MD/PhD Program Newsletter

Fall 2019

In This Issue

Contact MD/PhD

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Program Directors

Wally Whiteheart, PhD

Brandon Miller, MD PhD

Richard King, MD PhD

Directors' Welcome

These are exciting times for biomedical research at the University of Kentucky. UK's strategic plan for research recognizes the importance of strong clinical, translational, and basic sciences. UK's overall goal is to address key research questions and translate that knowledge into clinical applications that benefit human health. This has driven an institutional commitment to develop several prominent multidisciplinary centers of research excellence with new faculty recruitments and infrastructure investments. That emphasis is already paying off with record funding levels ($393 million in 2018), seminal research discoveries, and meaningful healthcare breakthroughs. MD/PhDs are at the nexus of these efforts due to their training in both basic research and the practice of medicine. Our MD/PhD program is critical to training the physicians/scientists who will lead the multidisciplinary research teams that accelerate the pace of discovery for the prevention, detection, diagnosis, and treatment of disease thereby improving the health of Kentucky and the nation.

You, our MD/PhD students, are excelling not only in your scientific achievements, but also in your academic records, leadership roles, and community service. You had another record year and a half for publications – 24 in the last 18 months. You are continuing to gain visibility by earning travel awards to present your high-caliber science at national and international meetings. Additionally, you are winning local and national awards for your work. Students in the program are successfully competing for NIH F30, AHA, and PEO fellowships for your research and it appears that more fellowships are on the way. Importantly, you all have some form of extramural funding for your research during graduate school. Upon completion of the program, our graduates are going on to high profile residency programs at major academic medical centers. These indictors demonstrate your success and the program's future trajectory.

As the new leaders of the program, Drs. King, Miller, and I are excited about the potential we see in our present students and our momentum for the journey ahead. Support from the College of Medicine leadership is further fueling that excitement. We are working to develop new activities and training opportunities to better prepare you to be future leaders in biomedical research. We look forward to working with you and helping you reach your goals as physician/scientists.

Wally

Introducing Our New Directors!

Dr. Sidney (Wally) Whiteheart

Dr. Whiteheart is a professor in the department of molecular and cellular biochemistry and joined the College of Medicine in 1994. He has been an active member of the college community, serving as chair of the faculty council, a member of the strategic plan executive oversight committee, and interim chair of his department. He has mentored more than 50 trainees and is an active researcher focusing on platelet function and cell biology, with two R01 grants and a VA Merit grant. As the director, he will provide oversight for the program; ensure appropriate infrastructure and integration with the Integrated Biomedical Sciences program, oversee the graduate mentor/advisory committees and the co-directors, and cultivate and maintain an open-door culture for the MD/PhD students.

Dr. Richard D. King

Dr. King is an associate professor of neurology and has mentored dozens of residents, medical students, and graduate students through their journey. He will apply this skill to enhance student recruitment, guide the first- and second-year medical students through their learning experiences, assist in the transition to third year, oversee clinical workshops, and develop and lead efforts to ensure student wellness. Dr. King earned his MD and PhD in neuroscience from Baylor College of Medicine and continued his training at Massachusetts General Hospital/Brigham & Women's Hospital, University of Texas, and the University of Utah. In 1994, he was awarded an MSTP scholarship and received the Rich Dickason Outstanding Physician Scientist award in 2002. His research interests focus on computer-based neural imaging methods and he is the site co-director for the Alzheimer's Disease Neuroimaging Initiative.

