

*DEPARTMENT OF
PHYSIOLOGY & BIOPHYSICS*

SYMPOSIUM

*“Epithelial transport, from molecules to
integrated tissue function in health and disease”*



MARCH 2, 2012

Symposium

*“Epithelial transport, from molecules to
integrated tissue function in health and disease”*

celebrating

Ulrich Hopfer, M.D., Ph.D.

Emeritus Professor
Physiology & Biophysics

Friday, March 2, 2012

*Department of Physiology and Biophysics
Case Western Reserve University
School of Medicine*

The Department of



*Physiology & Biophysics
has invited you to attend this
symposium in honor of the
accomplishments of
Ulrich Hopfer, M.D., Ph.D.
Dr. Hopfer is an internationally
recognized scientist whose academic
career spans over
35 years here at
Case Western Reserve University.*

*During this time period, he distinguished
himself for excellence in research and in teaching. Indeed,
postdoctoral fellows,
medical students, graduate students, and
undergraduates have all benefited from
his expertise.*

Adventure in Science

In 1963, I took a year off from medical school in Germany to study biochemistry in the Department of (then called) Physiological Chemistry at Johns Hopkins Medical School, supported by a Fulbright grant. The great experience during this year started a passion for research in the biomedical field. Therefore, after finishing my medical degree in Germany, I returned to the Department as a graduate student. During this time, the scientific discussions were exciting and centered around Mitchell's novel ideas of energy coupling in membranes through electrochemical gradients. I participated with the faculty in studying these physical-chemical concepts, and am very grateful to my mentors at Johns Hopkins (Lehninger, Lennarz, Thompson, and Gotterer) for providing such a supportive environment. For my post-doctoral training, Isselbacher's Gastrointestinal Unit at the Massachusetts General Hospital offered the ideal environment to test out these new concepts on vesicles of pure plasma membranes from the apical side of enterocytes. The results of these studies finally clarified the existence of secondary active transport for many nutrients and electrolytes. After a stint of two and a half years as junior faculty in Biochemistry at the Swiss Federal, I returned to the States and took a faculty position first in Anatomy and then in Physiology & Biophysics as it would allow me to pursue research in the biomedical field. During my stay in Switzerland and here at CWRU, I was blessed to have co-workers who would extend transport studies to many transporters, different types of plasma membranes, organelles (exocrine granules, cilia), and epithelial cells. Interaction with collaborators working on problems in cystic fibrosis and hypertension made my contributions relevant to human disease. I feel blessed having had wonderful co-workers and collaborators and support by NIH for over 30 years so that I could pursue my passion.

Welcome

The Department of Physiology & Biophysics is delighted to welcome you to the Symposium entitled “Epithelial transport, from molecules to integrated tissue function in health and disease.” This symposium recognizes the accomplishments of Dr. Ulrich Hopfer, a faculty member since 1974. Dr. Hopfer is an internationally recognized scientist who has distinguished himself as a scientific researcher, teacher, mentor, and advisor to students and to faculty. The impact of his contributions to the Department of Physiology & Biophysics and to the School of Medicine has assured excellence in graduate student education, postdoctoral training, and research supported through individual grants, center grants, and program project funding. Today’s symposium and festivities will highlight Dr. Hopfer’s graduate students and postdoctoral fellows from years past, as well as research collaborators.



-Dr. Carole Liedtke

SYMPOSIUM AGENDA

8:00am – 8:30am

Registration & Continental Breakfast

8:30am – 8:40am

**Welcome from Walter F. Boron, M.D., Ph.D.
-Case Western Reserve University**

8:40am – 9:20am

Robert J. Kolb, Ph.D.

-Medical University of South Carolina

Title: “The primary cilium, an organelle with single or multiple functions?”

9:20am – 10:00am

Robert C. De Lisle, Ph.D.

-University of Kansas

Title: “Intestinal pathophysiology in CF mice or, everything that can go wrong does (almost)”

10:00am—10:20am

Morning Break

(Refreshments served)

10:20am – 11:00am

Carol A. Bertrand, Ph.D.

