Oncology

Division Details

Division Data Summary

Research and Training Details

Number of Faculty	**20**
Number of Joint Appointment Faculty	**4**
Number of Research Fellows	**6**
Number of Research Students	**4**
Number of Support Personnel	**55**
Direct Annual Grant Support	**$1,789,135**
Direct Annual Industry Support	**$180,150**
Peer Reviewed Publications	**32**

Clinical Activities and Training

Number of Clinical Staff	**5**
Number of Clinical Fellows	**8**
Number of Other Students	**2**
Inpatient Encounters	**9,548**
Outpatient Encounters	**7,003**

Division Photo

Row 1: M O'Brien, B Lampkin, C Cost, D Adams
Row 2: B Weiss, R Nagarajan, M Absalon, B Mizukawa, J Perentesis
Row 3: R Drissi, J Geller, C Phillips
Row 4: L Chow, T Hummel, B Turpin, B DasGupta

Division Highlights

First clinical tumor profiling to guide therapy in relapsed leukemia

In a nationally unique program, the Division of Oncology is now creating molecular profiles of tumor cells from patients in real time in order to guide therapy. Initial efforts focus on relapsed leukemias, but the program will expand to include solid tumors. Although an array of novel molecularly targeted therapies are available to patients with relapsed and refractory cancers through consortium and investigator-initiated early phase clinical trials, it is sometimes unclear which therapies are most likely to show activity in a specific patient. Through the use of real-time tumor profiling technologies, Cincinnati Children's oncologists can assess which molecular pathways are fueling the growth of each patient's cancer and guide patients toward new drugs thought to be active in those pathways.

In a closely related initiative, the Childhood Cancer Drug Discovery Laboratory at Cincinnati Children's is screening a library of more than 340,000 potential drugs against childhood and young adult cancer cells collected through our specimen banking protocols to identify new candidate drugs. Simultaneously, we are using our specimen libraries to profile large numbers of cancer cells, identifying molecular signatures that may be represent new druggable targets

National awards recognize early-career faculty as among the next generation of leaders in translational oncology

Early-career faculty in the Division of Oncology continue to earn national recognition and substantial grant support for their translational cancer research programs. Lionel Chow, MD, PhD, Assistant Professor of Pediatrics in the Division of Oncology and a member of the Brain Tumors Program, received a prestigious Sontag Foundation Distinguished Scientist Award. The award, given to just five researchers nationally each year, provides $600,000 to support Dr. Chow's work on molecular targeting in high-grade astrocytoma. The Chow lab works to develop novel animal models of high-grade brain tumors and to identify and develop new targeted therapies, focusing on the PI3-Kinase/AKT/MTOR pathway.

Christine Phillips, MD, Assistant Professor of Clinical Pediatrics and a member of the Leukemia/Lymphoma Program, has received an AACR-FNAB Career Development Award for Translational Cancer Research to support her work to elucidate a genetic model of cytarabine sensitivity in children with acute myeloid leukemia.

Neuro-Oncology Program Launches International Diffuse Intrinsic Pontine Glioma Registry

Professor of Pediatrics and Medical Director of Neuro-Oncology Maryam Fouladi, MD, MSc, is the principal investigator of the newly launched International Diffuse Intrinsic Pontine Glioma (DIPG) Registry, a cooperative project to build a comprehensive registry of demographic, clinical, radiographic, and pathology data for DIPG, a rare pediatric brain tumor with a very poor prognosis. The registry is linked to a bioinformatics repository of molecular data generated from analysis of tumor samples. CCHMC is the coordinating center for the North American operations of the registry. The registry has embarked on two initial research projects: a study of long-term survivors of DIPG to attempt to correlate key clinical, radiographic, pathologic, and biological characteristics with outcome, and the first-ever epidemiological study to determine incidence patterns of DIPG in North America for 2000 – 2010. Collaborating investigators in Europe, Australia, and Asia expect to launch the registry in these regions in the upcoming year.

Significant Publications

Fouladi M, Stewart CF, Olson J, **Wagner LM**, Onar-Thomas A, Kocak M, Packer RJ, Goldman S, Gururangan S, Gajjar A, Demuth T, Kun LE, Boyett JM, Gilbertson RJ. **Phase I trial of MK-0752 in children with refractory CNS malignancies: a pediatric brain tumor consortium study.***Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 29(26):3529-3534. Sep 10 2011.

