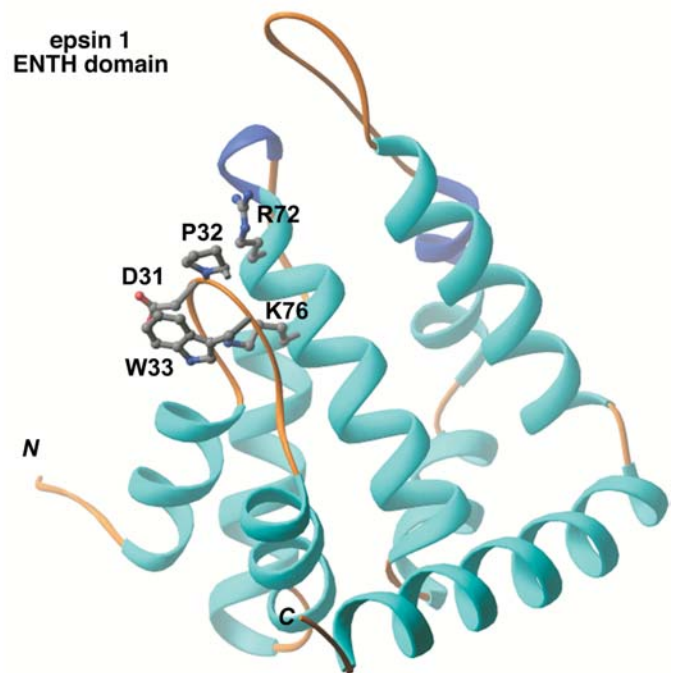
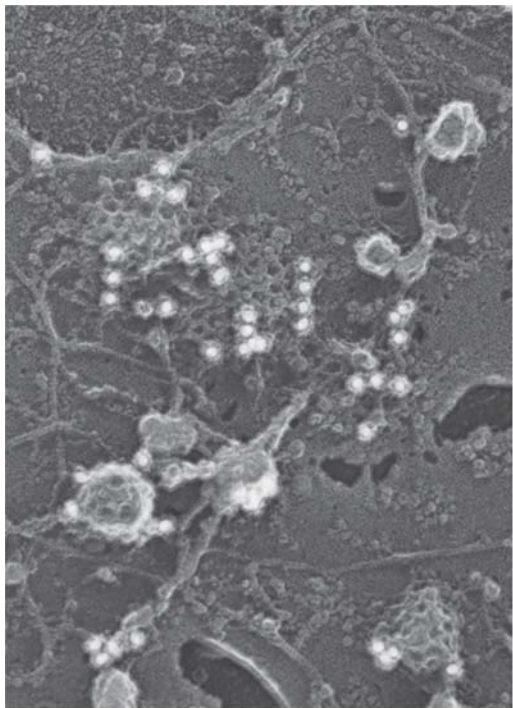


CELL BIOLOGY AND PHYSIOLOGY

FY01 ANNUAL REPORT

AND

FY03 BUSINESS PLAN



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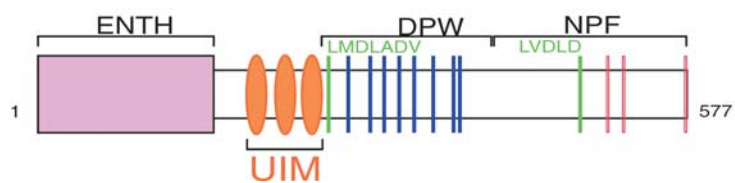


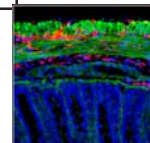


Table of Contents of CBP Annual Report

Cell Biology and Physiology Program Description	
General Description of Program	4
Research Activities	
Research Foci of Department	8
Centers of the Department	12
Faculty Data	18
CBP Organizational Chart	19
Research and Other Scholarly Activities	
Faculty Research Summaries	20
Faculty Study Sections	39
Faculty Advisor Committee Memberships	41
Faculty Sponsored Research Grants	43
Charts	48
CBP Seminar Series	52
Teaching Activities	
Cell Biology & Molecular Physiology Graduate Program	56
New Courses or Other Educational Innovations	56
CBMP Course Descriptions	56
Faculty Teaching Honors	60
Teaching Activities	61
CBMP Graduate Program Students	74
CBMP Students Graduated in 2001	75
Faculty Data	
Current CBP Faculty	76
New CBP Faculty	77
Faculty Honors, Recognition and Professional Affiliations	78
Faculty Presentations	87
Faculty Publications (1999-present)	
Peer Reviewed Publications	92
Abstracts, Chapters, Books, Reviews	120

On the cover:

In many cells, clathrin-coated vesicles represent the major vesicular carriers that transport material into the cell interior. The characteristic polyhedral 'honeycomb-like' coat is revealed in a rapid freeze-etch image of the inside surface of the plasma membrane (upper left). The assembling clathrin lattices are immunogold-labeled for epsin (the gold is seen as small white spheres), a protein composed of several domains (schematic below). The structure of the amino-terminal ENTH domain is also shown (upper right); this region binds directly to phospholipids and tethers epsin to the plasma membrane. In addition, 8 DPW tripeptide repeats and two clathrin binding sites link epsin to the forming clathrin coat directly. The function of epsin appears to be to synchronize clathrin coat formation with the incorporation of certain cargo into the coat, using the UIM region to sort ubiquitinated proteins. (Traub lab)



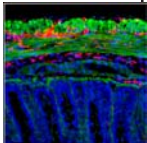
General Description: The Cell Biology and Physiology Program

This is a report of the research, teaching and service activities of members of the Department of Cell Biology and Physiology for the Academic Year 2000-01. In some instances, we have included expectations from AY2002, as they relate to notable accomplishments.

Research: The Department of Cell Biology and Physiology is one of five basic science departments of the School of Medicine. The department is housed in administrative and research space in the South Wing of the Biomedical Sciences Tower (SBST) and on the 8th floor of Scaife Hall. These modern facilities provide the faculty with research space designed specifically for their needs. The faculty research interests are diverse, as the name of the department implies. The research portfolio ranges from the study of fundamental cellular processes, including protein interactions and structures, to the control mechanisms that govern complex developmental and physiological regulatory processes in mammalian organisms. Thus, it is impossible to succinctly summarize the investigative interests of the faculty. Nevertheless, there are areas of concentrated effort that identify our strengths. In addition to research, our mission is also to instruct medical students in the disciplines of cell biology and physiology and to train young investigators for careers in academic or biotech based research.

Research in this department covers many areas of cell biology and physiology (see Faculty Research Interests, p. 20).

1. *Epithelial Cell Biology/Ion channels:* A significant fraction of our faculty are involved in an NIH (P50) and Cystic Fibrosis Foundation (RDP) funded center for research in the genetic disease, cystic fibrosis. Members of this group have focused on the detailed analysis the functions of ion channels (as the CF gene encodes a regulated ion channel in epithelial cells). Currently these studies are oriented toward identification of mechanisms that control ion channel activity and trafficking, and to questions regarding the role of the CF gene product in airway physiology and pathophysiology. Other members of this group are defining the role of pancreatic cell channels in the secretion of insulin and other hormones using novel fluorescent protein methods to track hormone release. Others use transgenic animals to identify the mechanisms responsible for cardiac electrical activity and the initiation and termination of cardiac arrhythmias. They have developed novel recording methods for this purpose that are being implemented by many laboratories worldwide.
2. *Reproductive and Metabolic Endocrinology:* A second major NIH-funded research center (U54) focuses on the hormonal and physiological processes that control neuroendocrine mechanisms, including ovulation, the onset of puberty, spermatogenesis, prostate development, glucose metabolism and satiety. Members of this group employ primate models of development and neuroendocrine regulation. They have developed mouse models for metabolic studies that permit hormone receptor manipulations in specific tissues.
3. *Muscle Development:* Another group of faculty investigates the development of muscle and its regeneration in response to trauma or disease, especially as concerns the muscular dystrophies.



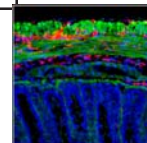
4. *Cell Biology:* Several members of the faculty focus their research efforts on basic mechanisms of cell-cell communication and protein trafficking. The latter includes studies of the protein interactions that contribute to internalization of plasma membrane and its associated proteins and the interactions and regulatory processes that lead to protein biogenesis and progression along the protein secretory pathway to the cell surface. These processes are often altered during oncogenesis.

Development of Novel Methods: Research techniques used in the department to study cell functions and their regulation are always in a state of flux. Cardiac imaging has been brought to a high level of resolution with the development of cameras and computational facilities that permit multi-mode data acquisition and online conversion of complex data arrays. It is now possible to image the beating hearts of transgenic mice that have conduction defects or ion channelopathies in real time in two dimensions across the entire heart. New camera and computational methods are under development that will allow acquisition of data from internal cardiac regions, so that the spread of excitation in three dimensions can be quantified. Similar methods are now being applied to the in vivo imaging of insulin secretion in pancreatic cells.

In recent years, the Center for Biologic Imaging has developed into a nationally recognized center that provides investigators in the Health Sciences with multi-line confocal microscopes and multi-mode, live-cell imaging systems. These systems and the expertise of the faculty and staff of the Center permit us to record concurrent multicolor multidimensional parameters in living tissues and cells. This, in turn, permits us to develop unique experimental designs and methods for data collection and analysis. An example of this capability is a technique developed by Dr. Peter Drain, one of our recently recruited junior faculty members. In an initiative towards genetic therapy for type I diabetes, he and his collaborators in the Department of Pediatrics are engineering, from stem cells and other progenitors, cells that mimic the glucose-responsive, insulin-secreting beta cells of the endocrine pancreas. Confocal, two-photon microscope technology enabled the identification of differentiated cell populations that are fluorescent by virtue of their synthesis and secretion of a fluorescent insulin surrogate. Physiological cell differentiation markers could then be identified in protocols designed to screen multiple cell populations for conditions that generate, select, and maintain insulin-secreting beta-like cells.

Another recently recruited member of our faculty has developed methods for tissue specific knockout of receptors for the metabolic regulatory hormone, leptin. His work has demonstrated for the first time that peripheral receptors are important in the regulation of metabolism, not only those in the central nervous system. His work implies that alterations in peripheral receptors are responsible for the development of adult onset diabetes.

Updating the Equipment Inventory: Within the department, we have established core facilities for imaging, quantitative assay of molecular expression and protein biochemistry that can be accessed by department faculty. This arrangement makes equipment and facilities available that cannot be accommodated in individual laboratories. In addition, the department is fully networked. Centralized servers perform the accounting and word processing/data/communication functions for department members. Last year, the department acquired a new fluorescence plate reader and

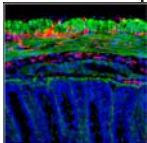


luminometer that permit faculty to run specialized live cell assays to probe a variety of cellular functions. We also acquired a gel documentation system that is generally useful for faculty research. Additional expenditures went toward updating departmental common equipment, centrifuges and rotors. The Department has funded expenditures in the last five years for recruitment, relocations and acquisitions of equipment, totaling more than \$500,000, from its internal development fund.

The Changing Faculty Roster: The second major challenge facing our department has been the recruitment and mentoring of new junior faculty (see New CBP Faculty, p.77). Since 1995, CBP has appointed 8 new tenure track Assistant Professors, two Professors, and a number of Research Assistant Professors, Research Associates and Postdoctoral Fellows. In the past year, with the help of Dr. Levine, we were able to attract a talented new member of the faculty. Dr. Sanford Leuba uses sophisticated optical methods to manipulate DNA and quantify the forces that hold chromatin together. His work is unique in attempting to address the energetics involved in disassembly of chromatin at the single molecule level. For this work, he uses atomic force microscopy and optical tweezers to physically perturb these structures and his work shows promise of defining the forces involved in DNA processive enzyme activities.

Facility Space and its Challenges: A major challenge for the department in the short term is how to achieve growth, both of existing programs and recruitment of new faculty in the face of limitations on space at the School of Medicine level. The department has achieved its initial goals in terms of faculty recruitment, but the environment lacks research expertise in certain critical areas, including developmental and structural biology and proteomics, to which this department should contribute. We are attempting to recruit new faculty in the face of this challenge. To determine the needs of existing faculty and to hopefully identify space for continued recruitment efforts, we have recently formed a space committee. The charge of this committee is to look at resource allocation in the spirit of a research community that wishes to continue to grow. Our next report should detail the initial outcome of this process, which has begun with the establishment of guidelines to govern the evaluation process. Our dilemma involves choosing between additional new investigators or providing “growing room” for its established faculty, both senior and junior members, who are successfully expanding their programs.

Research Support: As will be seen from detailed data (see Faculty Funding, Annual Departmental Funding History, and Faculty Funding Totals for 3 Years, pp. 43-51), the research grant income of the department has steadily risen during this same period. From 1995 to the present, CBP’s grant revenue has tripled. The faculty currently supports its research efforts through an aggressive grant application strategy that includes both individual and program grant support. Current sources of support include the National Institutes of Health, the Cystic Fibrosis Foundation, Circogen and Novartis Pharmaceutical Companies, the American Heart Association, the American Cancer Society, the Juvenile Diabetes Foundation International, the National Science Foundation, the Alfred P. Sloan Foundation, the GTE Foundation, the Whitaker Foundation, the Merck Education Program and The Parents Project.



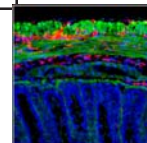
Our total sponsored research support has increased dramatically since the mid-1990's to a FY2001 level of \$6,916,845 in total grant dollars, which exceeded our projections by \$200,000. We project that our total grant income for FY2002 will reach \$7,322,862, and generate over \$1.9M in indirect cost revenue for the School. This achievement is indicative of the department's productivity. It is our hope and expressed goal that future physical stability and scientific maturation of the junior faculty will allow our department to continue this funding growth as well as to achieve our most important goal, to make significant scientific contributions to our respective fields.

Service: The faculty of Cell Biology and Physiology are active members in the larger scientific community. This report contains: Faculty Publications, p. 92; Faculty Honors, Recognition and Professional Affiliations, p. 78; and Faculty Study Section Activities, p. 39.

Teaching: The members of our faculty pursue an active involvement in the student recruitment, curricular development and teaching activities of the School of Medicine and the Interdisciplinary Biomedical Graduate Program (INTBP). See the various subsections in Teaching Activities, p. 61. We participate in the Graduate Admissions Committee, the MD/PhD Selection Committee, the Curriculum Committee and many course design committees in the School of Medicine. We teach extensively in Foundations of Biomedical Science for first year Graduate Students. Last year we initiated a new course in the Cell Biology and Molecular Physiology Graduate Program entitled 'Cell Biology of Normal and Disease States, which is being taught collectively by the junior faculty. Due to its success, the course has become our flagship course, one that is required of all students who are enrolled in the Program. We have had approximately ten students enrolled each of the two years that this course has now been given, and we hope that this experience will continue to generate student interest in joining the laboratories of the course instructors. We also expanded the student seminar/journal club offerings to represent three areas of interest to students and faculty: Cell Physiology; Reproductive Physiology; and Membrane Trafficking. Students in CBP must be enrolled in one journal club throughout their training and they receive credit for this offering during two semesters in which they are graded on their paper presentations. In the coming year, we plan to develop a new second level graduate course entitled 'Molecular Endocrinology', which will be taught by members of the department and the Division of Endocrinology. Depending on its success, this course may supplant the current offering: Integrative Physiology, which has become poorly subscribed in recent years. In addition, the new course is more closely aligned with the research interests of departmental faculty.

A description of the department and a summary of this report can be found at the department's website: www.cbp.pitt.edu. Our challenges for the coming year are discussed in the 2003 Business Plan (p. 144), which follows the reference material for this Annual Report.

Raymond A. Frizzell, Ph.D.
Chairman and Richard B. Mellon Professor
Cell Biology and Physiology



**Department of Cell Biology and Physiology
2001 Research Activities**

Biomedical research in the Department of Cell Biology and Physiology is directed in six major areas: Genetic Disorders of Ion Channels; Regulation of Gene Expression during Development; Membrane Traffic of Proteins and Lipids; Reproductive Biology; and Signal Transduction in Diabetes and Metabolism. The department is home of the School of Medicine's Structural Biology Imaging Center. It is also home to the Center for Research in Cystic Fibrosis, an effort supported both by an NIH Program Grant and a Cystic Fibrosis Foundation Center grant; and the Center for Research in Reproductive Physiology, which is sponsored by the NIH as part of its national cooperative research center program.

CBP's major faculty groupings (CBP has no formal Divisions) and research focus descriptions are shown below:

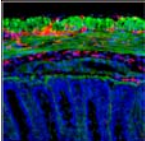
Genetic Disorders of Ion Channels

Bradbury, Neil
Bridges, Robert
Devor, Daniel
Frizzell, Raymond
Peters, Kathryn
Pilewski, Joseph
Salama, Guy
Sun, Fei

Inherited mutations in ion channels are responsible for many genetic diseases, including cystic fibrosis (CF). The department is home to a Specialized Center of Research in CF funded by the NIH (one of only two in the country) and the CF Foundation. Here, scientists are defining the factors that regulate ion channel activity and their expression on the plasma membrane. Inherited disorders of ion channels beyond CF include chronic obstructive pulmonary disease and hypertension. Program scientists are using biochemical, molecular expression, electrophysiologic, cell biologic and transgenic techniques to identify the channels involved in these processes and to define their regulation. Dr. Salama is using molecular engineering of ion channels and high-speed imaging to study the mechanisms responsible for the initiation and termination of cardiac arrhythmias.

Regulation of Gene Expression during Development

Onate, Sergio
Ontell, Martin P.
Ontell, Marcia
Stolz, Donna



Walker, Will
Washabaugh, Charles
Watkins, Simon

Identifying the factors that control gene expression is central to understanding how normal and malignant cell growth is regulated. Scientists in this program are identifying components of the gene transcription machinery that mediate signaling by steroid and peptide hormones, which control germ cell development and somatic cell differentiation. The regulation of gene expression is critical for many differentiated cell functions including fertility, hormone secretion, cell-cell communication and motor development. Members of this program are studying how alterations in these processes can lead to infertility, changes in wound healing, muscular dystrophy and cancer.

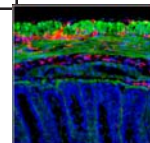
Membrane Traffic of Proteins and Lipids

Apodaca, Gerard
Aridor, Meir
Bradbury, Neil
Frizzell, Raymond
Murray, Sandra
Traub, Linton
Weisz, Ora

Much of modern cell biology is focused on the mechanisms that target proteins and lipids to their proper cellular destinations. The controlled movement of membranes is critical for the actions of growth factors, the secretion of hormones and neurotransmitters, the processing of antigens during the immune response, the maintenance of cell polarity and many other vital cell functions. Scientists in this program are identifying the cellular compartments involved in these processes and the mechanisms that regulate membrane flow between them. Success in this venture leads to identification of the cell's sorting and targeting machinery, high-resolution structures of the proteins that mediate these processes and an understanding of how the physical interactions among these proteins are regulated and how they govern trafficking.

Reproductive Biology

Onate, Sergio
Plant, Tony
Ryan, Kathleen
Sahu, Abhiram
Walker, William
Zeleznik, Anthony
Gay, Vernon



The neuroendocrine control of the hypothalamic-pituitary-gonadal axis is central to human sexual maturation and fertility. To better understand and intervene in human reproductive processes, program members utilize rhesus monkeys as a model system. For this work, the Center for Research in Reproductive Physiology maintains a colony of 350 rhesus monkeys. Studies of these animals are conducted in tandem with investigation of human pathophysiology, and contemporary molecular and cell imaging techniques are applied to physiological paradigms to study sex steroid regulation of gene expression in prostate, signal transduction pathways, stress, puberty, spermatogenesis, ovarian functions, aging and endocrine disruptors.

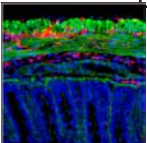
Signal Transduction in Diabetes and Metabolism

Zhao, Allan

Sahu, Abhiram

Drain, Peter

Regulated secretion of insulin by the pancreas and the actions of insulin and leptin in neuronal, muscle, fat and liver cells are critical for controlling the body's energy metabolism. Disruption of these processes leads to diabetes or obesity. Researchers in this program are defining the cell signaling mechanisms that control glucose-stimulated insulin secretion by pancreatic cells, and those that underlie the actions of insulin and leptin in the control of glucose and fat metabolism in central and peripheral tissues. By using cell models to identify the important response components, researchers are generating transgenic animal models to alter the expression of these signaling components to determine the mechanisms that lead to diabetes and obesity.



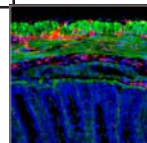
The Centers of the Department of Cell Biology and Physiology

The Department of Cell Biology and Physiology is the administrative home for three Centers:

The Center for Biologic Imaging is a world class, state of the art imaging Center which, as a School of Medicine core facility, serves virtually every investigator in the School.

The Center for Research in Cystic Fibrosis is funded by both the NIH and the Cystic Fibrosis Foundation.

The Center for Research in Reproductive Physiology is funded by the NIH and is part of a national network of like Centers.



Center for Biologic Imaging

Over the last several years, microscopy as a scientific tool has reinvented itself. It has changed from a group of principally descriptive methodologies, to a wide range of primary tools and techniques to investigate the molecular organization of organs, tissues and cells. Advances in microscope and camera design, fluorescent dye technology and the development of fluorescent proteins as well as the advent of inexpensive, powerful computers have made the simultaneous resolution and quantitation of multiple concurrent molecular markers for both protein and DNA at a sub-micron resolution a reality. Furthermore, using these same systems, it is possible to probe living cells using a rapidly expanding repertoire of dyes sensitive to changes in cellular pH or the concentration of specific intracellular ions, and to optically section and rebuild images of cells in 3 dimensions using confocal microscopy. The development of nanometer sized particulate markers has been an essential extension of these techniques, allowing the distribution of proteins and mRNA to be studied within cells at a molecular resolution using electron microscopy.

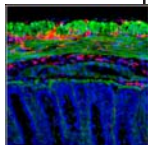
The recognition of the potential utility of these techniques to the rapidly expanding research community here at the University of Pittsburgh School of Medicine led to the formation of a centralized microscope imaging center; the Center for Biologic Imaging (CBI), six years ago. Since then the CBI has become an essential resource for most of the research programs within the medical school and collaborates extensively with most of the active research programs within the school.

Capacity of the Center:

The capacity of the Center is limited only by instrumentation, space and staff within the center. The Center for Biologic Imaging now provides a continuum of optical imaging technologies from routine histology to more exotic procedures such as EM *in situ* hybridization or fluorescent imaging of live cells with multiple fluorochromes in 3 dimensions or in time. This expansion has provided data for a large number of peer reviewed publications was sufficiently extensive to warrant authorship (listed below, table 2). The current staffing of the facility and available resources are described below.

The Director: Dr. Simon C. Watkins was recruited to the University of Pittsburgh from the Dana Farber Cancer Institute (DFCI) in Boston in 1991 to provide scientific leadership of the Center. He is a tenured Professor in the Department of Cell Biology and Physiology within the School of Medicine. His experience in microscopic methods covers most of the present light and electron microscopic methodologies.

The Assistant Director: Dr. Donna Beer-Stolz was recruited as an Assistant Professor in the Department of Cell Biology and Physiology. She joined the center a little under a year ago and is a very experienced cell biologist and electron microscopist. Her primary responsibility is to assist in the direction of the Cell And Tissue Imaging Core. She was recruited specifically to facilitate interactions between the Cell And Tissue Imaging Core and its users. Dr. Beer-Stolz's primary role lies in the management and development of the electron microscopy component of the center.



Postdoctoral Research Associates:

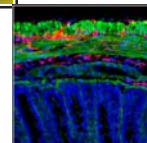
Drs Papworth, Burke and Guo form a leadership core within the Center for Biologic Imaging reporting to Drs. Watkins and Stolz. Their main function is the application and the development of 2 photon, live cell and electron optical methods within the center.

Technical Specialists: The technical base of the Center are all trained microscopists; In total 9 technical specialists work in the center. Furthermore we have a staff of three research assistants who provide general lab maintenance and photographic services. These staff are responsible for the processing and experimental manipulation of materials for light and electron microscopy. They assist users directly in the application of microscopic techniques, though equally they perform complete procedures for users who are not sufficiently experienced to perform their own experiments. They are also responsible for the day-to-day running of the Center, including management of microscope usage, microscope maintenance, bookkeeping, solution preparation, etc.

Administrative assistance: The primary administrative responsibilities are in the preparation of grants, and the monthly billing of charge-back users, processing Center for Biologic Imaging purchase requisitions and other general administrative duties.

Facilities:

The Center for Biologic Imaging is housed in the medical research center of the University of Pittsburgh Medical School in approximately 4000 sq ft. of space. This space has recently been completed and has been designed as a dedicated, state of the art imaging center, and has fully equipped microscopy suites, darkrooms, computer labs, and wet and dry bench space for light and electron microscopic preparations. Core equipment includes: 7 confocal Microscopes including 2P, Spectral hand held and multiple standard multiline confocals. 3 electron microscopes, 3 multimode live cell microscope, and 5 high end upright microscopes, all are entirely digital and equipped with CCD cameras. We also have 17 image processing stations (PCs Macs and SGIs) equipped with current image processing applications.



Cystic Fibrosis Research Center

Center Co-Directors:

Dr. Raymond A. Frizzell

Dr. Robert Bridges



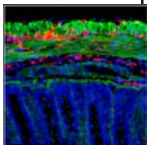
The Cystic Fibrosis Foundation established a Research Development Program Center for research in cystic fibrosis with a \$2 million grant in 1997. The primary goal of this Center is to focus the attention of investigators on multidisciplinary approaches designed to improve our understanding and treatment of cystic fibrosis (CF). In creating this Center, the CF Foundation took advantage of unique opportunities present at the School of Medicine and the Children's Hospital at the University of Pittsburgh, including a large and accessible patient population for pre-clinical and clinical research and excellent availability of patient lung tissue due to a large volume of transplant activity (greater than 50 lung transplants/year). The Center also provides the opportunity to engage excellent investigators in CF research in an institution that ranks 8th nationally in extramural support by the NIH. The University of Pittsburgh RDP Center is one of ten such Centers supported by the CF Foundation in North America. In addition to the RDP award, the Center was the recipient, in 1998, of a Specialized Center of Research (SCOR) award in CF from the NIH. This is one of only two such Centers nationally. The CF Research Center is directed by Raymond A. Frizzell, Ph.D., and co-directed by Robert J. Bridges, Ph.D.; both are leaders in CF research. The Center is housed in the Department of Cell Biology and Physiology in its 3rd floor Biomedical Science Tower facility.

