BIOGRAPHICAL SKETCH

NAME Liu, Ruisheng	POSITION TITLE Professor
eRA COMMONS USER NAME RUILIU1	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Jining Medical College, China	M.D	1982	Medicine
Shandong Medical University, China	M.S.	1991	Cardiovasology
Uppsala University, Sweden	Ph.D.	2002	Physiology & Cell Biology

A. Personal Statement

Tubuloglomerular feedback (TGF) is an intrarenal regulatory process by which increased flow *via* increases of NaCl delivery at the macula densa causes the afferent arteriole to constrict, thereby decreasing glomerular filtration rate (GFR) and tubular flow and preventing NaCl delivery to the distal nephron from increasing excessively. The mechanisms of TGF regulation have been studied both *in vitro* by microperfusion and *in vivo* by micropuncture. However, the long-term roles of TGF responsiveness are only assumptions from these acute experiments. We still do not know whether TGF play any roles in control of salt-water balance and hemodynamics. The major focus of our research is to determine the significance of TGF responsiveness in physiological and pathological situations, such as in volume homeostasis, salt-sensitive hypertension, acute kidney injury, chronic kidney diseases and diabetic nephropathy.

We utilize state-of-the-art and/or sophisticated techniques such as microperfusion of kidney tubules and arterioles *in vitro*, micropuncture *in vivo*, fluorescent imaging in perfused tubules or arterioles, laser capture microdissection, molecular biology, cell biology, whole-animal physiology, and tissue specific knockout and transgenic animal models.

B. Positions and Honors

Positions and Employment:

1984 – 1988 Resident, Internal Medicine, Guangrao Hospital of Dongying City, China

1988 – 1991 Fellowship, Cardiology Department, Shandong Medical University, Master's degree in Cardiology, China

1991 – 1998 Cardiologist, Cardiology Department, Shandong Province Hospital.

1998 – 2002 Ph.D. student/Postdoctoral Fellow, Department of Cell Biology, Uppsala University, Sweden.

2002 – 2007 Associate Staff Investigator/Research Scientist, Hypertension and Vascular Research Division, Henry Ford Hospital.

2007 – 2008 Senior Staff Investigator, Hypertension and Vascular Research Division, Henry Ford Hospital.

2008 – 2010 Assistant Professor, Department of Physiology & Biophysics, Director, Renal Microcirculatory Central Laboratory Division of Nephrology, Department of Medicine University of Mississippi Medical Center

2010 – 2014 Associate Professor, Department of Physiology & Biophysics, Director, Renal Microcirculatory Central Laboratory

Division of Nephrology, Department of Medicine
University of Mississippi Medical Center
2014 – date Professor, Department of Molecular Pharmacology and Physiology,
University of South Florida College of Medicine, Tampa FL

Honors and Awards:

2003 New Investigator Travel Award, American Heart Association.
2004 New Investigator Award for U.S. Fellows, American Heart Association.
2005 Young Investigator Award, Inter-American Hypertension Society.
2009 Excellence in Research Gold Award, University of Mississippi Medical Center

