BIOGRAPHICAL SKETCH

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NAME: Shapiro, Joseph I

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POSITION TITLE: Dean

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
University of Pennsylvania, Philadelphia, PA	B.A.	12/1976	Mathematics
UMDNJ-Rutgers College of Medicine, Newark, NJ	M.D.	12/1980	Medicine
Georgetown University Hospital IM		12/1983	Internal Medicine
University of Colorado IM/Nephrology		12/1987	Nephrology

A. Personal Statement

I have been an active clinical-translational scientist for the past 3 ½ decades. My clinical training has been in Nephrology, and my work has primarily addressed basic and clinical research relevant to this specialty. During these pursuits, my primary focus has been researching the effects of renal failure on the cardiovascular system. To this end, we have formulated a collaborative group formed by Dr. Zijian Xie and myself which includes Drs. Roy Silverstein, Yiliang Chen, David Kennedy, Jiang Tian, Steve Haller, Gustavo Blanco, Jiang Liu, Nader Abraham, Chris Cooper, Komal Sodhi and others who are well established researchers in their respective fields. This group has been effective at obtaining peer-reviewed grant support and publishing high impact papers. Although I am a Medical School Dean, I do manage to devote approximately 25% of my time to basic and clinical research as evidenced by my continued productivity. My research interests range from basic and translational science where I have studied the role of the NaK-ATPase oxidant amplification loop in the pathogenesis of different diseases. This proposed project is a application of the basic signaling work to focus on liver disease. I am very pleased to work with Dr. Silverstein who is an internationally known investigator with long standing interest in atherosclerosis. I have collaborated with Dr. Silverstein before, and I proud to say that I have co-mentored the aforementioned Dr. David Kennedy with him who has developed his own independent funding.

Following is the list of four most relevant papers to this study:

a. Kennedy, DJ, Y Chen, W Huang, J Viterna, J Liu, K Westall, J Tian, DJ Bartlett, WHW Tang, Z Xie, JI Shapiro and RL Silverstein. 2013. CD36 and Na/K-ATPase-alpha1 form pro-inflammatory signaling loop in kidney. Hypertension. 61:216-24. PMID: 23172921.
b. Sodhi, K, K Maxwell, Y Yan, J Liu, MA Chaudhry, M Getty, Z Xie, NG Abraham and JI Shapiro. 2015. pNaKtide inhibits Na/K-ATPase reactive oxygen species amplification and attenuates adipogenesis. Science Advances. 1:e1500781. PMID: 26601314.
c. Sodhi, K, A Nichols, A Mallick, X Wang, RL Klug, J Liu, K Srikanthan, P Goguet-Rubio, A Nawab, R Pratt, ML Lilly, JR Sanabria, Z Xie, NG Abraham and JI Shapiro. Sci. Rep. The Na/K-ATPase oxidant amplification loop regulates aging. Jun 26;8(1):9721. doi: 10.1038/s41598-018-26768-9. PMID: 29946187.
d. Chen Y, Yang M, Huang W, Chen W, Zhao Y, Schulte ML, Volberding PJ, Gerbec Z, Zimmermann MT, Zeighami A, Demos W, Zhang J, Knaack DA, Smith BC, Cui W, Malarkannan S, Sodhi K, Shapiro JI, Xie Z, Sahoo D, Silverstein RL. Mitochondrial Metabolic Reprogramming by CD36 Signaling Drives

Macrophage Inflammatory Responses. Circ Res. 2019 Oct 18. doi: 10.1161/CIRCRESAHA.119.315833. [Epub ahead of print] PubMed PMID: 31625810.