The Center focuses on three main areas of CF research: basic studies of the function, protein interactions and processing of the CF gene product, CFTR, the development of new pharmacological agents for treating CF, and participation in clinical studies. The Center also supports pilot/feasibility grants and postdoctoral or graduate student training stipends. These funding mechanisms allow the Center to encourage interactions between investigators with long-standing interests and accomplishments in CF research and to bring new investigators into the CF field.

Collaborative Arrangements: The principal investigators of the Center have a long-standing history of collaboration in CF research. In particular, Drs. Frizzell, Bridges, Bradbury and Devor have worked together in this area for more than ten years. Interactions with clinical investigators, especially Dr. Joseph Pilewski, of the Department of Medicine, and Dr. David Orenstein and colleagues at the CF Clinical Center at Children's Hospital provide for an effective clinical interface with the basic science components of the program.

Research and Clinical Cores:

The Cystic Fibrosis Research Center at the University of Pittsburgh provides a focal point for interactions among researchers having expertise in the areas of membrane biophysics, biochemis-



try, cell biology, molecular biology, medicinal chemistry and clinical research.

The principle strategy for achieving the Center's objectives lies in its structure, having core facilities for coordinating the efforts of diverse investigators. These facilities enable the translation of basic discoveries into pre-clinical and clinical projects. The cores also function to attract and train new investigators by providing funding for cores, pilot/feasibility projects and training. This makes it possible to "seed" research efforts that attract extramural support.

Core Facilities

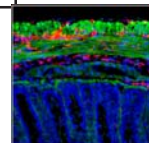
Molecular Biology/Gene Expression: The purpose of this core is to provide access to molecular reagents and techniques, to provide systems for gene expression, and standardized quality control over these procedures. This core provides constructs for expression of CFTR, the amiloride-sensitive Na channel, ENaC, and various regulatory reagents and enzymes. It interfaces with facilities for functional assays and protein expression. [Core Director: Fei Sun, Ph.D., Cell Biology and Physiology]

Cell and Tissue Imaging Core: This core is housed within the Center for Biologic Imaging of the Department of Cell Biology and Physiology. It provides investigators within the RDP with access to state-of-the-art imaging techniques. While its primary focus is immunocytochemistry, this core also provides for morphologic assessment of specimens, assessment of gene expression by in situ hybridization procedures, and modern image analysis techniques. [Core Director: Simon Watkins, Ph.D., Cell Biology and Physiology]

Drug Discovery: The purpose of this core is to provide pharmacological reagents designed to manipulate the properties of ion channels or regulators thereof. This core has drug design and synthetic capacities. It also accesses facilities and expertise in the Department of Chemistry. It provides experience and intuition for identification and optimization of lead compounds as well as promising reagents already certified for human use by the FDA. [Core Director: Robert J. Bridges, Ph.D., Cell Biology and Physiology]

Human Airway Cells: This core provides access to patient materials obtained as a result of lung transplant activities in the Department of Surgery. This core offers cultured human airway epithelia, organotypic cultures and human airway xenografts, to facilitate a variety of pre-clinical investigations. [Core Director: Joseph Pilewski, M.D., Department of Medicine, Division of Pulmonary and Critical Care Medicine]

Clinical Studies: This core provides facilities and personnel for implementing clinical trials. It provides procedures for identifying functional outcomes, monitored in terms of lung function, ion transport or gene expression. It maintains patient records and procedures for enrolling patients in clinical studies. [Core Director: Joseph Pilewski, M.D., Department of Medicine, Division of Pulmonary and Critical Care Medicine]



Center for Research in Reproductive Physiology

The mission of the Center for Research in Reproductive Physiology (CRRP) is to systematically study the fundamental physiological mechanisms that govern reproduction in higher primates and other mammalian species, integrating molecular, cellular, and system approaches, and to investigate the pathophysiological bases of specific states of human infertility. In addition, the CRRP is committed to provide pre-and postdoctoral level training in reproductive physiology and molecular endocrinology.

The CRRP was formally designated as a NICHHD Specialized Population Research Center (P-50) in 1974 with Dr. Ernst Knobil as its Director. In 1982 the CRRP was funded under the auspices of a Reproductive Sciences Center Core Grant (P-30) which continued until 2000. In April 2000, the CRRP was designated as a NICHHD Center in the Specialized Cooperative Program in Reproduction Research (SCCPRR). Dr. Tony M. Plant has served as Director of the CRRP since 1985.

Core Laboratories

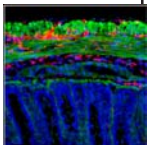
Cell Imaging Core

The Cell Imaging Core provides a centralized source of equipment, technical assistance and expertise for investigators requiring contemporary histochemical and quantitative imaging techniques. The services offered by this core include:

Providing and maintaining centralized equipment and reagents for immunohistochemistry and situ hybridization analyses including tissue sectioning, probe preparation, autoradiography and computer aided quantitative analysis. Optimizing in situ and immunohistochemical methods for detecting and quantifying specific mRNAs and proteins in monkey and rat tissues. Training CRRP members in the application of quantitative imaging methods (optical density, grain counting and unbiased stereological methods) to measure specific mRNAs and proteins.

Primate Core

The Primate Research Laboratory of the University of Pittsburgh School of Medicine became operational in 1967. The primate facilities have provided a unique regional resource for the study of reproductive processes in the monkey, an experimental model which serves as an excellent surrogate for humans. Since its inception, the Primate Research Laboratory has facilitated the acquisition of important information regarding the physiology of GnRH secretion and action, the control of the onset of puberty, the regulation of folliculogenesis and corpus luteum function, the control of spermatogenesis and the influences of metabolic demands upon reproductive function in males and females. Of major importance has been the development of a remote sampling system for use in monkeys in which continuous access to the venous system and cerebrospinal fluid is maintained in the absence of restraint or pharmacological sedation. With this system, blood samples can be collected from conscious animals and exogenous hormones and pharmacological agents can be delivered intravenously or directly to the central nervous system.



Radioimmunoassay Core

The RIA core offers validated radioimmunoassay services for a number of pituitary hormones, neuropeptides and steroid hormones including macaque LH, macaque FSH, rat LH, GnRH, cortisol, estradiol, testosterone and progesterone. In addition, commercial assay kits for human growth hormone, human leptin and human prolactin have been validated for use with macaque serum. In addition, the RIA core provides iodination services for cAMP and other proteins on an ad hoc basis for center investigators.

Training Program: Postdoctoral

The Center for Research in Reproductive Physiology (CRRP) of the University of Pittsburgh School of Medicine offers postdoctoral training which is funded by a Institutional National Research Service Award (NIH). These NIH fellowships are restricted to citizens and permanent residents of the US who have obtained the Ph.D. and/or M.D. degrees. In addition, research associate positions for non US citizens may be available through research grants awarded to the CRRP faculty.

Faculty Associated with Center (* denotes CBP faculty member):

Sarah L. Berga, M.D.

Neuroendocrine control of reproductive function

Judy L. Cameron, Ph.D.

Stress and the reproductive axis

Donald B. DeFranco, Ph.D.

Steroid hormone receptor trafficking

Robert B. Gibbs, Ph.D.

Estrogen, aging and cognitive function

Gary Marshall, Ph.D.

Regulation of spermatogenesis

*Sergio Onate, Ph.D.**

Steroid receptor co-activators and prostate function

*Tony M. Plant, Ph.D.**

Physiology of inhibin and neurobiology of puberty

*Abhiram Sahu, Ph.D.**

Leptin regulation of hypothalamic gene expression and feeding

*William H. Walker, Ph.D.**

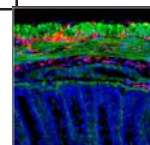
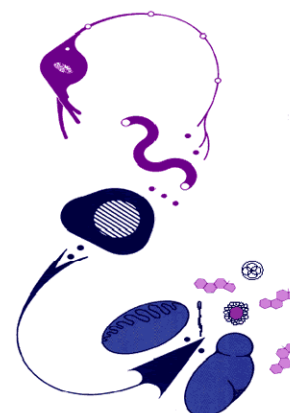
Transcriptional regulation in Sertoli cells

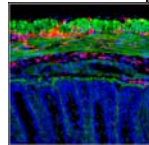
Selma F. Witchel, M.D.

Molecular genetic analysis of hyperandrogenism

*Anthony J. Zeleznik, Ph.D.**

Physiology and cell biology of ovarian function.



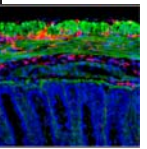
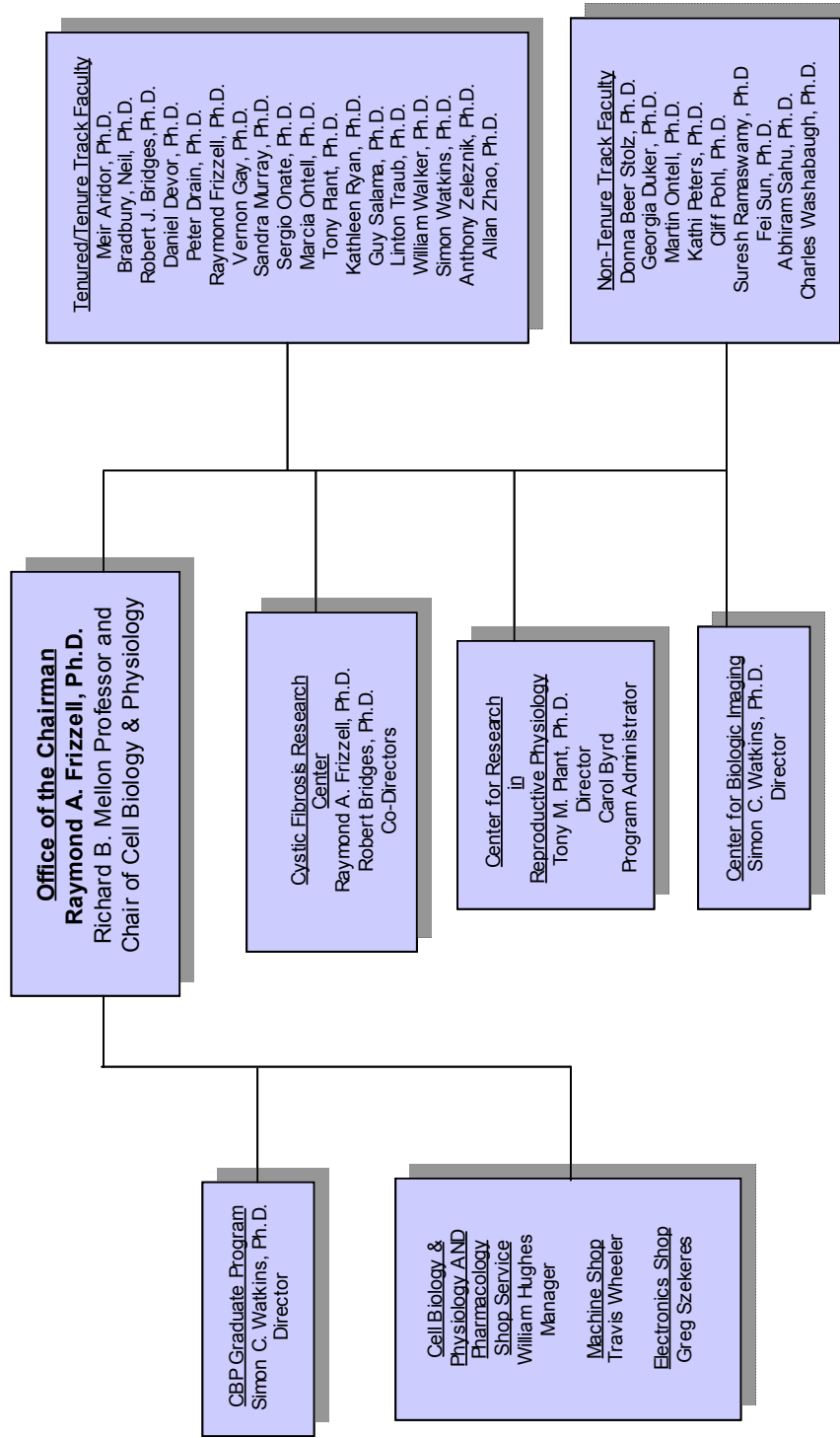


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[Current as of April 23, 2002]

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CBP ORGANIZATIONAL CHART FY02



Faculty Research Interests

William Ameredes, Ph.D. [Transferred to Department of Medicine, 12/31/01]

Visiting Research Assistant Professor

Dr. Ameredes' main interests include mechanisms of airway inflammation and the role of cytokines, particularly interleukin-10, in mediation of these responses. He is also interested in the paracrine function of airway smooth muscle in the regulation of airway responses and cell signalling during the process of inflammation and airway remodeling. The broad clinical application is the setting of asthma and other airway obstructive diseases. He is also interested in vascular eegulation within contracting skeletal and respiratory muscles, and phenotypic and functional adaptations of skeletal and cardiac muscle, in response to atrophic and hypertrophic stimuli. The applications in this case are acute responses, such as metabolic alterations during exercise and fatigue, and chronic responses, such as myosin expression shifts during aging, in the setting of cardiovascular disease, heart failure, and COPD.

Meir Aridor, Ph.D.

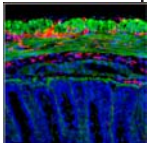
Assistant Professor

The endoplasmic reticulum (ER) is the first compartment of the secretor pathway. Plasma membrane receptors, ion channels, hormones and secreted enzymes are few examples of proteins which are being processed and sorted for vesicular transport in the ER. Mistakes in sorting lead to the development of variety of diseases, ranging from hemochromatosis, cystic fibrosis or hereditary emphysema to Pelizaeus-Merzbacher or Alzheimer's neurodegeneration. Viruses such as the cytomegalovirus, HIV-1 Epstein-Barr and many others manipulate ER sorting to evade immune surveillance, a specialized function of the compartment.

The main goal of the Aridor lab is to identify the molecular mechanisms which mediate cargo selection and ER export. Dr. Aridor's principal methods include utilizing a variety of molecular biochemical and cellular techniques to unravel the molecular basis of ER sorting. These include the identification and construction of dominant inhibitory proteins involved in ER export. Biochemical reconstitution assays with purified components, which recapitulate intermediate steps in the cargo selection process for biochemical analysis and morphological in vitro assays that enable the visualization of transport intermediates in real time.

Following the identification of COPII as the mediator of ER export and cargo selection, we have defined the interactions which mediate the direct recognition of the coat Sec23/24 subunits with cargo. We have found that multivalent interactions involving both temporal lipid modulation and protein-protein interactions operate to provide the required avidity to support cargo selection and export.

The long term goal of the lab is to identify the mechanisms which couple quality control, (protein folding and assembly) with ER export, ER degradation and with cell and tissue physiology. Model



cellular systems for ER related transport diseases are being established and adopted to unravel the molecular basis for these diseases.

Neil A. Bradbury, Ph.D.

Assistant Professor

Dr. Bradbury's research interests lie in the area of regulation of membrane protein trafficking in polarized epithelia. We have used the chloride channel protein CFTR as a paradigm for the cAMP dependent regulation of apical membrane endocytic events. We are interested in the protein-protein interactions between adaptins, clathrin, and CFTR involved in the endocytic internalization of CFTR. Interest also lies in the cAMP-dependent protein kinase (PKA) regulation of CFTR channel activity and trafficking and its mediation by binding of PKA to subcellular anchor proteins (AKAPs).

Robert J. Bridges, Ph.D.

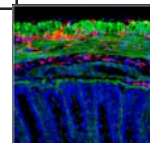
Professor and Co-Director of the Cystic Fibrosis Research Center

Dr. Bridges research is focused on epithelial ion channels. Studies examine the regulation, kinetics, biophysics, and pharmacology of chloride, potassium and sodium channels. A significant portion of his effort is toward the identification and optimization of new small ligands that modulate channel activity. Dr. Bridges is currently funded by three NIH grants, The Cystic Fibrosis Foundation and three pharmaceutical companies.

Each of the above funded projects has its own specific set of objectives: a) Mechanisms of Epithelial Bicarbonate Secretion (NIH); b) Protease Regulation of Airway Cell Sodium Transport (NIH); c) Fluctuation and Impedance Analysis of Chloride Secretion (NIH); d) Optimization of Benzimidazolones for Cl⁻ Secretion (CFF); e) Evaluation of the Ion Conductances and Capacitance Changes Involved in Airway Epithelia Cell Mucin Secretion (Novartis); f) Effects of CircaGen Compounds on CFTR Expression and Function (CircaGen); g) Proposal of the Evaluation of Genzyme Compounds on CFTR Expression and Function (Genzyme).

Principal methods employed are various electrophysiological methods including short circuit current studies, impedance analysis, fluctuation analysis, microelectrode studies, patch clamping, and whole cell capacitance measurements are used in our studies. In addition, we utilize various molecular biology and biochemical methods to study proteins. We also synthesize our own novel organic compounds as necessary.

The results in our lab have been notable. We have delineated the mechanism of bicarbonate secretion in Calu-3 cells. We've discovered that small molecules can be used to inhibit sodium transport in human bronchial epithelial cells (Invention disclosure submitted). We've demonstrated the inhibition of sodium transport by proteases results in a decrease in the number of active channels and not an alteration in their open probability. Finally, we've demonstrated the efficacy of several pharmaceutical company compounds for the treatment of Cystic Fibrosis.



Our future plans are to remain focused on the objectives of my funded projects and to attempt to obtain funding via a SBIR for the development of small molecule sodium transport inhibitors.

Daniel C. Devor, Ph.D.

Assistant Professor

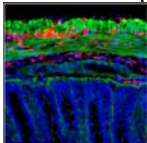
Dr. Devor's research interest is in determining the mechanisms by which Ca^{2+} -mediated agonists modulate both Cl^- secretion and Na^+ absorption across intestinal and airway epithelia. These processes are important in the pathology of both infectious secretory diarrhea and cystic fibrosis. Thus, a comprehensive understanding of the mechanisms underlying these processes would be expected to have therapeutic benefit. Specifically, his interest is in the regulation of the basolateral membrane K^+ channels which underlie these secretory and absorptive events. The mechanisms by which these conductances are regulated is being studied at both the single channel level as well as in the integrated epithelium. One of his goals is to understand the physiological regulation of these channels by known modulators of their activity (e.g., Ca^{2+} , PKC, PKA, arachidonic acid). In addition, his group has identified both novel pharmacological openers (e.g., benzimidazoles, chlorzoxazones) and inhibitors (e.g. imidazole antimycotics) of K^+ channel activity. By utilizing these recently identified pharmacological probes he is in a position to better understand the role of K^+ channels in Ca^{2+} -mediated responses; be they absorptive or secretory. Dr. Devor's long-term interest is in the molecular cloning and characterization of the basolateral membrane Ca^{2+} -activated K^+ channel. This will allow a more detailed understanding of its regulation by both physiological and pharmacological agents at the molecular level. Additionally, the cloning of this channel will allow studies designed to determine its localization along the crypt-villus axis of the intestine as well as in the glands of airway epithelia, thereby improving the understanding of the channels role in the absorptive and secretory functions of these tissues.

Peter F. Drain, Ph.D.

Assistant Professor

Diabetes is a devastating disease, the sixth leading cause of death due to disease in the US. Nearly \$50 billion is spent on diabetes in direct diabetes medical costs and an additional \$50 billion indirectly. Diabetes is caused by an inability to secrete appropriate amounts of insulin in response to changing blood glucose and over time the unregulated blood glucose leads to organ damage and death. My lab is interested in understanding how glucose metabolism is coupled to insulin secretion by focusing our molecular and cellular studies on the ATP-sensitive potassium (K-ATP) channels and peptide secretory granules of the insulin-secreting beta cell of the endogenous pancreas.

Our research objectives are to define the molecular and biophysical mechanisms by which the ATP-sensitive potassium (K-ATP) channel is inhibited by ATP, and how this inhibition is antagonized by MgADP. We also study the biogenesis, trafficking, and exocytosis of insulin secretory



granules, with particular regard to how changes in glucose metabolism speeds the rate of these processes.

The principal methods used combine the techniques of molecular biology, patch clamp electrophysiology, and confocal fluorescence microscopy, with live-cell imaging and transgenic techniques to integrate understanding at the molecular, cell, organ, and whole organism level.

Recent results include the establishment of a mechanism that demonstrates that ATP binding to the K-ATP channel energetically destabilizes the open state relative to the inhibited state as a critical and major mechanism by which ATP inhibits the K-ATP channel (J. Gen. Physiol. 119, 105-116, 2002). We have also succeeded demonstrated that proinsulin fusions to Fluorescent Proteins (GFP, YFP, and RFP) can be used for exquisitely fine spatial and temporal parameters characterizing insulin vesicle physiology including exocytotic release (Traffic, July 2002, in press).

Confocal fluorescence microscopy is aimed at better understanding the neurosecretory paradigm using insulin vesicle biogenesis, transport and K-ATP channel-regulated exocytosis as the model. A major challenge is to better understand at what subcellular sites and how K-ATP channel inhibition by ATP might stimulate insulin granule trafficking and exocytosis.

Future plans include a detailed confocal microscopic and biochemical study of where K-ATP channels reside throughout the cell and how their function might be differentiated according to subcellular site.

Georgia K. Duker, Ph.D.

Assistant Professor

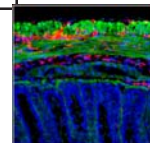
Dr. Duker is the curricula contributor, course director, lecturer and lab coordinator/instructor for a number of key Medical School and INTBP Graduate courses including Biomedicine: Past, Present & Future - Honors College Course, Graduate Histology, and the Histology lab.

Her research interests focus on normal cell structure/function correlations, especially with reference to membrane cycling. Previous projects include regulation of the macrophage C3 receptor by T lymphocytes and defects in retinal pigmented epithelial cell phagocytosis that may relate to retinal detachment.

Raymond A. Frizzell, Ph.D.

Professor, Department Chairman and Director of the Cystic Fibrosis Research Center

Dr. Frizzell's research is focused in the area of epithelial ion transport and cell biology. His principal interest is in the mechanisms responsible for epithelial electrolyte and fluid secretion, particularly the regulated secretion of NaCl that occurs in airways, intestines and exocrine glands. A central component of these processes is a protein kinase regulated Cl channel which lies at the apical membranes of salt secreting epithelial cells. This channel bears mutations in the human genetic



disease, cystic fibrosis (CF), and the protein product of this gene is termed the cystic fibrosis transmembrane conductance regulator (CFTR). Dr. Frizzell's laboratory was instrumental in identifying the functional defect in channel regulation in CF airway cells and in showing that expression of the CF gene would correct the defect in cAMP-stimulated Cl secretion that these cells display.

In recent years, this laboratory has been interested in the role of regulated membrane trafficking in expression of the secretory Cl channel. Using measurements of membrane capacitance to monitor cell surface area, we have demonstrated that cAMP produces a reversible increase in membrane insertion, only when cells express functional CFTR. There is close correlation between membrane insertion and the stimulation of Cl channel activity, suggesting that either CFTR itself contains the structural information required for its regulated traffic, or that this process occurs via protein-protein interactions that mediate the membrane insertion/retrieval events. Current research is aimed at defining the structures in CFTR that mediate these processes and the accessory traffic regulatory proteins. In particular, Dr. Frizzell is evaluating the role of SNARE proteins and the cysteine string protein in the regulated trafficking of CFTR and the epithelial sodium channel, ENaC. Modulation of the activity of these proteins influences the trafficking of these ion channels and this may be a regulatory mechanism for controlling channel density. Future work will explore this possibility as well as the additional role of these proteins in channel biogenesis.

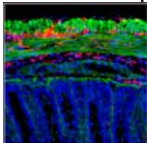
Vernon L. Gay, Ph.D.
Associate Professor

Regulation of the onset of puberty in the primate:

The temporal sequence of sexual maturation in primates is mandated by a prolonged interval (some ten years duration in the human) during which the rate of gonadotropin secretion is markedly decreased, if not totally absent. Over the past two decades numerous studies have centered on the search for a presumed inhibitory influence or, alternatively, the much delayed appearance of a stimulatory influence.

The objective of current research is to promulgate and refine an alternative hypothesis regarding the delayed onset of sexual development. The working hypothesis states that the process of sexual maturation in primates consists of a gradual and progressive accumulation of inter-neuronal connectivity and communication. The hypothesis further states that significant inhibitory and/or stimulatory systems are not required to explain the long interval of pituitary quiescence and takes into account the fact that we (Gay and Plant, 1988) have demonstrated that chemically induced synchronization of GnRH neurons in prepubertal monkeys is sufficient to produce pulsatile LH secretion compatible with the induction of full sexual development.

Working with patterns of gonadotropin secretion observed before and during puberty in the rhesus monkey and incorporating the known parameters of pituitary responsiveness to gonadotropin releasing hormone (GnRH), we have developed a computer program with simulates the gradual,



random connection of 1000 GnRH neurons over a period of months or years. The resultant patterns of (simulated) GnRH secretion are analyzed for their potential in stimulating or inhibiting gonadotropin secretion by the pituitary.

Our first (and very simple) computer simulation revealed GnRH secretory patterns which would have resulted in four sequential patterns of GnRH secretion: (1) Total desynchrony, (2) random, miniature, ineffective pulses, (3) a chaotic pattern of medium sized pulses which may be inhibitory or stimulatory depending on temporal patterns, (4) A highly effective pattern of GnRH pulses based on maximum synchronization of the majority of GnRH neurons.

