**Division Data Summary**

<table>
<thead>
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<th>Research and Training Details</th>
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<tr>
<td>Number of Faculty</td>
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<td>Number of Joint Appointment Faculty</td>
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<td>Number of Research Fellows</td>
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<table>
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<th>Clinical Activities and Training</th>
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<td>Number of Clinical Fellows</td>
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<td>Inpatient Encounters</td>
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**Significant Publications**


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.


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.


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 general-population 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.


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.


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)
Division Collaboration

Collaboration with Gastroenterology, Hepatology and Nutrition
Collaborating Faculty: K. Steinbrecher
Collitis-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

Collaboration with Experimental Hematology and Cancer Biology
Collaborating Faculty: Y. Zheng

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; Ophthalmology; 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

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.
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

Collaborating 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

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. Pruin
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 Behavioral Medicine and Clinical Psychology

Collaborating Faculty: M. Mitchell
Comprehensive Sickle Cell Center; Adherence to hydroxyurea therapy (K. Kalinyak, C. Joiner)

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


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


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


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 oncolytic herpes simplex virus type 1 transcriptionally targeted to midkine-positive 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. Shroyer

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


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


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; Ophthalmology; Pain Management; Human Genetics

Collaborating Faculty: R. Azizkhan; A. Dasgupta; R. Elluru; A. Lucky; M. Patel; T. Abruzzo; W. Ball; A.
Collaborating Faculty: R. Azizkhan; A. Dasgupta; R. Elluru; A. Lucky; M. Patel; T. Abruzzo; W. Ball; A. Zbojniewicz; K. Crone; A. Gupta; P. Eghtesady; K. Goldschneider; R. Hirsch; R. Hopkin; A. Kaul; P. Reddy; M. Rutter; J. Sorger; M. Sutton; R. Wood; K. Yakoboff; 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 Blessing, 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
Research Interests: Developing novel drugs for the treatment of children with recurrent or poor prognosis brain tumors

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, PhD, 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

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**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

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**Clinical Staff Members**

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

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**Trainees**

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

### Grant and Contract Awards

<table>
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<td>Severity Scale and Quality of Life Instrument for Infantile Hemangiomas</td>
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<td>Virotherapy for Neuroblastoma Stem Cells</td>
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<td>A Phase I Dose Escalation Study Of Intratumoral Herpes Simplex Virus-1 Mutant HSV 1716 in Patients with Non-Central Nervous System Solid Tumors</td>
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<td>Finding The Best Herpes Virus To Attack The Root of Neuroblastoma</td>
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Fouladi, M
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New England Research Institutes (National Institutes of Health)
U10HL083721  03/01/09 - 02/28/11  $3,465 / $3,465

**Sickle Cell Disease CTN- IMPROVE**
New England Research Institutes (National Institutes of Health)
U10HL083721  03/01/09 - 02/28/11  $1,925 / $1,925

Kalfa, T
**Rac1 and Rac2 Guanosine Triphosphatases in Erythroid Function and Differentiation**
National Institutes of Health
K08 HL 088126  02/11/08 - 11/30/12  $119,125 / $595,625

**TCD with Transfusions Changing to Hydroxyurea**
St Jude's Children's Hospital (National Institutes of Health)
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 Institutes of Health)
U01 HL 078787  04/01/06 - 07/31/10  $24,245 / $128,116

Mizukawa, B
**Characterization of Rac Proteins in Myeloid Leukemogenes**
Yale University School of Medicine (National Institutes of Health)
K12 HD 000850  07/01/08 - 06/30/11  $100,500 / $301,500

**Chemosensitization of the Leukemic Stem Cell Through Targeting its Interaction with the Marrow Niche**
Cancer Free Kids
07/01/09 - 06/30/11  $36,000 / $36,000

Morreale, R
**The Role of DEK in the Differentiation-Dependent HPV Life Cycle**
National Cancer Institute
F32 CA 138115  05/01/10 - 04/30/11  $50,054 / $50,054

