# Hematology/Oncology

## Division Photo

***First Row:*** *F. Smith, T. Kalfa, R. Gruppo;* ***Second Row:*** *S. Wells, M. Fouladi, T. Cripe;* ***Third Row:*** *K. Burns, S. Joshi, P. Mehta, L. Wagner;* ***Fourth Row:*** *K. Kalinyak;* ***Fifth Row:*** *R. Nagarajan, B. Weiss;* ***Sixth Row:*** *C. Joiner, R. Drissi, T. Hummel;* ***Seventh Row:*** *J. Perentesis, P. Malik*

## Division Data Summary

### Research and Training Details

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|---|---|
| Number of Faculty | 28 |
| Number of Joint Appointment Faculty | 7 |
| Number of Research Fellows | 3 |
| Number of Research Students | 1 |
| Number of Support Personnel | 187 |
| Direct Annual Grant Support | $4,397,168 |
| Direct Annual Industry Support | $143,650 |
| Peer Reviewed Publications | 55 |

### Clinical Activities and Training

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|---|---|
| Number of Clinical Staff | 4 |
| Number of Clinical Fellows | 12 |
| Number of Other Students | 1 |
| Inpatient Encounters | 1,197 |
| Outpatient Encounters | 13,753 |

## Faculty Members

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

**Vinod Balasa, MBBS,** Assistant Professor Clinical
**Research Interests:** Research activities related to sickle cell disease and Thrombophilia

**Jacob Bleesing, MD, PhD,** Assistant 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,** Associate 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
**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

**Matthew Hansen, MD,** Assistant Professor Clinical
**Research Interests:** Studying outcomes in Hurler's syndrome patients receiving hematopoietic stem cell transplants.

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

**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 ; *Director, Comprehensive Sickle Cell Center*
**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

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

**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 ; *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

**Laura Stadler, MEd, MD, MS,** Assistant Professor
Infectious Disease
Epidemiology of infectious diseases; cytomegalovirus (CMV); infections in immunocompromised hosts; international adoption; medical education

**Sualius Sumanas, PhD,** Assistant Professor
Developmental Biology

**Mary Sutton, MD,** Assistant Professor
Neurology

**David Williams, MD,** Professor
Experimental Hematology
Translational Research

## Clinical Staff Members

- **Sarita Joshi, MBBS, MD**
- **Teresa Finke, MD**
- **Grant Mussman, MD**
- **Gregory Wallace, DO**

## Trainees

- **Trent Hummel, MD,** PL-VII, Children's Hospital Medical Center - Akron
- **Eric Mullins, MD,** PL-VII, Vanderbilt University
- **Francis Eshun, MD,** PL-VI, Lincoln Medical Center
- **Sabine Mellor-Heineke, MD,** PL-VI, Staedtisches Klinikum Braunschweig
- **Ajay Perumbeti, MD,** PL-VI, Upstate Medical University
- **Philip Roehrs, MD,** PL-VI, Medical University of South Carolina
- **Lars Mueller, MD,** PL-V, Cincinnati Children's Hospital
- **Christine Phillips, MD,** PL-V, Children's Memorial Hospital Chicago
- **Melissa Rayburg, MD,** PL-V, University of Texas Health Science Center
- **Adrienne Hammill, MD, PhD,** PL-IV, Cincinnati Children's Hospital
- **Theodore Johnson, MD, PhD,** PL-IV, Medical College of Georgia
- **Kasiani Myers, MD,** PL-IV, Cincinnati Children's Hospital
- **Benjamin Mizukawa, MD,** PL-IV, Cincinnati Children's Hospital

# Significant Accomplishments in FY08

## Oncology Program Summary: Leukemia/Lymphoma Programs

A key focus of the Oncology Program is the translational development of new anti-cancer therapies built upon a foundation of investigation into the basic mechanisms of oncogenesis in childhood cancers. Fundamental cancer research is based in the Divisions of Hematology/Oncology and Experimental Hematology, along with integrated collaborations including other CCHMC Divisions, the University of Cincinnati, and the Ohio State University Comprehensive Cancer Center.