-University of Pittsburgh

Title: “SLC26A9 interactions with wild type and mutant CFTR”

11:00am – 11:40am

Frank Thévenod, M.D., Ph.D.

-University of Witten/Herdecke

Title: “Transport and toxicity of the metal cadmium in the kidney: A tale of ionic and molecular mimicry”

11:45am – 1:15pm

Box Lunch served in T-501, T-503, E-504, & E-546

1:30pm – 2:10pm

Michael Romero, Ph.D.

–Mayo Clinic

Title: “Slc4 & Slc26 bicarbonate transporters in pRTA, glaucoma, cystic fibrosis and nephrolithiasis”

2:10pm – 2:50pm

Heini Murer, Ph.D.

–University of Zürich

Title: “Molecular mechanisms of renal phosphate handling”

2:50pm-3:10pm

Afternoon Break

(Refreshments served)

3:10pm – 3:50pm

Pedro A. Jose, M.D., Ph.D.

–University of Maryland

Title: “You are what you eat and what your parents gave you: pharmacogenomics of essential hypertension”

3:50pm – 4:00pm

Introduction of Keynote Speaker: Dr. Walter Boron

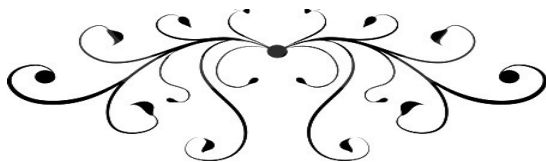
4:00—5:15pm

Keynote Speaker

William Catterall, Ph.D.

–University of Washington

Title: “Structure and function of voltage-gated sodium channels at atomic resolution”



RECEPTION AND DINNER

***CLEVELAND MUSEUM
OF
NATURAL HISTORY***

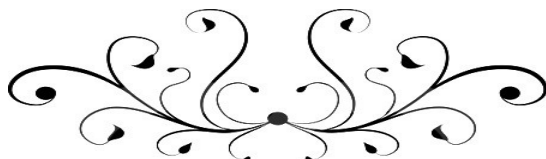
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(UNIVERSITY CIRCLE)
CLEVELAND, OH 44106***

RECEPTION

6:00PM—7:00PM

DINNER

7:00PM—9:00PM



Walter F. Boron M.D., Ph.D.
—Case Western Reserve University
Cleveland, Ohio
Cleveland, Ohio



*Dr. Boron is the David N. and Inez Myers/Antonio Scarpa Professor & Chairman of the Department of Physiology and Biophysics at Case Western Reserve University. He earned his AB in chemistry at Saint Louis University, and his M.D. and Ph.D. (Physiology & Biophysics) at Washington University in St. Louis. Dr. Boron joined Yale University as a postdoctoral fellow with Emile Boulpaep in 1978, and remained there for the next 29 years, serving as Chairman of the Department of Cellular & Molecular Physiology for three 3-year terms (1989-1998). In 2007 he returned to his hometown of Cleveland. Dr. Boron is the former President of the American Physiological Society (APS) and is currently Secretary-General of the International Union of Physiological Sciences (IUPS). He is the former editor-in-chief of *Physiological Reviews* and is the current editor-in-chief of *Physiology*. He and Emile Boulpaep co-edit the textbook *Medical Physiology*. Boron developed his life-long interest in acid-base transport and intracellular-pH regulation with his Ph.D. mentor Albert Roos as well as Paul De Weer, and his complementary interest in renal HCO_3^- transport with Boulpaep. His group currently focuses on three related areas: the molecular physiology of the Na^+ -coupled HCO_3^- transporters, molecular $\text{CO}_2/\text{HCO}_3^-$ sensors, and gas channels. Among Dr. Boron's previous honors are a Young Investigator Award (American Society of Nephrology/American Heart Association, 1986), the Robert F. Pitts Award (IUPS, 1993), the Gottschalk Award (APS, 1998), an NIH MERIT Award (2002), the Homer Smith Award (ASN, 2005), the Sharpey-Schafer Award (The Physiological Society, 2008), and the Palade Gold Medal (shared with William Catterall and Richard Tsien, Wayne State University, 2010).*

