2013 Research Annual Report

Experimental Hematology and Cancer Biology

Cincinnati Children's

Division Details

Division Data Summary

RESEARCH AND TRAINING DETAILS	
Number of Faculty	**24**
Number of Joint Appointment Faculty	**14**
Number of Research Fellows	**35**
Number of Research Students	**17**
Number of Support Personnel	**83**
Direct Annual Grant Support	**$7,783,205**
Direct Annual Industry Support	**$274,014**
Peer Reviewed Publications	**75**

Division Photo

Row 1: MD Filippe, L Privette-Vinnedge
Row 2: T Kalfa, E Grassman, R Drissi, M Azam
Row 3: F Guo, J Wu, R Meetei, C Lutzko, R Waclaw, H Van der loo, J Mulloy
Row 4: P Andreassen, N Nassar, L Chow, D Reynaud, D Starczynowski, B DasGupta, Y Zheng
Row 5: M Flick, J Cancelas, Q Pang, J Degen, G Huang

Research Highlights

Yi Zheng, PhD

Rational design of small molecule inhibitors targeting Rho GTPase activation cascade. We reported in *PNAS* and *Chemistry & Biology* the rational design of a small-molecule inhibitor of the RhoA activator, LARG, that helped stop the spread of laboratory cultured human breast cancer cells, especially when it was used with another chemical inhibitor known as Rhosin/G04 which is specific toward RhoA itself. The studies provide novel therapeutic principle for rational drug design and discovery.

Paul Andreassen, PhD

The Andreassen lab has recently demonstrated that the machinery for homologous recombination is linked to early events in DNA damage signaling by ubiquitin-dependent signaling and PALB2/FANCN. We have also generated novel insight into the function of RAD51 paralogs in DNA repair by finding that RAD51C/FANCO interacts with PALB2/FANCN.

Jose Cancelas, MD, PhD

The Cancelas Lab has been working on the following studies:

- Discovery and elucidation of the role of Vav3 in BCR-ABL lymphoblastic leukemia.

- Identification of connexin43 (Cx43) as a regulator of reactive oxygen content (ROS) in hematopoietic stem cells and description of a novel protective function of bone marrow stroma consisting of scavenging of ROS through Cx43.
- Elucidation of the role of Klf5 in stem cell adhesion and homing to the bone marrow with identification of Rab5 as the crucial downstream gene responsible for loss of integrin mediated cell adhesion in stem cells.
- In vivo demonstration of the safety of platelet additive solution Isoplate to maintain platelet storage for up to five days in a multicenter trial.
- In vivo demonstration of the ability of DMSO to freeze platelets and maintain their viability in a multicenter trial.

Jay Degen, PhD

The Degen Lab is genetically eliminating the fibrinogen binding motif recognized by the microglial integrin receptor CD11b/CD18;shown to inhibit perivascular microglial clustering and axonal damage within the central nervous system in a mouse model of multiple sclerosis.

In other work, the Degen Lab has shown thrombin-mediated proteolysis to be an unexpectedly powerful determinant of atherosclerosis in multiple distinct settings. These studies suggest that selective anticoagulants employed to prevent thrombotic events may also be remarkably effective in clinically impeding cardiovascular disease.

Finally, the Degen Lab has shown the host fibrin(ogen) and the *S. aureus*-encoded fibrinogen receptor, ClfA, to be dual determinants of bacterial virulence. These findings suggest that therapeutic interventions at the level of fibrinogen could be advantageous in *S. aureus* septicemia.

Matthew Flick, PhD

The Flick Lab has continued analysis of the pathogenesis of bacterial infection including a publication highlighting the mechanisms of microbe engagement of fibrinogen the pathogenesis of *S. aureus* septicemia.

In addition, the Flick Lab has initiated a new project, funded by an industry contract with Novo Nordisk, to study the efficacy of recombinant factor XIII in treating inflammatory arthritis.

Hartmut Geiger, PhD

The Geiger Lab published a paper in *Nature Medicine* on radiomitigation which received national attention.

Elke Grassman, PhD, HCLD

The Grassman Lab qualified four new specialized assays for patient monitoring for a thalassemia gene therapy trial.

The Grassman Lab published two papers in *Gene Therapy*. One was entitled, "Scale-up and manufacturing of clinical-grade self-inactivating gamma-retroviral vectors by transient transfection." The second paper was entitled, "Critical variables affecting clinical-grade production of the self-inactivating gamma-retroviral vector for the treatment of X-linked severe combined immunodeficiency."

Fukun Guo, PhD

The Guo Lab is studying the following:

- The role of mTOR in hematopoiesis.

- The role of Cdc42 in T cell activation.
- The role of RhoA in T cell development and activation.
- mTOR as a potential therapeutic target in T lymphocytic leukemia.

Carolyn Lutzko, PhD

The Lutzko Lab has developed specialized induced pluripotent stem cells from patients with blood diseases including neutropenia, sickle cell anemia and leukocyte adhesion deficiency. These specialized stem cells allow us to produce blood cells with the "disease" in the dish to directly develop and test gene, cell and drug therapies for these blood diseases.

Punam Malik, MD

The Malik Lab is working on:

- A clinical trial for gene therapy for sickle cell disease.
- Gene therapy for HLH with Drs. Jordan and Risna.
- A clinical trial for sickle nephropathy.

Ruhikanta Meetei, PhD

The Meetei Lab has:

- Discovered a 20kDa subunit of FA core complex protein and it was published in the journal *Blood*.
- Identified an important site of phosphorylation (S1045) in FANCM protein in response to DNA damage. This was published in the *Cancer Research* journal.

James Mulloy, PhD

The Mulloy Lab has:

- Defined the role that Thrombopoeitic/MPL/Bcl-xL plays downstream of the AML1-ETO oncogene.
- Established a chemotherapy regimen for AML in immunodeficient mice.

Nicolas Nassar, PHD

The Nassar Lab is working on the following:

- Rational design of a Vav/Rac inhibitor as a new therapy for high risk B-ALL.
- A novel and rationally designed Ras inhibitors for high rish B-ALL Multi-target therapy.

Dao Pan, PhD

The Pan Lab has reported in *PNAS* the development of a recombinant receptor-binding domain (Rb) of ApoE that enables protein delivery across the blood-brain barrier in mice when being tagged with a lysosomal enzyme as a fusion protein. The studies provide a noninvasive and BBB-targeted procedure for delivery of large molecule therapeutic agents to treat diseases involving the brain.

The Pan lab has also conducted preclinical evaluation of the blood-brain-barrier targeted Rb they recently developed, and showed that long-term systemic delivery of BBB-targeted IDUA-Rb could achieve superb neurological benefits over control protein with complete normalization of behavioral deficits in high-dosage groups and partial correction of brain pathology in medium group. This study has been presented at the 16th

Annual meeting of American Society of Cell and Gene Therapy, and Dr. Salim El-Amouri from the lab received a 2013 ASGCT Travel Award.

The Pan lab has recently demonstrated for the first time that megakaryocytes/platelets are capable of over-producing, packaging and storing a lysosomal enzyme which retains proper catalytic activity, lysosomal enzyme trafficking and endogenous M6PR-mediated uptake, as well as the ability of cross-correction in patient's cells. This study has been presented at the 2012 ASH meeting in December, and Dr. Mei Dai from the lab received ASH Abstract Achievement Award.

