BIOGRAPHICAL SKETCH

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NAME: **Ji Li**

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

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
Lanzhou University, Lanzhou	B.S.	06/1989	Biochemistry
Lanzhou University, Lanzhou	M.S.	06/1992	Biophysics
Lanzhou University, Lanzhou	Ph.D.	06/1998	Cell Biology
Sichuan University, Chengdu	Postdoc	06/2000	Molecular Medicine
NIH/National Institute on Aging, Baltimore	Postdoc	03/2002	Signal Transduction
Yale School of Medicine, New Haven	Postdoc	06/2003	Physiology

A. Personal Statement

I have the expertise, leadership, training, expertise and motivation necessary to successfully carry out the proposed research projects. I have a broad background in biochemistry and physiology, with specific training and expertise in key research areas for cardiovascular physiology and pharmacology. I finished my postdoctoral fellowship at the National Institute on Aging (NIA/NIH) and at Yale School of Medicine. To complement my skills in basic science, I have acquired new skills in translational research and disease-oriented investigations by working extensively with established clinical investigators and by frequently attending Cardiology Grand Rounds and other relevant cardiovascular disease lectures. As PI or Co-Investigator on several previous AHA-, ADA-, and NIH-funded grants, I laid the groundwork for the proposed research by spearheading novel projects related to understanding the role of stress inducible age related protein Sestrin2 in cardioprotection against ischemic insults. In addition, I successfully administered the projects (e.g. staffing and budget), collaborated with other researchers, and produced several peer-reviewed publications from each project. As a result of these previous experiences, I am aware of the importance of frequent communication among project members and of constructing a realistic research plan, timeline, and budget.

1. Ma, H., Wang, J., Thomas, D.P., Tong, C., Leng, L., Wang, W.K., Merk, M., Zierow, S., Bernhagen, J., Ren, J., Bucala, R. & **Li, J.** (2010). Impaired macrophage migration inhibitory factor (MIF)-AMPK activation and ischemic recovery in the senescent heart. *Circulation* 122:282-292. PMID: 20606117; PMCID: PMC2907453 (**This paper has been selected by Circulation Editors' Pick: Most Read Articles in Molecular Cardiology, *Circulation*, 124:e927, 2011**)
2. Morrison, A., Chen, L., Wang, J., Zhang, M., Yang, H., Ma, Y., Budanov, A., Lee, J.H., Karin, M. & **Li, J.** (2015) Sestrin2 promotes LKB1-mediated AMPK activation in the ischemic heart. *FASEB J* 29:408-417. PMID: 25366347; PMCID: PMC4314228
3. Quan, N., Sun, W., Wang, L., Chen, X., Bogan, J.S., Zhou, X., Cates, C., Liu, Q., Zheng, Y. & **Li, J.** (2017). Sestrin2 prevents age-related intolerance to ischemia and reperfusion injury by modulating substrate metabolism. *FASEB J* 31:4153-4167. PMID: 28592638

B. Positions and Honors

Positions and Employment

1992-1995	Instructor, Molecular Biology Laboratory, Cancer Research Center, Xiamen University, Xiamen, China
2003-2007	Associate Research Scientist, Division of Cardiovascular Medicine, Yale University School of Medicine, New Haven, CT
2007-2009	Assistant Professor, Division of Pharmaceutical Sciences, University of Wyoming School of Pharmacy, Laramie, WY
2009-2015	Assistant Professor, Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, University at Buffalo-SUNY, Buffalo, NY
2015-present	Associate Professor, Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS

