

## SABBATICAL LEAVE

### APPLICANT INFORMATION:

Name: Patrick J. Schultheis  
Department: Biological Sciences  
Office: SC 345  
Office Phone: x-5933  
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Date of initial applicant appointment to full-time faculty status: Fall 1999  
Date(s) of previous sabbatical leave(s): None

### ACADEMIC YEAR OR SEMESTER REQUESTED:

Spring semester 2009

### TITLE OF PROJECT:

Manuscript and Grant Preparation in Ion Transport Physiology and Training in Ratiometric Imaging

### SHORT PROJECT DESCRIPTION:

In this sabbatical leave application, the applicant requests a full semester in the spring of 2009 to devote to manuscript and grant preparation and to learning a sophisticated technique called ratiometric imaging, which is critical for meeting his research objectives. The applicant currently has funding through the National Institute of General Medical Sciences of NIH and the Kentucky Biomedical Research Infrastructure Network (KY-BRIN) to support his research in ion transport physiology. The basic goal of the applicant's research is to characterize five novel membrane transport proteins by determining where in the cell they are located and identifying what ion(s) they transport, both of which are necessary to understand their role in human health and disease. However, with teaching and committee responsibilities and as a supervisor of two full-time employees and undergraduate research students, the applicant has insufficient time to devote to writing papers, grants, and learning new techniques. Thus, the requested sabbatical leave will provide the applicant with large blocks of time where he can focus his efforts on writing and learning a technique critical to his research success.

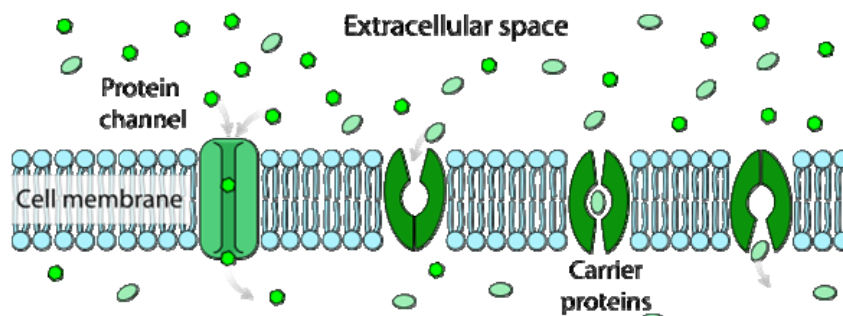
### DETAILED PROJECT DESCRIPTION:

#### Location of proposed work

Manuscript and grant writing will be carried out in the Department of Biological Sciences at NKU. The applicant will receive training in ratiometric imaging in the laboratory of Dr. Chip Montrose in the Department of Molecular and Cellular Physiology at the University of Cincinnati College of Medicine.

## Project Description

Cells represent the most basic unit of life. For cells to remain viable and carry out essential functions their internal composition must be carefully controlled. To achieve such control, cells possess a variety of membrane transport proteins that move ions such as sodium and calcium and other molecules across their membranes (figure 1). The importance of transport processes to normal cell function is underscored by the many disease states caused by mutations in genes encoding membrane transport proteins including a disease with which we are all familiar, cystic fibrosis.



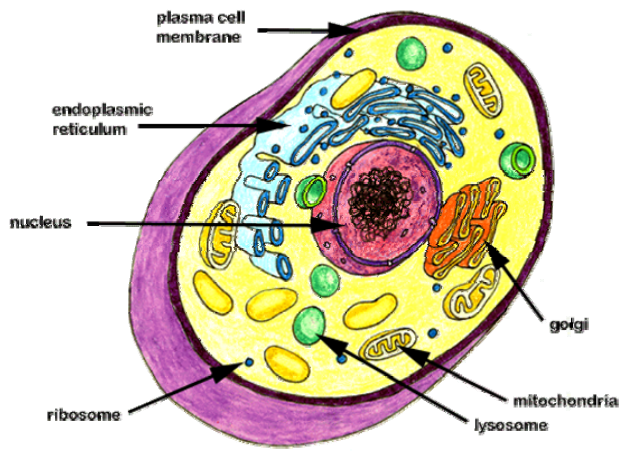
**Figure 1.** Membrane transport proteins (green) spanning the lipid bilayer or cell membrane (blue).

My work involves a specific class of membrane transport proteins called P-type ATPases. They use energy in the form of ATP to transport ions across cell membranes against their concentration gradients. P-type ATPases have been grouped into five subfamilies, termed P1-P5, based on the amino acid sequences that comprise the proteins. My lab recently identified five members of the P5 subfamily in mice, which we designated Atp13a1-Atp13a5. Our goal is to carry out a basic characterization of these transport proteins by determining where in the cell they are located and identifying what ion(s) they transport, both of which are critical if we are to develop a detailed understanding of their cellular and physiological functions. A longer term goal is to create genetically engineered mice in which the gene encoding each of the P5-ATPases is eliminated. Such animals are called “knockout mice” and serve as great research models for human disease states.

Because the P5-ATPases have been retained over evolutionary time in organisms as diverse as yeast and humans they are likely to carry out important cellular functions and possibly play an important role in human health and disease. As evidence of this, mutations in the gene encoding Atp13a2 have recently been shown to cause an inherited form of Parkinson’s disease.