Leukemia and lymphoma are the most common pediatric malignancies and accounts for approximately 40% to 45% of all childhood cancer. In coordinated efforts, CCHMC faculty members from the Divisions of Hematology/Oncology and Experimental Hematology lead an impressive array of research initiatives in the biology and therapy of leukemias and lymphomas which have been benchmarked by ability to gain competitive National Institutes of Health funding. Dr. Yi Zheng's NIH-funded laboratory is developing novel small molecular inhibitors of pathological signaling in leukemia cells. His group studies the function and mechanism of regulation of the Rho family small GTP-binding proteins of Ras superfamily. The Rho GTPases are a class of intracellular signal transducers that play important roles in the regulation of diverse cellular activities including action cytoskeleton reorganization, transcription activation, and DNA synthesis. The NIH-funded research group of Dr. Lee Grimes is studying the regulation of expression of cancer causing genes in leukemias through multiple NIH funded awards and is using this work to develop an understanding of the molecular bases of acute myeloid leukemia. He is also actively identifying and refining new drug targets for clinical intervention in leukemias. Dr. Hartmut Geiger is identifying the role of tumor suppressor genes in leukemias and therapeutic opportunities to exploit this pathway. Dr. John Perentesis' NIH-funded laboratory program is identifying molecular targets in leukemias in high-risk pediatric populations such as children with Down syndrome, as well a molecular predictors of outcome in leukemia and Hodgkin's lymphoma. His lab has also been active in the development of targeted therapies for leukemia. Dr. Andreassen is NIH funded to analyze and dissect the role of cancer gene checkpoint dysregulation in leukemias. Dr. Filippi is NIH-funded to understand some of the role of similar small molecules affecting normal and malignant hematopoietic stem cells as well as how these molecules impact the function of normal cells. Dr. Meetei is also funded through the NIH to study the function and regulation of DNA repair genes in blood cell precursors. Dr. James Mulloy's NIH-funded group is studying the role of specific core binding factor and other fusion target genes in the regulation of normal and leukemia cells. Dr. Stella Davies leads an extensive NIH-funded program to identify genetic risk factors for the development of leukemia as well as a parallel extensive effort in pharmacogenetics to provide a foundation for the optimization of personalized cancer therapies as well as new targeted agents. Her NIH funded laboratory is the center for national pharmacogenetic studies on the children treated on leukemia regimens through the National Children's Oncology Group, and 20,000 survivors of pediatric cancer through the Childhood Cancer Survivor Study. This work is a key element for the future development of personalized and predictive medicine efforts in pediatric and adult cancers. Translational clinical activities in the Oncology and Blood/Marrow Transplantation Programs are investigating the use of new targeted anti-cancer therapies and antibodies in the treatment of high-risk and relapsed pediatric leukemias and lymphomas.

## Blood and Marrow Transplantation Program Summary: Reducing the Side Effects of Bone Marrow Transplantation

Bone marrow transplantation is the only available cure for children with a variety of genetic diseases that cause metabolic abnormalities or bone marrow failure. The availability of better matched donors has improved the results of bone marrow transplantation have improved markedly in recent years. However, the short and long term side effects of transplant can still be severe, or even fatal. Faculty members of the stem cell transplant program at Cincinnati Children's Hospital have investigated the use of a less intense pre-transplant chemotherapy regimen and have shown that the results are excellent, with successful engraftment and reduced side-effects of treatment. The new reduced-intensity regimen has been used successfully to treat children with Schwachman-Diamond syndrome and Seckel syndrome, two bone marrow failure syndromes in which genetic instability commonly leads to severe side effects, or even death after treatment with conventional regimens. All the children treated with the new regimen had successful engraftment of their stem cells and survived their transplant. Outcomes were similarly in children with Hurler syndrome, a progressive and fatal metabolic disease. The investigators are hopeful that the new approach will allow preservation of fertility for at least a proportion of children, but long term follow-up is needed to confirm this.

## Hematology Program Summary: Comprehensive Sickle Cell Center

Sickle cell disease is one of the most common "single gene" disorders in the US, seriously affecting the health and well-being of almost 100,000 children and adults, and significantly shortening their life expectancy. The past two decades of basic and clinical research have generated a new opportunities for treating this disease of red blood cells. The Comprehensive Sickle Cell Center, led by Dr. Clinton Joiner, is fully engaged across a full spectrum of basic, translational, clinical and outcomes/adherence research. Over the past decade, the Sickle Cell Center has received over

$22 M in extramural research funding. In 2008 the Sickle Cell Center was awarded a new $6.4 M four-year grant from NHLBI to conduct three major projects: 1. Basic science research into ways to improve the hydration state of sickle red blood cells via gene transfer to hematopoietic stem cells (Dr. Clinton Joiner, PI). 2. Translational research to develop methodogies to alter hemoglobin expression via gene transfer to hematopoietic stem cells (Dr. Punam Malik, PI, Division of Experimental Hematology). 3. A project aimed at improving adherence to hydroxyurea therapy for sickle cell disease via individualized psychosocial interventions (Dr. Monica Mitchell, PI, Division of Psychology and Behavioral Medicine). The grant also funds a career development program for research faculty in hematology and a summer program to introduce high school students to laboratory research. Other NIH-funded, collaborative clinical research projects focus on therapies to prevent strokes in sickle cell disease; on pharmacological treatments for Hemoglobin SC disease; on the correlation between genetic polymorphisms and phenotypic diversity in sickle cell disease (Dr. Karen Kalinyak, PI). Another NHLBI-funded translational research project, in collaboration with the Divisions of Experimental Hematology and Pulmonary Medicine, investigates the relationships among sickle cell disease, inflammation, and lung disease (Dr. Malik).

