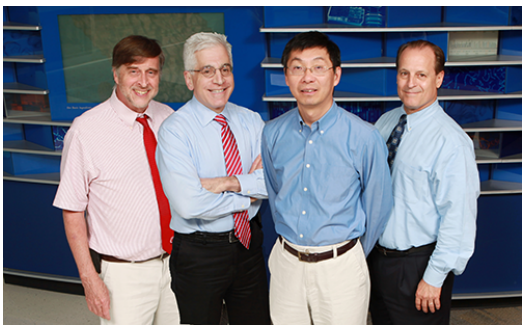
Cancer and Blood Diseases Institute

Division Details

RESEARCH AND TRAINING DETAILS	
Faculty	**77**
Joint Appointment Faculty	**23**
Research Fellows and Post Docs	**36**
Research Graduate Students	**26**
Total Annual Grant Award Dollars	**$21,010,094**
Total Annual Industry Award Dollars	**$1,841,497**



D Witte, J Perentesis, Y Zheng, R Ware

CLINICAL ACTIVITIES AND TRAINING	
Staff Physicians	**15**
Clinical Fellows	**15**
Inpatient Encounters	**2,196**
Outpatient Encounters	**29,819**

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Division Highlights

Qing Richard Lu, PhD

Dr. Qing Richard Lu's research continues to focus on glial cell fate specification and how glial progenitors transform into brain tumors including glioma and medulloblastoma under pathological conditions. Dr. Lu's lab has established a series of animal models for brain tumors. His recent work has demonstrated that transcription factor Olig2+ proliferative cells are the critical source of glioma growth and that Olig2 functions as a tumor-promoting factor for gliomas. Targeting Olig2 sensitizes brain tumor cells to chemotherapy. Hence, Olig2 is the molecular arbiter of genetic adaptability that makes high-grade gliomas aggressive and resistant to treatment. This work is recently published in *Cancer Cell*. Dr. Lu is also investigating the regulation of microenvironment and immunologic responses for enhancing brain cancer therapy.

Dr. Lu continues to study the underlying mechanisms of neurological diseases associated with white matter defects. The recent work of his team finds that a CHARGE syndrome-related chromatin-remodeling enzyme CHD7, which was previously thought as a ubiquitously expressed factor, is highly enriched in myelinating cells, oligodendrocytes, in the brain. His work further shows that Chd7 regulates the onset of myelination in the developing brain and myelin regeneration after injury, suggesting that Chd7 mutations contribute to white matter pathogenesis in CHARGE syndrome. This work is recently published in *Nature Neuroscience*. In addition, the study from his lab shows that a Mowat-Wilson syndrome requires related factor Zeb2 for the onset of peripheral myelination and remyelination. Zeb2 functions through recruiting histone deacetylases HDAC1/2 complexes to antagonize myelination block in the peripheral nervous system. This work is recently published in *Nature Neuroscience*. Furthermore, Dr. Lu's recent study shows that a myelinating cell-enriched microRNA, miR-219, can overcome myelination block in demyelinating disease conditions, and that treatment with this microRNA partially restores myelination

and limb function. This work is recently published in *Developmental Cell*. Dr. Lu is also developing new strategies to identify potential drugs and targets for brain repair.

Daniel T. Starczynowski, PhD

Dr. Daniel Starczynowski, PhD, has a long-standing interest in a family of poorly understood malignant blood diseases known as Myelodysplastic Syndrome (MDS). Ineffective treatment approaches, insufficient understanding of the underlying biology and pathogenesis, and lack of mouse models have all contributed to dismal outcomes for MDS patients. A major focus of Dr. Starczynowski's laboratory has been the intersection of inflammation and MDS, and how patients with MDS can develop acute myeloid leukemia. Namely, they have found aberrant activation of the Toll-like receptor (TLR) pathway in MDS hematopoietic stem cells (HSC), which are the disease-propagating cells, and now have evidence that TLR signaling is a major unifying driver of MDS pathogenesis. His research team recently found that overexpression of TRAF6, a protein that normally functions as an immune sensor of pathogens, impairs blood cell formation and drives the onset of MDS, through an unexpected mechanism involving ubiquitin modification of RNA binding proteins. While dissecting the role of TLR signaling in MDS HSC, Dr. Starczynowski's team has identified an essential function of TLR signaling in normal HSC, a finding that has implications in chronic inflammatory disorders, autoimmunity, and acute infections. As such, Dr. Starczynowski's research program has been developing transformative and innovative approaches to investigate the molecular, cellular, and genetic basis of MDS. Dr. Starczynowski's research program has three main long-term objectives: (1) To evaluate the developmental requirement of TLR signaling components in normal HSC function; (2) To dissect the genetic, molecular, and cellular underpinnings of MDS; and (3) To use the knowledge gained by our basic research to develop novel therapeutic modalities for the treatment of MDS.

