BIOGRAPHICAL SKETCH

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NAME: JIANG TIAN

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

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
Nanjing University, Nanjing, China	B.A	07/1988	Physiology
Chinese Academy of Preventive Medicine, Beijing, China	M.S	09/1991	Nutrition and Toxicology
University of Toledo, Toledo, Ohio	Ph. D	12/2006	Molecular Basis of Disease

A. Personal Statement

I am an Associate Professor in the Department of Biomedical Science at Joan C. Edward School of Medicine, Marshall University. My research focuses on the pathology of uremic cardiomyopathy. My laboratory uses partial nephrectomy (PNx), myocardial infarction (MI), transverse aortic constriction (TAC) animal models, as well as cell culture system to study the role of Na/K-ATPase in cardiac hypertrophy, fibrosis, apoptosis, and regeneration. I have been funded by NIH and AHA for related research with over 50 publications.

Na/K-ATPase is an important membrane protein that maintains cell ion homeostasis and regulates multiple signaling pathways. Reduction of Na/K-ATPase has been found in patients with heart failure and other chronic diseases. Our work demonstrated that reducing Na/K-ATPase α1 causes cardiac cell death, reduces cardiac hypertrophy, and decompensates muscle contraction in animal models of cardiomyopathy. We further demonstrated that mitochondria-related signaling pathways mediated the cardiac cell apoptosis induced by Na/K-ATPase reduction. In addition, we discovered that Na/K-ATPase-related Src and NFκB signaling pathways regulates miR-29b expression in cardiac tissue and cardiac fibroblasts, which contribute to the formation of tissue fibrosis. During the past decade, our laboratory has developed novel tools to interfere with Na/K-ATPase expression and its signaling functions. In collaboration with Dr. Zijian Xie and Dr. Shapiro's lab, we invented and demonstrated a novel peptide (pNaKtide) that can block Na/K-ATPase signaling and reduces cardiac fibrosis and hypertrophy in animal models of chronic kidney disease. We also established special vectors that can selectively express anti-fibrotic molecules in cells that have excessive collagen expression, which a useful research tool for tissue fibrosis.

My laboratory offers various opportunities for undergraduate, graduate, and medical students to receive training and conduct biomedical research. I have been a major advisor for several PhD and MD/PhD students and served as a thesis committee member for over 15 graduate students. I also successfully sponsored a postdoctoral fellow funded by a NIH F32 fellowship. One of my PhD students won the Biomedical Sciences Program Outstanding Student for 2019 Graduation Awards at the University of Toledo. I am currently sponsoring an undergraduate student at Marshall University who just received a Fellowship from NASA West Virginia Space Grant Consortium to perform biomedical research in my laboratory.

List of publications that mostly related with current project:

1. Drummond CA, Fan X, Haller ST, Kennedy DJ, Liu J, Tian J. Na/K-ATPase signaling mediates miR-29b-3p regulation and cardiac fibrosis formation in mice with chronic kidney disease. ***PLoS One***.

2018;13(5):e0197688. PubMed PMID: 29775473; PMCID: PMC5959191

2. Drummond CA, Hill MC, Shi H, Fan X, Xie JX, Haller ST, Kennedy DJ, Liu J, Garrett MR, Xie Z, Cooper CJ, Shapiro JI, Tian J. Na/K-ATPase signaling regulates collagen synthesis through microRNA-29b-3p in cardiac fibroblasts. *Physiological genomics*. **2016**; 48(3):220-9. PubMed PMID: 26702050; PMCID: PMC4773889.
3. Drummond CA, Sayed M, Evans KL, Shi H, Wang X, Haller ST, Liu J, Cooper CJ, Xie Z, Shapiro JI, Tian J. Reduction of Na/K-ATPase affects cardiac remodeling and increases c-kit cell abundance in partial nephrectomized mice. *Am J Physiol Heart Circ Physiol*. **2014**;306(12):H1631-43. PubMed PMID: 24748592; PMCID: PMC4059984.
4. Liu C, Bai Y, Chen Y, Wang Y, Sottejeau Y, Liu L, Li X, Lingrel JB, Malhotra D, Cooper CJ, Shapiro JI, Xie ZJ, Tian J. Reduction of Na/K-ATPase potentiates marinobufagenin-induced cardiac dysfunction and myocyte apoptosis. *The Journal of biological chemistry*. **2012**;287(20):16390-8. PubMed PMID: 22451662; PMCID: 3351339.