## Significant Publications in FY08

**Leukemia 22(2): 265-72**

Bhatla, D., R. B. Gerbing, T. A. Alonzo, **P. A. Mehta**, K. Deal, J. Elliott, S. Meshinchi, H. Geiger, **J. P. Perentesis**, B. J. Lange and **S. M. Davies** (2008). "DNA repair polymorphisms and outcome of chemotherapy for acute myelogenous leukemia: a report from the Children's Oncology Group."

This study demonstrated that patients with acute myeloid leukemia who were hetergeneous for the XRCC3 Thr241 Met allele has improved post-induction disease-free survival compared to children homozygous for the major or minor allele.

**Mol Ther16(5): 879-85**

Currier, M. A., R. A. Gillespie, N. M. Sawtell, Y. Y. Mahller, G. Stroup, M. H. Collins, H. Kambara, E. A. Chiocca and **T. P. Cripe** (2008). "Efficacy and safety of the oncolytic herpes simplex virus rRp450 alone and combined with cyclophosphamide."

This study suggest that the oncolytic herpes simplex virus, rRP450/CPA, is safe and should be studied further in childen with recurrent solid tumors.

**Cancer110(11): 2535-41**

**Fouladi, M.**, H. S. Nicholson, T. Zhou, F. Laningham, K. J. Helton, E. Holmes, K. Cohen, R. A. Speights, J. Wright and I. F. Pollack (2007). "A phase II study of the farnesyl transferase inhibitor, tipifarnib, in children with recurrent or progressive high-grade glioma, medulloblastoma/primitive neuroectodermal tumor, or brainstem glioma: a Children's Oncology Group study."

This phase II study of the farnesyl transferase inhibitor, tipifarnib, was not found to be effective in children with recurrent central nervous system malignancies.

**Blood110(1): 133-41**

**Palumbo, J. S.**, K. E. Talmage, J. V. Massari, C. M. La Jeunesse, M. J. Flick, K. W. Kombrinck, Z. Hu, K. A. Barney and J. L. Degen (2007). "Tumor cell-associated tissue factor and circulating hemostatic factors cooperate to increase metastatic potential through natural killer cell-dependent and-independent mechanisms."

This study showed that tumor-associated tissue factor is linked to metastasis throught a fibrinogen-dependent and platelet-dependent restriction in natural killer cell mediated clearance of micro-metastases.

**Clin Cancer Res13(18 Pt 1): 5418-25**

**Wagner, L. M.**, R. E. McLendon, K. J. Yoon, **B. D. Weiss**, C. A. Billups and M. K. Danks (2007). "Targeting methylguanine-DNA methyltransferase in the treatment of neuroblastoma."

This study showed that methylguanine-DNA methyltransferase is widely expressed in primary neuroblastoma tumors and may be a relevant therapeutic target.

## Division Highlights

**New viral and gene therapies for high-risk brain and other pediatric solid tumors**

Brain tumors and other pediatric solid tumors including neuroblastoma and rhabdomyosarcoma that cannot be completely resected are often fatal, and desperately need new approaches to therapy. CCHMC researchers are developing genetically engineered viruses, called “oncolytic viruses,” that show potent effects in killing cancer cells. In leading edge discoveries published in *Molecular Therapy*, *Cancer Research,* and *Cancer Gene Therapy,* CCHMC investigators have shown that oncolytic herpes simplex viruses can specifically target malignant sarcomas, inhibiting tumor growth and angiogenesis. In parallel clinical trials, patients at CCHMC with highly malignant brain tumors called glioblastoma multiforme are being treated with gene therapy that allows normal healthy blood cells to become resistant to the chemotherapies needed to treat these tumors. In these studies, a patient’s normal healthy blood stem cells are genetically modified to carry genes conferring resistance for the brain tumor chemotherapy drug temozolomide, allowing the patients to safely receive higher doses of the drug. Patients receive the genetically modified blood cells as well as high-dose temozolomide therapy and radiation for treatment of the glioblastoma multiforme. In related studies, our investigators have discovered the molecular mechanisms involved in events leading to the development of gene therapy-related complications, including leukemia. This work provides background for the development of safer gene therapy technologies.

**References**

Howe SJ, Mansour MR, Schwarzwaelder K, Bartholomae C, Hubank M, Kempski H, Brugman MH, Pike-Overzet K, Chatters SJ, de Ridder D, Gilmour KC, Adams S, Thornhill SI, Parsley KL, Staal FJ, Gale RE, Linch DC, Bayford J, Brown L, Quaye M, Kinnon C, Ancliff P, Webb DK, Schmidt M, von Kalle C, Gaspar HB, Thrasher AJ. Insertional mutagenesis combined with acquired somatic mutations causes leukemogenesis following gene therapy of SCID-X1 patients.

