BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. ***DO NOT EXCEED FIVE PAGES.***

NAME: Amanda Jo LeBlanc

eRA COMMONS USER NAME (credential, e.g., agency login): ALEBLANC

POSITION TITLE: Associate Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Indiana University (Bloomington, IN)	B.S.	08/2002	Exercise Science
University of Louisville (Louisville, KY)	M.S.	05/2004	Exercise Physiology
West Virginia University (Morgantown, WV)	Ph.D.	08/2008	Exercise Physiology
West Virginia University (Morgantown, WV)	Postdoctoral Fellowship	08/2009	Cardiovascular Toxicology
University of Louisville (Louisville, KY)	Postdoctoral Associate	12/2011	Cardiovascular Therapeutics

A. Personal Statement

I have an extensive research background in cardiovascular physiology, focusing most exclusively on myocardial perfusion and reactivity in models of both aging and gender-specific cardiology. My graduate research at WVU focused on the structural and functional microvascular alterations that occur with advancing age and gender in the heart. After I completed my Ph.D., my interest in translational research in cardiac physiology blossomed at the Cardiovascular Innovation Institute (CII) where I was able to learn various tissue-engineering techniques and improve my knowledge of overall cardiac physiology and function. My primary research areas as an independent investigator include: exploring sex differences related to regenerative medicine in the heart, particularly in an aging model, developing cell-based therapies designed to improve the function of the microcirculation, and progressing adipose-derived tissue-engineering technology into pre-clinical research phases. During 2013-2014 my career was disrupted due to the birth of my first child, and I took one year of leave from my tenure clock. However, upon returning to the field I immediately resumed my research projects and collaborations and successfully published corresponding author papers and received NIH-funded research grants.

B. Positions and Honors

Positions and Employment

1999-2002 Laboratory Technician, Geo. Pfau Sons Co. Jeffersonville, IN
2012-2014 Assistant Professor, Department of Obstetrics, Gynecology and Women's Health, University of Louisville, Louisville, KY
2013-2014 Associate appointment in Department of Physiology, University of Louisville, KY
2014-2017 Assistant Professor in Department of Physiology, University of Louisville, KY
2018- Associate Professor in Department of Physiology, University of Louisville, KY

Other Experience and Professional Memberships

2011- Review Editor for Frontiers in Vascular Physiology

2013-2014 Director for Resident/Fellow Research for the Department of Obstetrics, Gynecology and Women's Health
2013-2014 Director of Research Day for the Department of Obstetrics, Gynecology and Women's Health
2013 - Institutional Animal Care and Use Committee, University of Louisville
2013 - 2016 Membership Committee for The Microcirculatory Society
2013- American Heart Association National Peer Review Committee – Vascular Endothelial Biology 2
2015- Editorial Board for Microcirculation journal
2017 Conference Organizing Committee – "Cardiovascular Aging, New Frontiers and Old Friends" Westminster, CO, August 11-14, 2017
2017-2019 Secretary of The Microcirculatory Society
2018-2020 Communication Committee Member of the American Physiological Society

Professional Membership: American Heart Association, The Microcirculatory Society, American Physiological Society

Ad Hoc Manuscript Review: Aging, Aging Cell, AJP- Heart and Circulatory Physiology, AJP - Lung Cellular and Molecular Physiology, BMC Physiology, Cardiovascular Pathology, Cardiovascular Pharmacology, Cardiovascular Translational Research, Environmental Health Perspectives, Experimental Gerontology, Frontiers in Vascular Physiology, Inhalation Toxicology, Journal of Gerontology: Biological Sciences, Journal of Visual Experiments, Microcirculation, Plos One, Science Signaling, Stem Cell Research and Therapy, Stem Cell Translational Medicine, Toxicological Sciences, Toxicology and Applied Pharmacology

Grant Review

2013-2016 AHA National Peer Review Committee – Vascular Endothelial Biology 2
2016-2017 Early Career Reviewer for the Center for Scientific Review (CSR), National Institutes of Health
2017- NIH Aging Systems and Geriatrics (ASG) study section member, in-person study section meeting (February 13-14, San Diego, CA)
2017 AHA Vascular Disease Strategically Focused Research Network Review Committee member, Phase I
2018 NIH/NCCIH Special Emphasis Panel ZAT1 VS (09); "Training and Research Grants"
2018 NIH/BDCN Special Emphasis Panel 2018/10 ZRG1 BDCN-W(55) R