Dr. Brandon A. Miller

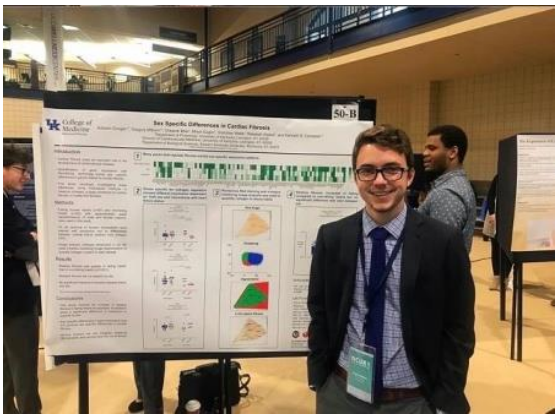
Dr. Miller is an assistant professor in the departments of neurosurgery and neuroscience and faculty associate in the Spinal Cord and Brain Injury Research Center. He is a current CCTS KL2 fellow and directs a research laboratory studying pediatric brain injury. Dr. Miller completed his MD and PhD training at The Ohio State University and will work to provide insight on career development and trajectory, lead a monthly clinical seminar, and assist with the transition of our MD/PhD students to their residencies and in networking with other physician-scientists.

Introducing Our New Students!

Aaron Silverstein

I grew up in Paducah, Kentucky and was homeschooled by my parents until I attended the University of Kentucky, graduating in 2019 with a B.S. in Psychology, a B.S. in Neuroscience, and a minor in Violin Performance. While an undergraduate, I conducted research in the Spinal Cord and Brain Injury Research Center (SCoBIRC) under Dr. Warren Alilain, using psychological and pharmacological perspectives to study therapies such as intermittent hypoxia after cervical spinal cord injury. In the summer preceding the start of M1, I rotated in UK MD/PhD Program Co-Director Dr. Brandon Miller's laboratory, also in SCoBIRC, studying intraventricular hemorrhage and hydrocephalus *in vitro.* I chose to stay at UK because of Dr. Alilain's exceptional mentorship and his facilitation of my exposure to the excellent advising and collaborative opportunities offered within SCoBIRC and beyond. In the future, I hope to continue research co-mentored by Dr. Alilain and Dr. Miller by applying intermittent hypoxia treatment to enhance recovery after life-threatening spinal cord or brain injury. In my free time I love experiencing life with my wife, Kelsey, spending time with our families, friends, and church family, rock climbing, playing soccer, bicycling, cooking, and exploring local breweries.

Gregory Milburn



I grew up in Louisville, Kentucky and graduated from the University of Kentucky with degrees in Biology and Chemistry. Throughout my undergraduate career I did cardiovascular and muscle physiology research with Dr. Kenneth Campbell at the University of Kentucky. During this time, I studied how demographic and clinical parameters influence the development of cardiac fibrosis in patients with heart failure. Additionally, using single muscle fiber experiments I investigated how altering the proportion of myosin heads in the super relaxed state can alter calcium sensitivity in skeletal muscle. These research experiences solidified my commitment to participate in cardiovascular research as it relates to heart failure and cardiac muscle. The University of Kentucky's MD/PhD program was an excellent fit for me due to the breadth of research and resources at the Saha Cardiovascular Research Center and the Gill Heart and Vascular Institute. In my free time, I enjoy running, cooking, and hiking with my dogs.

2019 Match Results

Greg Wehner
Diagnostic Radiology/Research
Barnes-Jewish Hospital, MO

Kristin Linscott
Pediatrics-Medical Genetics
University of Alabama Med Ctr-Birmingham, AL

Eseosa Ighodaro
Neurology
Mayo Clinic School of Grad Med Educ, MN

Christopher Brown
Neurology
Hospital of the University of Pennsylvania, PA

Recent PhD Defenses

The Role of CD8 T Cell Immunodominance and Regulatory T Cells in Neonatal Immunity to Influenza Virus
Luke Heil (M3)

Autologous Peripheral Nerve Grafts to the Brain for the Treatment of Parkinson's Disease
Andrew Welleford (M3)

Neuroprotective Strategies Following Experimental Traumatic Brain Injury: Lipid Peroxidation-Derived Aldehyde Scavenging and Inhibition of Mitochondrial Permeability Transition
Jacqueline Kulbe (M3)

Calibrated Short TR Recovery MRI for Rapid Measurement of Brain-Blood Partition Coefficient and Correction of Quantitative Cerebral Blood Flow
Scott Thalman (M3)