We conclude that the effectiveness of GnRH stimulation would vary greatly over the prepubertal interval in primates depending on the number of GnRH neurons able to communicate with each other. We propose to: (1) Obtain funding necessary to hire a computer programmer to refine the analysis; (2) To obtain funding for computer equipment adequate to the task of refining and displaying the data in a manner sufficient to demonstrate the extent of pituitary inhibition and/or stimulation which could be evoked in such a system; and (3) To obtain funding for experiments in primates in which intra-cranial infusion of growth factors would be used in an attempt to alter the rate of synaptic connection between GnRH neurons with a resultant alteration in the time to onset of adult patterns of pulsatile LH secretion.

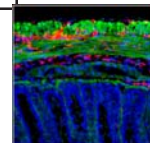
Sandra A. Murray, Ph.D.

Professor

Studies in Dr. Murray's lab are designed to test the hypothesis that gap junction protein dynamics are dependent on hormone stimulation. Specifically, the role of adrenocorticotropin (ACTH) and cyclic adenosine monophosphate (cAMP) in controlling connexin 43 (Cx43) gap junction channel trafficking, assembly, and degradation are in progress.

Our research objectives are: 1) To Measure and Characterize Connexin 43 Gap Junction Intracellular Transport and Degradation in ACTH and DbcAMP Treated Adrenal Cortical Cells; and 2) To Measure the Effects of ACTH and DbcAMP on Gap Junction Assembly in Adrenal Cortical Cells.

Gap junctions are cylindrical units composed of proteins called connexins. The sequences of several connexin gap junction proteins expressed in different tissues have been determined. Many cells express more than one of the 15 members of the connexin family that have now been identified. Connexins, once oligomerized into hemichannels (connexon), align in the cell membrane to form channels. Gap junction channels generally form between cells of the same type, however, they have also been found to form between cells of different types and channels composed of more than one connexin type have been reported. Once formed, gap junction channels provide pathways for the direct intercellular exchange of small molecules, including cAMP, Ca^{+2} , and inositol triphosphate, between adjoining cells. By the passage of such molecules, gap junctions have been suggested to play a pivotal role in embryonic development, cell proliferation, differentiation, hormone response and tissue homeostasis.



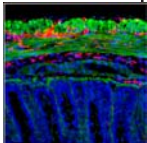
One member of the connexin family found in a large number of different cell types, connexin 43 gap junction protein (Cx43), has been demonstrated, at least in some cells, to take a classical route to the plasma membrane through the Golgi. The Cx43 molecules are thought to be synthesized in the endoplasmic reticulum, oligomerized into a hexameric hemichannel (connexon) in the Golgi and then transported to the cell surface. On the cell surface, they unite with similar connexons from apposing cells and aggregate to form gap junction plaques.

Recent live-cell imaging studies of fluorescently-tagged connexins reveal dynamic gap junction behavior both in the membrane and cytoplasm. Cx43 gap junction plaques within the plasma membrane were observed to form larger plaques by coalescing with one another. In addition, cytoplasmic Cx43 “packets” were observed both entering and exiting these previously formed gap junction plaques. All of these behaviors may influence the available number of junctional channels on the cell membrane and potentially affect cell function. The ultrastructural identity of the Cx43 packets, observed exiting gap junction plaques in live-cell imaging or the cytoplasmic Cx43 packets seen with immunocytochemistry, have not been elucidated. Some of these cytoplasmic packets that exit the gap junction plaque, however, may be the “annular” gap junctions described with electron microscopy.

The relationship of Cx43 packet trafficking seen in live cell imaging to increased gap junction plaque assembly, maintenance and function has not been demonstrated. More importantly, events involved in the assembly of connexin into functional gap junction plaques are poorly understood. However, the increase in gap junction protein synthesis and assembly is clearly influenced by peptide hormones and cAMP levels in some cell types. Thyroid stimulating hormone, for example, increases Cx43 and Cx32 expression in thyroid epithelial cells. Follicle stimulating hormone (FSH) increases cAMP levels and gap junction plaque number in intact ovary and cultured granulosa cells. Although phosphorylation of Cx43 gap junction proteins is not thought to be required for transport of Cx43 to the surface, it may be needed for plaque formation. The signals that regulate gap junction plaque formation however are not understood.

We have demonstrated that adrenocorticotropin (ACTH) increases Cx43 gap junction plaque number in adrenal cell cultures and in intact adrenal glands from hypophysectomized mice. Furthermore, gap junction protein expression in the adrenal cortex is zone dependent. The adrenal cortex is divided into the zonae glomerulosa, fasciculata and reticularis, each with morphologically and functionally distinct features. In the less ACTH-responsive cortical zone, where proliferation is highest, little Cx43 is expressed. In contrast, an abundance of Cx43 gap junction protein expression and lower proliferation rates were demonstrated in the highly ACTH-responsive zonae fasciculata and reticularis.

ACTH binds to its receptor and elicits a number of responses in the adrenal cortex mediated by cAMP acting through cAMP-dependent protein kinase (pKA). Cyclic AMP reversibly binds to pKA, freeing the catalytic subunit. The catalytic subunit can phosphorylate a substrate protein and thus bring about responses, including increased steroidogenesis, alteration in proliferation and presumably, the observed increased Cx43 gap junction assembly in the adrenal cortex. The



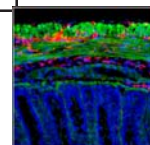
hormone triggered events at the cell surface, however, that result in increased numbers and/or sizes of gap junction plaques, have not been demonstrated.

Not only may hormone and cAMP levels influence gap junction formation, but they may also be involved in regulation of gap junction removal from the cell membrane and subsequent degradation. Both the proteasomal and lysosomal proteolytic pathways have been implicated in Cx43 turnover. Investigations with Brefeldin A suggest that proteasomal degradation occurs at the endoplasmic reticulum and the plasma membrane. In addition, lysosomal degradation has been demonstrated with electron microscopic techniques. In these studies it was suggested that gap junctions may be removed from the cell surface by an endocytotic mechanism and annular gap junction formation. The demonstration of acid phosphatase activity in gap annular gap junctions with electron microscopy, suggests that lysosomal degradation occurs following junctional internalization. The movement of packets of Cx43 from the gap junction plaque, seen in preliminary studies with live-cell imaging in our laboratory and by others, may confirm the early claims that gap junction plaques are internalized into the cytoplasm. In immunocytochemical studies DbcAMP treatment decreased the number of annular gap junctions in adrenal cortical cells while increasing the gap junction plaque size and number. However, the exact nature of the relationship between annular gap junction formation or degradation to cAMP levels has not been elucidated.

The relative rates of gap junction degradation and assembly may be important. The increase in connexin half-life at the cell surface resulting from a reduction in connexin removal from the plasma membrane and degradation would increase the amount of protein available for gap junction channel formation and channel mediated communication with surrounding cells. This regulation may be a post-translational means of altering intercellular communication. In preliminary live cell Cx43-GFP imaging experiments, we have observed gap junction packets entering and exiting surface gap junctions as well as the fusion of smaller gap junction plaques into larger plaques in adrenal cells in culture. We hypothesize that gap junction function may be regulated not only by channel gating but also by the assembly and removal of gap junction from the plasma membrane.

It is thought that the increased channel number could result not only from synthesis of new connexins but from increased assembly and decreased removal of the assembled gap junctions from the cell surface. We hypothesize that gap junction plaque assembly and degradation are regulated by peptide hormone stimulation. We are in the process of quantifying changes in the gap junction trafficking, assembly, and degradation in response to peptide hormone treatment in adrenocortical cell populations.

The significance of this work is that gap junction-mediated intercellular communication has been implicated in the development, differentiation and function of most cells of the body. Little is known about the regulation of gap junction assembly and even less is known about gap junction removal and degradation from the cell surface. Such information is critical in understanding of gap junctions and their role in hormonally responsive as well as other tissues. However, few studies have defined how hormone stimulation effects gap junction assembly or degradation. Understanding of gap junction-regulated endocrine cell function requires that gap junction dynamics be examined in hormone responsive tissues.



Our principal methods are to demonstrate gap junction trafficking in living cells, cDNA will be expressed in adrenal cells encoding for fluorescent Cx43-GFP or GFP-control vector with transfection techniques. For imaging cells expressing Cx43-GFP and grown on coverslips will be placed into closed system Biotechs Chamber temperature-controlled stage maintained at 37°C on a Zeiss microscope. Time lapse, immunocytochemistry, Western and northern blot techniques will be used to analyze gap junction gene products.

We come to four basic conclusions. We have demonstrated a zone specific Cx43 distribution within the adrenal gland which directly corresponds to dye communication patterns, proliferation and ACTH responsiveness in the gland. ACTH treatment of hypophysectomized mice results in an increase in gap junction expression within the ACTH responsive cortical zones (zona fasciculata and reticularis) while not affecting the expression in the less ACTH responsive, zona glomerulosa. 18 alpha-glycyrrhetic acid (GA), a known inhibitor of gap junction-mediated communication, was used to block intercellular communication in adrenal cultures. When cell communication was decreased by GA treatment, cellular response to stimulation was inhibited. Finally, proliferation rates were increased and steroidogenic responses to ACTH treatment were decreased in populations lacking Cx43 gap junctions.

Sergio A. Onate, Ph.D.

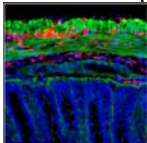
Assistant Professor

Dr. Onate's research interest is to gain an understanding of the molecular mechanism by which steroid hormones regulate gene expression during normal and malignant cell growth and development. Regulation of gene expression by steroid hormones is mediated by specific intracellular receptors. Steroid receptors (SR) belong to a large family of ligand-inducible transcription factors. Coactivators (such as SRC-1, CBP, p/CAF and TIF2) are important for steroid receptors to achieve full transcriptional gene activation. In addition, interaction with components of the general transcription machinery -including TFIIB (IIB), TFIID complex (IID) and members of the RNA polymerase (pol-II) complex- may provide the mechanism by which steroid receptors achieve the specificity required for the expression of different gene networks in target tissues. The prostate gland is highly responsive to sex steroid hormones and thus it is an attractive biological model to elucidate the molecular basis of steroid hormone action. Studies focus on the interactions of steroid hormone receptors with components of the general transcription machinery, including coactivators and/or adapter proteins that are relevant for target gene expression in the prostate gland. These studies are of clinical relevance because steroid hormone dysfunction is linked to the pathological progression of several diseases, including prostate cancer.

Marcia R. Ontell, Ph.D.

Professor

Dr. Marcia Ontell's research focuses on myogenesis, muscle signaling and myoneural integration,



muscle regeneration, muscle reaction to disease and trauma, gene therapy. Techniques used include: immunocytochemistry, gel electrophoresis, light, electron and confocal microscopy, morphometric analyses, in situ hybridization, competitive PCR, tissue culture, cell transfection, myoblast and stem cell transfer for muscle gene therapy, contractile properties of muscle, etc.

Martin P. Ontell, Ph.D.

Research Assistant Professor

Dr. Martin Ontell's research focuses on myogenesis, muscle signaling and myoneural integration, muscle regeneration, muscle reaction to disease and trauma, gene therapy. Techniques used include: immunocytochemistry, gel electrophoresis, light, electron and confocal microscopy, morphometric analyses, in situ hybridization, competitive PCR, tissue culture, cell transfection, myoblast and stem cell transfer for muscle gene therapy, contractile properties of muscle, etc.

Kathryn W. Peters, Ph.D.

Research Assistant Professor

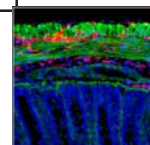
Numerous functions have been ascribed to the cystic fibrosis transmembrane conductance regulator (CFTR) and all of them rely on the proper trafficking of this protein into the apical plasma membrane. This premise is predicated on the majority of mutations that cause cystic fibrosis (CF) because misfolded CFTR protein remains in the endoplasmic reticulum, where it is degraded. Several lines of evidence suggest that intracellular movement of CFTR is through vesicles containing SNARE proteins and that upon stimulation, CFTR is inserted in to the plasma membrane.

Dr. Peters' research focuses on the identification and characterization of the proteins in these intracellular vesicles in which CFTR resides. The ultimate goal is to gather information that yields insight into protein-protein interactions responsible for translocating intracellular CFTR so that therapies to circumvent CF can be targeted to moving CFTR from within the cell to its functional location in the apical plasma membrane. These studies are completed with biochemical, molecular, and electrophysiological techniques which rely, in part, on cores within CBP. For example, numerous assays utilize the affinity of antibodies to their antigens; therefore we study cellular localization in collaboration with the imaging center.

Tony M. Plant, Ph.D.

Professor and Director of Center for Research in Reproductive Physiology

Dr. Plant's research is aimed at obtaining an integrative understanding, at both the systems and cellular levels, of the neurobiological mechanism that triggers the onset of puberty in man. The rhesus monkey is used as an experimental paradigm. Currently, his laboratory is exploring the notion that structural and/or functional changes in synaptic and glial inputs to the hypothalamic peptidergic GnRH neurons that drive the pituitary-gonadal axis are the key events underlying



the activation of this axis at puberty. Immunocytochemical procedures, combined with electron and confocal microscopy, are employed to study structural plasticity, while functional plasticity in the hypothalamus is examined by tracking protein and mRNA expression. Dr. Plant's laboratory is also interested in the role of gonadal peptides and locally produced paracrine factors in regulating pituitary function in the adult.

Clifford R. Pohl, Ph.D.

Adjunct Assistant Professor

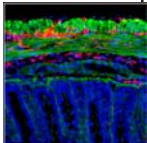
Dr. Pohl serves as Director of the Assay Core (Core C) of the Center for Research in Reproductive Physiology, which is supported by a U54 Cooperative Center grant from NICHD. The Core subserves several investigators at the Pittsburgh Center and also those at other US Institutions. Most notable, Dr. Pohl's Assay Core is setting up homologous radioimmunoassays for the baboon gonadotropins for colleagues at the University of Maryland. In addition, Dr. Pohl has decades of experience at iodinating proteins and he provides this service to several laboratories within the medical center. While Dr. Pohl does not perform independent research in the Department he is an integral component of Dr. Plant's team.

Suresh Ramaswamy, Ph.D.

Research Assistant Professor

Current thinking is that exposure to Hormonally Active Agents (HAA) prevalent in the environment accounts, in part, for an increase in the development of reproductive disorders in boys and a significant decline in sperm count in men. The putative, adverse effects of HAA on the development and maintenance of normal testicular functions may manifest indirectly by interfering along the hypothalamic-pituitary-testicular axis or directly at the level of the testis to compromise spermatogenesis. Although several *in vivo* studies using rodent models have addressed these issues, it is clear that extrapolation of the results from studies of rodents to human reproduction is hindered by confounding factors including species and strain differences among rodents. Moreover, the pattern of postnatal development of the hypothalamic-pituitary-testicular axis in higher primates leading to adulthood is strikingly different from that seen in rodents. In this regard, it is recognized that there is a particular need to determine the effects of endocrine disrupters on the development and health of children and adolescents.

Dr. Ramaswamy's research objective is to systematically examine, by integrating physiological, cellular, and molecular approaches, the direct effects of HAA on pubertal testicular development using the juvenile non-human primate (rhesus monkey) model. To this end, prepubertal primate 'testicular clamp' preparation is used as the experimental model, and, in the presence of HAA, precocious 'testicular puberty' is induced by stimulating the gonads of the immature monkey in a physiological manner with exogenous recombinant gonadotropins (FSH and LH). The focus of research is to identify in the primate testis the specific cell types



(Sertoli, Leydig, and stem germ cells), their endocrine/paracrine functions, and, in collaboration with other members of the Center for Research in Reproductive Physiology of the University of Pittsburgh, the cell signaling mechanisms and functional integrity of testicular genes that are vulnerable to the actions of HAA during puberty.

Preliminary results from an ongoing study of the biological effects of elevating levels of estradiol-17 β in the circulation of the male primate has indeed indicated that excess of estradiol is associated with a marked (up to 70%) inhibition in testosterone (T) secretion suggesting, at the outset, a direct effect at the level of LH-receptors and/or Leydig cell steroidogenic machinery.

Future studies are designed to examine whether estrogenic HAA prevalent in the environment indeed exhibit similar direct effects on primate testicular development during puberty.

Kathleen D. Ryan, Ph.D.

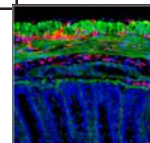
Associate Professor

Dr. Ryan serves as the Associate Director of the Office of Medical Education of the University's School of Medicine and as the Block Coordinator for the Basic Sciences Block in the Medical School curriculum. Dr. Ryan's laboratory is interested in the regulation of pubertal reproductive function in female mammals. In particular, we have evidence that hypothalamic dopamine may play a major part in imposition of the immature state in young females, and that changes in DA tone are required for activation of the adult reproductive capacity. Another focus of research is the role of the environment in the regulation of the onset of puberty in mammals.

Abhiram Sahu, Ph.D.

Research Associate Professor

Major research emphasis of this laboratory is to understand the neurochemical basis of feeding, obesity and diabetes with special emphasis on leptin and insulin signaling in the hypothalamus. We are currently investigating how orexigenic and anorectic signals in the hypothalamus mediate the satiety action of leptin, a long-sought satiety factor produced by adipocytes. In this regard, this laboratory has identified several hypothalamic peptidergic systems (e.g., galanin, melanin-concentrating hormone, pro-opiomelanocortin, neurotensin and NPY) that mediate the action of leptin on food intake and body weight regulation. Since obese individuals have more leptin in their blood, it is hypothesized that leptin resistance may be the major cause of obesity in human. Recently, we have developed an experimentally induced rat model with leptin resistance. Recent results include the demonstration of resistance in NPY neurons during the development of resistance to leptin's satiety action that occurs following chronic leptin infusion. We have also identified phosphatidylinositol-3 kinase (PI3K)-phosphodiesterase 3B (PDE3B)-cAMP pathway as an alternative mechanism of leptin signaling in the hypothalamus. We are currently addressing the questions of whether an alteration in leptin receptor activity and/ or defects in leptin signal transduc-



tion mechanisms (e.g. JAK/STAT and/or PI3K-PDE3B-cAMP pathway) in specific neuronal systems are responsible for the leptin resistance.

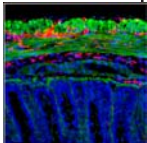
Another area of research is directed at elucidating neuroendocrine mechanisms that are involved in female reproductive aging, particularly in the development of menopause. In rodents, it has been established that an alteration in hypothalamic activity plays a major role in the development of irregular cyclicity, and subsequent acyclicity and anovulation in aged female rats. Research in our laboratory has shown that alteration in hypothalamic NPY neuronal activity may be responsible for the reproductive senescence in female rats. In women, however, while it is widely accepted that ovarian follicular depletion is the driving force for the menopause, the role of hypothalamus in the development of menopause is not clearly understood. Since rhesus monkey exhibits similar menstrual cycles and develops menopause like humans, we are using this animal to examine the role of hypothalamus in menopause.

Guy Salama, Ph.D.

Professor

A central goal of Dr. Salama's laboratory is to elucidate the mechanisms responsible for the initiation and termination of cardiac arrhythmias. An important step towards that end is to better understand the electrophysiology and function of the normal mammalian heart. To achieve these goals, they have developed the use of voltage-sensitive dyes and high temporal and spatial resolution optical techniques to map patterns of action potential (AP) propagation and repolarization. These novel methods are used to elucidate of the mechanisms that generate spatial heterogeneities of AP durations and the interplay between dispersion of repolarization (DOR) and anisotropic conduction velocities (CV). Several parameters play a role in producing non-uniformities of repolarization: the anisotropy of fiber structure is now found to influence DOR as well as CV and spatial heterogeneities of ionic channel expression and of AP duration restitution following a change in heart rate. Another related issue is to map AP propagation transmurally from endocardium to epicardium to elucidate the role of M-cells as (midwall cells) which may provide reentry pathways by forming a barrier of abrupt DOR. Animal models for cardiac arrhythmias include: acute ischemia in the guinea pig heart and 2 rabbit models of the long QT syndrome (LQTS). A number of mechanisms are being investigated as factors that promote arrhythmias in the LQTS: elevation of extracellular K^+ , sympathetic stimulation, and the role of spontaneous Ca^{2+} oscillation from the sarcoplasmic reticulum. Mapping spatial heterogeneities of intracellular Ca^{2+} transients in mammalian hearts using Ca^{2+} indicator dyes and imaging techniques. Once the normal heterogeneities of Ca^{2+} are determined, changes in Ca^{2+} transients will be analyzed in a wide range of physiological conditions to determined parameter that modulate Ca^{2+} transients. This laboratory has been at the forefront of the investigation of the role of sulfhydryl oxidation-reduction as a mechanisms to regulate Ca^{2+} release from the sarcoplasmic reticulum (SR). They are continuing this line of work in very exciting direction. We have found that nitric oxide (NO) and NO donors nitrosylate regulatory thiols on the SR Ca^{2+} release channel (e.g., ryanodine receptor) resulting in channel opening and release of Ca^{2+} from the SR. This mechanism seems to play a key role in Ca^{2+} homeostasis in striated muscles.

Also, we recently found that the actions of NO can be reversed by thioredoxin, thioredoxin



reductase, a thiol redox regulatory mechanism in mammalian cells which is linked to NADPH metabolism.

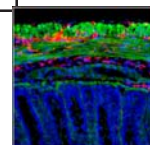
Donna Beer Stolz, Ph.D.

Research Assistant Professor and Assistant Director of the Center for Biologic Imaging

Liver Regeneration as a Model for Angiogenesis:

The healthy liver has the unique capacity to rapidly regenerate following a wide variety of mechanical and chemical insults. We utilize liver regeneration following 70% partial hepatectomy (PHx) to evaluate various aspects of liver growth and tissue remodeling. The basic liver architecture is represented as a structural unit comprised of one cell thick plates of parenchymal cells (hepatocytes) bounded on either side by sinusoidal endothelial cells (SEC). Following PHx, the hepatocytes undergo proliferation within the first 24 hr following resection, while the endothelial cells lining the liver sinusoid do not proliferate until 3-4 days after PHx. As a result, many avascular hepatic islands exist within the liver lobule and the subsequent proliferation and migration of the SEC into these islands provides a well-timed system to evaluate mechanisms underlying physiological angiogenesis. Additionally, the SEC are a very unique endothelium in that they are an undiaphragmed fenestrated endothelium resting on a non-basement membrane. Such specialization is an important feature of the sinusoids and deviation from this morphology is observed in various pathologies.

We are interested in describing the spatial and temporal signaling changes that accompany the growth and migration of the endothelium with respect to the hepatocytes during regeneration. We have been evaluating the roles of a variety of growth factors, their complimentary receptors, extracellular matrix molecules and their breakdown products as well as the involvement of cytokines, chemokines and their receptors in the revascularization process. The interplay of the SEC with the other non-parenchymal cells, such as the perisinusoidal stellate cells and resident macrophage Kupffer cells, also contribute to the progression of vascularization of the liver. The unique morphology of the SEC and ultrastructural changes that accompany revascularization provide quantifiable hallmarks into the specialization of the SEC in the progression of vascularization. In order to evaluate spatial and temporal regulation of the SEC proliferation, we routinely combine biochemical and imaging techniques. Since we employ an in vivo system, we developed a technique that allows for isolation and enrichment of the endothelial cell membrane from the liver during regeneration. We perfuse the liver with cationic colloidal silica, which uniformly non-covalently coats the vascular surfaces with a layer of dense silica. Subsequent homogenization of the liver allows for the coated endothelial cell membrane, which is now very dense, to be centrifugally isolated away from the rest of the liver. (Technique described in detail: Stolz, DB, MA Ross, HM Salem, W M Mars, GK Michalopoulos, K Enomoto. 1999. Cationic Colloidal Silica Membrane Perturbation as a Means of Examining Changes at the Sinusoidal Surface During Liver Regeneration. *Am. J. Path.* 155:1487-1498). Endothelial cell membranes isolated from liver at various times following PHx yield protein samples that can be analyzed for specific gene products including growth factor receptors and extracellular matrices that are upregulated on the endothelium during revascularization. While this gives us information that implicates involvement of specific growth factors endothelial cell growth and migration, it does not identify which endothelium have



upregulated these receptors. Temporal expression of these receptors are evaluated using immunofluorescence techniques on liver tissue.

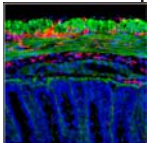
Using the combination of techniques described above we have shown that subsets of endothelium (i.e. large vessel vs. sinusoidal endothelium) upregulate different sets of receptors at various times during liver revascularization. (Ross, MA, CM Sander, TB Kleeb, SC Watkins, DB Stolz, 2001 Spatiotemporal expression of angiogenesis growth factor receptors during the revascularization of regenerating rat liver. *Hepatology*. 34:1135-1148). Correlative in vitro proliferation assays indicate that there are most likely synergistic interactions among a number of growth factors, and not just one is responsible for the endothelial growth. We also appreciate the ultrastructural changes that accompany liver revascularization. By using both transmission and scanning electron microscopy, we have determined that the fenestrations on the SEC change in both number and size during revascularization. Using vascular casting techniques we also show that the size and shape of the vasculature changes with relation to the avascular hepatic islands during liver angiogenesis. (Wack, KE, MA Ross, V Zegarra, SC Watkins, DB Stolz, 2001. Ultrastructural and zonal fenestration dynamics of sinusoidal endothelial cells during revascularization of regenerating rat livers. *Hepatology* 33:363-378). We are planning to extend our findings to liver revascularization following cold ischemic storage prior to liver transplantation, as endothelial cell damage is very acute under these conditions and can affect the short-term viability of the graft. We have also taken this approach to examining the role of SEC in regeneration events in KO mice that display delayed or non-optimized liver regeneration as the result of missing proteins. We are also would like to evaluate the role of these angiogenesis receptors in vascularization of liver tumors, both primary and secondary.

Fei Sun, Ph.D.

