

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE		
John R. Sedor, M.D.	Professor of Medicine and Physiology		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Univ. of Virginia, Charlottesville, VA	B.A.	1974	Russian Studies
Univ. of Virginia, Charlottesville, VA	M.D.	1978	Medicine
Univ. Hospitals/Case Western Reserve Univ.	–	1978-1981	Residency, Int. Med.
Univ. Hospitals/Case Western Reserve Univ.	–	1980-1984	Fellow-Nephrology

A. Positions and Honors.**Professional Experience**

- 1982-1984: Research Fellow, Drs. H. Abboud and M.J. Dunn, Case Western Reserve University
 1984-1990: Assistant Professor of Medicine, CWRU
 1990-1996: Associate Professor of Medicine, CWRU
 1991-2003: Director, Division of Nephrology & Hypertension, MetroHealth System Campus, CWRU, Cleveland, Ohio
 1992-1996: Associate Professor of Physiology and Biophysics
 1992-pres: Award of Tenure
 1996-pres: Professor of Medicine and Physiology and Biophysics, CWRU
 1998-2003: Director, O'Brien Renal Research Center, CWRU
 2003-pres: Vice President for Research, MetroHealth System Campus, CWRU, Cleveland, Ohio

Honors, Awards and Service:

Member General Medicine B IRG, NIH CSR, 2002-2004; Member, Medical Science Review Committee, Juvenile Diabetes Foundation International, 2000-2003, Established Investigatorship, American Heart Association, 1989-1994; Member, V.A. Nephrology Merit Review Board, 1992-1995; Member, Young Investigator Grant Review Committee, National Kidney Foundation, 1991-1994 & 1999-2002; Member, Cardiorenal Study Section, American Heart Association, 1990-1994; Member, Pathology A Study Section, 1993-1997; Member, Special Study Sections, NIDDK, 1989-pres; The Mather Charitable Foundation Young Scholar Award, 1987-1990; Trainee Research Award, Midwest Section, American Federation for Clinical Research, and Central Society for Clinical Research, 1983; John Lowey Research Grant, Kidney Foundation of Ohio, 1983-1984; Fellow, National Kidney Foundation, 1983-1984; R.H. Mohrman Research Fellowship, Kidney Foundation of Ohio, 1982-1983.

B. Selected publications

- Werber, H.I., S.N. Emancipator, M.L. Tykocinski and **J.R. Sedor**. The interleukin-1 gene is expressed by rat glomerular mesangial cells and is enriched in immune complex glomerulonephritis. *J. Immunol.* 138: 3207-3212, 1987.
 King, C.H., C.H. Goralnik, P.J. Kleinhenz, **J.R. Sedor**, and A.A.F. Mahmoud. Monoclonal antibody characterization of a chymotrypsin-like molecule on neutrophil membrane which is associated with cellular activation. *J. Clin. Invest.* 79: 1091-1098, 1987.
Sedor, J.R., S.W. Carey and S.N. Emancipator. Immune complexes stimulate superoxide release by cultured rat mesangial cells: dependence on Fc region of antibody. *J. Immunol.* 138: 3751-3757, 1987.
 Kester, M., M.S. Simonson, P. Mene' and **J.R. Sedor**. Interleukin-1 generates transmembrane signals from phospholipids through novel pathways. *J. Clin. Invest.* (Rapid Publication) 83: 718-723, 1989.
 Knauss, T.C., P. Mene', S.A. Ricanati, G.R. Dubyak, S.N. Emancipator and **J.R. Sedor**. Immune complex activation of rat glomerular mesangial cells: stimulation of phosphatidylinositol metabolism, cytosolic calcium, prostanoid production, and cell contraction. *Am. J. Physiol.* 257 (Renal, Fluid & Electrolyte 26): F478-485, 1989.
 Wiggins, R., N. Njoku and **J.R. Sedor**. Tissue factor production by cultured rat mesangial cells. *Kidney Int.* 37: 1281-

