BIOGRAPHICAL SKETCH

NAME: Amanda Jo LeBlanc

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

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

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 Fellow	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 sex-specific cardiology. My training focused on the structural and functional microvascular alterations that occur in the heart with advancing age and sex differences. Upon starting my own laboratory within the Cardiovascular Innovation Institute (CII) at the University of Louisville, I focused on translational research in cardiac physiology. I gained important skills in tissue-engineering techniques and mastered cardiac physiology and function. This led to my current line of investigation on regenerative medicine in aging-induced cardiovascular complications. My lab is developing cell-based therapies designed to improve the function of the microcirculation and also involved in advancing this adipose-derived tissue engineering technology to the preclinical phase. I have significant proficiency in multiple modes of (cardio)vascular reactivity assessment, including *ex vivo* (pressure myography, mesenteric window model), *in situ* (intravital microscopy, dorsal skin fold chamber), and *in vivo* (ultrasound, doppler, PV loop). The current funding proposal represents a continuation and expansion of my ESI R01 in translating important findings from preclinical models to the human microcirculation and associated systemic cardiovascular disease progressions.

Ongoing and Recently Completed Research Support

1. **NIH R01 AG053585-01** 3/01/17 – 2/28/23
   LeBlanc - PI
   Reversing Microvascular Dysfunction in Advancing Age
2. **NIH/NIDCR R01DE030103-01A1** 4/1/22 – 3/31/27
   Sandell-PI, **LeBlanc-co-I**
   Therapeutic Vascularization to Support Repair of Damaged Salivary Glands
3. **NIH 1P30ES030283-02** 7/15/20 – 3/31/25
   States-PI, **LeBlanc-co-I**
   University of Louisville Center for Integrative Environmental Health Sciences
4. **DOD W81XWH-19-RTRP-IDA -Proposal RT190021** 9/15/20- 9/14/23
   Kaufman-PI, **LeBlanc-co-I**
   Effect of Peritransplant C3d Blockade and Ischemia on Chronic Rejection and Vasculopathy in an Experimental OMC Flap Model of VCA

Key Publications

a) Rowe G, Tracy E, Beare JE, **LeBlanc AJ**. Cell therapy rescues aging-induced beta-1 adrenergic receptor and GRK2 dysfunction in the coronary microcirculation. Geroscience. 2022 Feb;44(1):329-348. doi: 10.1007/s11357-021-00455-6. Epub 2021 Oct 4. PMID: 34608562; PMCID: PMC8811091.

b) Tracy EP, Dukes M, Beare J, Rowe G, Nair R, **LeBlanc AJ**. Stromal Vascular Fraction Restores Vasodilatory Function by Reducing Oxidative Stress in Aging-Induced Coronary Microvascular Disease. Antioxid Redox Signal. 2022 Aug 11. doi: 10.1089/ars.2021.0249. Epub ahead of print. PMID: 35950616.

c) Lindsey ML, **LeBlanc AJ**, Ripplinger CM, Carter JR, Kirk JA, Hansell Keehan K, Brunt KR, Kleinbongard P, Kassiri Z. Reinforcing rigor and reproducibility expectations for use of sex and gender in cardiovascular research. Am J Physiol Heart Circ Physiol. 2021 Nov 1;321(5):H819-H824. doi: 10.1152/ajpheart.00418.2021. Epub 2021 Sep 15. PubMed PMID: 34524922.

B. Positions, Scientific Appointments, and Honors

Positions

2022- Division Chief of Research, Department of Cardiovascular and Thoracic Surgery, University of Louisville, Louisville, KY
2022- Associate Professor (tenured), Department of Cardiovascular and Thoracic Surgery, University of Louisville, Louisville, KY
2021- Core Leader, Pilot Project Program, Center for Integrative Environmental Health Sciences, University of Louisville, KY
2018- Tenured Associate Professor, Department of Physiology, University of Louisville, KY
2014-2017 Assistant Professor, Department of Physiology, University of Louisville, KY
2013-2014 Associate appointment, Department of Physiology, University of Louisville, KY
2012-2014 Assistant Professor, Department of Obstetrics, Gynecology and Women's Health, University of Louisville, Louisville, KY
1999-2002 Laboratory Technician, Geo. Pfau Sons Co., Jeffersonville, IN

