Institutes of Health	-	
K08 HL 088126	02/11/08 - 11/30/12	\$119,125 / \$595,625
TCD with Transfusions Changing to Hy		
St Jude's Children's Hospital (National Ins		
R01 HL 095647	08/21/09 - 07/31/11	\$27,730 / \$27,730
Kalinyak, K		
Stroke With Transfusions Changing To	Hydroxyurea	
St Jude's Children's Hospital (National Ins		
U01 HL 078787	04/01/06 - 07/31/10	\$24,245 / \$128,116
/izukawa, B		
Characterization of Rac Proteins in Mye	eloid Leukemogenes	
Yale University School of Medicine (Nation		
K12 HD 000850	07/01/08 - 06/30/11	\$100,500 / \$301,500
Chemosensitization of the Leukemic St Cancer Free Kids	em Cell Through Targeting its Interac	ction with the Marrow Niche
	07/01/09 - 06/30/11	\$36,000 / \$36,000
lorreale, R		+,
The Dele of DEK in the Differentiation	Demendent UDV Life Cycle	
The Role of DEK in the Differentiation- National Cancer Institute		\$50.054 / \$50.054
	Dependent HPV Life Cycle 05/01/10 - 04/30/11	\$50,054 / \$50,054
National Cancer Institute F32 CA 138115		\$50,054 / \$50,054
National Cancer Institute F32 CA 138115 //ullins, E Thrombin and Thrombin Targets in Alle	05/01/10 - 04/30/11	\$50,054 / \$50,054
National Cancer Institute F32 CA 138115 Iullins, E	05/01/10 - 04/30/11 ergic Airway Inflammation	
National Cancer Institute F32 CA 138115 Jullins, E Thrombin and Thrombin Targets in Alle	05/01/10 - 04/30/11	
National Cancer Institute F32 CA 138115 //ullins, E Thrombin and Thrombin Targets in Alle	05/01/10 - 04/30/11 ergic Airway Inflammation	
National Cancer Institute F32 CA 138115 <i>Iullins, E</i> Thrombin and Thrombin Targets in Alle American Society of Hematology <i>Iagarajan, R</i> Genetic Epidemiology of Osteosarcoma	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10	
National Cancer Institute F32 CA 138115 <b>Jullins, E</b> Thrombin and Thrombin Targets in Alle American Society of Hematology <b>Jagarajan, R</b> Genetic Epidemiology of Osteosarcoma University of Minnesota (National Cancer	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10	\$50,000 / \$100,000
National Cancer Institute F32 CA 138115 Iullins, E Thrombin and Thrombin Targets in Alle American Society of Hematology Iagarajan, R Genetic Epidemiology of Osteosarcoma	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10	\$50,000 / \$100,000
National Cancer Institute F32 CA 138115 <b>/ullins, E</b> Thrombin and Thrombin Targets in Alle American Society of Hematology <b>lagarajan, R</b> Genetic Epidemiology of Osteosarcoma University of Minnesota (National Cancer U01 CA 122371	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10	\$50,000 / \$100,000
National Cancer Institute F32 CA 138115 <b>Jullins, E</b> <b>Thrombin and Thrombin Targets in Alle</b> American Society of Hematology <b>Jagarajan, R</b> <b>Genetic Epidemiology of Osteosarcoma</b> University of Minnesota (National Cancer U01 CA 122371 <b>Palumbo, J</b>	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11	\$50,000 / \$100,000 \$9,561 / \$36,607
National Cancer Institute F32 CA 138115 <b>/ullins, E</b> Thrombin and Thrombin Targets in Alle American Society of Hematology <b>lagarajan, R</b> Genetic Epidemiology of Osteosarcoma University of Minnesota (National Cancer U01 CA 122371	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11	\$50,000 / \$100,000 \$9,561 / \$36,607
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National Cancer Institute F32 CA 138115 <b>Jullins, E</b> <b>Thrombin and Thrombin Targets in Alle</b> American Society of Hematology <b>Jagarajan, R</b> <b>Genetic Epidemiology of Osteosarcoma</b> University of Minnesota (National Cancer U01 CA 122371 <b>Palumbo, J</b> <b>Mechanisms Linking Metastasis to Tur</b> National Institutes of Health	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11 nor Procoagulant and Innate Immunit 07/20/06 - 06/30/11	\$50,000 / \$100,000 \$9,561 / \$36,607 <b>ty</b> \$242,750 / \$1,221,000