Honors

1999-2002 Alpha Beta Honorary (student-athlete with GPA 3.2+), Indiana University
2002-2004 Athletic Director's Honor Roll (student-athlete with GPA 3.0+), University of Louisville
2002-2004 Conference USA Commissioner's Honor Roll (student-athlete with cumulative 3.0+)
2002-2004 Red and Black Scholar (student-athlete 3.25 cumulative GPA), University of Louisville
2007 American Physiological Society CV Section Research Recognition Award, San Diego CA
2007 First Place Poster Presentation, E.J. Van Liere Research Day, West Virginia University
2007 Third Place Oral Presentation, E.J. Van Liere Convocation, West Virginia University
2007 8th World Congress for Microcirculation Zweifach Student Travel Award, Milwaukee WS
2009 1st Place Poster Presentation, Postdoctoral Fellow Division, E.J. Van Liere Research Day, West Virginia University
2010 9th World Congress for Microcirculation Postdoctoral Travel Award, Paris FR
2012 20th Annual NIA Summer Training Course in Experimental Aging Research, Buck Institute for Research on Aging, Novato, CA
2012 Faculty Excellence Award for contribution in patents, licenses, and options, University of Louisville
2014 University of Louisville Faculty Excellence Award for contribution in patents, licenses, and options
2015 Keynote Speaker for American Society for Extracorporeal Technology conference in San Antonio, TX
2016 Travel Grant from the European Society of Cardiology Council on Basic Cardiovascular Sciences, Florence, Italy
2018 Louisville Business First "Forty under 40"

Patent

9,844,514 - "Methods for Treating an Established Myocardial Infarction"- 12/19/2017

C. Contributions to Science

1. After testing the waters with various undergraduate research opportunities in human performance, my first foray into cardiovascular physiology was my doctoral dissertation work at West Virginia University. My early publications focused on identifying the age- and sex-related effects on vasoreactivity of the coronary microcirculation where I identified a gradual decline in the Flk-1/NO signaling pathway as age increases in males. In contrast, NO-mediated vasodilation was conserved until a much later age in females, but removing the ovarian hormones (at any age) resulted in an immediate decrease in vasomotor function unless estrogen was exogenously replaced at the time of surgery. These studies had significant implications related to the findings from the Women's Ischemia Syndrome Evaluation study, which found a possible relationship between hormone-replacement therapy and an increase in the risk for cardiovascular events in menopausal women. Our studies highlight the beneficial vascular effects of estrogen-replacement therapy in female rats, regardless of age, if initiated at the time of (surgical) menopause. These studies also highlight the completion of my training period where I became proficient in isolated microvascular physiology.

a) **LeBlanc AJ**, Shipley RD, Muller-Delp JM. Aging Impairs Flk-1 Signaling and NO-Mediated Vasodilation in Coronary Arterioles. *Am J Physiol Heart Circ Physiol* 295: H2280–H2288, 2008. PMID: 18835919, PMCID: PMC2614537
b) **LeBlanc, AJ**, Reyes R, Kang LS, Dailey RA, Stallone JN, Muller-Delp JM. Estrogen replacement improves while aging and loss of ovarian hormones impair flow-induced vasodilation in coronary arterioles. *AJP-Regulatory- Integrative and Comparative Physiology* 2009 Dec;297(6):R1713-23, PMID: 19812360, PMCID: PMC2803626
c) **LeBlanc AJ,** Chen B, Dougherty PJ, Reyes RA, Shipley RD, Korzick DH, Muller-Delp JM. Divergent effects of aging and sex on vasoconstriction to endothelin in coronary arterioles. *Microcirculation,* 2013 Jul;20(5):365-76. PMID: 23198990, PMCID: PMC3594502
d) Kang L, Chen B, Reyes R, **LeBlanc A**, Teng B, Mustafa S, Muller-Delp J. Aging and estrogen alter endothelial reactivity to reactive oxygen species in coronary arterioles. *Am J Physiol Heart Circ Physiol,* 300: H2105-15, 2011. PMID: 21441309, PMCID: PMC3119103

