

# Experimental Hematology and Cancer Biology

## RESEARCH AND TRAINING DETAILS



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## Research Highlights

### Yi Zheng, PhD

Rational design of small molecule inhibitors targeting Ras activation. In addition to continuing studies of novel signaling mechanisms regulating hematopoiesis and cancer progression, we reported in *Chemistry & Biology* and *The Journal of Biological Chemistry* the rational design and a screening approach of small-molecule inhibitors targeting Ras GEF, SOS1. The studies provide novel therapeutic tool and a screening platform for rational drug design and discovery.

## Paul Andreassen, PhD

DNA damage responses in human disease, including Fanconi anemia and breast cancer susceptibility. We reported in *Oncogene* our finding that RAD51C binds to the WD40 domain of PALB2, thereby integrating together multiple proteins, including BRCA1 and BRCA2, that are both Fanconi anemia and breast cancer susceptibility proteins.

## Elisa Boscolo, PhD

1. Identification of PI3KCA mutation in lymphatic malformation endothelial cells. We reported in *Angiogenesis* the presence and effect of activating PI3KCA mutation in endothelial cells from a lymphatic malformation resected from a patient.
2. Development of animal model for venous malformation. We reported in *The Journal of Clinical Investigation* (article is in press) a murine model of venous malformation (VM) dependent on endothelial TIE2-L914F mutation, same mutation found in VM patients.

## Jose Cancelas, MD, PhD

1. Pathogenesis of ELANE-mutant severe neutropenia revealed by induced pluripotent stem cells. We reported in *Journal of Clinical Investigation* the cellular biology basis of the development of severe congenital neutropenia by exon 3 mutations in the gene ELANE, using iPSC lines to model Koch's postulates.
2. Identification of angiotensin II as a major factor of mobilization of hematopoietic stem cells in health and disease. We reported in *Nature Communications* how hyperangiotensinemia is an independent factor regulating HSC/P mobilization to peripheral blood by controlling the processes of adhesion and de-adhesion of HSC/P to the vascular niches.
3. Identification of the role of osteoblastic autophagy in the retention of hematopoietic progenitors in the osteomac niche of the bone marrow. We reported in *Cell Reports* how the protein p62 is required to retain short-term repopulating and myeloid progenitor cells through inhibition of IKK/NF- $\kappa$ B/Ccl4 signaling at the bone marrow macrophage-osteoblast niche.
4. Optimized collection of functional human neutrophils for transfusion using a new automatic collector. We reported in *Transfusion* how the new Spectra Optia granulocyte apheresis system results in higher collection efficiency of viable, functional neutrophils in a randomized, crossover, multicenter trial.
5. We reported in three papers in *Transfusion* clinical studies using a novel storage solution for red blood cells, additive solution-7 (AS-7, SOLX).

## Marie-Dominique Filippi, PhD

1. Role of Rap1b in neutrophil migration and lung inflammation. We reported in the *Journal of Experimental Medicine* a novel signaling network that limits neutrophil migration into tissues and limits neutrophil-mediated lung inflammation. We identified a novel inhibitory pathway of neutrophil migration and inflammation, and provided critical new information on an ill-defined route of neutrophil migration. This is significant since there are very few identified inhibitors of inflammation; this could have broad impact for targeting excessive inflammatory reactions. This work led to a R01 award.
2. Role of p190-B RhoGAP in hematopoietic stem cell fate decision. We discovered a unique role for p190-B RhoGAP as a negative regulator of hematopoietic stem cell self-renewal by controlling HSC fate decision to self-renew or to commit to differentiation. P190-B is doing so by coordinating mitochondrial oxidative stress and stress signaling pathways belonging to TGF beta and p38MAPK signaling pathways. This work was the foundation of a R01 award.

## Matthew Flick, PhD

1. The role of the coagulation transglutaminase factor XIII in arthritis pathogenesis. We reported in *Blood* as a "Plenary Paper" that the coagulation transglutaminase factor XIII promotes inflammatory arthritis pathogenesis through mechanisms linked to fibrin-dependent promotion of local inflammation and fibrin independent mechanisms of enhanced osteoclastogenesis and cartilage/bone erosion. The study provides the novel proof of principal that therapeutic strategies targeting fXIII activity may prove beneficial in limiting arthropathies and other degenerative bone diseases.
2. The role of coagulation-driven platelet activation in cholestatic liver injury. In collaboration with James Luyendyk at Michigan State University, we reported in the *Journal of Thrombosis and Haemostasis* that platelet activation by thrombin through protease-activated receptor (PAR)-4 and platelet engagement of fibrin through integrin IIb 3 each exert hepatoprotective effects during chronic cholestasis. These studies provide critical cautionary insight into the potential use of anticoagulant drugs for the treatment of liver pathologies.  
Note: this manuscript was published as an "In Focus" article with a companion commentary article in the *Journal of Thrombosis and Haemostasis*.
3. The coagulation transglutaminase factor XIII and venous thrombosis. In collaboration with Alisa Wolberg at the University of North Carolina Chapel Hill, we reported in the *Journal of Clinical Investigation* that the fXIII-fibrinogen axis is a central determinant in venous thrombogenesis and identify FXIII as a potential therapeutic target for limiting venous thrombosis.  
Note: this article was featured on the cover of the *Journal of Clinical Investigation*.

## Hartmut Geiger, PhD

Co-authored with a group in Germany in *Nature* novel mechanisms on HSCs dormancy and DNA damage repair in HSCs. The study reveals that exit from dormancy provokes DNA damage that might result in stem cell exhaustion.

## Fukun Guo, PhD

1. Reported a new signaling role of mTOR in hematopoiesis and won a new National Institutes of Health (NIH) R21.
2. Reported new functions of Cdc42 and RhoA in T cell activation and differentiation.

## Kakajan Komurov, PhD

Research focuses on modeling and targeting the cell-autonomous and non-autonomous cancer cell vulnerabilities. Recently reported on the addiction of certain subtypes of cancers on the adaptive ER proteostasis pathways for survival, which has clear clinical implications. This study was published in *Science Signaling* with an accompanying focus.

## Qing Lu, PhD

1. Discovery of novel tumor suppressor genes in medulloblastomas and rational drug design targeting G-protein cascade. Reported in *Nature Medicine* that Gas was identified as a novel tumor suppressor in medulloblastoma principally by Sonic hedgehog signaling inhibition. Gas not only stimulates cyclic adenosine monophosphate (cAMP)-dependent signaling but also inhibits ciliary trafficking of hedgehog components. Elevation of cAMP inhibits medulloblastoma growth and augments smoothed inhibition to decrease tumor cell proliferation, highlighting Gas as a new therapeutic target.
2. Discovery of a tumor suppressor in establishing peripheral myelination. Reported in *Nature Communications* that a tumor suppressor LKB1/Par-4 controls the Schwann cell polarity to regulate their subsequent myelination events. Findings suggest that Schwann cell polarity may coordinate multiple signaling complexes to distribution of specific membrane components necessary to initiate and control myelin extent.