The Pan lab has recently demonstrated that long-term visceral phenotypic corrections could be further improved by stress erythropoiesis with complete normalization in spleen of MPS I mice with minimum HSC gene transfer (<1%) after lentiviral vector-mediated hematopoietic stem cell gene therapy using a erythroid/megakaryocytic promoter. These studies provide valuable preclinical information that may lead to future clinical trial. This study has been presented at the 16th Annual meeting of American Society of Cell and Gene Therapy, and Dr. Jing-fen Han, from the lab, has received a 2013 ASGCT Travel Award.

Qishen Pang, PhD

The study, "Link between abnormal HSC differentiation and disease progression in FA", shows that FA deficiency enhances Notch signaling in multipotential progenitors (MPPs), which is correlated with decreased phenotypic long-term HSCs and increased formation of MPP1 progenitors. The findings have implications for understanding the pathogenesis of BM failure and leukemia in FA, and suggest possible translational approaches to these devastating clinical complications. A manuscript describing these studies is in press in *J. Immunology*.

In addition, the study, "Targeting the FA pathway in sensitizing leukemia to chemotherapy", demonstrates that the mTOR kinase inhibitor pp242 enhances anti-tumor activity of conventional chemo-drugs *in vitro* and *in vivo* by suppressing FANCD2 and consequently augmenting DNA damage leading to apoptosis. The finding suggests that inhibition of the FA pathway coupled with chemo-therapy may be beneficial for cancer treatment. A manuscript describing these studies is in press in *Leukemia*.

Nancy Ratner, PhD

The Ratner Lab has published a paper in the *Journal of Neuroscience* showing that Rac1 controls Schwann cell myelination through cAMP and NF2/merlin. A critical role for cAMP downstream of the small GTPase Rac1 had not previously been defined *in vivo*.

The Ratner Lab published a paper showing Neurofibroma-associated macrophages play roles in tumor growth and response to pharmacological inhibition Acta Neuropathol. This shows for the first time that macrophages comprise 30% of cells in neurofibromas.

The Ratner Lab published a paper in *The Journal of Clinical Investigation* that shows MEK inhibition exhibits efficacy in human and mouse neurofibromatosis tumors. This paper shows that MEK inhibition shrinks most neurofibromas in an accurate mouse model of NF1 disease. The paper received considerable PR and two ongoing clinical trials have resulted from this work.

The Ratner Lab published a paper in *Cancer Research* that showsnPTEN and NF1 inactivation in Schwann cells produce a severe phenotype in the peripheral nervous system that promotes the development and malignant progression of peripheral nerve sheath tumors.

The Ratner Lab published a paper in *Sarcoma* showing thenconditional Inactivation of Pten with EGFR

Overexpression in Schwann Cells Models Sporadic MPNST.

The Ratner Lab published a paper in *Nature Genetics* showing the forward genetic screen for malignant peripheral nerve sheath tumor formation identifies new genes and pathways driving tumorigenesis. This is an important paper identifying novel potential driver mutations in MPNST, an incurable human sarcoma.

The Ratner Lab published a paper in *Cancer Discover* showing the Canonical Wnt/beta-catenin Signaling Drives Human Schwann Cell Transformation, Progression, and Tumor Maintenance. This is a paper identifying multiple modes for activating b-catenin signaling MPNST, an incurable human sarcoma.

The Ratner Lab published a paper in *Oncogen* showing EGFR-STAT3 signaling promotes formation of malignant peripheral nerve sheath tumors.

Damien Reynaud, PhD

The Reynaud laboratory was set up in March 2013 with the purchase of essential equipment. Recruitment and training of lab personnel (one research assistant and one postdoctoral fellow) has been initiated. The first set of experiments describing the hematopoietic compartments present in the neonate bone marrow have been performed.

Daniel Starczynowski, PhD

The Starczynowski Lab was awarded a Gabrielle's Angels Foundation Research Award.

The Starczynowski Lab published "Cytotoxic effects of Bortezomib in MDS/AML depend on autophagy-mediated lysosomal degradation of TRAF6 and repression of PSMA1" in *Blood* (July 2012).

Johannes van der Loo, BA, MS, PhD

The van der Loo Lab published a paper describing the development and scale-up for manufacturing of clinical-grade gamma-retroviral vectors in a bioreactor. The paper was published in the journal *Gene Therapy*.

The van der Loo Lab published a paper on the critical variables evaluated during the clinical-grade production of a self-inactivating gamma-retroviral vector for the treatment of X-linked severe combined immunodeficiency in an international multi-institutional phase I trial. The product is currently being used in London, Paris, Los Angeles, Boston and Cincinnati. The paper was published in the journal *Gene Therapy*.

The van der Loo Lab completed clinical manufacturing of three (3) lots of GMP-grade lentiviral vector for the treatment of Sickle Cell Anemia for a phase I trial to be opened at Cincinnati Children's (PI: Malik).

Ronald Waclaw, PhD

The Waclaw Lab is analyzing the role of the RASopathy gene, Shp2 (PTPN11) during mouse brain development. We have found that loss of Shp2 and misexpression of a Noonan Syndrome GOF mutation impacts the normal generation and differentiation of oligodendroctyes in the telencephalon. We are currently writing this manuscript for submission.

The Waclaw Lab is analyzing the role of the RASopathy gene, NF1 (neurofibromin) during mouse basal ganglia development. We have found that loss of NF1 impacts both the striatal differentiation and normal formation of striatal circuitry. We are currently writing a manuscript for submission.

Additionally, the Waclaw Lab is analyzing mouse models of glioma at "pre tumor" stages to determine the role of early developmental genes at early stages of gliomagensis. We have identified several candidate genes

normally expressed in progenitor niches of the telencephalon and are now characterizing several defined signaling pathways in combination with these factors.

Jianqiang Wu, MD, MS

The Wu Lab is studying the following: Stat3 in neurofibroma initiation and maintenance. miR-155 and RUNX function in neurofibroma formation and therapy.

Significant Publications

Chang, K.H., A. Sanchez-Aguilera, S. Shen, A. Sengupta, M.N. Madhu, A.M. Ficker, S.K. Dunn, A.M. Kuenzi, J.L. Arnett, R.A. Santho, X. Agirre, J.P. Perentesis, M.W. Deininger, **Y. Zheng**, X.R. Bustelo, D.A. Williams, and **J.A. Cancelas**. **Vav3 collaborates with p190-BCR-ABL in lymphoid progenitor leukemogenesis, proliferation, and survival**. *Blood*. 2012. 120:800-811.

Despite the introduction of tyrosine kinase inhibitor therapy, the prognosis for p190-BCR-ABL(+) acute lymphoblastic leukemia remains poor. This paper defines the cellular and molecular roles of the Rho GTPase guanine nucleotide exchange factor Vav in lymphoid leukemogenesis and explore the roles of Vav proteins in BCR-ABL-dependent signaling. The study concludes that Vav3 represents a novel specific molecular leukemic effector for multitarget therapy in p190-BCR-ABL-expressing acute lymphoblastic leukemia.

Chou, F.S., A. Griesinger, M. Wunderlich, S. Lin, K.A. Link, M. Shrestha, S. Goyama, **B. Mizukawa**, S. Shen, G. Marcucci, and **J.C. Mulloy**. **The thrombopoietin/MPL/Bcl-xL pathway is essential for survival and self-renewal in human preleukemia induced by AML1-ETO**. *Blood*. 2012. 120:709-719.