National Cancer Institute F32 CA 138115 <b>Nullins, E</b> <b>Thrombin and Thrombin Targets in Alle</b> American Society of Hematology <b>Iagarajan, R</b> <b>Genetic Epidemiology of Osteosarcoma</b> University of Minnesota (National Cancer U01 CA 122371 <b>Palumbo, J</b> <b>Mechanisms Linking Metastasis to Tun</b> National Institutes of Health R01 HL 085545 <b>Mechanisms Linking Metastasis to Tun</b> National Institutes of Health	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11 nor Procoagulant and Innate Immunit 07/20/06 - 06/30/11	\$50,000 / \$100,000 \$9,561 / \$36,607 <b>ty</b> \$242,750 / \$1,221,000
National Cancer Institute F32 CA 138115 Iullins, E Thrombin and Thrombin Targets in Alle American Society of Hematology Iagarajan, R Genetic Epidemiology of Osteosarcoma University of Minnesota (National Cancer U01 CA 122371 Valumbo, J Mechanisms Linking Metastasis to Tun National Institutes of Health R01 HL 085545 Mechanisms Linking Metastasis to Tun	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11 nor Procoagulant and Innate Immunit 07/20/06 - 06/30/11	\$50,000 / \$100,000 \$9,561 / \$36,607 <b>ty</b> \$242,750 / \$1,221,000 <b>ty</b>
National Cancer Institute F32 CA 138115 <b>Nullins, E</b> <b>Thrombin and Thrombin Targets in Alle</b> American Society of Hematology <b>Iagarajan, R</b> <b>Genetic Epidemiology of Osteosarcoma</b> University of Minnesota (National Cancer U01 CA 122371 <b>Palumbo, J</b> <b>Mechanisms Linking Metastasis to Tun</b> National Institutes of Health R01 HL 085545 <b>Mechanisms Linking Metastasis to Tun</b> National Institutes of Health R01 HL 085545	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11 hor Procoagulant and Innate Immunit 07/20/06 - 06/30/11 hor Procoagulant and Innate Immunit	\$50,000 / \$100,000 \$9,561 / \$36,607 ty \$242,750 / \$1,221,000 ty
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National Cancer Institute F32 CA 138115 Nullins, E Thrombin and Thrombin Targets in Alle American Society of Hematology lagarajan, R Genetic Epidemiology of Osteosarcoma University of Minnesota (National Cancer U01 CA 122371 Valumbo, J Mechanisms Linking Metastasis to Tum National Institutes of Health R01 HL 085545 Mechanisms Linking Metastasis to Tum National Institutes of Health R01 HL 085545 Verentesis, J Children's Oncology Group Phase I Children's Oncology Group (National Instituted U01 CA 097452	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11 nor Procoagulant and Innate Immunit 07/20/06 - 06/30/11 nor Procoagulant and Innate Immunit 07/01/09 - 06/30/11 tutes of Health) 08/01/07 - 07/31/11	\$50,000 / \$100,000 \$9,561 / \$36,607 <b>ty</b> \$242,750 / \$1,221,000 <b>ty</b> \$150,234 / \$150,234
National Cancer Institute F32 CA 138115 Nullins, E Thrombin and Thrombin Targets in Alle American Society of Hematology lagarajan, R Genetic Epidemiology of Osteosarcoma University of Minnesota (National Cancer U01 CA 122371 Palumbo, J Mechanisms Linking Metastasis to Tun National Institutes of Health R01 HL 085545 Mechanisms Linking Metastasis to Tun National Institutes of Health R01 HL 085545 Perentesis, J Children's Oncology Group Phase I Children's Oncology Group (National Institutes)	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11 nor Procoagulant and Innate Immunit 07/20/06 - 06/30/11 nor Procoagulant and Innate Immunit 07/01/09 - 06/30/11 tutes of Health) 08/01/07 - 07/31/11 a Grant	\$50,000 / \$100,000 \$9,561 / \$36,607 <b>ty</b> \$242,750 / \$1,221,000 <b>ty</b> \$150,234 / \$150,234
