Experimental Hematology

Division Photo

First Row: *F. Guo, D. Pan, M-D. Fiippi, T. Rizvi, N. Ratner, S. Wells;* ***Second Row:*** *Q. Pang, R. Meetei, T. Kalfa, P. Malik;* ***Third Row:*** *P. Andreassen, J. Mulloy, H. Vanderloo, J. Cancelas;* ***Fourth Row:*** *P. Andreassen, T. Cripe, Y. Zheng*

Division Data Summary

Research and Training Details

Number of Faculty	16
Number of Joint Appointment Faculty	10
Number of Research Fellows	21
Number of Research Students	12
Number of Support Personnel	93
Direct Annual Grant Support	$5,455,593
Peer Reviewed Publications	59

Clinical Activities and Training

Number of Clinical Fellows	3

Faculty Members

Yi Zheng, PhD, Professor ; *Division Director; Endowed Chair; Program Leader*
Research Interests: Signaling Program

Paul Andreassen, PhD, Assistant Professor
Research Interests: Leukemia Biology

Jose Cancelas, MD, PhD, Associate Professor ; *Program Leader*
Research Interests: Stem Cell Program

Marie-Dominique Filippi, PhD, Research Assistant Professor
Research Interests: Stem Cell Program

Hartmut Geiger, PhD, Assistant Professor

Research Interests: Stem Cell Program

Fukun Guo, PhD, Research Instructor
Research Interests: Signaling Program

Punam Malik, MD, Associate Professor ; *Program Leader; Director of Cores*
Research Interests: Molecular and Gene Therapy Program

Ruhikanta Meetei, PhD, Assistant Professor
Research Interests: Signaling Program

Shyra Miller, PhD, Research Assistant Professor
Research Interests: Cancer Biology

James Mulloy, PhD, Assistant Professor
Research Interests: Leukemia Biology Program

Dao Pan, PhD, Research Assistant Professor
Research Interests: Molecular and Gene Therapy Program

Qishen Pang, PhD, Associate Professor
Research Interests: Signaling Program

Nancy Ratner, PhD, Professor ; *Program Leader*
Research Interests: Cancer Biology Program

Lilith Reeves, MS, Field Service Associate Professor ; *Director*
Research Interests: Translational Cores

Tilat Aziz Rizvi, PhD, Research Assistant Professor
Research Interests: Cancer Biology Program

Johannes van der Loo, PhD, Field Service Assistant Professor
Research Interests: Vector Production

Joint Appointment Faculty Members

Christopher Baum, MD, Adjunct Associate Professor
Hanover Medical School
Gene Therapy

Tim Cripe, MD, PhD, Associate Professor
Hematology/Oncology
Musculoskeletal Tumor, Translational Research Trials

Timothy Crombleholme, MD, Professor
Surgery
Molecular Fetal Therapy

Stella Davies, MB, BS, PhD, MRCP, Professor
Hematology/Oncology
Blood and Marrow Transplantation, Leukemia Biology

Theodosia Kalfa, MD, PhD, Assistant Professor
Hematology/Oncology
Red Blood Cells and Sickle Cells

Thomas Leemhuis, MD, PhD, Associate Professor
Hoxworth Blood Center
Cell Manipulations

Thomas Moritz, MD, Adjunct Research Professor
Medical Hochschule Hannover
Blood Diseases

Christof VonKalle, MD, Adjunct Research Professor
NCT Heidelburg, Germany
Gene Therapy

Susanne Wells, PhD, Assistant Professor
Hematology/Oncology
Cancer Biology

David Williams, MD, Research Instructor
Children's Hospital Boston

Trainees

- **Zsuzsanna Adam, PhD,** 2006, University of Debrecen, Hungary
- **Shirin Akhter, PhD,** 2003, University of Windsor, Windsor Canada
- **Abdulla Mahmood Ali, PhD,** Indian Institute of Science, India
- **Paritha Arumugan, PhD,** University of Madras, Chennai, TamilNadu, India
- **Emily Bosco, PhD,** 2006, University of Cincinnati
- **HeeDon Chae, PhD,** Pohang University of Science and Technology, South Korea
- **Fu-Sheng Chou, MD,** 2004, National Taiwan University
- **Changhu Du, MD, PhD,** WanNan Medical College, Anhui, China, Guangzhou Institute of Respiratory Disease, Gangzhou Medical College, China
- **Wei Du, MD, PhD,** 2007, North China Coal Medical College, China, Division of Medicine, Graduate School, Tohoku University, Japan
- **Qiang Fan, PhD,** Fudan University, Shanghai, China
- **Brittany Goetz, ,**
- **Daniel Gonzalez-Nieto, PhD,** 2003, Autonoma University of Madrid, Spain
- **Matthew Grogg, PhD,** 2006, University of Dayton
- **Li Guo, PhD,** 2006, Institute of Neuroscience, Chinese Academy of Sciences, Shanghai, China
- **Devikala Gurusamy, ,**
- **Marnie Hall, PhD,** University of Cincinnati, College of Medicine
- **Tomoyasu Higashimoto, PhD,** 2005,
- **Paritha Ithayarasi, PhD,** 2004,
- **Gunnar Johanson, MS,** 2002, Umea Universitet, Sweden
- **Yashuhiko Kamikubo, ,**
- **Gregg Kottyan, ,**
- **Yun-Jung Lee, PhD,** Seoul National University , Seoul Korea
- **Jie Li, PhD,** Academy of Sciences, China
- **Kevin Link, PhD,** 2007, University of Cincinnati
- **Anuj Mankad, PhD,** 2006, Oregon Health and Science University, Portland, Oregon
- **Filippo Marchioni, PhD,** 2005, University of Bologna
- **Debra Mayes, PhD,** 2006, University of Arkansas for Medical Sciences
- **Rachel Mintz, ,**
- **Anjali Mishra, PhD,** 2006, Kanpur University, Kanpur, India
- **Kyle Mitts, BS,** Xavier University
- **Richard Morreale, PhD,** 2007, University of California
- **Deanna Patmore, BS,** 2007, Vorhees College
- **Ajay Perumbeti, MD,** 2006,
- **Ina Rattman, PhD,** University of Duisburg-Essen, Germany
- **Melissa Rawe, ,** University of Cincinnati
- **Keqin Ren, PhD,** University of Puerto Rico, San Juan, USA
- **Abel Sanchez-Aguilera, PhD,** 2006, Complutense University, Madrid, Spain
- **Amitava Sengupta, PhD,** Jadavpur University/Saha Institute of Nuclear Physics Kolkata, India
- **Xun Shang, PhD,** 2004, National University of Singapore
- **Thiyam Singh, PhD,** Central Drug Research Institute, India
- **Nisha Sipes, MS,** 2004, University of Cincinnati
- **Kristy Stengal, BS,** 2005, University of Cincinnati
- **Nambirajan Sundaram, PhD,** 2008,
- **Emily Krueger Thomas, PhD,** Vanderbilt University
- **Fabrizia Urbinati, PhD,** 2005, University of Modena, Italy

