Xudong Liao, PhD.

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EDUCATION

1998-2003 **Doctor of Philosophy in Biochemistry and Molecular Biology**

Peking Union Medical College & Chinese Academy of Medical Sciences, Beijing, China

1994-1998 **Bachelor of Science in Physiology and Biophysics with Honors**

College of Life Sciences, Peking University, Beijing, China

1996-1998 **Minor in Economics**

China Center for Economic Research, National School of Development, Peking University, Beijing, China

PROFESSIONAL EXPERIENCES

2015-present **Assistant Professor**

Case Cardiovascular Research Institute, Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio, USA

2012-2015 **Instructor**

Case Cardiovascular Research Institute, Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio, USA

2008-2011 **Research Associate**

Case Cardiovascular Research Institute, Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio, USA

2004-2008 **Postdoctoral Research Fellow**

Department of Molecular Genetics & Department of Molecular Cardiology, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, USA

2001-2003 **Visiting Scholar at Chinese Academy of Sciences**

Institute of Zoology, Chinese Academy of Sciences, Beijing, China

HONORS and AWARDS

2010 Jay D. Coffman Young Investigator Award, Society of Vascular Medicine, USA

2007 "Influential Paper in Cardiovascular Research of China" Award

National Center for CVD Control and Research, China

1998 Distinguished Graduate of Peking University

1997 XIYUE Scholarship of Peking University

PROFESSIONAL MEMBERSHIP

American Heart Association (AHA)

International Society of Interferon and Cytokines Research (ISICR)

Chinese Society of Pathology and Physiology

RESEARCH SUPPORT

2012-2016 PI, AHA SDG (completed): KLF4's Role in Myocardial Metabolism and Energetics

2018-2023 PI, NIH R01 (pending): Myeloid Control of Angiogenesis in the Heart

PERSONAL STATEMENT

I have over 18 years of experiences in cardiovascular research since graduate school. I have the expertise, training, and motivation necessary to successfully carry out biomedical research. I have a broad background in physiology, biochemistry and molecular biology, with extensive experience in the design, implementation, and application of molecular biology for study of cardiovascular diseases. My research includes cardiomyopathy, immunity and metabolism. My current efforts are focused on (a) transcriptional regulation of cardiac metabolism and mitochondrial biology; (b) roles of myeloid cells in cardiovascular health and diseases; and (c) transcriptional regulation of autophagy and its role in metabolic adaptation.

CONTRIBUTION TO SCIENCE

(a) My work on the role of KLF4 in the regulation of metabolism and mitochondrial function in the heart has led to the findings that KLF4 is critical to mitochondrial biogenesis, OXPHOS function, dynamics and autophagic clearance (mitophagy), all major aspects of the mitochondrial life cycle. Mechanistically, this work demonstrates that KLF4 binds to, cooperates with and is requisite for the PGC1-ERR complex, the master transcriptional regulator of metabolism and mitochondrial biology. Finally, this work discovers that KLF4 transcriptionally regulates autophagy. The applications of these findings are enormous as metabolism, mitochondrial function and autophagy is critical in almost all cell types.

Liao X, Haldar SM, Lu Y, Jeyaraj D, Paruchuri K, et al. Krüppel-like factor 4 regulates pressure-induced cardiac hypertrophy. *Journal of Molecular and Cellular Cardiology*. 2010; 49(2):334-8. PMID: 20433848. PMCID: PMC2885477.

Liao X, Zhang R, Lu Y, Prosdocimo DA, Sangwung P, et al. Kruppel-like factor 4 is critical for transcriptional control of cardiac mitochondrial homeostasis. *The Journal of Clinical Investigation*. 2015; 125(9):3461-76. PMID: 26241060. PMCID: PMC4588311

(b) My work on the role of KLF4 in myeloid cells has discovered KLF4 as a novel transcriptional regulator of macrophage polarization that suppresses inflammatory M1 polarization and augments anti-inflammatory M2 polarization. To date, KLF4 has been recognized as one of the pro-M2 transcription factors, among which are STAT6, PPAR-gamma, and IRF4, etc. My recent work in neutrophils has identified KLF4 as critical transcription factor in the regulation of neutrophil function. The application of these findings is very broad considering diverse roles of macrophages and neutrophils in vivo.

