BIOGRAPHICAL SKETCH

NAME: **Merry L. Lindsey, Ph.D.**

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

POSITION TITLE: Professor, Department of Physiology and Biophysics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Boston University, Boston, MA	B.A.	05/1992	Biology
Baylor College of Medicine, Houston, TX	Ph.D.	08/1999	Cardiovascular Sciences
Brigham and Women's Hospital and Harvard Medical School, Boston, MA	Postdoctoral Fellow	08/2002	Cardiovascular Sciences

A. Personal Statement

Dr. Lindsey was trained in cardiovascular sciences at Baylor College of Medicine and Harvard Medical School. She has >20 years' experience with all aspects of inflammatory and extracellular matrix (ECM) components of cardiac remodeling following myocardial infarction (MI) in several animal models (mouse, dog, rabbit, and pig,). In particular, she is a leading expert on matrix metalloproteinase (MMP) biology, ECM remodeling, and cardiac aging research. Dr. Lindsey brings physiology, cell biology, biochemistry, and proteomic expertise with *in vitro* and *in vivo* cardiac inflammatory and wound healing processes. She has served as PI on multiple funded projects and has trained >60 trainees, who have gone on to successful careers. She has extensive manuscript editing and reviewing experience. In summary, Dr. Lindsey has the research, mentoring, and leadership experience necessary for cardiac inflammation and extracellular matrix projects.

B. Positions and Honors

Positions

2002-2005 Asst Professor (tenure track), Dept of Surgery and Dept of Cell & Molecular Pharmacology & Experimental Therapeutics (dual appt), Medical Univ of South Carolina, Charleston, SC

2002-2007 Assoc Member/Member, Graduate Faculty, College of Graduate Studies, Program in Molecular & Cellular Biology & Pathobiology, Medical Univ of South Carolina, Charleston, SC

2005-2009 Assistant Professor (tenure track), Department of Medicine, Cardiology Division, and Department of Cellular and Structural Biology (cross-appointment); Member, Graduate School Faculty, The University of Texas Health Science Center, San Antonio, TX

2009-2012 Associate Professor with tenure, UTHSCSA, San Antonio, TX

2010-2013 Research Health Scientist, Audie L. Murphy VA Hospital, South Texas Veterans Health Care System

2012 Professor with tenure, Department of Medicine/ Division of Geriatrics, Gerontology and Palliative Medicine and Department of Cellular and Structural Biology (cross-appointment); Member, Graduate School Faculty, The University of Texas Health Science Center, San Antonio, TX

2013-present Professor (tenured 2015), Department of Physiology and Biophysics and Cardiology Division, Department of Medicine, University of Mississippi Medical Center, Jackson, MS

2013-present Research Health Scientist, G.V. (Sonny) Montgomery VA Medical Center, Jackson, MS

Selected Other Experience and Professional Memberships

2007-2013 Director, Cardiovascular Function Core, Barshop Institute for Longevity and Aging Studies, Nathan Shock Aging Center of Excellence, UTHSCSA

2009-2010 Interim Assistant Dean for Medical Student Research Programs, School of Medicine, UTHSCSA

2009-2013 Assoc Program Director, T32 (HL04776), Pathobiol of Occlusive Vasc Disease Training Grant

2010-2015 Director, San Antonio Cardiovascular Proteomics Center

2013-present Director, Mississippi Center for Heart Research, UMMC, Jackson, MS

Professional Memberships

- American Heart Association- Fellow, Council on Basic Cardiovascular Sciences and Council on Functional Genomics and Translational Biology; Chair, Cardiac Bio Reg 6 Study Section
- The American Physiological Society (2009-2013 Co-chair, CV Section Programming Committee; 2010-2013 Chair, Translational Physiology Interest Group; 2013-present Chair, CV Section)
- 2011- American Journal of Physiology: Heart and Circulatory Physiology
  - 2011 Consulting Editor
  - 2014 Associate Editor
  - 2015 Deputy Editor
  - Hosted 13 podcasts (http://ajpheart.podbean.com/)
- 2009-2017 Journal of Molecular and Cellular Cardiology;
  - 2008 Editorial Board
  - 2009 Guest Editor, Special Issue on ECM and Cardiovascular Remodeling
  - 2014 Associate Editor
  - 2015 Guest Editor, Special Issue on Fibrosis and Myocardial Remodeling
- 2015- Proteomics: Clinical Applications- Guest Editor, Special Issue on Tissue Damage, Repair, and Regeneration
- 2015 European Society of Cardiology, Heart Failure Association Workshop on Fibrosis; Working Group Member, Brussels, Belgium (March 2015)- only 1 of 2 US representatives
- 2015 NIH/NHLBI Workshop on *Refining Current Scientific Priorities and Identifying New Scientific Gaps in HIV-related Heart, Lung, and Blood Research*; Working Group Member, Bethesda, MD (December 2015)