- **Daren Wang, PhD,** 2004, Akita University Medical School, University of China Medical School, China
- **Aimee Warunek, ,**
- **Kristoffer Weber, MS,** 2007, University of Frankfurt, Germany
- **Junping Wei, MD,** 2004, Heibei Medical University School of Medicine,
- **Moran Jerabek Willemsen, MS,** 2005, University of Duisburg-Essen Medical School
- **Jon Williams, BS,** 2001, Muskingum College
- **Trisha Wise-Draper, BA,** 2005, Miami University
- **Haiming Xu, MS,** 2003, Shanghai Institute of Biochemistry

Significant Accomplishments in FY08

Rac GTPases as therapeutic targets in chronic myeloid leukemia and acute myeloid leukemia

Two milestone studies have been published in the journal Cancer Cell in November 2007 and June 2008, respectively, that involved collaborative efforts between several laboratories in the division and have important implications for future treatment of leukemia. In the work spearheaded by Drs. David Williams and Jose Cancelas, the investigators used a mouse model of chronic myeloid leukemia initiated by the BCR-ABL oncogene. They showed that the disease is greatly attenuated in a strain of mice that is defective in signaling through the Rac family of small GTPase proteins. When a Rac inhibitor was used, to mimic therapeutic intervention to treat human patients, there was also a very significant inhibition of leukemia growth, and these effects were also seen against BCR-ABL mutant proteins that develop in patients and are currently resistant to standard chemotherapy. This Rac inhibitor was identified by Dr. Yi Zheng, who also collaborated with the laboratory of Dr. James Mulloy on a model for acute myeloid leukemia. In this model, the investigators used human blood stem cells and introduced the leukemia oncogene MLL-AF9 into these cells, mimicking what happens in patients. The Mulloy lab is the only lab in the country to successfully transform a human blood stem cell to leukemia, which they transplanted into mice to establish an animal model for therapeutic testing of compounds on human leukemia cells. These investigators showed that the leukemia they created was highly sensitive to inhibition of the Rac signaling pathway, in fact much more sensitive than normal blood stem cells. These data demonstrate that the Rac signaling pathway plays a critical role in the growth and survival of chronic myeloid leukemia induced by BCR-ABL as well as acute myeloid leukemia induced by MLL-AF9. Therapeutic targeting of Rac could be a unique and important approach to treating leukemias. Dr. Zheng's lab is currently working with Amgen to develop new versions of this drug that could be used in human patients.

Mutation of Neurofibromatosis type 1 gene in neurofibroma formation

Neurofibromatosis type 1 (NF1) is an autosomal dominant inherited disease, affecting 1:3500 individuals worldwide. Nearly all (>90%) of NF1 patients develop plexiform and/or dermal neurofibromas composed of axons, Schwann cells, fibroblasts, perineurial cells, endothelial cells, and mast cells. Schwann cells are believed to be the primary pathogenic cells in neurofibromas because they show biallelic mutation at NF1. However, other cell types present in tumors, in the NF1+/- state, also show cell autonomous defects and have been proposed to be essential for neurofibroma formation. The Cancer Biology program, led by Dr. Nancy Ratner, discovered that the timing the NF1 gene mutation determines whether neurofibroma tumors will form (Cancer Cell, Feb. 2009). In this study, Ratner and her colleagues reported that if the NF1 gene mutated on day 12.5 of a mouse's embryonic development, neurofibroma tumors formed. If the gene mutated at other times during development, in cell culture studies, cells did not alter proliferation. The new data support a key mechanism in tumor development, in which loss of Nf1 at the correct time in development facilitates tumor formation in a wild-type environment. The discovery was made using the first successful robust neurofibromatosis 1 mouse neurofibroma model, a mouse that Ratner's team genetically altered to mimic the disease that occurs in humans. Riding on the success of this work, the "Cincinnati Center for Neurofibromatosis Research" was formed with Dr. Ratner as the Principal Investigator. The center will receive funding of one million dollars per year from the National Institutes of Health. Its goal is to identify and therapeutically target signaling pathways that underlie peripheral nerve tumors resulting from NF1 loss of function. The center combines the cutting edge basic science with the ongoing CCHMC pre-clinical therapeutics testing effort funded by the Children's Tumor Foundation, which is under the supervision of Dr. Tim Cripe.

Significant Publications in FY08

Li J, Sejas DP, Zhang X, Qiu Y, Nattamai KJ, Rani R, Rathburn KR, Geiger H, Williams DA, Bagby GC, Pang Q (2007). "TNF-alpha induces leukemic clonal evolution ex vivo in Fanconi anemia group C murine stem cells." J Clin Invest 117(11): 3283-95.

The molecular pathogenesis of the myeloid leukemias that frequently occur in patients with Fanconi anemia (FA) is not well defined. Hematopoietic stem cells bearing inactivating mutations of FA complementation group C (FANCC)

are genetically unstable and hypersensitive to apoptotic cytokine cues including IFN-gamma and TNF-alpha, but neoplastic stem cell clones that arise frequently in vivo are resistant to these cytokines. Reasoning that the combination of genetic instability and cytokine hypersensitivity might create an environment supporting the emergence of leukemic stem cells, we tested the leukemia-promoting effects of TNF-alpha in murine stem cells. TNF-alpha exposure initially profoundly inhibited the growth of Fancc-/- stem cells. However, longer-term exposure of these cells promoted the outgrowth of cytogenetically abnormal clones that, upon transplantation into congenic WT mice, led to acute myelogenous leukemia. TNF-alpha induced ROS-dependent genetic instability in Fancc-/- but not in WT cells. The leukemic clones were TNF-alpha resistant but retained their characteristic hypersensitivity to mitomycin C and exhibited high levels of chromosomal instability. Expression of FANCC cDNA in Fancc-/- stem cells protected them from TNF-alpha-induced clonal evolution. We conclude that TNF-alpha exposure creates an environment in which somatically mutated preleukemic stem cell clones are selected and from which unaltered TNF-alpha-hypersensitive Fancc-/- stem cells are purged.