Liao X, Sharma N, Kapadia F, Zhou G, Lu Y, et al. Krüppel-like factor 4 regulates macrophage polarization. *The Journal of Clinical Investigation*. 2011; 121(7):2736-49. PMID: 21670502. PMCID: PMC3223832.

Sharma N, Lu Y, Zhou G, **Liao X**, Kapil P, et al. Myeloid Krüppel-like factor 4 deficiency augments atherogenesis in ApoE-/- mice--brief report. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2012; 32(12):2836-8. PMID: 23065827. PMCID: PMC3574634.

Shen Y, Hong H, Sangwung P, Lapping S, Nayak L, Zhang L, Jain MK, and **Liao X**. KLF4 regulates neutrophil activation. *In submission*.

(c) My work on cardiac proteinase corin established critical approaches to detect corin zymogen activation and found the activation takes place on the cell membrane. This work paves the way for studies of corin zymogen activation and identification of PCSK6 as corin zymogen activator (Nature Medicine 2015).

Liao X, Wang W, Chen S, Wu Q. Role of glycosylation in corin zymogen activation. *The Journal of Biological Chemistry*. 2007; 282(38):27728-35. PMID: 17660514.

Wang W, **Liao X**, Fukuda K, et al. Corin variant associated with hypertension and cardiac hypertrophy exhibits impaired zymogen activation and natriuretic peptide processing activity. *Circulation Research*. 2008; 103(5):502-8. PMID: 18669922. PMCID: PMC2652846.

(d) My PhD thesis work on molecular and cellular mechanisms underlying pressure overload-induced hypertrophy discovered that mechanical stretch initiated intracellular calcium signaling, which was then relayed to nitric oxide signaling pathway to mediate cardiomyocytes' responses such as apoptosis. This work was published as four papers in peer-reviewed international SCI journals and the FASEB J paper was awarded "influential paper" by Chinese National Center for CVD Control and Research in 2007.

Liao X, Liu JM, Du L, Tang A, Shang Y, Wang SQ, Chen LY, Chen Q. Nitric oxide signaling in stretch-induced apoptosis of neonatal rat cardiomyocytes. *FASEB Journal*. 2006 Sep;20(11):1883-1885. PMID: 16877524.

Liao X, Wang X, Gu Y, Chen Q, Chen LY. Involvement of death receptor signaling in mechanical stretch-induced cardiomyocyte apoptosis. *Life Sciences*. 2005 May 27;77(2):160-174. PMID: 15862601.

Liao XD, Wang XH, Jin HJ, Chen LY, Chen Q., Mechanical stretch induces mitochondria-dependent apoptosis in neonatal rat cardiomyocytes and G2/M accumulation in cardiac fibroblasts. *Cell Research*. 2004 Feb;14(1):16-26. PMID: 15040886.

Liao XD, Tang AH, Chen Q, Jin HJ, Wu CH, Chen LY, Wang SQ. Role of Ca2+ signaling in initiation of stretch-induced apoptosis in neonatal heart cells. *Biochemical and Biophysical Research Communications*. 2003 Oct 17;310(2):405-411. PMID: 14521925.

INVITED TALKS

2016 **A KLF4-ERR Pathway Control Mitochondrial Biogenesis.**

FASEB Summer Research Conferences: KLF and Sp Transcription Factors in Disease and Regenerative Medicine. August 7–12, 2016, Snowmass, Colorado.

2014 **Krüppel-Like Factors and Metabolism.**

Peking Union Medical College and Shanghai Jiaotong University School of Medicine. October 2014. China.