Computational Tools for the Untargeted Assignment of FT-MS Metabolomics Datasets
Joshua Mitchell (M3)

Research Highlight

Two clinical trials at the University of Kentucky are currently underway that aim to develop a disease-modifying therapy that slows the progression of Parkinson's Disease. These trials are evaluating the safety and feasibility of an autologous peripheral nerve graft to the substantia nigra in combination with Deep Brain Stimulation (DBS) for the treatment of PD. My dissertation details analysis of the peripheral nerve tissue used in these trials with respect to tissue composition and gene expression, both of injury-naive human peripheral nerve as well as the post-conditioning injury nerve tissue used in the grafting procedure. RNA-sequencing analysis of sural nerve tissue pre- and post-conditioning show significant changes in gene expression corresponding with transdifferentiation of Schwann cells from a myelinating to a repair phenotype, release of growth factors, activation of macrophages and other immune cells, and an increase in anti-apoptotic and neuroprotective gene transcripts. These results reveal in vivo gene expression changes involved in the human peripheral nerve injury repair process, which has relevance beyond this clinical trial to the fields of Schwann cell biology and peripheral nerve repair. We also developed an animal model of the grafting procedure, termed Neuro-Avatars, which feature human graft tissue implanted into athymic nude rats. Survival and infiltration of human graft cells into the host brain were shown using immunohistochemistry of Human Nuclear Antigen. To connect the results of these laboratory studies to the clinical trial we compared the severity of motor symptoms before surgery to one year post-surgery in patients who received the analyzed graft tissue. In summary, this dissertation advances the translational science cycle by using clinical trial findings and samples to answer basic science questions that will in turn guide future clinical trial design.

- Andrew Welleford, M3

Awards

Society for Vascular Surgery – 2019 Vascular Research Initiatives Conference Poster Award
Jeff Chen (G5)

T32 Training Grant
Maddie Dunfee (G1)

NRSA F30 Predoctoral Fellowship
Brandon Farmer (G3)
"Astrocyte lipid droplets as a novel mechanism for impaired glucose metabolism in the E4 and AD brain"

American Heart Association Predoctoral Fellowship
Brandon Farmer (G3)
"Apolipoprotein E4 alters cerebral lipid metabolism"

Midwest Zebrafish Conference 2019 – Best Oral Presentation Award
Megan (Green) Haney

American Heart Association Predoctoral Fellowship
David Henson (G3)

University of Kentucky CCTS TL1 Predoctoral Training Program Fellowship
Laura Krueger (G3)

University of Kentucky Biology Department Merit Graduate Fellowship

Laura Krueger (G3)

CHARGE Syndrome Foundation – Davenport Fellowship
Laura Krueger (G3)

National TL1 Trainees (NTT) Committee – New Committee Member
Laura Krueger (G3)

CCTS TL1 Predoctoral Training Program Fellowship
Lincoln Shade (G1)

College of Medicine Fellowship for Excellence in Graduate Research
Zachary Winder (G2)

2019 Conferences

Vascular Discovery 2019 (Boston, MA)
Jeff Chen (G5)

Society for Neuroscience 2018 (San Diego CA)

University of Kentucky CCTS Spring Conference (Lexington KY)
Ryan Cloyd (G3)

SD IDeA 2019 (Sand Diego CA)
University of Kentucky CCTS Spring Conference (Lexington KY)
Maddie Dunfee (G1)

Alzheimer's Association International Conference (Los Angeles CA)
Kern Lipid Conference (Vail CO)
Southeastern Regional Lipid Conference (Asheville NC)
Brandon Farmer (G3)

University of Kentucky CCTS Spring Conference (Lexington KY)
Drew Farr (G1)

American Association of Immunology Annual Meeting 2019 (San Diego CA)
Luke Heil (M3)

15th Annual American Physician Scientist Association (APSA) Conference (Chicago IL)
2019 Association for Clinical and Translational Science Meeting (Washington DC)
14th International CHARGE Syndrome Conference (Dallas TX)
Laura Krueger (G3)

Society for Neuroscience Annual Meeting 2018 (San Diego CA)
University of Kentucky CCTS Spring Meeting 2019 (Lexington KY)

American Academy of Neurology Annual Meeting 2019 (Philadelphia PA)
American College of Physicians Kentucky Chapter Meeting 2019 (Lexington KY)
Andrew Welleford (M3)

Spring Alzheimer's Disease Center Meeting (Philadelphia PA)
Zachary Winder (G2)

Laura Krueger (G3) attending a camp for children with CHARGE as a Davenport Fellow at the 14th International CHARGE Syndrome Conference.