- 1285, 1990.
- Simonson M.S., J.A. Wolfe, M. Konieczkowski, **J.R. Sedor** and M.J. Dunn. Regulation of prostaglandin endoperoxide synthase gene expression in cultured rat mesangial cells: induction by serum via a protein kinase-C-dependent mechanism. *Molec. Endocrinol.* 5:441-451, 1991.
- Kusner, D.J., E.L. Luebbers, R.J. Nowinski, M. Konieczkowski, C.H. King and **J.R. Sedor**. Induction and release of neutrophil activating peptide-1/interleukin 8 from cultured human glomerular mesangial cells exposed to cytokines and lipopolysaccharide. *Kidney Int.* 39: 1240-1248, 1991.
- Nakazato, Y., M.S. Simonson, W.H. Herman, M. Konieczkowski and **J.R. Sedor**. Interleukin-1 amplifies receptor-mediated prostaglandin biosynthesis by induction of a nonpancreatic (Type II) phospholipase A₂. *J. Biol. Chem.* 266: 14119-14127, 1991.
- Nakazato, Y. and **J.R. Sedor**. Interleukin-1 α increases arachidonyl-CoA: lysophospholipid acyl transferase activity and stimulate [³H]arachidonate incorporation into membrane phospholipids. *Life Sciences* 50: 2075-2082, 1992.
- Sedor, J.R.**, Y. Nakazato and M. Konieczkowski. Interleukin-1 and the mesangial cell. *Kidney Int.* 41: 595-599, 1992.
- Sedor, J.R.** Cytokines, growth factors and glomerulonephritis. *Seminars in Nephrology* 12: 428-440, 1992.
- Konieczkowski, M. and **J.R. Sedor**. Cell-specific regulation of type II phospholipase A₂ expression in rat mesangial cells. *J. Clin. Invest.* 92: 2524-2532, 1993.
- Sedor, J.R.**, M. Konieczkowski, S. Huang, J.H. Gronich, Y. Nakazato, G. Gordon, C.H. King. Cytokines, mesangial cell activation and glomerular injury. *Kidney Int.* 43: 565-570, 1993.
- Gronich, J., M. Konieczkowski, M.H. Gelb, R.A. Nemenoff and **J.R. Sedor**. Interleukin-1 α causes rapid activation of cytosolic phospholipase A₂ by phosphorylation in rat mesangial cells. *J. Clin. Invest.* 93: 1224-1233, 1994.
- Schramek, H., Y. Wang, M. Konieczkowski, P.M. Rose, **J.R. Sedor** and M.J. Dunn. Endothelin-1 stimulates cytosolic phospholipase A₂ in Chinese hamster ovary cells stably expressing the human ET_A or ET_B receptor subtype. *Biochem. Biophys. Research Comm.* 199: 992-997, 1994.
- Ganz, M.B., R. Saxena, K. Hawkins, B. Saksa and **J.R. Sedor**. PDGF and IL-1 activate specific protein kinase C isoforms in mesangial cells. *Am. J. Physiol.* 271 (Renal, Fluid & Electrolyte 40), F108-F113, 1996.
- Singh, R., S. Huang, T. Guth, M. Konieczkowski and **J.R. Sedor**. The cytosolic domain of the type I interleukin-1 receptor spontaneously recruits signaling molecules to activate a proinflammatory gene. *J. Clin. Invest* 100: 419-428, 1997.
- Hricik, D.E., M. Chung-Park, and **J.R. Sedor**. Glomerulonephritis. *N. Eng. J. Medicine* 339: 888-99, 1998.
- Huang, S., M. Konieczkowski, J.R. Schelling and **J.R. Sedor**. Interleukin-1 stimulates the JNK N-terminal/stress-activated kinase by an arachidonate-dependent mechanism. *Kidney Int.* 55:1740-1749, 1999.
- Schelling, J.R., L. Zarif, A. R. Sehgal, Iyengar, S. and **J.R. Sedor**. Genetic susceptibility to end stage renal disease. *Current Opinion in Nephrology and Hypertension* 8: 465-472, 1999.
- Singh, R., B. Wang, A. Shirvaikar, S. Khan, S. Kamat, J.R. Schelling, M. Konieczkowski and **J.R. Sedor**. Rho family GTPases directly associate with the IL-1 receptor (IL-1R) cytosolic domain. Coordinate organization to drive cellular activation. *J. Clin. Invest.*, 103: 1561-1570, 1999.
- Covic, A., Goldsmith DJA, Panaghiu, L, Covic M, and **J.R. Sedor**. Analysis of the effect of hemodialysis on peripheral and central arterial pressure waveforms. *Kidney Int.* 57: 2634-2643, 2000.
- El-Meanawy, A., J.R. Schelling, S. Iyengar and **J.R. Sedor**. Serial analysis of gene expression (SAGE) is a valid tool to search for nephropathy susceptibility genes. *Am. J. Physiol. (Renal, Fluid and Electrolyte)* 279: F383-F392, 2000.
- Zarif, L., A. Covic, S. Iyengar, A. R. Sehgal, **J.R. Sedor** and J.R. Schelling. Inaccurate phenotyping may confound identification of hypertensive nephrosclerosis susceptibility loci. *Nephrol. Dial. Transplant* 15: 1801-1807, 2000.
- Covic, A., J.R. Schelling, M. Constantiner, S.I. Iyengar and **J.R. Sedor**. Serum C-peptide concentrations poorly phenotype type 2 diabetic end stage renal disease patients for genetic epidemiological analysis. *Kidney Int.*58:1742-1750, 2000.
- Schelling, J.R. and **J.R. Sedor**. Approach to the patient with proteinuria and the nephrotic syndrome. In: Kelly's *Textbook of Internal Medicine (Fourth Edition)*. H. D. Humes, Ed., J.B. Lippincott Co., Philadelphia, PA, pp 1098-1105, 2000.
- Covic, A.M.C., S. K. Iyengar, J. Olson, A. R. Sehgal, C. Jedrey, M. Kara, E. Sabbagh, **J. R. Sedor** and J.R. Schelling. A family-based strategy to identify genes for diabetic nephropathy. *Amer. J. Kidney Dis.* 37: 638-647, 2001.