Robert J. Kolb, Ph.D.
–Medical University of South Carolina
Charleston, South Carolina



Dr. Kolb is Assistant Professor of Pediatrics at the Medical University of South Carolina in Charleston, SC. He earned a B.A. in Biology (Ecology) at Maryville University (TN) and his Ph.D. (Cell Physiology and Biochemistry) at Georgia State University in Atlanta. Dr. Kolb trained as postdoctoral fellow in Dr. Hopfer's laboratory at CWRU, starting in 2000, and in Dr. Jing Zhou's laboratory at the Renal Division of Brigham and Women's Hospital and the Department of Genetics at Harvard Medical School, starting in 2004. In 2008, Dr. Kolb moved to the Department of Pediatrics at the Medical University of South Carolina as an Assistant Professor. He now heads a new Renal Pediatric Laboratory that focuses on pediatric and adult Glomerular and Ciliary Based Diseases. Dr. Kolb's interest in basic renal function and kidney disease stem from the studies with his Ph.D. mentor Dr. Delon Barfuss, which concerned renal cisplatin reabsorption in isolated perfused kidney tubules. At the same time, he developed an interest in cilia functions, which was reinforced with his discovery in Hopfer's laboratory that the primary cilium serves as a flow sensor that modulates the trafficking of the angiotensin type-1 receptor in the proximal tubule. In Dr. Zhou's lab he worked on the role of cilia in polycystic kidney disease and demonstrated the presence of cilia on podocytes. His group now focuses on the functional significance of primary cilia in several tissue types including the epithelial cells of the kidney, endothelial cells, and osteoblasts. Dr. Kolb and his recent mentee, Dr. Taka Saigusa, developed a project that has resulted in two local young investigator awards from the Southern Society of Clinical Investigation and a finalist for the young investigator award by the National Kidney Foundation.

Robert C. De Lisle, Ph.D.
–University of Kansas
Kansas City, Kansas



Dr. De Lisle earned his B.A. in biology, cum laude, from the University of Massachusetts, Boston in 1979. Under the mentorship of Dr. Ulrich Hopfer, he earned his Ph.D. from CWRU in 1984. The topic of his dissertation was the electrolyte properties of the pancreatic zymogen granule, and a major contribution was the idea that fluid transport from the pancreatic acinar cell is coupled to protein release via electrolyte permeabilities of the granule membrane. Dr. De Lisle was then a postdoctoral fellow with Drs. Seth Hootman and John A. Williams at the University of California, San Francisco, and then with Dr. Williams at the University of Michigan, Ann Arbor. With them, he continued work on the cell biology and physiology of protein secretion, and the relationship between pancreatic duct and acinar cells in development and disease. In 1990, he joined the anatomy & cell biology faculty at the University of Kansas School of Medicine, where he is currently an associate professor (tenured). In Kansas he continued to work on protein secretion, and also on the effects of cystic fibrosis (CF) on the gastrointestinal system. Using the Cfr knockout mouse, he has investigated the consequences of CF on small intestine function. Recent work includes investigations of excessive mucus accumulation, small intestinal microbial dysbiosis, altered innate immune activity, and dysmotility in the CF gut. His work also shows that interventions to improve gut hydration (laxative) or to reduce bacterial overgrowth (antibiotics) greatly improve gut function and health in CF.

Carol A. Bertrand, Ph.D.
-University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania



Dr. Bertrand is a Research Assistant Professor in the Department of Cell Biology at the University of Pittsburgh School of Medicine. She earned her B.S. in electrical engineering at the University of Colorado, and her Ph.D. (Biophysics and Biomedical Engineering) at Case Western Reserve University in Cleveland in the laboratory of Ulrich Hopfer. Dr. Bertrand joined the University of Pittsburgh in 2000 as a postdoctoral fellow with Dr. Ray Frizzell and Dr. Bob Bridges. Her current research centers on the biosynthesis and activity of chloride channels and anion exchangers that complement and may regulate the CFTR chloride channel, as well as the apical membrane permeability to bicarbonate. Dr. Bertrand holds several patents for medical electronic devices, and continues to devote effort towards the development and refinement of methods for performing electrophysiology and live cell fluorescence microscopy.