3. Discovery of a mechanism for Down syndrome. Reported in *Neurobiology of diseases* that mis-expression of a gene, Olig2, located in the Down syndrome critical region could cause a profound defect in brain development, suggesting that precocious elevation of Olig2 dosage in neural progenitor cells may contribute to developmental disorders including Down syndrome, where OLIG2 is triplicated on chromosomal 21.

### Carolyn Lutzko, PhD

Focused on the development of cell based studies for cancer and hPAP, as well as support and initiation of two cell and gene therapy clinical trials for sickle cell anemia and treatment of post-viral lymphoid disorders. Other studies focused on the development of induced pluripotent stem cells to study blood diseases such as neutropenia, and the development of methods to produce the large quantities of blood transfusion products required for future clinical use.

### Punam Malik, MD

1. Sickle cell disease — The Comprehensive Sickle Cell Center was one of eight recipients of the Excellence in Hemoglobinopathies Research Award. Currently studying the pathophysiology of sickle cell disease; particularly cardiopulmonary and renal pathologies. Successfully identified a unique sickle cardiomyopathy that is associated with a restrictive physiology and can explain the high incidence of sudden death in sickle cell disease. Completed a therapeutic trial for sickle nephropathy. Opened the Phase I/II Clinical Trial for Gene Therapy for Sickle Cell Disease.
2. **Gene therapy for HLH** — Gene therapy for HLH in Collaboration with **H. Gaspar**; **M. Jordan, MD**; and **K. Risma, MD, PhD**.
3. CAR T cell therapy for multiple myeloma — Working in collaboration with The Ohio State University (**OSU**) to develop lentiviral vectors to a CAR they have identified against multiple myeloma. The Translational Core is optimizing its translation to the clinic.

### Ruhikanta Meetei, PhD

Research focused on the role and regulation of FANCM-MHF complex in Fanconi anemia. As a collaborative project, it was reported that the crystal structure of a human MHF-DNA complex that reveals the DNA-binding mode of MHF. The structure suggests that MHF prefers branched DNA over double-stranded DNA because it engages two duplex arms. Biochemical analyses verify that MHF preferentially engages DNA forks or various four-way junctions independent of the junction-site structure. Furthermore, genetic experiments provide evidence that the observed DNA-binding interface of MHF is important for cellular resistance to DNA damage. These results offer insights into how the MHF complex recognizes branched DNA and stimulates FANCM activity at such a structure to promote genome maintenance.

### Jim Mulloy, PhD

1. Defined the role that the tumor suppressor FOXO1 plays in AML1-ETO AML.
2. Established a model for the most common MLL-fusion, MLL-AF4.

### Nicolas Nassar, PhD

Paper in press in *Blood*, "UBASH3B.Sts-1-CBL axis regulates myeloid proliferation in human AML1-ETO-induced Leukemia."

### Dao Pan, PhD

Innovative therapy for lysosomal storage diseases - preclinical evaluation of a innovative brain-crossing drug. Reported in *Molecular Therapy* about a preclinical study of blood-brain-barrier targeted IDUAe that can achieve long-term brain metabolic correction and normalization of behavioral deficits in a mouse model of MPS I by peripheral delivery of physiological levels (between normal carrier and wild-type) of IDUAe fusion protein. These results provide compelling evidence for CNS efficacy of IDUAe protein and its prospective translation to clinical application.

## Qishen Pang, PhD

1. Modeling FA hematopoietic stem cell transplantation ex vivo — This study demonstrates that a group of mesenchymal stromal cells (MSCs)-derived metabolites, glycerophospholipids and their endogenous inhibitor, regulated proliferation/differentiation of donor HSC and progenitor cells. This finding suggests that targeting glycerophospholipid biosynthesis in FA MSCs could be a therapeutic strategy to improve hematopoiesis and stem cell transplantation for FA patients. The study is in press in *Stem Cells*.
2. Generation and characterization of a Faap20 mouse model — Reported in *Stem Cells* that deletion of Faap20 in mice led to defects in the reproductive system and are susceptible to mitomycin C (MMC)-induced bone marrow failure. This novel mouse model which was recently generated may be a useful tool for investigating the regulation of the FA core complex and the mechanism underlying the pathophysiology of FA BM failure.

## Nancy Ratner, PhD

1. Dr. Ratner's preclinical therapeutics team continued preclinical testing in plexiform neurofibroma, and reported in *Pediatric Blood and Cancer* that MEK inhibition gives transient tumor shrinkage, reversed when drug is removed. With their 2013 report in *J. Clinical Investigation*, this study highlights the utility of MEK inhibition in NF1; this work has supported three new clinical trials of MEK inhibition in neurofibroma and a registration trial for the MEK inhibitor selumetinib.
2. Dr. Ratner published an invited comprehensive review for *Nature Reviews Cancer* entitled: "A RASopathy gene commonly mutated in cancer: the Neurofibromatosis type 1 tumor suppressor."

## Damien Reynaud, PhD

Won awards in studies of the mechanisms of hematopoiesis and leukemia initiation in the context of obesity.

## Daniel Starczynowski, PhD

Reported in *Cell Reports* that intrachromosomal gene regulator networks in del(5q) MDS/AML which results in sustaining TRAF6 signaling. This finding suggests that intra- and interchromosomal gene networks may expose therapeutic vulnerabilities in MDS/AML with specific cytogenetic alterations.

## Ronald Waclaw, PhD

1. Impact of RASopathy mutations during oligodendrogenesis. Studying the impact of RASopathy mutations during distinct stages of oligodendrocyte development. In addition, work will determine the role of MAPK signaling downstream of RASopathy induced oligodendrocyte defects.
2. Role of developmental genes/signaling pathways in gliomagenesis. Identifying early genes and signaling pathways during tumor formation in a mouse model of glioma in collaboration with [Lionel Chow, MD, PhD](#), in the [Division of Oncology](#).
3. Identifying new genes controlling regional development in the telencephalon. Studying the roles of two zinc finger proteins (536 and 704) that are expressed in distinct progenitor domains of the ventral telencephalon.

## Jianqiang Wu, MD, MS

Runx in neurofibroma formation. Reported in *Oncogene* that Runx1 contributes to neurofibromatosis type 1 neurofibroma formation.

## Mei Xin, PhD

1. Hippo signaling in endothelial cell development and disease. To define the role of the Hippo signaling effectors Yap and Taz in the vasculature, we have characterized Yap and Taz in endothelial cells by breeding Yap flox/flox mice and Yap

flox/flox;Taz flox/flox mice with two inducible endothelial specific Cre mouse lines, Tie2CreER (From Dr. Yi Zheng's lab) and Pdgfb-CreER to generate Yap eKO and Yap/Taz eKO mice, respectively.

2. Hippo signaling in lymphangiogenesis during development. To define the role of the Hippo signaling effector Yap in lymphangiogenesis, we have studied Yap in lymphatic endothelial cells by breeding Yap flox/flox mice with an inducible lymphatic endothelial specific Cre mouse line, Prox1CreERT2.

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## Significant Publications

Chang KH, Nayak RC, Roy S, Perumbeti A, Wellendorf AM, Bezold KY, Pirman M, Hill SE, Starnes J, Loberg A, Zhou X, Inagami T, **Zheng Y, Malik P, Cancelas JA**. **Vasculopathy-Associated Hyperangiotensinemia Mobilizes Haematopoietic Stem Cells/Progenitors through Endothelial  $\alpha(2)$ R and Cytoskeletal Dysregulation**. *Nat Commun*. 2015 Jan 9;6:5914.