AML1-ETO (AE) is a fusion product of translocation (8;21) that accounts for 40% of M2 type acute myeloid leukemia (AML). In addition to its role in promoting preleukemic hematopoietic cell self-renewal, AE represses DNA repair genes, which leads to DNA damage and increased mutation frequency. Although this latter function may promote leukemogenesis, concurrent p53 activation also leads to an increased baseline apoptotic rate. It is unclear how AE expression is able to counterbalance this intrinsic apoptotic conditioning by p53 to promote survival and self-renewal. This report shows that survival signaling through Bcl-xL is a critical and intrinsic component of a broader self-renewal signaling pathway downstream of AML1-ETO-induced MPL.

Fang, J., G. Rhyasen, L. Bolanos, C. Rasch, M. Varney, M. Wunderlich, S. Goyama, G. Jansen, J. Cloos, C. Rigolino, A. Cortelezzi, **J.C. Mulloy**, E.N. Oliva, M. Cuzzola, and **D.T. Starczynowski**. **Cytotoxic effects of bortezomib in myelodysplastic syndrome/acute myeloid leukemia depend on autophagy-mediated lysosomal degradation of TRAF6 and repression of PSMA1**. *Blood*. 2012. 120:858-867.

Bortezomib (Velcade) is used widely for the treatment of various human cancers; however, its mechanisms of action are not fully understood, particularly in myeloid malignancies. Bortezomib is a selective and reversible inhibitor of the proteasome. This work find that bortezomib induces proteasome-independent degradation of the TRAF6 protein, but not mRNA, in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) cell lines and primary cells. The studies present novel mechanisms by which TRAF6 is regulated through bortezomib/autophagy-mediated degradation and by which it alters MDS/AML sensitivity to bortezomib by controlling PSMA1 expression.

Flick, M.J., X. Du, J.M. Prasad, H. Raghu, J.S. Palumbo, E. Smeds, M. Hook, and **J.L. Degen**. **Genetic elimination of the binding motif on fibrinogen for the S. aureus virulence factor ClfA improves host survival in septicemia**. *Blood*. 2013. 121:1783-1794.

Fibrinogen can support host antimicrobial containment/clearance mechanisms, yet selected pathogens appear to benefit from host procoagulants to drive bacterial virulence. This paper explored the hypothesis that host

fibrin(ogen), on balance, supports Staphylococcus aureus infection in the context of septicemia. The findings indicate that host fibrin(ogen) and bacterial ClfA are dual determinants of virulence and that therapeutic interventions at the level of fibrinogen could be advantageous in S. aureus septicemia.

Patmore, D.M., S. Welch, P.C. Fulkerson, **J. Wu**, K. Choi, D. Eaves, J.J. Kordich, M.H. Collins, T.P. Cripe, and**N. Ratner**. **In vivo regulation of TGF-beta by R-Ras2 revealed through loss of the RasGAP protein NF1**. *Cancer research*. 2012. 72:5317-5327.

Ras superfamily proteins participate in TGF-β-mediated developmental pathways that promote either tumor suppression or progression. However, the specific Ras proteins, which integrate in vivo with TGF-β signaling pathways, are unknown. To resolve this question, the authors activated all Ras proteins in vivo by genetic deletion of the RasGAP protein Nf1 and examined mice doubly deficient in a Ras protein to determine its requirement in formation of TGF-β-dependent neurofibromas that arise in Nf1-deficient mice. The finding reveals R-Ras2 as a critical regulator of TGF-β signaling in vivo.

Division Publications

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2. Akunuru S, James Zhai Q, Zheng Y. **Non-small cell lung cancer stem/progenitor cells are enriched in multiple distinct phenotypic subpopulations and exhibit plasticity**. *Cell Death Dis*. 2012; 3:e352.
3. Azam M. **An in vitro screening to identify drug-resistant mutations for target-directed chemotherapeutic agents**. In: y zheng, ed. *Rational Drug Design - Methods Mol Biol*. New York: Springer; 2012:175-84.
4. Ballas SK, Kesen MR, Goldberg MF, Lutty GA, Dampier C, Osunkwo I, Wang WC, Hoppe C, Hagar W, Darbari DS, Malik P. **Beyond the definitions of the phenotypic complications of sickle cell disease: an update on management**. *ScientificWorldJournal*. 2012; 2012:949535.
5. Barger JF, Gallo CA, Tandon P, Liu H, Sullivan A, Grimes HL, Plas DR. **S6K1 determines the metabolic requirements for BCR-ABL survival**. *Oncogene*. 2013; 32:453-61.
6. Bell-Horwath TR, Vadukoot AK, Thowfeik FS, Li G, Wunderlich M, Mulloy JC, Merino EJ. **Novel ROS-activated agents utilize a tethered amine to selectively target acute myeloid leukemia**. *Bioorg Med Chem Lett*. 2013; 23:2951-4.
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8. Chang KH, Sanchez-Aguilera A, Shen S, Sengupta A, Madhu MN, Ficker AM, Dunn SK, Kuenzi AM, Arnett JL, Santho RA, Agirre X, Perentesis JP, Deininger MW, Zheng Y, Bustelo XR, Williams DA, Cancelas JA. **Vav3 collaborates with p190-BCR-ABL in lymphoid progenitor leukemogenesis, proliferation, and survival**. *Blood*. 2012; 120:800-11.
9. Chapman H, Waclaw RR, Pei Z, Nakafuku M, Campbell K. **The homeobox gene Gsx2 controls the timing of oligodendroglial fate specification in mouse lateral ganglionic eminence progenitors**. *Development*. 2013; 140:2289-98.
10. Chen L, Acciani T, Le Cras T, Lutzko C, Perl AK. **Dynamic regulation of platelet-derived growth**

factor receptor alpha expression in alveolar fibroblasts during realveolarization. *Am J Respir Cell Mol Biol*. 2012; 47:517-27.