C. Selected peer-reviewed publications (in chronological order).

1. Persson AEG, Gutierrez A, Pittner J, Ring A, Ollerstam A, Brown R, **Liu R**, Thorup C. Renal NO production and the development of hypertension. *Acta Physiol. Scand.* 2000;168: 169-174.
2. **Liu R**, Gutierrez AM, Ring A, and Persson AEG. Nitric oxide induces resensitization of P2Y nucleotide receptors in cultured rat mesangial cells. *J. Am. Soc. Nephrol.* 2002;13: 313-321.
3. **Liu R**, Bell PD, Peti-Peterdi J, Kovacs G, Johansson A, Persson AEG. Purinergic receptor signalling at the basolateral membrane of macula densa cells. *J. Am. Soc. Nephrol.* 2002;13: 1145-1151.
4. **Liu R**, Persson AEG. Effects of nitric oxide on P2Y receptor resensitization in spontaneously hypertensive rat mesangial cells*. J Hypertens.* 2002;20:1835-1842.
5. Persson A.E.G., Brown R, **Liu R**, Ollerstam A. Nitric oxide modulates and adenosine mediates the tubuloglomerular feedback mechanism. *Acta Physiol Scand.* 2002;176:91-94.
6. **Liu R**, Pittner J, Persson AEG. Changes of cell volume and nitric oxide concentration in macula densa cells caused by changes in luminal NaCl concentration*. J Am Soc Nephrol.* 2002;13:2688-2696.
7. **Liu R**. Regulatory functions of the juxtaglomerular apparatus. *PhD dissertation*, Uppsala University, Sweden, ISBN: 9155451993, 2002.
8. Pittner J, **Liu R**, Brown R, Wolgast M, Persson AEG . Visualization of nitric oxide production and intracellular calcium in juxtamedullary afferent arteriolar endothelial cells. *Acta Physiol Scand.* 2003;179:309-17.
9. Ren Y, **Liu R**, Carretero OA, Garvin JL. Increased intracellular Ca^{++} in the macula densa regulates tubuloglomerular feedback. *Kidney Int.* 2003;64:1348-55.
10. **Liu R**, Persson AEG. Angiotensin II Stimulates Calcium and Nitric Oxide Release From Macula Densa Cells Through AT1 Receptors. *Hypertension.* 2004;43:649-53.
11. Persson AEG, Ollerstam A, **Liu R**, Brown R. Mechanisms for macula densa cell release of renin. *Acta Physiol Scand*. 2004;181:471-4.
12. **Liu R**, Ren Y, Garvin J L, Carretero O A. Superoxide enhances tubuloglomerular feedback by constricting the afferent arteriole. *Kidney Int.* 2004;66:268-74.
13. Ren Y, Carretero OA, **Liu R**, Garvin GL. Role of macula densa adenosine triphosphate (ATP) in tubuloglomerular feedback. *Kidney Int*. 2004;66:1479-85.
14. **Liu R**, Persson AEG. Simultaneous changes of cell volume and cytosolic calcium concentration in macula densa cells caused by alterations of luminal NaCl concentration. *J Physiol.* 2005;563:895-901.
15. **Liu R**, Carretero OA, Ren Y, Garvin JL. Increased intracellular *p*H at the macula densa activates nNOS during tubuloglomerular feedback. *Kidney Int.* 2005;67:1837-43,
16. Ren Y, Garvin JL, **Liu R**, Carretero OA. Possible mechanism of efferent arteriole (Ef-Art) tubuloglomerular feedback. *Kidney Int.* 2007;71:861-6.
17. **Liu R**, Garvin JL, Ren Y, Pagano PJ, Carretero OA. Depolarization of the macula densa induces superoxide production via NAD(P)H oxidase. *Am J Physiol Renal Physiol.* 2007;292:F1867-72.
18. Ren Y, Garvin JL, **Liu R**, Carretero OA. Crosstalk between the connecting tubule and the afferent arteriole regulates renal microcirculation. *Kidney Int.* 2007;71:1116-21.