Other Experience and Professional Memberships

2000-2003	Member, American Society for Biochemistry and Molecular Biology (ASBMB)
2003-present	Member, American Heart Association and American Stroke Association (AHA/ASA)
2005-present	Member, American Diabetes Association (ADA)
2007-2011	Member, the Gerontological Society of America (GSA)
2010-2015	Member, American Society for Pharmacology & Experimental Therapeutics (ASPET)
2008-present	Member, The Academy of Cardiovascular Research Excellence (ACRE)
2006-2011	Member, American Heart Association (AHA) Grant Review Committee: Cardiology Regulation
2009-present	Member, American Diabetes Association (ADA) Research Grant Review Committee
2013-	Ad Hoc Member, NIH Myocardial Ischemia and Metabolism (MIM) Study Section
2014-	Ad Hoc Member, NIH Special Emphasis Panels Zrg1 BDCN-L02 SEP
2014-	Ad Hoc Member, NIH Special Emphasis Panels Zrg1 BDCN-N02 M SEP, Cognition, Diabetic Neuropathy and Metabolomics
2014-	Ad Hoc Member, DoD Peer Reviewed Medical Research Program, Discovery-Metabolic Disease (DIS-MD)
2015-	Ad Hoc Member, NIH Special Emphasis Panels ZDK1 GRB-7 (M1) 1, R13 Conference Grant Applications
2015-2016	Ad Hoc Member, NIH Aging Systems and Geriatrics (ASG) Study Section
2016-	Reviewer, AHA Committee of Strategically Focus Research Network-Heart Failure
2016-	Ad Hoc Member, NIH Surgery, Anesthesiology, and Trauma (SAT) Study Section
2016-	Ad Hoc Member, Department of Veterans Affairs (VA) Cardiovascular Studies-A (CARA) Study Section
2016-	Ad Hoc Member, NIH Cardiac Contractility, Hypertrophy, and Failure (CCHF) Study Section

Honors

1998	The Scientific & Technical Progress Award (2nd place) of Ministry of National Education of China
1999	The Excellent Paper Award (2nd place) of Chinese Hospital Pharmaceutical Society
2000	The Excellent Paper Award (3rd place) of Chinese Cell Biology Society
2002	NIH FARE (Fellow Award for Research Excellence) Award, Bethesda, MD
2006	Travel Award for the American Heart Association (AHA) Scientific Session, Chicago, IL
2008	Participant, 16th Annual Summer Training Course in Experimental Aging Research/NIH, June 14-19, Seattle, WA
2009	Seed Award, College of Health Sciences, University of Wyoming, Laramie, WY
2009	New Investigator Award, University of Wyoming, Laramie, WY
2016	Gold level of the Excellence in Research Awards, University of Mississippi Medical Center

C. Contribution to Science

1. ***Oxidative stress signaling pathways***. My early publications directly addressed the fact that natural antioxidants extracted from herb medicine can inhibit proliferation and induce apoptosis of tumor cells via modulating intracellular redox status. At the cellular level, oxidants elicit a wide spectrum of responses ranging from proliferation to growth arrest, to senescence, to death. The particular outcome observed varies significantly with cell type and conditions, but largely reflects the strength of the stimulus and the balance between the activities of a variety of signaling pathways that are activated. The mitogen-activated protein (MAP) kinases play a central role in orchestrating many short- and long-term changes in the cell in response to extracellular stimuli. The fact that a broad variety of extracellular signals conscript MAP kinase cascades to convey their specific messages suggests that MAP kinase cascades serve a myriad of purposes and the cascades need to be tightly controlled. The activities of all MAP kinases are regulated through reversible phosphorylation of two different amino acid residues in the Thr-Xaa-Tyr signature motifs in their kinase subdomain. In mammalian cells, inactivation of MAP kinases is primarily conducted by a family of dual-specificity MAP kinase phosphatases (MKPs) with MKP-1 being the archetype. By providing evidence and simple clinical approaches, this body of work has provided MKP-1 as a negative regulator of the macrophage inflammatory response and as a potential target for the development of anti-inflammatory drugs in relevant medical settings well into the future. I served as the primary investigator or co-investigator in all of these studies.

    a. **Li, J**., Gorospe, M., Hutter, D., Barnes, J., Keyse, S.M. & Liu, Y. (2001) Transcriptional induction of MKP-1 in response to stress is associated with histone H3 phosphorylation/acetylation. *Mol Cell Biol* 21: 8213-8224. PMID: 11689710; PMCID: PMC99986
    b. **Li, J**., Gorospe, M., Barnes, J. & Liu, Y. (2003) Tumor promoter arsenite stimulates histone H3 phosphoacetylation of proto-oncogenes c-fos and c-jun chromatin in human diploid fibroblasts. *J Biol Chem* 278:13183-13191. PMID: 12547826
    c. **Li, J**. & Holbrook, N.J. (2004) Elevated of gadd153/chop expression and enhanced c-Jun N-terminal protein kinase activation sensitize aged cells to ER stress. *Exp. Gerontology* 39:735-744. PMID: 15130668
    d. Yeung, E.D., Morrison, A., Plumeri, D., Wang, J., Tong, C., Yan, X., & **Li, J.** (2012) Alternol exerts prostate-selective antitumor effects through modulations of the AMPK signaling pathway. *Prostate* 72:165-172. PMID: 21538425