I have been fortunate to receive extramural funding to carry out this work and have recently hired a research assistant (Marquita Humphries) and post-doctoral associate (Dr. Anil Kumar Chava) to work on this project along with undergraduate students. We are making major progress toward meeting our experimental aims. To aid in the localization of the transporters, antibodies have been raised against peptides of each P5-ATPase. Moreover, we have engineered cells to express GFP (green fluorescent protein) tagged versions of each P5-ATPase. Fluorescence microscopy data generated by Ms. Humphries, Dr. Chava, and undergraduate student Jared Patton show that Atp13a1 localizes to the endoplasmic reticulum. Others have

shown that Atp13a2 resides in the lysosome (figure 2). Interestingly, both of these intracellular organelles are involved in protein processing and degradation, processes which are often



**Figure 2.** Schematic of a cell showing the plasma membrane and membrane bound organelles.

defective in various neurodegenerative disorders. Dr. Chava has also purified the Atp13a1 protein and we are ready to begin biochemical studies aimed at identifying which ion it transports.

We have also generated Atp13a1 knockout mice and are in the process of generating Atp13a2 knockout mice. The Atp13a1 knockout is not born live and dies sometime between 9 and 21 days gestation. Nonetheless, a great deal about the physiological function of Atp13a1 can be learned from histological examination of the fetuses. It is anticipated that the Atp13a2 knockout will be born live and serve as an excellent research model for Parkinson's disease.

Since hiring Ms. Humphries and Dr. Chava, the project has proceeded at an accelerated pace. As a result of this increased productivity I am requesting sabbatical leave to prepare manuscripts for publication and complete a grant renewal application so the work can continue to be funded. I also will spend time in the laboratory of Dr. Chip Montrose in the Department of Molecular and Cellular Physiology at the University of Cincinnati College of Medicine to gain expertise in ratiometric imaging, a powerful technique for measuring ion transport in live cells. This technique is critical for identifying which ion(s) the P5-ATPases transport. The requested sabbatical leave will provide the applicant with large blocks of time where he can focus his efforts on writing and learning a technique critical to his research success.

#### Impact of project on undergraduate research experiences

The Department of Biological Sciences has traditionally had a very strong undergraduate research program, particularly in the areas of ecology and environmental science. However, when I was hired at NKU as a molecular biologist in 1999 biomedical research in the department was somewhat limited. One of my goals was to increase the biomedical research capacity of the department by obtaining extramural funding to support my research in ion transport physiology and provide additional students with biomedical research experiences. I have been fortunate to have some success in these endeavors having received two NIH AREA (R15) awards and two awards through the Kentucky Biomedical Research Infrastructure Network (KY-BRIN). Since arriving at NKU, I have provided stipends for about three undergraduate students per summer and have had at least one undergraduate student per semester carry out research in the lab during the academic year. In the course of participating in the projects, students were introduced to and gained skills in a wide variety of molecular and cell biology techniques and presented their findings at local and regional meetings. In addition, seven former undergraduate research students have entered Ph.D. programs in molecular biology/biochemistry fields. To continue to

provide undergraduates with biomedical research experiences it is imperative that manuscripts be published in peer reviewed journals in order for future grant applications to be competitive.

#### VALUE OF THE PROJECT:

The sabbatical leave will be of value to my professional growth and status because it will increase my scholarly activity with respect to publications and extramural grant funding. As a consequence, my standing in the scientific community, particularly in the field of ion transport physiology will improve. Moreover, the leave should greatly enhance my chances of acquiring additional grant monies since the key to obtaining extramural funding from granting agencies such as NIH and NSF is adequate preliminary data and a strong publication record. The scholarly community will benefit because the P5-ATPases, though present in organisms as diverse as yeast, fish and humans, have been understudied. Dissemination of my research results on the basic function of the mammalian P5-ATPases in scientific journals should spur other members of the scientific community to direct some of their resources into the investigation of these transport proteins and lead to additional insights into their role in human health and disease. Along these lines, interest in Atp13a2, a member of the P5-ATPase subfamily, has greatly increased since a recent publication showing that mutations in the gene encoding this protein result in an inherited form of Parkinson's disease.

Because I often incorporate aspects of my own work into my lectures, students in the classroom will benefit from "real world" applications of research and better appreciate how significant basic cellular processes such as ion transport are to human health and disease. Moreover, the inclusion of students as co-authors on my manuscripts will also greatly enhance their chances of obtaining positions in industry, graduate or professional school. The University will be positively impacted by an increase in my scholarly activity and by indirect costs brought into the University through successful extramural grant applications. Success of my undergraduate research students should also enhance the reputation of the University and is likely to encourage talented high school students to seriously consider NKU as a viable option for their undergraduate work. Finally, the nonscientific community may benefit since insights into the basic function of the P5-ATPases may lead to a better understanding of disease states such as Parkinson's and possibly lead to novel treatments.

#### 8. GOALS AND CRITERIA:

The goals of the sabbatical leave are straightforward. I intend to submit two papers based on work completed in the 2007 and 2008 calendar years. The papers will be submitted to quality journals such as the Journal of Biological Chemistry or the Journal of Cell Science. A NIH R15 or R01 grant application will also be submitted to acquire funds to support my research efforts and to pay the salaries of undergraduate research students, my research assistant Marquita Humphries and post-doctoral associate Dr. Anil Kumar Chava. Time will also be spent in the laboratory of Dr. Chip Montrose in the Department of Molecular and Cellular Physiology at the University of Cincinnati College of Medicine to gain expertise in ratiometric imaging, a powerful technique for measuring ion transport in live cells using ion sensitive fluorescent dyes and a high speed digital imaging system. Such expertise is important for meeting some of our experimental objectives, most importantly of which is to identify the actual ion(s) transported by the P5-ATPases.