The purpose of this study was to estimate the maximum-tolerated dose (MTD), describe dose-limiting toxicities (DLTs), and characterize pharmacokinetic properties of MK-0752, a gamma secretase inhibitor, in children with refractory or recurrent CNS malignancies.Twenty-three eligible patients were enrolled: 10 males (median age, 8.1 years; range, 2.6 to 17.7 years) with diagnoses of brainstem glioma (n = 6), ependymoma (n = 8), medulloblastoma/primitive neuroectodermal tumor (n = 4), glioblastoma multiforme (n = 2), atypical teratoid/rhabdoid tumor (n = 1), malignant glioma (n = 1), and choroid plexus carcinoma, (n = 1). Seventeen patients were fully evaluable for toxicity. No DLTs occurred in the three patients enrolled at 200 mg/m(2)/dose. At 260 mg/m(2)/dose, DLTs occurred in two of six patients, both of whom experienced grade 3 ALT and AST. There were no grade 4 toxicities; non-dose-limiting grade 3 toxicities included hypokalemia and lymphopenia. Population pharmacokinetic values (% coefficient of variation) for MK-0752 were apparent oral clearance, 0.444 (38%) L/h/m(2); apparent volume of distribution, 7.36 (24%) L/m(2); and k(a), 0.358 (99%) hr(-1). Conclusion MK-0752 is well-tolerated in children with recurrent CNS malignancies. The recommended phase II dose using the 3 days on followed by 4 days off schedule is 260 mg/m(2)/dose once daily.

Haggstrom AN, Beaumont JL, Lai JS, **Adams DM**, Drolet BA, Frieden IJ, Garzon MC, Holland KE, Horii KA, Lucky AW, Mancini AJ, Metry DW, Morel KD, Newell BD, Nopper AJ, Siegel D, Swigonski NL, Cella D, Chamlin SL.

Measuring the severity of infantile hemangiomas: instrument development and reliability. *Archives of dermatology.* 148(2):197-202. Feb 2012.

The objective was to develop instruments that measure the severity of infantile hemangiomas (Hemangioma Severity Scale [HSS]) and the complications of infantile hemangiomas for longitudinal use (Hemangioma Dynamic Complication Scale [HDCS]). The HSS and the HDCS were developed through the collaborative effort of members of the Hemangioma Investigator Group Research Core, an expert multi-institutional research group. After development of the scales, 13 pediatric dermatologists used the HSS to score 20 different hemangiomas. In addition, 12 pediatric dermatologists used the HDCS to score hemangioma-related complications for 24 clinical scenarios. Interrater and intrarater reliability was measured for both scales. For the HSS, interrater reliability and intrarater reliability exceeded 99%. Similarly, the HDCS had a high rate of interrater agreement; for individual items, agreement among raters was 67% to 100%, with most clinical scenarios demonstrating greater than 90% agreement. Intrarater reliability was excellent for all individual items of the HDCS. The HSS and the HDCS are reliable scales that can be used to measure the severity of infantile hemangiomas, including the severity of complications for longitudinal use

Mizukawa B, Wei J, Shrestha M, Wunderlich M, Chou FS, Griesinger A, Harris CE, Kumar AR, Zheng Y, Williams DA, Mulloy JC. **Inhibition of Rac GTPase signaling and downstream prosurvival Bcl-2 proteins as combination targeted therapy in MLL-AF9 leukemia.** *Blood.* 118(19):5235-5245. Nov 10 2011.

The Rac family of small Rho GTPases coordinates diverse cellular functions in hematopoietic cells including adhesion, migration, cytoskeleton rearrangements, gene transcription, proliferation, and survival. The integrity of Rac signaling has also been found to critically regulate cellular functions in the initiation and maintenance of hematopoietic malignancies. Using an in vivo gene targeting approach, we demonstrate that Rac2, but not Rac1, is critical to the initiation of acute myeloid leukemia in a retroviral expression model of MLL-AF9 leukemogenesis. However, loss of either Rac1 or Rac2 is sufficient to impair survival and growth of the transformed MLL-AF9 leukemia. Rac2 is known to positively regulate expression of Bcl-2 family proteins toward a prosurvival balance. We demonstrate that disruption of downstream survival signaling through antiapoptotic Bcl-2 proteins is implicated in mediating the effects of Rac2 deficiency in MLL-AF9 leukemia. Indeed, overexpression of Bcl-xL is able to rescue the effects of Rac2 deficiency and MLL-AF9 cells are exquisitely sensitive to direct inhibition of Bcl-2 family proteins by the BH3-mimetic, ABT-737. Furthermore, concurrent exposure to NSC23766, a small-molecule inhibitor of Rac activation, increases the apoptotic effect of ABT-737, indicating the Rac/Bcl-2 survival pathway may be targeted synergistically.