B. Positions and Honors

Positions:

1991- 1998 Doctor of Public Health, Analysis Center of Sanitation & Anti-Epidemic Station of Ningxia, Yinchuan, China
1998- 2006 Research Assistant, Department of Pharmacology, University of Toledo, Toledo, OH.
2006- 2007 Post-Doc Fellow, Department of Pharmacology, University of Toledo, Toledo, OH
2007- 2012 Assistant Professor (research track), University of Toledo, Department of Medicine, Toledo, OH.
2012- 2015 Assistant Professor (tenure track), University of Toledo, Department of Medicine, Toledo, OH.
2015- 2020 Associate Professor, University of Toledo, Department of Medicine, Toledo, OH.
2020- Associate Professor, Marshall University, Biomedical Sciences Department/MIIR, Huntington, WV.

Other Experience and Professional Services and Memberships

- Internet Assisted Guest Reviewer for NIH RC1 grants (2009)
- Invited grant reviewer for British Heart Association (2017)
- Invited grant reviewer for Wellcome Trust (2018, 2019)

2016-2017 Faculty Senator at the University of Toledo
2016-2018 Member of Admission committee on Molecular Medicine Track at University of Toledo.
2018-2020 Member of the Institutional Animal Care and Use Committee (IACUC) at University of Toledo
2013-2019 Member of American Physiology Society (APS)
2012-present Professional Member of American Heart Association (AHA)

C. Contributions to Science

Demonstrated the role of Na/K-ATPase reduction on cardiac apoptosis and regeneration. We demonstrated that change in cellular Na/K-ATPase expression level significantly alters the course of how cardiotonic steroids (CTS) exerts effect on these cells. We have shown that reduction of Na/K-ATPase could potentiate CTS- and PNx-induced cardiac cell apoptosis through activation of caspase 9 and caspase 3. In addition, Na/K-ATPase is involved in the regulation of stem/progenitor cell signaling and function. We found that PNx increase c-kit positive progenitor cell expression in cardiac tissue, especially in the Na/K-ATPase reduced animals. We also demonstrated that Na/K-ATPase signaling potentiates bone marrow mesenchymal stromal cell adipogenesis. Na/K-ATPase is essential to cell survival, while reduction of Na/K-ATPase has been documented in patients and experimental animals with congestive heart failure, aging, diabetes with hypertension, and neurological disorders. In heart tissue biopsies from patients with dilated cardiomyopathy, Na/K-ATPase amount is decreased by up to 40%. Reduction of cardiac Na/K-ATPase is also connected to decreased cardiac contractile function in humans and in animals. Our recent work revealed novel tools to potentially fight against Na/K-ATPase reduction and cardiac cell apoptosis, including the discovery of an endogenous natural antisense RNA of Na/K-ATPase α1 subunit and a novel c-kit related mechanism for progenitor cell activation.

1. Shi H, Drummond CA, Fan X, Haller ST, Liu J, Malhotra D, Tian J. Hiding inside? Intracellular expression of non-glycosylated c-kit protein in cardiac progenitor cells. ***Stem cell research***. 2016;16:795-806. PubMed PMID: 27161312; PubMed Central PMCID: PMC4903953.
2. Drummond CA, Sayed M, Evans KL, Shi H, Wang X, Haller ST, Liu J, Cooper CJ, Xie Z, Shapiro JI, Tian J. Reduction of Na/K-ATPase affects Cardiac Remodeling and Increases c-kit cell abundance in Partial

