BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
Hopfer, Ulrich	Professor of Physiology & Biophysics and Medicine
eRA COMMONS USER NAME	
Uhopfer	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Goettingen, Germany	M.D.	1966	medicine
Johns Hopkins School of Medicine, MD	Ph.D.	1970	biochemistry
Harvard Medical Sch. & Mass. General Hosp.,	post-doct.	1970-71	biochemistry (medicine)
Duke University, NC	-	1985	mathematical modeling
Woods Hole Educ. Assoc., Woods Hole, MA	-	1988	imaging

A. Positions and Honors.

2002- Professor of Medicine, CWRU
1990- Director, Imaging Facility, Cystic Fibrosis Center, CWRU
1986- Professor, Physiology and Biophysics, CWRU
1983-88 Professor, Developmental Genetics and Anatomy, CWRU
1980-81 Visiting scientist, Max-Planck-Institute for Biophysics, Frankfurt, Germany
1974-83 Assistant/Associate Professor, Anatomy, Case Western Reserve University, Cleveland, Ohio
1972-74 Junior faculty, Biochemistry, Swiss Federal Institute of Technology, Zurich, Switzerland

Honors:

1983 Hoffmann-LaRoche Prize, GI Section, American Physiological Society
1976-81 Research Career Development Award
1975-76 Andrew Mellon Faculty Fellow
1998 J Am Soc Nephrol 9: 143-150 reprints as classical paper: Murer H, Hopfer U, Kinne R, Sodium/proton antiport in brush-border-membrane vesicles isolated from rat small intestine and kidney (Reprinted from Biochem J, vol 154, pg 597-604, 1976)

Professional Societies:

Ohio Physiological Society (treasurer/secretary 1995-1998) (1987), Society of General Physiologists (1984), American Physiological Society (1979), American Society for Biochemistry and Molecular Biology (1977), American Biophysical Society (1971)

Consultant/Editor/Editorial Board member:

1994-02 Associate editor, News in Physiological Sciences
1991-1998 Field editor, Pflügers Archiv, European Journal of Physiology
1981-1999 Editorial Board, Biochemical Journal
1978-93 Editorial Board, Membrane Biochemistry
1979-86 Editorial Board, American Journal of Physiology, Gastrointestinal and Liver Physiology
1986-94 Editorial Board, Archives Biochemistry and Biophysics
1981- Editorial Board, American Journal of Physiology, Cell Physiology
1975-78, 94-96 American Heart Assoc., Northeast Ohio Affiliate, NEO-Indiana Scientific Advisory Board
1978-2005 NIH ad hoc and chairing of Special Study Sections (1 to 2/year)
1979-91 Cystic Fibrosis Foundation., study section, RDP site visits,

B. Selected peer-reviewed publications (out of 151):

Ozdemir AM, Hopfer U, Erhard P, Monnier VM, Weiss MF (2005) Processing advanced glycation end product-modified albumin by the renal proximal tubule and the early pathogenesis of diabetic nephropathy. Ann N Y Acad Sci. 1043:625-36.

Zeng C, Yang Z, Wang Z, Jones J, Wang X, Altea J, Mangrum AJ, Hopfer U, Sibley DR, Eisner GM, Felder RA, Jose PA. Interaction of angiotensin II type 1 and D5 dopamine receptors in renal proximal tubule