Manuscript Reviewing

- Reviewer for >100 journals, including Aging Cell, American Journal of Physiology-Heart and Circulatory Physiology, Annals of Medicine, Cardiology, Cardiovascular Research, Circulation, Circulation Research, European Heart Journal, Hypertension, International Journal of Cardiology, Journal of Cardiac Failure, Journal of Molecular and Cellular Cardiology, Proteomics, and Thrombosis Research
  - have reviewed >884 manuscripts since 2007 (average of 8.2±1.9/ month)

Grant Reviewing

- 2005- Grant reviewer for funding agencies in Ireland, Austria, Hong Kong, Israel, Netherlands, and Qatar
- 2007- Grant reviewer for American Heart Association
- 2008- NIH Reviewer: Cellular Mechanisms in Aging and Development (CMAD) Study Section, Myocardial Ischemia and Metabolism (MIM) Study Section (2008-2016), Challenge Grants Panel 19 Study Section, numerous special emphasis panels (R15, R21, PPG), and R13 Conference Grant Study Section (NHLBI)

Meetings and Advisory Board Leadership

- 2011- Co-Organizer (with Dr. Thomas K. Borg), Keystone Symposia on Extracellular Matrix and Cardiovascular Remodeling
- 2010- Chair Pro Tempore, Medical Advisory Board, Saving tiny Hearts Foundation (http://www.savingtinyhearts.org/)

Social Media

- Founder, CV-ECM Linked in group (http://www.linkedin.com/groups/CV-ECM-3775394/about) with >145 international members
- AJP Heart podcasts (https://ajpheart.podbean.com/)- have recorded 15 podcasts

Selected Awards and Honors

- 2001 Trainee Abstract Award, Council on Basic Cardiovascular Sciences, American Heart Association Scientific Sessions, Anaheim, CA
- 2006 Leadership Education And Development (LEAD) Institute; UTHSCSA
- 2010 Leading Light Award, for exemplary leadership and outstanding achievement in healthcare, Healthcare Businesswomen's Association, San Antonio Chapter
- 2014 Distinguished Service Award, American Physiological Society, Translational Physiology Group, Experimental Biology (inaugural recipient; only 1 award was given)
- 2015 Translational Research Team Award, Excellence in Research Awards Ceremony, UMMC- awarded to the most outstanding translational research team of the year
- 2013-6 Silver, Gold, and Platinum Research Awards, Excellence in Research Awards Ceremony, UMMC

Mentoring
Have mentored/supervised >60 postdoctoral fellows, residents, PhD students, masters students, medical students, undergraduates, and high school students. These students have won multiple awards for their research, ranging from essay competitions to poster presentations to science fair projects to research grants (AHA postdoctoral fellowships, scientist development grants, and K99/R00 grants).

C. Contribution to Science (representative of >180 peer reviewed articles)

Mission Statement

Our team is dedicated to performing cardiovascular research that involves developing multidimensional approaches to examine the mechanisms whereby the left ventricle responds to injury; applying the knowledge gained to develop therapeutic strategies to prevent, slow, or reverse the progression to heart failure; disseminating our results to general, scientific, and medical communities; and training the next generation of scientists.

Research Focus: Cardiac inflammation and extracellular matrix (ECM) biology is the major research focus of our team, particularly changes that are the cause or effect of pathophysiological processes involved in tissue repair. Our main research areas can be divided into 5 overlapping themes, listed below followed by representative publications. While Dr. Lindsey has been publishing since 1998, all of the articles listed are recent (since 2010) to highlight our current expertise. The publications are listed in reverse chronological order.