Based on these goals, evidence for submission of manuscripts and a grant application, as well as correspondence between me and Dr. Montrose will serve as the criteria by which the success of my sabbatical leave is measured.

#### OTHER SUPPORT AND COMMITMENTS:

My current research support includes:

Characterization of the P5 Subfamily of P-type Transport ATPases in Mice  
NIH AREA Grant (R15) Award  
Award Type: Research Grant  
Role: Principal Investigator  
Project Period 3/1/2007 - 2/28/2009. Total Amount: \$150,000 (direct costs)

Characterization of Putative Magnesium-Transporting P-type ATPases  
NIH/NCRR-IDEA Networks of Biomedical Research Excellence Program (INBRE) Award  
Award Type: Research Grant  
Role: Principal Investigator  
Project Period 8/5/04 – 6/30/09 Total Amount: \$831,515 (direct costs)

Biology and Chemistry Interdisciplinary Summer Undergraduate Research Experience (iSURE)  
at Northern Kentucky University  
Merck/AAAS Undergraduate Science Research Program Grant  
Award Type: Research Grant  
Role: Senior Faculty on proposal Principal Investigator: Heather Bullen  
Project Period: 5/1/2005 – 8/31/2007 Total Amount: \$60,000

#### BACKGROUND OF APPLICANT RELEVANT TO THIS PROJECT:

The applicant received a Ph.D. in Molecular Biology from the Department of Molecular Genetics, Biochemistry and Microbiology at the University of Cincinnati College of Medicine in 1993 and carried out post-doctoral work in the same department for 5 years. He has been employed as an Assistant or Associate Professor in the Department of Biological Sciences at NKU since the fall of 1999.

The applicant has 18 years of research experience in the molecular biology of ion transport proteins including the Na,K-ATPase, Na/H exchangers, NaCl cotransporter, and members of the P5 subfamily of P-type transport ATPases. Moreover, he has 32 peer reviewed publications in this research area.

The applicant has secured continuous grant support for his research since being hired as an Assistant Professor at NKU in the fall of 1999.

The applicant teaches Genetics, Molecular and Cell Biology I and II (Bio 348 and Bio 349) and Advanced Molecular Biology (Bio 400) all of which involve topics relevant to his research.

PREVIOUS FBC AWARDS:

None

**Curriculum Vitae**  
**Patrick J. Schultheis, Ph.D.**

**Business Address:**

Department of Biological Sciences  
Northern Kentucky University  
Nunn Drive  
Highland Heights, KY 41099  
Phone: (859)-572-5933 (office), (859)-572-1471 (lab)  
FAX: (859) 572-5639  
Email: [Schultheisp@nku.edu](mailto:Schultheisp@nku.edu)  
Web page: <http://www.nku.edu/~schultheisp/>

**Home Address:**

1238 Meriweather Ave.  
Cincinnati, OH 45208  
Phone: (513)-533-3076

**Education:**

- 1984 B.S., Biology, (graduated *Summa Cum Laude*)  
University of Dayton, Dayton, Ohio
- 1986 M.S., Biology, University of Dayton, Dayton, Ohio  
Thesis Title: Antibody Response to Pyocin S2 in *Pseudomonas aeruginosa*  
Infected Mice.
- 1994 Ph.D., Molecular Genetics, Biochemistry, and Microbiology,  
University of Cincinnati, Cincinnati, Ohio  
Dissertation Title: Identification and Characterization of Amino Acid  
Determinants of Ouabain Sensitivity in the Na,K-ATPase  $\alpha$  Subunit.

**Post-doctoral Training:**

- 1994-1999 University of Cincinnati College of Medicine, Laboratory of Dr. Gary Shull.  
Research Project: Development of Animal Models for Genetic Diseases  
Involving Renal and Intestinal Epithelial Na<sup>+</sup> Transporters. Program of  
Excellence Investigator.

**Primary Appointments:**

- 1999-2005 Assistant Professor, Department of Biological Sciences, Northern Kentucky  
University, Highland Heights, Kentucky
- 2005-present Associate Professor, Department of Biological Sciences, Northern Kentucky  
University, Highland Heights, Kentucky

**Professional Societies:** Kentucky Academy of Sciences  
American Association for the Advancement of Science

Tri-Beta (Biology Honor Society)  
Sigma Xi  
Council on Undergraduate Research (CUR)

### Research Interests:

My general interest is in the molecular biology of ion transport. More specifically, I am characterizing members of the P<sub>5</sub> subfamily of P-type ATPases with respect to their ion specificity, cell-type specific expression, and membrane location. DNA microarray technology is also being used to identify novel genes involved in magnesium homeostasis (such as transporters of this biologically important cation) and disease states associated with magnesium deficiency.