J Clin Invest. 2008 Sep:118(9):3143-50.

Mahller YY, Vaikunth SS, Currier MA, Miller SJ, Ripberger MC, Hsu Y-H, Mehrian-Shai R, Collins MH, Crombleholme TM, Ratner N, Cripe TP. Oncolytic HSV and Erlotinib Inhibit Tumor Growth and Angiogenesis in a Novel Malignant Peripheral Nerve Sheath Tumor Xenograft Model. Mol Ther 15:279-286, 2007

Mahller YY, Vaikunth SS, Ripberger MC, Baird WH, Saeki Y, Cancelas JA, Crombleholme TM, Cripe TP. Tissue inhibitor of metalloproteinase-3 via oncolytic herpes virus inhibits tumor growth and vascular progenitors. Cancer Res 68:1170-1179, 2008

Modlich U, Schambach A, Brugman MH, Wicke DC, Knoess S, Li Z, Maetzig T, Rudolph C, Schlegelberger B, Baum C. Leukemia induction after a single retroviral vector insertion in Evi1 or Prdm16. Leukemia. 22(8):1519-28, 2008

**Leading-edge advances in leukemia research**

CCHMC leukemia researchers are among the first to successfully transform normal human blood stem cells into leukemia stem cells. This work is providing a new understanding of what causes pediatric leukemia, the most common cancer affecting children. When researchers programmed normal benign human umbilical cord blood cells to express a fusion of two genes important in childhood mixed-lineage leukemia (MLL), they were able to create leukemia stem cells able to transform into either acute myeloid leukemia (AML) or acute lymphoid leukemia (ALL) cells depending on the growth factor proteins present in the cell culture. By manipulating these growth factor proteins in the cells, they were also able to transform ALL cells into AML cells and vice versa. In order to facilitate research into new therapies, this same team of researchers used the human leukemia stem cells they developed to create new and more useful mouse models of MLL-associated ALL and mixed myeloid/lymphoid disease. This work has highlighted the critical importance of leukemia cells’ environment to the progression and form of the disease and has suggested exciting new targets for future drug development. Published in the prestigious journal *Cancer Cell,* this research has garnered significant national attention. In integrated parallel investigations, CCHMC scientists have developed novel drugs for targeting signaling pathways in these leukemias as well as other cancers. Importantly, these new drugs work to kill leukemia cells by targeting the core processes that make them malignant and spare normal cells. These new drugs also kill leukemia cells that have become otherwise resistant to traditional chemotherapy and are currently being refined for clinical trials.

**References**

Thomas EK, Cancelas JA, Zheng Y, Williams DA. Rac GTPases as key regulators of p210-BCR-ABL-dependent leukemogenesis. Leukemia. 22(5):898-904, 2008

Wei J. Wunderlich M. Fox C. Alvarez S. Cigudosa JC. Wilhelm JS. Zheng Y. Cancelas JA. Gu Y. Jansen M. Dimartino

JF. Mulloy JC. Microenvironment determines lineage fate in a human model of MLL-AF9 leukemia. Cancer Cell. 13(6):483-95, 2008

Williams DA, Zheng Y, Cancelas JA. Rho GTPases and regulation of hematopoietic stem cell localization. Methods Enzymol. 439:365-93, 2008

## Division Collaboration

**Collaboration with Experimental Hematology & Cancer Biology; Pediatric & Thoracic Surgery; Developmental Biology-Students**

**Collaborating Faculty: J. Cancelas; T. Crombleholme; W. Baird**

Tissue inhibitor of metalloproteinase-3 via oncolytic herpesvirus inhibits tumor growth and vascular progenitors. Cancer Res 68:1170-1179, 2008 (T. Cripe; Y. Mahller)

**Collaboration with Translational Research Trials Office; Infectious Diseases; Immunobiology**

**Collaborating Faculty: R. Gillespie; N. Sawtell; D. Hildeman**

Efficacy and safety of the oncolytic herpes simplex virus rRp450 alone and combined with cyclophosphamide. Mol Ther 16:879-885, 2008 (T. Cripe; M. Currier; Y. Mahller)

**Collaboration with Biomedical Informatics; Developmental Biology-Students**

**Collaborating Faculty: B. Sakthivel; B. Aronow; W. Baird**

Molecular analysis of human cancer cells infected by a multi-mutated oncolytic HSV-1 reveals a role for SOCS1 in virus replication. Cancer Gene Therapy, in press 2008 T. Cripe; Y. Mahller)

**Collaboration with Experimental Hematology & Cancer Biology; Pathology; Biostatistics & Epidemiology; Experimental Hematology & Cancer Biology**