Frank Thévenod, M.D., Ph.D.
-University of Witten/Herdecke
Witten, Germany



Dr. Thévenod is Professor and Chairman of the Institute of Physiology & Pathophysiology at Witten/Herdecke University, Germany. Thévenod earned his M.D. at Johann-Wolfgang-Goethe University in Frankfurt/Main and his Ph.D. (Cell Physiology) at Case Western Reserve University (CWRU) in Cleveland, Ohio. Dr. Thévenod was a resident in internal medicine/nephrology at Johann-Wolfgang-Goethe University, Frankfurt/Main and Hanover Medical School (Germany), and trained as a post-doctoral fellow at Max-Planck-Institute of Biophysics, Frankfurt/Main and the Department of Physiology and Biophysics at CWRU. In 1992 he returned to Germany where he became lecturer in the Department of Physiology at the University of the Saarland, Homburg. In 2000 he moved to the School of Life Sciences at the University of Manchester (United Kingdom) as a senior lecturer before obtaining his current position at Witten/Herdecke University in 2002. For almost 30 years Dr. Thévenod has been interested in membrane biology and physiology of exocrine and endocrine glands and renal epithelia. Dr. Thévenod's research on exocrine glands was initially influenced by his mentors Irene Schulz and Ulrich Hopfer. His interest in renal physiology and pathophysiology developed during his medical training with Karl M. Koch and was further stimulated by meeting the late Karl Julius Ullrich. After gaining his Habilitation in 1997, Dr. Thévenod has focused his research on membrane biology, physiology and molecular toxicology of the divalent transition metals cadmium and iron in the kidney with complimentary interests in cell death signaling and molecular carcinogenesis of toxic divalent metals.

Michael Romero, Ph.D.
–The Mayo Clinic
Rochester, Minnesota



*Dr. Romero's laboratory studies ion-solute movements across cell membranes. Membrane transporters, particularly in the kidney, account for ~10% of mammalian genomes and 50% of current drug targets. They want to understand and exploit this portion of the genome. Thus, they clone mammalian, vertebrate and invertebrate transporter SLC (SoLute Carrier) cDNAs and express the SLC proteins in *Xenopus* frog oocytes or mammalian cells. To study SLC clones, they functionally characterize the transporters using a range of strategies including electrophysiology, molecular biology, biochemistry, cell biology, whole organ, and integrative biological approaches. Generally, Dr. Romero's lab examines six issues in each project: (a) genetics/gene structure, (b) transport physiology, (c) protein localization, (d) protein structure, (e) protein - protein interactions and (f) functional roles in animal models and implications for disease. Previous studies have used *Drosophila* to elucidate function in epithelia. Recently his lab has taken advantage of the zebrafish genetic model to gain insight into the function of mammalian genes critical for renal uptake of monocarboxylates (lactate, pyruvate, short chain fatty acids, ketoacids). Presently they have cloned and analyzed function of anion transporters in the *Slc4* and *Slc26* gene families as well as the newly discovered Na^+ monocarboxylate transporters of the *Slc5* gene family.*