Morrison MA, Morreale RJ, Akunuru S, Kofron M, Zheng Y, **Wells SI**. **Targeting the human papillomavirus E6 and E7 oncogenes through expression of the bovine papillomavirus type 1 E2 protein stimulates cellular motility.***Journal of virology.* 85(20):10487-10498. Oct 2011.

Expression of the high-risk human papillomavirus (HPV) E6 and E7 oncogenes is essential for the initiation and maintenance of cervical cancer. The repression of both was previously shown to result in activation of their respective tumor suppressor targets, p53 and pRb, and subsequent senescence induction in cervical cancer cells. Consequently, viral oncogene suppression is a promising approach for the treatment of HPV-positive tumors. One well-established method of E6/E7 repression involves the reexpression of the viral E2 protein which is usually deleted in HPV-positive cancer cells. Here, we show that, surprisingly, bovine papillomavirus type 1 (BPV1) E2 but not RNA interference-mediated E6/E7 repression in HPV-positive cervical cancer cells stimulates cellular motility and invasion. Migration correlated with the dynamic formation of cellular protrusions and was dependent upon cell-to-cell contact. While E2-expressing migratory cells were senescent, migration was not a general feature of cellular senescence or cell cycle arrest and was specifically observed in HPV-positive cervical cancer cells. Interestingly, E2-expressing cells not only were themselves motile but also conferred increased motility to admixed HeLa cervical cancer cells. Together, our data suggest that repression

of the viral oncogenes by E2 stimulates the motility of E6/E7-targeted cells as well as adjacent nontargeted cancer cells, thus raising the possibility that E2 expression may unfavorably increase the local invasiveness of HPV-positive tumors.

Weiss BD, **Dasgupta R**, Gelfand MJ, Laor T, Yin H, Breneman JC, Lavigne R, Elluru RG, **Wagner LM**. **Use of sentinel node biopsy for staging parameningeal rhabdomyosarcoma**. *Pediatric blood & cancer.* 57(3):520-523. Sep 2011.

Identification of nodal involvement is important for treatment planning in patients with rhabdomyosarcoma, and is facilitated by sentinel node biopsy. Although it is employed primarily for extremity tumors, we report using sentinel node biopsy in a patient with parameningeal rhabdomyosarcoma arising in the ethmoid sinus. Lymphoscintigraphy with single photon emission computed tomography following injection of tracer at the tumor site helped identify contralateral cervical node involvement not previously recognized by physical exam, cross sectional imaging, or other functional imaging. This case demonstrates how information from sentinel node identification and biopsy can change therapy recommendations in patients with parameningeal rhabdomyosarcoma.