Scientific Appointments

2022 Chairperson of the AHA Fellowship Vascular Endothelial Biology Committee
2022- Chair, Institutional Animal Care and Use Committee, University of Louisville
2022 *Ad hoc* Member, NIH Aging Systems and Geriatrics (ASG) Study Section (2022/10)
2022 Chairperson, NIH Integrated Review Group (IRG) Fellowship Application Panel for Endocrinology, Nutrition, and Reproductive Sciences (2022/03)
2021- Associate Editor, *AJP-Heart and Circulatory Physiology*
2021- Member, Editorial Advisory Board, *AJP-Cell Physiology*
2021-2023 Member, Science Policy Committee, American Physiological Society
2021 Chairperson, NIH Brain Disorders and Clinical Neuroscience (BCDN) Special Emphasis Panel (2021/05): "Special Topics in Aging"
2021 Chairperson, American Heart Association (AHA) Fellowship "Vascular Endothelial 3" Committee
2021 Member, NIH Therapeutic Development and Preclinical Studies (TDPS) Study Section
2021 Medical College of Wisconsin Cancer Center Pilot Grant Program
2021 Member, NIH ASG Study Section
2020- Chair, School of Medicine Research Committee, University of Louisville
2020-2022 Review Editor, *Frontiers in Cardiovascular Medicine – Atherosclerosis and Vascular Medicine*
2020-2021 Member, Graduate Admissions Committee, Department of Physiology, University of Louisville
2020 Chairperson, NIH BDCN Special Emphasis Panel (2020/05): "Special Topics in Human Aging"
2020 Chairperson, NIH BDCN Special Emphasis Panel (2020/07): "Aging, Inflammation, and Neurological Topics"
2019- Member, International Liaison Committee for Microcirculation
2019 AHA Transformational Project Clinical-Population Sciences "Cardiac Biology/Regulation Clinical"
2019 Member, NIH BDCN Special Emphasis Panel (2019/05): ZRG1 BDCN-W (91) S
2019 Member, NIH Division of AIDS, Behavioral and Population Sciences (DABPS) Scientific Review Group (2019/05): HIV Comorbidities and Clinical Studies (HCCS)
2019 Member, NIH BDCN Special Emphasis Panel (2019/10): ZRG1 BDCN-W (92) S
2018-2021 Chair, School of Medicine Research Committee, University of Louisville
2018-2020 Member, Communications Committee, American Physiological Society
2018 Member, NIH/NCCIH Special Emphasis Panel ZAT1 VS (09): "Training and Research Grants"
2018 Member, NIH BDCN Special Emphasis Panel (2018/10): ZRG1 BDCN-W (55) R
2018 Member, NIH BDCN Special Emphasis Panel (2019/01): ZRG1 BDCN-L (55) R
2017- Member, NIH ASG Study Section

2017-2019 Secretary, The Microcirculatory Society
2017 Member, AHA Vascular Disease Strategically Focused Research Network Review Committee, Phase I
2017 Member, Conference Organizing Committee, "Cardiovascular Aging, New Frontiers and Old Friends," Westminster, CO, August 11-14, 2017
2016-2017 Early Career Reviewer, Center for Scientific Review (CSR), NIH
2015- Member, Editorial Board, *Microcirculation*
2013-2019 Member, Institutional Animal Care and Use Committee, University of Louisville
2013-2016 Member, Membership Committee, The Microcirculatory Society
2013-2016 Member, AHA National Peer Review Committee, Vascular Endothelial Biology 2
2013-2014 Director, Resident/Fellow Research, Department of Obstetrics, Gynecology and Women's Health
2013-2014 Director, Research Day, Department of Obstetrics, Gynecology and Women's Health
2011- Review Editor, *Frontiers in Vascular Physiology*

