

BIOGRAPHICAL SKETCH

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NAME: Yan, Yanling

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

POSITION TITLE: Assistant Professor of Clinical & Translational Sciences

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
Harbin Medical University, Harbin, China	M.D.	06/1991	Clinical Medicine
Liaoning Medical University, Jinzhou, China	M.S.	06/2004	Intenal Medicine (Cardiovascular Diseases)
University of Toledo Health Science Campus, Toledo	Ph.D	08/2012	Biomedical Science
Marshall University, JCE School of Medicine, Huntington	Postdoctoral	06/2015	Biomedical Science

A. Personal Statement

I have a broad background in clinical medicine (especially in cardiovascular diseases) and biomedical science, with specific training and expertise in the field of renal sodium (Na) handling and blood pressure regulation for this COBRE application. My experience as a physician together with my teaching experience provides me with a marvelous grasp of the underlying science as well as the clinical implications of my research work. I also realize the significance of translating from bench to bed. During my Ph.D work at UT, I described: (1) impairment of Na/K-ATPase signaling contributes to salt-sensitive hypertension in experimental Dahl salt-sensitive rats; and (2) how reactive oxygen species are involved in Na/K-ATPase signaling-mediated renal proximal tubular Na transport. During Posdoctoral training at Marshall, I demonstrated that the mutation of Pro222 of $\alpha 1$ Na/K-ATPase attenuates Na/K-ATPase signaling and prevents ouabain-inhibited sodium transport in renal proximal tubular cells. I produced 12 peer-reviewed publications from the above work. Now as an independent faculty member I have been extending the above project and building on adequate preliminary data for this proposal. In addition, I also laid the groundwork for the proposed research by developing the effective measures of oxidative stress, Na/K-ATPase signaling molecules, and other endosomal protein levels relevant to the renal Na handling, and by identifying (1) cardiotoxic steroids as an amplifier for reactive oxygen species through Na/K-ATPase signaling, including c-Src and ERK1/2; and (2) adaptation to a high salt or high fat diet is associated with marked increases in the carbonylation of intracellular proteins, and more specifically, that cardiotoxic steroids mediated signaling induces what appears to be widespread reversible carbonylation in proximal tubular cells. The current application builds logically on my prior work. Moreover, we work closely with Dr. Zijian Xie's group which has spearheaded the delineation of a signaling pool of Na/K-ATPase. Collaborating with Drs. Joseph I. Shapiro and Jiang Liu, we reported that the enzyme acts as an important signal transducer in renal epithelial cells, and that signal transduction through this system is important in proximal tubular Na handling. Therefore, an excellent scientific milieu has formed at Marshall specifically to study Na/K-ATPase signaling. In summary, I have demonstrated a record of accomplished and productive research projects in an area of high clinical relevance for obesity and hypertension patients, and my expertise and experience have prepared me to lead

the proposed project. I believe I can successfully perform all the studies in this application under the guidance of my mentor Dr. Gary Rankin. The support of COBRE will shape my development as a critical investigator.

1. Jiang Liu, **Yanling Yan**, Zijian Xie, Deepak Malhotra, Bina Joe and Joseph I Shapiro. Impairment of Na/K-ATPase signaling in renal proximal tubule contributes to Dahl salt-sensitive hypertension. *Journal of Biological Chemistry*, 2011, 286(26): 22806-13. PMID: PMC3123048
2. **Yanling Yan**, Steven Haller, Anna Shapiro, Nathan Malhotra, Jiang Tian, Zijian Xie, Deepak Malhotra, Joseph I. Shapiro and Jiang Liu. Ouabain-stimulated trafficking regulation of the Na/K-ATPase and NHE3 in renal proximal tubule cells. *Molecular and Cellular Biochemistry*, 2012, 367: 175-183. PMID: PMC3475650
3. **Yanling Yan**, Anna P. Shapiro, Steven Haller, Vinai Katragadda, Lijun Liu, Jiang Tian, Venkatesha Basrur, Deepak Malhotra, Zi-jian Xie, Nader G. Abraham, Joseph I. Shapiro, and Jiang Liu. The involvement of reactive oxygen species in a feed-forward mechanism of Na/K-ATPase mediated signaling transduction. *Journal of Biological Chemistry*, 2013, 288: 34249-34258. PMID: PMC3837165
4. Sodhi K, Maxwell K, **Yan Y**, Liu J, Chaudhry MA, Getty M, Xie Z, Abraham NG, Shapiro JI: pNaKtide inhibits Na/K-ATPase reactive oxygen species amplification and attenuates adipogenesis. *Science Advances* 2015, 1(9):e1500781. PMID: PMC4646828

B. Positions and Honors

Positions and Employment

- 1991-1997 Physician, The First Affiliated Hospital of Qiqihar Medical University (Former the First Heavy Mechanical Group Corporation Hospita), Qiqihar, China
- 1997-2001 Assistant Professor, Qinhuangdao Health School, Qinhuangdao, China
- 2004-2005 Assistant Professor, Yanshan University, Qinhuangdao, China
- 2005-2008 Associate Professor, Yanshan University, Qinhuangdao, China
- 2015- Assistant Professor, Marshall University, JCE School of Medicine, Huntington, WV

