

Division Details

Division Data Summary

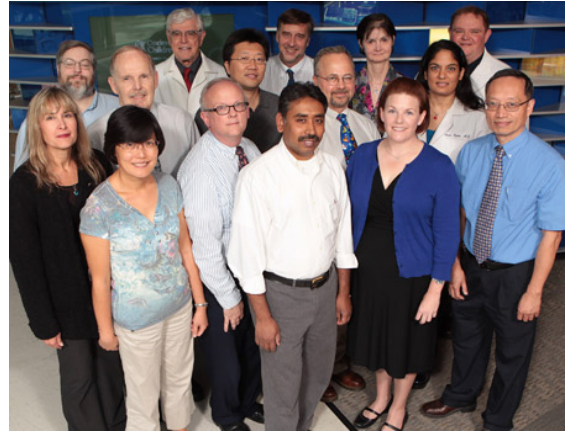
Research and Training Details

Number of Faculty	21
Direct Annual Grant Support	\$1,014,659
Peer Reviewed Publications	50

Clinical Activities and Training

Number of Clinical Staff	0
Number of Clinical Fellows	2
Inpatient Encounters	807,744
Outpatient Encounters	1,136,000

Division Photo



Row 1: L Miles, P Steele, M Azam, M O'Leary, P Tang

Row 2: K Wikenheiser-Brokamp, M Miles, G Huang, J Mortensen, A Gupta

Row 3: R McMasters, K Bove, D Witte, M Collins, T Boyd

Significant Accomplishments

Cancer Biology Program

Cincinnati Children's is a nationally recognized center for diagnostic evaluation and management of children with malignancies of the hematopoietic system, committed to developing a world class research program in cancer. This is the result of a joint program and commitment that includes the divisions of Hematology/Oncology Research, Immunobiology, Hematology and Pathology under the leadership of Yi Zheng, PhD, and Lee Grimes, PhD. This effort has brought together a team of collaborative and nationally recognized leaders in cancer cell research and has provided an infrastructure of core laboratories and technologies supported by these divisions to provide the latest technology and support to the growing research program. Faculty members of the Division of Pathology, including Gang Huang, PhD, and Mohammad Azam, PhD, have funded research programs supporting this effort. The success of this joint effort to establish a strong program in cancer biology was evident at the Ninth International Workshop on Molecular Aspects of Myeloid Stem Cell Development in Leukemia jointly sponsored by the Cancer and Blood Diseases Institute of Cincinnati, and division of Pathology and organized by Lee Grimes, PhD, Division of Immunobiology. This high profile and successful meeting brought investigators and leaders in the field of cancer biology from all across the United States, Europe, Canada, Australia and Japan.

Molecular Basis for Lung Disease

Kathryn Wikenheiser-Brokamp, PhD, studies the genetic and developmental basis of lung disease with specific interest in identifying the molecular basis of lung cancer and pediatric cystic lung disease. She has identified

critical functions for the RB/P16 and P53 tumor suppressant pathway in pulmonary epithelial cell growth in the context of lung development, injury repair and carcinogenesis. Her studies are supported by a National Institutes of Health RO1 grant and funding from the American Cancer Society. Wikenheiser-Brokamp is part of a multi-institutional, interdisciplinary team of physicians and researchers that recently discovered DICER1 mutations in a familial tumor predisposition syndrome that develop pleural pulmonary blastoma. She now leads a consortium towards elucidating how DICER1 and the micro RNAs it generates, controls organogenesis and oncogenesis. In addition, Wikenheiser-Brokamp has recently continued her research funding through the Saint Baldrick's Research Consortium grant support for basic science studies and development of the international pleural pulmonary blastoma treatment in biology registry.

Neuro-Oncology Program

Recently under the direction of Maryam Fouladi, MD, Cincinnati Children's has been selected to become a full member institution in the NCI Pediatric Brain Tumor Consortium. This consortium is the National Cancer Institute's primary mechanism for developing new drugs for children with brain tumors. The collaboration will involve Neurosurgery, Neuroimaging, Pathology, Neuropsychology, Neurology, Endocrinology, Physical Medical and Rehabilitation and the University of Cincinnati Department of Radiation Oncology to allow Cincinnati Children's to become a national center for the treatment and management of pediatric brain tumors. Lili Miles, MD, will head up the pathology diagnostic service and review of children referred for pediatric brain tumors. She will also work with the division to establish and provide core laboratory support to develop pathology-based markers to support this effort.