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B. Positions and Honors

Positions and Employment

1986-1991	University of Colorado: Director, Chronic Dialysis Service
1986-1987	University of Colorado: Instructor in Medicine
1987-1993	University of Colorado: Assistant Professor of Medicine
1989-1995	University of Colorado: Co-Director NMR Spectroscopy
1989-1997	University of Colorado: Co-Director Renal Transplant Physicians
1989-1993	University of Colorado: Assistant Professor of Radiology
1992-1997	Denver University: Adjunct Professor of Physics
1993-1997	University of Colorado: Associate Professor of Medicine
1993-1997	University of Colorado: Associate Professor of Radiology
1995-1997	Denver VAMC: Director, Renal Transplant Service
1996-1997	Denver VAMC: Section Head, Renal Diseases

University of Toledo (formerly Medical College of Ohio at Toledo):

1997-2012	Professor of Medicine & Physiology/Pharmacology
1997-1999	University of Toledo: Renal Division Head
1999-1999	University of Toledo: Interim Chairman of Medicine
1999-2012	University of Toledo: Chairman of Medicine
2004-2005	University of Toledo: Interim Chairman of Physiology
2006-2012	University of Toledo: Associate Dean for Business Development
2011-2012	University of Toledo Physicians, President
2012-present	Marshall University: Dean, College of Medicine
2012-present	Marshall University: Professor of Medicine

Honors

1974	Pi Mu Epsilon (Mathematics honor society)
1976	Graduated University of Pa. Magna cum Laude with distinction in Mathematics
1980	University of Medicine and Dentistry of New Jersey: Alpha Omega Alpha
1983	Georgetown University: Dudley P. Jackson Award
1985-87	Fellowship award
1988-92	American Heart Clinician-Scientist Award
1992-97	American Heart Association Established-Investigator Award
1992	Western Society for Clinical Investigation
1998	Medical College of Ohio Internal Medicine Faculty Teaching Award
2000	Central Society for Clinical Investigation
1999	American Society of Nephrology Chairman, Dialysis Hemodynamics Abstract Selection Committee.
2001	American Heart Association – Hypertension Fellow
2001	American Heart Association – Kidney Disease Fellow
2001	Fellow of the American College of Physicians
2002	Arnold P. Gold – Healthcare Foundation of New Jersey Humanism in Medicine Award
2003	Mercy Health Partners-Northern Region Endowed Chair of Excellence in Internal Medicine Education
2004	Fellow of the American Society of Nephrology
2009	St. Vs- UT Internal Medicine Excellence in Education Award
2009-present	America's Top Doctors
2009-present	America's Best Doctors
2012-present	Castle Connolly Top Doctors
2013-present	Phi Kappa Phi Honor Society
2013-present	American Physiological Society Cardiovascular Fellow

2014	Laurence Chan Endowed Lectureship (Inaugural Lecture).
2015	Harold J. Jeghers Memorial Lecture
2017	WV Immunization Society
2018	WV Diversity Award
2019	Master of the American College of Physicians (MACP)
2020	WV Healthcare Leadership Award

C. Contribution to Science

1. In vivo NMR spectroscopy applied to models of kidney disease. My first major contribution to Science occurred as the disciple of Drs. Laurence Chan and Robert W. Schrier in the development of in vivo NMR methods for studying renal biochemistry in living animals. This work applied to models acute kidney injury, chronic renal failure (section 3), urinary obstruction and renal transplant rejection is represented below.
    a. Shapiro, J.I., and L. Chan. 1987. P-31 nuclear magnetic resonance study of urinary obstruction in the rat. *J. Clin. Invest.* 80:1422-1427. PMID1422-7.
    b. Nakamoto, M., J.I. Shapiro, L. Chan, and R.W. Schrier. 1987. The invitro and invivo protective effect of atriopeptin III in ischemic acute renal failure in the rat. *J. Clin. Invest.* 80:698-705. PMID: 2957391.
    c. Shapiro, J.I., C.E. Haug, R. Weil,III, and L. Chan. 1988. P-31 NMR study of renal allograft rejection in the rat. *Transplant.* 45:17-21. PMID: 3680505.
    d. Burke, T.J., D. Malhotra and J.I. Shapiro. 2001. Effect of enhanced oxygen release from hemoglobin with RSR13 on acute renal failure in the rat. *Kidney Int.* 60:1407-1414.PMID: 11576354.