### Grants Awarded:

- 2006 NIH AREA Grant (R15) Award: Characterization of the P5 Subfamily of P-type Transport ATPases in Mice. P.I., Patrick Schultheis. Project Period 3/1/2007 - 2/28/2009. \$150,000 NIH/National Institute of General Medical Sciences R15 GM079608-01
- 2005 Merck/AAAS Undergraduate Science Research Program Grant: Biology and Chemistry Interdisciplinary Summer Undergraduate Research Experience (iSURE) at Northern Kentucky University. P.I., Heather Bullen. Senior Faculty on Proposal, Patrick Schultheis. Project Period, 5/1/2005 – 8/31/2007. \$60,000
- 2005 Kentucky NSF EPSCoR Research Enhancement Grant: Investigating Custom Dendrimer Interactions with Blood Brain Barrier Models. P.I., Kristi Martines. Co-P.I., Patrick Schultheis (1 summer month from 2005). Project Period 5/1/2005-8/31/06. \$22,479
- 2004 NIH/NCRR-IDEA Networks of Biomedical Research Excellence Program (INBRE) Award: Characterization of Putative Magnesium-Transporting P-type ATPases. Sub-Project Director, Patrick Schultheis. Project Period 8/5/04 – 6/30/09 \$831,515 (direct costs)
- Note: This is a subcontract award of the Kentucky Biomedical Research Infrastructure Network INBRE Program. This program provides support for research, teaching, and outreach in the biomedical sciences at regional universities in Kentucky. P.I., Nigel Cooper, University of Louisville. NIH/NCRR P20 RR16481-06
- 2003-2004 Center for Integrative Natural Science and Mathematics Research Award: Genetic Diversity Within and Among Populations of Cicada Killer Wasps. P.I. Jon Hastings, Co-investigators: Patrick Schultheis, Greg Dahlem, \$17,717.
- 2002 NIH AREA Grant (R15) Award: Magnesium Deficiency: A Global Gene Expression Study. P.I., Patrick Schultheis. Project Period 9/1/2002 - 8/31/2005. \$129,000 NIH/NIDDK R15 DK61940-01
- 2001-2002 KBRIN (Kentucky Biomedical Research Infrastructure Network) Award: Molecular Biology and Bioinformatics at NKU (P.I., Phil Schmidt; Co-P.I.s, Patrick Schultheis, Diana McGill, Gary Newell), \$175,788
- 2001-2002 KBRIN Supplement Award: Neurobehavioral Effects of Magnesium Deficiency in Mice (P.I., Mark Bardgett; Co-P.I., Patrick Schultheis), \$ 95,443

- 2001-2002 Center for Integrative Natural Science and Mathematics Research Award: Novel Actions of Antipsychotic Drugs on Hippocampal Function in Mice (Project Directors, Mark Bardgett and Patrick Schultheis), \$24,869
- 2001-2002 Center for Integrative Natural Science and Mathematics Research Award: A Collaborative Study of Magnesium Deficiency on Brain Serotonin Levels and Patterns of Behavior of Mice (Project Director, Ray Richmond; Co- project directors, Patrick Schultheis, Mark Bardgett, Diana McGill), \$34,000
- 2001 CUR Undergraduate Research Summer Fellowship. Identification of Novel Genes Involved in Magnesium Homeostasis: A Differential Expression Study (Patrick Schultheis), \$4,000
- 2000-2001 Center for Integrative Natural Science and Mathematics Research Award: DNA and Biotechnology Workshop for Teachers (Patrick Schultheis and Jon Hastings), \$13,810
- 2000-2001 Center for Integrative Natural Science and Mathematics Research Award: Involvement of Undergraduate Students in the Multidisciplinary Cell and Molecular Biology Research Program(Ray Richmond, Diana McGill, and Patrick Schultheis), \$35,000
- 1999-2000 Center for Integrative Natural Science and Mathematics Research Award: Identification of Novel Genes Involved in Magnesium Homeostasis by DNA Microarray Analysis (Co-PIs: Patrick Schultheis and Diana McGill), \$33,498
- 1999-2000 Center for Integrative Natural Science and Mathematics Research Award: Development of a Multidisciplinary Molecular and Cellular Biology Research Program (Project Director: Ray Richmond; Co- investigators, Patrick Schultheis and Diana McGill), \$35,068
- 1999-2000 Center for Integrative Natural Science and Mathematics Research Award: Enhancement of Multidisciplinary Laboratory Experiences: Using Light Absorbance as a Tool (Project Director: Diana McGill; co-investigator, Patrick Schultheis), \$20,000
- 1999 Kentucky Academy of Sciences Special Research Award: Cloning and Developmental Expression of a Putative Magnesium Transporter in *Dictyostelium discoideum* (P.I., Patrick Schultheis), \$13,000

**Other Awards:**

- 1995-1998 New Investigator Fellowship, Program of Excellence in Molecular Biology, University of Cincinnati College of Medicine
- 1988-1993 Full Graduate Tuition Fellowship, University of Cincinnati College of Medicine
- 1984-1986 Full Graduate Tuition Fellowship, University of Dayton
- 1985-1986 Summer Research Fellowships, University of Dayton
- 1985 Sigma Xi Grant-in-Aid of Research

**Departmental/University Service:**

University Benefits Committee  
 Member of Pre-Med Advisory Board  
 Chair, IACUC Committee (Institutional Animal Care and Use Committee)  
 Co-coordinator of Department of Biological Sciences Seminar Series  
 Departmental Scholarship Committee

Departmental Equipment Committee  
2004 Departmental Retreat Committee  
Environmental Toxicologist Search Committee  
Geneticist Search Committee  
Microbiologist Search Committee  
Computational Biologist Search Committee  
Reappointment, Promotion, and Tenure Committee  
Departmental Executive Committee  
Physiology/Neurobiology Search Committee (Chair)  
Departmental RPT Committee

**Other Service:**

President of NKU Chapter of Sigma Xi (national research honor society)  
Secretary of NKU Chapter of Sigma Xi  
Secretary of the Cell and Molecular Biology Section of the Kentucky Academy of Sciences

**Publications:**

Bardgett, M. E., Schultheis, P. J., Muzny, A., Riddle, M. D., & Wagge, J. R. (In press). Fear-induced conditioned lick suppression is reduced in magnesium-deficient mice. *Magnesium Research*.