Life Events

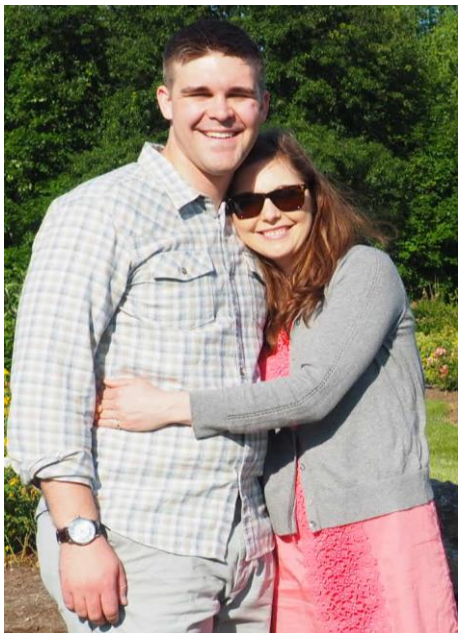
Andrew Welleford (M3) and his fiancé, Lauren, got engaged in August 2018.

Aaron Silverstein (M1) bought a new house in Lexington with his wife, Kelsey, in August 2019.

Left: T.J. Libecap (M2) married his wife, Emily, in March 2019.

Right: Ethan Glaser (M2) and his fiancé, Sarah, got engaged in September 2019.

Left: Tyler Hammond (G2) married his wife, Katrina, in July 2019.



Right: Maddie Dunfee (G1) and Drew Farr (G1) were married in October 2019.

Lexington Attractions


Downtown Lexington


University of Kentucky Arboretum


Keeneland


U of K Sporting Events


Mammoth Cave


Red River Gorge

2019 Publications (to date)

Peer-Reviewed Journal Publications

1. Wei M, **Haney MG**, Blackburn JS. Protein Tyrosine Phosphatase 4A3 (PTP4A3) modulates Src signaling in T-cell Acute Lymphoblastic Leukemia to promote leukemia migration and progression. *BioRxiv* open access. 2019 Jun.
2. **Chen, JZ** ; Sawada, H.; Moorleghen, JJ ; Weiland, M.; Daugherty, A.; Sheppard, MB "Aortic Strain Correlates with Elastin Fragmentation in Fibrillin-1 Hypomorphic Mice." *Circulation reports* 1, 5 (2019): 199-205.
3. Sawada, H.; **Chen, JZ** ; Wright, BC ; Moorleghen, JJ ; Lu, HS ; Daugherty, A. "Ultrasound Imaging of the Thoracic and Abdominal Aorta in Mice to Determine Aneurysm Dimensions." *Journal of visualized experiments : JoVE* 145 (2019)
4. **Farmer, B.C.**; Kluemper, J.; Johnson, L.A. Apolipoprotein E4 Alters Astrocyte Fatty Acid Metabolism and Lipid Droplet Formation. *Cells* 2019, 8, 182.
5. **Farmer B.C.**, Johnson LA, Hanson AJ. Effects of apolipoprotein E on nutritional metabolism in dementia. *Current Opinion in Lipidology*. 2019 Feb. PMID: 30550413
6. **Henson, D.**, Samman-Tahhan, A., Nardo, D. Quyyumi, A., Venditto, V. Association Between ApoA-I (Apolipoprotein A-I) Immune Complexes and Adverse Cardiovascular Events. *Atherosclerosis, Thrombosis and Vascular Biology*. 39(9), 1884-1892. 2019.
7. **Thalman, SW** ; Powell, DK ; Lin, AL "Novel Calibrated Short TR Recovery (CaSTRR) Method for Brain-Blood Partition Coefficient Correction Enhances Gray-White Matter Contrast in Blood Flow Measurements in Mice." *Frontiers in neuroscience* 13, (2019): 308.
8. Vechetti IJ, Jr ; **Wen, Y**.; Chaillou, T.; Murach, KA ; Alimov, AP ; Figueiredo, VC ; Dal-Pai-Silva, M.; McCarthy, JJ "Life-long reduction in myomiR expression does not adversely affect skeletal muscle morphology." *Scientific reports* 9, 1 (2019): 5483.

