Steven T. Haller, Ph.D.
Assistant Professor
University of Toledo College of Medicine and Life Sciences, Ph.D., 2012

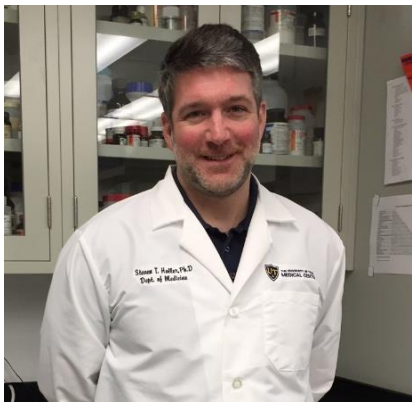
Atherosclerotic renal artery stenosis (RAS) is the leading cause of secondary hypertension (renovascular hypertension) and an important cause of ischemic renal injury. Impaired renal function is one of the most important contributors to adverse cardiovascular events and survival in this population. The focus of my research involves identifying the molecular targets leading to the development of renal fibrosis and renal dysfunction in RAS.

******See full length description below******

Steven T. Haller, Ph.D.
Assistant Professor of Medicine
Division of Cardiovascular Medicine, Department of Medicine

Office: 419-383-6859
Laboratory: 419-383-6823
Fax: 419-383-6863

Email: steven.haller@utoledo.edu



Education
B.S., Biology/Chemistry, University of Toledo, 2003
M.S., Molecular Basis of Disease, Medical University of Ohio, 2005
Ph.D., Biomedical Sciences, University of Toledo Health Science Campus, 2012

Postgraduate Training
University of Toledo Health Science Campus, Department of Medicine (Director: Professor Christopher J. Cooper, MD, Dean, College of Medicine and Life Sciences), 2012-2015

Academic Appointments
Assistant Professor of Medicine, Division of Cardiovascular Medicine, Department of Medicine, University of Toledo College of Medicine and Life Sciences

Awards and Commendations
American Heart Association Postdoctoral Fellowship, 2013-2015
European Society of Hypertension and International Society of Hypertension Travel Award, 2014
European Society of Hypertension and International Society of Hypertension Finalist for Young Investigator Award, 2014

Research Interest:

Atherosclerotic renal artery stenosis (RAS) is the leading cause of secondary hypertension (renovascular hypertension) and an important cause of ischemic renal injury. Our group and others have demonstrated that while contemporary therapies such as endovascular stenting and neurohormonal blockade address the renovascular hypertension associated with RAS, no treatment to date has been effective in treating or preventing the associated ischemic renal injury and subsequent renal dysfunction in these patients. As impaired renal function is one of the most important contributors to adverse cardiovascular events and survival in this population, new therapies based on a mechanistic understanding of ischemic renal disease are of paramount importance.

Soluble CD40 ligand (sCD40L) is expressed and secreted by activated platelets and plays a vital role in immunity, inflammation, and coagulation. In renal injury models sCD40L, signaling through the CD40 receptor in proximal tubular epithelial cells, activates the src family kinase Lyn and plasminogen activator inhibitor type-1 (PAI-1) resulting in a pro-inflammatory cascade that induces renal fibrosis (Figure 1). The CD40 receptor also exists in a soluble form (sCD40), which has been proposed to act as an antagonist to CD40 signaling. We have shown that atherosclerotic renal artery stenosis (RAS) is associated with significantly elevated levels of sCD40L. In RAS patients we have also demonstrated an inverse relationship between circulating sCD40 values and the rate of decline in kidney function over time. To expand on our clinical findings, we have transitioned into the Goldblatt two-kidney one clip (2K1C) animal model, which mimics the physiological complications associated with ischemic renal disease. Our preliminary findings in the 2K1C model strongly suggest that CD40 is an important mediator of renal fibrosis and renal dysfunction in experimental ischemic renal disease. With the assistance of Dr. Bina Joe, and the University of Toledo Center for Hypertension and Personalized Medicine we have created a novel CD40 mutant animal model, which we will use to define the role of CD40 signaling in the development of renal fibrosis.

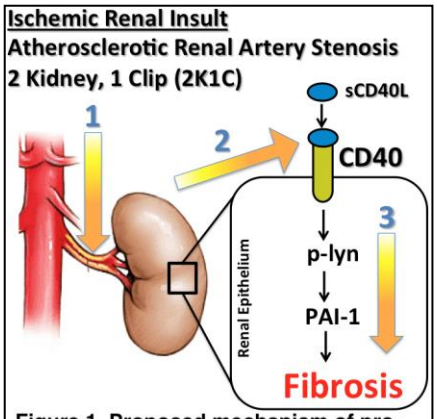


Figure 1. Proposed mechanism of pro-fibrotic CD40 signaling in renal ischemia.

Publications

http://www.ncbi.nlm.nih.gov/sites/myncbi/1z5sMUqCo7RAU/bibliography/47766132/public/?sort=date&direction=ascending

Folt DA, Evans KL, Brahmandam S, He W, Brewster PS, Yu S, Murphy TP, Cutlip DE, Dworkin LD, Jamerson K, Henrich W, Kalra PA, Tobe S, Thomson K, Holden A, Rayner BL, Grinfeld L, Haller ST, Cooper CJ. Regional and physician speciality-associated variations in the medical management of atherosclerotic renal artery stenosis. *J AM Soc Hypertens*. 2015;9:443-52.