National Cancer Institute F32 CA 138115 <b>Mullins, E</b> Thrombin and Thrombin Targets in Alle American Society of Hematology <b>Jagarajan, R</b> Genetic Epidemiology of Osteosarcoma University of Minnesota (National Cancer U01 CA 122371 <b>Palumbo, J</b> Mechanisms Linking Metastasis to Tun National Institutes of Health R01 HL 085545 Mechanisms Linking Metastasis to Tun National Institutes of Health R01 HL 085545 <b>Perentesis, J</b> Children's Oncology Group Phase I Children's Oncology Group (National Instituted U01 CA 097452 The Children's Oncology Group Chair's	05/01/10 - 04/30/11 ergic Airway Inflammation 07/01/08 - 06/30/10 a Institute) 05/01/07 - 04/30/11 nor Procoagulant and Innate Immunit 07/20/06 - 06/30/11 nor Procoagulant and Innate Immunit 07/01/09 - 06/30/11 tutes of Health) 08/01/07 - 07/31/11 a Grant	\$242,750 / \$1,221,000

		03/01/09 - 02/28/11	\$100,000 / \$200,000
HPV Replication Fanconi Anemia		on in FA Squamous Cell	
National Institute R01 CA 116316		08/01/09 - 07/31/11	\$146,211 / \$146,211
Role and Regu	ation of the Human	DEK Proto-Oncogene	. , ,,-
Role and Regu National Institute R01 CA 116316	es of Health	DEK Proto-Oncogene 04/01/06 - 02/28/11	\$172,353 / \$891,579
Wells, S			
-	bama-Birmingham (1	he Children's Tumor Foundation) 04/15/09 - 04/14/11	\$30,700 / \$30,700
Phase 1 Trial o	f Sorafenib in Child		
Weiss, B			
Cancer Free Kid	S	05/01/10 - 04/30/11	\$45,000 / \$45,000
	Neuroblastoma Ste	m Cells	
			φ, τ, φ, φ,
	Oncology Group Ch od Cancer Foundatic	a <b>irs Grant</b> n (National Institutes of Health) 03/01/03 - 02/28/11	\$114,444 / \$427,840
H46 MC 09233		06/01/08 - 05/31/11	\$185,000 / \$555,000
	le Cell Newborn Scr es & Services Admini-		
F32 CA 139931		09/15/09 - 09/14/11	\$47,210 / \$97,264
The Role of DE National Institute	K in Breast Cancer	Development and Therapy	
P50 NS 057531 Privette Vinnedge	1	09/15/08 - 06/30/13	\$296,437 / \$1,521,540
National Institute		tosis Research - Project 1	
National Childho U01 CA 097452	od Cancer Foundatio	<b>ublication Committee</b> n (National Institutes of Health) 09/1/06 - 07/31/11	\$12,490 / \$35,308
Children's Oncol U10CA098543	ogy Group (National	03/01/08 - 02/28/13	\$169,945 / \$223,04
	ology Group Phase ogy Group (National		\$26,311 / \$181,600
		# <b>19383</b> n (National Cancer Institute) 06/01/09 - 05/31/11	\$38,333 / \$38,33
		I n (National Institutes of Health) 06/01/09 - 05/31/11	\$18,721 / \$18,72
U01 CA 097452		n (National Institutes of Health) 06/01/09 - 05/31/11	\$21,143 / \$21,143

	Current Year Direct	\$5,100,417
dustry Contracts		
Kalinyak, K Novartis Pharmaceuticals		\$ 9,98
Fouladi, M Genentech		\$ 22,35
Geller, J ArQule, Inc		\$ 5,86
Gruppo, R Alexion Pharmaceuticals, Inc.		\$ 20,09
Baxter		\$ 51,96
Bayer		\$ 10,53
Grifols, Inc.		\$ 8,27
Wyeth Pharmaceuticals		\$ 3,92
Rho, Inc		\$ 10,22
Harris, R Alexion Pharmaceuticals, Inc.		\$ 1,77
Palumbo, J Novo Nordisk Pharmaceuticals		\$ 35,43
Perentesis, J CHLA - NANT		\$ 2,54
	Current Year Direct Receipts	\$182,957
unded Collaborative Efforts		
Perentesis, J Promoting Treatment Adherence in Adole	escent Leukemia	
National Institutes of Health		
Drotar, D	09/28/07 - 07/31/12	3 %
Neurofibromatosis Consortium Developm University of Alabama-Birmingham (Departn		
Schorry, E	07/01/08 - 06/30/10	5 %
Weiss, B		
Neurofibromatosis Consortium Developm University of Alabama-Birmingham (Departn		
Schorry, E	07/01/08 - 06/30/10	11 %
·	_	otal \$5,283,374