2014 **Transcriptional Control of Mitochondrial Homeostasis by KLF4.**

The 3rd International Conference on Cardiovascular Sciences. October 13-15, 2014. Wuhan, China.

2014 **Transcriptional Control of Cardiac Mitochondrial Homeostasis by KLF4.**

FASEB Summer Research Conferences: Biology and Pathobiology of Krüppel-Like Factors (KLFs). August 3–18, 2014, Snowmass, Colorado.

2012 **Klf4 orchestrates myocardial metabolism and energetics.**

FASEB Summer Research Conferences: Biology and Pathobiology of Krüppel-Like Factors (KLFs). August 5–10, 2012, Snowmass, Colorado.

2010 **Myeloid KLF4 regulates macrophage polarization.**

FASEB Summer Research Conferences: Biology and Pathobiology of Krüppel-Like Factors (KLFs). August 8–13, 2010, Steamboat Springs, Colorado.

2010 **Kruppel-like Factor 4 (KLF4) is an essential regulator of Macrophage Polarization and Insulin Resistance.**

The Society for Vascular Medicine (SVM) 21st Annual Scientific Sessions & 6th Annual Comprehensive Vascular Review. April 28–May 2, 2010. Cleveland, Ohio.

CONFERENCE PRESENTATION

2015 **KLF4 Regulates Mitochondrial Homeostasis in the Heart.**

American Heart Association Scientific Sessions 2015, November 7-10, 2015. Orlando, Florida. Poster presentation.

2015 **KLF4 and Cardiac Mitochondrial Homeostasis.**

Keystone Symposia: Mitochondria, Metabolism and Heart Failure (J5) joint with the meeting on Diabetes and Metabolic Dysfunction (J6), January 27-Febuary 1, 2015. Santa Fe, New Mexico. Poster presentation.

2014 **Klf4 orchestrates myocardial metabolism and mitochondrial function.**

Keystone Symposia: Growth and Wasting in Heart and Skeletal Muscle. January 26–31, 2014. Santa Fe, New Mexico. Poster presentation.

2006 **Signal-dependent activation of NFκB by unphosphorylated STAT3.**

Keystone Symposia: NF-kappaB: 20 Years on the Road from Biochemistry to Pathology. March 23-28, 2006. Banff, Alberta, Canada. Poster presentation.

PUBLICATIONS

Complete List of Published Work in MyBibliography.

1. **Liao X**#, Shen Y, Zhang R, Sugi K, Vasudevan NT, Alaiti MA, Sweet DR, Zhou L, Qing Y, Gerson SL, Fu C, Wynshaw-Boris A, Hu R, Schwartz MA, Fujioka H, Richardson B, Cameron MJ, Hayashi H, Stamler JS, Jain MK#. Distinct roles of resident and non-resident macrophages in non-ischemic cardiomyopathy. PNAS April 30, 2018. 201720065; published ahead of print April 30, 2018. #Corresponding author.
2. Zhang R, Shen Y, Zhou L, Sangwung P, Fujioka H, Zhang L, **Liao X**#. Short-term administration of Nicotinamide Mononucleotide preserves cardiac mitochondrial homeostasis and prevents heart failure. Journal of molecular and cellular cardiology. 2017; 112:64-73. PubMed [journal] PMID: 28882480 #Corresponding author.
3. Hsieh PN, Zhou G, Yuan Y, Zhang R, Prosdocimo DA, Sangwung P, Borton AH, Boriushkin E, Hamik A, Fujioka H, Fealy CE, Kirwan JP, Peters M, Lu Y, **Liao X**, Ramírez-Bergeron D, Feng Z, Jain MK. A conserved KLF-autophagy pathway modulates nematode lifespan and mammalian age-associated vascular dysfunction. Nature communications. 2017; 8(1):914. PubMed [journal] PMID: 29030550, PMCID: PMC5640649
4. Sangwung P, Zhou G, Lu Y, **Liao X**, Wang B, Mutchler SM, Miller M, Chance MR, Straub AC, Jain MK. Regulation of endothelial hemoglobin alpha expression by Kruppel-like factors. Vascular medicine (London, England). 2017; 22(5):363-369. PubMed [journal] PMID: 28825355
5. Zhang L, Zhang R, Tien CL, Chan RE, Sugi K, Fu C, Griffin AC, Shen Y, Burris TP, **Liao X**, Jain MK. REV-ERBα ameliorates heart failure through transcription repression. JCI insight. 2017; 2(17). PubMed [journal] PMID: 28878135, PMCID: PMC5621902
6. Sangwung P, Zhou G, Nayak L, Chan ER, Kumar S, Kang DW, Zhang R, **Liao X**, Lu Y, Sugi K, Fujioka H, Shi H, Lapping SD, Ghosh CC, Higgins SJ, Parikh SM, Jo H, Jain MK. KLF2 and KLF4 control endothelial identity and vascular integrity. JCI insight. 2017; 2(4):e91700. PubMed [journal] PMID: 28239661, PMCID: PMC5313061