11. Chen X, Skutt-Kakaria K, Davison J, Ou YL, Choi E, Malik P, Loeb K, Wood B, Georges G, Torok-Storb B, Paddison PJ. **G9a/GLP-dependent histone H3K9me2 patterning during human hematopoietic stem cell lineage commitment**. *Genes Dev*. 2012; 26:2499-511.
12. Chou FS, Griesinger A, Wunderlich M, Lin S, Link KA, Shrestha M, Goyama S, Mizukawa B, Shen S, Marcucci G, Mulloy JC. **The thrombopoietin/MPL/Bcl-xL pathway is essential for survival and self-renewal in human preleukemia induced by AML1-ETO**. *Blood*. 2012; 120:709-19.
13. Davalos D, Ryu JK, Merlini M, Baeten KM, Le Moan N, Petersen MA, Deerinck TJ, Smirnoff DS, Bedard C, Hakozaki H, Gonias Murray S, Ling JB, Lassmann H, Degen JL, Ellisman MH, Akassoglou K. **Fibrinogen-induced perivascular microglial clustering is required for the development of axonal damage in neuroinflammation**. *Nat Commun*. 2012; 3:1227.
14. Delaney MK, Liu J, Zheng Y, Berndt MC, Du X. **The role of Rac1 in glycoprotein Ib-IX-mediated signal transduction and integrin activation**. *Arterioscler Thromb Vasc Biol*. 2012; 32:2761-8.
15. Duan W, Gao L, Zhao W, Leon M, Sadee W, Webb A, Resnick K, Wu X, Ramaswamy B, Cohn DE, Shapiro C, Andreassen PR, Otterson GA, Villalona-Calero MA. **Assessment of FANCD2 nuclear foci formation in paraffin-embedded tumors: a potential patient-enrichment strategy for treatment with DNA interstrand crosslinking agents**. *Transl Res*. 2013; 161:156-64.
16. Dumont LJ, Cancelas JA, Dumont DF, Siegel AH, Szczepiorkowski ZM, Rugg N, Pratt PG, Worsham DN, Hartman EL, Dunn SK, O'Leary M, Ransom JH, Michael RA, Macdonald VW. **A randomized controlled trial evaluating recovery and survival of 6% dimethyl sulfoxide-frozen autologous platelets in healthy volunteers**. *Transfusion*. 2013; 53:128-37.
17. Dumont LJ, Cancelas JA, Graminske S, Friedman KD, Vassallo RR, Whitley PH, Rugg N, Dumont DF, Herschel L, Siegal AH, Szczepiorkowski ZM, Fender L, Razatos A. **In vitro and in vivo quality of leukoreduced apheresis platelets stored in a new platelet additive solution**. *Transfusion*. 2013; 53:972-80.
18. El-Amouri SS, Cao P, Miao C, Pan D. **Secreted luciferase for in vivo evaluation of systemic protein delivery in mice**. *Mol Biotechnol*. 2013; 53:63-73.
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20. Flick MJ, Du X, Prasad JM, Raghu H, Palumbo JS, Smeds E, Höök M, Degen JL. **Genetic elimination of the binding motif on fibrinogen for the S. aureus virulence factor ClfA improves host survival in septicemia**. *Blood*. 2013; 121:1783-94.
21. Geiger H, Pawar SA, Kerschen EJ, Nattamai KJ, Hernandez I, Liang HP, Fernández JÁ, Cancelas JA, Ryan MA, Kustikova O, Schambach A, Fu Q, Wang J, Fink LM, Petersen KU, Zhou D, Griffin JH, Baum C, Weiler H, Hauer-Jensen M. **Pharmacological targeting of the thrombomodulin-activated protein C pathway mitigates radiation toxicity**. *Nat Med*. 2012; 18:1123-9.
22. George A, Pushkaran S, Konstantinidis DG, Koochaki S, Malik P, Mohandas N, Zheng Y, Joiner CH, Kalfa TA. **Erythrocyte NADPH oxidase activity modulated by Rac GTPases, PKC, and plasma cytokines contributes to oxidative stress in sickle cell disease**. *Blood*. 2013; 121:2099-107.
23. Goyama S, Mulloy JC. **Making healthy stem cells: the new role of TPO**. *Cell Stem Cell*. 2013; 12:8-9.
24. Guo L, Moon C, Niehaus K, Zheng Y, Ratner N. **Rac1 controls Schwann cell myelination through cAMP and NF2/merlin**. *J Neurosci*. 2012; 32:17251-61.

25. Gutmann DH, Parada LF, Silva AJ, Ratner N. **Neurofibromatosis type 1: modeling CNS dysfunction**. *J Neurosci*. 2012; 32:14087-93.
26. Hennigan RF, Moon CA, Parysek LM, Monk KR, Morfini G, Berth S, Brady S, Ratner N. **The NF2 tumor suppressor regulates microtubule-based vesicle trafficking via a novel Rac, MLK and p38(SAPK) pathway**. *Oncogene*. 2013; 32:1135-43.
27. Hirai H, Kamio N, Huang G, Matsusue A, Ogino S, Kimura N, Satake S, Ashihara E, Imanishi J, Tenen DG, Maekawa T. **Cyclic AMP responsive element binding proteins are involved in 'emergency' granulopoiesis through the upregulation of CCAAT/enhancer binding protein βeta**. *PLoS One*. 2013; 8:e54862.
28. Horwitz MS, Corey SJ, Grimes HL, Tidwell T. **ELANE mutations in cyclic and severe congenital neutropenia: genetics and pathophysiology**. *Hematol Oncol Clin North Am*. 2013; 27:19-41, vii.
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34. Katayama K, Leslie JR, Lang RA, Zheng Y, Yoshida Y. **Left-right locomotor circuitry depends on RhoA-driven organization of the neuroepithelium in the developing spinal cord**. *J Neurosci*. 2012; 32:10396-407.
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p53-induced DNA damage response pathway in lymphoblastic leukemia. *Cancer Cell*. 2013; 23:200-14.

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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 physiopathologica role and novel approach of therapeutic targeting of Rho GTPase and mTOR signaling networks

Paul Andreassen, PhD, Associate Professor

Research Interests Understanding mechanisms of genome instability, including Fanconi Anemia and breast cancer susceptibility. This work includes investigation of cell cycle checkpoints, especially in their role in signaling the DNA damage response. We are also investigating ubiquitin-dependent signaling in coordinating DNA damage responses and DNA repair by homologous recombination. These studies are important for understanding the genetic basis for cancer. Also, given that DNA damaging agents are extensively utilized in treating cancer, understanding the function of pathways which respond to this damage is critical for improving therapeutic strategies.

Jose Cancelas, MD, PhD, Associate Professor

Leadership Program Leader, Stem Cell Program; Director, Flow Cytometry Core Facility

Research Interests Stem Cell Program

Jay Degen, PhD, Professor

Leadership Program Leader, Hemostasis and Thrombosis Program

Research Interests The long-term objective of this research program has been to understnd the mechanisms by which key hemostatic factors (e.g., prothrombin, fibrinogen, and plasminogen) contribute to diverse physiological processes (e.g., maintenance of vascular integrity, tissue repair, innate immunity) and debilitating or life-threatening pathological processes (e.g., vessel wall disease, malignancy, inflammatory disease). Because a rigorous understanding of these comples proceses can only be achieved in an easily-manipulated in vivo experimental setting, a major focus of this research program has been studies of gene-targeted mouse lines lacking or expressing mutant forms of selected hemostatic factors. We and others have firmly established that multiple proteolytic targets of thrombin are coupled to the control of inflammation processes in vitro and in vivo, including fibrinogen, factor XIII, protease-activated receptors and protein C. thrombin targets to antimicrobial host defense, neuroinflammatory disease and sickle cell disease. A more comprehensive understanding of the cross-talk between the hemostatic and inflammatory systems may reveal novel, safe and effective therapuetic strategies for the treatment of a wide spectrum of diseases.

Marie-Dominique Filippi, PhD, Assistant Professor

Research Interests Stem Cell Program

Matthew Flick, PhD, Assistant Professor

Research Interests Defining the mechanisms linking coagulation and fibrinolytic system components to physiological and pathological inflammation

Hartmut Geiger, PhD, Adjunct

Leadership Director, Comprehensive Mouse and Cancer Core

Research Interests Research in the Geiger Laboratory is mostly centered around hematopoiesis and HSCs. We primarily focus our analysis on stem cell aging, leukemia and DNA damage responses in this system. We also investigate mechanisms of aging of intestinal stem cells and mechanisms of therapy-induced myelodysplastic syndrome.