Professional Memberships American Heart Association (Council on Basic Cardiovascular Sciences and Council on Arteriosclerosis, Thrombosis and Vascular Biology), The Microcirculatory Society, American Physiological Society, North American Vascular Biology Organization

Patents:
2018 # 10,011,820 Adipose Stromal Vascular Cell Constructs
2017 # 9,844,514 Methods for Treating an Established Myocardial Infarction

Honors
2021 Leadership and Innovation in Academic Medicine graduate, University of Louisville
2018 Louisville Business First's "Forty under 40"
2018 12th Annual Division of Aging Biology New Investigators Forum, Bethesda, MD
2016 Travel Grant from the European Society of Cardiology Council on Basic Cardiovascular Sciences, Florence, Italy
2015 Keynote Speaker for American Society for Extracorporeal Technology conference in San Antonio, TX
2014 Faculty Excellence Award for Contribution in Patents, Licenses, and Options, University of Louisville
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
2010 9th World Congress for Microcirculation Postdoctoral Travel Award, Paris, France
2009 1st Place Poster Presentation, Postdoctoral Fellow Division, E.J. Van Liere Research Day, West Virginia University
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, WI

C. Contributions to Science

1. Coronary microvascular dysfunction in advanced age

The primary goal of my laboratory is to develop therapies treat coronary microvascular dysfunction in a model of advanced age. My lab has significantly contributed to understanding the mechanism how adipose-derived stromal vascular fraction cells protect against treat ischemia, thin endometrium, and most recently, coronary microvascular dysfunction. Key findings include changes in adrenergic responsiveness, reactive oxygen species crosstalk that contribute to microvascular dysfunction and associated cardiac defects.

- Tracy EP, Dukes M, Beare J, Rowe G, Nair R, **LeBlanc AJ**. Stromal Vascular Fraction Restores Vasodilatory Function by Reducing Oxidative Stress in Aging-Induced Coronary Microvascular Disease. Antioxid Redox Signal. 2022 Aug 11. doi: 10.1089/ars.2021.0249. Epub ahead of print. PMID: 35950616.

- Rowe G, Tracy E, Beare JE, **LeBlanc AJ**. Cell therapy rescues aging-induced beta-1 adrenergic receptor and GRK2 dysfunction in the coronary microcirculation. *Geroscience*, 2022 Feb;44(1):329-48. PMID: 34608562, PMCID: PMC8811091.
- Rowe G, Kelm NQ, Beare JE, Tracy E, Yuan F, **LeBlanc AJ**. Enhanced beta-1 adrenergic receptor responsiveness in coronary arterioles following intravenous stromal vascular fraction therapy in aged rats. *Aging* (Albany NY), 2019 Jul;11(13):4561-78. PMID: 31296794; PMCID: PMC6660031.
- Nevitt C, McKenzie G, Christian K, Austin J, Hencke S, Hoying J, **LeBlanc A**. Physiological levels of thrombospondin-1 decrease NO-dependent vasodilation in coronary microvessels from aged rats. Am J Physiol Heart Circ Physiol. 2016 Jun 1;310(11):H1842-50. doi: 10.1152/ajpheart.00086.2016. Epub 2016 May 3. PubMed PMID: 27199114; PubMed Central PMCID: PMC6345213

2. Impaired mitochondrial function in coronary microvascular dysfunction in cardiovascular aging

My lab has provided considerable evidence on the contribution of coronary microvascular dysfunction as a contributing event to aging-induced heart failure. We have identified mitochondrial defects including increases in mitochondrial fission and its regulators, including DRP1, as novel targets to treat cardiovascular aging phenotypes.

