BIOGRAPHICAL SKETCH

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NAME: Lu, Hong S.

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

POSITION TITLE: Associate Professor, Saha Cardiovascular Research Center and Department of Physiology

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
Zhejiang University School of Medicine, China	MD	06/1993	Medicine
Zhejiang University Sir Run Run Shaw Hospital, China	Residency	06/1995	Internal Medicine
Zhejiang University Sir Run Run Shaw Hospital, China	Clinical Fellow	05/1999	Cardiology
Kanazawa University Graduate School of Medical Sciences, Japan	PhD	03/2003	Molecular Genetics in Medical Sciences
University of Kentucky, Lexington, KY	Postdoctoral Scholar	06/2007	Atherosclerosis and Aortic Aneurysms

A. Personal Statement

I have been actively researching the pathogenesis and therapeutic targets of atherosclerosis and aortic aneurysms using multiple mouse models for over twenty years, with a long-term focus on the renin-angiotensin regulation in these two cardiovascular diseases.

Rigor, Reproducibility, and Transparency have always been the most important parts of my research philosophy. I have been the Senior Technical Review Editor of ATVB (Arteriosclerosis, Thrombosis, and Vascular Biology) since 2017 and a Technical Editor of Circulation Research since 2024. My role is to ensure that original research manuscripts adhere to the NIH principles and guidelines for rigor, reproducibility, and transparency in reporting original research.

Training History: Over the past decade, I have mentored more than 20 trainees. Most graduated trainees have continued in research and become independent investigators. I have served as Training Director of an AHA SFRN (Strategically Focused Research Network), mentor for AHA CDA (Career Development Award) recipients, and co-director of our institutional Undergraduate Summer Training in Cardiovascular Research program, which has received AHA Institutional Awards for Undergraduate Student Training (IAUS) and Supporting Undergraduate Research Experiences (SURE) Program. In addition to mentoring, I have reviewed undergraduate, predoctoral, and postdoctoral fellowship applications for the AHA since 2013.

Through my active involvement in research training and grant reviews for students and postdoctoral fellows, I am proud to contribute to the development and mentorship of the next generation of researchers.

Citations:

1. **Lu H**, Rateri D, Feldman DL, Charnigo RJ, Fukamizu A, Ishida J, Oesterling EG, Cassis LA, Daugherty A. Renin inhibition reduces hypercholesterolemia-induced atherosclerosis in mice. *J Clin Invest*. 2008; 118:984-993. (PMID: 18274671; PMCID: PMC2242618)
2. Ye F, Wang Y, Wu C, Howatt DA, Wu C-H, Balakrishnan A, Mullick AE, Graham MJ, Danser AHJ, Wang J-A, Daugherty A, **Lu HS**. Angiotensinogen and megalin interactions contribute to

atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2019; 39:150-155. (PMID: 30567480; PMCID: PMC6344256)

3. Amioka N, Franklin MK, Kukida M, Zhu L, Moorleghen JJ, Howatt DA, Katsumata Y, Mullick AE, Yanagita M, Martinez-Irizarry MM, Sandoval Jr RM, Dunn KW, Sawada H, Daugherty A, **Lu HS**. Renal proximal tubule cell-specific megalin deletion does not affect atherosclerosis but induces tubulointerstitial nephritis in mice fed a Western diet. *Arterioscler Thromb Vasc Biol*. 2025; 45:74-89. (PMID: 39569521; PMCID: PMC11668626)