Thomas EK, Cancelas JA, Chae H-D, Cox AD, Keller PJ, Perrotti D, Neviani Druker BJ, Setchell KDR, Zheng Y, Harris CE, Williams DA (2007). "Rac guanosine triphosphatases represent integrating molecular therapeutic targets for BCR-ABL-induced myeloproliferative disease." Cancer Cell12(5): 467-78.

Chronic myelogenous leukemia (CML) is a clonal myeloproliferative disease (MPD) initiated by expression of the p210-BCR-ABL fusion protein. We demonstrate in a murine model of p210-BCR-ABL-induced MPD that gene targeting of Rac1 and Rac2 significantly delays or abrogates disease development. Attenuation of the disease phenotype is associated with severely diminished p210-BCR-ABL-induced downstream signaling in primary hematopoietic cells. We utilize NSC23766, a small molecule antagonist of Rac activation, to validate biochemically and functionally Rac as a molecular target in both a relevant animal model and in primary human CML cells in vitro and in a xenograft model in vivo, including in Imatinib-resistant p210-BCR-ABL disease. These data demonstrate that Rac is an additional therapeutic target in p210-BCR-ABL-mediated MPD.

Wei J, Fox C, Wunderlich M, Alvarez S, Cigudosa JD, Wilhelm JE, Zheng Y, Cancelas J, Gu Y, Jansen M, DiMartino F, Mulloy JC 2008. "Microenvironment determines lineage fate in a human model of MLL-AF9 leukemia." Cancer Cell13(6): 483-95

Faithful modeling of mixed-lineage leukemia in murine cells has been difficult to achieve. We show that expression of MLL-AF9 in human CD34+ cells induces acute myeloid, lymphoid, or mixed-lineage leukemia in immunodeficient mice. Some leukemia stem cells (LSC) were multipotent and could be lineage directed by altering either the growth factors or the recipient strain of mouse, highlighting the importance of microenvironmental cues. Other LSC were strictly lineage committed, demonstrating the heterogeneity of the stem cell compartment in MLL disease. Targeting the Rac signaling pathway by pharmacologic or genetic means resulted in rapid and specific apoptosis of MLL-AF9 cells, suggesting that the Rac signaling pathway may be a valid therapeutic target in MLL-rearranged AML.

Wu J, Williams JP, Rizvi TA, Kordich JJ, Witte D, Meijer D, Stemmer-Rachamimov AO, Cancelas JA, Ratner N (2008). "Plexiform and dermal neurofibromas and pigmentation are caused by Nf1 loss in desert hedgehog-expressing cells." Cancer Cell13(2): 105-16.

Neurofibromatosis type 1 (Nf1) mutation predisposes to benign peripheral nerve (glial) tumors called neurofibromas. The point(s) in development when Nf1 loss promotes neurofibroma formation are unknown. We show that inactivation of Nf1 in the glial lineage in vitro at embryonic day 12.5 + 1, but not earlier (neural crest) or later (mature Schwann cell), results in colony-forming cells capable of multilineage differentiation. In vivo, inactivation of Nf1 using a DhhCre driver beginning at E12.5 elicits plexiform neurofibromas, dermal neurofibromas, and pigmentation. Tumor Schwann cells uniquely show biallelic Nf1 inactivation. Peripheral nerve and tumors contain transiently proliferating Schwann cells that lose axonal contact, providing insight into early neurofibroma formation. We suggest that timing of Nf1 mutation is critical for neurofibroma formation.

Yang L, Wang L, Kalfa T, Cancelas JA, Shange X, Pushkaran S, Mo J, Williams DA, Zheng, Y (2007). "Cdc42 critically regulates the balance between myelopoiesis and erythropoiesis." Blood110(12): 3853-61.

The Rho GTPase Cdc42 regulates adhesion, migration and homing, as well as cell cycle progression, of hematopoietic stem cells, but its role in multi-lineage blood development remains unclear. We report that inducible deletion of *cdc42* in *cdc42*-floxed mouse bone marrow by the interferon-responsive, *Mx1-Cre* mediated excision led to myeloid and erythroid developmental defects. Cdc42-deletion affected the number of early myeloid progenitors while suppressing erythroid differentiation. Cdc42 deficient mice developed a fatal myeloproliferative disorder manifested by significant leukocytosis with neutrophilia, myeloid hyper-proliferation, and myeloid cell infiltration into distal organs. Concurrently, Cdc42-deficiency caused anemia and splenomegaly accompanied with decreased bone

marrow BFU-E and CFU-E activities and reduced immature erythroid progenitors, suggesting that Cdc42-deficiency causes a block in the early stage of erythropoiesis. Cdc42 activity is responsive to stimulation by SCF, IL3, SDF-1, and fibronectin. The increased myelopoiesis and decreased erythropoiesis of the knockout mice are associated with an altered gene transcription program in hematopoietic progenitors, including upregulation of pro-myeloid genes such as PU.1, C/EBP1 and Gfi-1 in the common myeloid progenitors and granulocyte-macrophage progenitors and downregulation of pro-erythroid gene such as GATA-2 in the megakaryocyte-erythroid progenitors. Thus, Cdc42 is an essential regulator of the balance between myelopoiesis and erythropoiesis.

Division Highlights

Lilith Reeves, MS

Collaboration with National Toxicology Program for insertional mutagesis studies; Production of large scale GMP virus vector for international gene therapy trials

Tim Cripe, MD, PhD

Tissue inhibitor of metalloproteinase-3 via oncolytic herpesvirus inhibits tumor growth and vascular progenitors, published in *Cancer Res*

Hartmut Geiger, PhD

The retinoblastoma tumor suppressor is a critical intrinsic regulator for hematopoietic stem and progenitor cells under stress, published in Blood.