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 Rho GTPases in T cell biology

Kakajan Komurov, PhD, Assistant Professor

Research Interests Cancer systems biology; regulatory networks, bioinformatics

Carolyn Lutzko, PhD, Associate Professor

Leadership Director, Cell Processing Core; Co-Director, Cell Manipulations Lab; Director, Development Lab

Research Interests Research is focused on using stem cells to better understand and treat inherited blood disorders. One area of research is to develop induced pluripotent stem cells from patients with blood diseases. The lab then uses these pluripotent stem cells as a renewable source for blood cells to study in the laboratory, to study disease at the cellular level, and to test potential gene and drug therapeutics. In other studies, the lab is working with other physicians and scientists to translate cell and gene therapies for blood and other diseases from the basic lab into the clinic.

Punam Malik, MD, Professor

Leadership Professor of Pediatrics, University of Cincinnati College of Medicine; Program Leader, Molecular and Gene Therapy Program; Deputy Director, Comprehensive Sickle Cell Program

Research Interests Hemoglobinopathies, Stem Cell Biology, Gene Therapy

Ruhikanta Meetei, PhD, Assistant Professor

Research Interests Signaling and Drug Discovery Program

Shyra Miller, PhD, Assistant Professor

Research Interests Cancer Biology and Neural Tumors Program

James Mulloy, PhD, Associate Professor

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

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

Nicolas Nassar, PhD, Associate Professor

Research Interests We combine biphysical, biochemical and celular approaches to elucidate the structure/function relationship of signaling proteins and to inhibit them in disease.

Dao Pan, PhD, Assistant Professor

Research Interests Research focus is on combining translational and basic research on virus-mediated, in vivo and ex-vivo, gene transfer into stem cells, as well as their potential application for gene therapy of patients with inherited or acquired diseases, with the particular goal of ameliorating the central nervous system abnormalities and bone diseases.

Qishen Pang, PhD, Associate Professor

Research Interests Research focuses on the function of Fanconi Anemia (FA) proteins in hematopoiesis, with specific emphasis on elucidating the mechanisms by which the FA proteins regulate the hematopoietic stem cells in the context of bone marrow failure and leukemia development. These studies utilize cellular, genetic, and molecular techniques to identify and characterize critical pathways that regulate hematopoietic stem cell function.

Nancy Ratner, PhD, Professor

Leadership Program Leader, Cancer Biology and Neural Tumors; Endowed Chair

Research Interests Neurofibromatosis/Cancer Biology/Nervous system development

Damien Reynaud, PhD, Assistant Professor

Research Interests The overall goal of our research is to characterize the systemic and environmental signals that specifically affect the developing hematopoiesis at the time of birth and to investigate the contribution of these signals to the leukemogenic process in children.

Daniel Starczynowski, PhD, Assistant Professor

Research Interests Molecular and cellular basis of hematologic malignancies

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 Practicies

(cGMP)

Ronald Waclaw, PhD, Assistant Professor

Research Interests Impact of RASopathy mutations on brain development,genetic control of regional development in the mouse telencephalon, role of developmental genes during gliomagenesis

Jianqiang Wu, MD, MS, Instructor

Research Interests Preclinal trial of neurofibrom a, cancer stem/progenitor cells

Joint Appointment Faculty Members

Mohammed Azam, PhD, Assistant Professor (Cancer Pathology)

Research Interests Hematology Malignancy Program

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

Research Interests The Chow Lab studies High-Grade Gliomas which are aggressive brain tumors in adults and children with limited treatment options. Using a combination of novel and robust laboratory models coupled with the study of human tumor material, the lab's goals are to better understand the cellular origins and molecular underpinnings of these diseases in order to design and test novel therapies that will improve patient outcome.

Biplab DasGupta, PhD, Assistant Professor (Oncology)

Research Interests Our laboratory is interested in understanding the function of energy and nutrient sensing enzymes during normal brain development and in brain cancer. We use a variety of methods incuding in vitro culture systems, knockout and transgenic mouse models and ex vivo techniques to examine metabolic regulation in neural tissue.

Rachid Drissi, PhD, Assistant Professor (Oncology)

Research Interests Cancer Biology and Neural Tumors Program

Leighton Grimes, PhD, Associate Professor (Immunobiology)

Research Interests Hematology Malignancy Program

Gang Huang, PhD, Assistant Professor (Cancer Pathology)

Research Interests Cancer develops through a series of DNA and non-DNA related changes that progressively drive normal cells into highly malignant derivatives and the distinct mutations can cause the same cancer via their effects on the same regulatory network. The key regulators for blood cell development are DNA binding proteins and chromatin (proteins packed DNA) modification enzymes, which are often targeted by mutations or chromosomal translocations in human blood cancer. Research in Dr. Gang Huang's laboratory focuses on the DNA binding proteins and chromatin (proteins packed DNA) modification enzymes in blood cell normal development and cancer. This research will provide new insight into the interplay between DNA binding proteins and chromatin modification enzymes in normal blood development and leukemia. It will also help to develop drugs which will benefit the future clinical treatments.

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

Research Interests Hematology Malignancy Program

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

Research Interests Hematology Malignancy program

Benjamin Mizukawa, MD, Instructor (Oncology)

Research Interests Hematological Malignancy Program

Eric Mullins, MD, Assistant Professor (Hematology)

Research Interests Hemostasis and Thrombosis Program

Joseph Palumbo, MD, Associate Professor (Hematology)

Research Interests Hemostasis and Thrombosis Program

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

Research Interests Hematology and Gene Therapy Program

LIsa Privette Vinnedge, PhD, Instructor (Oncology)

Research Interests Advanced breat cancer (BC) has poor survivial rates and is the second leading cause of cancer deaths. Mortality is a result of tumor recurrence and disease progression, which are caused by a drug-resistant BC stem cell (BCSC) population. Identifying novel molecular mechanisms is crucial for developing new treatments that may target BCSCs, a potential candidate is the frequently upregulated, chromatin remodeling protein, DEK. My work indicates that DEK (1) promotes tumor initation and oncogenic phenotypes, (2) increases Wnt/beta-catenin pathway activity, and (3) is an estrogen receptor (ER-alpha) target gene that promotes tamoxifen drug resistence. Of importance, DEK inhibition correlates with fewer BCSC numbers, decreased overt lung metastases in murine models, and Wnt pathway inhibition. Finally, the loss of DEK enhances the cytotoxicity of the chemotherapeutic drug cisplatin. Current work focuses on 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.

Susanne Wells, PhD, Associate Professor (Oncology)

Research Interests The long term goal of my research program is to identify viral and cellular modifiers of epithelial cancers, and to explore the therapeutic targeting of such modifiers for the purpose of new cancer treatments. Versatile human and murine tumor models, and my board interest in viral tumor etiology and biology form the basis for our research. In past years, we hae explored translational directions which offer unique training opportunities. An emergin theme is organismal and cellular preference for certain DNA repair mechanisms, a major determinant of genome instability, cancer susceptibiity and response to treatment. For instance, Fanconi Anemia (AF) patients exhibit an aberrant choice of repair in every cell of the body contributes to the susceptibility of children with FA to leukemia nad solid tumors, as well as to life-threatening toxicities of chemotherapy.