B. Positions, Scientific Appointments, and Honors

Positions

2022 - Present	Associate Professor (Regular Title Series with Tenure), Saha Cardiovascular Research Center and Department of Physiology, University of Kentucky, Lexington, KY
2020 - 2022	Assistant Professor (Regular Title Series), Saha Cardiovascular Research Center and Department of Physiology, University of Kentucky, Lexington, KY
2015 - 2020	Associate Professor (Research Title Series), Saha Cardiovascular Research Center and Department of Physiology, University of Kentucky, Lexington, KY
2012 - 2015	Assistant Professor (Research Title Series), Saha Cardiovascular Research Center, University of Kentucky, Lexington, KY
2010 - 2011	Assistant Professor (Research Title Series), Department of Cell Biology and Anatomy, University of South Carolina School of Medicine, Columbia, SC
2008 - 2009	Assistant Professor (Research Title Series), Saha Cardiovascular Research Center, University of Kentucky, Lexington, KY
2007 - 2008	Scientist III, Saha Cardiovascular Research Center, University of Kentucky, Lexington, KY
1998 - 1999	Visiting scholar, the First Department of Internal Medicine, Fukui Medical University, Fukui, Japan

Scientific Appointments

2024 - Present	Technical Editor, Circulation Research
2024 - Present	Grant Reviewer of AVI Special Emphasis Panel in the National Institutes of Health (ad hoc)
2023	Grant Reviewer of Quebec-Flanders Research Program, Canada
2022 - Present	Senior Technical Editor, ATVB (Arteriosclerosis, Thrombosis, and Vascular Biology)
2022 - Present	Associate Editor, Global Translational Medicine
2021 - Present	Grant Reviewer (mail-in) of European Science Foundation (ESF)
2021 - Present	Associate Editor in Cardiovascular Pharmacology and Drug Discovery, Frontiers in Cardiovascular Medicine
2021 - 2023	Guest Theme Editor of Women in Cardiovascular Therapeutics, Frontiers in Cardiovascular Medicine
2021 - 2022	Guest Editor of Aortic Aneurysms: Heterogeneity and Molecular Mechanisms, Biomolecules
2021 - 2022	Guest Theme Editor of Novel Epigenetic Medicine and Cardiovascular Diseases, Frontiers in Cardiovascular Medicine
2021	Chair of Institutional Undergraduate Student Fellowship Committee of American Heart Association
2020 - 2022	Guest Theme Editor of Cardiovascular Fibrosis and Related Diseases, Frontiers in Cardiovascular Medicine
2020 - 2021	Co-Chair of Fellowships Vascular Biology 1 Committee of American Heart Association
2020 - Present	Associate Editor of BMC Cardiovascular Disorders
2019 - 2021	Editorial Board, Journal of Thoracic Disease
2019 - 2020	GBD (Global Burden of Disease)-NHLBI-JACC Global Burden of Cardiovascular Diseases Writing Group (Aortic Aneurysm section)
2019 - 2020	Co-Chair of Institutional Undergraduate Student Fellowship Committee of American Heart Association
2017 - 2022	Technical Editor, ATVB
2013 - 2021	Vascular Biology Committee of American Heart Association
2013 - Present	Editorial Board, ATVB
2013 - 2022	Undergraduate Student Fellowship Committee of American Heart Association

Honors

2025	David A. Dichek Mid-Career Investigator Award of Arteriosclerosis, Thrombosis, and Vascular Biology (a Journal of the American Heart Association)

2014, 2016 - 2022 Top reviewer award of ATVB (Journal)
2006 New Investigator Travel Award, ATVB Council of the American Heart Association
2005 Finalist, Junior Women's Award, ATVB Council of the American Heart Association
2004 New Investigator Travel Award, ATVB Council of the American Heart Association

C. Contributions to Science

The Renin-Angiotensin System and Atherosclerosis
The renin-angiotensin system has been recognized as an increasingly complex system over the past 20 years. My research work has determined (1) the effects of different components of the renin-angiotensin system on hypercholesterolemia-induced atherosclerosis, (2) molecular mechanisms by which these renin-angiotensin components contribute to atherosclerosis, and (3) optimal targets of the renin-angiotensin system for treating atherosclerosis. Our recent studies have provided new insights into AGT being regulated by megalin, a protein that mediates the reabsorption of proteins in the kidney.