- Tracy EP, Nair R, Rowe G, Beare JB, Beyer AM, **LeBlanc AJ**, Adipose Stromal Vascular Fraction Reverses Mitochondrial Dysfunction and Hyperfission in Aging-Induced Coronary Microvascular Disease. Accepted – August 2022 to *Am J Physiol Heart Circ Physiol.*
- Ait-Aissa K , Norwood-Toro LE, Terwoord J, Young M, Paniagua LA, Hader SN., Hughes WE, Hockenberry JC, Beare JE, Linn J, Kim J, Betts DH, **LeBlanc AJ**, Gutterman D.D, Beyer A.M., Non-canonical role of telomerase in regulation of microvascular redox environment with implications for coronary artery disease. Accepted to *Function* in August 2022
- Kelm NQ, Beare JE, Weber GJ, **LeBlanc AJ**. Thrombospondin-1 mediates Drp-1 signaling following ischemia reperfusion in the aging heart. FASEB Bioadv. 2020 May;2(5):304-314. doi: 10.1096/fba.2019-00090. eCollection 2020 May. PubMed PMID: 32395703; PubMed Central PMCID: PMC7211039. Barati MT, Ketchem CJ, Merchant ML, Kusiak WB, Jose PA, Weinman EJ, **LeBlanc AJ**,
- Kelm NQ, Beare JE, **LeBlanc AJ**. Evaluation of Coronary Flow Reserve After Myocardial Ischemia Reperfusion in Rats. J Vis Exp. 2019 Jun 28;(148). doi: 10.3791/59406. PubMed PMID: 31305512; PubMed Central PMCID: PMC6996202.

3.Cell Therapy as treatment for heart disease.

With my initial faculty appointment at the Cardiovascular Innovation Institute and growing interest in translational research in the field of cardiac physiology, my lab contributed to understanding the potential of remedying heart disease through potential cell therapies focusing on coronary physiology. This effort resulted invention of 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. In addition, we found 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 using this cell patch.

- **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*, 2012 Feb;302:H973-82. PMID: 22140045, PMCID: PMC3322738.
- **LeBlanc AJ**, Krishnan L, Sullivan CJ, Williams SK, Hoying JB. Microvascular repair: Post-angiogenesis vascular dynamics. *Microcirculation*, 2012 Nov;19(8):676-95. PMID: 22734666, PMCID: PMC3842172.
- ***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 Transl Med,* 2013 Nov;2(11):896-905. PMID: 24106337, PMCID: PMC3808204. (*Indicates corresponding author)
- 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. *Exp Gerontol*, 2015 Mar;63:18-26. PMID: 25617825, PMCID: PMC4346434.

4. Environmental Toxicology – impact of cardiac and microvascular function

During my post graduate training I extended my expertise in the coronary microcirculation in the field of cardiovascular toxicology. My work identified that pulmonary exposure to nanoparticle aerosols as a critical component of cardiovascular complications (e.g., asbestos epidemic). I solely developed and setup the isolated vessel research program in my mentor'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. These efforts resulted in the first studies describing deleterious vasodilatory effects in coronary arterioles following inhalation exposure to normal environmental levels of TiO_2.

- **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*, 2008;13-7.
- **LeBlanc AJ**, JL Cumpston, BT Chen, D Frazer, V Castranova, TR Nurkiewicz. Nanoparticle inhalation impairs endothelium-dependent vasodilation in subepicardial arterioles. *J Toxicol Environ Health A*, 2009;72(24):1576-84. PMID: 20077232, PMCID: PMC2808198.
- **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. *Cardiovasc Toxicol*, 2010 Mar;10(1):27-36. PMID: 20033351, PMCID: PMC2825710.

5. Age- and sex-related effects on vasoreactivity of the coronary microcirculation

During my graduate work I identified a gradual decline in the Flk-1/NO signaling pathway as age increases in male rats. 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 WISE study, which found a possible relationship between HRT 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.

- **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*, 2008 Dec;295:H2280-8. PMID: 18835919, PMCID: PMC2614537.
- **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. *Am J Physiol Regul Integr Comp Physiol*, 2009 Dec;297(6):R1713-23. PMID: 19812360, PMCID: PMC2803626.
- 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,* 2011 Jun;300:H2105-15. PMID: 21441309, PMCID: PMC3119103.
- **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.

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