Trainees

Shailaja Akunuru, PhD, 2010, University of Cincinnati
Gregory Bick, BS, 2010, Case Western Reserve
Gasilina Anjelika, , 2011
Kyung-Hee Chang, PhD, PGY-5, University of Florida
Wei Du, MD, PhD, 2007, Tohoku University School of Medicine, Japan
Marthe-Sandrine Eiymo Mwa Mpollo, Grad Student, University of Montreal
Salim El-Amouri, PhD, PL-3, Medical University of South Carolina
Chris Evelyn, PhD, 2009, University of Michigan
Yuxin Feng, PhD, 2008, University of Cincinnati
Susuma Goyama, PhD, 2009, Graduate School of Medicine, University of Tokyo
Paritha Arumugan, PhD, CCHMC
Li Guo, PhD, 2006, Chinese Academy of Sciences, Shanghai, China
Ajay Perumbeti, MD, Northeastern Ohio Medical University

Vikram Kohli, PhD, Yr-1
Rachel Mantyla, , University of Cincinnati
Kimberly Breving, MS, CCHMC
Leesa Sampson, PhD, 2010, Vanderbilt University
Edwin Jousma, MS, CCHMC
Shan Lin, Grad Student, 2010, Tsinghua University, Beijing China
Kevin Link, PhD, 2007, University of Cincinnati
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Debra Mayes, PhD, 2006, University of Arkansas
Xiaoyi Chen, MD, 2012, West China Medical School, Sichuan University
Nicholas Olshavsky, 3rd year Post-doc, 2010, University of Cincinnati
Jung-Young Park, PhD, 2010, National Institutes of Health
Ami V. Patel, PhD, 2009, University of Louisville
Deanna Patmore, BS, PGY-IV, South Carolina
TingTing Zhang, PhD, 2012, University of Alabama at Birmingham
Junqi Yang, PhD, PL-1, University of Cincinnati
Garrett Rhyasen, BSc, PGY-2, University of Victoria
Wen Chai, BS, PGY-1, University of Minnesota
Haley Titus-Mitchell, MS, PGY-II, Wright State University
Melinda Varney, PhD, PDF-2, Marshall University, WV
Shiv Viswanathan, PhD, 2003, University of Cincinnati
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Shuangmin Zhang, PhD, PL-2, University of Texas
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Benjamin Mizukawa, MD, 2008, University of Utah School of Medicine
Ryan Brooks, Grad Student, 2013
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Lisa Trump, PhD, PGY-2, University of Illinois, Urbqana Champaign
Jing Fang, MD, PhD, PDF-2, Maine Medical Center Research Institute
Hongyan Zhu, PhD, PGY-1, University of Cincinnati
Mei Dai, PhD, PL-2, Institute of Materia Medica, Chinese Academy of Sciences, P.R. China
Jing-Fen Han, PhD, PL-2, University of Medicine & Dentistry of New Jersey
Juana Serrano-Lopez, PhD, PGY-5, University of Cordoba Argentina
Shanmuganathan Chandrakasan, MD, Children's Hospital of Michigan
Jed Kendall, BS, PGY-II, Brigham Young University
Nihal Bakeer, MD, CCHMC
Meghan Brundage, MS, PGY-VI, University of Cincinnati
Preeti Tandon, PhD, 2011, University of Cincinnati
Mathieu Sertorio, PhD, 2012, University Aix-Marseille II. INSERM, France
Kwangmin Choi, PhD, 2010, Indiana University
Xiaoli Li, PhD, 2011, Chinese Center for Disease Control and Prevention
Surya Amarachintha, PhD, 2011, Bowling Green State University
Navin Ravishankar, Grad Student, 2012
Ramesh Nayak, PhD, PGY-2, University of Texas at Tyler
Ashley Ficker, BS, 2009, University of Cincinnati

Cuiping Zhang, PhD, PGY-2, Peking Union Medical College, China
Ming Liu, PhD, 2010, Sichuan University China
Matt Grogg, PhD, 2006, University of Dayton
Swarnava Roy, PhD, 2010, NIH
Harini Raghu, PhD, 2009, University of Cincinnati
Swati Tiwari, , 2011, University of Delhi
Archana Shaesta, Grad Student, 2011, Missouri State University
Jeffrey Vassallo, PhD, 2012, BMS Lehy University
Marnie Hall, PhD, 2006, CCHMC
Laura Murley, PhD, 2012
Arun Pradhan, PhD, 2007, U Pennsylvania
Abdullah Ali, PhD, 2006, IISC
Thiyam Ramsingh, PhD, 2005

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Division Collaboration

Biomedical Informatics » Bruce Aronow
Grant

BMT » Stella Davies
Grant

Immunobiology » Lee Grimes
Grant

Neonatology and Pulmonary Biology » Vladimir Kalinichenko
Thesis Committee

Division of Developmental Biology » Raphael Kopan
Thesis Committee

BMT » Ashish Kumar
Thesis Committee

Biomedical Informatics » Jaroslaw Meller
Grant, Publication

Hematology » Joe Palumbo
Grant, Publication

Oncology » John Perentesis
Grant

Developmental Biology » Jim Wells
Thesis Committee

Oncology » Susa Wells

Grant, publication

Neonatology and Pulmonary Biology » Jeffrey Whitsett

Publication

Pathology » Kathryn Wikenheiser-Brokamp

Thesis Committee

Reproductive Scienees » Satoshi Namekawa

The function of DNA repair proteins in meiosis

Bone Marrow Transplantation/Immune Deficiency » Stella Davies

Prenatal EGFR-STAT3 pathway promotes NF1 peripheral nerve tumorigenesis and transformation

Imaging Resource Center » RS Dunn

Neurofibroma-associated macrophages play roles in tumor growth and response to pharmacological inhibition

Diagnostic Immunology Lab; Bone Marrow Transplantation/Immune Deficiency » A Filipovich

Prenatal origin of Monosomy 7 in very young children

Cancer Pathology/Immunobiology » Lee Grimes

Klf5 controls bone marrow homing of stem cells and progenitors through Rab5-mediated membrane β1/β2-integrin expression.

Cancer Pathology/Immunobiology » Lee Grimes

Kruppel-Like-Factor 5 (Klf-5) controls hematopoietic stem cell/progenitor bone marrow homing and lodging through Rab5-mediated expression of active β1 integrin.

Biostatistics & Epidemiology/Bone Marrow Transplantation » Kim Mo

Neurofibroma-associated macrophages play roles in tumor growth and response to pharmacological inhibition.

Bone Marrow Transplantation/Immune Deficiency » Ashish Kumar

P190-B RHOGAP is critical for the hematopoietic stem and progenitor cell niche.

Radiology » D Lindquist

An EGFR-STAT3 pathway promotes NF1 peripheral nerve tumorigenesis and transformation.

Bone Marrow Transplantation and Immune Deficiency » P Mehta

Quercetin: Novel targeted chemoprevention for Fanconi anemia patients

Bone Marrow Transplantation and Immune Deficiency » P Mehta

Prenatal origin of Monosomy 7 in very young children.

Immunobiology » H Olsson

Klf5 controls bone marrow homing of stem cells and progenitors through Rab5-mediated membrane β1/β2-integrin expression.

Immunobiology » H Olsson

Kruppel-Like-Factor 5 (Klf-5) controls hematopoietic stem cell/progenitor bone marrow homing and lodging through Rab5-mediated expression of active β1 integrin.

Oncology » J Perentesis

Clinical Study

Oncology » J Perentesis

Vav3 collaborates with p190-BCR-ABL in lymphoid progenitor leukemogenesis, proliferation and survival.