**Collaborating Faculty: G. Johansson; M. Collins; K. Mi-Ok; N. Ratner**

Effective in vivo targeting of the mTOR pathway in malignant peripheral nerve sheath tumors. Mol Cancer Ther 7:1237-1245, 2008. (T. Cripe; Y. Mahller; J. Perentesis)

**Collaboration with Endocrinology; Behavioral Medicine & Clinical Psychology**

**Collaborating Faculty: S. Rose; Doug Ris**

A pilot study of oxandrolone in children with Fanconi Anemia and severe bone marrow failure (F. Smith)

**Collaboration with Surgical Services**

**Collaborating Faculty: R. Azizkhan**

COG, Surgery services for Oncology patients

**Collaboration with UC Radiation Oncology**

**Collaborating Faculty: J. Breneman**

Radiation Oncology clinical services for Hem/Onc patients; COG

**Collaboration with Human Genetics**

**Collaborating Faculty: Liming Bao; T Smolarek**

COG; Genetic services for HemOnc Patients

**Collaboration with Pathology**

**Collaborating Faculty: M. Collins**

COG; Pathology services

**Collaboration with Behavioral Medicine and Clinical Psychology**

**Collaborating Faculty: D. Drotar**

COG; Adherence Research

**Collaboration with Behavioral Medicine & Clinical Psychology**

**Collaborating Faculty: D. Ris**

COG; NeuroPsych services, Neuropsychology research, Fanconi Anemia research

**Collaboration with Radiology**

**Collaborating Faculty: M. Gelfand**

COG; Cancer Nuclear Mecine services

**Collaboration with Orthopaedics**

**Collaborating Faculty: CT Mehlman**

COG; Brain Tumor research and clinical services

**Collaboration with Experimental Hematology**

**Collaborating Faculty: J. Mulloy**

Leukemia Research; COG

**Collaboration with Endocrinology**

**Collaborating Faculty: S. Rose**

COG; FA research, NeurOncology Research, Endocrinology services as part of clinic

**Collaboration with University of Cincinnati**

**Collaborating Faculty: George Thomas**

COG; Drug Development

**Collaboration with Pediatric & Thoracic Surgery**

**Collaborating Faculty: G. Tiao**

COG; Cancer Surgery

**Collaboration with Clinical Pharmacology**

**Collaborating Faculty: A. Vinks**

COG; Developmental Therapeutics research

**Collaboration with Anesthesia**

**Collaborating Faculty: N. Weidner**

COG; Paliative care and pain

**Collaboration with PM&R**

**Collaborating Faculty: D. Pruit**

NeuroOncology Clinic

**Collaboration with University of Cincinnati - Oncology**

**Collaborating Faculty: M Gerena-Lewis**

Medical Oncology and NeuroOncology services

## Mentions in Consumer Media

- America's Best Children's Hospitals U.S. News & World Report , Magazine
- Viral Therapy Slows Pediatric Tumors in Mice Forbes , Magazine

## Division Publications


1. Absalon MJ, McCarville MB, Liu T, Santana VM, Daw NC, Navid F. **Pulmonary nodules discovered during the initial evaluation of pediatric patients with bone and soft-tissue sarcoma.** *Pediatr Blood Cancer.* 2008; 50: 1147-53.
2. Adams DM, Wentzel MS. **The role of the hematologist/oncologist in the care of patients with vascular anomalies.** *Pediatr Clin North Am.* 2008; 55: 339-55.
3. Adams DM, Zhou T, Berg SL, Bernstein M, Neville K, Blaney SM. **Phase 1 trial of O6-benzylguanine and BCNU in children with CNS tumors: a Children's Oncology Group study.** *Pediatr Blood Cancer.* 2008; 50: 549-53.
4. Friedlander SL, Dooms KT, Seroogy CM, Voss CY, Agger WA, Zhang K, Bleesing J, Filipovich AH. **Adolescent presentation of x-linked lymphoproliferative disease.** *Ann Allergy Asthma Immunol.* 2008; 100: 398-400.
5. Kahwash SB, Fung B, Savelli S, Bleesing JJ, Qualman SJ. **Autoimmune lymphoproliferative syndrome (ALPS): a case with congenital onset.** *Pediatr Dev Pathol.* 2007; 10: 315-9.
6. Cripe TP. **Can less really be more? Using lessons from leukemia and cancer stem cells to make sense of oral maintenance for metastatic sarcoma.** *Pediatr Blood Cancer.* 2008; 50: 737-8.
7. Currier MA, Gillespie RA, Sawtell NM, Mahller YY, Stroup G, Collins MH, Kambara H, Chiocca EA, Cripe TP. **Efficacy and safety of the oncolytic herpes simplex virus rRp450 alone and combined with cyclophosphamide.** *Mol*

*Ther.* 2008; 16: 879-85.

