BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
Major, Michael B.	**Assistant Professor of Cell and Developmental Biology**
eRA COMMONS USER NAME **BEN_MAJOR**	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Michigan State University, MI	B.S.	1997	Microbiology
University of Utah/Huntsman Cancer Institute, UT	Ph.D	2004	Oncological Sciences
University of Washington, WA	Postdoctoral	2009	Pharmacology

A. Personal Statement

My lab studies how perturbation of specific signal transduction pathways contributes to the initiation, progression and dissemination of cancer. We employ a "systems level" integrative discovery platform to characterize pathway dynamics in normal and cancer cell models. More specifically, we use mass spectrometry-based proteomics to define the protein-protein interaction networks for a particular signaling pathway. We then annotate the nodes within the network for function, as determined by functional genomics and small molecule screening. Integration of these data with cancer-associated mutation data and cancer-associated gene expression data yields a powerful tool for oncological discovery—a cancer annotated physical/functional map for a specific signaling pathway of interest. The models and hypotheses produced though integrative screening are challenged through mechanistic studies employing cultured human cancer cells, zebrafish, mice and *in vitro* biochemical systems.

Using these technologies, my lab is interrogating two signaling pathways in the context of non-small cell lung cancer (NSCLC), colon cancer and chronic myelogenous leukemia: the WNT signaling pathway and the KEAP1/NRF2 antioxidant response pathway. We have found that these pathways functionally communicate in models of NSCLC and colon cancer, and have identified several likely mediators of the cross-talk. Additionally, the integrative approach has revealed numerous pathway-specific proteins. Generally speaking, our work addresses the mechanics and significance of the communication between these pathways, the underlying mechanism(s) driving pathway activation or inactivation in cancer and the potential to exploit any discoveries for diagnostic and therapeutic ends.

B. Positions and Honors.

Positions and Employment

2009- Assistant Professor of Cell and Developmental Biology, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

Honors

1999 Pharmaceutical Research and Manufacturers of America (PhRMA) Foundation Advanced Predoctoral Fellowship in Pharmacology and Toxicology.
2010 Sidney Kimmel Scholar Award
2010 NIH Director's New Innovator Award

C. Selected Peer-reviewed publications (showing 16 of 16).

1. Priscila F. Siesser, Marta Motolese, Matthew P. Walker, Dennis Goldfarb, Kelly Gewain, Feng Yan, Rima M. Kulikauskas, Andy J. Chien, Linda Wordeman and Michael B. Major. FAM123A Binds

Microtubules and Inhibits the Guanine Nucleotide Exchange Factor ARHGEF2 to Decrease Actomyosin Contractility. ***Science Signaling.*** In Press