Research Assistant Professor

The cystic fibrosis transmembrane conductance regulator (CFTR) is an epithelial Cl channel. Mutations in CFTR gene cause cystic fibrosis (CF), the most common lethal genetic disease in Caucasian population. More than 900 different mutations have been found in the CFTR gene from CF patients. However, deletion of phenylalanine located in position of 508 in the CFTR gene product (deltaF508CFTR) accounts for more than 90% of CF patients and is associated with a very severe form of the disease. Studies on both wide type of CFTR and deltaF508CFTR showed that less than 30% of newly synthesized CFTR protein reaches to plasma membrane while all deltaF508CFTR protein retains in ER and is degraded by ubiquitin-proteasome pathway. Inhibition of ubiquitin-proteasome pathway promotes CFTR proteins to form aggregates in ER rather than to move to plasma membrane. Interestingly, deltaF508CFTR still behaves Cl channels as long as the protein can get to plasma membrane by so called "chemical chaperons". Dr. Sun's research is focused on the protein trafficking involved in both wt CFTR and deltaF508CFTR. His primary interest is to elucidate the mechanism(s) that are responsible for the retention of CFTR proteins in ER and to biochemically alter the retention and facilitate deltaF508CFTR trafficking to plasma membrane.

Using molecular biology, protein chemistry, immunofluorescence, and electrophysiological tech-



niques, Dr. Sun found that a portion of deltaF508CFTR protein can traffic to plasma membrane by co-expression of deltaF508CFTR with a small domain from CFTR with deletion of phenylalanine. These “rescued” deltaF508CFTR protein generated more than 10% of its wtCFTR Cl currents. Collaborating with Drs. Robbins and Mi in the Department of Molecular Genetics and Biochemistry, Dr. Sun is able to show CFTR Cl currents in airway epithelial cells derived from CF patients with deltaF508 homozygous transduced this small protein fused with PTD peptide. The mechanism underlying of this “rescue” is under studies. Future work will explore a possibility that deltaF508CFTR protein is anchored in ER by interacting with another protein. The results from these studies will not only provide the understanding how CFTR proteins traffic but also initiate insight of therapeutic potential for CF.

Linton M. Traub, Ph.D.

Assistant Professor

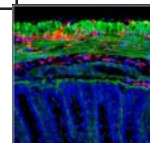
Many molecules enter the cell interior within clathrin-coated vesicles, in a process termed endocytosis. This membrane trafficking process is critical to the way we move and think. At the tip of each axon, synaptic vesicles (packages of neurotransmitter) release their contents when the nerve is stimulated by fusing with the cell surface. This releases the neurotransmitter into the synaptic cleft. Almost instantly, the limiting membrane of the synaptic vesicle is then retrieved from the plasma membrane within clathrin-coated vesicles. Endocytosis is thus tightly coupled to exocytosis, the stimulated release of neurotransmitter. Failure to recover synaptic-vesicle membrane results in both morphological disruption of the nerve terminal and defective neurotransmission. Clathrin-coated vesicles are also the primary vehicles used for the uptake of extracellular nutrients like lipoprotein particles and iron. Many viruses also utilize the clathrin-dependent internalization pathway as the principle mode of entry into the cell.

Dr. Traub’s lab studies the mechanisms and molecules involved in clathrin-coat assembly. To understand how these complex structures assemble within only a minute or two, we use biochemical, cell biological and structural approaches to unravel the protein-protein interactions that orchestrate the formation of this elaborate protein-sorting machine. We are currently focusing on a group of proteins termed endocytic ‘accessory’ proteins. We have documented that the accessory proteins epsin, huntingtin-interacting protein 1 (HIP1) and Disabled-2 (Dab2) are able to synchronously coordinate binding to phospholipid membranes, cargo selection and clathrin lattice assembly. We propose that there are several discrete cargo-selecting components of the clathrin coat in addition to the major AP-2 adaptor complex. The utility of expressing multiple cargo sorting proteins is that it allows cells to regulate endocytosis of certain cargo without impinging upon the trafficking of other molecules. We now intend to follow up our observations by using cell-based systems to carefully validate the role of epsin and Dab2 in the selection of distinct cargo and dissect out the functional consequences of mutating different functional regions of these proteins.

William H. Walker, Ph.D.

Assistant Professor

Gene Regulation in Mammalian Spermatogenesis



One of the major focuses of study in the walker laboratory is the regulation of CREB transcription factor activity in Sertoli cells through the FSH-dependent signaling cascade. This work has led to the understanding that FSH binding to Sertoli cells results in rapid phosphorylation and activation of CREB causing the activation of CREB-dependent gene transcription. Our recent studies have demonstrated that CREB is an essential Sertoli cell gene required for the survival of spermatocytes. By employing a strategy in which an adenovirus was used to deliver a phosphorylation defective CREB mutant only to Sertoli cells *in vivo*, it was found that the lack of Sertoli cell CREB activity disrupted spermatogenesis. Using a battery of adenovirus constructs expressing dominant negative or positive CREB proteins as well as classical molecular biology and quantitative real time PCR techniques, studies are underway to identify CREB-regulated genes in Sertoli cells required to support spermatogenesis.

A second major focus of study is the regulation of Sertoli cell gene expression by the NF- κ B transcription factor. Previously uncharacterized in the testis, we have found that NF- κ B is constitutively active in Sertoli cells and can be activated further by the cytokine TNF- κ which is produced by adjacent round spermatids. NF κ B and TNF- κ were shown to activate the CREB androgen receptor genes in transient transfection assays. These studies identify NF- κ B as a modulator of the FSH and androgen signaling pathways required for Sertoli cells to sustain spermatogenesis. An adenovirus expressing a dominant negative repressor of NF- κ B activity is presently being used to identify additional genes induced by NF- κ B in Sertoli cells.

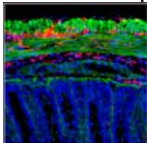
In a study currently in progress I have found that CREB is phosphorylated and activated rapidly after addition of androgen to primary Sertoli cells. This finding is highly significant as it suggests that the phosphorylation of CREB may be one mechanism by which testosterone is able to support spermatogenesis in the absence of FSH. The characterization of the signaling pathways responsible for testosterone-mediated CREB phosphorylation and the effects upon CREB-mediated transcription are underway.

Another study underway, describes the FSH-mediated induction a repressor of helix-loop-helix transcription factors named Id2. Preliminary studies show that the Id2 protein represses transcription from the androgen receptor promoter suggesting that transient induction of Id2 may be responsible for the reported delayed induction of androgen receptor gene expression by FSH and cAMP. As Id2 activity is also required for the proliferation of many cell types, studies are planned to determine whether Id2 may play an important role in the FSH-induced expansion of Sertoli cells prior to puberty.

In summary, our goals are to characterize the factors that modulate gene expression in the testis of rodents and monkeys and identify genes that are critical for the progression of spermatogenesis. The results of this work may then lead to information needed to provide therapies for infertility and solutions for male contraception.

Techniques being employed:

Gene therapy, cDNA cloning and subcloning, RNase protection and Northern analyses of gene expression, transient and stable cell transfection measurements of RNA transcription, *in situ*



hybridization and immunocytochemistry quantitation of mRNA and protein expression in vivo, differential display of RNA, GST-fusion protein co-immunoprecipitation measures of protein interaction measurements, and initiation of primary cell cultures.

Charles Washabaugh, Ph.D.

Research Assistant Professor

The main focus of my research deals with the expression of the genes responsible for muscle development and regeneration. Using competitive RT-PCR, the expression levels of muscle-specific genes, such as the myosin light chains and heavy chains, muscle and brain-type creatine kinases as well as the myogenic regulatory factors (MyoD, Myf-5, Myf-6 and Myogenin), are under examination in aneural developing soleus and EDL muscles and also during the denervation-reinnervation of adult hindlimb muscles. In addition, we currently are examining gene expression during myogenesis in MyoD and Myf-5 in knockout mice. Another line of investigation deals with the development of nerve muscle interactions and Acetylcholine receptor (AChR) cluster distribution in MyoD knockout mice. Techniques used include: Immunocytochemistry, gel electrophoresis, light, electron and confocal microscopy, in situ hybridization, quantitative competitive RT-PCR.

Simon C. Watkins, Ph.D.

Professor and Director of the Center for Biologic Imaging

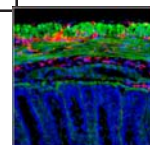
All skeletal muscle fibers are enveloped in a sarcolemma. Structurally it is composed of the muscle fiber basal lamina, plasma membrane and underlying cytoskeleton. It is a highly complex structure and is critical in ensuring appropriate muscle structure and function. A subset of interconnected molecules within this structure may be defined as the dystrophin cytoskeleton. Mutations in these molecules are responsible for a number of diseases including Duchenne muscular dystrophy (dystrophin deficiency), congenital muscular dystrophy (merosin deficiency) and the sarcoglycanopathies. In each case the failure of a single component of the dystrophin cytoskeleton leads to a debilitating, commonly lethal myopathy.

At the present time little is known about the process of development, assembly and integration of the dystrophin cytoskeleton and its potential role(s) in establishing and maintaining normal muscle function. Understanding these processes and defining what goes wrong in disease is the focus of Dr. Watkins' research efforts.

Various methodologies are employed in this research: Optical methods (multimode, multicolor deep tissue imaging methods coupled with fluorescent imaging tools and immunoelectron microscopy).

Recent results are described in the following publications:

Mizuno Y, Thompson TG, Guyon JR, Lidov HG, Brosius M, Imamura M, Ozawa E, Watkins SC, Kunkel LM. Desmuslin, an intermediate filament protein that interacts with alpha-dystrobrevin and



desmin. Proc Natl Acad Sci U S A. 2001 May 2;98(11):6156-61.

Takada F, Woude DL, Tong HQ, Thompson TG, Watkins SC, Kunkel LM, Beggs AH. Myozenin: An alpha-actinin- and gamma-filamin-binding protein of skeletal muscle Z lines. Proc Natl Acad Sci U S A. 2001 Feb 13;98(4):1595-1600.

We have been performing many of these studies on in vitro material over extended culture periods. This is working well, however, fundamental blocks in spectral separation and maintenance of cell health have arisen, we have now found solutions to these problems. Use 2p and spectral separation tools to increase sensitivity and temporal resolution of molecular events.

Anthony J. Zeleznik, Ph.D.

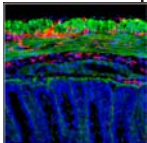
Professor

Dr. Zeleznik's research interests are focused on the physiology and cell biology of ovarian function. At the physiological level, we are interested in understanding how the events that transpire during the menstrual cycle (follicular development, ovulation, corpus luteum formation and regression) are precisely regulated by the interactions between hypothalamus, the pituitary and the ovary and how other factors such as IGF-I and insulin may modify this system. At the cellular and molecular level, we are interested in understanding the mechanisms by which the response of the ovary to the gonadotropic hormones changes as a function of the maturational status of the ovary. Towards this end, we are interested in identifying the intracellular signaling pathways activated by the gonadotropic hormones and whether they change in relationship to ovarian cellular differentiation. To accomplish this, replication defective adenovirus vectors that stimulate or inhibit the cAMP and other intracellular signaling systems are being used in vitro and in vivo.

Allan Z. Zhao, Ph.D.

Assistant Professor

Obesity and type 2 diabetes have become serious health concerns in western societies. In the United States alone, approximately 25% of the population are obese, more than 60% are overweight. The American Diabetes Association estimates that currently there are about 15 million people in the U.S. who are type 2-diabetic. Our research interest is focused on the molecular signaling events underlying the actions of leptin and insulin, two very important hormones that regulate our bodyweight, food-intake as well as glucose and fat metabolism. Our work involves a wide range of disciplines, including biochemistry, molecular biology and pharmacology. We are also making different transgenic and gene-targeting models to mimic the situations in human obesity and type 2 diabetes.



Faculty Study Sections 2000-2001

Neil A. Bradbury, Ph.D.
Assistant Professor

Cystic Fibrosis Foundation Research Development Project, Internal Reviewer University of Alabama at Birmingham
Cystic Fibrosis Foundation Research Development Project, Internal Reviewer University of Pittsburgh School of Medicine
Cystic Fibrosis Trust, U.K.
Cystic Fibrosis Foundation, External Reviewer
Veteran's Association, Merit Review Board, External Reviewer

Daniel C. Devor, Ph.D.
Assistant Professor

ad hoc reviewer for Cystic Fibrosis Foundation
ad hoc reviewer for Department of Veterans Affairs

Peter F. Drain, Ph.D.
Assistant Professor

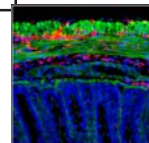
ad hoc referee for National Science Foundation

Marcia R. Ontell, Ph.D.
Professor

Study Section, National Institutes of Health, Respiratory and Applied Physiology Regular Member (on assignment to new Skeletal Muscle Biology Study Section)
Reviewer, MRC-Canada
Reviewer, Assoc. Francaise Contre les Myopathies
Reviewer, Italian Teleton
Reviewer, Competitive Medical Research Fund, University of Pittsburgh

Tony M. Plant, Ph.D.
Professor

Extramural Grant Reviewer for NSF



Abhiram Sahu, Ph.D.

Research Associate Professor

Reviewer, National Science Foundation

Reviewer, United States Department of Agriculture NRICGP Proposals

Guy Salama, Ph.D.

Professor

NIH Member of SBIR review group November 14, 2000, SRA, Dr. Michael Lang.

Member of the Mid-5 Study Section of the Western Pennsylvania Affiliate of the AHA review group on Cell Signaling March 20th, 2000; March 27, 2001.

NIH Member of SBIR review group April 6, 2001, SRA, Dr. Michael Lang.

Simon C. Watkins, Ph.D.

Professor

NIH study Section BSRG, Large instrumentation (optical instruments). September 28-29th

NIH study Section ZRG SBIR (Imaging) October 26th 2000

NIH study Section, Imaging Instrumentation Development R01s October 27th 2000

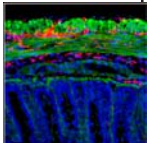
NIH-NCI study section development of novel imaging technologies December 7-8th 2000

NIH study section Cystic Fibrosis P30's December 11th 2000

NIH study section ZRG1-CBY-2 December 15th 2000

NIH study section ZRG1-SSU January 19th 2001

NIH study section DRG1 MMG February 26th 2001



Faculty Advisory Committee Memberships

Ameredes, William [Transferred to Department of Medicine, 12/31/01]

Visiting Research Assistant Professor

Research Advisory Committee - Children's Hospital of Pittsburgh

Bradbury, Neil

Assistant Professor

Cystic Fibrosis Research Center Internal Advisory Committee, University of Pittsburgh School of Medicine

Bridges, Robert

Professor

Cell Biology and Physiology Chairman's Advisory Committee

Frizzell, Raymond

Professor

Mount Desert Island Biological Laboratory Trustees
Medical Advisory Council, Cystic Fibrosis Foundation

Murray, Sandra

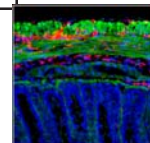
Professor

Research Advisory Committee - Morehouse School of Medicine
Child Health Research Center Grant Advisory Committee
NIMH Training Grant Faculty Advisory Committee
Advisory Board Member for Survival Skills and Ethics Program
Cell Biology and Physiology Chairman's Advisory Committee

Ontell, Marcia

Professor

Parent's Project for Muscular Dystrophy Advisory Committee
Duchenne Muscular Dystrophy Research Center of University of Pittsburgh
Internal Advisory Committee



Cell Biology and Physiology Chairman's Advisory Committee

Plant, Tony

Professor

Member, Health Sciences Animal Research Advisory Committee

Watkins, Simon

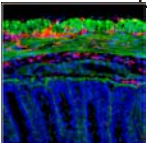
Professor

Research Advisory Board, Childrens Hospital, University of Pittsburgh
Research Advisory Committee, University of Pittsburgh School of Medicine
Cell Biology and Physiology Chairman's Advisory Committee

Zeleznik, Tony

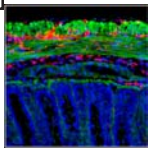
Professor

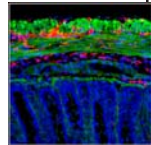
Magee-Womens Research Institute Steering Committee



Cell Biology and Physiology Sponsored Research Funding

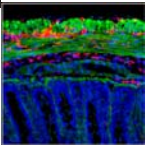
PI	Agency Name	Title	Annual DC	Annual IDC
Bradbury, Neil	National Institute of Health	CFTR Regulation by Targeted Kinase and Phosphatase	\$109,097	\$55,193
	Cystic Fibrosis Foundation	Regulation of CFTR Removal from the Cell Surface	\$60,000	\$4,801
	Cystic Fibrosis Foundation	Inhibition of CFTR Endocytosis	\$27,510	\$0
	Circagen	The Effect of the Compounds Upon Their Efficacy in Increasing the Trafficking of the CF Protein out of the ER and Its Maturation Through the Golgi	\$22,518	\$12,160
Bridges, Robert	National Institute of Health	Fluctuation and Impedance Analysis of Chloride Secretion	\$126,038	\$63,018
	National Institute of Health	Mechanisms of Epithelial Bicarbonate Secretion	\$92,000	\$44,563
	Cystic Fibrosis Foundation	Mechanisms of Bicarbonate Secretion	\$49,980	\$3,999
	Cystic Fibrosis Foundation	Optimization of Benzimidazolones for Cl Secretion	\$60,000	\$4,801
	Bayer	Phase IV Studies 95'-96' Objectives	\$39,101	\$21,115
	Novartis	Evaluation of the Ion Conductances and Capacitance Changes Involved in Airway Epithelial Cell Mucin Secretion	\$70,866	\$19,134
	Circagen	The Effect of the Compounds Upon Their Efficacy in Increasing the Trafficking of the CF Protein out of the ER and Its Maturation Through the Golgi	\$22,518	\$12,160
Devor, Dan	National Institute of Health	Potassium Channel Properties of Airway Cells	\$49,946	\$24,973
	National Institute of Health	Regulation of HIK1 in Secretory Diarrhea	\$130,190	\$65,095
	Am Physiological Soc	Lazaro J Mandel Young Investigator Award	\$3,000	\$0
Drain, Peter	National Science Foundation	Stoichiometry of the Inhibitory ATP Site and Inhibition Gate of the ATP Sensitive Potassium Channel	\$76,668	\$38,332
	Children's Hospital (JDF)	Quantitative Live b-Cell Fluorescence Imaging of Normal and Enhanced Stimulus-Evoked Insulin Secretion	\$57,882	\$3,359

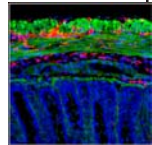




Frizzell, Raymond	National Institute of Health	SCOR: CFTR in Airway Cell Function	\$171,408	\$82,361
	National Institute of Health	SCOR: CFTR in Airway Cell Function	\$0	\$0
	National Institute of Health	Traffic Regulatory Proteins and Enac	\$159,415	\$79,707
	Cystic Fibrosis Foundation	HTS Assays for Cell surface CFTR	\$130,826	\$10,466
	Cystic Fibrosis Foundation	Program Enrichment-Admin.	\$0	\$0
	Burroughs Wellcome Fund	Wellcome Visiting Professorship in the Basic Medical Sciences	\$4,165	\$0
	Cystic Fibrosis Foundation	Research Training	\$63,200	\$0
	Cystic Fibrosis Foundation	Structure-Function Relations in CFTR Traffic	\$33,500	\$0
	Cystic Fibrosis Foundation	Structure-Function Relations in CFTR Traffic	\$34,185	\$0
	Cystic Fibrosis Foundation	SNARE Proteins and Epithelial CFTR Traffic	\$6,096	\$0
Gangopadhyay, N.*	Cystic Fibrosis Foundation	Molecular Biology/Gene Expression	\$67,346	\$0
Murray, Sandra	National Science Foundation	Role of Gap Junction Expression in Adrenal Function	\$74,556	\$37,277
	ASCB	Role of Gap Junction in Adrenal Cortical Cell Function	\$1,834	\$0
Onate, Sergio	CMRF	Steroid Receptor Co-Activators Expression and Activity in Prostate Cancer	\$25,000	\$0
Ontell, Marcia	National Institute of Health	Improving Muscle function through Gene Delivery	\$12,050	\$6,025
	National Institute of Health	Myogenic Factors: Muscle Maturation and Regeneration	\$176,180	\$76,060
	Muscular Dystrophy Assoc. Parent Project	Muscle Regeneration and Myogenic Regulatory Factors	\$60,185	\$4,815
		Enhancement to Dystrophic Muscle Mass and Functional Capacity	\$68,609	\$6,529
Peters, Kathryn	CMRF	Sodium Bicarbonate Cotransporter Expression in the Airway	\$9,375	\$0

Plant, Tony	National Institute of Health	Physiology and Pathophysiology of the Primate Gonad	\$0	\$0
	National Institute of Health	Physiology and Pathophysiology of the Primate Gonad	\$119,561	\$83,691
	National Institute of Health	Physiology and Pathophysiology of the Primate Gonad	\$32,642	\$16,621
	National Institute of Health	Physiology and Pathophysiology of the Primate Gonad	\$160,154	\$64,105
	National Institute of Health	Physiology and Pathophysiology of the Primate Gonad	\$47,679	\$21,810
	National Institute of Health	The Role of Neuronal Plasticity in Primate Puberty	\$217,467	\$108,734
	National Institute of Health	The Mediodorsal Thalamic Nucleus in Schizophrenia	\$11,624	\$930
	National Institute of Health	Postdoctoral Training in Reproductive Physiology	\$51,776	\$3,973
	Glaxo Wellcome	NPY and Feeding in the Rhesus Monkey	\$2,276	\$1,503
	Ramaswamy, Suresh	CMRF	Studies of the Hypothesis that Environmental Estrogens Inhibit Sperm Production in Primates	\$20,000
Sahu, Abhiram	National Institute of Health	The Role of the Hypothalamic Pituitary Axis in Menopause	\$29,150	\$14,575
	National Institute of Health	Leptin Action on Hypothalamic Peptides Governing Feeding	\$171,769	\$82,079
	Cystic Fibrosis Foundation	The Role of CFTR in Hypothalamic Peptide Secretion	\$27,510	\$0
Salama, Guy	National Institute of Health	Factors that Initiate Arrhythmias in Long QT Syndrome	\$89,941	\$41,112
	National Institute of Health	Mechanisms of Repolarization-Induced Arrhythmias in Mice	\$178,458	\$50,145
	National Institute of Health	Mechanisms of Cytokine Induced Arrhythmias in Congestive Heart Failure	\$11,085	\$5,542
	American Heart Association	Spatio-temporal Heterogeneities of Cai and Action Potentials in Long QT Syndrome & Torsade	\$16,000	\$0
	American Heart Association	Site of Action of Nitric Oxide (NO) on Cardiac Tyrodine Receptor	\$16,000	\$0
	American Heart Association	Role of Dispersion of Repolarization in Triggering Ventricular Tachycardia	\$16,000	\$0
	American Heart Association	Mechanisms of Ventricular Arrhythmias in Genetically Manipulated Mice w/ Long QT Syndrome	\$22,000	\$0