7. Shen Y, Hong H, Sangwung P, Lapping S, Nayak L, Zhang L, Jain MK[#], **Liao** X[#]. KLF4 Regulates Neutrophil Activation. Blood Advances. 2017, 1:662-668. PMID:29296708 [#]Corresponding author.

8. Chowdhury SK, Liu W, Zi M, Li Y, Wang S, Tsui H, Prehar S, Castro S, Zhang H, Ji Y, Zhang X, Xiao R, Zhang R, Lei M, Cyganek L, Guan K, Millar CB, **Liao X**, Jain MK, Boyett MR, Cartwright EJ, Shiels HA, Wang X. Stress-Activated Kinase Mitogen-Activated Kinase Kinase-7 Governs Epigenetics of Cardiac Repolarization for Arrhythmia Prevention. Circulation. 2017; 135(7):683-699. PubMed [journal] PMID: 27899394

9. Zhang L, Prosdocimo DA, Bai X, Fu C, Zhang R, Campbell F, **Liao X**, Coller J, Jain MK. KLF15 Establishes the Landscape of Diurnal Expression in the Heart. Cell reports. 2015; 13(11):2368-2375. PubMed [journal] PMID: 26686628

10. **Liao X**[#], Zhang R, Lu Y, Prosdocimo DA, Sangwung P, Zhang L, Zhou G, Anand P, Lai L, Leone TC, Fujioka H, Ye F, Rosca MG, Hoppel CL, Schulze PC, Abel ED, Stamler JS, Kelly DP, Jain MK[#]. Kruppel-like factor 4 is critical for transcriptional control of cardiac mitochondrial homeostasis. The Journal of clinical investigation. 2015; 125(9):3461-76. PubMed [journal] PMID: 26241060, PMCID: PMC4588311 [#]Corresponding author.

11. Han S, Zhang R, Jain R, Shi H, Zhang L, Zhou G, Sangwung P, Tugal D, Atkins GB, Prosdocimo DA, Lu Y, Han X, Tso P, **Liao X**, Epstein JA, Jain MK. Circadian control of bile acid synthesis by a KLF15-Fgf15 axis. Nature communications. 2015; 6:7231. NIHMSID: NIHMS683746 PubMed [journal] PMID: 26040986, PMCID: PMC4457302

12. Prosdocimo DA, John JE, Zhang L, Efraim ES, Zhang R, **Liao X**, Jain MK. KLF15 and PPARα Cooperate to Regulate Cardiomyocyte Lipid Gene Expression and Oxidation. PPAR research. 2015; 2015:201625. PubMed [journal] PMID: 25815008, PMCID: PMC4357137

