

# BIOMEDICAL & VETERINARY SCIENCES GRADUATE PROGRAM



## ANNOUNCES

The Doctor of Philosophy Seminar  
and Examination of

### **Benjamin T. Ledford**

**Keratose Hydrogels Promote Vascular  
Smooth Muscle Differentiation from c-kit<sup>+</sup>  
Human Cardiac Stem Cells: Underlying  
Mechanism and Therapeutic Potential**

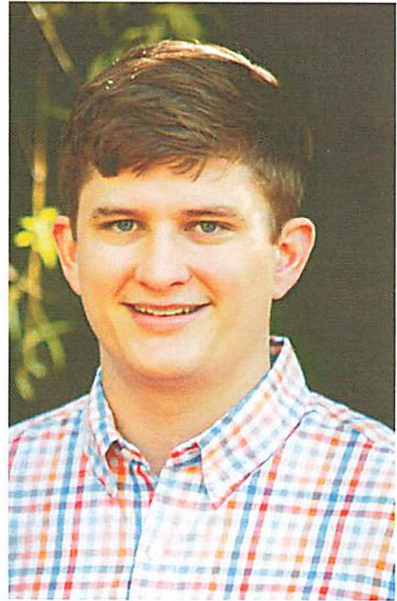
**Tuesday, January 30, 2018**

**1:00 pm**

**VMIA Classroom 220**

## **Bio**

Benjamin T. Ledford grew up in Wolf Creek, North Carolina. He graduated cum laude, from North Carolina State University with a bachelor's degree in Biochemistry in the Spring of 2013. In the Fall of 2013, Benjamin received a scholarship from the ICTAS doctoral scholars program and joined Dr. Jia-Qiang He's lab to begin his Ph.D. in Biomedical Sciences and Pathobiology. The focus of his Ph.D. work has been the use of human cardiac stem cells (hCSCs) and keratin based biomaterials for regenerative medicine applications. Specifically, he investigated the mechanisms behind keratin hydrogel mediated vascular smooth muscle differentiation (VSMC) of hCSCs, and the use of these cells to re-vascularize tissues in a mouse model of critical limb ischemia.



Benjamin is interested in tissue engineering and regenerative medicine. Additionally, he has also greatly enjoyed training and mentoring undergraduate students in the research lab. Benjamin hopes to pursue a career in academia or industry in the field of regenerative medicine.

## **Funded by**

ICTAS Doctoral Scholars Program  
VMCVM Office of Research and Graduate Studies

## Lay Language Abstract

Cardiovascular disease is the leading cause of mortality in the United States, responsible for 1 out of every 4 deaths, and accounting for over 200 billion dollars in health care related cost. There are several available therapies which offer a temporary solution; however, only a heart transplant can fully resolve heart failure, and donor organ shortages severely limit this therapy. Cardiac stem cells are a promising alternative therapy to treat cardiovascular disease by replacing damaged cardiac tissue; however, low cell viability, low retention/engraftment, and uncontrollable in vivo differentiation after transplantation has limited the efficacy of stem cell therapy. Tissue engineering solutions offer potential tools to overcome current limitations of stem cell therapy. Keratin proteins extracted from human hair have shown therapeutic potential in a wide range of applications including cardiac regeneration. My studies utilize human hair-derived keratin biomaterials to modulate c-kit<sup>+</sup> human cardiac stem cell (hCSC) differentiation and explored the capability of differentiated cells to regenerate vascular tissue. My dissertation demonstrated that keratin biomaterials modified c-Kit<sup>+</sup> hCSC differentiation and produced VSMCs (a major component of vascular tissue), and that TGF- $\beta$ 1 signaling was key in producing this differentiation pattern. Additionally, our keratin differentiated hCSCs were able to recover vascular tissue and blood perfusion in a critical limb ischemia (CLI) mouse model. Results demonstrated that our cells increased both blood flow and the density of vascular tissue. Future studies should explore potential protein-protein interactions between KOS, TGF- $\beta$ 1 and its associated proteins. Additionally, we should plan animal studies that examine the efficacy of our cells to regenerate cardiac tissue in a myocardial infarction disease model.

## Publications

**Ledford B., Simmons. J, Chen M., Fan H., Barron C, Liu Z. Van Dyke M. and He J. Q.** Keratose Hydrogels Promote Vascular Smooth Muscle Differentiation from C-kit Positive Human Cardiac Stem Cells. *Stem Cells and Development*. 2017 26(12): 888-900.

Chen, M., H. Fan, **B. T. Ledford**, Z. Farah, C. Barron, Z. Liu and J. Q. He. Impacts of femoral artery and vein excision versus femoral artery excision on the hindlimb ischemic model in CD-1 mice. *Microvasc Res*.2016; 110: 48-55.

Chen M, Kan LJ, **Ledford BT** and He JQ. Tattooing Various Combinations of Ears, Tail, and Toes to Identify Mice Reliably and Permanently. *J Am Assoc Lab Anim*. 2016; 55: 189-98.

Kan L, Smith A, Chen M, **Ledford B**, et al. Rho-Associated Kinase Inhibitor (Y-27632) Attenuates Doxorubicin-Induced Apoptosis of Human Cardiac Stem Cells. *PLoS One*. 2015; 10: e0144513.

Kwiatkowski A, Piatkowski M, Chen M, **Ledford B**, et al. Superior angiogenesis facilitates digit regrowth in MRL/MpJ mice compared to C57BL/6 mice. *Biochem Biophys Res Commun*. 2016.