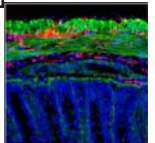




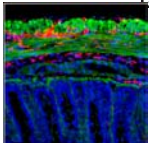
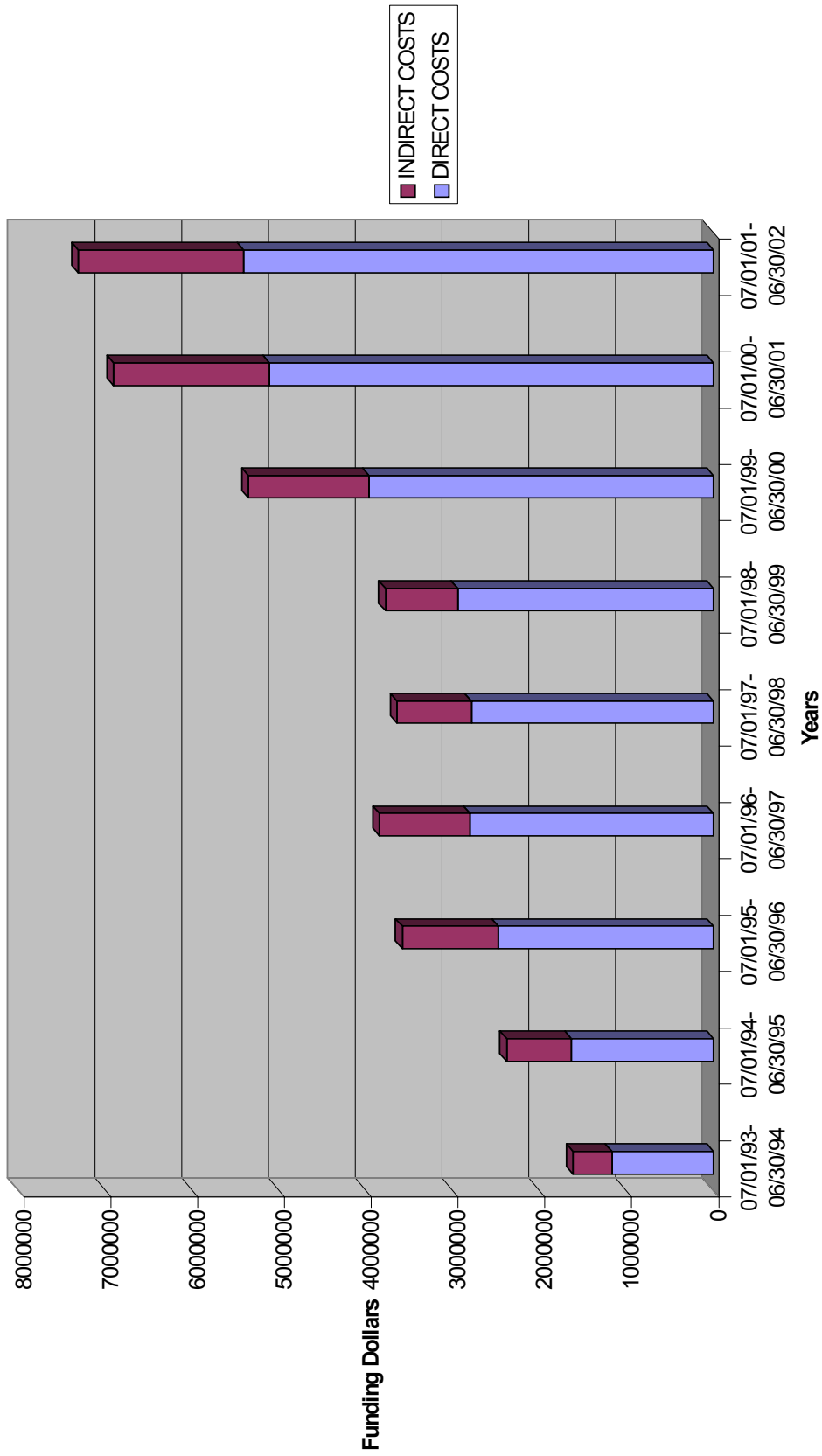
Singh, Ashvani*	Cystic Fibrosis Foundation Beacon	Drug Chemistry Core Beacon Lab Contract	\$40,000 \$8,100	\$0 \$8,100
	National Institute of Health National Institute of Health	Liver Regeneration as a Model for Angiogenesis Postoperative Ileus Induced by Surgical Trauma	\$64,161 \$5,826	\$32,081 \$2,914
Traub, Linton	National Institute of Health	Clathrin-Coated Vesicles and Lysosome Function	\$109,633	\$54,817
Walker, William	National Institute of Health	Regulation of Testis Gene Expression by cAMP and CREB	\$51,999	\$26,000
	National Institute of Health	Regulation of Testis Gene Expression by cAMP and CREB	\$60,900	\$4,872
	National Institute of Health	Determination of the Role of CREB in Spermatogenesis	\$34,524	\$0
Watkins, Simon	National Institute of Health	Cancer Center Support Grant	\$19,055	\$9,527
	National Institute of Health	Generation of Animal Models of Arthritis by Gene Transfer	\$20,312	\$10,157
	National Institute of Health	Pathogenesis & Treatment of Experimental Peritonitis	\$23,854	\$11,927
	National Institute of Health	Post-Traumatic Sepsis: Regulation of LPS Binding Protein	\$32,705	\$16,353
	National Institute of Health	Molecular Biology of Hemorrhagic Shock	\$59,622	\$29,811
	National Institute of Health	Cancer Therapy with Activated Natural Killer Cells	\$52,385	\$26,193
	National Institute of Health	Echocardiographic Study of the Coronary Microvasculature	\$4,377	\$2,189
	National Institute of Health	Metallothionein & Reactive Oxygen and Nitrogen Species	\$4,698	\$2,349
	National Institute of Health	Dendritic Cell Biology and Therapy (Core C)	\$74,227	\$37,114
	National Institute of Health	Growth Inhibition by IL-2 of IL-2R & Oral Carcinomas	\$4,639	\$2,320
	National Institute of Health	DNA Based Adjuvant Immunization for HIV	\$5,550	\$2,775
	National Institute of Health	Role of Endothelin in Liver Cirrhosis and Its Complications	\$5,514	\$2,757
	National Institute of Health	Liver Specific Non-Viral Vectors Imaging Core-C	\$12,995 \$65,135	\$6,498 \$26,305
	National Institute of Health	Caspase-Mediated Neuronal Death After Head Injury Model Systems Toward Development of Human Gene Therapy	\$12,224 \$87,550	\$6,111 \$43,775

	National Institute of Health	Cell & Tissue Imaging Core	\$51,376	\$25,689
	National Institute of Health	Cell & Tissue Imaging Core	\$48,704	\$0
	National Institute of Health	Cell & Tissue Imaging Core	\$102,250	\$6,249
	National Institute of Health	Hepatocyte: Kupffer Cell Interactions in Surgical Sepsis	\$54,178	\$27,089
	National Institute of Health	Molecular Mechanisms in Traumatic Brain Injury: Bench to Bedside	\$3,324	\$1,629
	National Institute of Health	Cytokine Gene Therapy of Cancer	\$34,955	\$17,478
	National Institute of Health	Molecular Contributor to Stem Cell Quiescence	\$4,631	\$2,316
	National Institute of Health	Cardiovascular Gene Therapy Center	\$50,079	\$25,040
	National Institute of Health	JSM 6335F FE Scanning Electron Microscope	\$79,400	\$0
	National Institute of Health	Blocking Intimal Hyperplasia Following Vascular Trauma	\$8,000	\$3,993
	Cystic Fibrosis Foundation	Cystic Fibrosis Research Development Program	\$40,000	\$0
	American Cancer Society	Molecular Contributors to Stem Cell Quiescence	\$1,497	\$374
	Genetic Therapy Inc.	Cryo-Electron Microscopy Study	\$17,500	\$0
Zeleznik, Anthony	National Institute of Health	Regulation of the Primate Corpus Luteum	\$157,696	\$76,336
	National Institute of Health	Physiology and Pathophysiology of the Primate Gonad	\$137,031	\$64,851
Zhao, Allan	OB/Nutrition Center-UPMC	Developing A Genetic Model with Peripheral Leptin Resistance	\$11,250	\$0
	American Diabetes Association	Development and Study of a Genetic Model with Peripheral Leptin Resistance	\$86,957	\$13,043
	CMRF Dean's Support	Study of Peripheral Leptin Resistance	\$25,000	\$0

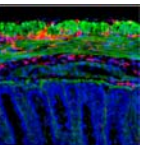
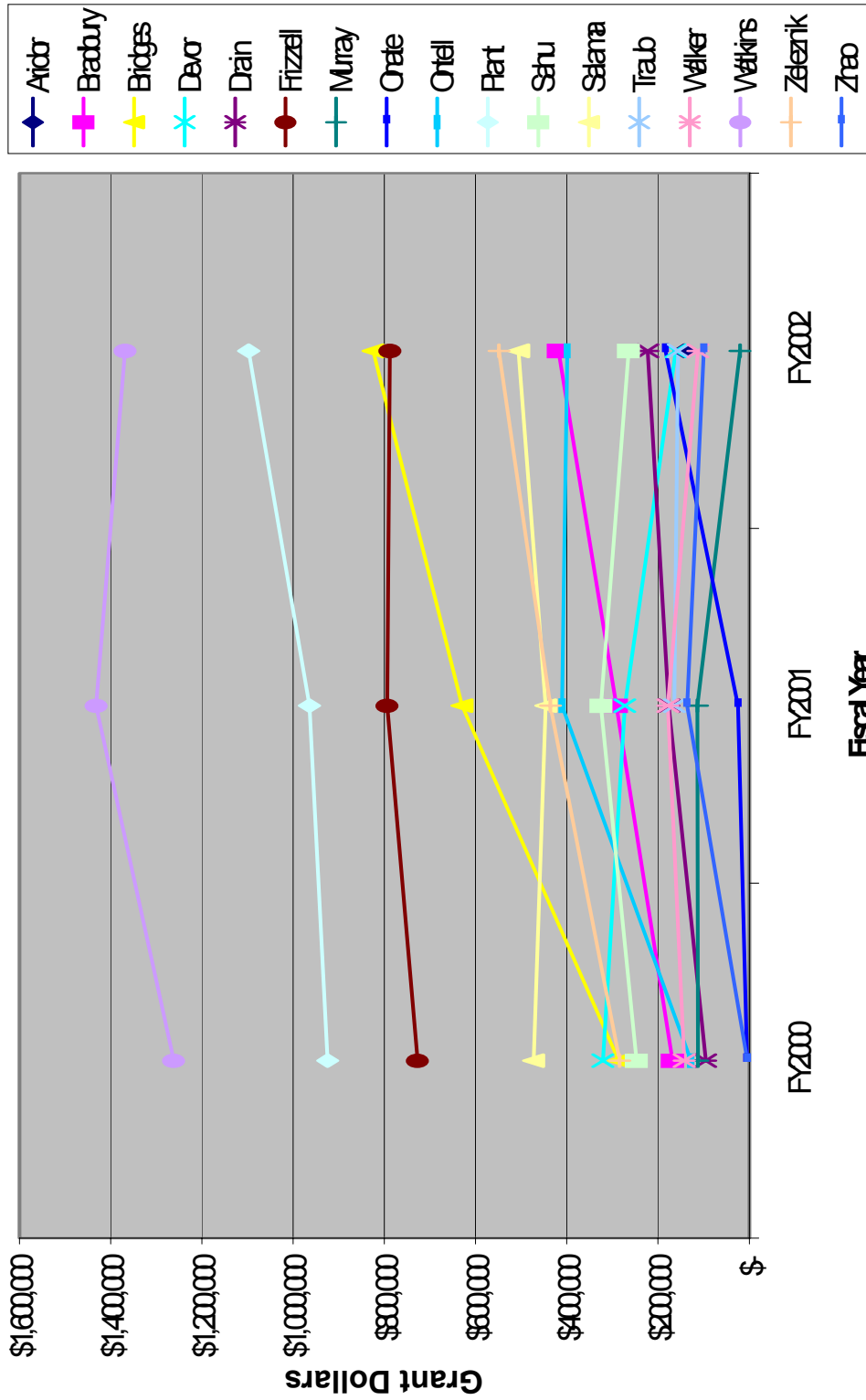
*Left University of Pittsburgh during reporting year.



CBP Sponsored Funding History



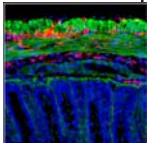
OB FACULTY FUNDING HISTORY (3 YEARS)

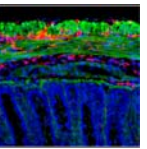
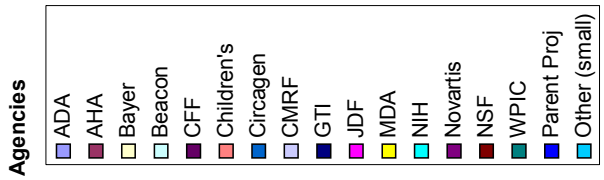
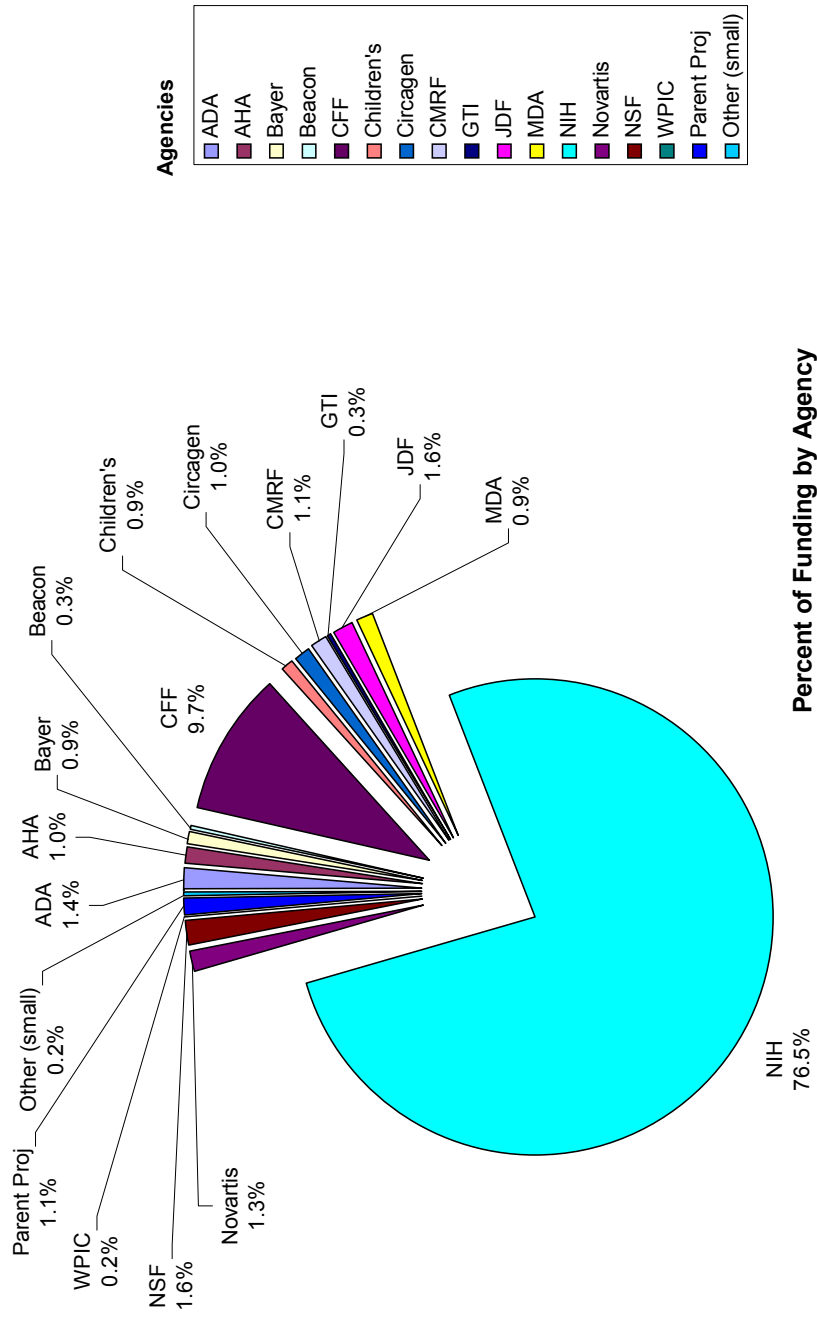


Cell Biology and Physiology Department NIH Rankings

[NOTE: We must use the ranking developed for Physiology departments since there is no ranking developed for Cell Biology departments.]

Year	Rank	NIH Funding
FY01	27	\$6,104,958
FY00	32	\$4,990,137
FY99	29	\$4,325,111
FY98	46	\$2,690,162
FY97	37	\$2,805,231
FY96	30	\$3,116,435





CBP Seminar Series - 2000-2001

September 27, 2000

Linton M. Traub, Ph.D.

Assistant Professor

Department of Cell Biology and Physiology

University of Pittsburgh

“Molecular Interactions During Endocytic Clathrin-Coat Assembly”

October 25, 2000

Rajesh Agarwal, Ph.D.

Professor

Center for Cancer Causation and Prevention

AMC Cancer Research Center

“Cell Signaling and Regulators of Cell Cycle and Apoptosis as Molecular Targets for Prostate Cancer Intervention”

November 15, 2000

Peter F. Drain, Ph.D.

Assistant Professor

Department of Cell Biology and Physiology

University of Pittsburgh

“When Inhibition Leads to Release: Mechanisms Underlying K_{ATP} Channel Regulated Insulin Vesicle Exocytosis”

November 29, 2000

Kevin Strange, Ph.D.

Professor

Department of Anesthesiology and Pharmacology

Vanderbilt University School of Medicine

“New Insights Into CIC Anion Channel Biology: Functional and Molecular Identification and Physiological Roles of a C. Elegans Cell Cycle-Regulated CIC-2 Ortholog”

January 10, 2001

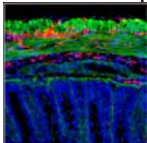
Peter A. Friedman, Ph.D.

Professor

Department of Pharmacology

University of Pittsburgh

“Renal Calcium Channels: Is ECaC the Whole Story?”



January 24, 2001

Michael S. Marks, Ph.D. (Mickey)

Department of Pathology and Laboratory Medicine

University of Pennsylvania School of Medicine

“Melanosome Biogenesis: How Does One Generate a Bizarre Lysosome-Related Organelle?”

January 31, 2001

Robert F. Gilmour, Ph.D.

Professor

Department of Biomedical Sciences, Section of Physiology

Cornell University

“A Mechanism for Ventricular Fibrillation”

February 21, 2001

William B. Guggino, Ph.D.

Professor

Department of Physiology

Johns Hopkins University

“Role of the PDZ Domain in the Processing, Trafficking and Assembly of CFTR into a Macromolecular Complex”

February 28, 2001

William N. Zagotta, Ph.D.

Associate Professor

Department of Physiology and Biophysics

University of Washington School of Medicine

“Molecular Mechanisms of Activation in Cyclic Nucleotide-Gated Ion Channels”

March 7, 2001

John C. Lawrence, Ph.D.

Professor

Departments of Pharmacology and Medicine

University of Virginia School of Medicine

“mTOR Signalling in Insulin Action”

March 14, 2001

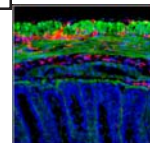
Paul Allen, M.D., Ph.D.

Professor

Department of Anesthesia

Brigham and Women’s Hospital

“RyR Structure Function Studies”



March 14, 2001

Nancy L. Weigel, Ph.D.

Associate Professor

Department of Cell Biology

Baylor College of Medicine

“The Roles of Androgen Receptors and Vitamin D Receptors in Regulating Androgen-Dependent and Androgen-Independent Prostate Cancer Growth”

March 21, 2001

Daniel R. Storm, Ph.D.

Professor

Department of Pharmacology

University of Washington

“Mechanisms Underlying Neuroplasticity: Role of the Erk MAP Kinase and cAMP Signal Transduction Systems”

March 28, 2001

Norman Hecht, Ph.D.

University of Pennsylvania

“Post-Transcriptional Regulation of Gene Expression in Male Germ Cells: Intracellular and Intercellular mRNA Transport”

April 4, 2001

Sergio Onate, Ph.D.

Assistant Professor

Department of Cell Biology and Physiology

University of Pittsburgh

“Steroid Receptor And Coactivator Function in Prostate Cancer”

April 11, 2001

Mark Anderson, Ph.D.

Vanderbilt University

“Cardiomyopathy and the Arrhythmogenic Phenotype”

April 18, 2001

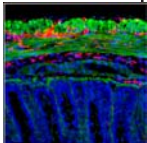
Andre Terzic, M.D., Ph.D.

Director, Cardiovascular Research Lab

Department of Internal Medicine

Mayo Clinic, Rochester

“Enzymology of an Ion Channel: The Paradigm of the ATP-Sensitive K⁺ Conductance”



May 2, 2001

Allan Zhao, Ph.D.

Assistant Professor

Department of Cell Biology and Physiology

University of Pittsburgh

“Leptin Signaling and Bodyweight Regulation”

May 16, 2001

J. Kevin Foskett, Ph.D.

Professor, Department of Physiology

University of Pennsylvania School of Medicine

“Regulating Cystic Fibrosis Chloride Channel Activity by Protein Interactions with its Tail”

May 30, 2001

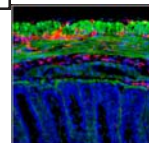
Harry Blair, Ph.D.

Professor

Departments of Pathology and Cell Biology and Physiology

University of Pittsburgh

“Bone Turnover is Inseperable from Bone Morphogenesis: A Unified View
of Continuing Differentiation and Apoptosis in the Skeleton”



The Graduate Program in Cell Biology and Molecular Physiology

The program in Cell Biology and Molecular Physiology has a rich tradition of scientific training and discovery. Graduates of the Ph.D. program are now chairs of departments at six major U.S. medical schools. Today, the department brings together basic and clinical research faculty who are dedicated to their research programs and to the training of students. Among the medical school departments, this faculty is uniquely focused on integrative biology; that is, using the tools of genetics and molecular biology to understand the integrated functions of cells and organisms in the era following description of the human genome.

Our program offers the opportunity to interact with multiple, well supported faculty with international reputations. Students receive stipends throughout their training, which is a rich experience going far beyond formal classroom training, including numerous journal clubs, research conferences and the opportunity to attend national and international meetings.

The central theme of integrative biology in our program plays out in research projects that are focused on important diseases, including heart disease, cancer and diabetes, as well as inherited disorders of developmental and reproductive functions.

New Courses

Academic Year 2000-2001

Cell Biology of Normal & Disease States

Course Number: 2880

Course Director: *Raymond Frizzell, Ph.D.*

Spring, 2001

CMBP Graduate Courses Descriptions

Academic year 2000-2001

Title: MS Thesis Research

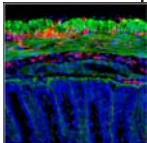
Course Number: 2800

Course Director: *Simon Watkins*

When: Fall Term, Spring Term, Summer Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: A directed research project which results in a thesis for a Master's Degree.



Title: Topics in Integrative Physiology

Course Number: 2820

Course Director: *Anthony Zeleznik*

When: Fall Term

Prerequisites: "A working knowledge of Biology, Biochemistry and Physics"

Core Course for: Cell Biology and Molecular Physiology Program

Description: Rather than the usual survey of organ systems which is typical of most physiology courses, this course will focus on the experimental approaches used to analyze complex homeostatic mechanisms in the intact mammalian organism. An attempt will be made to show how molecular and cellular methodologies can be integrated with classical physiological approaches to answer important questions about the survival and function of the whole animal. The subject matter will be taught through lectures, problem-solving sessions, and examination of original papers.

Title: Cell and Molecular Physiology

Course Number: 2830

Course Director: *Raymond Frizzell*

When: Spring Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Core Course for: Cell Biology and Molecular Physiology Program

Description: This course consists of lectures, problem-solving sessions, and examination of original papers. A main focus will be on the application of modern biophysical and molecular-genetic approaches in the analysis of cellular function. Topics include: 1) membrane transport; pumps, channels, and bio-electrical potentials; 2) excitable membranes; 3) regulation of ion channels; 4) absorptive and secretory functions of epithelia; 5) signal transduction; 6) molecular motors, cell motility, and muscle contraction.

Title: Regulation of Membrane Traffic

Course Number: 2840

Course Director: *Gerard Apodaca/Ora Weisz*

When: Summer Term

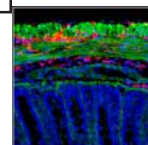
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Core Course for: students in the Program in Cell Biology and Molecular Physiology with research focus in cellular biology

The focus of this course is to analyze membrane/protein traffic along both the biosynthetic and endocytic pathways. Particular emphasis will be placed on how this traffic is regulated and how it is disrupted during disease. The topics change each year and are tailored to the interests of the students. The topics this year include, the role of dynamin and dynamin-associated proteins in receptor-mediated endocytosis, the function of Rab5 and its effector EEA1, regulation of traffic between early and late endosomes, quality control in the ER-associated degradation pathway, viral strategies for subversion of host cell defenses, regulation of trafficking of the TGN-associated proteinase furin, down-regulation of MHC class I by the HIV Nef protein, and transport between the secretory pathway and the cytosol.

Title: Research Seminar/Cellular Physiology

Course Number: 2851



Course Director: *Peter Drain*

When: Fall Term, Spring Term

Prerequisites: Medical or Graduate Student

Advanced research seminar with journal club format specializing in current aspects of molecular and cellular physiology.

Title: Research Seminar/Membrane Trafficking

Course Number: 2852

Course Director: *Gerard Apodaca*

When: Fall Term, Spring Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Core Course for: students in the Program in Cell Biology and Molecular Physiology with research focus in cellular biology

Description: Advanced research seminar with journal club format specializing in current aspects of cell-cell communication, cell signaling, and membrane/protein traffic.

Title: Research Seminar/Reproductive Physiology

Course Number: 2853

Course Director: *Tony Plant*

When: Fall Term, Spring Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: Advanced research seminar with journal club format specializing in current aspects of reproductive physiology.

Title: Multiparametric Microscopic Imaging

Course Number: 2860

Course Director: *Simon Watkins*

When: Summer Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: 1) a lecture/lab course which immerses students in the theory and practical aspects of modern microscopic imaging. The fields will cover the theory and implementation of all types of light and electron microscopy and computer aided imaging. Students will be expected to reach a functional capability in a selected technology.

Title: Histology

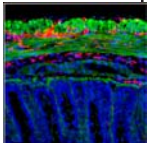
Course Number: 2870

Course Director: *Georgia Duker*

When: Summer Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: The objective of this lecture/lab course is to comprehend the relationship between structure and function at the cell, organ and organ system levels. Focus is placed on the integration of cell biology, classical histology and basic physiology of each of the organ systems, with the exclusion of the central nervous system. This knowledge is applied by building



skills in the interpretation of light and electronmicrographic images of cells and organs. This course is a requirement for those graduate students wishing to serve as teaching fellows in Histology for the Medical School.

Title: Cell Biology of Normal & Disease States

Course Number: 2880

Course Director: *Raymond Frizzell*

When: Spring Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: This course will extend basic knowledge of cell and molecular biology obtained in Foundations of Biomedical science. The lectures will focus on four or five intensely active research areas of cell biology. Basic principles will be reinforced by considering disease states in which these processes are defective. Examples: cell growth and cancer, cell polarity and protein targeting, diseases of ion channels, cell biology of diabetes. Lectures and discussion groups.

Title: Directed Study

Course Number: 2890

Course Director: *Simon Watkins*

When: Fall Term, Spring Term, Summer Term

Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: This course provides the student an opportunity to carry out a specific laboratory project in any area of interest in Cell Biology or Physiology.

Title: Ph.D. Dissertation Research

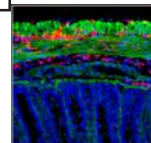
Course Number: 3800

Course Director: *Simon Watkins*

When: Fall Term, Spring Term, Summer Term

Prerequisites: Successful completion of the Comprehensive Examination
INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: After advancement to candidacy for the Ph.D. degree, students enroll in this course to pursue original experimental laboratory research. The results of which will provide the substance of their doctoral dissertation. A minimum of forty credits of this course are required for the Ph.D. degree in the School of Medicine.