Division Publications

1. Chen W, Wagner L, Boyd T, Nagarajan R, Dasgupta R. **Extralobar pulmonary sequestration presenting with torsion: a case report and review of literature**. *J Pediatr Surg*. 2011; 46:2025-8.
2. Chernoguz A, Crawford K, Donovan E, Vandersall A, Berglund C, Cripe TP, Frischer JS. **EGFR inhibition fails to suppress vascular proliferation and tumor growth in a Ewing's sarcoma model**. *J Surg Res*. 2012; 173:1-9.
3. Chow LM, Baker SJ. **Capturing the molecular and biological diversity of high-grade astrocytoma in genetically engineered mouse models**. *Oncotarget*. 2012; 3:67-77.
4. Dorris K, Fouladi M, Davies SM, Perentesis JP, Lawrence JM, Chow LM, Assa'ad A, Uygungil B, Jodele S. **Severe allergic reactions to thiol-based cytoprotective agents mesna and amifostine in a child with a supratentorial primitive neuroectodermal tumor**. *J Pediatr Hematol Oncol*. 2011; 33:e250-2.
5. Drissi R, Wu J, Hu Y, Bockhold C, Dome JS. **Telomere shortening alters the kinetics of the DNA damage response after ionizing radiation in human cells**. *Cancer Prev Res (Phila)*. 2011; 4:1973-81.
6. Elmeliegy MA, Carcaboso AM, LM LC, Zhang ZM, Calabrese C, Throm SL, Wang F, Baker SJ, Stewart CF. **Magnetic resonance imaging-guided microdialysis cannula implantation in a spontaneous high-grade glioma murine model**. *J Pharm Sci*. 2011; 100:4210-4214.
7. Eshelman-Kent D, Kinahan KE, Hobbie W, Landier W, Teal S, Friedman D, Nagarajan R, Freyer DR. **Cancer survivorship practices, services, and delivery: a report from the Children's Oncology Group (COG) nursing discipline, adolescent/young adult, and late effects committees**. *J Cancer Surviv*. 2011; 5:345-57.
8. Fadell MF, 2nd, Jones BV, Adams DM. **Prenatal diagnosis and postnatal follow-up of rapidly involuting congenital hemangioma (RICH)**. *Pediatr Radiol*. 2011; 41:1057-60.
9. Fisher MJ, Loguidice M, Gutmann DH, Listernick R, Ferner RE, Ullrich NJ, Packer RJ, Tabori U, Hoffman RO, Ardern-Holmes SL, Hummel TR, Hargrave DR, Bouffet E, Charrow J, Bilaniuk LT, Balcer LJ, Liu GT. **Visual outcomes in children with neurofibromatosis type 1-associated optic pathway glioma following chemotherapy: a multicenter retrospective analysis**. *Neuro Oncol*. 2012; 14:790-7.
10. Fouladi M, Stewart CF, Olson J, Wagner LM, Onar-Thomas A, Kocak M, Packer RJ, Goldman S, Gururangan S, Gajjar A, Demuth T, Kun LE, Boyett JM, Gilbertson RJ. **Phase I trial of MK-0752 in children with refractory CNS malignancies: a pediatric brain tumor consortium study**. *J Clin Oncol*. 2011; 29:3529-34.
11. Franz DN, Weiss BD. **Molecular therapies for tuberous sclerosis and neurofibromatosis**. *Curr Neurol*

Neurosci Rep. 2012; 12:294-301.
12. Gamis AS, Alonzo TA, Gerbing RB, Hilden JM, Sorrell AD, Sharma M, Loew TW, Arceci RJ, Barnard D, Doyle J, Massey G, Perentesis J, Ravindranath Y, Taub J, Smith FO. **Natural history of transient myeloproliferative disorder clinically diagnosed in Down syndrome neonates: a report from the Children's Oncology Group Study A2971**. *Blood*. 2011; 118:6752-9; quiz 6996.
13. Haggstrom AN, Beaumont JL, Lai JS, Adams DM, Drolet BA, Frieden IJ, Garzon MC, Holland KE, Horii KA, Lucky AW, Mancini AJ, Metry DW, Morel KD, Newell BD, Nopper AJ, Siegel D, Swigonski NL, Cella D, Chamlin SL. **Measuring the severity of infantile hemangiomas: instrument development and reliability**. *Arch Dermatol*. 2012; 148:197-202.
14. Hammill AM, Wentzel M, Gupta A, Nelson S, Lucky A, Elluru R, Dasgupta R, Azizkhan RG, Adams DM. **Sirolimus for the treatment of complicated vascular anomalies in children**. *Pediatr Blood Cancer*. 2011; 57:1018-24.
15. Hochman M, Adams DM, Reeves TD. **Current knowledge and management of vascular anomalies, II: malformations**. *Arch Facial Plast Surg*. 2011; 13:425-33.
16. Kaimal V, Chu Z, Mahller YY, Papahadjopoulos-Sternberg B, Cripe TP, Holland SK, Qi X. **Saposin C coupled lipid nanovesicles enable cancer-selective optical and magnetic resonance imaging**. *Mol Imaging Biol*. 2011; 13:886-97.
17. Kavanaugh GM, Wise-Draper TM, Morreale RJ, Morrison MA, Gole B, Schwemberger S, Tichy ED, Lu L, Babcock GF, Wells JM, Drissi R, Bissler JJ, Stambrook PJ, Andreassen PR, Wiesmuller L, Wells SI. **The human DEK oncogene regulates DNA damage response signaling and repair**. *Nucleic Acids Res*. 2011; 39:7465-76.
18. Knapke S, Nagarajan R, Correll J, Kent D, Burns K. **Hereditary cancer risk assessment in a pediatric oncology follow-up clinic**. *Pediatr Blood Cancer*. 2012; 58:85-9.
19. Maugans T, Sheridan RM, Adams D, Gupta A. **Cutaneous vascular anomalies associated with neural tube defects: nomenclature and pathology revisited**. *Neurosurgery*. 2011; 69:112-8; discussion 118.
20. Meyers AB, Towbin AJ, Serai S, Geller JI, Podberesky DJ. **Characterization of pediatric liver lesions with gadoxetate disodium**. *Pediatr Radiol*. 2011; 41:1183-97.
21. Mizukawa B, Wei J, Shrestha M, Wunderlich M, Chou FS, Griesinger A, Harris CE, Kumar AR, Zheng Y, Williams DA, Mulloy JC. **Inhibition of Rac GTPase signaling and downstream prosurvival Bcl-2 proteins as combination targeted therapy in MLL-AF9 leukemia**. *Blood*. 2011; 118:5235-45.
22. Morrison MA, Morreale RJ, Akunuru S, Kofron M, Zheng Y, Wells SI. **Targeting the human papillomavirus E6 and E7 oncogenes through expression of the bovine papillomavirus type 1 E2 protein stimulates cellular motility**. *J Virol*. 2011; 85:10487-98.
23. Myers K, Davies SM, Harris RE, Spunt SL, Smolarek T, Zimmerman S, McMasters R, Wagner L, Mueller R, Auerbach AD, Mehta PA. **The clinical phenotype of children with Fanconi anemia caused by biallelic FANCD1/BRCA2 mutations**. *Pediatr Blood Cancer*. 2012; 58:462-5.
24. Myers KC, Bleesing JJ, Davies SM, Zhang X, Martin LJ, Mueller R, Harris RE, Filipovich AH, Kovacic MB, Wells SI, Mehta PA. **Impaired immune function in children with Fanconi anaemia**. *Br J Haematol*. 2011; 154:234-40.
25. Phillips CL, Miles L, Jones BV, Sutton M, Crone K, Fouladi M. **Medulloblastoma with melanotic differentiation: case report and review of the literature**. *J Neurooncol*. 2011; 103:759-64.
26. Sharkawi E, Hamedani M, Fouladi M. **Eyelid squamous cell carcinoma in situ treated with topical 5-fluorouracil**. *Clin Experiment Ophthalmol*. 2011; 39:915-6.
27. Sharp SE, Gelfand MJ, Absalon MJ. **Altered FDG uptake patterns in pediatric lymphoblastic lymphoma patients receiving induction chemotherapy that includes very high dose corticosteroids**. *Pediatr Radiol*. 2012; 42:331-6.