Dr. Cancelas, in collaboration with Dr. P. Malik and collaborators, discovered that plasma levels of angiotensin II (Ang-II), commonly increased in vasculopathies, is involved in increased circulating haematopoietic stem cells and progenitors (HSC/P) in patients with organ failure of vascular origin, particularly sickle cell disease.

Kumar S, Xu J, Kumar RS, Lakshmikanthan S, Kapur R, Kofron M, Chrzanowska-Wodnicka M, **Filippi MD**. **The Small Gtpase Rap1b Negatively Regulates Neutrophil Chemotaxis and Transcellular Diapedesis by Inhibiting Akt Activation**. *J Exp Med*. 2014 Aug 25;211(9):1741-58.

Dr. M. Filippi's group reported a new molecular mechanism of neutrophil regulation, through cascade of events regulated by Rap1b-PI3K/SHP1-Akt signaling, that underlies neutrophil response to infections and inflammatory injuries.

Raghu H, Cruz C, Rewerts CL, Frederick MD, Thornton S, Mullins ES, Schoenecker JG, Degen JL, **Flick MJ**. **Transglutaminase Factor Xiii Promotes Arthritis through Mechanisms Linked to Inflammation and Bone Erosion**. *Blood*. 2015 Jan 15;125(3):427-37.

Rheumatoid arthritis is a chronic inflammatory disease characterized by synovial hyperplasia, inflammatory cell infiltration, irreversible cartilage and bone destruction, and exuberant coagulation system activity within joint tissue. Dr. M. Flick, together with Drs. Degen and E. Mullin, demonstrate that the coagulation transglutaminase, factor XIII (fXIII), drives arthritis pathogenesis by promoting local inflammatory and tissue degradative and remodeling events. Their discovery suggest therapeutic strategies targeting fXIII activity may prove beneficial in limiting arthropathies and other degenerative bone diseases.

Shen YA, Chen Y, Dao DQ, Mayoral SR, **Wu L**, Meijer D, Ullian EM, Chan JR, **Lu QR**. **Phosphorylation of Lkb1/Par-4 Establishes Schwann Cell Polarity to Initiate and Control Myelin Extent**. *Nat Commun*. 2014 Sep 26;5:4991.

The Schwann cell (SC)-axon interface represents a membrane specialization that integrates axonal signals to coordinate cytoskeletal dynamics resulting in myelination. Dr. R. Lu and collaborators have found that LKB1/Par-4 is asymmetrically localized to the SC-axon interface and co-localizes with the polarity protein Par-3. Their findings suggest that SC polarity may coordinate multiple signalling complexes that couple SC-axon contact to the redistribution of specific membrane components necessary to initiate and control myelin extent.

Fang J, Barker B, Bolanos L, Liu X, Jerez A, Makishima H, Christie S, Chen X, Rao DS, **Grimes HL, Komurov K**, Weirauch MT, **Cancelas JA**, Maciejewski JP, **Starczynowski DT**. **Myeloid Malignancies with Chromosome 5q Deletions Acquire a Dependency on an Intrachromosomal Nf-Kappab Gene Network**. *Cell Rep*. 2014 Sep 11;8(5):1328-38.

Chromosome 5q deletions (del[5q]) are common in high-risk (HR) myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Dr. D. Starczynowski's lab reported that del(5q) HR MDS/AML employs an intrachromosomal gene

network involving loss of miR-146a and haploid overexpression of p62 via NF- $\kappa$ B to sustain TRAF6/NF- $\kappa$ B signaling for cell survival and proliferation. Their work indicate that interfering with the p62-TRAF6 signaling complex represents a therapeutic option in miR-146a-deficient and aggressive del(5q) MDS/AML.

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## Division Publications

1. Aleman MM, Byrnes JR, Wang JG, Tran R, Lam WA, Di Paola J, Mackman N, Degen JL, Flick MJ, Wolberg AS. **Factor XIII activity mediates red blood cell retention in venous thrombi.** *J Clin Invest.* 2014; 124:3590-600.
2. Boscolo E, Coma S, Luks VL, Greene AK, Klagsbrun M, Warman ML, Bischoff J. **AKT hyper-phosphorylation associated with PI3K mutations in lymphatic endothelial cells from a patient with lymphatic malformation.** *Angiogenesis.* 2015; 18:151-62.
3. Brundage ME, Tandon P, Eaves DW, Williams JP, Miller SJ, Hennigan RH, Jegga A, Cripe TP, Ratner N. **MAF mediates crosstalk between Ras-MAPK and mTOR signaling in NF1.** *Oncogene.* 2014; 33:5626-36.
4. Cancelas JA. **Non-Malignant Hematopathology.** In: LM McManus, RN Mitchell, eds. *Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms.* Oxford UK: Elsevier; 2014.
5. Cancelas JA, Dumont LJ, Maes LA, Rugg N, Herschel L, Whitley PH, Szczepiokowski ZM, Siegel AH, Hess JR, Zia M. **Additive solution-7 reduces the red blood cell cold storage lesion.** *Transfusion.* 2015; 55:491-8.
6. Cancelas JA, Padmanabhan A, Le T, Ambruso DR, Rugg N, Worsham DN, Pinkard SL, Graminske S, Buck J, Goldberg J, Bill J. **Spectra Optia granulocyte apheresis collections result in higher collection efficiency of viable, functional neutrophils in a randomized, crossover, multicenter trial.** *Transfusion.* 2014; 55:748-755.
7. Carmo M, Risma KA, Arumugam P, Tiwari S, Hontz AE, Montiel-Equihua CA, Alonso-Ferrero ME, Blundell MP, Schambach A, Baum C, Malik P, Thrasher AJ, Jordan MB, Gaspar HB. **Perforin gene transfer into hematopoietic stem cells improves immune dysregulation in murine models of perforin deficiency.** *Mol Ther.* 2015; 23:737-45.
8. Casbon AJ, Reynaud D, Park C, Khuc E, Gan DD, Schepers K, Passegue E, Werb Z. **Invasive breast cancer reprograms early myeloid differentiation in the bone marrow to generate immunosuppressive neutrophils.** *Proc Natl Acad Sci U S A.* 2015; 112:E566-75.
9. Chang KH, Nayak RC, Roy S, Perumbeti A, Wellendorf AM, Bezold KY, Pirman M, Hill SE, Starnes J, Loberg A, Zhou X, Inagami T, Zheng Y, Malik P, Cancelas JA. **Vasculopathy-associated hyperangiotensinemia mobilizes haematopoietic stem cells/progenitors through endothelial AT(2)R and cytoskeletal dysregulation.** *Nat Commun.* 2015; 6:5914.
10. Chang KH, Sengupta A, Nayak RC, Duran A, Lee SJ, Pratt RG, Wellendorf AM, Hill SE, Watkins M, Gonzalez-Nieto D, Aronow BJ, Starczynowski DT, Civitelli R, Diaz-Meco MT, Moscat J, Cancelas JA. **p62 is required for stem cell/progenitor retention through inhibition of IKK/NF-kappaB/Ccl4 signaling at the bone marrow macrophage-osteoblast niche.** *Cell Rep.* 2014; 9:2084-97.
11. Cole HA, Ohba T, Nyman JS, Hirotaka H, Cates JM, Flick MJ, Degen JL, Schoenecker JG. **Fibrin accumulation secondary to loss of plasmin-mediated fibrinolysis drives inflammatory osteoporosis in mice.** *Arthritis Rheumatol.* 2014; 66:2222-33.
12. Cui Y, Tong H, Du X, Li B, Gale RP, Qin T, Liu J, Xu Z, Zhang Y, Huang G, Jin J, Fang L, Zhang H, Pan L, Hu N, Qu S, Xiao Z. **Impact of TET2, SRSF2, ASXL1 and SETBP1 mutations on survival of patients with chronic**