19. **Liu R,** Carretero OA, Ren Y, Wang H, Garvin JL. Intracellular pH regulates superoxide production by the macula densa. PMCID: PMC2536876. *Am J Physiol Renal Physiol*. 2008;295:F851-6.
20. Ren Y, D'Ambrosio M, Wang H, **Liu R**, Garvin JL, Carretero OA. Heme oxygenase metabolites inhibit tubuloglomerular feedback (TGF). PMCID: PMC2576153; *Am J Physiol Renal Physiol* 2008;295: F1207-F1212.
21. Ren Y, Garvin JL, **Liu R**, Carretero OA. Cross-talk between arterioles and tubules in the kidney. PMCID: PMC2697568, *Pediatr Nephrol.* 2009;24(1):31-5.
22. Zhang R, Harding P, Garvin JL, Juncos R, Peterson E, Luis A. Juncos LA, **Liu R**. Isoforms and functions of NAD(P)H oxidase at the macula densa. PMCID: PMC2688698, *Hypertension*. 2009;53:556-563. (***** selected as the **top paper** of *Hypertension* for 2009 in basic science)
23. **Liu R** and Juncos LA. GTPase-Rac enhances depolarization-induced superoxide production by the macula densa during tubuloglomerular feedback. PMCID: PMC2828178, *Am J Physiol Regul Integr Comp Physiol* 2010;298: R453-R458,
24. Fu Y, Zhang R, Lu D, Liu H, Chandrashekar K, Juncos LA, **Liu R**. NOX2 is the primary source of AngII induced superoxide in the macula densa. PMCID: PMC2838666, *Am J Physiol Regul Integr Comp Physiol.* 2010;298:R707-12.
25. Lu D, Fu Y, Lopez-Ruiz AF, Zhang R, Juncos R, Liu H, Manning RD Jr, Juncos LA, **Liu R**. Salt sensitive splice variant of nNOS expressed in the macula densa cells. PMCID: PMC2886819, *Am J Physiol Renal Physiol.* 2010;298:F1465-71.
26. Ren Y, D'Ambrosio MA, **Liu R**, Pagano PJ, Garvin JL, Carretero OA. Enhanced myogenic response in the afferent arteriole of spontaneously hypertensive rats. PMCID: PMC2886653, *Am J Physiol Heart Circ Physiol.* 2010;298:H1769-75.
27. Zhu X, Manning RD, Jr., Lu D, Gomez-Sanchez CE, Fu Y, Juncos LA, **Liu R.** Aldosterone stimulates superoxide production in macula densa cells. PMCID: PMC3174554, *Am J Physiol Renal Physiol.*, 2011;301:F529-35.
28. Wang H, Garvin JL, D'Ambrosio MA, Falck JR, Leung P, **Liu R**, Ren Y, Carretero OA. Heme oxygenase metabolites inhibit tubuloglomerular feedback in vivo. PMCID: PMC3075027, *Am J Physiol Heart Circ Physiol.* 2011;300:H1320-6
29. Lai E, Wang Y, Persson E, Manning D, **Liu R**. Pressure induces intracellular calcium changes in juxtaglomerular cells in perfused afferent arterioles. *Hypertension Res.* 2011;34:942-8
30. Fu Y, Hall JE, Lu D, Lin L, Manning, RD, Cheng L, Gomez-sanchez CE, Juncos LA, **Liu R**. Aldosterone Blunts Tubuloglomerular Feedback by Activating Macula Densa Mineralocorticoid Receptors. PMCID: PMC3299000, *Hypertension.* 2012;59:599-606.
31. Lu Y, Fu Y, Ge Y, Juncos LA, Reckelhoff JF, **Liu R**. The vasodilatory effect of testosterone on renal afferent arterioles. PMCID: PMC3322301, *Gender Medicine.* 2012;9:103-11.
32. Chandrashekar K, Lopez-Ruiz A, Juncos R, Nath K, Stec DE, Vera T, **Liu R**, Juncos LA. The Modulatory Role of Heme Oxygenase on Subpressor Angiotensin II-Induced Hypertension and Renal Injury. PMCID: PMC3312292, *Int J Hypert*. 2012; 2012:392890.
33. Ge Y, Gannon KP, Gousset M, **Liu R**, Murphey B, Drummond H. Impaired myogenic constriction of the renal afferent arteriole in a mouse model of reduced βENaC expression. PMCID: PMC3378172, *Am J Physiol Renal Physiol.*, 2012; 302:F1486-93.
34. Burke M, Pabbidi MR, Fan F, Ge Y, **Liu R**, Williams JM, Sarkis AB, Lazar J, Jacob HJ, Roman RJ. Genetic Basis of the Impaired Renal Myogenic Response in FHH Rats. PMCID: PMC3602705 *Am J Physiol Renal Physiol., 2013; 304:F565-77.*
35. Zhang Q, Lin L, Lu Y, Liu H, Duan Y, Zhu X, Zou C, Manning RD, Jr., **Liu R**. Interaction between nitric oxide and superoxide in the macula densa in aldosterone-induced alterations of tubuloglomerular feedback. PMCID: PMC3566515, *Am J Physiol Renal Physiol.*, 2013;304:F326-32.
36. Fu Y, Lu Y, Liu E, Zhu X, Mahajan GJ, Lu D, Roman RJ, **Liu R**. Testosterone enhances tubuloglomerular feedback by increasing superoxide production in the macula densa. PMCID: PMC3652076, *Am J Physiol Regul Integr Comp Physiol.* 2013;304:F726-33.
37. Soljancic A, Lopez-Ruiz AF, Chandrashekar K, Maranon RO, **Liu R**, Reckelhoff JF, Juncos LA. Protective Role of Testosterone in ischemia-reperfusion-induced acute kidney injury. *Am J Physiol Regul Integr Comp Physiol.* 2013;304:R951-8.