Jose Cancelas, MD, PhD

FIP1L1/PDGFRa synergizes with SCF to induce systemic mastocytosis in a murine model of chronic eosinophilic leukemia/hypereosinophilic syndrome, published in Blood

Susa Wells, PhD

Papillomavirus E6 and E7 proteins and their cellular targets, published in *Front Biosci*

James Mulloy, PhD

p53 signaling in response to increased DNA damage sensitizes AML1-ETO cells to stress-induced death, published in *Blood*

Qishen Pang, PhD

Defective homing is associated with altered Cdc42 activity in cells from patients with Fanconi anemia group A, published in *Blood*

Punam Malik, MD

Improved human beta-globin expression from self-inactivating lentiviral vectors carrying the chicken hypersensitive site-4 (cHS4) insulator element, published in *Mol Ther*

Dao Pan, PhD

Progression of multiple behavioral deficits with various ages of onset in a murine model of Hurler syndrome, published in *Brain Res*

Ruhikanti Meetei, PhD

FAAP100 is essential for activation of the Fanconi anemia-associated DNA damage response pathway, published in *EMBO J*

Christof VonKalle, PhD

High-resolution insertion-site analysis by linear amplification-mediated PCR (LAM-PCR), published in *Nat Methods*

Christopher Baum, MD

Physiological promoters reduce the genotoxic risk of integrating gene vectors, published in *Mol Ther*

Stella Davies, MB, BS, PhD, MRCP

Pharmacogenetics of minimal residual disease response in children with B-precursor acute lymphoblastic leukemia: a report from the Children's Oncology Group, published in *Blood*

David Williams, MD

Rac1 is essential for intraembryonic hematopoiesis and for the initial seeding of fetal liver with definitive hematopoietic progenitor cells, published in *Blood*

Yi Zheng, PhD

Rac1 controls the formation of midline commissures and the competency of tangential migration in ventral telencephalic neurons, published in *J Neurosci*

Fukun Guo, PhD

Rac GTPase isoforms Rac1 and Rac2 play a redundant and crucial role in T-cell development, published in *Blood*

Division Collaboration

Collaboration with Hematology/Oncology

Collaborating Faculty: Dr. Wagner

MGMT Toxicology Program for Insertional Mutagenesis studies clinical trial

Collaboration with Hematology/Oncology

Collaborating Faculty: Dr. Cripe

HSV Animal Safety studies clinical trial

Collaboration with Allergy and Immunology

Collaborating Faculty: Dr. Rothenberg

FIP1L1/PDGFRa in chronic eosinophilic leukemia. Published in *Blood*.

Collaboration with Pulmonary Biology

Collaborating Faculty: Dr. Whitsett

Transcriptional control of lung stem cells, NIH/NHLBI funded project

Collaboration with Surgery

Collaborating Faculty: Dr. Crombleholme

Tissue inhibitor of metalloproteinase-3 via oncolytic herpesvirus inhibits tumor growth and vascular progenitors. Published in *Cancer Res.*

Collaboration with Infectious Diseases; Immunobiology

Collaborating Faculty: Dr. Sawtell; Dr. Hildeman

Efficacy and safety of the oncolytic herpes simplex virus rRp450 alone and combined with cyclophosphamide. Published in *Mol Ther*.

Collaboration with Biomedical Informatics

Collaborating Faculty: Dr. Aronow

Molecular analysis of human cancer cells infected by a multi-mutated oncolytic HSV-1 reveals a role for SOCS1 in virus replication. Published in *Cancer Gene Therapy.*

Collaboration with Pathology; Hematology/Oncology

Collaborating Faculty: Dr. Collins; Dr. Perentesis

Effective in vivo targeting of the mTOR pathway in malignant peripheral nerve sheath tumors. Published in *Mol Cancer Ther*.

Collaboration with Developmental Biology

Collaborating Faculty: Dr. Kuan

Generating preliminary data in support of R01 application on gene therapy for CNS manifestations in MPS I via BBB-targeted protein delivery.

Collaboration with Hematology/Oncology

Collaborating Faculty: Dr. Joiner

Sickle Cell Center grant (awarded 4/2008) Project 4— genetic manipulation of red cell volume regulation.

Collaboration with Immunobiology

Collaborating Faculty: Dr. Hildeman

Rac GTPase isoforms, Rac1 and Rac2, play redundant and critical role in T-cell development, published in *Blood*.

Collaboration with Developmental Biology

Collaborating Faculty: Dr. Kuan

Rac GTPase in mammalian brain development, funded NIH R01 grant; Rac1 controls the formation of midline commissures and the competency of tangential migration in ventral telencephalic neurons, published in *J. Neuroscience*

Collaboration with Pathology

Collaborating Faculty: Dr. Mo

Cdc42 critically regulates the balance between myelopoiesis and erythropoiesis, published in *Blood*

Collaboration with Hematology/Oncology

Collaborating Faculty: Dr. Smith

Defective adhesion, migration and homing are associated with altered Cdc42 activity in cells from Fanconi anemia patients, published in *Blood*

Collaboration with Pathology

Collaborating Faculty: Dr. Setchell

Rac guanosine triphosphatases represent integrating molecular therapeutic targets for BCR-ABL-induced myeloproliferative disease. Published in *Cancer Cell*.

Mentions in Consumer Media

- Leukaemia/Mixed Up Nature Rev Cancer , Web Site
- Potential Viral Therapy Weapon for Difficult Cancers is Safe and Effective in Study Science Daily , Web Site
- Potential Viral Therapy Weapon for Difficult Cancers is Safe and Effective in Study Think Gene , Web Site
- Potential Viral Therapy Weapon for Diffcult Cancers is Safe and Effective in Study Science Centric , Web Site
- Potential Viral Therapy Weapon for Difficult Cancers is Safe and Effective in Study Bio Medicine , Web Site