8. Mahller YY, Vaikunth SS, Ripberger MC, Baird WH, Saeki Y, Cancelas JA, Crombleholme TM, Cripe TP. **Tissue inhibitor of metalloproteinase-3 via oncolytic herpesvirus inhibits tumor growth and vascular progenitors.** *Cancer Res.* 2008; 68: 1170-9.
9. Blanco JG, Leisenring WM, Gonzalez-Covarrubias VM, Kawashima TI, Davies SM, Relling MV, Robison LL, Sklar CA, Stovall M, Bhatia S. **Genetic polymorphisms in the carbonyl reductase 3 gene CBR3 and the NAD(P)H:quinone oxidoreductase 1 gene NQO1 in patients who developed anthracycline-related congestive heart failure after childhood cancer.** *Cancer.* 2008; 112: 2789-95.
10. Davies S. **Who evaluates and counsels related donors?.** *Biol Blood Marrow Transplant.* 2007; 13: 1526-7.
11. Davies SM, Borowitz MJ, Rosner GL, Ritz K, Devidas M, Winick N, Martin PL, Bowman P, Elliott J, Willman C, Das S, Cook EH, Relling MV. **Pharmacogenetics of minimal residual disease response in children with B-precursor acute lymphoblastic leukemia: a report from the Children's Oncology Group.** *Blood.* 2008; 111: 2984-90.
12. Gardner SL, Carreras J, Boudreau C, Camitta BM, Adams RH, Chen AR, Davies SM, Edwards JR, Grovas AC, Hale GA, Lazarus HM, Arora M, Stiff PJ, Eapen M. **Myeloablative therapy with autologous stem cell rescue for patients with Ewing sarcoma.** *Bone Marrow Transplant.* 2008; 41: 867-72.
13. Lee SJ, Joffe S, Artz AS, Champlin RE, Davies SM, Jagasia M, Kernan NA, Loberiza FR, Jr., Soiffer RJ, Eapen M. **Individual physician practice variation in hematopoietic cell transplantation.** *J Clin Oncol.* 2008; 26: 2162-70.
14. Mulrooney DA, Dover DC, Li S, Yasui Y, Ness KK, Mertens AC, Neglia JP, Sklar CA, Robison LL, Davies SM. **Twenty years of follow-up among survivors of childhood and young adult acute myeloid leukemia: a report from the Childhood Cancer Survivor Study.** *Cancer.* 2008; 112: 2071-9.
15. Pentz RD, Haight AE, Noll RB, Barfield R, Pelletier W, Davies S, Alderfer MA, Hinds PS. **The ethical justification for minor sibling bone marrow donation: a case study.** *Oncologist.* 2008; 13: 148-51.
16. Bullock JZ, Villanueva JM, Blanchard C, Filipovich AH, Putnam PE, Collins MH, Risma KA, Akers RM, Kirby CL, Buckmeier BK, Assa'ad AH, Hogan SP, Rothenberg ME. **Interplay of adaptive th2 immunity with eotaxin-3/c-C chemokine receptor 3 in eosinophilic esophagitis.** *J Pediatr Gastroenterol Nutr.* 2007; 45: 22-31.
17. Filipovich AH. **Diagnosis and manifestations of chronic graft-versus-host disease.** *Best Pract Res Clin Haematol.* 2008; 21: 251-7.
18. Filipovich AH. **Hemophagocytic lymphohistiocytosis and other hemophagocytic disorders.** *Immunol Allergy Clin North Am.* 2008; 28: 293-313, viii.
19. Hazen MM, Woodward AL, Hofmann I, Degar BA, Grom A, Filipovich AH, Binstadt BA. **Mutations of the hemophagocytic lymphohistiocytosis-associated gene UNC13D in a patient with systemic juvenile idiopathic arthritis.** *Arthritis Rheum.* 2008; 58: 567-70.
20. Horne A, Trottestam H, Arico M, Egeler RM, Filipovich AH, Gadner H, Imashuku S, Ladisch S, Webb D, Janka G, Henter JI. **Frequency and spectrum of central nervous system involvement in 193 children with haemophagocytic lymphohistiocytosis.** *Br J Haematol.* 2008; 140: 327-35.
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## Grants, Contracts, and Industry Agreements

### Grant and Contract Awards — Annual Direct / Project Period Direct

**Browne, A**

**Delivery and Production of a Secretable Universal Cancer Biomarker and its Detection in the Blood by a Novel Continuous Sampling Microtechnology**
Cancer Free Kids
05/01/08 - 04/30/09 — $35,000 / $35,000

**Burns, K.**

**Survivorship Conference Grant**
The National Children's Cancer Society
11/01/07 - 10/31/08 — $20,000 / $20,000

**Cripe, T**

**Identifying and Targeting the Source of Neuroblastoma Metastasis**
Cancer Free Kids
05/01/08 - 04/30/09 — $25,000 / $25,000