2. After I completed my Ph.D., I combined my expertise in the coronary microcirculation with the field of cardiovascular toxicology during my post-doctoral training at WVU. Given the rate that nanotechnology was permeating modern society, the cardiovascular consequences of pulmonary exposure to nanoparticle aerosols was an unexplored area of research and extremely critical to ascertain (note the asbestos epidemic). I solely developed and setup the isolated vessel research program in Dr. Timothy Nurkiewicz's laboratory, while expanding my *in situ* isolated vessel skill set and gained valuable experience in one of the key future research areas, toxicological exposures. In just 12 months, I published two first-author manuscripts, which were the first studies to describe deleterious vasodilatory effects in coronary arterioles following inhalation exposure to normal environmental levels of TiO_2. A book chapter was also published for the proceedings of an international conference in which I gave a presentation, and generated multiple abstracts for national and international meetings.

a) **LeBlanc AJ**, JL Cumpston, BT Chen, D Frazer, V Castranova, TR Nurkiewicz. Nanoparticle inhalation impairs endothelium-dependent vasodilation in subepicardial arterioles. *J Toxicology and Environmental Health – Part A*, 2009;72(24):1576-84, PMID: 20077232, PMCID: PMC2808198
b) **LeBlanc AJ**, AM Moseley, BT Chen, D Frazer, V Castranova and TR Nurkiewicz. Nanoparticle inhalation impairs coronary microvascular reactivity via a local reactive oxygen species-dependent mechanism. *Cardiovascular Toxicology*, 2010 Mar;10(1):27-36. PMID: 20033351, PMCID: PMC2825710

c) **LeBlanc, AJ**, Y Hu, J Muller-Delp, BT Chen, D Frazer, V Castranova, TR Nurkiewicz. Particulate matter inhalation impairs coronary microvascular reactivity. *Proceedings of 25th European Conference on Microcirculation*, 13-17, 2008.

3. As my interest in translational research in cardiac physiology blossomed, the next logical step was a position at the Cardiovascular Innovation Institute where I had space to thread out my interests in remedying heart disease through potential cell therapies, while keeping some familiarity of coronary physiology. My mentors (Drs. Williams and Hoying) and I invented an autologous 3-D epicardial cell patch that preserved coronary blood flow reserve following myocardial infarction (MI). Importantly, we found that an increase in the number of vessels in an injured/ischemic area did not correlate with perfusion or cardiac function. I published a second manuscript (and first corresponding author paper) on the use of autologous adipose-derived regenerative cells in the repair of an established MI, which reinforced the finding that whatever time-point the cell patch was applied following MI, the progressive worsening of cardiac and microvascular function could be halted through the use of this cell patch.

a) **LeBlanc AJ,** Hoying JB, Touroo J, Williams SK. Adipose stromal vascular fraction construct protects coronary microvascular function after acute myocardial infarction. *Am J Physiol Heart Circ Physiol* 302: H973-82, 2012. PMID: 22140045, PMCID: PMC3322738
b) **LeBlanc AJ**, Krishnan L, Sullivan CJ, Williams SK, Hoying JB. Microvascular Repair: Post-Angiogenesis Vascular Dynamics. *Microcirculation*, 19(8): 676-695, 2012. PMID: 22734666, PMCID: PMC3842172
c) ***LeBlanc AJ**, Nguyen QT, Touroo JS, Aird AL, Chang RC, Ng CK, Hoying JB, Williams SK. Adipose-derived cell construct stabilizes heart function and increases microvascular perfusion in an established infarct. *Stem Cells Translational Research,* 2(11): 896-905, 2013, PMID: 24106337, PMCID: PMC3808204. ***Indicates corresponding author.**

4. The primary goal of my burgeoning laboratory is to develop a cell-based therapy using age-specific adipose-derived stem cells to treat coronary microvascular dysfunction in a model of advanced age. While evaluating the angiogenic properties of these regenerative cells, I found that the cells isolated from old donors demonstrated far less *in vivo* vasculogenic potential than cells from a young donor, even though *in vitro* angiogenic characteristics were similar between the two age groups. This finding carries significant weight as many preclinical trials propose to utilize autologous cells from donors to treat many types of ischemic diseases. My laboratory is now studying mechanisms to improve the angiogenic capabilities of these adipose-derived regenerative cells from old donors to increase autologous application of this cell therapy.