Mullins, E
**Thrombin and Thrombin Targets in Allergic Airway Inflammation**
American Society of Hematology
07/01/08 - 06/30/10  $50,000 / $100,000

Nagarajan, R
**Genetic Epidemiology of Osteosarcoma**
University of Minnesota (National Cancer Institute)
U01 CA 122371  05/01/07 - 04/30/11  $9,561 / $36,607

Palumbo, J
**Mechanisms Linking Metastasis to Tumor Procoagulant and Innate Immunity**
National Institutes of Health
R01 HL 085545  07/20/06 - 06/30/11  $242,750 / $1,221,000

**Mechanisms Linking Metastasis to Tumor Procoagulant and Innate Immunity**
National Institutes of Health
R01 HL 085545  07/01/09 - 06/30/11  $150,234 / $150,234

Perentesis, J
**Children's Oncology Group Phase I**
Children's Oncology Group (National Institutes of Health)
U01 CA 097452  08/01/07 - 07/31/11  $22,545 / $65,683

**The Children's Oncology Group Chair's Grant**
Children's Oncology Group (National Institutes of Health)
U10 CA 098543  03/01/08 - 02/28/13  $36,881 / $134,556

**Children's Oncology Group Phase I**
National Childhood Cancer Foundation (National Institutes of Health)  
U01 CA 097452 06/01/09 - 05/31/11 $21,143 / $21,143  

**Children's Oncology Group Phase I**  
National Childhood Cancer Foundation (National Institutes of Health)  
U01 CA 097452 06/01/09 - 05/31/11 $18,721 / $18,721

**Children's Oncology Chair Award #19383**  
National Childhood Cancer Foundation (National Cancer Institute)  
U10 CA 098543 06/01/09 - 05/31/11 $38,333 / $38,333

**Children's Oncology Group Phase I (Per Patient)**  
Children's Oncology Group (National Institutes of Health)  
U01CA097452 08/01/07 - 07/31/10 $26,311 / $181,600

**The Children's Oncology Group Chair Grant (Per patient)**  
Children's Oncology Group (National Institutes of Health)  
U10CA098543 03/01/08 - 02/28/13 $169,945 / $223,041

**Children's Oncology Group New Publication Committee**  
National Childhood Cancer Foundation (National Institutes of Health)  
U01 CA 097452 09/1/06 - 07/31/11 $12,490 / $35,308

**Cincinnati Center for Neurofibromatosis Research - Project 1**  
National Institutes of Health  
P50 NS 057531 09/15/08 - 06/30/13 $296,437 / $1,521,540

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 $47,210 / $97,264

Shook, L  
**Cincinnati Sickle Cell Newborn Screening Network**  
Health Resources & Services Administration  
H46 MC 09233 06/01/08 - 05/31/11 $185,000 / $555,000

Smith, F  
**The Children's Oncology Group Chairs Grant**  
National Childhood Cancer Foundation (National Institutes of Health)  
U10 CA 098543 03/01/03 - 02/28/11 $114,444 / $427,840

Wang, P-Y  
**Virotherapy for Neuroblastoma Stem Cells**  
Cancer Free Kids  
05/01/10 - 04/30/11 $45,000 / $45,000

Weiss, B  
**Phase 1 Trial of Sorafenib in Children w/ NF1**  
University of Alabama-Birmingham (The Children's Tumor Foundation)  
04/15/09 - 04/14/11 $30,700 / $30,700

Wells, S  
**Role and Regulation of the Human DEK Proto-Oncogene**  
National Institutes of Health  
R01 CA 116316 04/01/06 - 02/28/11 $172,353 / $891,579

**Role and Regulation of the Human DEK Proto-Oncogene**  
National Institutes of Health  
R01 CA 116316 08/01/09 - 07/31/11 $146,211 / $146,211

**HPV Replication and Transformation in FA Squamous Cell**  
Fanconi Anemia Research Fund  
03/01/09 - 02/28/11 $100,000 / $200,000

**Fanconi Anemia and HPV Transformation**
### Industry Contracts

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Total $5,283,374