2. Dr. Shapiro has been active in clinical research. Notably he was the PI of the National Analgesic Nephropathy study and served as a co-investigator and enrollment chairman for the CORAL study. Relevant clinical research papers include:
    a. Cooper CJ, Murphy TP, Cutlip DE, Jamerson K, Henrich W, Reid DM, Cohen DJ, Matsumoto AH, Steffes M, Jaff MR, Prince MR, Lewis EF, Tuttle KR, Shapiro JI, Rundback JH, Massaro JM, D'Agostino RB, and Dworkin LD. 2014. Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis. N.Engl.J.Med. 370:13-22. PMID: 24245566.
    b. Murphy TP, Cooper CJ, Pencina KM, D'Agostino R, Massaro J, Cutlip DE, Jamerson K,Matsumoto AH, Henrich W, Shapiro JI, Tuttle KR, Cohen DJ, Steffes M, Gao Q, Metzger DC,Abernethy WB, Textor SC, Briguglio J, Hirsch AT, Tobe S, Dworkin LD. 2016. Relationship of Albuminuria and Renal Artery Stent Outcomes: Results from the CORAL Randomized Clinical Trial (Cardiovascular Outcomes With Renal Artery Lesions). Hypertension. 68:1145-52. PMID: 27647847.
    c. Chen T, Brewster P, Tuttle KR, Dworkin LD, Henrich W, Greco BA, Steffes M, Tobe S, Jamerson K, Pencina K, Massaro JM, D'Agostino RB Sr, Cutlip DE, Murphy TP, Cooper CJ, Shapiro JI. Prediction of cardiovascular outcomes with machine learning techniques: application to the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) study. 2019. In J Nephrol Reonvasc Dis. 12:49-58. PMID 30962703.
    d. Cooper EL, Xie Y, Nguyen H, Brewster PS, Sholl H, Sharrett M, Ren K, Chen T, Tuttle KR, Haller ST, Jamerson K, Murphy TP, D'Agostino RB Sr, Massaro JM, Henrich W, Cooper CJ, Cutlip DE, Dworkin LD, Shapiro JI. Early Rapid Decline in Kidney Function in Medically Managed Patients With Atherosclerotic Renal Artery Stenosis. J Am Heart Assoc. 2019 Jun 4;8(11):e012366. doi: 10.1161/JAHA.119.012366. Epub 2019 Jun 1. PMID: 31433717

3. Oxidant stress in chronic renal failure progression. The mechanisms by which chronic kidney injury appears to inexorably progress has been an important topic for some time. We (including Drs. Laurence Chan and Robert W. Schrier) were among the first to identify that the metabolic rate of the chronic renal failure kidney was increased an uncoupled from sodium transport. We have subsequently linked this to progressive renal fibrosis and our work with the Na/K-ATPase as a signal transducer.
    a. Shapiro, J.I., D.C.H. Harris, R.W. Schrier, and L. Chan. 1990. Attenuation of hypermetabolism in the remnant kidney by dietary phosphate restriction in the rat. *Am. J. Physiol.* 258:F183-188. PMID:2301590.
    b. Fedorova, L, V Raju, N El-Okdi, A Shidyak, S Vetteth, D Kennedy, S Vetteth, D Giovannucci, AY Bagrov, O Fedorova, JI Shapiro and D Malhotra. 2009. Cardiotonic steroid hormone marinobufagenin induces renal fibrosis: Implications of epithelial to mesenchymal transition. *Am.J.Physiol.* 296:F922-34. PMID: 1916701.

c. Haller, ST, CA Drummond, Y Yan, J Liu, J Tian, D Malhotra and JI Shapiro. 2013. Passive immunization against marinobufagenin attenuates renal fibrosis and improves renal function in experimental renal disease. Am.J.Hyperten. 27:603-9. PMID:24014658.
d. Haller ST, Kumarasamy S, Folt DA, Wuescher LM, Stepkowski S, Karamchandani M, Waghulde H, Mell B, Chaudry M, Maxwell K, Upadhyaya S, Drummond CA, Tian J, Filipiak WE, Saunders TL, Shapiro JI, Joe B and Cooper CJ. 2017. Targeted disruption of CD40 in a genetically hypertensive rat model attenuates renal fibrosis and proteinuria independent of blood pressure. Kidney Int. 91:365-374. PMID: 27692815.