28. Wagner LM, Smolarek TA, Sumegi J, Marmer D. **Assessment of minimal residual disease in ewing sarcoma**. *Sarcoma*. 2012; 2012:780129.
29. Wani K, Armstrong TS, Vera-Bolanos E, Raghunathan A, Ellison D, Gilbertson R, Vaillant B, Goldman S, Packer RJ, Fouladi M, Pollack I, Mikkelsen T, Prados M, Omuro A, Soffietti R, Ledoux A, Wilson C, Long L, Gilbert MR, Aldape K. **A prognostic gene expression signature in infratentorial ependymoma**. *Acta Neuropathol*. 2012; 123:727-38.
30. Weiss BD, Dasgupta R, Gelfand MJ, Laor T, Yin H, Breneman JC, Lavigne R, Elluru RG, Wagner LM. **Use of sentinel node biopsy for staging parameningeal rhabdomyosarcoma**. *Pediatr Blood Cancer*. 2011; 57:520-3.
31. Wu J, Dombi E, Jousma E, Scott Dunn R, Lindquist D, Schnell BM, Kim MO, Kim A, Widemann BC, Cripe TP, Ratner N. **Preclincial testing of sorafenib and RAD001 in the Nf(flox/flox) ;DhhCre mouse model of plexiform neurofibroma using magnetic resonance imaging**. *Pediatr Blood Cancer*. 2012; 58:173-80.
32. You J, Wells SI. **Human Pappillomaviruses and cancer**. *Cancer associated viruses*. New York: Springer; 2012:463-487.