Haller ST, Drummond CA, Yan Y, Liu J, Tian J, Malhotra D, Shapiro JI. Passive immunization against marinobufagenin attenuates renal fibrosis and improves renal function in experimental renal disease. *AM J Hypertension*. 2014;27:603-609.
Sayed M, Drummond CA, Evans KL, Haller ST, Liu J, Xie Z, Tain J. Effects of Na/K-ATPase and its ligands on bone marrow stromal cell differentiation. *Stem Cell Res*. 2014;13:12-23.

Yu MS, Folt DA, Drummond CA, Haller ST, Cooper EL, Brewster P, Evans KL, Cooper CJ. Endovascular verses medical therapy for atherosclerotic renovascular disease. *Curr Atheroscler Rep*. 2014;16:459

Evans KL, Tuttle KR, Folt DA, Dawson T, Haller ST, Brewster PS, He W, Jamerson K, Dworkin LD, Cutlip DE, Murphy TP, D'Agostino RB Sr, Henrich W, Cooper CJ. Use of renin-angiotensin inhibitors in people with renal artery stenosis. *Clin AM J Soc Nephrol*. 2014;9:1199-206.

Drummond CA, Sayed M, Evans KL, Shi H, Wang X, Haller ST, Liu J, Copper 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:H1631-43.

Haller ST, Evans KL, Folt DA, Drummond CA, Cooper CJ. Mechanisms and treatments for renal artery stenosis. *Discov Med*. 2013;16:255-260.

Haller ST, Kalra PA, Ritchie JP, Chrysochou T, Brewster P, He W, Yu H, Shapiro JI, Cooper CJ. Effect of CD40 and sCD40L on Renal Function and Survival in Patients with Renal Artery Stenosis. *Hypertension*. 2013;61:894-900.

Fedorova LV, Tamirisa A, Kennedy DJ, Haller ST, Budny G, Shapiro JI, Malhotra D. Mitochondrial impairment in the fifth-sixth nephrectomy model of chronic renal failure: proteomic approach. BMC Nephrol. 2013;4:209.

Yan Y, Shapiro AS, Haller S, Katragadda V, Liu L, Tian J, Basrur V, Malhotra D, Xie ZJ, Abraham NG, Shapiro JI, Liu J. Involvement of reactive oxygen species in a feed-forward mechanism of Na/K-ATPase-mediated signal transduction. *J Biological Chem*. 2013;288:34249-34258.

Drummond CA, Buddny G, Haller ST, Liu J, Yan Y, Xie Z, Malhotra D, Shapiro JI, Tian J. Gender differences in the development of uremic cardiomyopathy following partial nephrectomy: role of progesterone. *J Hypertens (Los Angel)*. 2013.;31:2.

Haller S, Kennedy DJ, Shidyak A, Budny G, Malhotra D, Fedorova OV, Shapiro JI, Bagrov AY. Monoclonal antibody against marinobufagenin reverses cardiac fibrosis in rats with chronic renal failure. *Am J Hypertension*. 2012;25:690-6.

Yan Y, Haller S, Shapiro A, Malhotra N, Tian J, Xie Z, Malhotra D, Shapiro, JI, Liu J. Ouabain-stimulated trafficking regulation of the Na/K-ATPase and NHE3 in renal proximal tubule cells. *Mol Cell Biochem*, 2012;367:175-183.

Haller S, Adlakha S, Reed G, Brewster P, Kennedy D, Burket MW, Colyer W, Yu H, Zhang D, Shapiro JI, Cooper CJ. Platelet activation in patients with atherosclerotic renal artery stenosis undergoing stent revascularization. *Clin J Am Soc Nephrol*. 2011;6:2185-91.

Yu H, Zhang D, Haller S, Kanjwal K, Colyer W, Brewster P, Steffes M, Shapiro JI, Cooper CJ. Determinants of renal function in patients with renal artery stenosis. *Vasc Med*. 2011;16:331-8.

Kolmakova EV, Haller ST, Kennedy DJ, Isachkina AN, Budny GV, Frolova EV, Piecha G, Nikitina ER, Malhotra D, Fedorova OV, Shapiro JI, Bagrov AY. Endogenous cardiotonic steroids in chronic renal failure. *Nephrol Dial Transplant*. 2011;26:2912-9.

Tian J, Haller S, Periyasamy S, Brewster P, Zhang H, Adlakha S, Fedorova OV, Xie ZJ, Bagrov AY, Shapiro JI, Cooper CJ. Renal ischemia regulates marinobufagenin release in humans. *Hypertension*. 2010;56:914-9.

Kanjwal K, Cooper CJ, Virmani R, Haller S, Shapiro JI, Burket MW, Steffes M, Brewster P, Zhang H, Colyer WR Jr. (2010) Predictors of embolization during protected renal artery angioplasty and stenting: Role of antiplatelet therapy. *Catheter Cardiovasc Interv. 2010;*76:16-23.

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;54:1313-20.

Kanjwal K, Haller S, Steffes M, Virmani R, Shapiro JI, Burket MW, Cooper CJ, Colyer WR Jr. (2009) Complete versus partial distal embolic protection during renal artery stenting. *Catheter Cardiovasc Interv,* 2009;73:725-30.

Cooper CJ, Haller ST, Colyer W, Steffes M, Burket MW, Thomas WJ, Safian R, Reddy B, Brewster P, Ankenbrandt MA, Virmani R, Dippel E, Rocha-Singh K, Murphy TP, Kennedy DJ, Shapiro JI, D'Agostino RD, Pencina MJ, Khuder S. Embolic protection and platelet inhibition during renal artery stenting. *Circulation*, 2008;117:2752-60.