Division Publications

1. Trobridge GD, Beard BC, Gooch C, Wohlfahrt M, Olsen P, Fletcher J, Malik P, Kiem HP. **Efficient transduction of pigtailed macaque hematopoietic repopulating cells with HIV-based lentiviral vectors.** *Blood.* 2008; 111: 5537-43.
2. Arumugam PI, Scholes J, Perelman N, Xia P, Yee JK, Malik P. **Improved human beta-globin expression from self-inactivating lentiviral vectors carrying the chicken hypersensitive site-4 (cHS4) insulator element.** *Mol Ther.* 2007; 15: 1863-71.
3. Galla M, Schambach A, Towers GJ, Baum C. **Cellular restriction of retrovirus particle-mediated mRNA transfer.** *J Virol.* 2008; 82: 3069-77.
4. Heuser M, Argiropoulos B, Kuchenbauer F, Yung E, Piper J, Fung S, Schlenk RF, Dohner K, Hinrichsen T, Rudolph C, Schambach A, Baum C, Schlegelberger B, Dohner H, Ganser A, Humphries RK. **MN1 overexpression induces acute myeloid leukemia in mice and predicts ATRA resistance in patients with AML.** *Blood.* 2007; 110: 1639-47.
5. Meyer J, Rhein M, Schiedlmeier B, Kustikova O, Rudolph C, Kamino K, Neumann T, Yang M, Wahlers A, Fehse B, Reuther GW, Schlegelberger B, Ganser A, Baum C, Li Z. **Remarkable leukemogenic potency and quality of a constitutively active neurotrophin receptor, deltaTrkA.** *Leukemia.* 2007; 21: 2171-80.
6. Schiedlmeier B, Santos AC, Ribeiro A, Moncaut N, Lesinski D, Auer H, Kornacker K, Ostertag W, Baum C, Mallo M, Klump H. **HOXB4's road map to stem cell expansion.** *Proc Natl Acad Sci U S A.* 2007; 104: 16952-7.
7. Thornhill SI, Schambach A, Howe SJ, Ulaganathan M, Grassman E, Williams D, Schiedlmeier B, Sebire NJ, Gaspar HB, Kinnon C, Baum C, Thrasher AJ. **Self-inactivating gammaretroviral vectors for gene therapy of X-linked severe combined immunodeficiency.** *Mol Ther.* 2008; 16: 590-8.
8. Akbar H, Kim J, Funk K, Cancelas JA, Shang X, Chen L, Johnson JF, Williams DA, Zheng Y. **Genetic and pharmacologic evidence that Rac1 GTPase is involved in regulation of platelet secretion and aggregation.** *J Thromb Haemost.* 2007; 5: 1747-55.
9. Ghiaur G, Ferkowicz MJ, Milsom MD, Bailey J, Witte D, Cancelas JA, Yoder MC, Williams DA. **Rac1 is essential for intraembryonic hematopoiesis and for the initial seeding of fetal liver with definitive hematopoietic progenitor cells.** *Blood.* 2008; 111: 3313-21.

10. 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.
11. 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.
12. Azizkhan RG, Crombleholme TM. **Congenital cystic lung disease: contemporary antenatal and postnatal management.** *Pediatr Surg Int.* 2008; 24: 643-57.
13. Crombleholme TM, Shera D, Lee H, Johnson M, D'Alton M, Porter F, Chyu J, Silver R, Abuhamad A, Saade G, Shields L, Kauffman D, Stone J, Albanese CT, Bahado-Singh R, Ball RH, Bilaniuk L, Coleman B, Farmer D, Feldstein V, Harrison MR, Hedrick H, Livingston J, Lorenz RP, Miller DA, Norton ME, Polzin WJ, Robinson JN, Rychik J, Sandberg PL, Seri I, Simon E, Simpson LL, Yedigarova L, Wilson RD, Young B. **A prospective, randomized, multicenter trial of amnioreduction vs selective fetoscopic laser photocoagulation for the treatment of severe twin-twin transfusion syndrome.** *Am J Obstet Gynecol.* 2007; 197: 396 e1-9.
14. Gordon A, Kozin ED, Keswani SG, Vaikunth SS, Katz AB, Zoltick PW, Favata M, Radu AP, Soslowsky LJ, Herlyn M, Crombleholme TM. **Permissive environment in postnatal wounds induced by adenoviral-mediated overexpression of the anti-inflammatory cytokine interleukin-10 prevents scar formation.** *Wound Repair Regen.* 2008; 16: 70-9.
15. Heineke J, Auger-Messier M, Xu J, Oka T, Sargent MA, York A, Klevitsky R, Vaikunth S, Duncan SA, Aronow BJ, Robbins J, Crombleholme TM, Molkentin JD. **Cardiomyocyte GATA4 functions as a stress-responsive regulator of angiogenesis in the murine heart.** *J Clin Invest.* 2007; 117: 3198-210.
16. Livingston JC, Lim FY, Polzin W, Mason J, Crombleholme TM. **Intrafetal radiofrequency ablation for twin reversed arterial perfusion (TRAP): a single-center experience.** *Am J Obstet Gynecol.* 2007; 197: 399 e1-3.
17. Livingston JC, Malik KM, Crombleholme TM, Lim FY, Sibai BM. **Mirror syndrome: a novel approach to therapy with fetal peritoneal-amniotic shunt.** *Obstet Gynecol.* 2007; 110: 540-3.
18. Parvadia JK, Keswani SG, Vaikunth S, Maldonado AR, Marwan A, Stehr W, Erwin C, Uzvolgyi E, Warner BW, Yamano S, Taichman N, Crombleholme TM. **Role of VEGF in small bowel adaptation after resection: the adaptive response is angiogenesis dependent.** *Am J Physiol Gastrointest Liver Physiol.* 2007; 293: G591-8.
19. Michelfelder E, Gottliebson W, Border W, Kinsel M, Polzin W, Livingston J, Khoury P, Crombleholme T. **Early manifestations and spectrum of recipient twin cardiomyopathy in twin-twin transfusion syndrome: relation to Quintero stage.** *Ultrasound Obstet Gynecol.* 2007; 30: 965-71.
20. 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.
21. Hansen MD, Filipovich AH, Davies SM, Mehta P, Bleesing J, Jodele S, Hayashi R, Barnes Y, Shenoy S. **Allogeneic hematopoietic cell transplantation (HCT) in Hurler's syndrome using a reduced intensity preparative regimen.** *Bone Marrow Transplant.* 2008; 41: 349-53.
22. Mehta PA, Davies SM. **Allogeneic transplantation for childhood ALL.** *Bone Marrow Transplant.* 2008; 41: 133-9.
23. Daria D, Filippi MD, Knudsen ES, Faccio R, Li Z, Kalfa T, Geiger H. **The retinoblastoma tumor suppressor is a critical intrinsic regulator for hematopoietic stem and progenitor cells under stress.** *Blood.* 2008; 111: 1894-902.
24. Monk KR, Wu J, Williams JP, Finney BA, Fitzgerald ME, Filippi MD, Ratner N. **Mast cells can contribute to axon-glial dissociation and fibrosis in peripheral nerve.** *Neuron Glia Biol.* 2007; 3: 233-44.
25. Bhatla D, Gerbing RB, Alonzo TA, Mehta PA, Deal K, Elliott J, Meshinchi S, Geiger H, Perentesis JP, Lange BJ, Davies SM. **DNA repair polymorphisms and outcome of chemotherapy for acute myelogenous leukemia: a report from the Children's Oncology Group.** *Leukemia.* 2008; 22: 265-72.
26. Li J, Sejas DP, Zhang X, Qiu Y, Nattamai KJ, Rani R, Rathbun KR, Geiger H, Williams DA, Bagby GC, Pang Q. **TNF-alpha induces leukemic clonal evolution ex vivo in Fanconi anemia group C murine stem cells.** *J Clin Invest.* 2007; 117: 3283-95.
27. Zychlinski D, Schambach A, Modlich U, Maetzig T, Meyer J, Grassman E, Mishra A, Baum C. **Physiological promoters reduce the genotoxic risk of integrating gene vectors.** *Mol Ther.* 2008; 16: 718-25.
28. Higashimoto T, Urbinati F, Perumbeti A, Jiang G, Zarzuela A, Chang LJ, Kohn DB, Malik P. **The woodchuck hepatitis virus post-transcriptional regulatory element reduces readthrough transcription from retroviral vectors.** *Gene Ther.* 2007; 14: 1298-304.
29. Johansson G, Mahller YY, Collins MH, Kim MO, Nobukuni T, Perentesis J, Cripe TP, Lane HA, Kozma SC, Thomas G, Ratner N. **Effective in vivo targeting of the mammalian target of rapamycin pathway in malignant peripheral nerve sheath tumors.** *Mol Cancer Ther.* 2008; 7: 1237-45.