Heini Murer, Ph.D.
–University of Zürich
Switzerland



Professor Heini Murer was born in Beckenried (Switzerland). Dr. Murer earned his M.Sc. in Biology from the University of Fribourg (Fribourg, Switzerland) and his Ph.D. in Biochemistry at the Institute of Biochemistry of the same institution, his Ph.D. supervisor was Prof. P. Portmann. The next three years he spent as a Postdoc at the ETH Zurich at the Laboratory of Biochemistry under the tutelage of Prof. G. Semenza. From there he went in 1975 to the Max-Planck Institute in Frankfurt and joined the Renal Physiology Laboratory. In 1979 he joined the faculty of the Department of Biochemistry at the University of Fribourg as an Assistant Professor. In 1981 he moved on to professorship at the Institute of Physiology of the University of Zurich where he awarded his distinguished professorship in 1996. He was Head of Department for 8 years. From March 2006 to August 2010 Heini Murer served as Vice-president for Medicine and the Sciences at the University of Zurich. In August 2010 he became an Emeritus. Awards and prizes: Cloëtta Prize (Switzerland), Homer Smith Award (USA), Otto Nägeli Prize (Switzerland), Adolf Fick Prize (Germany), Franz Volhard Medal (Germany), Robert Berliner Lectureship (USA), Robert Pitts Memorial Lectureship (IUPS; USA), Donald W. Seldin Award (National Kidney Foundation; USA), Richard Award (ISN), Borelli Medaille (Italy) and Johann-Melchior-Wyrsch Prize (Switzerland). He is an honorary Member of the American Physiological Society, a member of the Academia Europea and the German Academy of Science Research Leopoldina.

Pedro A. Jose, M.D., Ph.D.
-University of Maryland
Baltimore, Maryland



Pedro A. Jose, M.D., Ph.D. is Professor of Medicine, University of Baltimore School of Medicine, and Adjunct Professor of Physiology and Biophysics, Georgetown University School of Medicine. Dr. Jose received his M.D. degree, magna cum laude, meritissimus, from the University of Santo Tomas, Philippines, placed first in the Philippine National Board Examinations. He received his Ph.D. degree in Physiology (dissertation defended with distinction) from Georgetown University. He was President of the American Society of Pediatric Nephrology. Dr. Jose has chaired Study Sections and Emphasis Panels of the NIH and serves on the editorial boards of several journals. His publications (>310) have been cited more than 6,000 times, with 31 cited more than 50 times, 16 of which were more than 100 times; 4 have been chosen as covers of scientific journals and 4 have been the subject of editorial commentaries. His studies have resulted in a US patent (# 6,660,474), and awards (e.g., Lewis K. Dahl Memorial, 2007 Ernest H. Starling Distinguished Lecture, and an NIH MERIT award). Dr. Jose is currently funded by seven NIH grants (three as Principal Investigator, two as Project Director in two Program Project Grants, one as Core Director in a Center Grant, and one as a collaborating investigator) and one grant from pharma. His current work investigates the pathogenesis of salt-sensitive hypertension, pharmacogenetics and pharmacogenomics of essential hypertension, gastro-renal communication, and insulin resistance. Studies range from molecular biology to integrative physiology in mice, rats, and humans. Deciphering the role of variations of the GRK4 gene in the causation of human essential hypertension was the second advance and discovery cited by the Director of the National Heart, Lung, and Blood Institute for its FY 2004 Budget Justification to the US Congress.

William Catterall, Ph.D.
–University of Washington
Seattle, Washington



Dr. Bill Catterall received a B.A. in Chemistry from Brown University in 1968, a Ph.D. in Physiological Chemistry from Johns Hopkins in 1972, and postdoctoral training in neurobiology and molecular pharmacology as a Muscular Dystrophy Association Fellow with Dr. Marshall Nirenberg at the National Institutes of Health from 1972 to 1974. Following three years as a staff scientist at NIH, he joined the University of Washington in 1977 as Associate Professor of Pharmacology, became Professor in 1981, and Chair in 1984. Dr. Catterall discovered the voltage-gated sodium and calcium channel proteins, which initiate electrical and chemical signaling in excitable cells, and his work has contributed much to understanding their structure, function, regulation, and molecular pharmacology. Dr. Catterall is a member of several science academies, including the US National Academy of Science, the Institute of Medicine, and the Royal Society of London, UK. Dr. Catterall has received numerous awards, including the Gairdner International Award of Canada in 2010.

Keynote Speaker

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