Division Publications

1. Assa'ad AH, Gupta SK, Collins MH, Thomson M, Heath AT, Smith DA, Perschy TL, Jurgensen CH, Ortega HG, Aceves SS. **An antibody against IL-5 reduces numbers of esophageal intraepithelial eosinophils in children with eosinophilic esophagitis.** *Gastroenterology*. 2011; 141:1593-604.
2. Brown NM, Lindley SL, Witte DP, Setchell KDR. **Impact of perinatal exposure to equol enantiomers on reproductive development in rodents.** *Reproductive Toxicology*. 2011; 32:33-42.
3. Bulmer JN, Burton GJ, Collins S, Cotechini T, Crocker IP, Croy BA, Cvitic S, Desforjes M, Deshpande R, Gasperowicz M, Groten T, Haugen G, Hiden U, Host AJ, Jirkovska M, Kiserud T, Konig J, Leach L, Murthi P, Pijnenborg R, Sadekova ON, Salafia CM, Schlabritz-Loutsevitch N, Stanek J, Wallace AE, Westermeier F, Zhang J, Lash GE. **IFPA Meeting 2011 workshop report II: Angiogenic signaling and regulation of fetal endothelial function; placental and fetal circulation and growth; spiral artery remodeling.** *Placenta*. 2012; 33 Suppl:S9-S14.
4. Chamulitrat W, Zhang W, Xu W, Pathil A, Setchell K, Stremmel W. **Hepatoprotectant ursodeoxycholy lysophosphatidylethanolamide increasing phosphatidylcholine levels as a potential therapy of acute liver injury.** *Front Physiol*. 2012; 3:24.
5. Chen H, Zheng J, Xue L, Meng Y, Wang Y, Zheng B, Fang F, Shi S, Qiu Q, Jiang P, Lu Z, Mo JQ, Lu J, Guan MX. **The 12S rRNA A1555G mutation in the mitochondrial haplogroup D5a is responsible for maternally inherited hypertension and hearing loss in two Chinese pedigrees.** *Eur J Hum Genet*. 2012; 20:607-12.
6. Clarkson TB, Utian WH, Barnes S, Gold EB, Basaria SS, Aso T, Kronenberg F, Frankenfeld CL, Cline JMA, Landgren BM, Gallagher JC, Weaver CM, Hodis HN, Brinton RD, Maki PM, Setchell KDR, Setchell DR, Allmen TI, Messina MJ, Shu XO, Ishimi Y, Wong WW, Kim H. **The role of soy isoflavones in menopausal health: Report of the North American Menopause Society/Wulf H. Utian Translational Science Symposium in Chicago, IL (October 2010).** *Menopause*. 2011; 18:732-753.