30. Yang L, Wang L, Kalfa TA, Cancelas JA, Shang X, Pushkaran S, Mo J, Williams DA, Zheng Y. **Cdc42 critically regulates the balance between myelopoiesis and erythropoiesis.** *Blood.* 2007; 110: 3853-61.
31. Raynard S, Zhao W, Bussen W, Lu L, Ding YY, Busygina V, Meetei AR, Sung P. **Functional role of BLAP75 in BLM-topoisomerase IIIalpha-dependent holliday junction processing.** *J Biol Chem.* 2008; 283: 15701-8.
32. Durig J, Ebeling P, Grabellus F, Sorg UR, Mollmann M, Schutt P, Gothert J, Sellmann L, Seeber S, Flasshove M, Duhrsen U, Moritz T. **A novel nonobese diabetic/severe combined immunodeficient xenograft model for chronic lymphocytic leukemia reflects important clinical characteristics of the disease.** *Cancer Res.* 2007; 67: 8653-61.
33. Ebeling P, Eisele L, Schuett P, Bauer S, Schuette J, Moritz T, Seeber S, Flasshove M. **Docetaxel and gemcitabine in the treatment of soft tissue sarcoma - a single-center experience.** *Onkologie.* 2008; 31: 11-6.
34. Eisele L, Klein-Hitpass L, Chatzimanolis N, Opalka B, Boes T, Seeber S, Moritz T, Flasshove M. **Differential expression of drug-resistance-related genes between sensitive and resistant blasts in acute myeloid leukemia.** *Acta Haematol.* 2007; 117: 8-15.
35. Rattmann I, Kleff V, Feldmann A, Ludwig C, Sorg UR, Opalka B, Moritz T, Flasshove M. **Reliable generation of stable high titer producer cell lines for gene therapy.** *Intervirology.* 2007; 50: 197-203.
36. Schutt P, Rebmann V, Brandhorst D, Wiefelsputz J, Ebeling P, Opalka B, Seeber S, Nowrousian MR, Moritz T, Grosse-Wilde H. **The clinical significance of soluble human leukocyte antigen class-I, ICTP, and RANKL molecules in multiple myeloma patients.** *Hum Immunol.* 2008; 69: 79-87.
37. Sorg UR, Kleff V, Fanaei S, Schumann A, Moellmann M, Opalka B, Thomale J, Moritz T. **O6-methylguanine-DNA-methyltransferase (MGMT) gene therapy targeting haematopoietic stem cells: studies addressing safety issues.** *DNA Repair (Amst).* 2007; 6: 1197-209.
38. Troeger A, Siepermann M, Escherich G, Meisel R, Willers R, Gudowius S, Moritz T, Laws HJ, Hanenberg H, Goebel U, Janka-Schaub GE, Mahotka C, Dilloo D. **Survivin and its prognostic significance in pediatric acute B-cell precursor lymphoblastic leukemia.** *Haematologica.* 2007; 92: 1043-50.
39. Welt A, Schutt P, Derks C, Ebeling P, Muller S, Metz K, Anhuf J, Moritz T, Seeber S, Nowrousian MR. **Long-term results of a phase-I/II study of sequential high-dose chemotherapy with autologous stem cell transplantation in the initial treatment of aggressive non-Hodgkin's lymphoma.** *Tumori.* 2007; 93: 409-16.
40. Pan D, Sciascia A, 2nd, Vorhees CV, Williams MT. **Progression of multiple behavioral deficits with various ages of onset in a murine model of Hurler syndrome.** *Brain Res.* 2008; 1188: 241-53.
41. Wang D, Worsham DN, Pan D. **Co-expression of MGMT(P140K) and alpha-L-iduronidase in primary hepatocytes from mucopolysaccharidosis type I mice enables efficient selection with metabolic correction.** *J Gene Med.* 2008; 10: 249-59.
42. Kleff V, Sorg UR, Bury C, Suzuki T, Rattmann I, Jerabek-Willemsen M, Poremba C, Flasshove M, Opalka B, Trapnell B, Dirksen U, Moritz T. **Gene therapy of beta(c)-deficient pulmonary alveolar proteinosis (beta(c)-PAP): studies in a murine in vivo model.** *Mol Ther.* 2008; 16: 757-64.
43. Wu J, Williams JP, Rizvi TA, Kordich JJ, Witte D, Meijer D, Stemmer-Rachamimov AO, Cancelas JA, Ratner N. **Plexiform and dermal neurofibromas and pigmentation are caused by Nf1 loss in desert hedgehog-expressing cells.** *Cancer Cell.* 2008; 13: 105-16.
44. Thomas EK, Cancelas JA, Chae HD, Cox AD, Keller PJ, Perrotti D, Neviani P, Druker BJ, Setchell KD, Zheng Y, Harris CE, Williams DA. **Rac guanosine triphosphatases represent integrating molecular therapeutic targets for BCR-ABL-induced myeloproliferative disease.** *Cancer Cell.* 2007; 12: 467-78.
45. Thomas EK, Cancelas JA, Zheng Y, Williams DA. **Rac GTPases as key regulators of p210-BCR-ABL-dependent leukemogenesis.** *Leukemia.* 2008; 22: 898-904.
46. Schmidt M, Schwarzwaelder K, Bartholomae C, Zaoui K, Ball C, Pilz I, Braun S, Glimm H, von Kalle C. **High-resolution insertion-site analysis by linear amplification-mediated PCR (LAM-PCR).** *Nat Methods.* 2007; 4: 1051-7.
47. Schwarzwaelder K, Howe SJ, Schmidt M, Brugman MH, Deichmann A, Glimm H, Schmidt S, Prinz C, Wissler M, King DJ, Zhang F, Parsley KL, Gilmour KC, Sinclair J, Bayford J, Peraj R, Pike-Overzet K, Staal FJ, de Ridder D, Kinnon C, Abel U, Wagemaker G, Gaspar HB, Thrasher AJ, von Kalle C. **Gammaretrovirus-mediated correction of SCID-X1 is associated with skewed vector integration site distribution in vivo.** *J Clin Invest.* 2007; 117: 2241-9.
48. Chae HD, Lee KE, Williams DA, Gu Y. **Cross-talk between RhoH and Rac1 in regulation of actin cytoskeleton and chemotaxis of hematopoietic progenitor cells.** *Blood.* 2008; 111: 2597-605.
49. Ball CR, Pilz IH, Schmidt M, Fessler S, Williams DA, von Kalle C, Glimm H. **Stable differentiation and clonality of murine long-term hematopoiesis after extended reduced-intensity selection for MGMT P140K transgene expression.** *Blood.* 2007; 110: 1779-87.