38. Ge Y, Murphy SR, Lu Y, Falck J, **Liu R**, Roman RJ. Endogenously produced 20-HETE modulates myogenic and TGF response in microperfused afferent arterioles. *Prostaglandins Other Lipid Mediat.* 2013;102:42-48.
39. Brewer J, **Liu R**, Lu Y, Scott J, Wallace K, Wallukat G, Moseley J, Herse F, Dechend R, Martin JN Jr, Lamarca B. Mechanisms of angiotensin II type I receptor autoantibody-enhanced renal and blood pressure response during pregnancy. *Hypertension.* 2013;62:886-92.
40. Zhang J, Chandrashekar K, Lu Y, Duan Y, Qu P, Wei J, Juncos LA, **Liu R**. Enhanced expression and activity of Nox2 and Nox4 in the macula densa in Ang II-induced hypertensive mice. *Am J Physiol Renal Physiol*. 2014;306:F344-50.
41. Liu ZZ, Schmerbach K, Lu Y, Perlewitz A, Nikitina T, Cantow K, Seeliger E, Persson PB, Patzak A, **Liu R**, Sendeski MM. Iodinated contrast media cause direct tubular cell damage, leading to oxidative stress, low nitric oxide, and impairment of tubulo-glomerular feedback. *Am J Physiol Renal Physiol*. *Am J Physiol Renal Physiol*. 2014;306:F846-72.
42. Ge Y, Murphy SR, Fan F, Williams JM, Falck JR, **Liu R**, Roman RJ. Role of 20-HETE in the impaired myogenic and TGF responses of the Af-Art of Dahl Salt-sensitive rats. *Am J Physiol Renal Physiol*. 2014 307:F509-15.
43. Song J, Yan Lu Y, Lai EY, Wei J, Wang L, Chandrashekar K, Wang S, Shen C, Luis A. Juncos LA, **Liu R**. Oxidative status in the macula densa modulates tubuloglomerular feedback responsiveness in Ang II-induced hypertension. *Acta Physiologica.* 2014 (in press)

Research Support

ACTIVE

R01DK099276 (**Liu**) 06/01/2014—05/31/2018 3.6 calendar
NIH/NIDDK $995,064
Primary cilia and modulation of the renal microcirculation
Role: PI

The major goal of this project is to study the role of primary cilia on the macula densa regulated by the tubular flow in control of renal hemodynamics and salt-water balance.

R01DK098582 (Liu) 09/01/2013– 05/31/2017 3.6 calendar
NIH/NIDDK $1,327,000
Tubuloglomerular feedback and salt-sensitive hypertension.
Role: PI

The major goals of this project are to study the expression and role of splice variants of NOS1 expressed in the macula densa in control of tubuloglomerular feedback, salt-water balance and blood pressure.

13POST14220006 (Mentor) 01/011/2013– 12/31/2014
AHA post-doctoral fellowship award for Y. Lu. $99,000
Nitric oxide in the macula densa protects against Ang II-induced hypertension and renal injury
Role: Mentor

This project examines the protective role of nitric oxide in the macula densa in the development of hypertension and renal injury.

PAST

11POST7840039 (Mentor) 7/1/2011– 6/31/2013
AHA post-doctoral fellowship award for Y. Fu. $98,000
Renal NO bioavailability and hypertension.
Role: Mentor
This project investigates the interactions between nitric oxide and superoxide in the macula densa in hypertensive animals.

R01HL086767-03 (Liu) 08/10/2007 – 05/31/2012
NIH/NHLBI $1,650,000
Regulation of Macula Densa Superoxide during Tubuloglomerular Feedback.
Role: PI
The major goal of this study is to investigates the factors regulate superoxide production by the macula densa during tubuloglomerular feedback.

R01HL086767-02S1 (Liu) 07/15/2009 - 06/30/2011
NIH/NHLBI $217,856
Regulation of Macula Densa Superoxide during Tubuloglomerular Feedback.
Role: PI
This is an administrate supplement award for grant R01HL086767.

R01 DK073401(Juncos) 7/1/2006– 6/30/2011
NIH/NIDDK $1,525,000
Subpressor ANGII Determines Acute & Chronic Renal Injury.
Role: Co-Investigator
The major goals of this project are to define the how the balance between inflammation (MCP-1) and heme oxygenase affect renal function and determine the severity/progression of hypertension and renal injury.

SDG – AHA (0630288N) (Liu) 01/01/2006 – 12/31/2009
AHA $260,000
Regulation of Macula Densa NAD(P)H Oxidase Activity during Tubuloglomerular Feedback.
Role: PI
This study investigates some of the factors regulate NAD(P)H oxidase activity of the macula densa during tubuloglomerular feedback.

Grant-in-Aid – AHA (0555563Z) (Ren) 7/1/2005 -- 6/30/2007
Mechanisms of myogenic response in spontaneously hypertensive rat (SHR)
Role: Co-Investigator
This study investigates factors that are involved in myogenic response in hypertensive animals.