Human Genetics » C Prada

Neurofibroma-associated macrophages play roles in tumor growth and response to pharmacological inhibition.

Human Genetics » R Raman

P190-B RHOGAP is critical for the hematopoietic stem and progenitor cell niche.

Genetics; Pathology » T Smolarek

Prenatal origin of Monosomy 7 in very young children.

Oncology » Susa Wells

Role and Regulation of the Human DEK Proto-Oncogene

Neonate & Pulmonary Biology » J Whitsett

Kruppel-Like-Factor 5 (Klf-5) controls hematopoietic stem cell/progenitor bone marrow homing and lodging through Rab5-mediated expression of active β1 integrin.

Neonate & Pulmonary Biology » J Whitsett

Klf5 controls bone marrow homing of stem cells and progenitors through Rab5-mediated membrane β1/β2-integrin expression.

Genetics; Pathology » S Zimmerman

Prenatal origin of Monosomy 7 in very young children.

Hematology » Joe Palumbo

Cancer Research; Co-Investigators

Hematology » Eric Mullins

Neuroinflammatory Disease Research

Pathology » David Witte

Disease Pathogenesis Research

Pathology » S Kumar Shanmukhappa

Pathobiology of Sickle Cell Disease

Hematology » Eric Mullins

Co-Investigators

Rheumatology » Sherry Thornton

Co-Investigators

Immunology » Senad Divanovic

Co-Investigators

Hematology » Theodosia Kalfa

Set up clinical test for diagnosis of erythrocyte cytoskeleton disorder

BMT » Perinda Mehta

Support of Fanconi Anemia Program

BMT » Lisa Filipovich

Support of hte SCID-X1 gene transfer trial

Human Genetics » Kejian Zhang

Support Development of Specialized Fanconi Anemia Testing

Critical Care Medicine » Basilia Zingarelli

Experiments

Immunobiology; » Lee Grimes
Provided Reagents and performed experiments

Neonatology and Pulmonary Biology » Bruce Trapnell and Jeff Whitsett
Development of Gene Therapy for hPAP and development of markers to identify lung stem cells

Molecular Cardiovascular Biology » Stephanie Ware
Development of iPSC models of cariomyopathy

Immunobiology » Lee Grimes
Development of anti-viral Cytotoxic T Lymphocytes

BMT » Lisa Filipovich
xSCID Gene Therapy

Immunology Center - Immunobiology » Michael Jordan and Kimberly Risma
Gene Therapy for HLH

Pulmonary » Jeff Whitsett, Neeni Hensley, and Tim LeCras
Pulmonary pathology in Sickle Cell Disease

Heart Institute » Jeffrey Towbin, Tim Kimball, and Michael Taylor
Cardiac aspects of Sickle Cell Disease

Cellular and Molecular Immunology » Lee Grimes
Xenograft leukemia models

Cellular and Molecular Immunology » Clair Chougnet
Humanizing Mice

Cellular and Molecular Immunology » Julio Aliberti
Humanizing Mice

BMT » Ashish Kumar
Role of Meis1 in AML

Pathology » Gang Huang
Role of RUNX1 in AML

Rheumatology » John Harley
Immune response to EBV in humanized mice

Hematology » Joe Palumbo
Role of thrombin in AML

Cellular and Molecular Immunology » Fred Finkelman
Human mast cell development in humanized immunodeficient mice

Allergy and Immunology » Patty Fulkerson
Human eosinophil progenitor cell development in humanized immunodeficient mise

Allergy and Immunology » Nives Zimmerman
Human eosinophil cell development in humanized immundeficient mice

Cellular and Molecular Immunology » Michael Jordan
Role of Interferon gamma in a xenograft anemia model

Human Genetics » Greg Grabowski

Gene therapy for Gaucher disease - leading to dual-PI R01 application

BMT » Stella Davies, Parinda Mehta, and Kasiani Myers

Oxidative stress and bone marrow failure in FA

Endocrinology » Susan Rose and

Endocrine defect in FA children

Pediatric Gastroenterology, Hepatology and Nutrition » Kris Steinbrecher

Inflammatory responses in FA hematopoiesis

Bioinformatics » Bruce Aronow

Publication

Ophthalmology » Richard Lang

New DOD grant funded

Radiology » Diana Lindquist

DOD grant; publication

Oncology » John Perentesis

NIH Grant; publication

Pathology; » Margaret Collins

NIH grant; publications

Cellular and Molecular Immunobiology » Lee Grimes

Gfi1 and TIFAB genetic interaction

Neonatology and Pulmonary Biology » Vladimir Kalinichenko

Studying the transcription factor Foxm1 in the development of forebrain neurons. Foxm1 expression is associated with high-grade compared to low-grade gliomas.

Oncology » Lionel Chow

Study the role of Foxm1 in a genetic model of high-grade astrocytoma

Oncology » Biplab DasGupta

Study the downstream mechanisms of abnormal Shp2 signaling caused from Shp2-GOF mutations observed in Noonan Syndrome.

Radiology » Diana Lindquist

Mouse MRI

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
AKUNURU, S		
Training Programs in Cancer Therapeutics National Institutes of Health(University of Cincinnati)		
T32 CA 117846	09/14/12-08/31/14	$48,435
ANDREASSEN, P		

14th Annual Midwest DNA Repair Symposium
National Institutes of Health(University of Cincinnati)
R13 CA 168317 04/01/12-03/31/13 $6,000

FANCD2 Monoubiquitination in DNA Damage Responses
National Institutes of Health
R01 HL 085587 07/08/08-06/30/13 $222,750

CANCELAS-PEREZ, J

Rational Design of a Vav/Rac Inhibitor as a New Therapy
The Leukemia and Lymphoma Society
10/01/12-09/30/15 $180,018

CHOI, K

Regulation of Cellular Growth and Differentiation
National Institutes of Health(University of Cincinnati)
T32 CA020624 09/30/12-08/31/13 $21,122

DEGEN, J

Analysis of Staphylococcus Aureus Host Interactions
National Institutes of Health(Texas A & M)
R01 AI 020624 09/30/10-08/31/13 $49,971

DEGEN, J / MALIK P (MPI)

Hemostatic Factors and Sickle Cell Disease
National Institutes of Health
R01 HL 112603 01/01/12-11/30/16 $238,000

FENG, Y

Targeting Bone Marrow Niche to Eradicate Childhood Acute Myeloid Leukemia
Cancer Free Kids
06/01/13-05/31/14 $25,000

FILIPPI, M

Regulation of Neutrophil Migration and Polarity
National Institutes of Health
R01 HL 090676 03/01/10-02/28/15 $235,620

FLICK, M

Mechanisms Linking the Hemostatic Protease Thrombin to Arthritic Disease
National Institutes of Health
R01 AR 056990 08/10/09-07/31/14 $171,072

Cincinnati Rheumatic Disease Core Center (Core 2)

National Institutes of Health

P30 AR 047363 08/25/11-06/30/16 $52,222

GEIGER, H

Activated Protein C for Treatment of Radiation Combined Injury

National Institutes of Health(Blood Center of Wisconsin, Inc.)