13. Hale AT, Tian H, Anih E, Recio FO 3rd, Shatat MA, Johnson T, **Liao X**, Ramirez-Bergeron DL, Proweller A, Ishikawa M, Hamik A. Endothelial Kruppel-like factor 4 regulates angiogenesis and the Notch signaling pathway. The Journal of biological chemistry. 2014; 289(17):12016-28. PubMed [journal] PMID: 24599951, PMCID: PMC4002108

14. Prosdocimo DA, Anand P, **Liao X**, Zhu H, Shelkay S, Artero-Calderon P, Zhang L, Kirsh J, Moore D, Rosca MG, Vazquez E, Kerner J, Akat KM, Williams Z, Zhao J, Fujioka H, Tuschl T, Bai X, Schulze PC, Hoppel CL, Jain MK, Haldar SM. Kruppel-like factor 15 is a critical regulator of cardiac lipid metabolism. The Journal of biological chemistry. 2014; 289(9):5914-24. PubMed [journal] PMID: 24407292, PMCID: PMC3937660

15. Lu Y, Zhang L, **Liao X**, Sangwung P, Prosdocimo DA, Zhou G, Votruba AR, Brian L, Han YJ, Gao H, Wang Y, Shimizu K, Weinert-Stein K, Khrestian M, Simon DI, Freedman NJ, Jain MK. Kruppel-like factor 15 is critical for vascular inflammation. The Journal of clinical investigation. 2013; 123(10):4232-41. PubMed [journal] PMID: 23999430, PMCID: PMC3785338

16. Tugal D, **Liao X**, Jain MK. Transcriptional control of macrophage polarization. Arteriosclerosis, thrombosis, and vascular biology. 2013; 33(6):1135-44. PubMed [journal] PMID: 23640482

17. Zhou G, Hamik A, Nayak L, Tian H, Shi H, Lu Y, Sharma N, **Liao X**, Hale A, Boerboom L, Feaver RE, Gao H, Desai A, Schmaier A, Gerson SL, Wang Y, Atkins GB, Blackman BR, Simon DI, Jain MK. Endothelial Kruppel-like factor 4 protects against atherothrombosis in mice. The Journal of clinical investigation. 2012; 122(12):4727-31. PubMed [journal] PMID: 23160196, PMCID: PMC3533563

18. Sharma N, Lu Y, Zhou G, **Liao X**, Kapil P, Anand P, Mahabeleshwar GH, Stamler JS, Jain MK. Myeloid Krüppel-like factor 4 deficiency augments atherogenesis in ApoE-/- mice--brief report. Arteriosclerosis, thrombosis, and vascular biology. 2012; 32(12):2836-8. NIHMSID: NIHMS419335 PubMed [journal] PMID: 23065827, PMCID: PMC3574634

19. **Liao X**, Sharma N, Kapadia F, Zhou G, Lu Y, Hong H, Paruchuri K, Mahabeleshwar GH, Dalmas E, Venteclef N, Flask CA, Kim J, Doreian BW, Lu KQ, Kaestner KH, Hamik A, Clément K, Jain MK.

Krüppel-like factor 4 regulates macrophage polarization. The Journal of clinical investigation. 2011; 121(7):2736-49. PubMed [journal] PMID: 21670502, PMCID: PMC3223832