50. Muller LU, Milsom MD, Kim MO, Schambach A, Schuesler T, Williams DA. **Rapid lentiviral transduction preserves the engraftment potential of Fanca(-/-) hematopoietic stem cells.** *Mol Ther.* 2008; 16: 1154-60.
51. Sherafat-Kazemzadeh R, Mehta SN, Care MM, Kim MO, Williams DA, Rose SR. **Small pituitary size in children with Fanconi anemia.** *Pediatr Blood Cancer.* 2007; 49: 166-70.
52. Williams DA, Zheng Y, Cancelas JA. **Rho GTPases and regulation of hematopoietic stem cell localization.** *Methods Enzymol.* 2008; 439: 365-93.
53. Wu X, Tu X, Joeng KS, Hilton MJ, Williams DA, Long F. **Rac1 activation controls nuclear localization of beta-catenin during canonical Wnt signaling.** *Cell.* 2008; 133: 340-53.
54. Wise-Draper TM, Wells SI. **Papillomavirus E6 and E7 proteins and their cellular targets.** *Front Biosci.* 2008; 13: 1003-17.
55. Krejci O, Wunderlich M, Geiger H, Chou FS, Schleimer D, Jansen M, Andreassen PR, Mulloy JC. **p53 signaling in response to increased DNA damage sensitizes AML1-ETO cells to stress-induced death.** *Blood.* 2008; 111: 2190-9.
56. 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.* 2008; 13: 483-95.
57. Castilho RM, Squarize CH, Patel V, Millar SE, Zheng Y, Molinolo A, Gutkind JS. **Requirement of Rac1 distinguishes follicular from interfollicular epithelial stem cells.** *Oncogene.* 2007; 26: 5078-85.
58. Liu N, Zhang G, Bi F, Pan Y, Xue Y, Shi Y, Yao L, Zhao L, Zheng Y, Fan D. **RhoC is essential for the metastasis of gastric cancer.** *J Mol Med.* 2007; 85: 1149-56.
59. Tan W, Palmby TR, Gavard J, Amornphimoltham P, Zheng Y, Gutkind JS. **An essential role for Rac1 in endothelial cell function and vascular development.** *FASEB J.* 2008; 22: 1829-38.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards — Annual Direct / Project Period Direct

Baum, C

Prevention of Insertional Mutagenesis In Gene Therapy
National Institutes of Health
R01 CA 107492 — 08/01/05 - 05/31/09 — $149,813 / $611,913

Bosco, E

Training Program in Cancer Therapeutics
National Institutes of Health (University of Cincinnati)
T32 CA 117846 — 02/01/07 - 01/31/09 — $22,736 / $59,732

Cancelas, J

Rac in p190-BCR/ABL Induced Acute Lymphoblastic Leukemia
Alex's Lemonade Stand Foundation
07/01/07 - 06/30/09 — $100,000 / $200,000

Inhibition of Rac GTPases in the Therapy of Chronic Myelogenous Leukemia
Department of Defense - Army
W81XWH-07-1-0297 — 04/01/07 - 03/31/10 — $150,261 / $450,000

Filippi, M

The Role of the Small GTPase RhoA in Hematopoietic Stem Cell Engraftment
American Heart Association - National
0635027N — 07/01/06 - 06/30/10 — $59,091 / $236,364

Geiger, H

The Role of the RB Protein in Leukemia Progression
Cancer Free Kids
05/01/08 - 04/30/09 — $40,000 / $40,000

Genomic Integrity and DNA-Repair Pathways in Aging
Ellison Medical Foundation
07/01/05 - 06/30/09 — $46,296 / $185,184

Oncogenic Events in Thyroid Neoplasia
National Institutes of Health (Sloan-Kettering Institute for Cancer Research)
R01 CA 072597 | 01/01/08 - 12/31/09 | $12,875 / $26,136

Young Stem Cell Potential in Aged Mice
National Institutes of Health
R21 DK 077762 | 04/01/08 - 03/31/10 | $125,000 / $275,000

Molecular Mechanism of Age-Related Decline of Nonhomologous DNA and Joining
National Institutes of Health (University of Rochester)
R01 AG 02737 | 07/01/06 - 06/30/11 | $5,364 / $28,207

Pathways to Mutagenesis in Vivo and in Stem Cells
National Institutes of Health (University of Cincinnati)
R01 ES 012695 | 08/15/06 - 06/30/10 | $5,259 / $28,207

Guo, F

Genetic and Biochemical Evaluation of Rac1 GTPase Signaling Mechanism in Primary Cells
American Heart Association - Ohio
0765194B | 07/01/07 - 06/30/09 | $55,000 / $110,000

Link, K

Training Program in Cancer Therapeutics
National Institutes of Health (University of Cincinnati)
T32 CA117846 | 02/01/08 - 01/31/09 | $49,346 / $49,346

Malik, P

Gene Therapy Using Hematopoietic Stem Cells
National Institutes of Health (Children's Hospital Los Angeles)
P01 HL 073104 | 12/15/06 - 03/31/08 | $210,033 / $227,880

Lentiviral Vectors for Gene Therapy for Beta-Thalassemia
National Institutes of Health
R01 HL 070135 | 09/01/06 - 03/31/09 | $76,974 / $196,544

Role of Placenta Growth Factor in Sickle ACS
National Institutes of Health
R01 HL 079916 | 09/01/06 - 05/31/09 | $610,906 / $1,767,492

Cincinnati Comprehensive Sickle Cell Center - Project 5
National Institutes of Health
U54 HL070871 | 06/15/08 - 03/31/12 | $389,734 / $1,558,936