Other Experience and Professional Memberships

- 2007-2009 Peer reviewer, *Journal of Electrocardiology*
- 2011-2012 Member, Association for Women in Science
- 2012-2013 Member, American Heart Association
- 2013-2014 Member, American Physiology Society
- 2014- Member, American Society of Nephrology

Honors

- 2000 Excellence in Teaching, Qinhuangdao Health School, China
- 2001 Excellent Teacher, Board of Health of Qinhuangdao, China
- 2007 Excellence in Teaching, Yanshan University, China
- 2008 The University of Toledo Sister Cities Scholarship for Excellent Faculty in Qinhuangdao City, China
- 2013 Poster Finalist and Winner, JCE School of Medicine, Marshall University, Huntington, WV

C. Contribution to Science

1. My publications have described a novel regulating mechanism in which endogenous cardiotonic steroids through the Na/K-ATPase/Src/reactive oxygen species (ROS) cascades, induce the endocytosis of basolateral Na/K-ATPase and redistribution of apical Na proton exchanger 3 (NHE3, responsible for maintaining the balance of sodium and water) in the renal proximal tubule. These changes lead to decreases in transcellular Na transport and a net increase in urinary Na excretion. These publications document this regulating process is impaired in the Dahl salt-sensitive rat. This body of work will provide proof-of-principle for the notion that the Na/K-ATPase/Src/ROS signaling is not only responsible for renal Na handling and blood pressure regulation, but also can be manipulated with molecular or pharmacologic strategies, leading to new targets for interventions in hypertension.

- a. Jiang Liu, **Yanling Yan**, Zijian Xie, Deepak Malhotra, Bina Joe and Joseph I Shapiro. Impairment of Na/K-ATPase signaling in renal proximal tubule contributes to Dahl salt-sensitive hypertension. *Journal of Biological Chemistry*, 2011, 286(26): 22806-13. PMID: PMC3123048
 - b. **Yanling Yan**, Steven Haller, Anna Shapiro, Nathan Malhotra, Jiang Tian, Zijian Xie, Deepak Malhotra, Joseph I. Shapiro and Jiang Liu. Ouabain-stimulated trafficking regulation of the Na/K-ATPase and NHE3 in renal proximal tubule cells. *Molecular and Cellular Biochemistry*, 2012, 367: 175-183. PMID: PMC3475650
 - c. **Yanling Yan**, Anna P. Shapiro, Steven Haller, Vinai Katragadda, Lijun Liu, Jiang Tian, Venkatesha Basrur, Deepak Malhotra, Zi-jian Xie, Nader G. Abraham, Joseph I. Shapiro, and Jiang Liu. The involvement of reactive oxygen species in a feed-forward mechanism of Na/K-ATPase mediated signaling transduction. *Journal of Biological Chemistry*, 2013, 288: 34249-34258. PMID: PMC3837165
 - d. Sodhi K, Maxwell K, **Yan Y**, Liu J, Chaudhry MA, Getty M, Xie Z, Abraham NG, Shapiro JI: pNaKtide inhibits Na/K-ATPase reactive oxygen species amplification and attenuates adipogenesis. *Science Advances* 2015, 1(9):e1500781. PMID: PMC4646828
2. In addition to the contributions described above, I am also active in collaborative research. Our laboratory has demonstrated that sustained increases in the circulating concentrations of cardiotoxic steroids cause fibrosis of several organs, notably heart and kidney. Thus, it appears that there is a trade-off whereby increases in cardiotoxic steroids allow one to maintain Na homeostasis on a high salt diet or in the presence of chronic kidney disease, but the sustained elevations appear to cause fibrosis of the heart and kidney. This body of work will address this pathway and could ultimately be translated into a clinical therapy.
- a. Jiang Liu, David J. Kennedy, **Yanling Yan**, Joseph I. Shapiro. Reactive Oxygen Species Modulation of Na/K-ATPase Regulates Fibrosis and Renal Proximal Tubular Sodium Handling. *International Journal of Nephrology*, 2012: 381320. PMID: PMC3299271
 - b. Christopher A Drummond, George Buddny, Steven T Haller, Jiang Liu, **Yanling Yan**, Zi-jian Xie, Deepak Malhotra, Joseph I Shapiro, Jiang Tian. Gender differences in the development of uremic cardiomyopathy following partial nephrectomy: Role of progesterone. *Journal of Hypertension*, 2013, 2: 109. PMID: PMC3880896
 - c. Steven T Haller, Christopher A Drummond, **Yanling Yan**, Jiang Liu, Jiang Tian, Deepak Malhotra, Joseph I Shapiro. Passive immunization against marinobufagenin attenuates renal fibrosis and improves renal function in experimental renal disease. *American Journal of Hypertension*, 2013, 27(4): 603-609. PMID: PMC3958603

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1TiTu7Bw5qAD/bibliography/48531405/public/?sort=date&direction=ascending>

D. Research Support
None