a. **Lu H**, Balakrishnan A, Howatt DA, Wu C, Charnigo R, Liau G, Cassis LA, Daugherty A. Comparative effects of different modes of renin-angiotensin system inhibition on hypercholesterolemia-induced atherosclerosis. *Br J Pharmacol. 2012:165*:2000-2008. (PMID: 22014125; PMCID: PMC3372847)
b. **Lu H**, Wu C, Howatt DA, Balakrishnan A, Moorleghen JJ, Chen X, Zhao M, Graham MJ, Mullick AE, Crooke RM, Feldman DL, Cassis LA, Vander Kooi CW, Daugherty A. Angiotensinogen exerts effects independent of angiotensin II. *Arterioscler Thromb Vasc Biol. 2016:36*:256-265. (PMID: 26681751; PMCID: PMC4732917)
c. Ye F, Wang Y, Wu C, Howatt DA, Wu CH, Balakrishnan A, Mullick AE, Graham MJ, Danser AHJ, Wang J, Daugherty A, **Lu HS**. Angiotensinogen and megalin interactions contribute to atherosclerosis. *Arterioscler Thromb Vasc Biol. 2019:39*:150-155. (PMID: 30567480; PMCID: PMC6344256)
d. Wu C-H, Wu C, Howatt DA, Moorleghen JJ, Cassis LA, Daugherty A, **Lu HS**. Two amino acids proximate to the renin cleavage site of angiotensinogen do not affect blood pressure and atherosclerosis in mice. *Arterioscler Thromb Vasc Biol. 2020:40*:2108-2113. (PMID: 32640904; PMCID: PMC7483780)

The Renin-Angiotensin Regulation and Atherosclerosis in Nonhuman Primates
There are many differences in the renin-angiotensin regulations between mice and humans. There are also many differences in atherosclerosis between mice and humans. To enhance the human relevance of our research work, we studied the renin-angiotensin regulation and atherosclerosis in a nonhuman primate model.

a. Kukida M, Cai L, Ye D, Sawada H, Katsumata Y, Franklin MK, Hecker PI, Campbell KS, Danser AHJ, Mullick AE, Daugherty A, Temel RE, Lu HS. Renal angiotensinogen is predominantly liver-derived in nonhuman primates. *Arterioscler Thromb Vasc Biol*. 2021:41; 2851-2853 (PMID: 34496634; PMCID: PMC8551028).

Pathogenesis and Therapeutics of Aortic Aneurysms and Dissections
Since 2003, I have been studying aortic aneurysms and dissections, including (1) mechanisms by which hypercholesterolemia contributes to angiotensin II-induced aortic aneurysmal development, (2) the complex pathogenesis and molecular mechanisms that are related to the renin-angiotensin system, (3) heterogeneity of pathogenesis and molecular mechanisms of ascending thoracic aortic aneurysms and dissections, and (4) potential therapeutic strategies for aortic aneurysms and dissections. The collaborative work between Dr. Daugherty and me led to one patent for inhibiting angiotensinogen to attenuate aortic pathology in Marfan syndrome.

a. **Lu H**, Howatt DA, Balakrishnan A, Moorleghen JJ, Rateri DL, Cassis LA, Daugherty A. Subcutaneous angiotensin II infusion using osmotic pumps induces aortic aneurysms in mice. *J Vis Exp*. 2015:103. (PMID: 26436287; PMCID: PMC4692630)
b. **Lu H**, Howatt DA, Balakrishnan A, Graham MJ, Mullick AE, Daugherty A. Hypercholesterolemia induced by a PCSK9 gain-of-function mutation augments angiotensin II-induced abdominal aortic aneurysms in C57BL/6 mice. *Arterioscler Thromb Vasc Biol*. 2016:36:1753-1757. (PMID: 27470509; PMCID: PMC5001883).
c. Chen JZ, Sawada H, Ye D, Katsumata Y, Kukida M, Ohno-Urabe S, Moorleghen JJ, Franklin MK, Howatt DA, Sheppard MB, Mullick AE, **Lu HS**, Daugherty A. Deletion of AT1a receptor or inhibition of