Faculty, Staff, and Trainees

Faculty Members

John Perentesis, MD, FAAP, Professor

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

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

Michael Absalon, MD, PhD, Assistant Professor

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

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

Denise M. Adams, MD, Professor

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

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

Karen Burns, MD, Assistant Professor

Leadership Clinical Director, Cancer Survivor Center

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

Lionel Chow, MD, Assistant Professor

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

Timothy Cripe, MD, PhD, Professor

Leadership Research Director, Musculoskeletal Tumor Program; Co-Medical Director, Office for Clinical and Translational Research; Director of Pilot and Collaborative Studies, Center for Clinical and Translational Science and Training

Research Interests Mechanistic, preclinical, and clinical studies of oncolytic virotherapy, antiangiogenesis, and signal transduction inhibitors for sarcomas, neuroblastoma and other pediatric solid tumors

Biplab Dasgupta, PhD, Assistant Professor

Research Interests Brain development, energy metabolism, brain cancer

Rachid Drissi, MD, Assistant Professor

Research Interests Replicative senescence, telomere disruption signaling to DNA damage pathways

Maryam Fouladi, MD, FRCP, Professor

Leadership Medical Director, Neuro-Oncology Program; Cincinnati Children's Principal Investigator, Collaborative Ependymoma Research Network (CERN)

Research Interests Novel drug development for the treatment of children with recurrent or poor prognosis brain tumors

James I. Geller, MD, Associate Professor

Leadership Medical Director, Kidney and Liver Tumors Program; Co-Medical Director, Retinoblastoma Program

Research Interests Developmental therapeutics for pediatric solid tumors, especially liver and kidney tumors and retinoblastoma

Adrienne Hammill, MD, Assistant Professor

Research Interests New approaches to the assessment and treatment of hemangiomas and vascular malformations

Trent Hummel, MD, Instructor

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

Beatrice Lampkin, MD, Professor Emerita

Research Interests Blood and bone marrow morphology and the significance thereof in relationship to patients' case histories

Benjamin Mizukawa, MD, Instructor

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

Rajaram Nagarajan, MD, Assistant Professor

Leadership Outpatient and Inpatient Clinical Director; Director of Cancer Control and Outcomes Research, Cancer Survivor Center

Research Interests Bone tumors; functional and quality of life outcomes following cancer therapy

Maureen O'Brien, MD, Assistant Professor

Leadership Associate Director, Leukemia/Lymphoma Program

Research Interests High-risk acute lymphoblastic leukemia; novel therapies for relapsed leukemia and lymphoma; complications of leukemia therapy

Christine Phillips, MD, Instructor

Research Interests Developmental therapeutics for acute myeloid leukemia; pharmacogenomics of cytarabine

and other chemotherapeutic agents

Lars Wagner, MD, Associate Professor

Leadership Medical Director, Musculoskeletal Tumor Program; Cincinnati Children's Principal Investigator, Sarcoma Alliance for Research Through Collaboration (SARC)

Research Interests Developmental therapeutics for neuroblastoma, sarcomas, and brain tumors

Brian D. Weiss, MD, Associate Professor

Leadership Associate Director for Safety and Compliance, Cancer and Blood Diseases Institute; Medical Director, Neuroblastoma Program; Cincinnati Children's Principal Investigator, New Approaches to Neuroblastoma Therapy Consortium (NANT)

Research Interests Targeted agents for neurofibromatosis type 1-related malignancies (including plexiform neurofibromas, optic pathway gliomas, and juvenile myelomonocytic leukemia); chemotherapy safety

Susanne Wells, MD, Associate Professor

Leadership Director, Epithelial Carcinogenesis and Stem Cell Program

Research Interests Epithelial malignancies, human papillomavirus biology and new targets of the HPV E6/E7 oncogenes, the role of epithelial stem cells in carcinogenesis

Joint Appointment Faculty Members

Mi-Ok Kim, PhD, Associate Professor (Center for Epidemiology and Biostatistics)
Ahna Pai, PhD, Assistant Professor (Adherence Psychology)
Saulius Sumanas, PhD, Assistant Professor (Developmental Biology)
Mary Sutton, MD, Associate Professor (Neurology)

Clinical Staff Members

- **Carina Braeutigam, MD**
- **Vasudha Narayanaswamy, MD**

Trainees

- **Michael Bishop, MD**, PL-VI, Children's Mercy Hospital, Kansas City
- **Christopher Dandoy, MD**, PL-V, Miami Children's Hospital
- **Kathleen Dorris, MD**, PL-VII, Children's Memorial Hospital, Northwestern University
- **Sarah Fitzgerald, MD**, PL-VI, Rainbow Babies & Children's Hospital/University of Cleveland
- **Dawn Pinchasik, MD**, PL-V, Children's Hospital of Pittsburgh
- **Jennifer Pope, MD**, PL-VI, Medical College of Wisconsin
- **Ralph Salloum, MD**, PL-V, Detroit Medical Center/Wayne State University
- **Jennifer Williams, MD**, PL-V, T.C. Thompson Children's Hospital/University of Tennessee

Division Collaboration

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

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

Biomedical Informatics; Biostatistics and Epidemiology; Clinical Pharmacology; Pathology; Radiology » B.