cells. Hypertension. 2005 Apr;45(4):804-10. Epub 2005 Feb 7.
Zeng C, Hopfer U, Asico LD, Eisner GM, Felder RA, Jose PA (2005) Altered AT_1 receptor regulation of ETB receptors in renal proximal tubule cells of spontaneously hypertensive rats. Hypertension (IASH) accepted for publication
Zeng C, Wang Z., Hopfer U, Asico LD, Eisner GM, Felder RA, Jose PA (2005) AT_1 Receptor Loses the Ability to Upregulate D_1 Dopamine Receptors in Renal Proximal Tubule Cells from SHRs. Hypertension (IASH) accepted for publication
Zeng C, Wang Z, Asico LD, Hopfer U, Eisner GM, Felder RA, Jose PA. (2005) Aberrant ETB receptor regulation of AT receptors in immortalized renal proximal tubule cells of spontaneously hypertensive rats. Kidney Int. 68(2):623-31
Gorodeski GI, Hopfer U, Liu CC, Margles E. Estrogen acidifies vaginal pH by up-regulation of proton secretion via the apical membrane of vaginal-ectocervical epithelial cells. Endocrinology. 2005 Feb;146(2):816-24. Epub 2004 Oct 21.
Pinho MJ, Serrao MP, Gomes P, Hopfer U, Jose PA, Soares-da-Silva P. Over-expression of renal LAT1 and LAT2 and enhanced L-DOPA uptake in SHR immortalized renal proximal tubular cells. Kidney Int. 2004 Jul;66(1):216-26
Pedrosa R, Gomes P, Hopfer U, Jose PA, Soares-da-Silva P. Gi{alpha}3 protein-coupled dopamine D3 receptor-mediated inhibition of renal NHE3 activity in SHR proximal tubular cells is a PLC-PKC-mediated event. Am J Physiol Renal Physiol. 2004 Nov;287(5):F1059-F1066. Epub 2004 Jul 20
Kolb, Robert J., Woost, Philip G., and Hopfer, Ulrich (2004) Membrane Trafficking of Angiotensin Receptor Type 1 and Mechano-chemical Signal Transduction in Proximal Tubule Cells. *Hypertension*. 44:352-359
Zeng C, Wang D, Asico LD, Welch WJ, Wilcox CS, Hopfer U, Eisner GM, Felder RA, Jose PA. Aberrant D1 and D3 dopamine receptor transregulation in hypertension. Hypertension. 2004 Mar;43(3):654-60. Epub 2004 Jan 19.
Bertrand CA. Danahay H. Poll CT. Laboisse C. Hopfer U. Bridges RJ. Niflumic acid inhibits ATP-stimulated exocytosis in a mucin-secreting epithelial cell line. *Am J Physioly - Cell Physiology. 286(2):C247-55, 2004 Feb.*
Pedrosa Rui, Pedro Gomes, Chunyu Zeng, Ulrich Hopfer, Pedro A Jose, and Patrício Soares-da-Silva. Dopamine D3 receptor-mediated inhibition of Na+/H+ exchanger activity in normotensive and spontaneously hypertensive rat proximal tubular epithelial cells British Journal of Pharmacology (2004) 142, 1343–1353
Orosz DE, Philip G. Woost, Robert J. Kolb1, Margaret B. Finesilver, Wenwu Jin, Phyllis S. Frisa, Chee-Keong Choo, Chung-Fai Yau, Kwok-Wah Chan, Martin I. Resnick, Janice G. Douglas, John C. Edwards, James W. Jacobberger, and Ulrich Hopfer. (2004) Growth, immortalization, and differentiation potential of normal adult human proximal tubule cells. In Vitro Cellular and Developmental Biology-Animal. 2004 Jan;40(1):22-34.
Zeng C, Luo Y, Asico LD, Hopfer U, Eisner GM, Felder RA, Jose PA. Perturbation of D1 dopamine and AT1 receptor interaction in spontaneously hypertensive rats. Hypertension. 2003 Oct;42(4):787-92. Epub 2003 Aug 04.
Zeng C. Asico LD. Wang X. Hopfer U. Eisner GM. Felder RA. Jose PA. Angiotensin II regulation of AT1 and D3 dopamine receptors in renal proximal tubule cells of SHR. *Hypertension. 41:724-9, 2003*
Krug, A.W., Papavassiliou, F., Hopfer, U., Ullrich, K.J., Gekle, M. (2003) Aldosterone stimulates surface expression of NHE3 in renal proximal brush borders. Pfluegers Arch. (Eur. J. Physiol) 446: 492-496
Gross, E, Hawkins, K, Pushkin, A, Sassani, O, Dukkipati, E, Abuladze, N, Hopfer, U, and Kurtz, I. (2001) Phosphorylation of Ser982 in the sodium bicarbonate cotransporter kNBC1 shifts the HCO_3^- : Na+ stoichiometry from 3 : 1 to 2 : 1 in murine proximal tubule cells. J. Physiol. 537: 659-665
Hopfer, U (2001) A Maxwell's demon type of membrane transport: Possibility for active transport by ABC type transporters? Journal of Theoretical Biology 214, 539-547
Shu C, Shen H, Hopfer U, Smith D (2001) Mechanism of intestinal absorption and renal reabsorption of an orally active ACE inhibitor: Uptake and transport of foinopril in cell cultures. Drug Metabolism & Disposition 29: 1307-1315
Yu, P., Asico, LD, Eisner, GM, Hopfer, U, Felder, RA, Jose, PA (2000) Renal protein phosphatase 2A activity and spontaneous hypertension in rats. Hypertension 36: 1053-1058

C. Research Support.

Ongoing Research Projects:

Type: NIH PO1-HL41618-13 (PI: U. Hopfer) 6/1/00-4/30/06
Project 2 (PI: U. Hopfer)
AT2 receptor signaling in the kidney
Angiotensin II is a major hormone involved in sodium homeostasis and blood pressure regulation. The interrelationship between intrarenal and systemic angiotensin II levels as well as the roles of proximal tubular angiotensin receptors type 1 and 2 for proximal tubular sodium reabsorption are not well delineated, but are clearly very important for understanding the influence of renal sodium excretion on blood pressure. To better understand regulation of proximal tubular electrolyte transport by angiotensin II at the cellular level, we have generated new cell lines from this tubule segment and are in the process of characterizing angiotensin II-mediated signaling, particularly as it pertains to regulation of electrolyte transport. In differentiated, polarized cells, AT1 and AT2 accumulate in a central, apical area close to the primary cilium. The receptors move to the apical surface with fluid movement across the apical surface, suggesting a new paradigm of mechanochemical coupling. The new model suggests that fluid flow is sensed by the cilium and controls externalization of receptors to the apical plasma membrane. The model provides a rationale for the constitutively high intrarenal angiotensin II concentrations that have been observed in vivo. We also have generated proximal tubule cell lines from AT1a, AT2, AT1a/AT1b KO mice. These different cell models will be used to examine angiotensin receptor expression, interactions, membrane trafficking, and signaling via AT1 and AT2 receptors.

Research Projects completed during the last 3 years:

Type: grant from Cystic Fibrosis Foundation 12/1/99 - 11/30/02
Regulated exocrine secretion of mucin in a goblet cell line.
PI: Ulrich Hopfer
Many epithelial cells are specialized to synthesize large amounts of macromolecules (enzymes, mucins) that are destined for secretion into the external milieu. The macromolecules are stored inside cells in a highly condensed form in secretory granules. The secretory granules undergo a regulated process of fusion with the plasma membrane which sets in motion the process of exocytosis of the granule content and recycling of the granule membrane. To better understand the process of mucin exocytosis, we have studied the relationship between regulated granule fusion and secretion of electrolytes as a function of secretagogues in a colonic mucin producing cell line. Regulated mucin electrolyte secretion was studied by epithelial electrophysiology (quasi steady-state and impedance measurements) partitioning of the fluorescent dye FM1-43 into surface membranes, and pharmacological manipulations that affect the cellular fusion apparatus or chloride secretion.