2. ***AMPK signaling in ischemic heart***. In addition to the contributions described above, with a team of collaborators, I directly documented the effects of macrophage migration inhibitor factor (MIF) on cardiac AMP-activated protein kinase (AMPK) activity. This work allowed us to demonstrate definitively that small molecular compounds of MIF agonist can trigger cardiac AMPK signaling and limit cardiac ischemic damage by augmentation of the affinity between MIF and its receptor, CD74. These original results inform our thinking of how cardiac AMPK signaling pathways respond to MIF and other endogenous cytokines, and they have significant mechanistic and physiological implications

    a. **Li, J**., Miller, E.J., Ninomiya-Tsuji, J., Russell, R.R. & Young, L.H. (2005) AMP-activated protein kinase activates p38 mitogen-activated protein kinase by increasing p38 MAPK recruitment to TAB1 in the ischemic heart. *Circulation Res.*97:872-879. PMID: 16179588
    b. Miller, E.J.*, **Li, J.*,** Leng, L., McDonald, C., Atsumi, T., Bucala, R. & Young, L.H. (*equal contribution). (2008). Macrophage migration inhibitory factor stimulates AMP-activated protein kinase. *Nature* 451:578-582. PMID:18235500
    c. Tong, C., Morrison, A., Yan, X., Zhao, P., Yeung, E.D., Wang, J., Xie, J. & **Li, J**. (2010) Microphage migration inhibitory factor deficiency augments cardiac dysfunction in Type 1 diabetic murine cardiomyocytes. *J Diabetes* 2:267-274. PMID: 20923497; PMCID: PMC2991593
    d. Wang, J., Tong, C., Yan, X., Yeung, E., Gandavadi, S., Hare, A.A., Du, X., Chen, Y., Xiong, H., Ma, C., Leng, L., Young, L.H., Jorgensen, W.L., **Li, J***. & Bucala, R*. (*Corresponding authors) (2013) Limiting cardiac ischemic injury by pharmacologic augmentation of MIF-AMPK signal transduction. *Circulation* 128:225-236. PMID: 23762877; PMCID: PMC3781594

3. ***The application of AMPK agonist for cardiovascular diseases.*** I have been successful in building comprehensive models for the cardioprotection of AMPK against myocardial infarction caused by ischemia and reperfusion. My research has been able to explain the kinetic mechanisms by which endogenous cytokines modulate cardiac AMPK signaling pathways and to characterize the role of protease activated receptor-1 in the endogenous activated protein C (APC) mediated cardioprotection against ischemic injury.

    a. Wang, J., Yang, L., Rezaie, A.R. & **Li, J.** (2011) Activated protein C protects against myocardial ischemia/reperfusion injury through AMP-activated protein kinase signaling. *J Thromb Haemost* 9:1308-1317. PMID: 21535395; PMCID: PMC3129410
    b. Morrison, A., Yan, X., Tong, C. & **Li, J.** (2011) Acute rosiglitazone treatment is cardioprotective against ischemia/reperfusion injury by modulating AMPK, Akt, and JNK signaling in non-diabetic mice. *Am J Physiol-Heart Cir Physiol* 301:H895-H902. PMID: 21666107
    c. **Li, J.,** Qi, D., Cheng, H., Hu, X., Miller, E.J., Wu, X., Russell, K.S., Mikush, N., Zhang, J., Xiao, L., Sherwin, R.S. & Young, L.H. (2013) Urocortin 2 autocrine/paracrine and pharmacologic effects to activate AMP-activated protein kinase in the heart. *Proc Natl Acad Sci USA* 110:16133-16138. PMID: 24043794; PMCID: PMC3791748
    d. Xue, M., Chen, X., Guo, Z., Liu, X., Bi, Y., Yin, J., Hu, H., Zhu, P., Zhuang, J., Cates, C., Rousselle, T. & **Li, J.** (2017) L-Carnitine attenuates cardiac dysfunction by ischemic insults through Akt signaling pathway. *Toxicol Sci* 160:341-350.