Aronow, M. Kim, A. Vinks, D. Witte, M. Gelfand, and A. Towbin

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

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

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

Surgical Services » R. Azizkhan and G. Tiao

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

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

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

Human Genetics » L. Bao and T. Smolarek

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

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

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

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

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

Radiology » M. Gelfand and A. Towbin

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

Endocrinology » S. Rose and M. Rutter

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

Physical Medicine and Rehabilitation » D. Pruitt

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

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

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

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

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

University of Cincinnati Drug Discovery Center » R.Papoian

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

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

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

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

Human Genetics; Neurology; Clinical Pharmacology; Radiology; Neurosurgery; Ophthalmology; Orthopaedic Surgery; Physical Medicine and Rehabilitation; Pathology » E. Schorry, R. Hopkin, A. Vinks, A.

Towbin, S. Sharp, M. Gelfand, M. Sutton, M. Collins, D. Pruitt, C. West, A. Crawford, and K. Crone

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

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

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

Pathology » L. Miles

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

Human Genetics » X. Qi

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

Pathology » L. Miles

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

Neurosurgery » C. Stevenson

Xenograft models of pediatric brain tumors (L. Chow)

Obstetrics and Gynecology » L. Ayensu-Coker

Fertility Consultation Service for oncology patients (K. Burns)

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

Cincinnati chapter of the Oncofertility Consortium

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

Phosphoproteomic analysis of glioblastoma (B. DasGupta)

UC Drug Discovery Center » R. Papoian

Small molecule inhibition of AMP kinase (B. DasGupta)

Developmental Biology » K. Campbell

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

Pathology » K. Setchell

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

Imaging Research Center » D. Lindquist

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

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

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

Ophthalmology » J. Augsburger

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

Human Genetics; Pathology; Surgical Services » N. Leslie, A. Gupta, and 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)

Human Genetics » N. Leslie

Pediatric Hereditary Cancer Predisposition Clinic (J. Geller)

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

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

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

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

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

Phase I trial of HSV1716 (J. Geller)

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

Phase I trial of JX-594 (J. Geller)

Radiology; General and Thoracic Surgery; Pathology » A. Towbin, D. von Allmen, and K. Bove

Director: Multidisciplinary Solid Tumor Board - a weekly educational session pertaining to solid tumors, for all levels of care providers (J. Geller).

Radiology; Ophthalmology » T. Abruzzo and J. Augsburger

Protocol Chair: CCHMC IARB1 **–** (IND# 111358) **-** A Pilot Study of Intra-Ophthalmic Artery Topotecan Infusion for the Treatment of Retinoblastoma (J. Geller).

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

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

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

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

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

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

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

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

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

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

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

EYA4 in MPNST (T. Cripe)

Immunobiology » D. Hildeman

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

Surgical Services; Otolaryngology; Dermatology; Radiology; Pathology; Cardiology; Gastroenterology,

Hepatology and Nutrition; Urology; Endocrinology; Orthopaedics; Neurology; Pulmonary Medicine; Ophthalmology; Pain Management and Palliative Care; Human Genetics » R. Azizkhan, A. Dasgupta, R. Elluru, A. Lucky, M. Patel, T. Abruzzo, W. Ball, A Zbojniewicz, K. Crone, A. Gupta, P. Eghtesday, K. Goldchneider, R. Hirsch, R. Hopkin, A. Kaul, P. Reddy, M. Rutter, J. Sorger, M. Sutton, R. Wood, K. Yakuboff, J. Taylor, M. Yang, M. Seid, B. Dickie, J. McCarthy, K. Shah, C. Merrow, A. Schwentker, E. Mundt, M. Visscher, L. Burns, D. Neilson, and N. Weidner

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

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

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

Pathology » D. Witte

Cincinnati Children's to develop an assay for High-grade patents eligibility (R. Drissi)

Center for Professional Excel Rsch & EBP » R. Pickler

Local and Systemic Responses and Epi-Genetic Influences on Preterm Birth among Hispanic Women (R. Drissi)

Biology » G. Guasch

To determine telomerase activity and telomere length in cells over-expressing hTERT (R. Drissi)