- Miao, M., B.-R. Wei, D. M. Peehl, Q. Li, T. Alexandrou, J. R. Schelling, J. S. Rhim, **J. R. Sedor**, E. Burnett and B. Wang. EphA Receptor Tyrosine Kinase Activation Inhibits Ras/MAPK Pathway. *Nat. Cell Biol* 3: 527-530, 2001.
- Jarad G, B. Wang, S. Khan, J. DeVore, H. Miao, K.L. Wu, S.L. Nishimura, B.A. Wible, M. Konieczkowski, **J.R. Sedor** and Schelling JR. Fas activation induces renal tubular epithelial cell β 8 integrin expression and function in the absence of apoptosis. *J. Biol. Chem.* 277: 47826-47833, 2002.
- Iyengar, S.K., J.R. Schelling and **J.R. Sedor**. Approaches to Understanding Susceptibility to Nephropathy: From Genetics to Genomics. *Kidney Int.*, 61 (Suppl 1): 61-67, 2002.
- Schelling, J.R., M.A. El-Meanawy, T. Dodig, S. Barathan, S.K. Iyengar and **J.R. Sedor**. Generation of kidney transcriptomes using serial analysis of gene expression. *Exp. Nephrol.*, 10: 82-92, 2002.
- Schelling, J.R., S. Sinha, M. Konieczkowski and **J.R. Sedor**. Myofibroblast differentiation: specialized membrane domains and cell phenotype. *Exp. Nephrol* 10: 313-319, 2002.
- Wu KL, S. Khan, L. Wang, G. Jarad, R.T. Miller, M. Konieczkowski, **J.R Sedor** and J.R. Schelling. Renal tubular epithelial cell apoptosis is associated with caspase cleavage of the NHE1 Na⁺/H⁺ exchanger. *Am. J. Physiol. (Renal Physiology)*, 284: F829-839, 2003 (epub: November 26, 2002).
- Liu, J., L. Zhang, D. Wang, H. Shen, M. Jiang, P. Mei, P.S. Hayden, **J.R. Sedor** and H. Hu. Congenital diaphragmatic hernia, kidney agenesis and cardiac defects associated with Slit3-deficiency in mice. *Mech. Dev.* 120:1059-70, 2003.
- Hayden, P.S., S.K. Iyengar, J.R. Schelling and **J.R. Sedor**. The relationship of genotype to development of vasculopathy. *Curr. Opin. Nephrol. Hypertens.* 12: 71-78, 2003.
- M.A. El-Meanawy, J.R. Schelling, S. Barathan, S.K. Iyengar and **J.R. Sedor**. Serial analysis of gene expression (SAGE). In: *Methods in Molecular Medicine (volume 86): Renal Disease. Techniques and Protocols*. M.S. Goligorsky, Ed. The Humana Press, Totowa, NJ, chapter 17, 2002.
- Liu, J., L. Zhang, D. Wang, H. Shen, M. Jiang, P. Mei, P.S. Hayden, **J.R. Sedor** and H. Hu. Congenital diaphragmatic hernia, kidney agenesis and cardiac defects associated with Slit3-deficiency in mice. In press, *Mech. Dev.*, 2003.
- Iyengar, S.K., K.A. Fox, M. Schachere, F. Manzoor, M.E. Slaughter, A.M. Covic, S.M. Orloff, P.S. Hayden, J.M. Olson, J.R. Schelling, and **J.R. Sedor**. Linkage analysis of candidate loci for end stage renal disease due to diabetic nephropathy. *J. Amer. Soc. Neph.* 14: S195-S201, 2003.
- The Family Investigation of Nephropathy and Diabetes Research Group (includes **J.R. Sedor**). Genetic determinants of nephropathy. The family investigation of diabetes and nephropathy (FIND). *J. Amer. Soc. Neph.* 14: S202-S204, 2003.
- Hayden, P.S., M.A. El-Meanawy, J.R. Schelling, and **J.R. Sedor**. DNA expression analysis: SAGE (Serial Analysis of Gene Expression), microarrays and kidney disease. *Curr. Opin. Nephrol. Hypertens.* 12: 407-414, 2003.
- Jarad, G.; J.S. Simske, **J.R. Sedor**, J.R. Schelling. Nucleic acid-based techniques for post-transcriptional regulation of molecular targets. *Curr. Opin. Nephrol. Hypertens.* 12: 415-421, 2003.
- Gandhi, P. N., R.M. Gibson, X. Tong, J. Miyoshi, Y. Takai, M. Konieczkowski, **J.R. Sedor** and AL. Wilson-Delfosse. An activating mutant of Rac1 that fails to interact with Rho GDP-dissociation inhibitor stimulates membrane ruffling in mammalian cells. *Biochem. J.*, 378: 409-19, 2004 (epub November 21, 2003).
- Knowler, W.C., J. Coresh, R.C. Elston, B.I. Freedman, S.K. Iyengar, P.L. Kummel, J. Olson, R. Plaetke, **J.R. Sedor**, and M.F. Seldin on behalf of the Family Investigation of Nephropathy and Diabetes Research Group. The family investigation of diabetes and nephropathy (FIND). Design and Methods. *J. Diabetes Complications*, in press, 2004.
- Srichai, M.B., M. Konieczkowski, S. Barathan, P. S. Hayden, S. Khan, P. Mundel, S.B. Lee, L.A. Bruggeman, J.R. Schelling, and **J.R. Sedor**. A WT1 co-regulator controls podocyte phenotype by shuttling between adhesion structures and nucleus. In Press, *J.Biol.Chem.* 279: 14398-408, 2004 (Epub January 20, 2004).
- Wu K.L., S. Khan, A. Mukherjee, S. Lakhe-Reddy, C.A. Obejero-Paz, M. Konieczkowski, **J.R. Sedor**, and J.R. Schelling. The NHE1 Na⁺/H⁺ exchanger recruits ERM proteins to regulate Akt-dependent cell survival signaling. *J.Biol. Chem.* 279: 26280-26286, 2004 (Epub pub Apr 19, 2004).
- Jarad, G., S. Lahke-Reddy, J. Blatnick, M. Koepke, S. Khan, M.A. El-Meanawy, A.S. O'Connor, **J.R. Sedor**, and J.R. Schelling. Renal phenotype is exacerbated in *lpr* and *Os* double mutant mice. *Kidney. Int.*, in press, 2004.