Publications

1. Dombi E; Baldwin A; Marcus LJ; Fisher MJ; Weiss B; Kim A; Whitcomb P; Martin S; Aschbacher-Smith LE; Rizvi TA. **Activity of Selumetinib in Neurofibromatosis Type 1-Related Plexiform Neurofibromas.** *The New England journal of medicine*. 2016; 375:2550-2560.

2. Rotz SJ; Dandoy CE; Davies SM. **ST2 and Endothelial Injury as a Link between GVHD and Microangiopathy.** *The New England journal of medicine*. 2017; 376:1189-1190.

3. Fang J; Liu X; Bolanos L; Barker B; Rigolino C; Cortelezzi A; Oliva EN; Cuzzola M; Grimes HL; Fontanillo C. **A calcium- and calpain-dependent pathway determines the response to lenalidomide in myelodysplastic syndromes.** *Nature Medicine*. 2016; 22:727-734.

4. Kesarwani M; Kincaid Z; Gomaa A; Huber E; Rohrabaugh S; Siddiqui Z; Bouso MF; Latif T; Xu M; Komurov K. **Targeting c-FOS and DUSP1 abrogates intrinsic resistance to tyrosine-kinase inhibitor therapy in BCR-ABL-induced leukemia.** *Nature Medicine*. 2017; 23:472-482.

5. Cabezas-Wallscheid N; Buettner F; Sommerkamp P; Klimmeck D; Ladel L; Thalheimer FB; Pastor-Flores D; Roma LP; Renders S; Zeisberger P. **Vitamin A-Retinoic Acid Signaling Regulates Hematopoietic Stem Cell Dormancy.** *Cell*. 2017; 169:807-823.e19.

6. Cavalli FMG; Remke M; Rampasek L; Peacock J; Shih DJH; Luu B; Garzia L; Torchia J; Nor C; Morrissy AS. **Intertumoral Heterogeneity within Medulloblastoma Subgroups.** *Cancer Cell*. 2017; 31:737-754.e6.

7. Lin S; Luo RT; Ptasinska A; Kerry J; Assi SA; Wunderlich M; Imamura T; Kaberlein JJ; Rayes A; Althoff MJ. **Instructive Role of MLL-Fusion Proteins Revealed by a Model of t(4;11) Pro-B Acute Lymphoblastic Leukemia.** *Cancer Cell*. 2016; 30:737-749.

8. Torchia J; Golbourn B; Feng S; Ho KC; Sin-Chan P; Vasiljevic A; Norman JD; Guilhamon P; Garzia L; Agamez NR. **Integrated (epi)-Genomic Analyses Identify Subgroup-Specific Therapeutic Targets in CNS Rhabdoid Tumors.** *Cancer Cell*. 2016; 30:891-908.

9. Niederkorn M; Starczynowski DT. **GMP-ing to Spatial Conclusions about Emergency and Leukemic Myelopoiesis.** *Cell Stem Cell*. 2017; 20:579-581.

10. Ramaswamy V; Hielscher T; Mack SC; Lassaletta A; Lin T; Pajtler KW; Jones DTW; Luu B; Cavalli FMG; Aldape K. **Therapeutic Impact of Cytoreductive Surgery and Irradiation of Posterior Fossa Ependymoma in the Molecular Era: A Retrospective Multicohort Analysis.** *Journal of Clinical Oncology*. 2016; 34:2468-2477.

11. von Stackelberg A; Locatelli F; Zugmaier G; Handgretinger R; Trippett TM; Rizzari C; Bader P; O'Brien MM; Brethon B; Bhojwani D. **Phase I/Phase II Study of Blinatumomab in Pediatric Patients With Relapsed/Refractory Acute Lymphoblastic Leukemia.** *Journal of Clinical Oncology*. 2016; 34:4381-4389.

12. Fang J; Bolanos LC; Choi K; Liu X; Christie S; Akunuru S; Kumar R; Wang D; Chen X; Greis KD. **Ubiquitination of hnRNPA1 by TRAF6 links chronic innate immune signaling with myelodysplasia.** *Nature Immunology*. 2017; 18:236-245.

13. Wu LMN; Wang J; Conidi A; Zhao C; Wang H; Ford Z; Zhang L; Zweier C; Ayee BG; Maurel P. **Zeb2 recruits HDAC-NuRD to inhibit Notch and controls Schwann cell differentiation and remyelination.** *Nature Neuroscience*. 2016; 19:1060-1072.