**myelomonocytic leukemia.** *Exp Hematol Oncol.* 2015; 4:14.

13. Delaney MK, Liu J, Kim K, Shen B, Stojanovic-Terpo A, Zheng Y, Cho J, Du X. **Agonist-induced platelet procoagulant activity requires shear and a Rac1-dependent signaling mechanism.** *Blood.* 2014; 124:1957-67.
14. Derderian SC, Togarrati PP, King C, Moradi PW, Reynaud D, Czechowicz A, Weissman IL, MacKenzie TC. **In utero depletion of fetal hematopoietic stem cells improves engraftment after neonatal transplantation in mice.** *Blood.* 2014; 124:973-80.
15. Diao HJ, Low WC, Milbreta U, Lu QR, Chew SY. **Nanofiber-mediated microRNA delivery to enhance differentiation and maturation of oligodendroglial precursor cells.** *J Control Release.* 2015; 208:85-92.
16. Dumont LJ, Cancelas JA, Maes LA, Rugg N, Whitley P, Herschel L, Siegal AH, Szczepiorkowski ZM, Hess JR, Zia M. **Overnight, room temperature hold of whole blood followed by 42-day storage of red blood cells in additive solution-7.** *Transfusion.* 2015; 55:485-90.
17. Dumont LJ, Cancelas JA, Maes LA, Rugg N, Whitley P, Herschel L, Siegal AH, Szczepiorkowski ZM, Hess JR, Zia M. **The bioequivalence of frozen plasma prepared from whole blood held overnight at room temperature compared to fresh-frozen plasma prepared within eight hours of collection.** *Transfusion.* 2015; 55:476-84.
18. El-Amouri SS, Dai M, Han JF, Brady RO, Pan D. **Normalization and improvement of CNS deficits in mice with hurler syndrome after long-term peripheral delivery of BBB-targeted iduronidase.** *Mol Ther.* 2014; 22:2028-37.
19. Evelyn CR, Biesiada J, Duan X, Tang H, Shang X, Papoian R, Seibel WL, Nelson S, Meller J, Zheng Y. **Combined rational design and a high throughput screening platform for identifying chemical inhibitors of a Ras-activating enzyme.** *J Biol Chem.* 2015; 290:12879-98.
20. Evelyn CR, Duan X, Biesiada J, Seibel WL, Meller J, Zheng Y. **Rational design of small molecule inhibitors targeting the Ras GEF, SOS1.** *Chem Biol.* 2014; 21:1618-28.
21. Fabbiano S, Menacho-Marquez M, Sevilla MA, Albarran-Juarez J, Zheng Y, Offermanns S, Montero MJ, Bustelo XR. **Genetic dissection of the vav2-rac1 signaling axis in vascular smooth muscle cells.** *Mol Cell Biol.* 2014; 34:4404-19.
22. Fang J, Barker B, Bolanos L, Liu X, Jerez A, Makishima H, Christie S, Chen X, Rao DS, Grimes HL, Komurov K, Weirauch MT, Cancelas JA, Maciejewski JP, Starczynowski DT. **Myeloid malignancies with chromosome 5q deletions acquire a dependency on an intrachromosomal NF-kappaB gene network.** *Cell Rep.* 2014; 8:1328-38.
23. Flach J, Bakker ST, Mohrin M, Conroy PC, Pietras EM, Reynaud D, Alvarez S, Diolaiti ME, Ugarte F, Forsberg EC, Le Beau MM, Stohr BA, Mendez J, Morrison CG, Passegue E. **Replication stress is a potent driver of functional decline in ageing haematopoietic stem cells.** *Nature.* 2014; 512:198-202.
24. Geiger H, Denking M, Schirmbeck R. **Hematopoietic stem cell aging.** *Curr Opin Immunol.* 2014; 29:86-92.
25. Geiger H, Zheng Y. **Regulation of hematopoietic stem cell aging by the small RhoGTPase Cdc42.** *Exp Cell Res.* 2014; 329:214-9.
26. Gonsalves CS, Li C, Mwa Mpollo MS, Pullarkat V, Malik P, Tahara SM, Kalra VK. **Erythropoietin mediated expression of Placenta Growth Factor is regulated via activation of hypoxia inducible factor -1alpha and post-transcriptionally by mir214 in Sickle Cell Disease.** *Biochem J.* 2015; 468:409-423.
27. Gopal YN, Rizos H, Chen G, Deng W, Frederick DT, Cooper ZA, Scolyer RA, Pupo G, Komurov K, Sehgal V, Zhang J, Patel L, Pereira CG, Broom BM, Mills GB, Ram P, Smith PD, Wargo JA, Long GV, Davies MA. **Inhibition of mTORC1/2**



**overcomes resistance to MAPK pathway inhibitors mediated by PGC1alpha and oxidative phosphorylation in melanoma.** *Cancer Res.* 2014; 74:7037-47.

28. Goyama S, Wunderlich M, Mulloy JC. **Xenograft models for normal and malignant stem cells.** *Blood.* 2015; 125:2630-40.
29. Grimes HL, Meyer SE. **A 2-way miRror of red blood cells and leukemia.** *Blood.* 2015; 125:1202-3.
30. Hacein-Bey-Abina S, Pai SY, Gaspar HB, Armant M, Berry CC, Blanche S, Bleesing J, Blondeau J, de Boer H, Buckland KF, Caccavelli L, Cros G, De Oliveira S, Fernandez KS, Guo D, Harris CE, Hopkins G, Lehmann LE, Lim A, London WB, van der Loo JC, Malani N, Male F, Malik P, Marinovic MA, McNicol AM, Moshous D, Neven B, Oleastro M, Picard C, Ritz J, Rivat C, Schambach A, Shaw KL, Sherman EA, Silberstein LE, Six E, Touzot F, Tsytsykova A, Xu-Bayford J, Baum C, Bushman FD, Fischer A, Kohn DB, Filipovich AH, Notarangelo LD, Cavazzana M, Williams DA, Thrasher AJ. **A modified gamma-retrovirus vector for X-linked severe combined immunodeficiency.** *N Engl J Med.* 2014; 371:1407-17.
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34. Kesarwani M, Huber E, Kincaid Z, Azam M. **A method for screening and validation of resistant mutations against kinase inhibitors.** *J Vis Exp.* 2014; .
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38. Kumar S, Xu J, Kumar RS, Lakshmikanthan S, Kapur R, Kofron M, Chrzanowska-Wodnicka M, Filippi MD. **The small GTPase Rap1b negatively regulates neutrophil chemotaxis and transcellular diapedesis by inhibiting Akt activation.** *J Exp Med.* 2014; 211:1741-58.
39. Lane A, Segura-Cabrera A, Komurov K. **A comparative survey of functional footprints of EGFR pathway mutations in human cancers.** *Oncogene.* 2014; 33:5078-89.
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41. Lee MP, Ratner N, Yutzey KE. **Genome-wide Twist1 occupancy in endocardial cushion cells, embryonic limb buds, and peripheral nerve sheath tumor cells.** *BMC Genomics*. 2014; 15:821.
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# Faculty, Staff, and Trainees

## Faculty Members

**Yi Zheng, PhD**, Professor

**Leadership** Co-Director, CBDI; Director, EHCB; Endowed Chair; Program Leader, Cell Signaling and Drug Discovery Program

**Research Interests** The physiopathological role and novel approach of therapeutic targeting of Rho GTPase and mTOR signaling networks.