R33 AI 080557 09/13/10-08/31/13 $77,488

Molecular Mechanisms and Therapies for Radiation-Induced Myelodysplastic Syndrome

Edward P Evans Foundation(University of Kentucky)

04/01/12-03/31/17 $181,818

GOYAMA, S

Suppressing a Tumor Suppressor RUNX1: A Novel Approach to Treat Pediatric Acute Leukemia

Cancer Free Kids

07/01/12-06/30/13 $40,000

HENNIGAN, R

Regulation of Intracellular Trafficking in NF2

Department of Defense

W81XWH1310136 06/01/13-05/31/16 $129,421

KOMUROV, K

Targeting Metabolic Vulnerabilities of ERBB2-Driven Breast Cancer

Ride Cincinnati Foundation

04/01/13-03/31/14 $40,000

LIN, S

Identification of Drug Development Pathway for Improving Prognosis of Pediatric Leukemia

Cancer Free Kids

05/01/12-04/30/13 $30,000

LUTZKO, C

NHLBI Progenitor Cell Biology Institute - Pilot Study

National Institutes of Health(University of Maryland)

U01 HL 099997 03/01/13-02/28/14 $58,905

MALIK, P

Ameliorating Sickle Nephropathy and Pulmonary Hypertension

National Institutes of Health

R34 HL 108752 08/18/11-06/30/14 $150,000

Development of Safe and Efficient Gene Therapy Strategies

National Institutes of Health(Fred Hutchinson Cancer Research Center)

R01 HL 098489 01/21/10-12/31/14 $43,333

PLGF-H1F1a-mIRNA Axis in Sickle Pulmonary Hypertension

National Institutes of Health(University of Southern California)

R01 HL 111372 01/01/12-12/31/16 $161,480

Cincinnati Cell Characterization Core

National Institutes of Health(University of Maryland)

U01 HL 099997 09/30/10-04/30/14 $316,697

Cincinnati Cell Characterization Core - per assay

National Institutes of Health(University of Maryland)

U01 HL 099997 09/30/10-04/30/14 $247,368

MULLOY, J

Genotype and Phenotype of Chemoresistant AML

National Institutes of Health

R21 CA 168369 03/01/13-02/28/15 $130,500

Rac Signaling in MLL Leukemia

The Leukemia and Lymphoma Society

07/01/10-06/30/15 $104,702

OSHAVSKY, N

Regulation of Cellular Growth and Differentiation

National Institutes of Health(University of Cincinnati)

T32 CA 059268 12/6/12-04/30/13 $21,122

PAN, D

Genetic Therapy for CNS Manifestations in MPS I via BBB-Targeted Protein Delivery

National Institutes of Health

R01 NS 064330 09/30/08-08/31/13 $214,375

PANG, Q

Role of FA Proteins in Hematopoiesis

National Institutes of Health

R01 HL 076712 04/01/10-03/31/15 $235,620

Role of Tumor Necrosis Factor in Leukemogenesis

The Leukemia and Lymphoma Society

07/01/08-06/30/13 $103,115

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

National Institutes of Health

R01 CA 157537 02/01/11-12/31/15 $195,050

PATEL, A

Neurofibromatosis Postdoctoral Traineeship

The Ohio State University

06/01/13-05/31/14 $46,092

RATNER, N

Can Targeting Fat Cure MPNST?

Cancer Free Kids

06/01/13-05/31/14 $30,000

Cincinnati Center for Neurofibromatosis Research

National Institutes of Health

P50 NS 057531 09/15/08-06/30/13 $1,068,273

Ratner, N	Project A	$48,069
Cripe, T	Project B	$106,147
Rizvi, T	Project C	$81,328
Perentesis, J	Project 1	$297,056
Ratner, N	Project 2	$225,064
Ratner, N	Project 3	$276,814

Identification of Molecular and Cellular Contributors to Neurofibroma Formation and Growth

Department of Defense

W81XWH1210133 07/01/12-06/30/15 $221,965

In Vivo Testing of Anti-Oxidants in Nf1 CNS

The Children's Tumor Foundation

07/01/12-06/30/13 $45,455

Mitogenic Activities in Neurofibromatosis

National Institutes of Health

R01 NS 028840 09/15/11-07/31/16 $231,250

SAMPSON, L

mTOR Signaling in Murine Intestinal Stem Cell and Progenitor Homeostasis

National Institutes of Health

F32 DK 097879 12/01/12-11/30/14 $52,605

STARCZYNOWSKI, D

Defining the Role and Therapeutic Potential of TNF Recep

Gabrielle's Angel Fnd for Cancer Research

06/01/13-05/31/16 $68,182

Deregulation of TIFAB in Myelodysplastic Syndrome

American Society of Hematology

	07/01/11-06/30/14	$50,000

Identification and Characterization of Genes in del(5q) Myelodysplastic Syndrome

National Institutes of Health

R01 HL 111103	12/15/11-11/30/16	$238,000

Regulation and Function of TIFAB in Myelodysplastic Synd

Department of Defense

W81XWH1110468	06/01/11-05/31/14	$132,295

TANDON, P

Training Programs in Cancer Therapeutics

National Institutes of Health(University of Cincinnati)

T32 CA 117846	09/14/12-08/31/14	$48,435

VARNEY, M

Environmental Carcinogenesis and Mutagenesis

National Institutes of Health(University of Cincinnati)

T32 ES 007250	05/01/12-04/30/14	$6,894

WU, J

STAT3 in Neurofibroma Tumorigenesis and Therapy

Department of Defense Army

W81XWH1110259	07/01/11-06/30/14	$132,862

Exploring the Plexiform Neurofibroma Interactone

Neurofibromatosis Therapeutic Accleration Program(John Hopkins University)

	05/15/13-05/14/15	$292,910

ZHENG, Y

Cincinnati Center for Excellence in Molecular Hematology

National Institutes of Health

P30 DK 090971	07/01/10-06/30/13	$505,315

Zheng, Y	Admin Core	$91,497
Grabowski, G	Genomics and Genetic Core	$63,001
Cancelas, J	Cell Analysis and Sorting Core	$65,112
Malik, P	Translational Core	$163,824
Mulloy, J	Xenotransplant and Transgenic Core	$68,765
Zheng, Y	Summer Students	$30,370

Pharmacological Rejevention of Aged Hematopoietic Stem Cells
National Institutes of Health(P2D Bioscience)

R34 AG 042986	08/15/12-07/31/13	$84,870

Rac GTPase-Specific Small Molecular Inhibitors
National Institutes of Health

R01 CA 141341	03/24/09-01/31/14	$151,943

Training Program in Pediatric Hematologic and Oncologic Diseases
National Institutes of Health

T32 HL 091805	09/01/08-08/31/13	$155,456

Digestive Health Center: Bench to Bedside Pilot Study
National Institutes of Health

P30 DK 078392	06/01/13-05/31/14	$50,000

ZHENG, Y / MULLOY, J

Targeting Cdc42 in Leukemia Stem Cells
National Institutes of Health

R01 CA 150547	03/10/10-01/31/15	$189,199

ZHENG,Y/ GEIGER, H

Lineage Determination and Tissue HomeOstasis in the Aged Hematopoietic System
National Institutes of Health

R01 AG 040118	08/01/11-07/31/16	$250,000

Current Year Direct **$7,783,205**

Industry Contracts

MULLOY, J

Celgene Cellular Therapeutics	$164,254
NovImmune SA	$8,916
Seattle Genetics	$37,668

GRASSMAN, E

Battelle Memorial Institute	$63,176

Current Year Direct Receipts **$274,014**

Total **$8,057,219**