7. Clerici C, Nardi E, Battezzati PM, Asciutti S, Castellani D, Corazzi N, Giuliano V, Gizzi S, Perriello G, Di Matteo G, Galli F, Satchell KD. **Novel soy germ pasta improves endothelial function, blood pressure, and oxidative stress in patients with type 2 diabetes.** *Diabetes Care.* 2011; 34:1946-8.
8. Coe A, Collins MH, Lawal T, Loudon E, Levitt MA, Pena A. **Reoperation for Hirschsprung disease: pathology of the resected problematic distal pull-through.** *Pediatr Dev Pathol.* 2012; 15:30-8.
9. Das A, Green JV, Henson M, DeBurger B, Mortensen J. **Cases in Clinical Microbiology. Case Twenty One: A Case of Asymptomatic Pulmonary Nodules.** *Journal of Continuing Education Topics & Issues.* 2012; 14:10-14.
10. Dickinson SI, Mo J, Cauling HS. **Lymphadenopathy with Predominant Follicular Patterns.** *Non-Neoplastic Hematopathology and Infections.* Hoboken, NJ: Wiley-Blackwell; 2012:249-284.
11. Fernandez NC, Mortensen J. **Cases in Clinical Microbiology. Urinary Schistosomiasis: A Rare Cause of Hematuria in the United States.** *Journal of Continuing Education Topics and Issues.* 2012; 14:46-50.
12. Grom AA, Jordan MB, Mo JQ. **Disorders of Macrophages and Dendritic Cells.** *ACP Medicine Atlas of Dermatology: Cutaneous Manifestations of Systemic Diseases.* Hamilton, Ontario: Decker Publishing; 2012.
13. Henderson CJ, Abonia JP, King EC, Putnam PE, Collins MH, Franciosi JP, Rothenberg ME. **Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis.** *J Allergy Clin Immunol.* 2012; 129:1570-8.
14. Huang G, Zhao X, Wang L, Elf S, Xu H, Sashida G, Zhang Y, Liu Y, Lee J, Menendez S, Yang Y, Yan X, Zhang P, Tenen DG, Osato M, Hsieh JJD, Nimer SD. **The ability of MLL to bind RUNX1 and methylate H3K4 at PU.1 regulatory regions is impaired by MDS/AML-associated RUNX1/AML1 mutations.** *Blood.* 2011; 118:6544-6552.
15. Huppert JS, Bennett K, Kollar LM, Pattullo L, Mortensen JE. **MRSA: rare in the vagina.** *J Pediatr Adolesc Gynecol.* 2011; 24:315-6.
16. Karakukcu C, Karakukcu M, Unal E, Patisroglu T, Ozdemir MA, Torun YA, Tang PH. **Coenzyme Q10 levels in beta-thalassemia and its association with ferritin levels and chelation therapy.** *Hemoglobin.* 2012; 36:219-29.
17. King BA, Boyd JT, Kingma PS. **Pulmonary maturational arrest and death in a patient with pulmonary interstitial glycogenosis.** *Pediatr Pulmonol.* 2011; 46:1142-5.
18. Kupert E, Anderson M, Liu Y, Succop P, Levin L, Wang J, Wikenheiser-brocamp K, Chen P, Pinney SM, Macdonald T, Dong Z, Starnes S, Lu S. **Plasma secretory phospholipase A2-IIa as a potential biomarker for lung cancer in patients with solitary pulmonary nodules.** *BMC Cancer.* 2011; 11:513.
19. Ladd PE, Emery KH, Salisbury SR, Laor T, Lovell DJ, Bove KE. **Juvenile dermatomyositis: correlation of MRI at presentation with clinical outcome.** *AJR Am J Roentgenol.* 2011; 197:W153-8.
20. Laor T, Stanek J, Leach JL. **Diprosopus tetraophthalmus: CT as a complement to autopsy.** *Br J Radiol.* 2012; 85:e10-3.
21. Levantini E, Lee S, Radomska HS, Hetherington CJ, Alberich-Jorda M, Amabile G, Zhang P, Gonzalez DA, Zhang J, Basseres DS, Wilson NK, Koschmieder S, Huang G, Zhang DE, Ebralidze AK, Bonifer C, Okuno Y, Gottgens B, Tenen DG. **RUNX1 regulates the CD34 gene in haematopoietic stem cells by mediating interactions with a distal regulatory element.** *EMBO Journal.* 2011; 30:4059-4070.
22. Levy M, Trivedi A, Zhang J, Miles L, Mattis AN, Kim GE, Lassman C, Anders RA, Misdraji J, Yerian LM, Xu H, Dhall D, Wang HL. **Expression of glypican-3 in undifferentiated embryonal sarcoma and mesenchymal hamartoma of the liver.** *Hum Pathol.* 2012; 43:695-701.
23. Lu Z, Chen H, Meng Y, Wang Y, Xue L, Zhi S, Qiu Q, Yang L, Mo JQ, Guan MX. **The tRNAMet 4435A>G mutation in the mitochondrial haplogroup G2a1 is responsible for maternally inherited hypertension in a Chinese pedigree.** *Eur J Hum Genet.* 2011; 19:1181-6.
24. Luo G, Gerrety M, DeBurger B, Pfeiffer J, McMasters R, Mortensen J. **Cases in Clinical Microbiology. Case**