20. **Liao X**, Haldar SM, Lu Y, Jeyaraj D, Paruchuri K, Nahori M, Cui Y, Kaestner KH, Jain MK. Krüppel-like factor 4 regulates pressure-induced cardiac hypertrophy. Journal of molecular and cellular cardiology. 2010; 49(2):334-8. NIHMSID: NIHMS201597 PubMed [journal] PMID: 20433848, PMCID: PMC2885477
21. Wang FZ, Weber F, Croce C, Liu CG, **Liao X**, Pellett PE. Human cytomegalovirus infection alters the expression of cellular microRNA species that affect its replication. Journal of virology. 2008; 82(18):9065-74. PubMed [journal] PMID: 18596100, PMCID: PMC2546905
22. Wang W, **Liao X**, Fukuda K, Knappe S, Wu F, Dries DL, Qin J, Wu Q. Corin variant associated with hypertension and cardiac hypertrophy exhibits impaired zymogen activation and natriuretic peptide processing activity. Circulation research. 2008; 103(5):502-8. NIHMSID: NIHMS94934 PubMed [journal] PMID: 18669922, PMCID: PMC2652846
23. **Liao X**, Wang W, Chen S, Wu Q. Role of glycosylation in corin zymogen activation. The Journal of biological chemistry. 2007; 282(38):27728-35. PubMed [journal] PMID: 17660514
24. Yang J, **Liao X**, Agarwal MK, Barnes L, Auron PE, Stark GR. Unphosphorylated STAT3 accumulates in response to IL-6 and activates transcription by binding to NFkappaB. Genes & development. 2007; 21(11):1396-408. PubMed [journal] PMID: 17510282, PMCID: PMC1877751
25. Lei X, Chen Y, Du G, Yu W, Wang X, Qu H, Xia B, He H, Mao J, Zong W, **Liao X**, Mehrpour M, Hao X, Chen Q. Gossypol induces Bax/Bak-independent activation of apoptosis and cytochrome c release via a conformational change in Bcl-2. FASEB journal : official publication of the Federation of American Societies for Experimental Biology. 2006; 20(12):2147-9. PubMed [journal] PMID: 16935937
26. **Liao X**, Liu JM, Du L, Tang A, Shang Y, Wang SQ, Chen LY, Chen Q. Nitric oxide signaling in stretch-induced apoptosis of neonatal rat cardiomyocytes. FASEB journal : official publication of the Federation of American Societies for Experimental Biology. 2006; 20(11):1883-5. PubMed [journal] PMID: 16877524
27. **Liao X**, Wang X, Gu Y, Chen Q, Chen LY. Involvement of death receptor signaling in mechanical stretch-induced cardiomyocyte apoptosis. Life sciences. 2005; 77(2):160-74. PubMed [journal] PMID: 15862601
28. Sun Y, Zhou J, **Liao X**, Lü Y, Deng C, Huang P, Chen Q, Yang X. Disruption of Smad5 gene induces mitochondria-dependent apoptosis in cardiomyocytes. Experimental cell research. 2005; 306(1):85-93. PubMed [journal] PMID: 15878335
29. **Liao XD**, Wang XH, Jin HJ, Chen LY, Chen Q. Mechanical stretch induces mitochondria-dependent apoptosis in neonatal rat cardiomyocytes and G2/M accumulation in cardiac fibroblasts. Cell research. 2004; 14(1):16-26. PubMed [journal] PMID: 15040886
30. Liu XW, **Liao XD**, Cong XF. The effects of homoeysteine on HUVECs apoptosis. Chinese Journal of Pathophysiology. 2004, 20(12):2185-2188.
31. **Liao XD**, Tang AH, Chen Q, Jin HJ, Wu CH, Chen LY, Wang SQ. Role of Ca2+ signaling in initiation of stretch-induced apoptosis in neonatal heart cells. Biochemical and biophysical research communications. 2003; 310(2):405-11. PubMed [journal] PMID: 14521925
32. Ji R, Zhang J, Wang SW, **Liao XD**, Chen LY. D-galactose induces replicative senescence of rat pulmonary microvascular endothelial cells. Chinese Science Bulletin (2003);48(6):575-581.
33. Lei XY, **Liao XD**, Zhang GY, Dai YR. Flow cytometric evidence for hydroxyl radical-induced apoptosis in tobacco protoplasts. ACTA BOTANICA SINICA 45 (8): 944-948 AUG 2003.
34. **Liao X** and Chen LY. TPO and its receptor c-MPL. Foreign Medical Sciences (Section Of Blood Transfusion And Hematology) (2000); 23(6):286-289. (Review in Chinese)