angiotensinogen synthesis attenuates thoracic aortic pathology in fibrillin-1$^{C1041G/+}$ mice. *Arterioscler Thromb Vasc Biol*. 2021; 41:2538-2550. *Featured Article* (PMID: 34407634; PMCID: PMC8458261)

d. Sawada H, Katsumata Y, Higashi H, Zhang C, Li Y, Morgan S, Lee LH, Singh SA, Chen JZ, Moorleghen JJ, Howatt DA, Rateri DL, Shen YH, LeMaire SA, Aikawa M, Majesky MW, **Lu HS**, Daugherty A. Second heart field-derived cells contribute to angiotensin II-mediated ascending aortopathies. *Circulation* 2022; 145:987-1001. (PMID: 35143327; PMCID: PMC9008740).

Molecular Genetics of Hypercholesterolemia and Coronary Atherosclerotic Disease in Patients with Familial Hypercholesterolemia

My graduate training at Kanazawa University Graduate Program of Medicine (Japan) focused on molecular genetic analysis in patients with familial hypercholesterolemia. One major project was to identify potentially functional single nucleotide polymorphisms (SNP) of the estrogen receptor α gene in hypercholesterolemia-associated coronary artery disease. I have also completed a project that determined associations between cholesteryl ester transfer protein (CETP) and LDL (low-density lipoprotein) receptor SNPs and hypercholesterolemia.

a. **Lu H**, Higashikata T, Inazu A, Nohara A, Yu W, Shimizu M, Mabuchi H. Association of estrogen receptor-alpha gene polymorphisms with coronary artery disease in patients with familial hypercholesterolemia. *Arterioscler Thromb Vasc Biol*. 2002:22:817-823. (PMID: 12006396)
b. **Lu H**, Inazu A, Moriyama Y, Higashikata T, Kawashiri MA, Yu W, Okamura T, Mabuchi H. Haplotype analyses of cholesteryl ester transfer protein gene promoter: a clue to an unsolved mystery of TaqIB polymorphism. *J Mol Med* 2003:81:246-255. (PMID: 12700892)
c. Yu W, Nohara A, Higashikata T, **Lu H**, Inazu A, Mabuchi H. Molecular genetic analysis of familial hypercholesterolemia: spectrum and regional difference of LDL receptor gene mutations in Japanese population. *Atherosclerosis*. 2002:165:335-342. (PMID: 12417285)
d. Mabuchi H, Higashikata T, Nohara A, **Lu H**, Yu W, Nozue T, Noji Y, Katsuda S, Kawashiri MA, Inazu A, Kobayashi J, Koizumi J. Cutoff point separating affected and unaffected familial hypercholesterolemic patients validated by LDL receptor gene mutants. *J Arterioscler Thromb*. 2005:12:35-40. (PMID: 15725694)

Mechanisms of Volume Overload-induced Cardiac Dysfunction

During my short-term (2010-2011) relocation to the University of South Carolina School of Medicine, I used rat models to study mechanisms of cardiac dysfunction associated with sex differences and mast cell biology. We found that mast cell-mediated mechanisms in females are a critical contributor to cardiac dysfunction.

a. **Lu H**, Meléndez GC, Levick SP, Janicki JS. Volume overload has differential effects on the initial phase of cardiac remodeling in female rats with and without ovariectomy. *Am J Physiol Heart Circ Physiol* 2012; 302: H811-817. (PMID: 22160000; PMCID: PMC3353795)
b. Li J, **Lu H***, Plante E, Melendez GC, Levick SP, Janicki JS. Stem cell factor is responsible for the rapid response in mature mast cell density in the acutely stressed heart. *J Mol Cell Cardiol* 2012; 53: 469-474. (PMID: 22850284; PMCID: PMC3438908) *Co-first author.

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