- Twenty Two: A Disseminated Infection.** *Journal of Continuing Education Topics and Issues.* 2012; 14:22-25.
25. Maugans T, Sheridan RM, Adams D, Gupta A. **Cutaneous vascular anomalies associated with neural tube defects: Nomenclature and pathology revisited.** *Neurosurgery.* 2011; 69:112-118.
 26. Melvin A, Litsky A, Mayerson J, Stringer K, Melvin D, Juncosa-Melvin N. **An artificial tendon to connect the quadriceps muscle to the tibia.** *J Orthop Res.* 2011; 29:1775-82.
 27. Miles MV, Miles L, Horn PS, DeGrauw TJ. **Enzyme inducing antiepileptic drugs are associated with mitochondrial proliferation and increased cytochrome c oxidase activity in muscle of children with epilepsy.** *Epilepsy Res.* 2012; 98:76-87.
 28. Molho-Pessach V, Rios JJ, Xing C, Setchell KD, Cohen JC, Hobbs HH. **Homozygosity mapping identifies a bile acid biosynthetic defect in an adult with cirrhosis of unknown etiology.** *Hepatology.* 2012; 55:1139-45.
 29. Nkinin SW, Stringer JR, Keely SP, Setchell KDR, Giner JL, Kaneshiro ES. **Pneumocystis carinii sterol 14 α -demethylase activity in saccharomyces cerevisiae erg11 knockout mutant: Sterol biochemistry.** *Journal of Eukaryotic Microbiology.* 2011; 58:383-392.
 30. O'Leary MF. (Febrary 2, 2012) **Hematocrit.** Medscape Reference. .
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 32. Pardo AC, Do T, Ryder T, Meyer A, Miles L, Wong BL. **Combination of steroids and ischial weight-bearing knee ankle foot orthoses in Duchenne's muscular dystrophy prolongs ambulation past 20 years of age-a case report.** *Neuromuscul Disord.* 2011; 21:800-2.
 33. Schroer KT, Gibson AM, Sivaprasad U, Bass SA, Ericksen MB, Wills-Karp M, Lecras T, Fitzpatrick AM, Brown LA, Stringer KF, Hershey GK. **Downregulation of glutathione S-transferase pi in asthma contributes to enhanced oxidative stress.** *J Allergy Clin Immunol.* 2011; 128:539-48.
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 35. Sheridan RM, Gupta A, Miethke A, Knisely AS, Bove KE. **Multiple dysplastic liver nodules in PFIC2 underscore risk for neoplasia associated with functional BSEP deficiency.** *Am J Surg Pathol.* 2012; 36:785-6.
 36. Sheridan RM, Michelfelder EC, Choe KA, Divanovic A, Liu C, Ware S, Stanek J. **Ductus arteriosus aneurysm with massive thrombosis of pulmonary artery and fetal hydrops.** *Pediatr Dev Pathol.* 2012; 15:79-85.
 37. Sourris KC, Harcourt BE, Tang PH, Morley AL, Huynh K, Penfold SA, Coughlan MT, Cooper ME, Nguyen TV, Ritchie RH, Forbes JM. **Ubiquinone (coenzyme Q10) prevents renal mitochondrial dysfunction in an experimental model of type 2 diabetes.** *Free Radic Biol Med.* 2012; 52:716-23.
 38. Spergel JM, Rothenberg ME, Collins MH, Furuta GT, Markowitz JE, Fuchs G, 3rd, O'Gorman MA, Abonia JP, Young J, Henkel T, Wilkins HJ, Liacouras CA. **Reslizumab in children and adolescents with eosinophilic esophagitis: results of a double-blind, randomized, placebo-controlled trial.** *J Allergy Clin Immunol.* 2012; 129:456-63, 463 e1-3.
 39. Stanek J. **Utility of diagnosing various histological patterns of diffuse chronic hypoxic placental injury.** *Pediatr Dev Pathol.* 2012; 15:13-23.
 40. Stanek J. **Chorionic disk extravillous trophoblasts in placental diagnosis.** *Am J Clin Pathol.* 2011; 136:540-7.
 41. Stanek J, Biesiada J. **Sensitivity and specificity of finding of multinucleate trophoblastic giant cells in decidua in placentas from high-risk pregnancies.** *Hum Pathol.* 2012; 43:261-8.