**Oncolytic HSV Therapy in Immunocompetent Sarcoma Models**
National Institutes of Health
R01 CA 114004 — 07/01/06 - 05/31/11 — $172,353 / $866,912

**Cincinnati NF1 Preclinical Testing Center**
The Children's Tumor Foundation
12/01/07 - 05/31/11 — $25,000 / $720,000

**Cincinnati NF1 Preclinical Testing Center**
The Children's Tumor Foundation
06/01/08 - 05/31/11 — $232,000 / $720,000

**Davies, S**

**The Children's Oncology Group Chairs Grant**
National Institutes of Health (National Childhood Cancer Foundation)
U10 CA 098543 — 03/01/08 - 02/28/13 — $11,663 / $58,465

**The Children's Oncology Group Chairs Grant - Methotrexate**
National Institutes of Health (National Childhood Cancer Foundation)
U10 CA 098543-S1 — 03/01/08 - 02/28/13 — $11,693 / $58,468

**COG Pediatric Blood and Marrow Transplant (Per Patient)**
National Institutes of Health (National Childhood Cancer Foundation)
U01 HL 069294 — 09/01/06 - 08/31/08 — $4,763 / $22,610

**Predictors Of Adult Leukemia**
National Institutes of Health (University of Minnesota)

R01 CA 107143 04/01/05 - 02/28/10 $11,712 / $56,904

**Genetic Epidemiology of Basal Cell Carcinoma in Childhood Cancer Survivors**
University of Cincinnati Center for Environmental Genetics
04/01/08 - 03/31/09 $25,000 / $25,000

**Novel Molecular and Cellular Therapies in Fanconi Anemia**
National Institutes of Health (Children's Hospital Boston)
R01 HL 081499 04/01/08 - 03/31/10 $166,839 / $333,678

**Childhood Cancer Survivor Study**
National Institutes of Health (St. Jude's Children's Hospital)
U54 CA 055727 12/01/05 - 11/30/10 $50,000 / $643,729

**Antileukemic Effect of NK Cells in HCT for Pediatric AML**
National Institutes of Health (St. Jude's Children's Hospital)
R01 CA 120583 08/01/07 - 06/30/12 $8,716 / $43,580

## Fouladi, M

**Children's Oncology Group Phase I/Pilot Consortium**
National Institutes of Health (National Childhood Cancer Foundation)
U01 CA 097452 08/01/07 - 07/31/12 $21,877 / $21,877

**The Pediatric Brain Tumor Consortium**
National Institutes of Health (St. Jude's Children's Hospital)
U01 CA 081457 04/01/08 - 03/31/09 $11,127 / $11,127

## Glass, D.

**Fascanto II Flow Cytometer and SVC Fascanto II Violet**
Health Resources and Services Administration
C76 HF 09978 06/01/08 - 05/31/09 $473,707 / $473,707

## Gruppo, R

**Hemophilia Comprehensive Care & Prevention Core Center for Bleeding Disorders**
Maternal and Child Health Bureau (Hemophilia Foundation of Michigan)
5H30MC0015-11 10/01/97 - 05/31/09 $14,760 / $124,190

**Hemophilia Prevention Network**
Centers for Disease Control and Prevention (Hemophilia Foundation of Michigan)
U27 CCU 51382 10/01/97 - 09/29/08 $22,295 / $134,771

**Hemophilia and Thrombosis Center**
Cascade Hemophilia Consortium (Hemophilia Foundation of Michigan)
06/01/03 - 05/31/09 $58,200 / $239,458

## Joiner, C

**Cincinnati Sickle Cell Project**
Ohio Department of Health
31-6-006-1-CC-08 07/01/07 - 06/30/08 $117,368 / $117,368

**Cincinnati Comprehensive Sickle Cell Center**
National Institutes of Health
U54 HL 070871 06/15/08 - 03/31/12 $1,005,115 / $4,067,809

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|---|---|---|
| Mitchell, M | Project 3 | 108,644 |
| Joiner, C | Project 4 | 298,056 |
| Malik, P | Project 5 | 389,734 |
| Joiner, C | Admin Core | 103,681 |
| Joiner, C | Scholar | 105,000 |

**Cincinnati Comprehensive Sickle Cell Center**
National Institutes of Health
U54 HL070871-05S 06/15/08 - 03/31/09 $184,862 / $184,862

**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

**Kalinyak, K**

**Silent Cerebral Infarct Multi-Center Clinical Trial**
National Institutes of Health (Washington University)
U01 NS 042804 | 09/30/03 - 06/30/10 | $3,665 / $502,371

**Stroke With Transfusions Changing To Hydroxyurea**
National Institutes of Health (St. Jude's Children's Hospital)
U01 HL 078787 | 04/01/06 - 06/30/11 | $28,975 / $138,180