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
ADAMS, D		
Phase II Study of Rapamycin for Complicated Vascular Anomalies		
Food and Drug Administration		
R01 FD 003712	09/25/09-07/31/13	$248,540
CHOW, L		
Micro-RNA Expression in Pediatric High-Grade Glioma		
Bear Necessities Pediatric Cancer Fdn		
-	08/01/11-07/31/12	$40,000
Micro-RNA Expression in Pediatric High-Grade Glioma		
Childhood Brain Tumor Foundation		
-	09/01/11-08/31/13	$22,727
Molecular Targeting of High-Grade Astrocytoma		
The Sontag Foundation		
-	10/01/11-09/30/15	$130,435
Molecular Targeting of Pediatric High-Grade Glioma		
St. Baldrick's Foundation		
	07/01/11-06/30/14	$110,000
CRIPE, T		
Neurofibromatosis Preclinical Consortium Center Award		
The Children's Tumor Foundation		
2011-05-003	07/01/11-06/30/13	$136,364
Phase I Study of HSV1716 in Pediatric Non-CNS Solid Tumors		
Food and Drug Administration		

R01 FD 003717 09/01/10-08/31/13 $152,618

Acidic Phospholipid-Selective Treatment for Neuroblastoma
National Institutes of Health(University of Cincinnati)
R01 CA 158372 09/27/11-07/31/13 $12,760

DORRIS, K

Molecular Epidemiology in Children's Environmental Health
National Institutes of Health(University of Cincinnati)
T32 ES010957 10/01/10-09/30/12 $52,293

DRISSI, R

Biology Studies in the First Phase I Trial of a Telomerarase Inhibitor in Children with Refractory or Recurrent Solid Tumors and Lymphomas
Children's Cancer Research Fund
08/01/11-07/31/12 $40,000

FOULADI, M

Children's Oncology Group Phase I / Pilot Consortium
National Institutes of Health(National Childhood Cancer Foundation)
U10 CA 097452 09/16/11-07/31/12 $25,662

Establishment of an International Diffuse Intrinsic Pontine Glioma (DIPG) Registry
The Cure Starts Now Foundation
01/01/12-12/31/12 $155,000

The Pediatric Brain Tumor Consortium
National Institutes of Health(St Jude's Children's Hospital)
U01 CA 081457 04/01/08-03/31/13 $93,908

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

HAMMILL, A

Ontogeny and Quantitative Multimodal Skin Imaging of Infantile Hemangiomas
The Society for Pediatric Dermatology
07/01/11-06/30/12 $6,500

PERENTESIS, J

Children's Oncology Group Phase I
National Institutes of Health(National Childhood Cancer Foundation)
U01 CA 097452 08/01/07-07/31/11 $23,918

Children's Oncology Group Phase I / Pilot Consortium
National Institutes of Health(National Childhood Cancer Foundation)
U01 CA 097452 09/01/06-07/31/12 $26,124

Cincinnati Children’s Hyundai Scholar in Cancer Survivorship
Hyundai Hope on Wheels
10/01/11-12/01/12 $100,000

Children's Oncology Group Phase I / Pilot Consortium - Per Patient
National Institutes of Health(National Childhood Cancer Foundation)
U01 CA 097452 09/01/06-07/31/12 $38,058

Children's Oncology Group Chair - Per Patient
National Institutes of Health(National Childhood Cancer Foundation)
U10 CA 098543 03/01/11-02/28/12 $57,840

POPE, J

Analysis of Antioxident Polymorphisms in Patients with Down Syndrome and CML
St. Baldrick's Foundation
07/01/10-06/30/12 $70,804

WANG, P-Y

Virotherapy on Primary Neuroblastoma Cells
Alex's Lemonade Stand Foundation
07/01/10-06/30/12 $41,250

WELLS, S

Fanconi Anemia and HPV Transformation
National Institutes of Health
R01 CA 102357 09/28/09-08/31/14 $191,834

Current Year Direct **$1,789,135**

Industry Contracts

FOULADI, M
Genentech, Inc $30,800

GELLER, J
Bayer HealthCare Pharmaceuticals, Inc. $25,000

WEISS, B
CHLA - NANT $15,574

ABSALON, M
Children's Healthcare of Atlanta $3,332

CRIPE, T
Jennerex Biotherapeutics $88,250

WAGNER, L
Abraxis BioScience, LLC $16,178
Amgen, Inc $1,016

Current Year Direct Receipts **$180,150**

Funded Collaborative Efforts

WELLS, S

Fanconi Anemia as a Model for Susceptibility to Human Papillomavirus Infection
National Institutes of Health
Butsch-Kovacic 07/01/11-06/30/16 3%

Total **$1,969,285**