Bardgett ME, **Schultheis PJ**, McGill DL, Richmond RE, Wagge JR. Magnesium deficiency impairs fear conditioning in mice. *Brain Res*. 2005 Mar 15;1038(1):100-6.

Noonan WT, Woo AL, Nieman ML, Prasad V, **Schultheis PJ**, Shull GE, Lorenz JN. Blood pressure maintenance in NHE3-deficient mice with transgenic expression of NHE3 in small intestine. *Am J Physiol Regul Integr Comp Physiol*. 2005 Mar;288(3):R685-91.

**Schultheis PJ**, Hagen TT, O'Toole KK, Tachibana A, Burke CR, McGill DL, Okundade GW, Shull GE. Characterization of the P<sub>5</sub> subfamily of P-type transport ATPases in mice. *Biochem. Biophys. Res. Comm.* 323: 731-738, 2004.

Bachmann O, Riederer B, Rossmann H, Groos S, **Schultheis PJ**, Shull GE, Gregor M, Manns MP, Seidler U

The Na<sup>+</sup>/H<sup>+</sup> exchanger isoform 2 is the predominant NHE isoform in murine colonic crypts and its lack causes

NHE3 upregulation. *Am J Physiol Gastrointest Liver Physiol*. 287: G125-33, 2004.

Woo AL, Noonan WT, **Schultheis PJ**, Neumann JC, Manning PA, Lorenz JN, Shull GE. Renal function in NHE3-deficient mice with transgenic rescue of small intestinal absorptive defect. *Am J Physiol Renal Physiol*. 284: F1190-8, 2003.

Miller ML, Judd LM, Van Driel IR, Andringa A, Flagella M, Bell SM, **Schultheis PJ**, Spicer Z, Shull GE. The unique ultrastructure of secretory membranes in gastric parietal cells depends upon the presence of H<sup>(+)</sup>,K<sup>(+)</sup>-ATPase. *Cell Tissue Res*. 309:369-80, 2002.

- Gawenis LR, Stien X, Shull GE, **Schultheis PJ**, Woo AL, Walker NM, Clarke LL. Intestinal NaCl transport in NHE2 and NHE3 knockout mice. *Am J Physiol Gastrointest Liver Physiol.* 282: G776-84, 2002.
- Ledoussal C, Lorenz JN, Nieman ML, Soleimani M, **Schultheis PJ**, Shull GE. Renal salt wasting in mice lacking NHE3 Na(+)/H(+) exchanger but not in mice lacking NHE2. *Am J Physiol Renal Physiol.* 281: F718-27, 2001.
- Park K, Evans RL, Watson GE, Nehrke K, Richardson L, Bell SM, **Schultheis PJ**, Hand AR, Shull GE, Melvin JE. Defective fluid secretion and NaCl absorption in the parotid glands of Na<sup>+</sup>/H<sup>+</sup> exchanger-deficient mice. *J Biol Chem.* 276: 27042-50, 2001
- Mennone A, Biemesderfer D, Negoianu D, Yang CL, Abbiati T, **Schultheis PJ**, Shull GE, Aronson PS, Boyer JL. Role of sodium/hydrogen exchanger isoform NHE3 in fluid secretion and absorption in mouse and rat cholangiocytes. *Am J Physiol Gastrointest Liver Physiol.* 280: G247-54, 2001.
- Brooks HL, Sorensen AM, Terris J, **Schultheis PJ**, Lorenz JN, Shull GE, Knepper MA. Profiling of renal tubule Na<sup>+</sup> transporter abundances in NHE3 and NCC null mice using targeted proteomics. *J Physiol.* 530: 359-66, 2001.
- Boivin GP, **Schultheis PJ**, Shull GE, Stemmermann GN. Variant form of diffuse corporal gastritis in NHE2 knockout mice. *Comp Med.* 50: 511-5, 2000.
- Lee MG, Ahn W, Choi JY, Luo X, Seo JT, **Schultheis PJ**, Shull GE, Kim KH, Muallem S. Na(+)-dependent transporters mediate HCO<sub>3</sub>(-)<sup>3</sup> salvage across the luminal membrane of the main pancreatic duct. *J Clin Invest.* 105: 1651-8, 2000.
- Choi JY, Shah M, Lee MG, **Schultheis PJ**, Shull GE, Muallem S, Baum M. Novel amiloride-sensitive sodium-dependent proton secretion in the mouse proximal convoluted tubule. *J Clin Invest.* 105: 1141-6, 2000.
- Shull, G.E., Miller, M.L., **Schultheis, P.J.** Lessons from genetically engineered animal models: absorption and secretion of ions in the gastrointestinal tract. *Am J Physiol. Gastrointest Liver Physiol.* 278: G185-90, 2000. Review.
- Evans, R.L., Bell, S.M., **Schultheis, P.J.**, Shull, G.E., and Melvin, J.E. Targeted disruption of the Nhe1 gene prevents muscarinic agonist-induced up-regulation of Na(+)/H(+) exchange in mouse parotid acinar cells. *J Biol Chem.* 274: 29025-29030, 1999.
- Lorenz J.N., **Schultheis P.J.**, Traynor T., Shull G.E., Schnermann, J. Micropuncture analysis of single-nephron function in NHE3-deficient mice. *Am J Physiol.* 277:F447-F453, 1999.
- Wang T., Yang C.L., Abbiati T., **Schultheis P.J.**, Shull G.E., Giebisch G., Aronson P.S. Mechanism of proximal tubule bicarbonate absorption in NHE3 null mice. *Am J Physiol.* 277:F298-302, 1999.
- Melvin J.E., Park K., Richardson L., **Schultheis P.J.**, Shull G.E. Mouse down-regulated in adenoma (DRA) is an intestinal Cl(-)/HCO<sub>3</sub>(-)<sup>3</sup> exchanger and is up-regulated in colon of mice lacking the NHE3 Na(+)/H(+) exchanger. *J Biol Chem.* 274:22855-61, 1999.
- Nakamura S., Amlal H., **Schultheis P.J.**, Galla J.H., Shull G.E., Soleimani M. HCO<sub>3</sub>-3 reabsorption in renal collecting duct of NHE-3-deficient mouse: a compensatory response. *Am J Physiol.* 276:F914-21, 1999.