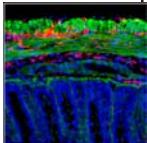


Faculty Teaching Honors - 2000-2001

Georgia K. Duker, Ph.D.
Assistant Professor

Excellence in Education Award as a “Basic Science & Organ Systems Lecturer” from the Medical Graduating Class of 2002

Excellence in Education Award as a “Small Group Facilitator” From the Medical Graduating Classes of 2003 and 2004



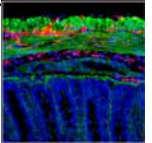
**CBP Faculty Teaching Activities
Academic Year 2001**

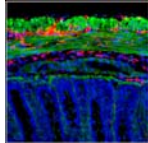
Ameredes, William

Hemodynamics		8/16/2000	MS 2
Physiology	BFH Cardiovascular Course	8/31/2000	MS 2
Respiratory Mechanics I	Pulmonary Phys., Pathophys., Pulmonary Disorders	10/3/2000	MS 2
Respiratory Mechanics II	Pulmonary Phys., Pathophys., Pulmonary Disorders	10/4/2000	MS 2
Workshop I - Pulmonary Physiology	Pulmonary Phys., Pathophys., Pulmonary Disorders	10/6/2000	MS 2
Workshop II - Pulmonary Function Tests	Pulmonary Phys., Pathophys., Pulmonary Disorders	10/12/2000	MS 2
Workshop III - Pulmonary Pathophysiology	Pulmonary Phys., Pathophys., Pulmonary Disorders	10/20/2000	MS 2
Muscle/Motors I	Cell and Molecular Physiology 2830	3/27/2001	PhD
Muscle/Motors II	Cell and Molecular Physiology 2830	4/3/2001	PhD
Muscle/Motors I & II	Cell and Molecular Physiology 2830	4/24/2001	PhD

Aridor, Meir

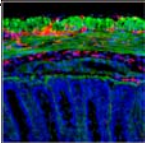
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	9/27/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	10/4/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	10/11/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	10/18/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	10/25/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	11/1/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	11/8/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	11/15/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	11/22/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	11/29/2000	PhD
Journal Group	Membrane-protein trafficking (MSCBMP 2852)	12/6/2000	PhD
Endoplasmic Reticulum	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	1/3/2001	MSc, MD/PhD, PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	1/10/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	1/17/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	1/24/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	1/31/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/7/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/21/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/28/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/7/2001	PhD

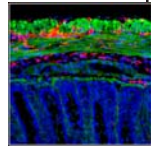




Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	3/12/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/14/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/21/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/28/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	4/9/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	4/23/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	5/7/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	5/21/2001	PhD
Membrane Trafficking course	Regulation of Membrane Traffic (MSCBMP 2840)	6/28/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/14/01	PhD
Bradbury, Neil			
PBL-CSM Introduce Case 1	Cell Structure Metabolism & Nutrition	10/13/2000	MS 1
PBL-CSM Resolve Case 1	Cell Structure Metabolism & Nutrition	10/18/2000	MS 1
PBL - Nutrition Introduce Case 2	Cell Structure Metabolism & Nutrition	10/20/2000	MS 1
PBL - CSM Introduce Case 3	Cell Structure Metabolism & Nutrition	10/23/2000	MS 1
PBL - Resolve Case 2	Cell Structure Metabolism & Nutrition	10/25/2000	MS 1
PBL - Resolve Case 3	Cell Structure Metabolism & Nutrition	10/27/2000	MS 1
PBL - CSMN Introduce Case 4	Cell Structure Metabolism & Nutrition	10/30/2000	MS 1
PBL - Resolve Case 4	Cell Structure Metabolism & Nutrition	11/1/2000	MS 1
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/18/2000	MS 1
Action Potentials	Cellular Comm. And Signaling	12/18/2000	MS 1
Synapses	Cellular Comm. And Signaling	12/20/2000	MS 1
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/21/2000	MS 1
Cell Surface Receptors	Cellular Comm. And Signaling	1/2/2001	MS 1
Disorders of Insulin Action	Cellular Comm. And Signaling	1/3/2001	MS 1
Receptor Signaling thru G Proteins & Tyrosins Kinases	Cellular Comm. And Signaling	1/5/2001	MS 1
Disorders of Insulin Action	Cellular Comm. And Signaling	1/8/2001	MS 1
Reg. of the Endocytic Pathway	INTBP 2000	10/12/2000	PhD
Molecular Basis of Cystic Fibrosis I	Cell Biology and Molecular Physiology	2/7/2001	Ph.D.
Structure and Function of Epithelia	Cell Biology and Molecular Physiology	2/13/2001	Ph.D.
Molecular Basis of Cystic Fibrosis II	Cell Biology of Normal and Disease States	2/14/2001	Ph.D.
Structure and Function of Epithelia	Cell Biology and Molecular Physiology	2/20/2001	Ph.D.
Molecular Basis of Cystic Fibrosis III	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	2/21/2001	Ph.D.
Scientific Methods & Values	Scientific Ethics - INTBP 2290	5/14/2001	Ph.D.
Responsible Training/Trainee Prac	Scientific Ethics - INTBP 2290	5/16/2001	Ph.D.

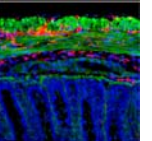
Use of Animals in Research	Scientific Ethics - INTBP 2290	5/21/2001	Ph.D.
Office of Research Integrity	Scientific Ethics - INTBP 2290	5/23/2001	Ph.D.
Scientific Methods & Values	Scientific Ethics - INTBP 2290	6/12/2001	Ph.D.
Responsible Training/Trainee Prac	Scientific Ethics - INTBP 2290	6/19/2001	Ph.D.
<u>Bridges, Robert</u>			
Cystic Fibrosis/Ion Channel Transport	ILS - Molecular Medicine	11/3/2000	MS 4
Physiology of Duodenum & Small Intestine	Digestion and Nutrition	11/29/2000	MS 2
Large Intestine; Water & Electrolyte Absorption	Digestion and Nutrition	12/4/2000	MS 2
Cellular Physiology	Cell Biology and Molecular Physiology	1/9/2001	Ph.D.
Cellular Physiology	Cell Biology and Molecular Physiology	1/16/2001	Ph.D.
<u>Devor, Daniel</u>			
Small group (PBL)	Specialized Tissue Course	1/17/2001	MS-1
Small group (PBL)	Specialized Tissue Course	1/24/2001	MS-1
Potassium channel assembly	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	2/7/2001	Ph.D.
Potassium channel trafficking	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	2/14/2001	Ph.D.
Epithelial Transport I	Cell Biology and Molecular Physiology	3/13/2001	Ph.D.
Epithelial Transport II	Cell and Molecular Physiology	3/20/2001	Ph.D.
<u>Drain, Peter</u>			
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	3/12/2001	PhD
1.0 Insulin Biosynthesis and Secretory Vesicle Assembly	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	3/14/2001	MSc, MD/PhD, PhD
2.0 Electrical Excitability in the Cell	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	3/14/2001	MSc, MD/PhD, PhD
3.0 Stimulation-Secretion Coupling in the Cell	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	3/21/2001	MSc, MD/PhD, PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	4/9/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	4/23/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	5/7/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	5/21/2001	PhD
<u>Duker, Georgia</u>			
Cell Membranes & Organelle Synthesis	Prematriculation Program Class of 2004	7/14/2000	MS 1
Cell Biology - Mitochondria	Prematriculation Program Class of 2004	7/17/2000	MS 1

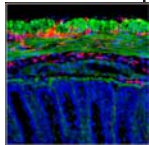




Cell Biology - Cytoskeleton	Prematriculation Program Class of 2004	7/18/2000	MS 1
Cell Biology - Secretions & Endocytosis	Prematriculation Program Class of 2004	7/18/2000	MS 1
Cell Biology - Cell Cycle	Prematriculation Program Class of 2004	7/19/2000	MS 1
Cell Biology - Extracellular Matrix	Prematriculation Program Class of 2004	7/19/2000	MS 1
Hemodynamics	BFH Cardiovascular Course	8/16/2000	MS 2
Physiology	BFH Cardiovascular Course	8/31/2000	MS 2
Renal Anatomy and Histology	BFH/ Renal Organ System and Hypertension	9/12/2000	MS 2
Renal Anatomy and Histology	BFH/ Renal Organ System and Hypertension	9/12/2000	MS 2
Membrane Structure	Cell Structure Metabolism & Nutrition	10/10/2000	MS 1
Membrane Transport	Cell Structure Metabolism & Nutrition	10/10/2000	MS 1
Intracellular Compartments	Cell Structure Metabolism & Nutrition	10/12/2000	MS 1
Secretion, Lysosomal & Membrane Proteins	Cell Structure Metabolism & Nutrition	10/12/2000	MS 1
Review	Cell Structure Metabolism & Nutrition	10/12/2000	MS 1
Endocytic Pathway	Cell Structure Metabolism & Nutrition	10/13/2000	MS 1
Structure & Biogenesis of Mitochondria & Peroxisomes	Cell Structure Metabolism & Nutrition	10/13/2000	MS 1
PBL - CSM Resolve Case 1	Cell Structure Metabolism & Nutrition	10/18/2000	MS 1
Pretest Review	Cell Structure Metabolism & Nutrition	10/19/2000	MS 1
PBL - Nutrition Introduce Case 2	Cell Structure Metabolism & Nutrition	10/20/2000	MS 1
Biochemistry Exam 1	Cell Structure Metabolism & Nutrition	10/23/2000	MS 2
PBL - CSM Introduce Case 3	Cell Structure Metabolism & Nutrition	10/23/2000	MS 1
PBL - Resolve Case 2	Cell Structure Metabolism & Nutrition	10/25/2000	MS 1
PBL - Resolve Case 3	Cell Structure Metabolism & Nutrition	10/27/2000	MS 1
PBL - CSM Introduce Case 4	Cell Structure Metabolism & Nutrition	10/27/2000	MS 1
PBL - Resolve Case 4	Cell Structure Metabolism & Nutrition	10/30/2000	MS 1
PBL - Intro Case 5	Cell Structure Metabolism & Nutrition	11/1/2000	MS 1
PBL - Nutrition Intro Case 6	Cell Structure Metabolism & Nutrition	11/7/2000	MS 1
PBL - Resolve Case 5	Cell Structure Metabolism & Nutrition	11/8/2000	MS 1
PBL - Resolve Case 6	Cell Structure Metabolism & Nutrition	11/10/2000	MS 1
Introduction to Histology, Part I	Cell Structure Metabolism & Nutrition	11/13/2000	MS 1
Introduction and Oral Cavity	Digestion & Nutrition	11/17/2000	MS 2
Esophagus / Stomach	Digestion & Nutrition	11/20/2000	MS 2
Introduction to Histology, Part II	Digestion & Nutrition	11/21/2000	MS 2
Large and Small Intestine	Digestion & Nutrition	11/28/2000	MS 2
Pancreas, Biliary Tree, Liver	Digestion & Nutrition	11/30/2000	MS 2
Histology & Pathology (Review Session)	Digestion & Nutrition	12/6/2000	MS 2
Practical: GI Histology & Pathology	Digestion & Nutrition	12/15/2000	MS 2
	Digestion & Nutrition	12/19/2000	MS 2

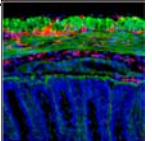
Female Reproductive Tract	Reproductive & Developmental Biology	1/2/2001	MIS 2
Male Reproductive Tract	Reproductive & Developmental Biology	1/4/2001	MIS 2
Prostate and Testes	Reproductive & Developmental Biology	1/4/2001	MIS 2
Epithelium I	Specialized Tissue	1/11/2001	MIS 1
Epithelium I	Specialized Tissue	1/11/2001	MIS 1
Ovary and Breast	Reproductive & Developmental Biology	1/11/2001	MIS 2
Connective Tissue I	Specialized Tissue	1/12/2001	MIS 1
Connective Tissue II	Specialized Tissue	1/12/2001	MIS 1
Connective Tissue	Specialized Tissue	1/12/2001	MIS 1
Applications - Epithelium/Connective Tissue	Specialized Tissue	1/16/2001	MIS 1
Nervous Tissue	Specialized Tissue	1/17/2001	MIS 1
Case Intro: Pulmonary Fibrosis	Specialized Tissue	1/17/2001	MIS 1
Cartilage and Bone Tissues	Specialized Tissue	1/18/2001	MIS 1
Cartilage and Bone Growth and Dev	Specialized Tissue	1/18/2001	MIS 1
Cartilage/Bone	Specialized Tissue	1/18/2001	MIS 1
Applications: Nervous Tissue	Specialized Tissue	1/18/2001	MIS 1
Cervix and Uterus	Reproductive & Developmental Biology	1/18/2001	MIS 2
Development	Specialized Tissue	1/19/2001	MIS 1
Muscle Tissue	Specialized Tissue	1/22/2001	MIS 1
Applications: Development/Catilage/Bone	Specialized Tissue	1/23/2001	MIS 1
Vascular Tissue	Specialized Tissue	1/24/2001	MIS 1
Case Resolution	Specialized Tissue	1/24/2001	MIS 1
Applications: Muscle and Vascular Tissue	Specialized Tissue	1/25/2001	MIS 1
Open Lab Review	Specialized Tissue	1/25/2001	MIS 1
Practical: Specialized Tissues	Specialized Tissue	1/26/2001	MIS 1
Case 1-1	Integrated Case Studies	4/4/2001	MIS 2
Case 1-2&3	Integrated Case Studies	4/5/2001	MIS 2
Case 1-Resolution	Integrated Case Studies	4/6/2001	MIS 2
Case 6-1	Integrated Case Studies	4/23/2001	MIS 2
Case 6-2&3	Integrated Case Studies	4/24/2001	MIS 2
Case 6-Resolution	Integrated Case Studies	4/25/2001	MIS 2
Case 7-1&2	Integrated Case Studies	4/26/2001	MIS 2
Case 7-Resolution	Integrated Case Studies	4/27/2001	MIS 2
Case 10-1	Integrated Case Studies	5/7/2001	MIS 2
Case 10-2&3	Integrated Case Studies	5/8/2001	MIS 2
Case 10-Resolution	Integrated Case Studies	5/9/2001	MIS 2
Case 11-1&2	Integrated Case Studies	5/10/2001	MIS 2

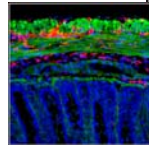




Case 11-Resolution	Integrated Case Studies	5/11/2001	MS 2
The Wrist	Musculoskeletal	5/11/2001	MS 1
The Knee	Musculoskeletal	5/16/2001	MS 1
Histology Lab Normal Bone, Cartilage & Muscle	Musculoskeletal	5/21/2001	MS 1
Inflammatory Diseases	Musculoskeletal	5/24/2001	MS 1
Degenerative Diseases	Musculoskeletal	5/29/2001	MS 1
PBL-CSM Introduce Case 1	Cell Structure Metabolism & Nutrition	10/13/2001	MS 1
Frizzell, Raymond			
Clinical Perspectives II- Cystic Fibrosis	Cell Communication & Signaling	1/8/2001	MS-1
Intensive Laboratory Research Experience	Structure & Function of Polarized Epithelial Cells	6/3/2001	MS-1
Intensive Laboratory Research Experience	Structure & Function of Polarized Epithelial Cells	6/3/2001	MS-1
Intensive Laboratory Research Experience	Structure & Function of Polarized Epithelial Cells	6/4/2001	MS-1
Intensive Laboratory Research Experience	Structure & Function of Polarized Epithelial Cells	6/5/2001	MS-1
Intensive Laboratory Research Experience	Structure & Function of Polarized Epithelial Cells	6/6/2001	MS-1
Intensive Laboratory Research Experience	Structure & Function of Polarized Epithelial Cells	6/7/2001	MS-1
Intensive Laboratory Research Experience	Structure & Function of Polarized Epithelial Cells	6/8/2001	MS-1
Membrane Transport	Found. of Biomedical Science	10/20/2000	CS
Electrical Signaling in Neurons; Membrane Ion Channels	Cell & Molecular Physiology	1/23/2001	CS
Ion Channels	Cell & Molecular Physiology	1/30/2001	CS
Synaptic Release of Neurotransmitters	Cell & Molecular Physiology	2/6/2001	CS
Gay, Vernon			
Hemodynamics	BFH Cardiovascular Course	8/16/2000	MS 2
Physiology	BFH Cardiovascular Course	8/31/2000	MS 2
PBL	Integrated Case Studies	4/9/2001	MS 2
PBL	Integrated Case Studies	4/10/2001	MS 2
PBL	Integrated Case Studies	4/11/2001	MS 2
PBL	Integrated Case Studies	4/16/2001	MS 2
PBL	Integrated Case Studies	4/17/2001	MS 2
PBL	Integrated Case Studies	4/18/2001	MS 2
PBL	Integrated Case Studies	4/23/2001	MS 2
PBL	Integrated Case Studies	4/24/2001	MS 2
PBL	Integrated Case Studies	4/25/2001	MS 2
PBL	Integrated Case Studies	5/3/2001	MS 2
PBL	Integrated Case Studies	5/4/2001	MS 2

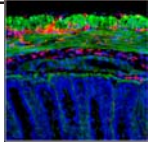
Cardiovascular	MSCBMP 2820	8/31/2000	PhD
Cardiovascular	MSCBMP 2820	9/5/2000	PhD
Cardiovascular	MSCBMP 2820	9/7/2000	PhD
Cardiovascular	MSCBMP 2820	9/12/2000	PhD
Cardiovascular	MSCBMP 2820	9/14/2000	PhD
Cardiovascular	MSCBMP 2820	9/19/2000	PhD
Cardiovascular	MSCBMP 2820	9/21/2000	PhD
<u>Murray, Sandra</u>			
The Thoracic Wall	Human Body	8/28/2000	MIS 1
Dissection of The Thoracic Wall	Human Body	8/28/2000	MIS 1
Dissection of The Thoracic Wall	Human Body	8/29/2000	MIS 1
Dissection of The Pleural Wall	Human Body	8/30/2000	MIS 1
Dissection of the Heart	Human Body	8/31/2000	MIS 1
Dissection of the Mediastinum	Human Body	9/1/2000	MIS 1
Complete Dissection of the Mediastinum	Human Body	9/1/2000	MIS 1
Abdominal Wall, Formation of Inguinal Canal	Human Body	9/5/2000	MIS 1
Dissection of the Abdominal Wall	Human Body	9/5/2000	MIS 1
Dissection of Scrotum, Spermatic Cord, Etc.	Human Body	9/6/2000	MIS 1
Dissection of the Blood Supply	Human Body	9/7/2000	MIS 1
Dissection of the Blood Supply	Human Body	9/8/2000	MIS 1
Dissection of the Posterior Abdominal Wall	Human Body	9/11/2000	MIS 1
Hemisection of the Pelvis	Human Body	9/12/2000	MIS 1
The Perineum	Human Body	9/13/2000	MIS 1
Pelvis Dissection	Human Body	9/14/2000	MIS 1
Pelvis Dissection: Male & Female	Human Body	9/15/2000	MIS 1
Frist examination	Human Body	9/19/2000	MIS 1
Pterygopalatin Fossa Demonstration	Human Body	9/28/2000	MIS 1
Examination II Head and Neck	Human Body	10/6/2000	MIS 1
Endocrine Systems: Adreanal Gland	MSCMP2730-mol. Mech of tissue growth and diff	2/18/2001	PhD
<u>Onate, Sergio</u>			
Cytosol/Nuclei trafficking	MSBMG 3510	10/10/2000	PhD
Cytosol/Nuclei trafficking	MSBMG 3510	10/12/2000	PhD
Nuclear/Cyto Trafficking I	INTBP 2000	10/16/2000	PhD
Cyto/Nuclear Trafficking II	INTBP 2000	10/16/2000	PhD

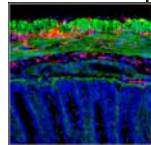




Nuclear receptors and disease	MSCBP 2880	1/17/2001	PhD
Nuclear receptors and disease	MSCBP 2880	1/24/2001	PhD
Ontell, Marcia			
Epithelium and Connective Tissue Lab Review	Specialized Tissue	1/10/2001	MS 1
Epithelium I	Specialized Tissue	1/11/2001	MS 1
Connective Tissue	Specialized Tissue	1/12/2001	MS 1
Nervous Tissue lab review	Specialized Tissue	1/12/2001	MS 1
Applications - Epithelium/Connective Tissue	Specialized Tissue	1/16/2001	MS 1
Nervous Tissue	Specialized Tissue	1/17/2001	MS 1
Case Intro: Pulmonary Fibrosis	Specialized Tissue	1/17/2001	MS 1
Cartilage/Bone	Specialized Tissue	1/18/2001	MS 1
Applications: Nervous Tissue	Specialized Tissue	1/18/2001	MS 1
Development	Specialized Tissue	1/19/2001	MS 1
Muscle Tissue Lab Review	Specialized Tissue	1/19/2001	MS 1
Striated Muscle I	Specialized Tissue	1/22/2001	MS 1
Striated Muscle II	Specialized Tissue	1/22/2001	MS 1
Muscle Tissue	Specialized Tissue	1/22/2001	MS 1
exam preparation-final and summative	Specialized Tissue	1/22/2001	MS 1
Striated Muscle III	Specialized Tissue	1/23/2001	MS 1
Applications: Development/Catilage/Bone	Specialized Tissue	1/23/2001	MS 1
Vascular Tissue	Specialized Tissue	1/24/2001	MS 1
Case Resolution	Specialized Tissue	1/24/2001	MS 1
Applications: Muscle and Vascular Tissue	Specialized Tissue	1/24/2001	MS 1
exam-written and practical	Specialized Tissue	1/25/2001	MS 1
Review of labs 1-7	Specialized Tissue	1/26/2001	MS 1
Myogenic Regulatory factors	MSCMP2730-mol. Mech of tissue growth and diff	1/25/01	MS 1
Myogenic Regulatory factors	MSCMP2730-mol. Mech of tissue growth and diff	4/6/2001	PH.D.
		4/15/2001	PH.D.
Plant, Tony			
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/18/2000	MS 1
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/21/2000	MS 1

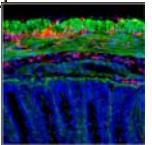
<u>Ryan, Kathleen</u>					
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/21/2000		MIS 1	
Content, Eval. & Grading of Bas Sci Core Crs	Class of 2004 - Orientation	8/11/2000		MIS 1	
Hemodynamics	BFH Cardiovascular Course	8/16/2000		MIS 2	
Physiology	BFH Cardiovascular Course	8/31/2000		MIS 2	
PBL-CSM Introduce Case 1	Cell Structure Metabolism & Nutrition	10/13/2000		MIS 1	
PBL-CSM Resolve Case 1	Cell Structure Metabolism & Nutrition	10/18/2000		MIS 1	
PBL - CSM Introduce Case 3	Cell Structure Metabolism & Nutrition	10/23/2000		MIS 1	
PBL - Resolve Case 2	Cell Structure Metabolism & Nutrition	10/25/2000		MIS 1	
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/18/2000		MIS 1	
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/21/2000		MIS 1	
Initial Sessions	Reproductive and Developmental Biology	1/2/2001		MIS 2	
Menstrual Cycle	Reproductive and Developmental Biology	1/3/2001		MIS 2	
Breast/Lactation	Reproductive and Developmental Biology	1/3/2001		MIS 2	
Resolution / Case Initiation	Reproductive and Developmental Biology	1/5/2001		MIS 2	
Androgen Insensitivity	Reproductive and Developmental Biology	1/5/2001		MIS 2	
Resolution/ Initial Session	Reproductive and Developmental Biology	1/10/2001		MIS 2	
Fetal / Neonatal Adaptation	Reproductive and Developmental Biology	1/11/2001		MIS 2	
Resolution/ Initial Session	Reproductive and Developmental Biology	1/12/2001		MIS 2	
Resolution/ Initial Session	Reproductive and Developmental Biology	1/16/2001		MIS 2	
Puberty	Reproductive and Developmental Biology	1/17/2001		MIS 2	
Contraception	Reproductive and Developmental Biology	1/17/2001		MIS 2	
Resolution	Reproductive and Developmental Biology	1/18/2001		MIS 2	
Adulthood, Menopause / Aging	Reproductive and Developmental Biology	1/19/2001		MIS 2	
Mechanisms / Infertility	Reproductive and Developmental Biology	1/19/2001		MIS 2	
<u>Salama, Guy</u>					
Electrical Activity of the Heart I	BFH Cardiovascular Course	8/15/2000		MIS 2	
Electrical Activity of the Heart II	BFH Cardiovascular Course	8/15/2000		MIS 2	
Electrical Activity of the Heart III	BFH Cardiovascular Course	8/16/2000		MIS 2	
Electrophysiology of the Heart	Cell Physiology	4/16/2001		PhD	
Electrophysiology of the Heart	Cell Physiology	4/17/2001		PhD	
Electrophysiology of the Heart	Cell Physiology	4/23/2001		PhD	
Excitation-Contraction coupling	Cell Physiology	4/24/2001		PhD	
Excitation-Contraction coupling	Cell Physiology	4/27/2001		PhD	

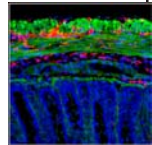




Stolz, Donna Beer					
Electrical Activity of the Heart III				8/16/2000	MS 2
PBL-CSM Resolve Case 1			Cell Structure Metabolism & Nutrition	10/18/2000	MS 1
PBL - Nutrition Introduce Case 2			Cell Structure Metabolism & Nutrition	10/20/2000	MS 1
PBL - Resolve Case 2			Cell Structure Metabolism & Nutrition	10/25/2000	MS 1
PBL - Intro Case 5			Cell Structure Metabolism & Nutrition	11/7/2000	MS 1
PBL - Nutrition Intro Case 6			Cell Structure Metabolism & Nutrition	11/8/2000	MS 1
PBL - Resolve Case 5			Cell Structure Metabolism & Nutrition	11/10/2000	MS 1
PBL - Resolve Case 6			Cell Structure Metabolism & Nutrition	11/13/2000	MS 1
Epithelium I			Specialized Tissue	1/11/2001	MS 1
Connective Tissue			Specialized Tissue	1/12/2001	MS 1
Applications - Epithelium/Connective Tissue			Specialized Tissue	1/16/2001	MS 1
Nervous Tissue			Specialized Tissue	1/17/2001	MS 1
Case Intro: Pulmonary Fibrosis			Specialized Tissue	1/17/2001	MS 1
Cartilage/Bone			Specialized Tissue	1/18/2001	MS 1
Applications: Nervous Tissue			Specialized Tissue	1/18/2001	MS 1
Development			Specialized Tissue	1/19/2001	MS 1
Muscle Tissue			Specialized Tissue	1/22/2001	MS 1
Applications: Development/Catilage/Bone			Specialized Tissue	1/23/2001	MS 1
Vascular Tissue			Specialized Tissue	1/24/2001	MS 1
Case Resolution			Specialized Tissue	1/24/2001	MS 1
Applications: Muscle and Vascular Tissue			Specialized Tissue	1/25/2001	MS 1
PBL-CSM Introduce Case 1			Cell Structure Metabolism & Nutrition	10/13/2001	MS 1
Protein Import into Mitochondria and Peroxisomes			Foundations in Biomedical research	10/5/2000	GSI
Angiogenesis and Vasculogenesis			Mol mechan of Tissue Growth and Differentiation	1/17/2001	GSI
Traub, Linton					
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	9/27/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	10/4/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	10/11/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	10/18/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	10/25/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	11/1/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	11/8/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	11/15/2000	PhD
Journal discussion group			Membrane-protein trafficking (MSCBMP 2852)	11/22/2000	PhD