4. ***Impaired AMPK signaling in aging****.* We have identified an anti-aging protein, Sirtuin 1 (SIRT1), which acts as a regulator of the cardiac AMPK signaling cascade. This new discovery calls attention to the possibility that cardiac SIRT1 could be a good pharmacological target for modulating the aging-related increases in susceptibility to ischemia and reperfusion mediated cardiac injury. This possibility has not been explored, and it motivates me to develop a new project to investigate the basis of the observed differences between young and aged hearts and to delineate the mechanisms that control the cardiac resistance to ischemic insults.

    a. Wang, J., Ma, H., Tong, C., Zhang, H., Lawlis, G.B., Li, Y., Zang, M., Ren, J., Nijland, M., Ford, S.P., Nathanielsz, P.W. & **Li, J.** (2010) Overnutrition and maternal obesity in sheep pregnancy alter the JNK-IRS-1 signaling cascades and cardiac function in the fetal heart. *FASEB J* 24:2066-2076. PMID: 20110268; PMCID: PMC2874473
    b. Tong, C., Morrison, A., Mattison, S., Qian, S., Bryniarski, M., Rankin, B., Wang, J., Thomas, D.P. & **Li, J.** (2013) Impaired SIRT1 nucleocytoplasmic shuttling in the senescent heart during ischemic stress. *FASEB J* 27:4332-4342. PMID: 23024374; PMCID: PMC3804750
    c. Sun, W., Quan, N., Wang, L., Chu, D., Cates, C., Liu, Q., Zheng, Y., & **Li, J.** (2016) Cardiac-specific deletion of the Pdha1 gene sensitizes hearts to toxicological actions of ischemic stress. *Toxicol Sci* 151:193-203. PMID: 26884059; PMCID: PMC4914805
    d. Yang, H., Sun, W., Quan, N., Wang, L., Chu, D., Cates, C., Liu, Q., Zheng, Y. & **Li, J.** (2016) Cardioprotective actions of Notch1 against myocardial infarction via LKB1-dependent AMPK signaling pathway. *Biochem Pharmacol* 108:47-57. PMID: 27015742; PMCID: PMC4959604

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40092542/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

1R01AG049835 (PI: Li, J) 04/15/15-03/31/20
NIH/NIA
SIRT1 Signaling in the Adaptive Metabolic Response
The major goals of this project are to investigate the molecular mechanisms by which SIRT1 signaling mediates cardioprotection against ischemia and reperfusion injury.
Role: PI

1-17-IBS-296 (PI: Li, J) 01/01/17-12/31/19
American Diabetes Association (ADA)
Glucose Transporter Trafficking in the Ischemic Heart
The major goal of this project is to investigate the regulation of glucose transporter translocation in the heart during ischemic stress conditions.
Role: PI

1R01HL12587701 (PI: Tan, Y) 05/01/17-03/31/22
NIH/NHLBI
A Novel Mechanism of Stromal Cell-derived Factor 1 Protection against Diabetic Cardiomyopathy
The major goal of this project is to characterize the role of AMPK signaling in the cardioprotective effects of SDF1 against diabetic cardiomyopathy.
Role: Co-Investigator (Li, J)

Completed Research Support (within 3 years)

1-14-BS-131 (PI: Li, J) 01/01/14-12/31/16
American Diabetes Association (ADA)
Glucose Metabolism in the Ischemic Heart
The major goals of this project are to investigate how the AMPK signaling regulates the glucose metabolism in the hearts.
Role: PI

R21AG044820 (PI: Li, J) 06/01/14-05/31/16
NIH/NIA
Role of AMPK in Prevention of Age-related Cardiomyopathy
The major goal of this project was to characterize the role of AMPK signaling pathway in cardiomyopathy in response to ischemic insults.
Role: PI

2R01HL101917-02 (PI: Rezie, A) 12/01/14-06/30/15
NIH/NHLBI
Protease Activated Receptor-1 Signaling by Coagulation Proteases
The major goal of this project was to investigate the molecular mechanisms by which Activated protein C (APC) mediates cardioprotection against ischemia and reperfusion injury.
Role: Sub-Award PI

12GRANT11620029 (PI: Li, J) 07/01/12-06/30/15
American Heart Association (AHA)
Optimizing Cardiac Function in Aging via a Novel Signaling Pathway
The major goals of this project were to investigate the molecular mechanisms by which MIF signaling mediates cardioprotection against ischemia and reperfusion injury.
Role: PI

1F31AG043291-A1 (PI: Alex Morrison, Mentor: Ji Li) 04/01/13-03/30/15
NIH/NIA
A Novel Signaling Component in the Senescent Heart
Role: Mentor