1. Macrophage, neutrophil, and fibroblast roles in LV remodeling post-MI
Macrophage and neutrophils are primary leukocyte responders in the MI setting; and the fibroblast is the source of the extracellular matrix (ECM) scar that forms post-MI. Our team is focused on understanding how these cell types coordinate to regulate cardiac remodeling, including how macrophage and neutrophil polarization helps initiate, amplify, and turn off inflammation post-MI over time and how fibroblasts coordinate the transition from wound debridement to scar formation. The following publications document our expertise in this arena:

a) Ma Y, Iyer RP, de Castro Brás LE, Toba H, Yabluchanskiy A, DeLeon KY, Hall ME, Lange RA, and **Lindsey ML**. Chapter 4. Cross Talk Between Inflammation and Extracellular Matrix Following Myocardial Infarction. In *Inflammation in Heart Failure*. Editors: Blankesteijn WM and Altara R. Elsevier. 67-79 (2015).
b) Ma Y, de Castro Brás LE, Toba H, Iyer RP, Hall ME, Winniford MD, Lange RA, Tyagi SC, and **Lindsey ML**. Myofibroblasts and the extracellular matrix network in post-myocardial infarction cardiac remodeling. Pflugers Arch. 466(6):1113-27 (2014) PMC4033805 *Accepted on first submission (was among the top 10 downloaded articles for this journal, with >600 downloads between June and September 2014).*
c) Zamilpa R, Ibarra J, de Castro Brás LE, Ramirez TA, Nguyen N, Halade GV, Zhang J, Dai Q, Dayah T, Chiao YA, Lowell W, Ahuja SS, D'Armiento J, Jin YF, and **Lindsey ML**. Transgenic overexpression of matrix metalloproteinase-9 in macrophages attenuates the inflammatory response and improves left ventricular function post-myocardial infarction. J Mol Cell Cardiol. Nov; 53(5):599-608 (2012). PMC3472138
d) Ma Y, Halade GV, and **Lindsey ML**. Extracellular Matrix and Fibroblast Communication Following Myocardial Infarction. Journal of Cardiovascular Translational Research. 5(6):848-7 (2012). PMC3518752

2. Matrix Metalloproteinase (MMP) roles in LV remodeling post-MI
Our team leads the effort to understand how MMPs serve as upstream signaling molecules to coordinate remodeling. While many groups measure MMPs as output signals, we are one of a few groups who investigate the downstream effect of MMP activity. The following publications document our expertise in this arena:

a) Iyer RP, Patterson NL, Zouein FA, Ma Y, Dive V, de Castro Brás LE, and **Lindsey ML**. Early Matrix Metalloproteinase-12 Inhibition Worsens Post-Myocardial Infarction Cardiac Dysfunction by Delaying Inflammation Resolution. International Journal of Cardiology. 185:198-208 (2015). PMC4406852
b) Iyer RP, De Castro Brás LE, Jin YF, and **Lindsey ML**. Translating Koch's Postulates to Identify Matrix Metalloproteinase Roles in Post-Myocardial Infarction Remodeling: The Cardiac Metalloproteinase Actions (CarMA) Postulates. Circulation Research, 114(5):860-71 (2014). PMC3972011
c) Ma Y, Halade GV, Zhang J, Ramirez TA, Levin D, Voorhees A, Jin Y-F, Han H-C, Manicone AM, and **Lindsey ML**. Matrix Metalloproteinase-28 Deletion Exacerbates Cardiac Dysfunction and Rupture Following Myocardial Infarction in Mice by Inhibiting M2 Macrophage Activation. Circulation Research. 112:675-88(2013). PMC3597388
d) Iyer RP, Patterson NL, Fields GB, and **Lindsey ML.** The History of Matrix Metalloproteinases (MMPs): Milestones, Myths, and Misperceptions. Am J Physiol Heart Circ Physiol. Oct; 303(8):H919-30 (2012). PMC3469639

3. Aging influences on LV remodeling

A major co-morbidity for cardiovascular disease is aging, yet many basic science research projects do not evaluate aging animal models. We have extensively evaluated the effects of aging on normal cardiac physiology as well as during the MI response. The following publications document our expertise in this arena:

a) Yabluchanskiy A, Ma Y, DeLeon-Pennell KY, Altara R, Halade GV, Voorhees AP, Nguyen NT, Jin Y-F, Winniford MD, Hall ME, Han H-C, and **Lindsey ML**. Myocardial Infarction Superimposed on Aging: MMP-9 Deletion Promotes M2 Macrophage Polarization. Journal of Gerontology: Biological Sciences. In press (2015).
b) Ma Y, Chiao YA, Clark R, Flynn ER, Yabluchanskiy A, Ghasemi O, Zouein F, **Lindsey ML**, and Jin Y-F. Deriving a cardiac ageing signature to reveal MMP-9-dependent inflammatory signalling in senescence. Cardiovasc Res. 106: 421-431 (2015).
c) Yabluchanskiy A, Ma Y, Chiao YA, Lopez EF, Voorhees A, Toba H, Hall ME, Han H-C, **Lindsey ML**, and Jin Y-F. Cardiac aging is initiated by matrix metalloproteinase-9 mediated endothelial dysfunction. American Journal of Physiology: Heart and Circulatory Physiology. 306:H1398-H1407 (2014).
d) Chiao YA, Ramirez TA, Zamilpa R, Okoronkwo SM, Dai Q, Zhang J, Jin Y-F, and **Lindsey ML**. Matrix Metalloproteinase-9 Deletion Attenuates Myocardial Fibrosis and Diastolic Dysfunction in Ageing Mice. Cardiovascular Research. Dec 1;96(3):444-55 (2012). PMC3500048

4. Proteomics as a tool to investigate LV remodeling

From 2010-2015, our team was one of 7 NHLBI funded proteomics centers (Dr. Lindsey, PI). The focus of our center was ECM proteomics, which is very difficult due to relative low abundance and high insolubility issues. Also included in this theme is cell secretomics, to understand the individual cell contributions to the extracellular environment. We have developed proteomic methods to monitor ECM proteomes and isolated cell secretomes during the time continuum of remodeling. The following publications document this expertise:

a) **Lindsey ML**, Iyer RP, Zamilpa R, Yabluchanskiy A, DeLeon-Pennell KY, Hall ME, Kaplan A, Zouein FA, Bratton D, Flynn ER, Cannon PL, Tian Y, Jin Y-F, Lange RA, Tokmina-Roszyk D, Fields GB, and de Castro Brás LE. A Novel Collagen Matricryptin Reduces Left Ventricular Dilation Post-myocardial Infarction by Promoting Scar Formation and Angiognesis. J Am Coll Cardiol. 66(12):1364-74. (2015).
b) de Castro Brás LE, Ramirez TA, Deleon-Pennell KY, Chiao YA, Ma Y, Dai Q, Halade GV, Hakala K, Weintraub ST, and **Lindsey ML**. Texas 3-Step decellularization protocol: Looking at the cardiac extracellular matrix. Journal of Proteomics 86:43-52 (2013) PMC3879953
c) Patterson NL, Iyer RP, Bras LD, Li Y, Andrews TG, Aune GJ, Lange RA, and **Lindsey ML**. Using proteomics to uncover extracellular matrix interactions during cardiac remodeling. Proteomics Clin Appl. 7(7-8):516-527 (2013). PMC3815558
d) **Lindsey ML**, Weintraub ST, and Lange RA. Using Extracellular Matrix Proteomics to Understand Left Ventricular Remodeling. Circ Cardiovasc Genet. 5:01-07 (2012). PMC3282021

5. Mathematical modeling of LV remodeling

Working with Dr. Yu-Fang Jin at UTSA, our team develops network analyses and builds mathematical models that encapsulate the molecular, cellular, and tissue level processes involved in LV remodeling both during aging and MI. The following publications document our expertise in this arena:

a) Nguyen NT, **Lindsey ML**, and Jin YF. Systems analysis of gene ontology and biological pathways involved in post-myocardial infarction responses. BMC Genomics Supplement Issue for ICIBM. In press (2015)
b) Nguyen NT, Zhang X, Wu C, Lange RA, Chilton RJ, **Lindsey ML**, and Jin YF. Integrative Computational and Experimental Approaches to Establish a Post-Myocardial Infarction Knowledge Map. PLoS Computation Biology, 10(3): e1003472. (2014). PMC3961365
c) Wang Y, Yang T, Ma Y, Halade GV, Zhang J, **Lindsey ML**, and Jin Y-F. Mathematical modeling and stability analysis of macrophage activation in left ventricular remodeling post-myocardial infarction. BMC Genomics. Oct 26;13 Suppl 6:S6-21 (2012). PMC3481436
d) Jin YF, Han HC, Berger J, Dai Q, and **Lindsey ML**. Combining Experimental and Mathematical Modeling to Reveal Mechanisms of Macrophage-Dependent Left Ventricular Remodeling. BMC Systems Biology, 5(1):60 (2011). PMC3113236