Mankad, A

Characterization of the FANCA Protein and Patient Derived FANCA Mutants
Fanconi Anemia Research Foundation
08/01/06 - 07/31/08 | $35,000 / $70,000

Mayes, D

Training Program in Cancer Therapeutics
National Institutes of Health (University of Cincinnati)
T32 CA 117846 | 12/01/06 - 08/31/08 | $29,232 / $66,228

Meetei, R

Role of FAAP250/FANCM Enzymatic Activities in the FA-DNA Repair Function
American Society of Hematology
07/01/06 - 12/31/08 | $75,000 / $150,000

Defining the Fanconi Anemia-DNA Repair Pathway by Protein Association Analysis
Fanconi Anemia Research Foundation
10/01/07 - 09/30/09 | $75,000 / $150,000

Function and Regulation of FADCM in Fanconi Anemia
National Institutes of Health
R01 HL 084082 | 05/01/07 - 04/30/12 | $250,000 / $1,250,000

Milsom, M

Genetic Correction of the Fanconi Anemia Stem Cell Defects
National Blood Foundation
07/01/07 - 02/29/08 $32,500 / $32,500

Morreale, R

Training Program with Regulations of Cellular Growth and Differentiation
National Institutes of Health (University of Cincinnati)
T32 CA 059268 08/01/07 - 07/31/09 $36,996 / $75,972

Mulloy, J

Genetic Screen for Pathways Cooperating with AML1-ETO in Leukemia Induction
Ohio Cancer Research Associates
07/01/06 - 06/30/08 $22,727 / $45,454

The Role of CBFb-MYH11 in Acute Myeloid Leukemia
National Institutes of Health
R01 CA 118319 04/15/06 - 02/28/11 $172,353 / $861,765

Microenvironment and Flt3 Signaling in MLL Leukemia
Gabrielle's Angel Foundation for Cancer Research
06/01/08 - 05/31/11 $68,182 / $204,545

The Role of CBFb-MYH11 in Acute Myeloid Leukemia
National Institutes of Health
R01 CA 118319-S1 06/01/08 - 02/29/11 $84,987 / $201,058

Pang, Q

Role Of Nucleophosmin in FA-Evolved Leukemia
National Institutes of Health
R01 CA 109641 07/09/04 - 04/30/09 $194,378 / $998,939

Role of FA Protein Complexes in Hematopoiesis
National Institutes of Health
R01 HL 076712 07/05/05 - 06/30/09 $237,045 / $968,215

Ratner, N

Compound Screening for NF1 Drug Discovery
University of Cincinnati Cancer Center
08/01/07 - 07/31/08 $40,000 / $40,000

Modelling Brain Defects In NF1
Department of Defense - Army
W81XWH-06-1-0114 11/15/05 - 11/14/08 $244,111 / $715,948

Mitogenic Activities In Neurofibromatosis
National Institutes of Health
R01 NS 028840 03/22/06 - 01/31/11 $217,837 / $1,354,456

Schwann Cells in Neurofibromatosis Type 2 (NF2)
National Institutes of Health
R01 CA 118032 08/13/07 - 05/31/12 $190,000 / $950,000

Wei, J

A Novel Model of MLL-AF9 Leukemia Using Primary HSPC in NOD/SCID Mice
American Society of Hematology
07/01/07 - 06/30/09 $50,000 / $100,000

Williams, D

Rac Proteins in Hematopoietic Cell Survival and Function
National Institutes of Health (Children's Hospital Boston)
R01 DK 062757 09/01/07 - 02/28/08 $78,964 / $78,964

Targeting Rac GTPases in Bcr-abl-Induced Chronic Myelogenous Leukemia
The Leukemia and Lymphoma Society

	10/01/05 - 11/30/07	$180,018 / $540,000

RhoH GTPase in Hematopoiesis and Cancer
National Institutes of Health (Children's Hospital Boston)

R01 CA113969	12/01/07 - 02/28/08	$34,424 / $34,424

Chemoresistance and Stem Cell Selection
National Institutes of Health (Children's Hospital Boston)

R01 DK074310	01/01/08 - 02/29/08	$6,729 / $6,729

Zheng, Y

Interaction of Rho GTPases with Regulators and Effectors
National Institutes of Health

R01 GM 060523	07/01/04 - 06/30/09	$164,984 / $707,895

Targeting RhoA in Lymphomagenesis
National Institutes of Health

R03 CA 125830	09/15/06 - 08/31/08	$48,550 / $98,550

Rho GTPase-Activating Proteins In Cancer
National Institutes of Health

R01 CA 105117	03/01/04 - 02/28/09	$155,502 / $819,650

Dbl-Like Regulators of Small GTP-Binding Proteins
National Institutes of Health

R01 GM 053943	04/01/05 - 03/31/09	$189,636 / $774,572

Cell Type and Stimulus-Specific Role of CDC42 in Blood
National Institutes of Health

R01 HL 085362	07/01/06 - 05/31/11	$242,750 / $1,221,000

Rac GTPases as Targets in Lymphomagenesis
National Institutes of Health

R01 CA 125658	02/10/07 - 01/31/12	$190,000 / $950,000

Current Year Direct	**$5,455,593**

Service Collaborations

Reeves, L

Industry: Proj N1 GAD	$ 277,366
Industry: Proj N1 NPY	$ 63,515
Industry: Proj J1	$ 44,746
Industry: GOSH	$ 62,630
Industry: Necker	$ 62,630
Industry: Nationwide	$ 32,330
Industry: GeneDx	$ 2,773
Industry: Hoxworth (QC, CAP, CFU)	$ 25,913
Industry: OSU (CD, WC)	$ 20,088
Industry: GRI	$ 2,370
Industry: Shriners	$ 1,196
Industry: DanaFarber Institute	$ 763
Industry: UK	$ 494
Industry: UC	$ 1,728
NTP Battelle	$ 162,120

Current Year Direct	**$760,662**

Funded Collaborative Efforts

Cancelas, J

Transcriptional Control of Respiratory Epithelial Progenitor Cells
National Institutes of Helath

Whitsett, Jeffery	09/28/07 - 06/30/11	10 %

Pan, D

Cincinnati Comprehensive Sickle Cell Center
National Institutes of Health

Joiner, Clinton	06/15/08 - 03/31/12	15 %

Ratner, N

Cincinnati NF1 Preclinical Testing Center
The Children's Tumor Foundation

Cripe, Timothy	12/01/07 - 05/31/11	10 %

Total $6,216,255