42. Stanek J, Biesiada J. **Clustering of maternal-fetal clinical conditions and outcomes and placental lesions.** *Am J Obstet Gynecol.* 2012; 206:493 e1-8.
43. Strait RT, Hicks W, Barasa N, Mahler A, Khodoun M, Kohl J, Stringer K, Witte D, Van Rooijen N, Susskind BM, Finkelman FD. **MHC class I-specific antibody binding to nonhematopoietic cells drives complement activation to induce transfusion-related acute lung injury in mice.** *J Exp Med.* 2011; 208:2525-44.
44. Straumann A, Aceves SS, Blanchard C, Collins MH, Furuta GT, Hirano I, Schoepfer AM, Simon D, Simon HU. **Pediatric and adult eosinophilic esophagitis: similarities and differences.** *Allergy.* 2012; 67:477-90.
45. Strother DR, London WB, Schmidt ML, Brodeur GM, Shimada H, Thorner P, Collins MH, Tagge E, Adkins S, Reynolds CP, Murray K, Lavey RS, Matthay KK, Castleberry R, Maris JM, Cohn SL. **Outcome after surgery alone or with restricted use of chemotherapy for patients with low-risk neuroblastoma: results of Children's Oncology Group study P9641.** *J Clin Oncol.* 2012; 30:1842-8.
46. Sun Y, Liou B, Xu YH, Quinn B, Zhang W, Hamler R, Setchell KD, Grabowski GA. **Ex vivo and in vivo effects of isofagomine on acid beta-glucosidase variants and substrate levels in Gaucher disease.** *J Biol Chem.* 2012; 287:4275-87.
47. Tang PH, Miles MV. **Measurement of oxidized and reduced coenzyme Q in biological fluids, cells, and tissues: an HPLC-EC method.** *Methods Mol Biol.* 2012; 837:149-68.
48. Wang L, Gural A, Sun XJ, Zhao X, Perna F, Huang G, Hatlen MA, Vu L, Liu F, Xu H, Asai T, Deblasio T, Menendez S, Voza F, Jiang Y, Cole PA, Zhang J, Melnick A, Roeder RG, Nimer SD. **The leukemogenicity of AML1-ETO is dependent on site-specific lysine acetylation.** *Science.* 2011; 333:765-9.
49. Yan X, Wang X, Wang Z, Sun S, Chen G, He Y, Mo JQ, Li R, Jiang P, Lin Q, Sun M, Li W, Bai Y, Zhang J, Zhu Y, Lu J, Yan Q, Li H, Guan MX. **Maternally transmitted late-onset non-syndromic deafness is associated with the novel heteroplasmic T12201C mutation in the mitochondrial tRNAHis gene.** *J Med Genet.* 2011; 48:682-90.
50. Yin H, Boyd T, Pacheco MC, Schonfeld D, Bove KE. **Rectal biopsy in children with Down syndrome and chronic constipation: Hirschsprung disease vs non-hirschsprung disease.** *Pediatr Dev Pathol.* 2012; 15:87-95.

Faculty, Staff, and Trainees

Faculty Members

David Witte, MD, Professor

Leadership Division Director

Research Interests Renal pathology, molecular pathology

Mohammad Azam, PhD, Assistant Professor

Research Interests Cancer Biology and Neural Tumors Program

Kevin E Bove, MD, Professor

Research Interests Pediatric liver disease, biliary atresia

J. Todd Boyd, DO, Assistant Professor

Research Interests Pulmonary pathology, graduate medical education

Margaret H Collins, MD, Professor

Research Interests Pediatric gastrointestinal pathology, especially pediatric eosinophilic gastrointestinal disorders, pediatric inflammatory bowel disease, pediatric bowel motility disorders

Anita Gupta, MD, Assistant Professor

Research Interests Liver tumor pathology, vascular anomalies

Gang Huang, PhD, Assistant Professor

Research Interests Cancer pathology

Richard L McMasters, MD, Assistant Professor

Research Interests Hematopathology

Lili Miles, MD, Associate Professor

Leadership Director, Training Program

Research Interests Brain tumor, epilepsy research, neuromuscular diseases and NASH liver

Michael Miles, PharmD, Professor

Research Interests Neuropathology of mitochondrial disease

Jun Q Mo, MD, Associate Professor

Research Interests Hematopathology

Joel E Mortensen, PhD, Associate Professor

Leadership Director, Diagnostic Infectious Disease Lab

Research Interests Microbiology

Mandy F O'Leary, MD, Assistant Professor

Research Interests Transfusion medicine

Kenneth D Setchell, PhD, Professor

Leadership Director, Mass Spec Lab

Research Interests Biochemistry, Bile acids, Sterol and cholesterol metabolism, Steroids, Liver disease, Liver transplantation, Gastroenterology, Nutrition/Diet, Phytochemicals, Isoflavones/Lignans, Breast cancer, Colon cancer, Mass spectrometry – biomedical mass spectrometry, Chromatography, Analytical Biochemistry, Assay development, Therapeutic drug monitoring, Pharmacokinetics and metabolism, Genetics