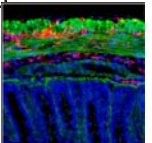
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	11/29/2000	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	12/6/2000	PhD
Lysosomal enzyme delivery	Cell Biology of Norm. and Dis. States (MSCBMP 2880)	1/10/2001	MSc, MD/PhD, PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	1/17/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	1/24/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	1/31/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/7/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/14/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/21/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	2/28/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/7/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	3/12/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/14/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/21/2001	PhD
Journal discussion group	Membrane-protein trafficking (MSCBMP 2852)	3/28/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	4/9/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	4/23/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	5/7/2001	PhD
Methods & Logic in Cell Physiology	Research Seminars in Cell Physiology (MSCBMP 2851)	5/21/2001	PhD
Membrane Trafficking course	Regulation of Membrane Traffic (MSCBMP 2840)	6/14/2001	PhD
Membrane Trafficking course	Regulation of Membrane Traffic (MSCBMP 2840)	6/21/2001	PhD
Walker, William			
PBL - Intro Case 5	Cell Structure Metabolism & Nutrition	11/7/2000	MS 1
PBL - Resolve Case 5	Cell Structure Metabolism & Nutrition	11/10/2000	MS 1
Male Reproduction	Reproductive and Developmental Biology	1/4/2001	MS 2
Hypothesis Generation and Testing	INTBP2005	8/29/2000	PhD
Stabilization of phage T4 lysozyme	INTBP2005	9/5/2000	PhD
Selective alteration of a substrate specificity	INTBP2005	9/8/2000	PhD
Replisome assembly	INTBP2005	9/15/2000	PhD
CAP and RNA polymerase interactions	INTBP2005	9/19/2000	PhD
YY1 facilitates the association	INTBP2005	9/22/2000	PhD
Disruption of splicing	INTBP2005	9/26/2000	PhD
Herpes simplex virus gene expression	INTBP2005	9/29/2000	PhD
CREB Transcription factors	MSBMG 3510	10/10/2000	PhD
CREB Transcription factors	MSBMG 3510	10/12/2000	PhD





Cell Cycle and Mitosis	MSCBP 2880	1/17/2001	PhD
Cell Cycle and Mitosis	MSCBP 2880	1/24/2001	PhD
Watkins, Simon			
Cytoskeleton 1	Cell Structure Metabolism & Nutrition	10/11/2000	MS 1
Cytoskeleton 2	Cell Structure Metabolism & Nutrition	10/11/2000	MS 1
Review	Cell Structure Metabolism & Nutrition	10/13/2000	MS 1
PBL-CSM Resolve Case 1	Cell Structure Metabolism & Nutrition	10/18/2000	MS 1
Pretest Review	Cell Structure Metabolism & Nutrition	10/19/2000	MS 1
PBL - Nutrition Introduce Case 2	Cell Structure Metabolism & Nutrition	10/20/2000	MS 1
PBL - CSM Introduce Case 3	Cell Structure Metabolism & Nutrition	10/23/2000	MS 1
PBL - Resolve Case 2	Cell Structure Metabolism & Nutrition	10/25/2000	MS 1
PBL - Resolve Case 3	Cell Structure Metabolism & Nutrition	10/27/2000	MS 1
PBL - CSMN Introduce Case 4	Cell Structure Metabolism & Nutrition	10/30/2000	MS 1
PBL - Resolve Case 4	Cell Structure Metabolism & Nutrition	11/1/2000	MS 1
PBL - Intro Case 5	Cell Structure Metabolism & Nutrition	11/7/2000	MS 1
PBL - Nutrition Intro Case 6	Cell Structure Metabolism & Nutrition	11/8/2000	MS 1
PBL - Resolve Case 5	Cell Structure Metabolism & Nutrition	11/10/2000	MS 1
PBL - Resolve Case 6	Cell Structure Metabolism & Nutrition	11/13/2000	MS 1
Case 2-1	Integrated Case Studies	4/9/2001	MS 2
Case 2-2	Integrated Case Studies	4/10/2001	MS 2
Case 2-Resolution	Integrated Case Studies	4/11/2001	MS 2
Case 3-1&2	Integrated Case Studies	4/12/2001	MS 2
Case 3-Resolution	Integrated Case Studies	4/13/2001	MS 2
Case 4-1	Integrated Case Studies	4/16/2001	MS 2
Case 4-2&3	Integrated Case Studies	4/17/2001	MS 2
Case 4-Resolution	Integrated Case Studies	4/18/2001	MS 2
Case 12-1	Integrated Case Studies	5/14/2001	MS 2
Case 12-2&3	Integrated Case Studies	5/15/2001	MS 2
Case 12-Resolution	Integrated Case Studies	5/16/2001	MS 2
PBL-CSM Introduce Case 1	Cell Structure Metabolism & Nutrition	10/13/2001	MS 1
Imaging	Foundations	10/3/2000	PhD.
cytoskeleton	Foundations	10/3/2000	PhD.

<u>Zeleznik, Tony</u>				
PBL-CSM Introduce Case 1	Cell Structure Metabolism & Nutrition	10/13/2001	MS 1	
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/18/2000	MS 1	
Initial Sessions	Reproductive and Developmental Biology	1/2/2001	MS 2	
Menstrual Cycle	Reproductive and Developmental Biology	1/2/2001	MS 2	
Menstrual Cycle	Reproductive and Developmental Biology	1/3/2001	MS 2	
Disorders of Insulin Action	Cellular Comm. And Signaling	1/3/2001	MS 1	
Resolution / Case Initiation	Reproductive and Developmental Biology	1/5/2001	MS 2	
Androgen Insensitivity	Reproductive and Developmental Biology	1/5/2001	MS 2	
Disorders of Insulin Action	Cellular Comm. And Signaling	1/8/2001	MS 1	
Resolution / Initial session	Reproductive and Developmental Biology	1/10/2001	MS 2	
Resolution / Initial session	Reproductive and Developmental Biology	1/12/2001	MS 2	
Contraception	Reproductive and Developmental Biology	1/17/2001	MS 2	
Mechanisms / Infertility	Reproductive and Developmental Biology	1/19/2001	MS 2	
Case 3 -1&2	Integrated Case Studies	4/12/2001	MS 2	
Case 3-Resolution	Integrated Case Studies	4/13/2001	MS 2	
Case 4-1	Integrated Case Studies	4/16/2001	MS 2	
Case 4-2&3	Integrated Case Studies	4/17/2001	MS 2	
Case 4-Resolution	Integrated Case Studies	4/18/2001	MS 2	
Case 7-1&2	Integrated Case Studies	4/26/2001	MS 2	
Case 7-Resolution	Integrated Case Studies	4/27/2001	MS 2	
Case 9-1&2	Integrated Case Studies	5/3/2001	MS 2	
Case 9-Resolution	Integrated Case Studies	5/4/2001	MS 2	
Disorders of Motor Weakness	Cellular Comm. And Signaling	12/21/2001	MS 1	
<u>Zhao, Allan</u>				
Insulin and Leptin Signaling	Molecular Basis of Disease and Normal States	3/23/2000	Ph.D.	
Insulin and Leptin Signaling	Molecular Basis of Disease and Normal States	3/30/2001	Ph.D.	



CBMP and Other Program Graduate Students

July 1, 2000 through June 30, 2001

Graduate Students Assigned to the CBMP Program:

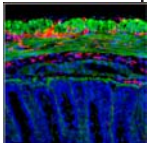
	<u>Current status</u>	<u>CBMP Mentor</u>
Frank J. Delfino	7 th year	Dr. Will Walker
Mark Ellis	2 nd year	Dr. Ora Weisz
Matthew O. Fraser	Extended	Dr. William DeGroat
Aaron C. Gerlach	6 th year	Dr. Dan Devor
Som-Ming Leung	6 th year	Dr. Gerry Apodaca
Uzma S. Shah	7 th year	Dr. Sandra Murray
Fei Sun	6 th year	Dr. Ray Frizzell
Steven T. Truschel	5 th year	Dr. Gerry Apodaca
Kelly M. Weixel	6 th year	Dr. Neil Bradbury
Raul Esteban Rojas	3 nd year	Dr. Gerry Apodaca
Edward Chi Yu Wang	3 nd year	Dr. Gerry Apodaca

Graduate Students Assigned to the INTBP Program but affiliated with the CBMP Program :

Marjet Heitzer	Dr. Sergio Onate
Christopher Lewarchik	Dr. Raymond Frizzell

Graduate Students Assigned to CBP faculty from Other Graduate Programs:

Kevin Davis	Biological Sciences	Dr. Sandra Murray
Bum-Rak Choi	Neuroscience	Dr. Guy Salama
Linda Baker	Bioengineering	Dr. Guy Salama



CBMP Graduates

2000-2001 Academic Year

Frank Delfino, mentored by Dr. Will Walker, successfully defended his thesis on September 25, 2000, earning his Ph.D. Dr. Delfino accepted a postdoctoral appointment at the University of Pittsburgh School of Medicine, Department of Molecular Genetics & Biochemistry.

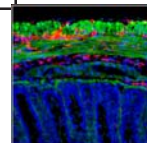
Matthew O. Fraser, mentored by Dr. William DeGroat, successfully defended his thesis on March 27, 2001, earning his Ph.D. Dr. Fraser accepted a postdoctoral appointment at the University of Pittsburgh School of Medicine, Department of Pharmacology.

Aaron C. Gerlach, mentored by Dr. Dan Devor, successfully defended his thesis on September 19, 2000, earning his Ph.D. Dr. Gerlach accepted a postdoctoral appointment at the Vollum Institute for Advanced Biomedical Research, Oregon Health Sciences University.

Juanjuan Qi, mentored by Dr. Ray Frizzell, successfully defended her thesis on April 25, 2000 and successfully completed all the requirements on May 4, 2001, earning her Ph.D. Dr. Qi accepted a postdoctoral appointment at Verizon in Dallas, TX.

Other Program Graduates:

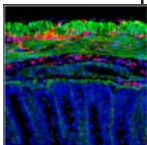
Bum-Rak Choi, of the Neuroscience Program and mentored by CBP's Dr. Guy Salama, successfully defended his thesis on May 25, 2001, earning his Ph.D. Dr. Choi accepted a postdoctoral appointment at the University of Pittsburgh School of Medicine with Dr. Guy Salama.



**CELL BIOLOGY AND PHYSIOLOGY
CURRENT FACULTY ROSTER
(Effective April 30,2002)**

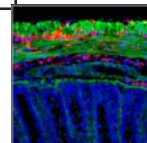
LAST NAME	FIRST NAME	Tenure TITLE	Status
Bridges	Robert	Professor	Tenured
Frizzell	Raymond	Professor	Tenured
Murray	Sandra	Professor	Tenured
Ontell	Marcia	Professor	Tenured
Plant	Tony	Professor	Tenured
Salama	Guy	Professor	Tenured
Watkins	Simon	Professor	Tenured
Zeleznik	Tony	Professor	Tenured
Gay	Vernon	Associate Professor	Tenured
Ryan	Kathleen	Associate Professor	Tenured
Aridor	Meir	Assistant Professor	Tenure Track
Bradbury	Neil	Assistant Professor	Tenure Track
Devor	Dan	Assistant Professor	Tenure Track
Drain	Peter	Assistant Professor	Tenure Track
Onate	Sergio	Assistant Professor	Tenure Track
Traub	Linton	Assistant Professor	Tenure Track
Walker	William	Assistant Professor	Tenure Track
Zhao	Allan	Assistant Professor	Tenure Track
Duker	Georgia	Assistant Professor	Non-tenure Track
Pohl	Clifford	Adjunct Assistant Professor	Non-tenure Track
Sahu	Abhiram	Research Associate Professor	Non-tenure Track
Ontell	Martin	Research Assistant Professor	Non-tenure Track
Peters	Kathryn	Research Assistant Professor	Non-tenure Track
Ramaswamy	Suresh	Research Assistant Professor	Non-tenure Track
Stolz	Donna	Research Assistant Professor	Non-tenure Track
Sun	Fei	Research Assistant Professor	Non-tenure Track
Washabaugh	Charles	Research Assistant Professor	Non-tenure Track
Ameredes	William	Visiting Res. Assistant Professor*	Non-tenure Track

*Transferred back to Department of Medicine, Division of Pulmonary, Allergy, and Critical Care Medicine, 12/31/01



**CELL BIOLOGY AND PHYSIOLOGY
NEW FACULTY APPOINTMENTS (1996-YTD2002)**

NAME	CBI RANK	DATE	RANK AT ORIGIN	START
Recent Tenure Track Appointments:				
None since September, 2000				
Anticipated Tenure Track Appointments:				
Leuba, Sanford	Assistant Professor	9/1/02		Research Fellow National Institutes of Health
Research Appointments:				
Sun, Fei	Res. Assistant Prof.	11/1/01		Research Associate Cell Biology and Physiology University of Pittsburgh
Ramaswamy, S.	Res. Assistant Prof. CRRP Primate Center Director	4/1/01		Research Associate Cell Biology and Physiology University of Pittsburgh



CBP Faculty Honors, Recognition and Professional Affiliations - 2000-2001

William T. Ameredes, Ph.D. [Transferred to Department of Medicine, 12/31/01]

Visiting Research Assistant Professor

Member, American Physiological Society

Member, Sigma Xi Honorary Scientific Society

Member, Comparative Respiratory Society

Member, Ohio Physiological Society

Member, Biophysical Society

Member, American Thoracic Society

ad hoc reviewer for Chest

ad hoc reviewer for American Journal of Physiology

ad hoc reviewer for Journal of Applied Physiology

ad hoc reviewer for Comparative Biochemistry and Physiology

ad hoc reviewer for Medicine and Science in Sports and Exercise

ad hoc reviewer for Journal of Nutrition

ad hoc reviewer for Canadian Journal of Applied Physiology

ad hoc reviewer for Journal of Leukocyte Biology

Meir Aridor, Ph.D.

Assistant Professor

Alon career award

Young investigator career award to establish new research program in Israel (**Award declined**).

Neil A. Bradbury, Ph.D.

Assistant Professor

Member of *the Biochemical Society*

Member of *American Physiological Society*

Member of the *American Society for Cell Biology*

Member Editorial Board: *American Journal of Physiology*

Reviewer for American Journal of Physiology: Cell Physiology

ad hoc reviewer for American Journal of Physiology: Lung Physiology

ad hoc reviewer for Journal of Clinical Investigation

ad hoc reviewer for Journal of Biological Chemistry

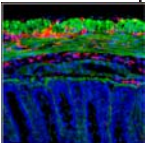
ad hoc reviewer for Cell and Tissue Research

ad hoc reviewer for Urology

ad hoc reviewer for Prostaglandins

ad hoc reviewer for Laboratory Investigation

ad hoc reviewer for *In Vitro* Cell Research



Robert J. Bridges, Ph.D.
Professor

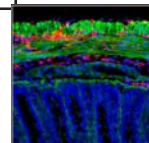
American Physiology Society
Society of General Physiologists
ad hoc reviewer for American Journal of Physiology: Cell Physiology
ad hoc reviewer for Journal of General Physiology
ad hoc reviewer for Journal of Membrane Biology
ad hoc reviewer for Journal of Membrane Biology
ad hoc reviewer for Journal of Pharmacological and Experimental Therapeutics
ad hoc reviewer for Toxicology Science

Daniel C. Devor, Ph.D.
Assistant Professor

Member, Long-Range Planning Committee: American Physiological Society
Editorial Board: American Journal of Physiology: Cell Physiology
ad hoc reviewer for Nature
ad hoc reviewer for Journal of Clinical Investigation
ad hoc reviewer for Journal of Biological Chemistry
ad hoc reviewer for American Journal of Physiology: Gastrointestinal and Liver Physiology
ad hoc reviewer for American Journal of Physiology: Renal Physiology
ad hoc reviewer for Journal of Physiology
ad hoc reviewer for Journal of Membrane Biology
ad hoc reviewer for Journal of Cellular Physiology
ad hoc reviewer for Gastroenterology
ad hoc reviewer for Comparative Biochemistry and Physiology
ad hoc reviewer for Biochimica et Biophysica Acta
ad hoc reviewer for Cystic Fibrosis Foundation
ad hoc reviewer for Department of Veterans Affairs

Peter F. Drain, Ph.D.
Assistant Professor

Member, Biophysical Society
Member, American Association for the Advancement of Science
Member, Society of General Physiologists
ad hoc reviewer for Nature
ad hoc reviewer for Neuron
ad hoc reviewer for Cell
ad hoc reviewer for Proc. Natl. Acad. Sci.,



ad hoc reviewer for J. Biol. Chemistry
ad hoc reviewer for J. Gen. Physiol.
ad hoc reviewer for Am. J. Physiology: Cell Physiology
ad hoc reviewer for Am. J. Physiology: Endocrinology.
ad hoc reviewer for National Science Foundation

Georgia K. Duker, Ph.D.

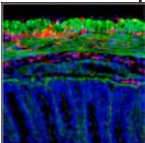
Assistant Professor

Coordinator for Graduate Teaching Fellows in Histology for 1st & 2nd year medical school curriculum
Young Women in Science Day, University of Pittsburgh School of Medicine event for 100 7th grade girls from Pittsburgh Public Schools, lab instructor
Dean's Applicant Interview Committee for University of Pittsburgh School of Medicine
Planning Committee – "Science 2001 – A Research Festival"
Chancellor's Distinguished Teaching Award Committee
Medical Illustrations – Posters for the Senior Vice Chancellors's Research Seminar series
Advisor – Medical Student Life Drawing Interest Group

Raymond A. Frizzell, Ph.D.

Professor

Richard Beatty Mellon Professor of Cell Biology and Physiology
American Society for Cell Biology
Member at Large, Medical Advisory Council, Cystic Fibrosis Foundation
Council, Society of General Physiologists
Salt and Water Club
American Physiological Society
Society of General Physiologists
Member, Mount Desert Island Biological Laboratory
Trustee, Mount Desert Island Biological Laboratory
Vice Chairman, Medical Advisory Council, Cystic Fibrosis Foundation
Journal Editing and Review (Ad Hoc):
Associate Editor, American Journal of Physiology: Cell Physiology
International Editorial Board, Gene Therapy
American Journal of Physiology
The Journal of Clinical Investigation
The Journal of General Physiology
American Journal of Respiratory Cell & Molecular Biology
Proceedings of the National Academy of Sciences



Vernon L. Gay, Ph.D.

Associate Professor

Member, Society for the Study of Reproduction
Member, Endocrine Society
Member, International Society of Neuroendocrinology
Editorial Board, Endocrinology
Editorial Board, Biology of Reproduction
ad hoc reviewer for Science
ad hoc reviewer for Neuroendocrinology
ad hoc reviewer for Proc. Soc. Exper. Biol. Med.
ad hoc reviewer for Journal of Reproduction and Fertility
ad hoc Consultant, NICHD (Site visits), NSF (Grant applications)

Sandra M. Murray, Ph.D.

Professor

Member, American Society for Cell Biology, Minorities Affairs Committee
Council Member, American Society for Cell Biology
Member, Society for In Vitro Biology
Member, The Pittsburgh Cancer Institute
Member, Corporation of the Marine Biological Laboratory
Member, Cell Transplant Society
Publications Committee, The Endocrine Society
Member, American Physiological Society
Member, International Society for Preventive Oncology
Research Advisory Committee. Morehouse School of Medicine.

Sergio A. Onate, Ph.D.

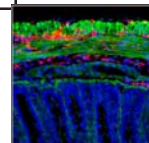
Assistant Professor

Member, American Society for Microbiology
Member, AAAS

Marcia R. Ontell, Ph.D.

Professor

Member, New York Academy of Science
Member, Tissue Culture Association Inc.
Member, American Society for Cell Biology
Member, Electron Microscopy Society of America



Member, Society for Neuroscience
Reviewer, MRC-Canada
Reviewer, Assoc. Francaise Contre les Myopathies
Reviewer, Italian Teleton
Reviewer, Competitive Medical Research Fund
ad hoc reviewer for Journal of Neuropathology and Experimental Neurology)
ad hoc reviewer for Experimental Neurology
ad hoc reviewer for Muscle and Nerve
ad hoc reviewer for Anatomical Record
ad hoc reviewer for Journal of Anatomy and Embryology
ad hoc reviewer for Histochemistry
ad hoc reviewer for Neuroscience
ad hoc reviewer for Developmental Biology
ad hoc reviewer for Journal of Cell Biology
ad hoc reviewer for Developmental Dynamics
Member, American Association of Anatomists

Martin Ontell, Ph.D.

Research Assistant Professor

Member, New York Academy of Sciences
Member, The American Society for Cell Biology

Kathryn W. Peters, Ph.D.

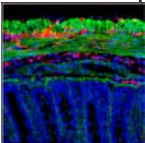
Research Assistant Professor

Member, Society of General Physiologists

Tony M. Plant, Ph.D.

Professor

Member, The Endocrine Society
Member, The Society for the Study of Reproduction
Member, American Physiological Society
Member, Pittsburgh Neuroscience Society
Member, Society for Neuroscience
Member, International Society for Neuroendocrinology
Member, International Neuroendocrine Federation
Member, American Neuroendocrine Society
Member, American Society of Andrology
ad hoc reviewer for Endocrinology



ad hoc reviewer for Neuroendocrinology
ad hoc reviewer for American Journal of Physiology
ad hoc reviewer for Journal of Endocrinology
ad hoc reviewer for Nature
ad hoc reviewer for Proceedings of Society of Experimental Biology and Medicine
ad hoc reviewer for Life Sciences, Journal of Clinical Endocrinology and Metabolism
ad hoc reviewer for Journal of Andrology
ad hoc reviewer for Biology of Reproduction
ad hoc reviewer for Journal of Neuroscience
ad hoc reviewer for Proceedings of the National Academy of Sciences, U.S.A.
ad hoc reviewer for Journal of Comparative Neurology
ad hoc reviewer for Journal of Pediatrics
ad hoc reviewer for Journal of Neuroendocrinology

Suresh Ramaswamy, Ph.D.

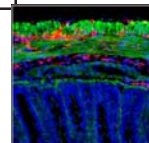
Research Assistant Professor

American Association for the Advancement of Science
The Endocrine Society (USA)
Society for the Study of Reproduction (USA)
ad hoc reviewer for Biology or Reproduction (Publication of the Society for the Study of Reproduction)

Abhiram Sahu, Ph.D.

Research Associate Professor

Member, Society for the Study of Reproduction
Member, The Endocrine Society
Member, International Society of Neuroendocrinology
Member, Society for Neuroscience
Member, Society for the Study of Ingestive Behavior
Member, American Association for the Advancement of Science
ad hoc reviewer for Physiology and Behavior
ad hoc reviewer for Trends in Endocrinology and Metabolism
ad hoc reviewer for Brain Research
ad hoc reviewer for Endocrinology
ad hoc reviewer for Molecular Brain Research
ad hoc reviewer for Journal of Endocrinology
ad hoc reviewer for Pharmacology Biochemistry and Behavior
ad hoc reviewer for Neuroendocrinology
ad hoc reviewer for Journal of Neuroendocrinology
ad hoc reviewer for Nutritional Neuroscience



Guy Salama, Ph.D.

Professor

Member, Biophysical Society
Member, Society of General Physiologists
Member, Marine Biological Laboratory, Member of the Corporation
Member, Basic Science Council of the American Heart Association
Member, North American Society of Pacing and Electrophysiology, NASPE
Editorial Board, Cell Calcium
ad hoc reviewer for Archives of Biochemistry & Biophysics Science
ad hoc reviewer for Nature
ad hoc reviewer for Circulation Research
ad hoc reviewer for Circulation
ad hoc reviewer for Biophysical Journal
ad hoc reviewer for Cardiovascular Research
ad hoc reviewer for Circulation
ad hoc reviewer for Am. J. Physiology
ad hoc reviewer for Annals of Biophysics and Bioengineering
ad hoc reviewer for Life Sciences
ad hoc reviewer for FASEB
ad hoc reviewer for J. Neuroscience

Donna Beer Stolz, Ph.D.

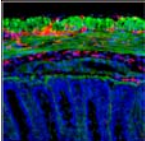
Research Assistant Professor

Member, American Society for Cell Biology
Member, Microscopy Society of America
Member, North American Vascular Biology Association
Member, American Society for the Study of Liver Diseases
Member, American Society for Investigative Pathology
Member, Society of Regenerative Medicine and Stem Cell Biology
Member, American Liver Foundation Liver Scholar Award, American Liver Foundation

Linton M. Traub, Ph.D.

Assistant Professor

Member, American Society for Cell Biology
ad hoc reviewer for Blood
ad hoc reviewer for EMBO Journal
ad hoc reviewer for FASEB Journal
ad hoc reviewer for FEBS Letters



ad hoc reviewer for Immunity
ad hoc reviewer for Molecular Biology of the Cell
ad hoc reviewer for Journal of Biological Chemistry
ad hoc reviewer for Journal of Cell Biology
ad hoc reviewer for Proceedings of the National Academy of Sciences
ad hoc reviewer for Traffic.