a) Nevitt CD, McKenzie G, Christian K, Austin J, Hencke S, Hoying JB, **LeBlanc AJ**. Physiological Levels of Thrombospondin-1 Decrease NO-Dependent Vasodilation in Coronary Microvessels from Aged Rats. *Am J Physiol Heart Circ Physiol.* In press, May 2016, PMID: 27199114
b) Aird AL, Nevitt CD, Christian K, Williams SK, Hoying JB, **LeBlanc AJ**. Adipose – derived stromal vascular fraction cells isolated from old animals exhibit reduced capacity to support the formation of microvascular networks. *Experimental Gerontology,* 63: 18-26, March 2015. PMID: 25617825, PMCID: PMC4346434
c) Hunter RK, Nevitt CD, Gaskins JT, Keller BB, Bohler HC, **LeBlanc AJ**. Adipose-derived stromal vascular fraction cell effects on a rodent model of thin endometrium. *Plos One* 10(12): e0144823, 2015. PMID: 26657744, PMCID: PMC4684382
d) ***LeBlanc AJ**, Kelm NQ. Thrombospondin-1, free radicals, and the coronary microcirculation: the aging conundrum. *Antioxidants and Redox Signaling*. Aug 1 2017 Epub ahead of print, *Corresponding author, PMID: 28762749

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1XYGbkPaMuRQi/bibliography/47575137/public/?sort=date&direction=ascending

D. Research Support

Current Research Support

1. **Jewish Heritage Foundation for Excellence** (LeBlanc, PI) July 1, 2016-June 30, 2019
   "Microvascular Dysfunction in Women's Hearts: A Novel Diagnosis and Treatment Regime"
   The major goal of this project is to develop a new diagnostic and cell-based therapy for patients with microvascular angina

2. **Helmsley Restorative Medicine Center: Spinal Cord Injury and Cardiovascular Function** (LeBlanc, co-Investigator) Jan 1, 2016 – December 31, 2018

3. **NIH R01 AG053585-01** (LeBlanc – PI) March 1, 2017 – February 28, 2022
   "Reversing microvascular dysfunction in advancing age".
   The goal of this project is to explore the dynamics of autologous cell therapy for microvascular dysfunction in a model of advanced age

4. **NIH 1T32HL134644-01A1** (Mentor) May 1, 2017 – April 30, 2022
   "Current Trends in Stem Cell Therapies"
   The intent of this program is to provide focused post-doctoral training in the biology and application of cell-based therapies.

5. **Department of Defense RTR grant** (PI: Kaufman, LeBlanc co-I) Sep 15, 2013 – Sep 14, 2018
   W81XWH-13-2-0057 CRMRP-RTR-DMRDP
   "Positioning Vascularized Composite Allotransplantation in the Spectrum of Transplantation"
   This project is a collaboration between our four centers to determine the mechanisms of rejection and vasculopathy in VCA allografts using experimental model studies and to refine and standardize clinical management of VCA recipients.

Completed Research Support

1. **Kosair Charities Pediatric Heart Research Pilot Grant** Nov 2011- Jan 2013
   (LeBlanc, PI)
   "Age-related differences in SVF-assisted coronary microvascular repair"
   This study determined the greatest source potential for creating a stromal vascular fraction construct and its ability to support microvascular repair in areas of coronary ischemia in the adolescent heart.

2. **AHA Beginning Grant-in-Aid** Jan. 1, 2012 – June 30, 2014
   (LeBlanc, PI)
   "Improving coronary microcirculation in advanced age through cell-based therapy"
   This purpose of this grant is to promote the first independent step of a junior scientist. The primary goal of this study was to develop a cell-based therapy using age-specific adipose-derived stem cells to treat coronary microvascular dysfunction in a model of advanced age.

3. **University of Louisville Intramural Research Incentive Grant** Jan 2013- Dec 2013
   (LeBlanc, PI)
   "Regenerative potential of adipose-derived stem cells during advancing age in women"

4. **NIH R21 AG047474-01** Sept. 1, 2014 – June 30, 2015
   "Dopamine-mediated regulation of blood pressure in aging: Role of NHERF-1" (LeBlanc, co-PI).

5. **VV Cooke Foundation** (LeBlanc – co-Investigator, 2% effort) Dec 1, 2015 – Nov 30, 2016
   "Studies in Women's Heart Health", Pilot program
   The goal is to perform pilot studies in support of a pre-clinical investigation of cell therapy for microvascular angina.