**Marsh, R**

**Investigation into the Clinical and Molecular Pathogenesis of XIAP Deficiency**
Histiocytosis Association of America
11/01/07 - 10/31/08 | $48,500 / $48,500

**Muller, L**

**Optimization of Gene Therapy Technology for FA, an Inherited Cancer Predisposition and Bone Marrow Failure Syndrome**
St. Baldrick's Foundation
07/01/07 - 06/30/08 | $61,875 / $61,875

**Nagarajan, R**

**Genetic Epidemiology of Osteosarcoma**
National Institutes of Health (University of Minnesota)
U01 CA 122371 | 05/01/07 - 04/30/11 | $9,013 / $36,607

**Palumbo, J**

**Hemostatic Factors and Tumor Biology**
National Institutes of Health
K08 HL 074363 | 07/15/03 - 06/30/08 | $120,750 / $603,750

**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

**Partin-Welch, P**

**Oncology Education and Support Group/Family Specials Needs Program**
Bear Necessities Pediatric Cancer Foundation
07/01/07 - 06/30/08 | $5,000 / $5,000

**Perentesis, J**

**Children's Oncology Group Phase I Consortium**
National Institutes of Health (National Childhood Cancer Foundation)
U01 CA 097542 | 08/01/07 - 07/31/12 | $21,250 / $106,250

**Children's Oncology Group Phase I Consortium (Per Patient)**
National Institutes of Health (National Childhood Cancer Foundation)
U01 CA 097542 | 08/01/07 - 07/31/12 | $23,354 / $116,772

**Children's Oncology Group - Committee**
National Institutes of Health (National Childhood Cancer Foundation)
U01 CA 097542 | 08/01/07 - 07/31/12 | $11,441 / $57,205

**Molecular Studies of Down Syndrome Leukemia**
National Institutes of Health
R01 CA 111778 | 01/01/05 - 12/31/08 | $178,395 / $652,146

**Personalized Neuroblastoma Cancer Signatures and Targeted Therapy**
Cancer Free Kids
05/01/08 - 04/30/09 | $40,000 / $40,000

**Chairman's Award Children's Oncology Group**
National Institutes of Health (National Childhood Cancer Foundation)
U10 CA 098543 03/01/08 - 02/28/13 $23,325 / $116,625

**Chairman's Award Children's Oncology Group (Per Patient)**
National Institutes of Health (National Childhood Cancer Foundation)
U10 CA 098543 03/01/03 - 02/28/13 $97,909 / $418,715

**Shook, L**

**Cincinnati Sickle Cell Newborn Screening Network**
Health Resources and 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 Institutes of Health (National Childhood Cancer Foundation)
U10 CA 098543 03/01/08 - 02/28/13 $108,925 / $544,628

**Sumegi, J**

**Molecular Characterization of Novel Variant Translocation in Sarcomas of Children**
American Cancer Society - Ohio
09/01/07 - 08/31/08 $25,000 / $25,000

**Search for Growth Inhibitory Genes in Ewing's Sarcoma by Epigentic Profiling**
La Fondation des Gouverneurs de l'espoir for Ewing Family Tumors (University of Nebraska)
01/01/08 - 12/31/08 $46,262 / $92,524

**Wagner, L.**

**Children's Oncology Group Phase I ADVL0414 Study Chair**
National Institutes of Health (National Childhood Cancer Foundation)
U01 CA 097452 08/01/07 - 07/31/12 $20,251 / $101,255

**Identification of Response Markers in Children Receiving Combination Therapy with Chemotherapy and Bevacizumab**
Cancer Free Kids
05/01/08 - 04/30/09 $20,000 / $20,000

**Wells, S.**

**Fanconi Anemia and HPV Associated Disease**
Fanconi Anemia Research Foundation
01/01/07 - 12/31/08 $75,000 / $150,000

**Role and Regulation of the Human DEK Proto-Oncogene**
National Institutes of Health
R01 CA 116313 04/01/06 - 02/28/11 $172,353 / $916,579

**Current Year Direct** **$4,397,168**

## Industry Contracts

**Balasa, V**
Novartis Pharmaceuticals $ 36,599

**Cripe, T**
Crusade Laboratories Limited $ 38,078

**Gruppo, R**
Baxter Healthcare Corp. $ 11,562
Wyeth Pharmaceuticals $ 12,570

**Harris, R**
Alexion Pharmaceuticals, Inc. $ 2,118
NANT $ 6,622

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|---|---|
| **Joiner, C** | |
| Icagen Inc. | $ 2,257 |
| **Smith, F** | |
| Clinical Trials Office | $ 33,844 |
| **Current Year Direct Receipts** | **$143,650** |
| **Current Year Direct** | **$143,650** |
| **Total** | **$4,540,818** |