2. Shelly Sorrells, Seth Carbonneau, Erik Harrington, Aye T. Chen, Bridgid Hast, Brett Milash, Ujwal Pyati, Michael B. Major,Yi Zhou, Rodney A. Stewart, Leonard I. Zon, A. Thomas Look, and Cicely Jette. Ccdc94 Functions in the Prp19 Complex to Protect Cells from Radiation-Induced Apoptosis by Inhibiting the Transcription of p53. ***PLoS Genetics***. In Press
3. Duncan, J.S., Whittle, M.C., Nakamura, K., Abell, A.N., Midland, A.A., Zawistowski, J.S., Johnson, N.L., Granger, D.A., Vincent Jordan, N., Darr, D.B., Usary, J., Kuan, P.F., Smalley, D.M., Major, B., He, X., Hoadley, K., Zhou, B. Sharpless, N.E., Perou, C.M., Kim, W.Y., Gomez, S.H., Chen, X., Jin, J., Frye, S.V., Earp, H.S., Graves, L.M., Johnson, G.L. (2012) Dynamic Reprogramming of the Kinome In Response to Targeted MEK Inhibition In Triple Negative Breast Cancer. ***Cell***. 2012 Apr 13; 149(2):307-21. PMID: 22500798
4. Camp ND, James RG, Dawson DW, Yan F, Davison JM, Houck SA, Tang X, Zheng N, Major MB*, Moon RT*. Wilms tumor gene on the X chromosome (WTX) inhibits the degradation of NRF2 through comptetitive binding to KEAP1. ***Journal of Biological Chemistry***. 2012 Jan 3. Epub PMID: 22215675
5. Chung N, Marine S, Smith EA, Liehr R, Smith ST, Locco L, Hudak E, Kreamer A, Rush A, Roberts B, Major MB, Moon RT, Arthur W, Cleary M, Strulovici B, Ferrer M. A 1,536-well ultra-high-throughput siRNA screen to identify regulators of the Wnt/beta-catenin pathway. ***Assay Drug Dev Tech***., Jun 2010:8(2):286-94. PMID:20578927
6. Jason D. Berndt, Travis L. Biechele, Randall T. Moon, and Michael B. Major. Integrative Analysis of Genome-Wide RNA Interference Screens. ***Science Signaling***. 2009 12 May Vol. 2, Issue 70, p. pt4. PMID: 19436058
7. Richard G. James, Travis L. Biechele, William H. Conrad, Nathan D. Camp, Daniel M. Fass, Michael B. Major, Karen Sommer, XianHua Yi, Brian S. Roberts, Michelle A. Cleary, William T. Arthur, Michael MacCoss, David J. Rawlings, Stephen J. Haggerty and Randall T. Moon. Bruton's Tyrosine Kinase Binds CDC73 and Negatively Regulates Wnt/β-catenin signaling. ***Science Signaling***., 26 May 2009 Vol. 2, Issue 72, p. ra25. PMID: 19471023
8. Jason D. Berndt, Randall T. Moon and Michael B. Major. b-Catenin gets Jaded, and it is VHL's fault. ***Trends in Biological Science.*** 2009 Mar Vol. 34, p.101-104. PMID: 19217300
9. Andy J. Chien, Erin C. Moore, Anke S. Lonsdorf, Rima M. Kulikauskas, Bonnie Gould Rothberg, Aaron J. Berger, Michael B. Major, Sam T. Hwang, David L. Rimm, and Randall T. Moon. Activated Wnt/b-catenin signaling in melanoma is associated with decreased proliferation in patient tumors and a murine melanoma model. ***Proceedings of the National Academy of Scienc*****es**. 2009 Jan 27;106(4):1193-1198. PMID: 19144919
10. Michael B. Major, Brian S. Roberts, Jason D. Berndt, Shane Marine, Jamie Anastas, Namjin Chung, Marc Ferrer, XianHua Yi, Cristi L. Stoick-Cooper, Priska D. von Haller, Lorna Kategaya, Andy Chien, Stephane Angers, Michael MacCoss, Michele A. Cleary, William T. Arthur and Randall T. Moon. An Integrative Molecular Screening Approach Identifies Regulators of Wnt/β-catenin Signal Transduction. ***Science Signaling***. 2008 Nov 11;1(45) PMID: 19001663
11. De Ferrari GV, Papassotiropoulos A, Biechele T, De-Vrieze FW, Avila ME, Major MB, Myers A, Sáez K, Henríquez JP, Zhao A, Wollmer MA, Nitsch RM, Hock C, Morris CM, Hardy J, Moon RT. Common genetic variation within the Low-Density Lipoprotein Receptor-Related Protein 6 and late-onset Alzheimer's disease. ***Proceedings of the National Academy of Scienc*****es**. 2007 May 29;104(22):9434-9439. PMID: 17517621
12. Michael B. Major, Nathan D. Camp, Jason D. Berndt, XianHua Yi, Seth J. Goldenberg, Charlotte Hubbert, Travis L. Biechele, Anne-Claude Gingras, Ning Zheng, Michael J. MacCoss, Stephane Angers, Randall T. Moon. Wilms Tumor Suppressor WTX Negatively Regulates Wnt/β-catenin Signaling. ***Science***. 2007. May 18;316(5827):1043-1046. PMID: 17510365
13. Qisheng Zhang, Michael B. Major, Shinichi Takanashi, Nathan D. Camp, Naoyuki Nishiya, Eric C. Peters, Mark H. Ginsberg, Peter G. Schultz , Randall T. Moon, and Sheng Ding. Small-molecule synergist of the Wnt/b-catenin signaling pathway. ***Proceedings of the National Academy of Scienc*****es**. 2007 May 1;104(18):7444-7448. PMID: 17460038

14. Cristi L. Stoick-Cooper, Gilbert Weidinger, Kimberly J. Riehle, Charlotte Hubbert, Michael B. Major, Nelson Fausto and Randall T. Moon. Distinct Wnt signaling pathways have opposing roles in appendage regeneration. ***Development****.* 2007. 134:479-489. PMID: 17185322
15. Susanne Kloeker, Michael B. Major, David A. Calderwood, Mark H. Ginsberg, David A. Jones, and Mary C. Beckerle. The Kindler syndrome protein is regulated by TGFβ and involved in integrin-mediated adhesion. ***Journal of Biological Chemistry****.* 2004 Feb 20;279(8):6824-33. PMID: 14634021
16. Michael B. Major and David A. Jones. Identification of a Gadd45β 3-prime enhancer that mediates SMAD3 and SMAD4 dependent transcriptional induction by TGFβ. ***Journal of Biological Chemistry***. 2004 Feb 13;279(7):5278-5287. PMID: 14630914

D. Research Support.

Not Assigned Major (PI) 07/01/2010-06/30/2012
Sidney Kimmel Scholar Award
"New Functional Components of the KEAP1 Tumor Suppressor Protein Complex"
The goal of the awarded project is to identify and validate novel regulators of the KEAP1/NRF2 signaling pathway in models of lung cancer.

DP2 OD007149-01 Major (PI) 9/30/2010-9/29/2015
"Exploitation of Near-Haploid Human Cells for Functional Gene Discovery"
The goal of the awarded project is to develop and employ stable near-haploid human cells for genetic dissection of disease-relevant signal transduction pathways.

Not Assigned Major (co-PI w/ D. Neil Hayes) 1/1/2012-12/31/2012
Greensboro Golfers Against Cancer
"A needle in a haystack: Finding key 'driver mutations' from thousands of passenger mutations in individual cancer patients"
The goal of this pilot grant is to ascertain whether novel driver mutations can be probabilistically scored based on their proximity to known oncogenes and tumor suppressors within a protein interaction network.