4. Scaffolding function of the Na/K-ATPase and its implications toward signaling, renal salt handling and hypertension. I am extremely proud to be part of the group that delineated the Na/K-ATPase-Src-EGFR-ROS signal cascade resulting from the scaffolding function of the alpha1 subunit of the Na/K-ATPase with Src. We were the first to identify this cascade and have worked for the better part of the last 20 years to define its role in pathophysiology. I must at this point admit that my colleague, Zijian Xie, conceived of the overall scaffolding function concept whereas my personal contributions were to uncover the ligand mediated endocytosis of the Na/K-ATPase and the potential role in renal sodium transport and hypertension (where Dr. Jiang Liu, a former fellow played a critical role) as well as to delineate the implications of this signal cascade to the subject of uremic cardiomyopathy.
    a. Xie, Z., P. Kometiani, J. Liu, J.I. Shapiro and A. Askari. 1999. Intracellular reactive oxygen species mediate the linkage of Na+/K+-ATPase to hypertrophy and its marker genes in cardiac myocytes. *J. Biol. Chem.* 274:19323-8. PMID: 10383443
    b. Liu, J., S.M. Periyasamy, W. Gunning, O.V. Fedorova, A.Y. Bagrov, D. Malhotra, Z Xie, and J.I. Shapiro. 2002. Effects of cardiac glycosides on sodium pump expression and function in LLC-PK1 and MDCK cells. *Kidney Int.* 62:2118-2125. PMID: 12427136
    c. Liu, J., M. Liang, L. Liu, D. Malhotra, Z. Xie, and J.I.Shapiro. 2005. Ouabain induced endocytosis of the plasmalemmal Na/K-ATPase in LLC-PK1 cells requires caveolin-1. *Kidney Int*. 67: 1844-1854. PMID: 15200429
    d. Wang W, Shapiro JI. Quantum Modeling: A Bridge between the Pumping and Signaling Functions of Na/K-ATPase. Int J Mol Sci. 2018 Aug 9;19(8). pii: E2347. doi: 10.3390/ijms19082347. PubMed PMID: 30096926;

5. Role of cardiotonic steroid signaling in the pathogenesis of uremic cardiomyopathy. Back in the 1960s, Neil Bricker and others postulated that a circulating inhibitor of the Na/K-ATPase might be involved in the pathogenesis of progressive renal failure (see section 3 above) and the symptom complex of uremia. Our group, working with Drs. Alexei Bagrov and Olga Fedorova, have explored the role of the Na/K-ATPase signal cascade in the pathogenesis of the cardiomyopathic aspect of uremia (uremic cardiomyopathy). In particular, we have causally linked such signaling to the cardiac fibrosis which complicates uremic cardiomyopathy. We have also explored different novel therapies of this important clinical complication of chronic renal failure.