**Paul Andreassen, PhD**, Associate Professor

**Research Interests** DNA damage response mechanisms in Fanconi anemia and breast cancer susceptibility, and application of this knowledge to improve cancer therapy.

**Elisa Boscolo, PhD**, Assistant Professor

**Research Interests** The Boscolo Laboratory is focused on the study of vascular anomalies.

**Jose Cancelas, MD, PhD**, Professor

**Leadership** Program Leader, Stem Cell Program; Deputy Director, Hoxworth Blood Center (HBC); Division Director, Research HBC Division; Research and Medical Director, Cellular Therapies (HBC)

**Research Interests** Hematopoietic stem cell biology in health and disease: molecular and cellular mechanisms that control tissue homeostasis.

**Jay Degen, PhD**, Professor

**Leadership** Program Leader, Hemostasis and Thrombosis Program

**Research Interests** The mechanisms linking hemostatic factors to thromboinflammatory disease processes, including sickle cell disease, neuroinflammatory disease and sepsis.

**Marie-Dominique Filippi, PhD**, Associate Professor

**Research Interests** The role of signaling pathways in controlling hematopoietic cell fate decision and self-renewal and in controlling neutrophil migration and associated lung inflammation.

**Matthew Flick, PhD**, Assistant Professor

**Leadership** Director, Rheumatology P30 Animal Models of Inflammatory Disease Core; IACUC Committee Member

**Research Interests** Defining the mechanisms of coagulation factor-mediated regulation of the pathogenesis of infectious, inflammatory and malignant diseases.

**Hartmut Geiger, PhD**, Adjunct

**Leadership** Director, Comprehensive Mouse and Cancer Core

**Research Interests** Stem cell biology in health and disease; stem cell aging.

**Elke Grassman, PhD, HCLD**, Assistant Professor

**Leadership** Director, Translational Trials Development and Support Laboratory

**Research Interests** Support phase I/II gene transfer trials with specialized patient testing and preclinical safety studies.

**Fukun Guo, PhD**, Assistant Professor

**Research Interests** Pathological and pathophysiological role of Rho GTPases and mTOR pathway in T and B cells.

**Kakajan Komurov, PhD**, Assistant Professor

**Research Interests** Modeling and targeting cancer vulnerabilities with a focus on ER stress mechanism.

**Qing Lu, PhD**, Professor

**Leadership** Scientific Director, Brain Tumor Center

**Research Interests** Glial cells regulation under physiologic and pathologic conditions and novel approach of therapeutic targeting of gliomas and medulloblastomas.

**Carolyn Lutzko, PhD**, Associate Professor

**Leadership** Director of Development; Director, Cell Processing Core; Director, Viral Vector core; Interim Director, Translational Trials Development and Support Laboratory

**Research Interests** Development and evaluation of induced pluripotent stem cell models of blood disease; development of cell and gene therapies from basic research to clinical study.

**Punam Malik, MD**, Professor

**Leadership** Marjory J. Johnson Chair of Gene and Cell Therapy; Professor of Pediatrics; Program Leader, Molecular and Gene Therapy; Director, Comprehensive Sickle Cell Program; Director, Translational Core Laboratory

**Research Interests** Hemoglobinopathies; hematopoiesis; gene therapy for hematopoietic disorders.

**Ruhikanta Meetei, PhD**, Associate Professor

**Research Interests** Identifying and characterizing proteins comprising the FA-core and Bloom syndrome complexes which are associated with chromosome instability, highly elevated cancer incidence and hypersensitivity to a variety of genotoxic drugs.

**Shyra Miller, PhD**, Assistant Professor

**Research Interests** Genomics and informatics of NF1.

**Jim Mulloy, PhD**, Professor

**Leadership** Co-Leader, Hematologic Malignancies Program; Associate Director, Hem/Onc/BMT Fellowship Program

**Research Interests** Dissection of the molecular pathogenesis of MLL-fusion leukemia and AML and AML1-ETO-associated AML, using human xenograft models and experimentally generated human AML.

**Nicolas Nassar, PhD**, Associate Professor

**Research Interests** Biophysical, biochemical and cellular approaches to elucidate the structure/function relationship of signaling proteins and rational targeting in diseases.

**Dao Pan, PhD**, Associate Professor

**Research Interests** Virus-mediated gene transfer into stem cells as well as their potential application for gene therapy of patients with inherited or acquired diseases, with a goal of ameliorating the central nervous system abnormalities and bone disease.

**Qishen Pang, PhD**, Professor

**Research Interests** Function of Fanconi anemia (FA) proteins in hematopoiesis and bone marrow failure syndromes.

**Nancy Ratner, PhD**, Professor

**Leadership** Beatrice C. Lampkin Endowed Chair in Cancer Biology; Leader, Neural Tumors and Cancer Biology Program; Co-Leader, RASopathy Program

**Research Interests** NF1 signaling pathways and RASopathies and NF1 tumors including neurofibroma and malignant peripheral nerve sheath tumor and pre-clinical therapeutics.

**Damien Reynaud, PhD**, Assistant Professor

**Research Interests** Contribution of the metabolic environment to leukemia initiation and progression; adipokine network associated with obesity and its role in normal and pathological hematopoiesis; mechanism of leukemic transformation in neonates.

**Daniel Starczynowski, PhD**, Associate Professor

**Research Interests** Molecular and cellular basis of myelodysplastic syndromes and role of innate immune signaling in HSC function.

**Johannes van der Loo, BA, MS, PhD**, Associate Professor

**Leadership** Director, Vector Production Facility; Director, Aseptic Processing Laboratories; Director, Viral Vector Core; Chair, Institutional Biosafety Committee

**Research Interests** Production of research grade viral vectors and development and scale-up of viral vector manufacturing for early phase clinical application in compliance with current good manufacturing practices (cGMP).

**Ronald Waclaw, PhD**, Assistant Professor

**Research Interests** Molecular genetic control of cellular diversity in the forebrain; impact of RASopathy mutations on brain development; role of developmental genes in gliomagenesis.