Bell, S.M., Schreiner, C.M., **Schultheis, P.J.**, Miller, M.L., Evans, R.L., Vorhees, C.V., Shull, G.E., and Scott, W.J. Targeted Disruption of the Murine NHE1 Locus Induces Ataxia, Growth Retardation, Seizures, and Increased Mortality. *Am. J. Physiol.* 276: C788-C795, 1999.

Baird, N.R., Orlowski, J., Szabo, E.Z., Zaun, H.C., **Schultheis, P.J.**, Menon, A.G., and Shull, G.E. Molecular Cloning, Genomic Organization, and Functional Expression of Na<sup>+</sup>/H<sup>+</sup> Exchanger Isoform 5 (NHE5) from Human Brain. *J. Biol. Chem.* 274: 4377-4382, 1999.

**Schultheis, P.J.**, Lorenz, J., Meneton, P., Riddle, T.M., Duffy, J., Doetschman, T., Flagella, M., Nieman, M., Miller, M.L., and Shull, G.E. Phenotype Resembling Gitelman's Syndrome in Mice Lacking the Apical Na<sup>+</sup>-Cl<sup>-</sup> Cotransporter of the Distal Convolute Tubule. *J. Biol. Chem.* 273:29150-29155, 1998.

Lee, M.G., **Schultheis, P.**, Shull, G., Bookstein, C., Chang, E., Donowitz, M., Park, K., Muallem, S. Membrane Limited Expression, and Regulation of Na<sup>+</sup>-H<sup>+</sup> Exchanger Isoforms by P<sub>2</sub> Receptors in the Rat Submandibular Duct. *J. Physiol. (London)* 513: 341-357, 1998.

**Schultheis, P.J.**, Clarke, L.L., Meneton, P., Miller, M.L., Harline, M., Soleimani, M., Riddle, T., Duffy, J.J., Doetschman, T., Wang, T., Giebisch, G., Aronson, P.S., Lorenz, J., and Shull, G.E. Renal and Intestinal Absorptive Defects in Mice Lacking the NHE3 Na<sup>+</sup>/H<sup>+</sup> Exchanger. *Nature Genet.* 19: 282-285, 1998.

**Schultheis, P.J.**, Clarke, L.L., Meneton, P., Harline, M., Boivin, G.P., Stemmermann, G., Duffy, J.J., Doetschman, T., Miller, M.L., and G.E. Shull. Targeted Disruption of the Murine Na<sup>+</sup>/H<sup>+</sup> Exchanger Isoform 2 Gene Causes Reduced Viability of Gastric Parietal Cells and Loss of Net Acid Secretion. *J. Clin. Invest.* 101: 1243-1253, 1998.

Meneton, P., **Schultheis, P.J.**, Greeb, J., Nieman, M., Liu, L.H., Clarke, L.L., Duffy, J.J., Doetschman, T., Lorenz, J.N., and G.E. Shull. Increased Sensitivity to K<sup>+</sup> Deprivation in Colonic H,K-ATPase-Deficient Mice. *J. Clin. Invest.* 101:536-542, 1998.

Wang, Z., **Schultheis, P.J.**, and Shull, G. Three N-terminal Variants of the AE2 Cl<sup>-</sup>/HCO<sub>3</sub><sup>-</sup> Exchanger are Encoded by mRNAs Transcribed from Alternative Promoters. *J. Biol. Chem.* 271: 7835-7843, 1996.

Johnson, C. L., **Schultheis, P.J.**, Lingrel, J. B., Johnson, C. G., and Wallick, E.T. Comparison of the Effects of Potassium on Ouabain Binding to Native and Site-directed Mutants of Na, K-ATPase. *Arch. Biochem. Biophys.* 317: 133-141, 1995.