Podium Presentations:

9. **Haney MG**, University of Kentucky, Markey Cancer Center Research Day, Lexington, KY, 2019. *A Protein Tyrosine Phosphatase 4A3 (PRL-3)/Wnt signaling axis as a novel therapeutic target in Acute Lymphoblastic Leukemia (ALL) relapse.*
10. **Haney MG**, Zebrafish Disease Models Society, Boston, MA, 2019. *A Protein Tyrosine Phosphatase 4A3 (PRL3)/Wnt Signaling Axis as a Novel Therapeutic Target in Acute Lymphoblastic Leukemia Relapse*
11. **Haney MG**, Midwest Zebrafish Meeting, Lexington, KY 2019. *A Protein Tyrosine Phosphatase 4A3 (PRL3)/Wnt Signaling Axis as a Novel Therapeutic Target in Acute Lymphoblastic Leukemia Relapse*

Poster Presentations:

12. **Haney MG**, Miller AK, Wei M, Blackburn JS, "A Protein Tyrosine Phosphatase 4A3 (PRL3)/Wnt Signaling Axis as a Novel Therapeutic Target in Acute Lymphoblastic Leukemia (ALL) Relapse." Gordon Research Conference, Wnt Signaling, Mount Snow, VT, 2019.
13. **Haney MG**, Miller AK, Blackburn JS, "A Protein Tyrosine Phosphatase 4A3 (PRL-3)/Wnt Signaling Axis as a Novel Therapeutic Target in Acute Lymphoblastic Leukemia (ALL) Relapse." Zebrafish Disease Models Society, Boston, MA, 2019.
14. **Haney MG**, Miller AK, Blackburn JS, "A Protein Tyrosine Phosphatase 4A3 (PRL-3)/Wnt signaling axis as a novel therapeutic target in Acute Lymphoblastic Leukemia (ALL) relapse" University of Kentucky, Markey Cancer Center Research Day, Lexington, KY, 2019.
15. **Haney MG**, Miller AK, Blackburn JS, "A Protein Tyrosine Phosphatase 4A3 (PRL-3)/Wnt signaling axis as a novel therapeutic target in Acute Lymphoblastic Leukemia (ALL) relapse" Midwest Zebrafish Meeting, Lexington, KY, 2019.
16. **Haney MG**, Miller AK, Blackburn JS, "A Protein Tyrosine Phosphatase 4A3 (PRL-3)/Wnt signaling axis as a novel therapeutic target in Acute Lymphoblastic Leukemia (ALL) relapse." University of Kentucky, Center for Clinical and Translational Sciences Conference, Lexington, KY, 2019.
17. **Haney MG**, Dockins SD, Blackburn JS, "Optimization of human cancer cell xenografts into zebrafish larvae for high-throughput drug screening." American Academy of Physicians/American Society of Clinical Investigators/American Physician Scientists Association Annual Meeting, Chicago, IL, 2019.
18. **Haney MG**, Miller AK, Blackburn JS, "A Protein Tyrosine Phosphatase 4A3 (PRL-3)/Wnt signaling axis as a novel therapeutic target in Acute Lymphoblastic Leukemia (ALL) relapse." American Association for Cancer Research Annual Meeting, Atlanta, GA, 2019.