Complete List of Published Works in My Bibliography: (note this myNCBI file includes 5 references from the Han lab that were supported by grants to Dr. Lindsey; she is not a co-author on these 5 publications)
https://www.ncbi.nlm.nih.gov/sites/myncbi/merry.lindsey.1/bibliography/41659911/public/?sort=date&direction=descending

D. Research Support

Ongoing

Systems Biology of Fibroblast Polarization Following Myocardial Infarction
R01 HL129823 Lindsey (PI) 05/01/16-04/30/20 NIH/NHLBI
The goal is to define upstream fibroblast mechanisms of post-MI LV remodeling.

Systems Biology of Macrophage Polarization Following Myocardial Infarction
R01 HL075360 Lindsey (PI) 07/01/04-05/31/19 NIH/NHLBI
The goal is to define upstream macrophage mechanisms of post-MI LV remodeling.

Matrix Metalloproteinase-9 Roles in the Aging Myocardial Response to Ischemia
Merit Award Lindsey (PI) 10/01/09-03/31/19 Veterans Administration
The goal is to define how aging influences the inflammatory and fibrotic responses to MI.

A Community Effort to Translate Protein Data to Knowledge: An Integrated Platform
U54GM114833 Lindsey, Ping (Co-PI) 09/29/14-04/30/18 NIH/NIGMS
The goal is to fuse cutting-edge big data innovations and cardiovascular medicine.

Mississippi Center for Clinical and Translational Research
U54GM115428 Wilson, James G (PI) 08/18/16-07/31/21 NIH/NIGMS
MCCTR focuses on clinical and translational obesity research that can reduce obesity and its morbidities.
Role: Co-investigator (Lead, Tracking & Evaluation Core)

Aptamer Proteomics of Cardiometabolic and Renal Traits in African Americans
HL133870 Wilson, James G and Gerstzen, Robert E (Co-PI) 04/01/2017 – 02/28/2021 NIH/NHLBI
The goal is to profile aptamer-based proteomic markers in the African American Jackson Heart Study cohort and validates results using the Southern Community Study cohort. Role: Co-investigator

Grants with Mentor Roles:

- **MMP-9 Generated Collagen C-peptide Roles in Post-myocardial Infarction Remodeling**
  AHA14SDG18860050 de Castro Brás, Lisandra (PI) 01/01/14-12/31/17 Role: Consultant/Mentor
  Goal: to determine the roles of collagen fragments generated by MMP-9 on post-MI remodeling.
- **Neutrophil polarization in post-myocardial infarction cardiac remodeling**
  AHA15SDG22930009 Ma, Yonggang (PI) 01/01/15-12/31/18 Role: Consultant/Mentor
  Goal: to determine neutrophil phenotypes, polarization mechanisms, and roles during post-myocardial infarction left ventricular remodeling.
- **T-cell regulation of cardiac remodeling**
  VA1IK2BX003922-01 DeLeon-Pennell, Kristine (PI) 06/01/17-05/31/22 Role: Consultant/Mentor
  Goal: to determine T-cell roles in post-MI remodeling
- **Hypertension and Cardiorenal Diseases Research Training Program**
  NIHT32HL105324 Granger, Joey (PI) 09/20/10-08/31/20 Role: Mentor
- **Mississippi Center of Excellence in Perinatal Research**
  NIHP20GM121334 Reckelhoff, Jane (PI) 06/08/17-05/31/22 Role: Mentor

Selected Completed (representative of >$20M in grant funding received to date)

NHLBI UTHSCSA Cardiovascular Proteomics Center
NHLBI contract Lindsey (PI) 08/15/10-08/14/15 NIH/NHLBI
The goal was to develop novel and innovative proteomic technologies to identify predictive markers of adverse LV remodeling post-MI, focusing on extracellular matrix fragment generation as a key initiating event.

DHA Mechanisms in Obesity-Mediated Cardiac Remodeling Post-Myocardial Infarction
K99 AT006704 Halade (PI) 08/01/11-06/30/13 (K99 phase) NIH/NCCAM
The goal was to determine how obesity mediates the LV response to MI, both in the basal state and with DHA treatment. Role: Mentor