**Schultheis, P.J.**, Wallick, E.T., and Lingrel, J.B. Kinetic Analysis of Ouabain Binding to Native and Mutated Forms of Na,K-ATPase and Identification of a New Region Involved in Cardiac Glycoside Interactions. *J. Biol. Chem.* 268: 22686-22694, 1993.

**Schultheis, P.J.** and Lingrel, J.B. Substitution of Transmembrane Residues with Hydrogen Bonding Potential in the  $\alpha$  Subunit of Na,K-ATPase Reveals Alterations in Ouabain Sensitivity. *Biochem.* 32: 544-550, 1993.

#### **Genebank Submissions:**

Accession Numbers BK005557 and BK005558 – third party annotations of *Atp13a3* and *Atp13a4* genes

#### **Gene Nomenclature:**

Submitted official names for mouse *Atp13a1-Atp13a5* genes to the Mouse Genomic Nomenclature Committee

#### **Abstracts/Poster/Oral Presentations:**

Schultheis PJ, Hagen TT, \*O'Toole KK, Tachibana A, \*Burke CR, McGill DL, Okunade GW, Shull GE  
Characterization of the P5 subfamily of P-type Transport ATPases in Mice. KAS Annual Meeting,  
Murray State University, November 2004

Boyce, R, Miller, C, Hagen, T and Schultheis, PJ. DNA Microarray Analysis of Liver Gene Expression  
Profiles in Magnesium Deficient Mice, Poster Presentation, UT-ORNL\_KBRIN Bioinformatics Summit,  
April 1-3, 2005, Lake Barkley State Park, Cadiz, KY.

Localization of Atp13a1-GFP and Atp13a2-GFP Fusion Proteins. J. Walter, R. Baldrige, D.R. Hahn,  
C.R. Burke, P.M. Gulleman, D.L. McGill, K.H. Martines and P.J. Schultheis. 2006 National IDEa  
Symposium of Biomedical Research Excellence (NISBRE), Washington, D.C.

### **Conferences Attended (did not present):**

2006 Lingrel Symposium. University of Cincinnati College of Medicine, Cincinnati, Ohio. Themes  
included Membrane Transport, Signaling and Gene Regulation and Development. Speakers included  
Nobel Laureates Peter Agre and Timothy Hunt.

### **Invited Presentations/Lectures:**

Applications of DNA chip and microarray technology. Presented at local Tri-Beta chapter initiation meeting,  
Northern Kentucky University. Fall 99.

A chip off the old DNA block: applications of DNA chip and microarray technology. Local Sigma Xi  
lecture series, Northern Kentucky University, February 2000.

Invited speaker at NIH AREA Grant Writing Workshop. 2003 Kentucky Academy of Sciences Meeting,  
Western Kentucky University, Bowling Green Kentucky

Guest lecture on magnesium homeostasis for graduate course in Molecular Physiology, Department of  
Zoology, Miami University, Oxford, Ohio, Spring 2004.

Guest lecture on magnesium homeostasis for graduate course in Molecular Physiology, Department of  
Zoology, Miami University, Oxford, Ohio, Spring 2005.

### **Courses Taught:**

Bio 202	Microbiology for Health Professionals
Bio 202L	Microbiology for Health Professionals Lab
Bio 150L	Introductory Biology: Lab
Bio 150R	Introductory Biology: Recitation
Bio 400	Advanced Molecular Biology
Bio 400 L	Advanced Molecular Biology Lab
Bio 340	Principles of Research
Bio/Che 482	Biochemistry Lab
Bio 120L	General Biology Lab (nonmajors)
Bio 348	Genetics, Molecular and Cell Biology I
Bio 349	Genetics, Molecular and Cell Biology II
Bio 349L	Genetics, Molecular and Cell Biology Lab

### **Undergraduate Research Mentoring:**

Numerous students have earned research credit (Bio 399, Techniques in Biology and/or Bio 492, Directed Research) under my supervision during the semester or have carried out research in my lab during the summer. Two others have completed their Honors Theses in my lab and several have presented their findings at regional meetings. In addition, several of my former research students are currently attending graduate or medical school.

### **Student Abstracts/Research Presentations:**

\*denotes student presenter

1. Cloning and Developmental Expression of a Putative Magnesium Transporter in *Dictyostelium discoideum*. Rachel DiTrapani, Emily McElhinney, Kenny Jones, and \*Brian Dundas. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Poster. Presented at KAS 2000 Meeting, University of Kentucky, Lexington, KY.
2. Cloning and Developmental Expression of a Putative Magnesium Transporter in *Dictyostelium discoideum*. \*Brian Dundas. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Poster. Presented at regional Tri-beta meeting in New Orleans, LA, spring 2001. **(note: Brian won first place in the poster competition).**
3. Magnesium Deficiency: A Global Gene Expression Study. \*Rachel DiTrapani and Tamara Hagen. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Poster. Presented at 2001 KAS/TAS meeting Murfreesboro, TN.
4. Magnesium Deficiency: A Global Gene Expression Study. \*Rachel DiTrapani and Tamara Hagen, Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Poster. 2002 Posters on the Capitol, Frankfort, KY
5. Magnesium Deficiency: A Global Gene Expression Study. \*Tamara Hagen and Rachel DiTrapani. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Poster. 2002 CUR Poster on the Hill, Washington D.C. **(note: Tamara was one of only 60 students nationwide selected to present their work)**
6. Identification of a Putative Magnesium Transporting P-type ATPase. \*Alicia Blaker. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Oral Presentation. 2002 Kentucky Academy of Sciences Meeting, Northern Kentucky University, Highland Heights, KY.
7. Identification of a Putative Magnesium Transporting P-type ATPase. \*Tamara Hagen and Alicia Blaker. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Oral Presentation. Celebration of Student Research and Creativity, Spring 2003, Northern Kentucky University, Highland Heights, KY.
8. Characterization of Antibodies Raised Against Synthetic Peptides of a Novel P-type ATPase. \*Kate O'Toole. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Poster Presentation. Posters at the Capitol, January 2004, Frankfort, Kentucky.
9. Characterization of Antibodies Raised Against Synthetic Peptides of a Novel P-type ATPase. \*Kate O'Toole. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Poster Presentation. Tri-beta, Regional Conference (2004), Memphis, TN.
10. Characterization of Antibodies Raised Against Synthetic Peptides of a Novel P-type ATPase. \*Kate O'Toole. Sponsored by Patrick J. Schultheis of the Department of Biological Sciences. Tri-beta, National Convention (2004), Mesa State University, Grand Junction, CO. **(won Brooks Award, given to the top oral presentation)**