C. Research Support

ONGOING

R01 DK064719 Sedor P.I. 7/1/2003 – 6/30/2008
 “Mechanisms of Glomerulosclerosis”

Agency: NIDDK

In vitro and in vivo experiments characterize a previously undiscovered regulator of podocyte phenotype, which is part of a growing family of cell adhesion complex molecules that may translate extracellular information into altered gene expression by shuttling between cytoplasm and nucleus.

T32 DK 07474 Sedor PI 7/1/2004 – 12/31/2009 (years 21-26)

Agency: NIDDK

CWRU Nephrology Training Grant

The major goals of this project are to train nephrology fellows for careers in biomedical research.

U01 DK 57329 Sedor PI 9/30/99 – 9/29/2006

Agency: NIDDK

Genetic Regulation of Renal Disease Progression (FIND: Family Investigation of Nephropathy & Diabetes Consortium)

The major goals of this project are to characterize the intermediate phenotypes of proteinuria and GFR change, and to assess linkage of genomic regions with the intermediate, quantitative phenotypes of proteinuria and GRF change.

R01 DK59997 Schelling P.I. 9/1/2002 – 8-31-2006

“Renal Disease Progression in African Americans”

Agency: NIDDK

The major goal of this grant is to determine whether African Americans are at increased genetic risk for development of progressive diabetic nephropathy.

COMPLETED

P50 DK 54178 Sedor PI 9/1/1998 – 8/31/2003

CWRU O’Brien Renal Research Center

“Regulation of mesangial cell activation by glomerular microenvironment”

Agency: NIDDK

The major goals of this center are to define molecular mechanisms of renal disease. Project 1 tests the hypothesis that cell-cell and cell-matrix interactions control mesangial cell activation.

T32 DK 07474 Sedor PI 7/1/1998 – 6/30/2003

Agency: NIDDK

CWRU Nephrology Training Grant

The major goals of this project are to train nephrology fellows for careers in biomedical research.

R01 DK54644 Iyengar PI 7/1/1998 – 6/30/2003

Agency: NIDDK

Genetic Susceptibility to end-stage renal disease

The goals of this project are to analyze candidate genes for susceptibility to diabetic nephropathy by collecting sib-pairs or other family members.

DK 38558 Sedor PI 4/1/1995 - 3/31/2002

NIDDK

Mechanisms of Glomerular Immune Injury

The major goals of this project are to define the role of resident glomerular cells in mediating progressive glomerular injury.

K08 DK02281 Schelling PI 5/1/1994 – 4/30/1999

NIDDK

Nuclear and plasma membrane angiotensin II signaling

The major goals of this project are to characterize angiotensin II-activated cytosolic and nuclear signals.