**Jianqiang Wu, MD, MS**, Assistant Professor

**Research Interests** Runx family genes and microRNAs in NF1 neurofibroma formation.

**Mei Xin, PhD**, Assistant Professor

**Research Interests** The role of Hippo signaling in cardiovascular development and disease.

## Joint Appointment Faculty Members

**Mohammed Azam, PhD**, Assistant Professor (Pathology)

**Research Interests** Hematology malignancy and novel drug resistance mechanisms.

**Lionel Chow, MD, PhD**, Assistant Professor (Oncology)

**Research Interests** The cellular origins and molecular underpinnings of high-grade gliomas in order to design and test novel therapies that will improve patient outcome.

**Biplab DasGupta, PhD**, Assistant Professor (Oncology)

**Research Interests** Function of energy and nutrient sensing enzymes during normal brain development and in brain cancer.

**Rachid Drissi, PhD**, Assistant Professor (Oncology)

**Research Interests** Telomere in cancer biology and neural tumor therapy.

**Leighton Grimes, PhD**, Associate Professor (Immunobiology)

**Research Interests** Hematology malignancy and transcription network of hematopoiesis.

**Gang Huang, PhD**, Assistant Professor (Pathology)

**Research Interests** The interplay between DNA binding proteins and chromatin modification enzymes in normal blood development and leukemia; mouse modeling of MDS.

**Theodosia Kalfa, MD, PhD**, Assistant Professor (Hematology)

**Research Interests** Benign hematology; red blood cell biology and sickle cell disease mechanism.

**Ashish Kumar, MD, PhD**, Associate Professor (Bone Marrow Transplantation and Immune Deficiency)

**Research Interests** Novel mechanism of MLL leukemia and future therapy.

**Adam Lane, PhD**, Instructor (Bone Marrow Transplantation and Immune Deficiency)

**Research Interests** Biostatistics.

**Benjamin Mizukawa, MD**, Assistant Professor (Oncology)

**Research Interests** Cell polarity and signaling in AML.

**Eric Mullins, MD**, Assistant Professor (Hematology)

**Research Interests** Hemostasis factors and coagulation.

**Joseph Palumbo, MD**, Associate Professor (Hematology)

**Research Interests** Hemostasis in cancer initiation and metastasis.

**Lisa Privette Vinnedge, PhD**, Instructor (Oncology)

**Research Interests** The molecular functions of DEK in BCSCs and pre-clinical studies of genetic inhibition of DEK as a means to enhance therapeutic response to several classes of drugs, thus hopefully resulting in improved patient survival.

**William Seibel, PhD**, Assistant Professor (Oncology)

**Research Interests** Drug discovery and medicinal chemistry.

**Janos Sumegi, MD, PhD**, Professor (Blood and Marrow Transplantation and Immune Deficiency)

**Research Interests** Immunodeficiency and novel mechanism of childhood sarcomas.

**Susanne Wells, PhD**, Associate Professor (Oncology)

**Research Interests** Identifying viral and cellular modifiers of epithelial cancers and to explore the therapeutic targeting of such modifiers for the purpose of new cancer treatments.

## Trainees

- **Shailaja Akunuru, PhD**, PGY-4, University of Cincinnati
- **Gregory Bick, BS**, PGY-5, Case Western Reserve University
- **Gasilina Anjelika**, , 2011
- **Wei Du, MD, PhD**, PGY-8, Tohoku University School of Medicine, Japan
- **Marthe-Sandrine Eiyemo Mwa Mpollo, Grad Student**, University of Montreal
- **Chris Evelyn, PhD**, 2009, University of Michigan
- **Susuma Goyama, PhD**, PGY-5, Graduate School of Medicine, University of Tokyo
- **Paritha Arumugam, PhD**, Cincinnati Children's
- **Leesa Sampson, PhD**, 2010, Johns Hopkins University
- **Shan Lin, Grad Student**, 2010, Tsinghua University, Beijing China
- **Kevin Link, PhD**, 2007, University of Cincinnati
- **Huiqing Li, MS**, University of Cincinnati
- **Xiaoyi Chen, MD**, 2012, West China Medical School, Sichuan University
- **Jung-Young Park, PhD**, 2010, National Institutes of Health
- **Ami V. Patel, PhD**, PGY-6, University of Louisville
- **TingTing Zhang, PhD**, PGY-4, University of Alabama at Birmingham
- **Junqi Yang, PhD**, PGY-4, University of Cincinnati
- **Haley Titus-Mitchell, MS**, PGY-6, Wright State University
- **Melinda Varney, PhD**, PGY-4, Marshall University, WV
- **Shuangmin Zhang, PhD**, PGY-4, University of Texas
- **Benjamin Mizukawa, MD**, 2008, University of Utah School of Medicine
- **Lisa Trump, PhD**, PGY-4, University of Illinois, Urbana Champaign
- **Mei Dai, PhD**, PGY-5, Institute of Materia Medica, Chinese Academy of Sciences, PR China
- **Jing-Fen Han, PhD**, PGY-6, University of Medicine & Dentistry of New Jersey
- **Juana Serrano-Lopez, PhD**, PGY-7, University of Cordoba Spain
- **Shanmuganathan Chandrakasan, MD**, Children's Hospital of Michigan
- **Jed Kendall, BS**, PGY-4, Brigham Young University



- **Nihal Bakeer, MD**, Cincinnati Children's
- **Preeti Tandon, PhD**, PGY-4, University of Cincinnati
- **Mathieu Sertorio, PhD**, PGY-4, University Aix-Marseille II. INSERM, France
- **Xiaoli Li, PhD**, PGY-5, Chinese Center for Disease Control and Prevention
- **Surya Amarachintha, PhD**, PGY-4, Bowling Green State University
- **Ramesh Nayak, PhD**, PGY-7, University of Texas at Tyler
- **Ashley Ficker, BS**, 2009, University of Cincinnati
- **Cuiping Zhang, MD**, PGY-4, Peking Union Medical College, China
- **Harini Raghu, PhD**, PGY-5, VIT University, Vellore, India
- **Swati Tiwari, Grad Student**, 2011, University of Delhi
- **Archana Shrestha, Grad Student**, 2011, Missouri State University
- **DanYang He, BS**, Grad S, UT Southwestern Medical Center
- **Laiman Wu, PhD**, PGY-3, University of Edinburgh, UK
- **Chuntao Zhao, PhD**, PGY-4, Nankai University
- **Minqing Jiang, BS**, Grad S, East Chinese University
- **Fanghui Lu, MS**, Grad S, Sichuan University, China
- **Xulian He, PhD**, PGY-6, Sichuan University, China
- **Ahmad Reyes, MD**, Syria University
- **Yuan Lin, PhD**, University of Rochester
- **Mark Jordan Althoff, BS**, 2013, Murray State University
- **Kodanda Nalapreddy, PhD**, PGY-4, Harvard University
- **Khalid Kalim, PhD**, PGY-2, Deutsche Rheuma-Forschungszentrum, Germany
- **Bhushan Lokesh, PhD**, PGY-4, Indian Institute of Science
- **Jonathan Fletcher, BS**, PGY-3, University of Michigan
- **Cindy Wong, Grad Student**, Michigan State University
- **Sachin Kumar, PhD**, PGY-5, University of New Delhi, India
- **Ashwini Hinge, PhD**, PGY-5, University of Pune, India
- **Hongzhu Liu, MS**
- **Jung-Mi Lee, PhD**, PGY-2
- **Michael Goodman, MD**, Washington University, St. Louis