Rachel Sheridan, MD, Assistant Professor

Research Interests Liver pathology, biliary atresia

Jerzy W Stanek, MD, PhD, Professor

Research Interests Pathology and pathomechanisms of in-utero hypoxia, particularly in the placenta; Pathology of perinatal mortality and morbidity

Paul E Steele, MD, Associate Professor

Leadership Medical Director, Clinical Lab

Research Interests Clinical lab medicine

Keith F Stringer, MD, Assistant Professor

Research Interests Microscopic techniques for assessing mRNA expression, protein production and cellular identity in eukaryotic tissues

Peter Tang, PhD, Assistant Professor

Research Interests Special chemistry

Kathryn Wikenheiser-Brokamp, MD, PhD, Associate Professor

Research Interests Genetic and developmental basis of lung disease, lung cancer and pediatric cystic lung disease

Hong Yin, MD, Assistant Professor

Research Interests Renal pathology, tumor pathology

Trainees

- **Michael Baker, MD**, PGY-V, Dartmouth-Hitchcock Medical Center, NH
- **Amanda Baker, MD**, PGY-IV, Indiana University - Ball Memorial Hospital

Division Collaboration

Human Genetics » Gregory Grabowski MD

Providing technical and professional support for NIH study to characterize a metabolic disease animal model.

Gastroenterology, Hepatology and Nutrition » Mitch Cohen MD, Jorge Bezerra MD, Xiaonan Han PhD, and Noah Shroyer PhD

Digestive Health Center: Integrated morphology core lab, provides technical and professional support to members of the DHC involved in basic and translational research in gastrointestinal tract.

Gastroenterology, Hepatology and Nutrition » James Heubi MD, John Bucuvalas MD, Jorge Bezerra MD, and Kathleen Campbell MD

Director of Pathology Core for multicenter BARC and CLIC studies on biliary atresia and other chronic liver disorders in children.

Endocrinology » Stuart Handwerger MD

Providing technical and professional support for NIH placental studies.

Rheumatology » John Harley MD, Sue Thompson PhD, and Hermine Brunner MD

Providing pathology professional and technical support for establishment of Biorepository service and support for Rheumatology core lab for Cincinnati Rheumatic Diseases Center and multicenter study for lupus nephritis.

Allergy and Immunology » Marc Rothenberg MD and Pablo Abonia MD

Providing professional support for the Cincinnati Center for Eosinophilic Disorders program and related research.

Hematology/Oncology » Maryam Fouladi MD and Richard Dressi PhD

Providing pathology professional and technical support for multicenter referral service for the High Grade Glioma program and basic research program.

Hematology/Oncology Research » Yi Zheng PhD, James Mulloy PhD, and Jose Cancelas MD, PhD

Joint development of Leukemia Biology program at CCHMC

Division of Hematology/Oncology; Department of Pediatric Surgery » Denise Adams MD, Richard Azizkhan MD, and Anusa Dasgupta MD

Hemangioma/vascular malformation clinical program. Providing professional diagnostic and technical pathology support for multidisciplinary patient care program.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct

BOVE, K

Clinical Center for Cholestatic Liver Disease in Children
National Institutes of Health

U01 DK 062497	09/10/09-05/31/14	\$34,200
SIMPSON, D		
Role of Rb/p16 Pathway in Pulmonary Progenitor Cell Regulation		
National Institutes of Health		
F30 HL 097609	08/11/09-08/10/13	\$32,621
WIKENHEISER-BROKAMP, K		
Mechanisms of Dicer1 Function in Lung Organogenesis and Cystic Lung Disease		
National Institutes of Health		
R01 HL 109265	06/15/11-05/31/15	\$258,699
Mechanisms Underlying DICER1 Suppression of Pleuropulmonary Blastoma Initiation		
St. Baldrick's Foundation		
	07/01/11-06/30/12	\$184,204
Rb-p16 Regulatory Pathway in Lung Carcinogenesis		
American Cancer Society National		
RSG-10-194-01-TBG	07/01/10-06/30/14	\$150,000
Role of Rb Family in Lung Epithelial Response to Injury		
National Institutes of Health		
R01 HL 079193	04/01/10-03/31/14	\$247,500
WITTE, D		
Digestive Health Center - Integrative Morphology Core		
National Institutes of Health		
P30 DK 078392	06/01/12-05/31/17	\$107,435
Current Year Direct		\$1,014,659
Total		\$1,014,659