11. Western Blot Analysis of a Putative P-type ATPase Magnesium Transporter. O'Toole, KK. Senior Honors Thesis Presentation, Celebration of Student Research and Creativity, Northern Kentucky University, Highland Heights, KY, April 2004.
12. Genomic Organization and Primary Structure of a Novel Family of P-type ATPases. O'Toole, KK. KAS Annual Meeting, Murray State University, November 2004. **3rd place poster Life Sciences section**
13. Genomic Organization and Primary Structure of a Novel Family of P-type ATPases. O'Toole, KK. 2005 Celebration of Student Research and Creativity, Northern Kentucky University, April 2005. Faculty sponsor, Patrick Schultheis.
13. The Use of Randomly Amplified DNA Fingerprinting to Evaluate the Relationship Between Eastern and Western Cicada Killer Wasps. David Hahn, Jack Defevers, Angela Mendell. KAS Annual Meeting, Murray State University, November 2004. Faculty Mentors: Jon Hastings, Patrick Schultheis. **(2<sup>nd</sup> place oral presentation in Cell and Molecular Biology Section)**
14. The Use of Randomly Amplified DNA Fingerprinting to Evaluate the Relationship Between Eastern and Western Cicada Killer Wasps. David Hahn, Jack Defevers, Angela Mendell. 2005 Celebration of Student Research and Creativity, Northern Kentucky University, April 2005. Faculty sponsors: Jon Hastings, Patrick Schultheis.
15. Localizing a Novel Ion Transporter in the Rat Brain. Katie Clark and Kyle Minor. 2005 Celebration of Student Research and Creativity, Northern Kentucky University, April 2005. Faculty sponsors: Kristi Martines, Patrick Schultheis.
16. Analysis of P<sub>5</sub>-ATPase Gene Expression in Mouse Brain by In Situ Hybridization. David Hahn and Chuck Burke. 2005 Merck/AAAS Interdisciplinary Summer Research Celebration. Department of Biological Sciences, Chemistry, Physics and Geology, and Psychology, Northern Kentucky University. September 2005. **(won 2<sup>nd</sup> place award in poster competition).**
17. Use of Tagged Expression Constructs to Characterize the Intercellular Location and Ion Specificity of Five Novel P<sub>5</sub>-type ATPases. David R. Hahn, Pete M. Gulleman, Charles R. Burke, and Heather J. Meeks. Northern Kentucky University. (Sponsored by Patrick Schultheis). 91<sup>st</sup> Annual Meeting of the Kentucky Academy of Sciences, Eastern Kentucky University and Berea College, Richmond, KY, November 2005. (oral presentation).
18. Analysis of P<sub>5</sub>-ATPase Gene Expression in Mouse Brain by *in situ* Hybridization. Chuck Burke, David R. Hahn, Patrick Schultheis, and Kristi Martines. Northern Kentucky University. (Sponsored by Patrick Schultheis). 91<sup>st</sup> Annual Meeting of the Kentucky Academy of Sciences, Eastern Kentucky University and Berea College, Richmond, KY, November 2005. (poster presentation).
19. Localization of Atp13a1-GFP and Atp13a2-GFP Fusion Proteins. J. Walter, R. Baldrige, D.R. Hahn, C.R. Burke, P.M. Gulleman, D.L. McGill, K.H. Martines and P.J. Schultheis. 2006 Merck/AAAS Interdisciplinary Summer Research Celebration. Department of Biological Sciences, Chemistry, Physics and Geology, and Psychology, Northern Kentucky University. September 2006.
20. Subcellular Localization of Two P-type ATPases, Atp13a1 and Atp13a2. Ryan D. Baldrige, Adam C. Ketron, John R. Ledford, Jennifer M. Walter, Kristi Martines, Diana L. McGill, Patrick Schultheis. 92<sup>nd</sup> Annual Meeting of the Kentucky Academy of Sciences, Morehead State University, Morehead, Kentucky. November 2006.

21. Subcellular Localization of Two P-type ATPases, Atp13a1 and Atp13a2. Ryan D. Balridge, Adam C. Ketron, John R. Ledford, Jennifer M. Walter, Kristi Martines, Diana L. McGill, Patrick Schultheis. Posters at the Capitol, Frankfort Ky, January 2006.