- **Madeline Niederkorn, BSc**, GS-1, University of Cincinnati
- **Courtney Stockman**,
- **Maxwell Norris**,
- **Vase Bare**,
- **Mitchell Springer, PhD**, PGY-2, University of Pittsburgh
- **Michael Boateng**, , Antwi
- **Yi Lin, PhD**, PGY-1, Wuhan University, P.R. China
- **Zheng Zhang, PhD**, University of Cincinnati
- **Xian Li, PhD**, PGY-1, Shanghai Institute of Materia Medica
- **Megan Desai, PhD**, PGY-7, University of Cordoba, Spain
- **Shailaja Hedge, PhD**, PGY-2, Penn State University
- **Chancal Sur Chowdhury, PhD**, PGY-1, University of Basel, Switzerland
- **Jose Javier, BA**, GS-1, Franklin and Marshall College, Lancaster, PA
- **Deena Kahn, PhD**, PGY-1, Virginia Tech University
- **Yuan Li, MS**, University of Cincinnati
- **Vakus Mohanty, BS**, PGY-3, Baylor College of Medicine
- **Haibo Wang, PhD**, Beijing University
- **Liguo Zhang, PhD**, Chinese Academia Sinica
- **Jinchen Wang, BS**, Zhejiang University
- **Molly Smith, BSc**, GS-11, University of Wisconsin
- **Katelyn Melgar, BSc**, MSTP-I, Bucknell University
- **Jing Fang, MD/PhD**, PGY-IV, Shanghai Second Medical University, China
- **Laura Barreyro, PhD**, PGY-1, Albert Einstein College of Medicine
- **Tomoya Muto, PhD**, PGY-1, Chiba University, Japan

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## Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct

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Akunuru, S

Training Programs in Cancer Therapeutics

National Institutes of Health(University of Cincinnati)

T32 CA117846	9/14/2012-8/31/2015	\$47,244
<b>Bari, V</b>		
<b>Targeting Sts-1 in Acute Myeloid Leukemia</b>		
American Society of Hematology		
	7/1/2014-6/30/2015	\$42,000
<b>Boscolo, E</b>		
<b>Role of NOTCH Signaling during Pathological Blood Vessel Formation and Maturation</b>		
Charles H. Hood Foundation		
	8/1/2014-12/31/2014	\$12,258
<b>Venous Malformations (VM): A Murine Model to Identify Therapies to Target Aberrant Venous Development</b>		
National Institutes of Health		
R01 HL117952	8/7/2014-4/30/2018	\$221,626
<b>Cancelas-Perez, J</b>		
<b>Atypical Protein Kinase C as Safe, Effective Target in Leukemic Stem Cells</b>		
Cancer Free Kids		
	7/1/2014-6/30/2015	\$48,000
<b>Rational Design of a Vav/Rac Inhibitor as a New Therapy for High-Risk B-ALL</b>		
The Leukemia and Lymphoma Society		
	10/1/2012-9/30/2015	\$180,018
<b>Validation of a Rationally Designed Guanine Nucleotide Exchange Factor Inhibitor in Lymphoblastic Leukemia</b>		
Wm Lawrence & Blanche Hughes Foundation (University of Southern California)		
	1/1/2014-12/31/2016	\$90,909
<b>Chang, K</b>		
<b>Angiotensin in Stem Cell Recruitment and Mobilization</b>		
National Blood Foundation		
	7/1/2014-6/30/2016	\$37,500
<b>Degen, J</b>		
<b>Analysis of Staphylococcus Aureus Host Interactions</b>		

National Institutes of Health (Texas A & M University Health Science Center)

R01 AI020624

9/30/2010-8/31/2015

\$49,458

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**Degen, J / Malik, P**

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**Hemostatic Factors and Sickle Cell Disease**

National Institutes of Health

R01 HL112603

1/1/2012-11/30/2016

\$246,250

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**Filippi, M**

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**Regulation of Hematopoietic Stem Cell Self-Renewal by GTPase Activating Protein**

American Society of Hematology

3/1/2015-2/28/2016

\$150,000

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**Geiger, H**

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**Molecular Mechanisms in Therapies for Radiation Induced Myelodysplastic Syndrome**

Edward P. Evans Foundation (University of Kentucky)

4/01/2015-9/30/2015

\$90,909

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**Guo, F**

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**Novel Signaling Function of Cdc42 GTPase In Vivo**

National Institutes of Health

R01 GM108661

5/1/2014-2/28/2018

\$175,000

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**Hennigan, R**

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**Regulation of Intracellular Trafficking in NF2**

Department of Defense Army

W81XWH1310136

6/1/2013-5/31/2016

\$137,289

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**Komurov, K**

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**Exploiting Proteotoxic Stress in Therapy-Refractory HER2+ Breast Cancers**

National Institutes of Health

R01 CA193549

5/1/2015-4/30/2020

\$228,750

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**Modeling and Targeting the Hexosamine Pathway in Drug Resistance**

Susan G Komen for the Cure

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8/1/2013-7/31/2016

\$120,000

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**Lin, S**

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**Discovery of Novel Therapeutic Targets for the Treatment of MLL-AF4 Infant Acute Lymphoblastic Leukemia**

Cancer Free Kids

7/1/2014-6/30/2015

\$40,000

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**Lu, Q**

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**The Establishment of Schwann Cell Polarity and the Inflation of Myelination**

National Institutes of Health (University of California - San Francisco)

R01 NS062796

5/1/2014-4/30/2019

\$78,750

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**Molecular Mechanisms of Oligodendrocyte Differentiation and Myelination**

National Institutes of Health

R01 NS072427

10/1/2013-8/31/2015

\$212,231

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**Chromatin Remodeling Control of CNS Myelination and Remyelination**

National Institutes of Health

R01 NS075243

10/1/2013-3/31/2017

\$218,750

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**A Novel Model of Medulloblastoma to Define Cancer Pathways and Molecular Targets**

National Institutes of Health

R01 NS078092

10/1/2013-3/31/2017

\$218,750

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**MicroRNA Control of Myelination and Remyelination in the Central Nervous System**

National Multiple Sclerosis Society

10/1/2013-6/30/2015

\$197,394

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**Histone Deacetylase Control of CNS Myelination and Remyelination**

National Multiple Sclerosis Society

4/1/2015-3/31/2018

\$223,553

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**Lutzko, C**

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**CS1 Chimeric Antigen Receptor-Based Immunotherapy**

American Cancer Society National(Ohio State University)

1/1/2015-12/31/2018

\$50,000

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**Malik, P**

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**Gene Therapy for Sickle Cell Anemia**

Doris Duke Charitable Foundation

9/1/2013-8/31/2016

\$150,000

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**Cincinnati Cell Characterization Core - Per case Reimbursement**

National Institutes of Health(University of Maryland)

5/01/2011-4/30/2015

\$177,042

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**PLGF-HIF1a-miR Axis in Sickle Pulmonary Hypertension**

National Institutes of Health (University of Southern California)