Kan L, Thayer P, Fan H, **Ledford B**, Chen M, et al. Polymer microfiber meshes facilitate cardiac differentiation of c-kit<sup>+</sup> human cardiac stem cells. *Exp Cell Res*. 2016.

### Presentations

#### Oral Presentations:

**Ledford B.**, Chen M., Van Dyke M., and He J.Q. TGF-  $\beta$ 1 Signaling is Crucial in Differentiation of Human Cardiac Stem Cells on Keratose Hydrogels. Selected for Oral Presentation TERMIS Charlotte North Carolina (12/2017)

**Ledford B.**, Chen M., Baron K., Van Dyke M., and He J.Q. Keratose Hydrogels Promote Vascular Smooth Muscle Differentiation from c-kit<sup>+</sup> Human Cardiac Stem Cells: Underlying Mechanism and Therapeutic Potential. Oral Presentation Department of Animal Science Blacksburg Virginia (10/2017)

**Ledford B.**, Simmons J., Kan L., Chen M., Van Dyke M., and He J.Q. Keratose Hydrogels Promote Smooth Muscle Differentiation from c-Kit<sup>+</sup> Human Cardiac Stem Cells. Selected for Oral Presentation Muscle Research Meeting Blacksburg Virginia (11/2016)

**Ledford B.**, Simmons J., Kan L., Chen M., Van Dyke M., and He J.Q. Keratose Hydrogels Promote Smooth Muscle Differentiation from c-Kit<sup>+</sup> Human Cardiac Stem Cells. Selected for Oral Presentation BMES Minneapolis Minnesota (10/2016)

**Ledford B.** and He J.Q. Biomaterial Mediated Stem Cell Therapy as a Promising Regenerative Medicine Approach. Oral Presentation BMVS Blacksburg Virginia (11/2015)

Poster Presentations:

**Ledford B.,** Simmons J., Chen M., Barron C., Van Dyke M., and He J.Q. Activation of TGF- $\beta$  Signaling Pathway Promotes Smooth Muscle Differentiation from c-Kit<sup>+</sup> Human Cardiac Stem Cells on Keratose Hydrogels. Biofabrication Winston Salem North Carolina (10/2016).

**Ledford B.,** Simmons J., Kan, L.; Chen M., Van Dyke M., He. J.Q. Keratin Hydrogel-facilitated Differentiation of Smooth Muscle Cells from Human Cardiac Stem Cells Improves Blood Perfusion in Ischemic Limb of Immunodeficient Mice. Blacksburg Virginia (4/2016).

**Ledford, Benjamin;** Simmons, Jamelle; Kan, Lijuan Kan; Chen, Miao; Mark, Van Dyke; He, Jia-Qiang. Keratin Hydrogel-facilitated Differentiation of Smooth Muscle Cells from Human Cardiac Stem Cells Improves Blood Perfusion in Ischemic Limb of Immunodeficient Mice Blacksburg Virginia (3/2016).

**Ledford B.,** Simmons J., Kan L., Chen M., Van Dyke M., and He J.Q. Keratin Hydrogels Promote Smooth Muscle Differentiation from c-Kit<sup>+</sup> Human Cardiac Stem Cells. Selected for poster presentation at NHLBI Symposium on Cardiovascular Regenerative Medicine Bethesda Maryland (9/2015).

**Ledford B.,** Simmons J., Kan L., Chen M., Van Dyke M., and He J.Q. Keratin Hydrogels Facilitate Differentiation of Human Cardiac Stem Cells into Smooth Muscle. ICTAS Doctoral Scholar Meeting (4/2015).

**Ledford, Benjamin;** Simmons, Jamelle; Kan, Lijuan Kan; Chen, Miao; Mark, Van Dyke; He, Jia-Qiang. Keratin Hydrogel Facilitates Cultivation of Human Cardiac Stem Cells BMVS Symposium Blacksburg Virginia (3/2015).

**Ledford, Benjamin;** Simmons, Jamelle; Kan, Lijuan Kan; Chen, Miao; Mark, Van Dyke; He, Jia-Qiang. Keratin Hydrogel Facilitates Cultivation of Human Cardiac Stem Cells ViaCOM Reaserch Day (2/2015).

**Ledford, Benjamin;** Simmons, Jamelle; Kan, Lijuan Kan; Chen, Miao; Mark, Van Dyke; He, Jia-Qiang. Keratin Hydrogel Facilitates Cultivation of Human Cardiac Stem Cells in 3D Format NCTERMS Durham North Carolina (10/2014).

## Awards and Academic Achievements

ICTAS Doctoral Scholar

Gamma Beta Phi Society

Vector Laboratories Photo Contest Honorable Mention

## Examination Graduate Committee

### **Major Advisor/Chair:**

Jia-Qiang He Ph.D.

Assistant Professor, Stem Cell Physiology

Department of Biomedical Sciences & Pathobiology

### **Graduate Advising Committee Members:**

Mark Van Dyke Ph.D.

Associate Professor of Biomedical Sciences and Engineering

Robert Gourdie Ph.D.

Professor, Virginia Tech Carilion Research Institute

Director, Cardiovascular & Regenerative Biology Center, VTCRI

William Huckle Ph.D.

Associate Professor of Cell Biology/Pharmacology

Biomedical Sciences & Pathobiology

Department of Biomedical Sciences & Pathobiology

## External Examiner

### **Gangjian Qin, MD, FAHA**

Professor, Department of Biomedical Engineering

Director, Molecular Cardiology Program

Vice Chair of Research

School of Medicine

University of Alabama at Birmingham

Seminar:

**Novel Regulators of Stem Cells in the Cardiovascular System**

Tuesday, January 30, 2018

10:00 am

VMIA Classroom 220