14. He D; Wang J; Lu Y; Deng Y; Zhao C; Xu L; Chen Y; Hu YC; Zhou W; Lu QR. **lncRNA Functional Networks in Oligodendrocytes Reveal Stage-Specific Myelination Control by an lncOL1/Suz12 Complex in the CNS.** *Neuron*. 2017; 93:362-378.

15. Chandrakasan S; Marsh RA; Uzel G; Holland SM; Shah KN; Bleesing J. **Outcome of patients with NEMO deficiency following allogeneic hematopoietic cell transplant.** *Journal of Allergy and Clinical Immunology*. 2017; 139:1040-1043.e2.

16. de la Morena MT; Leonard D; Torgerson TR; Cabral-Marques O; Slatter M; Aghamohammadi A; Chandra S; Murguia-Favela L; Bonilla FA; Kanariou M. **Long-term outcomes of 176 patients with X-linked hyper-IgM syndrome treated with or without hematopoietic cell transplantation.** *Journal of Allergy and Clinical Immunology*. 2017; 139:1282-1292.

17. Du W; Amarachintha S; Wilson A; Pang Q. **The immune receptor Trem1 cooperates with diminished DNA damage response to induce preleukemic stem cell expansion.** *Leukemia*. 2017; 31:423-433.

18. Itkin T; Kumari A; Schneider E; Gur-Cohen S; Ludwig C; Brooks R; Kollet O; Golan K; Khatib-Massalha E; Russo CM. **MicroRNA-155 promotes G-CSF-induced mobilization of murine hematopoietic stem and progenitor cells via propagation of CXCL12 signaling.** *Leukemia*. 2017; 31:1247-1250.

19. Varney ME; Choi K; Bolanos L; Christie S; Fang J; Grimes LH; Maciejewski JP; Inoue JI; Starczynowski DT. **Epistasis between TIFAB and miR-146a: neighboring genes in del(5q) myelodysplastic syndrome.** *Leukemia*. 2017; 31:491-495.

20. Byrnes JR; Wilson C; Boutelle AM; Brandner CB; Flick MJ; Philippou H; Wolberg AS. **The interaction between fibrinogen and zymogen FXIII-A(2)B(2) is mediated by fibrinogen residues gamma 390-396 and the FXIII-B subunits.** *Blood*. 2016; 128:1969-1978.

21. Chandrakasan S; Jayavaradhan R; Ernst J; Shrestha A; Loberg A; Dexheimer P; Jordan M; Pang Q; Aronow B; Malik P. **KIT blockade is sufficient for donor hematopoietic stem cell engraftment in Fanconi anemia mice.** *Blood*. 2017; 129:1048-1052.

22. Holtan SG; Khera N; Levine JE; Chai X; Storer B; Liu HD; Inamoto Y; Chen GL; Mayer S; Arora M. **Late acute graft-versus-host disease: a prospective analysis of clinical outcomes and circulating angiogenic factors.** *Blood*. 2016; 128:2350-2358.

23. Lounder DT; Khandelwal P; Dandoy CE; Jodele S; Grimley MS; Wallace G; Lane A; Taggart C; Teusink-Cross AC; Lake KE. **Lower levels of vitamin A are associated with increased gastrointestinal graft-versus-host disease in children.** *Blood*. 2017; 129:2801-2807.

24. McGann PT; Hernandez AG; Ware RE. **Sickle cell anemia in sub-Saharan Africa: advancing the clinical paradigm through partnerships and research.** *Blood*. 2017; 129:155-161.

25. Mehta PA; Davies SM; Leemhuis T; Myers K; Kernan NA; Prockop SE; Scaradavou A; O'Reilly RJ; Williams DA; Lehmann L. **Radiation-free, alternative-donor HCT for Fanconi anemia patients: results from a prospective multi-institutional study.** *Blood*. 2017; 129:2308-2315.

26. Rubin TS; Zhang K; Gifford C; Lane A; Choo S; Bleesing JJ; Marsh RA. **Perforin and CD107a testing is superior to NK cell function testing for screening patients for genetic HLH.** *Blood*. 2017; 129:2993-2999.

27. Shaw MA; Kombrinck KW; McElhinney KE; Sweet DR; Flick MJ; Palumbo JS; Cheng M; Esmon NL; Esmon CT; Brill A. **Limiting prothrombin activation to meizothrombin is compatible with survival but significantly alters hemostasis in mice.** *Blood*. 2016; 128:721-731.