R01 HL111372

1/1/2012-12/31/2016

\$156,500

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**Cincinnati Center of Excellence in Hemoglobinopathies Research**

National Institutes of Health

U01 HL117709

8/15/2013-5/31/2018

\$1,067,021

Quinn, C

Translational Research Skills  
Development Core

\$221,382

Kalfa, T

Research Project 1

\$130,506

Malik, P

Research Project 2

\$556,365

Quinn, C

Research Project 3

\$216,958

Kalfa, T

Summer Students

\$41,810

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**Mulloy, J****Conferring in vivo Metabolic Resistance to a Highly Selective Anti-AML Agent**

National Institutes of Health(University of Cincinnati)

R21 CA185370

5/1/2014-2/28/2016

\$25,000

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**Targeting the Core Binding Factor Tumor Suppressor in MLL-fusion AML**

National Institutes of Health(P2D Bioscience)

R43 CA176907

8/1/2014-1/31/2015

\$47,115

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**Rac Signaling in MLL leukemia**

The Leukemia and Lymphoma Society

7/1/2010-6/30/2015

\$104,762

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**Nassar, N**

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**Novel Rationally Designed Ras Inhibitors for B-ALL Multi-Target Therapy**

The Leukemia and Lymphoma Society

10/1/2013-9/30/2016

\$180,018

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**Pan, D**

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**Gaucher Disease: Treatment of Neurodegenerative Disease**

National Institutes of Health

R01 NS086134

9/1/2013-5/31/2018

\$270,887

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**Pang, Q**

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**Targeted Improvement in Stem Cell Therapy for Leukemia and Bone Marrow Failure Syndromes**

National Institutes of Health

R01 CA157537

2/1/2011-12/31/2015

\$207,500

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**Ratner, N**

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**Identification of Molecular and Cellular Contributors to Neurofibroma Formation and Growth**

Department of Defense Army

W81XWH1210133

7/1/2012-6/30/2015

\$225,819

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**Mitogenic Activities in Neurofibromatosis**

National Institutes of Health

R01 NS028840

9/15/2011-7/31/2016

\$228,937

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**Disordered Regulation of Wnt/Beta-catenin Signaling in MPNST Development and Maintenance**

National Institutes of Health(University of Minnesota)

R01 NS086219

8/15/2014-6/30/2019

\$152,382

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**Brain Dysfunction in Neurofibromatosis**

National Institutes of Health

R01 NS091037

4/1/2015-3/31/2020

\$223,993

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**Ras Proteins in Nerve Tumorigenesis**

National Institutes of Health

R37 NS083580

4/1/2014-3/31/2019

\$250,000

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**Can Targeted Therapy Prevent Neurofibroma Growth in Mice**

Neurofibromatosis Therapeutic

3/1/2015-2/28/2017

\$46,735

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**Identification of Neurofibroma Growth and Drug Resistance Pathways**

Neurofibromatosis Therapeutic(Johns Hopkins University)

2/1/2014-1/31/2016

\$124,000

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**Neurofibroma Preclinical Therapeutics**

The Children's Tumor Foundation

7/15/2013-7/14/2016

\$275,720

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**Ratner, N**

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**Novel Combinatorial Therapies for Malignant Peripheral Nerve Sheath Tumors**

National Institutes of Health

R21 NS084885

7/1/2014-6/30/2016

\$301,615

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**Reynaud, D**

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**Systemic Metabolic Disorders and Leukemic Clonal Dominance**

Conquer Cancer Foundation

7/1/2014-6/30/2016

\$60,000

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**Springer, M**

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**Training Programs in Cancer Therapeutics**

National Institutes of Health(University of Cincinnati)

T32 CA11786

8/1/2013-7/31/2015

\$41,364

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**Starczynowski, D**

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**Chronic Innate Immune Signaling in the Pathogenesis of MDS**

Edward P. Evans Foundation

7/1/2014-6/30/2016

\$200,000

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**Defining the Role and Therapeutic Potential of TNF Receptor-Associated Factor 6 in Myelodysplastic Syndromes**

Gabrielle's Angel Fnd for Cancer Research

6/1/2013-5/31/2016

\$68,182

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**Molecular Pathogenesis of Myelodysplastic Syndromes**

National Institutes of Health



R01 DK102759	8/15/2014-5/31/2017	\$150,000
<b>Identification and Characterization of Genes in del(5q) Myelodysplastic Syndrome</b>		
National Institutes of Health		
R01 HL111103	12/15/2011-11/30/2016	\$246,250
<b>Role of TRAF6 in Myelodysplastic Syndromes</b>		
National Institutes of Health		
R01 HL114582	8/1/2014-4/30/2018	\$251,741
<b>Tandon, P</b>		
<b>Characterizing the Role of Specific Ras Proteins in Neurofibroma and MPNST Formation</b>		
National Institutes of Health		
F32 NS083249	9/1/2013-8/31/2015	\$53,282
<b>Waclaw, R</b>		
<b>Signaling Pathways Regulating Oligodendrocyte Development and Function</b>		
National Institutes of Health		
R01 NS088529	4/1/2015-2/29/2020	\$218,750
<b>Wu, L</b>		
<b>Functional Study of Transcriptional Regulator Sip1 in CNS Myelination and Remyelination</b>		
National Multiple Sclerosis Society		
	10/1/2013-9/30/2016	\$54,804
<b>Zheng, Y</b>		
<b>Therapeutic Targeting of LARG-RhoA-ROCK Signaling Axis in Childhood Leukemia</b>		
Alex's Lemonade Stand Foundation		
	7/1/2013-6/30/2015	\$125,000
<b>Cincinnati Center for Excellence in Molecular Hematology</b>		
National Institutes of Health		
P30 DK090971	9/30/2010-6/30/2015	\$453,441
<b>Targeting Cdc42 for Bone Marrow Transplant Therapies</b>		
National Institutes of Health		

R01 CA193350	5/1/2015-4/30/2020	\$228,750
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**Rho GTPase Inhibitors for Refrigerated Platelet Storage**

National Institutes of Health(P2D Bioscience)

R43 HL123103	8/1/2014-7/31/2015	\$58,008
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**Novel Anti-inflammatory Drug Targeting NOX2 in Acute Lung Injury**

National Institutes of Health(Cleveland Clin Lerner Col of Med of CWRU)

U54 HL119810	8/1/2014-7/31/2015	\$50,000
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**Zheng, Y / Geiger, H****Lineage Determination and Tissue Homeostasis in the Aged Hematopoietic System**

National Institutes of Health

R01 AG040118	8/01/2011-5/31/2016	\$218,750
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**Current Year Direct****\$9,810,007**

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**Industry Contracts**

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**Flick, M**

Novo Nordisk		\$30,739
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**Mulloy, J**

Celgene Cellular Therapeutics		\$31,656
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Seattle Genetics, Inc		\$12,556
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**Grassman, E**

Battelle Memorial Institute		\$14,879
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**Current Year Direct Receipts****\$89,830**

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**Funded Collaborative Efforts**

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**Flick, M****Animal Models of Inflammatory Disease Core**

National Institutes of Health

Thompson, S	8/25/2011-6/30/2016	10%
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Total

\$9,899,837

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