Nephrectomized Mice. ***Am J Physiol Heart Circ Physiol***. 2014. Epub 2014/04/22. PubMed PMID: 24748592; Central PMCID: PMC4059984.
3. Liu C, Bai Y, Chen Y, Wang Y, Sottejeau Y, Liu L, Li X, Lingrel JB, Malhotra D, Cooper CJ, Shapiro JI, Xie ZJ, Tian J. Reduction of Na/K-ATPase potentiates marinobufagenin-induced cardiac dysfunction and myocyte apoptosis. ***The Journal of biological chemistry***. 2012;287(20):16390-8. Epub 2012/03/28. PubMed PMID: 22451662; PMCID: 3351339.
4. Sayed M, Drummond CA, Evans KL, Haller ST, Liu J, Xie Z, Tian J. Effects of Na/K-ATPase and its ligands on bone marrow stromal cell differentiation. ***Stem cell research***. 2014;13(1):12-23. Epub 2014/05/06. PubMed PMID: 24793006; PMCID: PMC4090276.

Demonstration of Na/K-ATPase/Src complex and its signaling function: My early work during PhD and postdoctoral training in Dr. Zijian Xie's laboratory has demonstrated that Na/K-ATPase can work as a signal-transducing receptor in addition to its canonic function as an ion pump. We have demonstrated that Na/K-ATPase directly interacts with Src and forms a receptor-like complex. The interaction involves multiple domains from both proteins, specifically, the SH2 domain of Src associates with the CD2 domain of Na/K-ATPase while the Src kinase domain binds with the CD3 domain of Na/K-ATPase. Binding of cardiotonic steroids (CTS) such as ouabain to Na/K-ATPase dissociates the Src kinase domain from Na/K-ATPase and thus causes Src activation. In addition, identification of the Na/K-ATPase/Src interaction domains led to our discovery of a 20-amino acid peptide (called pNaKtide) that can effectively inhibit Src activity, which became an important tool specifically regulating Na/K-ATPase signaling functions. This peptide has been granted the patent in US, in which I am a co-inventor.

1. Tian J, Cai T, Yuan Z, Wang H, Liu L, Haas M, Maksimova E, Huang XY, Xie ZJ. Binding of Src to Na+/K+-ATPase forms a functional signaling complex. ***Molecular biology of the cell***. 2006;17(1):317-26. Epub 2005/11/04. doi: 10.1091/mbc.E05-08-0735. PubMed PMID: 16267270; PMCID: 1345669.
2. Liang M, Cai T, Tian J, Qu W, Xie ZJ. Functional characterization of Src-interacting Na/K-ATPase using RNA interference assay. ***The Journal of biological chemistry.*** 2006;281(28):19709-19. PubMed PMID: 16698801.
3. Li Z, Cai T, Tian J, Xie JX, Zhao X, Liu L, Shapiro JI, Xie Z. NaKtide, a Na/K-ATPase-derived peptide Src inhibitor, antagonizes ouabain-activated signal transduction in cultured cells. ***The Journal of biological chemistry***. 2009;284(31):21066-76. Epub 2009/06/10. doi: 10.1074/jbc.M109.013821. PubMed PMID: 19506077; PMCID: 2742871.
4. Li Z, Zhang Z, Xie JX, Li X, Tian J, Cai T, Cui H, Ding H, Shapiro JI, Xie Z. Na/K-ATPase mimetic pNaKtide peptide inhibits the growth of human cancer cells. ***The Journal of biological chemistry.*** 2011;286(37):32394-403. Epub 2011/07/26. doi: 10.1074/jbc.M110.207597. PubMed PMID: 21784855; PMCID: 3173162.

Established the link of Src/NFκB/miR-29b signaling and cardiac fibrosis. We have shown that PNx induces cardiac hypertrophy and fibrosis through activation of Src/NFκB signaling pathway, which downregulates the microRNA-29b-3p (miR-29b-3p) and increases the collagen synthesis in cardiac fibroblast and in cardiac tissue. A novel peptide, pNaKtide, was developed together with our collaborators to inhibit this signaling pathway to reverse the expression level of miR-29b-3p, and reduces fibrosis and hypertrophy in cardiac tissue.