    a. Kennedy, D.J., S. Vetteth, S.M. Periyasamy, M. Kanj, L. Fedorova, S. Khouri, M. B. Kahaleh, Z. Xie, D. Malhotra, N. Kolodin, E. G. Lakatta, O.V. Fedorova, A.Y. Bagrov and J.I. Shapiro. 2006. Central role for the cardiotonic steroid, marinobufagenin, in the pathogenesis of experimental uremic cardiomyopathy. *Hypertension*. 47:488-495. PMID: 16446397.
    b. Tian, J, A Shidyak, SM Periyasamy, S Haller, S Oweis, , M Taleb, N El-Okdi, J Elkareh, S Gupta, OV Fedorova, CJ Cooper, Z Xie, D Malhotra, AY Bagrov and JI Shapiro. 2009. Spironolactone attenuates uremic cardiomyopathy by antagonizing the signaling of cardiotonic steroids through the Na/K-ATPase. Hypertension. 54:1313-20. PMID: 19884563.
    c. Haller, ST, Y Yan, CA Drummond, J Tian, DJ Kennedy, VY Shilova, Z Xie, J Liu, CJ Cooper, D Malhotra, JI Shapiro, OV Fedorova and AY Bagrov. 2017. Rapamycin attenuates cardiac fibrosis in experimental uremic cardiomyopathy by reducing marinobufagenin levels and inhibiting downstream pro-fibrotic signaling. Kidney Int. 91:365-374. PMID: 27692815.
    d. Liu J, Tian J, Chaudhry M, Maxwell K, Yan Y, Wang X, Shah PT, Khawaja AA, Martin R,Robinette TJ, El-Hamdani A, Dodrill MW, Sodhi K, Drummond CA, Haller ST, Kennedy DJ,Abraham NG, Xie Z, and Shapiro JI. Attenuation of Na/K-ATPase Mediated Oxidant Amplification with pNaKtide Ameliorates Experimental Uremic Cardiomyopathy. Sci Rep. 2016 Oct 4;6:34592. doi: 10.1038/srep34592 PMID: 27698370

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/joseph.shapiro.1/bibliography/48602179/public/?sort=date&direction=ascending

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

Ongoing Research Support
Brickstreet Foundation Endowment: Corpus is approximately 5M dollars. Approximately 4% interest per year invested to study role of the Na/K-ATPase oxidant amplification loop in animal models of disease. I serve as the PI for this endowment.

Huntington Foundation Endowment: Corpus is approximately 1.5M dollars. Approximately 4% interest per year invested to study role of Na/K-ATPase oxidant amplification loop in animal models of aging. I serve as the PI for this endowment.

National Institutes of Health. 1P20GM121299-01. Appalachian Center for Cellular Transport in Obesity Related Disorders. PI: Uma Sundaram, M.D. Period 7/01/2018 - 6/30/2023. JI Shapiro serves 1/12th time as a faculty mentor to COBRE investigators.

Completed Research Support
National Institutes of Health (NHLBI SMARTT Program (RSA-000456, 455))
09/26/17-02/28/19 Role of Dr. Shapiro: Co-Investigator 5% Effort.
SMARTT program has approved the provision of regulatory affair assistance and small molecular manufacture services to enable progression of pNaktide for the treatment of uremic cardiomyopathy toward IND submission.

NIH RO1 (HL109015, 2011-2016) JI Shapiro and Z Xie Co-PIs. Receptor Na/K-ATPase Antagonists As Novel Therapeutics For Renal/Cardiac Diseases. In this project which has just finished a no-cost extension (2017), the aim are to define the potential therapeutic role of novel antagonists which we've developed to the Na/K-ATPase signal cascade in the context of experimental models of uremic cardiomyopathy. My role was as a joint PI (it is a multiple PI application) focusing in particular on the experiments utilizing animal models. This project has just finished a no-cost extension.

NIH RO1 (2011-2016, 250K per year.) Na/K-ATPase reduction in renal disease-related cardiac dysfunction. PI – Jiang Tian, PhD, Co-PI JI Shapiro, MD. HL105649. The aims of this project are to define the roles of cardiotonic steroid induced apoptosis and other signaling events in the pathogenesis of uremic cardiomyopathy as well as examine potential linkage of such signaling to cardiovascular outcomes in the CORAL population. My primary role with this project is to oversee the clinical-translational components as well as provide insights related to my expertise with animal models of uremic cardiomyopathy. This project has just finished a no-cost extension.

NIH RO1 (2004-2012) Cardiovascular outcomes in renal atherosclerotic lesions (CORAL). PI Christopher Cooper, M.D., HL071556, National enrollment committee chairman and site co-PI, JI Shapiro, M.D. The objective of the CORAL study was to determine whether renal arterial stenting was advantageous to patients with atheromatous renal artery stenosis. In addition to being part of the team that conceived of this study, my primary role in the project was to serve as enrollment chairman for the project.