1. Drummond CA, Fan X, Haller ST, Kennedy DJ, Liu J, **Tian J**. Na/K-ATPase signaling mediates miR-29b-3p regulation and cardiac fibrosis formation in mice with chronic kidney disease. ***PLoS One***. **2018**;13(5):e0197688. Epub 2018/05/19. doi: 10.1371/journal.pone.0197688. PubMed PMID: 29775473; PMCID: PMC5959191.
2. Xie JX, Fan X, Drummond CA, Majumder R, Xie Y, Chen T, Liu L, Haller ST, Brewster PS, Dworkin LD, Cooper CJ, **Tian J**. MicroRNA profiling in kidney disease: Plasma versus plasma-derived exosomes. ***Gene***. **2017**;627:1-8. Epub 2017/06/08. doi: 10.1016/j.gene.2017.06.003. PubMed PMID: 28587849; PMCID: PMC5534180.
3. Drummond CA, Hill MC, Shi H, Fan X, Xie JX, Haller ST, Kennedy DJ, Liu J, Garrett MR, Xie Z, Cooper CJ, Shapiro JI, Tian J. Na/K-ATPase signaling regulates collagen synthesis through microRNA-29b-3p in cardiac fibroblasts. ***Physiological genomics***. 2016; 48(3):220-9. PubMed PMID: 26702050; PMCID: PMC4773889.
4. Tian J, Shidyak A, Periyasamy SM, Haller S, Taleb M, El-Okdi N, Elkareh J, Gupta S, Gohara S, Fedorova OV, Cooper CJ, Xie Z, Malhotra D, Bagrov AY, Shapiro JI. Spironolactone attenuates experimental uremic cardiomyopathy by antagonizing marinobufagenin. ***Hypertension.*** 2009;54(6):1313-20. Epub 2009/11/04.

PubMed PMID: 19884563; PMCID: 2783263.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/16QDvygXfLzku/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH R01, HL-137004 (PI: David Kennedy) 04/01/2017 – 03/31/2022
Counter Regulatory Mechanisms of Cardiotonic Steroids in Cardio-Renal Syndrome
Role: Co-investigator (10% effort)

WV- NASA (PI, Jiang Tian) 05/16/2020 - 05/15/2021
Preserving Na/K-ATPhase as a Protection of Heart Function Following Myocardial Infraction (MI)
Role: PI, Mentor of Marshall Undergraduate student Dominic Collins

Completed Research support

Biomedical Research Innovation Program from University of Toledo, (PI). 05/01/2019-06/30/2020

R01 HL105649 Tian (PI) (including two year no-cost extension) 12/15/2011-11/30/2018
NIH/NHLBI
Na/K-ATPase Reduction in Renal Disease-Related Cardiac Dysfunction
The overall goal of this project is to test the hypothesis that in renal insufficiency reduction of Na/K-ATPase and sustained increase of cardiotonic steroids may cause cardiac cell death and heart chamber dilation. It will also test the role of signaling Na/K-ATPase complex in this process.
Role: PI

R01 HL109015 Xie & Shapiro (PI) 6/1/2011 to 5/31/2015
NIH/NHLBI
Receptor Na/K-ATPase Antagonists as Novel Therapeutics for Renal/Cardiac Diseases
The major goal of this project is to provide proof of the concept that the newly identified antagonists of the receptor Na/K-ATPase could be used to reduce cardiac remodeling *in vivo*.
Role: Co-investigator

AHA NCRP Clinical Research Program 098027N Tian (PI) 01/01/2009 to 12/31/2010
Endogenous Cardiotonic Steroids, A New Risk Factor of Adverse Cardiac Events in Patients With Renal Artery Stenosis.
The goal of this project is to test if renal ischemia induces elevation of endogenous cardiotonic steroids and the association with cardiac fibrosis in patients with renal artery stenosis.
Role: PI

Funding from Nerium Biotech Inc. Tian (PI) 11/1/2012 to 04/30/2013
Cosmetic products in collagen Synthesis
The goal of this project is to test the effect of a product in regulating collagen synthesis in fibroblasts.
Role: PI