William H. Walker, Ph.D.

Assistant Professor

Member, Endocrine Society
Member, American Association for the Advancement of Science
Member, American Society for Cell Biology
ad hoc reviewer for Endocrinology, Molecular Endocrinology

Charles Washabaugh, Ph.D.

Research Assistant Professor

Member of the University of Dayton Research Council, 1992-1994
ad hoc reviewer for The Anatomical Record, 1998-present
ad hoc reviewer for Biochimica et Biophysica Acta

Simon C. Watkins, Ph.D.

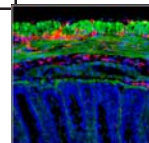
Professor

Ph.D. (Honoris Causae), University of Umea Sweden.
ad hoc reviewer for Muscle and Nerve
ad hoc reviewer for Journal of Neurological Sciences
ad hoc reviewer for Journal of Cell Biology
ad hoc reviewer for Agents and Actions
ad hoc reviewer for American Journal of Pathology
ad hoc reviewer for Journal of Immunology
ad hoc reviewer for J. Rheumatol

Anthony J. Zeleznik, Ph.D.

Professor

Member, The Endocrine Society
Member, Society for the Study of Reproduction
Member, American Fertility Society

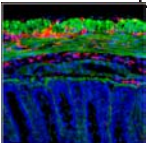
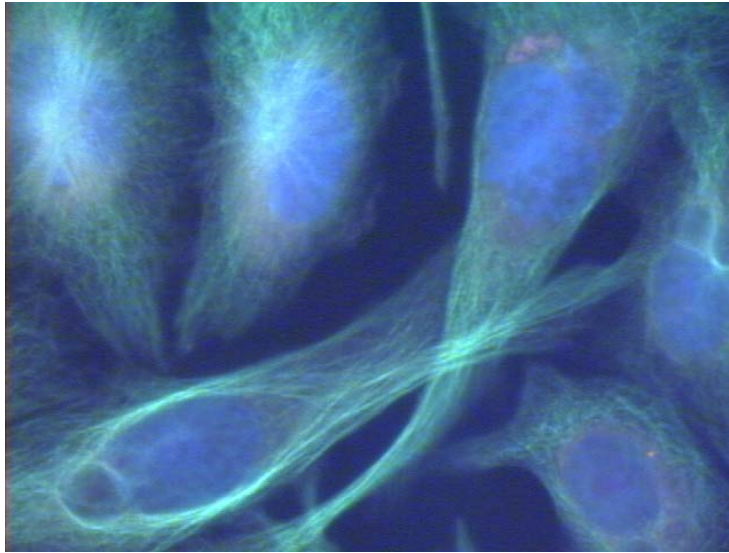


ad hoc reviewer for American Journal of Physiology
ad hoc reviewer for Biology of Reproduction
ad hoc reviewer for Endocrinology
ad hoc reviewer for Journal of Clinical Endocrinology and Metabolism
ad hoc reviewer for Journal of Clinical Investigation
ad hoc reviewer for Proceedings of the National Academy of Sciences

Allan Z. Zhao, Ph.D.

Assistant Professor

Career & Development Award, American Diabetes Association
Member, American Society for Pharmacology and Experimental Therapeutics (ASPET)
Member, American Association for the Advancement of Science (AAAS)
Member, American Diabetes Association (ADA)



Faculty Presentations - 2000-2001

William T. Ameredes, Ph.D. [Transferred to Department of Medicine, 12/31/01]

Visiting Research Assistant Professor

“Effects of (R) and (S)-enantiomers of beta-agonists on non-contractile function of airway smooth muscle cells.” Sepracor Scientific Research Forum, New Orleans, LA, Sept. 23, 2000.

“IL-4 Upregulation in Airway Immune Cells of Sensitized and Airway Challenged IL-10 Knockout Mice.” American Thoracic Society Annual Meeting, San Francisco, CA, May 21, 2001.

Neil A. Bradbury, Ph.D.

Assistant Professor

“Endocytosis and cystic fibrosis: Mechanisms of protein traffic.” Inaugural Senior Vice Chancellor Research Seminar, University of Pittsburgh School of Medicine, February 2000.

“Molecular mechanisms of ion channel endocytosis”. University of Wales College of Medicine, June 2001.

“CFTR binds directly to the mu subunit of AP-2”, Cystic Fibrosis Foundation, Williamsburg Conference '00, Williamsburg, VA, May 2000.

“Intermediary proteins in CFTR function”, North American Cystic Fibrosis Conference, Baltimore, MD, November 2000.

“How much specificity is there for inhibiting or stimulating CFTR trafficking?”, Cystic Fibrosis Foundation, Williamsburg Conference '01, Williamsburg, VA, June 2001.

Daniel C. Devor, Ph.D.

Assistant Professor

September 1999, University of Pittsburgh. Department of Cell Biology and Physiology, Pittsburgh, PA

December 1999, Yale University, Department of Cell and Molecular Physiology, New Haven, CT

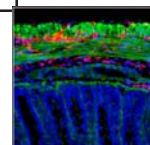
November 2000, SUNY at Buffalo, Dept. of Physiology and Biophysics, Buffalo, NY

May 2001, University of Pittsburgh, Renal Division, Pittsburgh, PA

September 2001, Kansas State University, Dept. of Anatomy and Physiology, Manhattan, KS

“Will K⁺ Channel Modulators be of benefit in Cystic Fibrosis?” Cystic Fibrosis Foundation Williamsburg Conference 2000, Williamsburg, VA, May 19-23, 2000.

“Kinase-dependent regulation of hIK1 is conferred by a C-terminal domain.” Biophysical Society meeting, Boston, MA, February 17-21, 2001.



Peter F. Drain, Ph.D.

Assistant Professor

“Mechanisms linking ATP binding and gate closure when the K_{ATP} channel is inhibited by ATP,”
Cardiology Seminar Series sponsored by Merck, Mayo Clinic, Rochester Minnesota
30 October 2000

“When inhibition Leads to Release: The Role of the K_{ATP} Channel in Glucose-Stimulated Insulin
Release,” University of Pittsburgh School of Medicine, Department of Medicine Seminar, Wednes-
day 27 June 2001.

Raymond A. Frizzell, Ph.D.

Professor

Johns-Hopkins University, Seminar, “Regulation of CFTR Density in the Plasma Membrane”,
December 1, 2000.

Emory University School of Medicine, Department of Cell Biology Seminar, “Of Strings and
SNARES: Two Tails of CFTR Traffic”, October 31, 2001.

Sandra M. Murray, Ph.D.

Professor

Adrenal 2000 Conference, Toronto, Canada June 16-18, 2000

American Society for Cell Biology, Gap Junction Symposium, Washington, D.C., Dec. 2001

Sergio A. Onate, Ph.D.

Assistant Professor

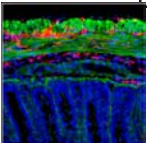
E. Lilly Co. Cincinnati, Ohio, Fall, 2001

Case Western University, Cleveland, Ohio. Spring, 2000

Kathryn W. Peters, Ph.D.

Research Assistant Professor

Regulation of CFTR Traffic by SNAP-25 and VAMP2. The Fourteenth Annual North American
Cystic Fibrosis Conference. Baltimore, Maryland. November 10, 2000



Tony M. Plant, Ph.D.

Professor

The Postnatal Ontogeny of the Hypothalamic-Pituitary-Gonadal Axis in the Rhesus Monkey, 55th Meeting of the Midwest Teratology Association, Greenfield
The Effects of Sex Hormones on the Initiation of Puberty in Primates. XIV Meeting of the Latin American Pediatric Endocrinology Society, Ushuaia
Circulating Leptin as a Signal for Triggering the Initiation of Puberty. XIV Meeting of the Latin American Pediatric Endocrinology Society, Ushuaia
The Role of Testicular Inhibins in the Control of FSH in Primates, Ares-Serono Foundation International Workshop on Inhibins, Activins and Follistatins. Melbourne
Puberty, Ares-Serono Foundation International Conference on Reproductive Competence: Pathology and Therapeutic Interventions, Santiago
Hypothalamic Plasticity and Our Adulthood, National Institute of Immunology, New Delhi
The Neurobiology of Primate Puberty, Indian Institute of Science, Bangalore
The Role of Inhibin in Regulating the Male Reproductive Axis, Institute for Research in Reproduction, Bombay
The Neurobiology of the Onset of Puberty, Pakistan Academy of Sciences, Islamabad
The Hypothalamic Pituitary Testicular Axis in the Monkey: Ongoing Studies, Massachusetts General Hospital, Boston
The Operation of the FSH-Inhibin Feedback Loop in Regulating Spermatogenesis in the Monkey, Bioqual, Inc., Rockville
The Control of the Onset of Primate Puberty, 83rd Annual Meeting of The Endocrine Society, Denver
Regulation of Primate Spermatogenesis by the FSH-inhibin Feedback Loop, 34th Annual Meeting of the Society for the Study of Reproduction, Ottawa

Abhiram Sahu, Ph.D.

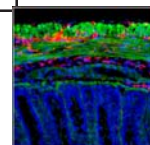
Research Associate Professor

The Center for Research in Reproductive Physiology Seminar, Department of Cell Biology and Physiology, University of Pittsburgh Medical School. Leptin action in the hypothalamus. Pittsburgh, PA, March 22, 2000.

Guy Salama, Ph.D.

Professor

September 19-20, 2000, Department of Pharmacology at Ohio Medical School of Toledo: "Mechanisms underlying arrhythmias in long QT syndrome"
Speaker at the XII Congress on High Altitude Physiology: Regulation of Ryanodine receptor activity and force by nitric oxide, Arica, Chile.
Speaker at a symposium on Ca²⁺ dependent mechanisms of cardiac pathology at the AHA



meeting: "Putting it all together: Ca²⁺ oscillations in the whole heart.
Invited Seminar speaker at Vanderbilt University by John Wikswo on: Control of Fibrillation Dynamics by the local refractory period"
Invited speaker on behalf of the Oxygen Society of Greater Washington and the Department of Anesthesiology and Physiology of the Uniformed Services University of the Health Sciences by Dr. Leslie McKinney.
Chairman of Session at NASPE, May 4, 2001 "Basic Science: Cell-cell coupling and arrhythmias.
Chairman of Session at NASPE, May 5, 2001 "Basic Science: Histology of the Venous System- Substrate for Arrhythmias

Linton M. Traub, Ph.D.
Assistant Professor

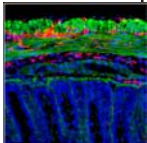
Dept. of Biochemistry, St. Louis University School of Medicine, 1999.
"Hormonal and Neural Peptide Biosynthesis" Gordon Conference, New Hampshire, 2000.

Simon C. Watkins, Ph.D.
Professor

Not your Fathers Microscope, Discovery Weekend, University of Pittsburgh October 28th 2000
Imaging: the future, University of Umea, Umea Sweden November 17th 2000
NIEHS retreat, Raleigh Durham, Imaging session, "Imagining the future" December 4-5th 2000
From little animals to Moving molecules, Department of Environmental Health, University of Pittsburgh Jan 14th 2001
Imagining the future, Cornell School of Veterinary Medicine. February 27th 2001
Imaging Death, April 4th 2001 Apoptosis work group, University of Pittsburgh
From Little Animals to Moving Molecules, April 6th 2001 Optical Imaging Seminar Series, UPCI,
Imaging Opportunities: Biomedical imaging in the 21st Century. Cystic Fibrosis Research Center University of North Carolina May 31st 2001
Imaging the future, Optical opportunities in the 21st century. University of Pittsburgh, Department of Pathology June 6th 2001
Not your Fathers Microscope, Discovery Weekend, University of Pittsburgh October 28th 2000
Imaging: the future, University of Umea, Umea Sweden November 17th 2000
NIEHS retreat, Raleigh Durham, Imaging session, "Imagining the future" December 4-5th 2000

Charles Washabaugh, Ph.D.
Research Assistant Professor

"Effects of steroid hormones on amphibian limb regeneration" Department of Biology, Westminster College, New Wilmington, PA. , 1993.



Anthony J. Zeleznik, Ph.D.

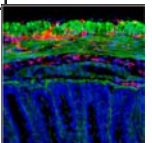
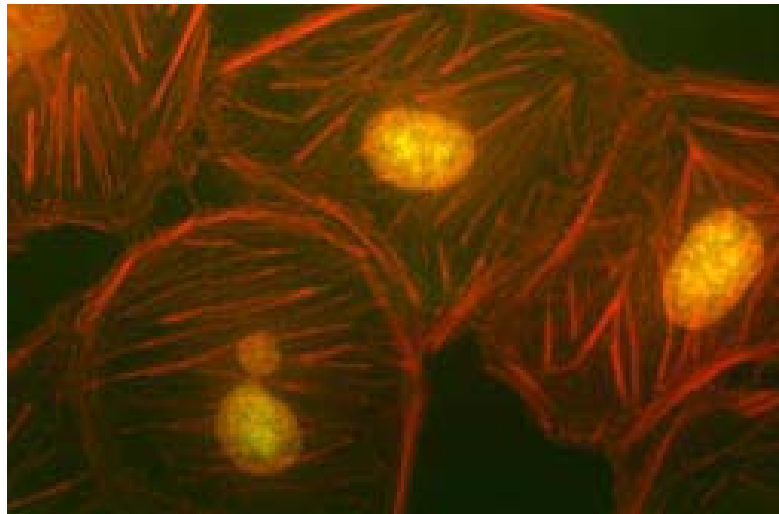
Professor

Society for the Study of Reproduction - "Follicle Selection in Primates...Many are Called But Few Are Chosen"

Buenos Aires - Ferring Symposia - "Gonadotropic Control Of Prepubertary Follicular Development"

University of Michigan - Reproductive Sciences Program - "Physiology and Cell Biology of the Primate Ovarian Cycle"

European Society for Human Reproduction and Embryology (ESHRE) Meeting. "Gonadotropin Physiology in the Natural Menstrual Cycle" Lausanne, Switzerland.



**Peer Reviewed Publications
1999-2001**

William T. Ameredes, Ph.D.
Visiting Research Assistant Professor

Ameredes BT, Provenzano MA. Influence of nitric oxide on vascular resistance and muscle mechanics during tetanic contractions in situ. *J. Appl. Physiol.* 87(1): 142-151, 1999.

Ameredes BT, Watchko JF, Daood MJ, Rosas JF, Donahoe MP, and Rogers RM. Growth hormone restores aged diaphragm myosin composition and performance after chronic undernutrition. *J. Appl. Physiol.* 87(4): 1253-1259, 1999.

Ameredes BT, Watchko JF, Daood MJ, Rosas JF, Donahoe MP, and Rogers RM. Growth hormone improves body mass recovery with refeeding after chronic undernutrition-induced muscle atrophy in aging male rats. *J. Nutr.* 129: 2264-2270, 1999.

DeRosimo JF, Washabaugh CH, Ontell MP, Daood MJ, Watchko JF, Watkins SC, Ameredes BT, Ontell M. Enhancement of adult muscle regeneration by primary myoblast transplantation. *Cell Transplantation.* 9: 369-377, 2000.

Ameredes BT, Zhan WZ, Prakash YS, Vandenboom R, and Sieck GC. Power fatigue of the rat diaphragm muscle. *J. Appl. Physiol.* 89: 2215-2219, 2000.

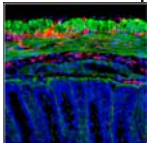
Ameredes BT, Zamora R, Gibson KF, Billiar TR, Dixon-McCarthy B, Calhoun WJ. Increased nitric oxide production by airway immune cells of sensitized and challenged IL-10 knockout mice. *J. Leukocyte Biol.* 70: 000-000, 2001.

Ameredes BT, Zamora R, Gibson KF, Billiar TR, Dixon-McCarthy B, Calhoun WJ. IL-18 production by airway cells is downregulated with airway inflammation in IL-10 knockout mice. (submitted)

Ameredes BT, Brechue WF, and Stainsby WN. Maximal VO₂ with shortening contractions at maximal power: dependence on preload and afterload (in preparation).

Meir Aridor, Ph.D.
Assistant Professor

M. Aridor, S. I. Bannykh, T. Rowe and W. E. Balch (1999) Cargo can Modulate COPII Vesicle Formation from the Endoplasmic reticulum. *J. Biol. Chem.* 274 4389-4399



M. Aridor and W. E. Balch (1999) Integration of Endoplasmic Reticulum Signaling in Health and Disease. *Nature Medicine* 5, 745-751

Allan BB, Weissman J, Aridor M, Moyer B, Chen CD, Yoo JS, Balch WE (2000) Stage specific assays to study biosynthetic cargo selection and role SNAREs in export from the endoplasmic reticulum and delivery to Golgi. *Methods*; 20: 411-6

M. Aridor and W.E. Balch (2000) Drug Delivery: Regulating the export of ER cargo *Science* 287 816-817

M. Aridor and L. A. Hannan (2000) Traffic Jam: A compendium of Human Diseases that affect Intracellular Transport Processes. *Traffic*, 1 836-851

M. Aridor and W. E. Balch (2000) Kinase signaling initiates COPII recruitment and Export from the Mammalian Endoplasmic Reticulum, *J. Biol. Chem.*, 275 35673-35676

Weissman JT, Aridor M. and W.E. Balch (2001) Purification and Properties of rat liver Sec23-Sec24 complex. *Method Enzymol.* 329 431-438

M. Aridor, K. N. Fish, S. I. Bannykh, J. T. Weissman, Roberts T. H., J. Lippincott Schwartz J. and W. E. Balch, (2001) The Sar1 GTPase coordinates biosynthetic cargo selection with Endoplasmic Reticulum Export Site Assembly. *J. Cell. Biol.* 152 213-229

Mingdong H, Weissman, JT., Beraud-dufour S., Luan P., Wang C., Chen W., M. Aridor, Wilson IA., Balch WE, (2001), Crystal Structure of Sar1-GDP at 1.7 Å resolution and the role of the N-terminus in ER export. *J. Cell Biol.* In press

Neil A. Bradbury, Ph.D.

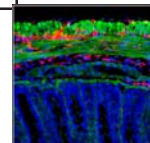
Assistant Professor

Bradbury, N.A., Clark, J.A., Watkins, S.C., Widnell, C., Smith, H.S., and Bridges, R.J. (1999). Characterization of the internalization pathways of the cystic fibrosis transmembrane conductance regulator (CFTR). *Am. J. Physiol.* 276:L659-L668

Weixel, K. and Bradbury, N.A. (1999). The carboxyl terminus of CFTR binds the endocytic adaptor complex AP-2. *J. Biol. Chem.* 275:3655-3660.

Sun, F., Hug, M., Bradbury, N.A., and Frizzell, R.A. (2000). Protein kinase A associates with cystic fibrosis transmembrane conductance regulator via an interaction with ezrin. *J. Biol. Chem.* 275:14360-14366.

Singh, A.K., Schultz, B.D., Katzenellenbogen, J.A., Price, E.M., Bridges, R.J. and Bradbury, N.A. (2000). Estrogen inhibition of CFTR-mediated chloride secretion. *J. Pharm. Exp. Ther.* 295:195-204.



Bradbury, N.A. (2000). Protein kinase-A mediated secretion of mucin from human colonic epithelial cells. *J. Cell Physiol.* 185:408-415.

Sun, F., Hug, M., Bradbury, N.A. and Frizzell, R.A. (2000). E3KARP mediates the association of ezrin and PKA with CFTR in airway cells. *J. Biol. Chem.* 275:29539-29546.

Yaroslavskiy, B.B., Stolz, D., Watkins, S.C., Alber, S.M., Bradbury, N., and Steinman, R.A. (2001). p27Kip1 localizes to detergent-insoluble microdomains within lymphocyte membranes. *Mol. Med.* 7:49-58.

Weixel, K.M. and Bradbury, N.A. (2001). Endocytic adaptor complexes bind the C-terminal domain of CFTR. *Pflugers Arch. – Eur. J. Physiol.* 443(Suppl. 1):S70-S74.

Bradbury, N.A. (2001). cAMP signaling cascades and CFTR: is there more to learn? *Pflugers Arch. – Eur. J. Physiol.* 443(Suppl. 1):S85-S91.

Weixel, K.M. and Bradbury, N.A. (2001). The mu subunit of AP-2 directs CFTR to the clathrin endocytic pathway. *J. Biol. Chem.* (Submitted).

Robert J. Bridges, Ph.D.

Professor

Bradbury, N.A., Clark, J.A., Watkins, S.C., Widnell, C., Smith, H.S., and Bridges, R.J. (1999). Characterization of the internalization pathways of the cystic fibrosis transmembrane conductance (CFTR). *Am. J. Physiol.* 276:L659-L668.

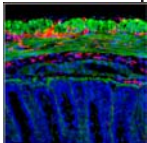
Devor, D.C., Singh, A.K., Lambert, L.C., DeLuca, A., Frizzell, R.A., and Bridges, R.J. (1999). Bicarbonate and chloride secretion in Calu-3 human airway epithelial cells. *J. Gen. Physiol.* 113:743-760.

Schultz, B.D., Frizzell, R.A., and Bridges, R.J. (1999). Rescue of dysfunctional $\Delta F508$ -CFTR chloride activity by IBMX. *J. Memb. Biol.* 170:51-66.

Schultz, B.D., Singh, A.K., Devor, D.C., and Bridges, R.J. (1999). Pharmacology of CFTR chloride channel activity. *Physiol. Rev.* 79:S109-S144.

Singh, A.K., Devor, D.C., Gerlach, A.C., Gondor, J., Pilewski, J.M., and Bridges, R.J. (2000). Stimulation of Cl⁻ secretion by chlorzoxazone, an activator of basolateral membrane K_{Ca} channels. *J. Pharm. Exp. Therap.* 292:778-787.

Devor, D.C., Bridges, R.J., and Pilewski, J.M. (2000) Pharmacological modulation of ion transport across wild-type and $\Delta F508$ CFTR-expressing human bronchial epithelia. *Am. J. Physiol.* 279:C461-C479.



Singh, A.K., Schultz, B.D., Katzenellenbogen, J.A., Price, E.M., Bridges, R.J., and Bradbury, N.A. (2000). Estrogen inhibition of cystic fibrosis transmembrane conductance regulator-mediated chloride secretion. *J. Pharmacol. Exp. Ther.* 295:195-204.

Singh, S., Syme, C.A., Singh, A.K., Devor, D.C., and Bridges, R.J. (2001). Benzimidazolone activators of chloride secretion: Potential therapeutics for cystic fibrosis and chronic obstructive pulmonary disease. *J. Pharmacol. Exp. Ther.* 296:600-611.

Danahay, H., Withey, L., Poll, C.T., van de Graaf, S.F.J., and Bridges, R.J. (2001). Protease-activated receptor-2-mediated inhibition of ion transport in human bronchial epithelial cells. *Am. J. Physiol.* 280:C1455-C1464.

Tamada, T., Hug, M.J., Frizzell, R.A. and Bridges, R.J. (2001). Microelectrode and impedance analysis of anion secretion in Calu-3 cells. *J. Pancreas* 2(4 Suppl):219-228.

Hug, M.J. and Bridges, R.J. (2001). pH regulation and bicarbonate transport of isolated porcine submucosal glands. *J. Pancreas* 2(4Suppl):274-279.

Bridges, R.J., Newton, B.B., Pilewski, J.M., Devor, D.C., Poll, C.T., and Hall, R.L. (2001). Na⁺ transport in normal and CF human bronchial epithelial cells is inhibited by BAY 39-9437. *Am. J. Physiol.* 281:L16-L23.

Danahay, H., Atherton, H., Bridges, R.J., and Poll, C.T. (2001). Interleukin 13 induces a hypersecretory ion transport phenotype in human bronchial epithelial cells. (in press).

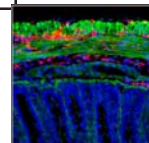
Danahay, H., Poll, C.T. and Bridges, R.J. (2001). A novel non-radioisotope, fluorescence-based Na⁺-flux assay suitable for transepithelial transport studies. *Journal of Pharmacological and Toxicological Methods*. (Submitted).

Lambert, L.C., Cassell, G.H. and Bridges, R.J. (2000). *Mycoplasma fermentans* potassium channel: A prokaryote channel with eukaryotic channel properties. *Journal of Membrane Biology*. (Submitted).

Singh, A.K., Bradbury, N.A., Schultz, B.D. and Bridges, R.J. (2000). Iodoglibenclamide inhibits and photo labels CFTR. (Manuscript in preparation).

Singh, A.K., Juneja, R.K., Atwood, J.L. and Bridges, R.J. (2000). TS-TM-calix[4]arene: A subnanomolar chloride channel blocker. (Manuscript in preparation).

Schultz, B.D., Singh, A.K., Bradbury, N.A., Aguilar-Bryan, L., Frizzell, R.A. and Bridges, R.J. (2000). Diarylsulfonylureas selectively modulate CFTR channel gating. (Manuscript in Preparation).



Daniel C. Devor, Ph.D.
Assistant Professor

Devor, D.C., A.K. Singh, L.C. Lambert, A. DeLuca, R.A. Frizzell, and R.J. Bridges. Bicarbonate and chloride secretion in Calu-3 human airway epithelial cells. *J. Gen. Physiol.* 113:743-760, 1999.

Devor, D.C. and J.M. Pilewski. UTP inhibits Na⁺ absorption in wild type and Δ F508 CFTR expressing human bronchial epithelia. *Am. J. Physiol.* 45:C827-837, 1999.

Syme, C.A., A.C. Gerlach, A.K. Singh and D.C. Devor. Pharmacological activation of the cloned intermediate- and small-conductance Ca²⁺-activated K⁺ channels, hIK1 and rSK2. *Am. J. Physiol.* 278: C589-C600, 2000.

Gerlach, A.C., N.N. Gangopadhyay and D.C. Devor. Kinase-dependent regulation of the intermediate conductance, calcium-dependent potassium channel, hIK1. *J. Biol. Chem.* 275: 585-598, 2000.

Devor, D.C., R.J. Bridges and J.M. Pilewski. Pharmacological modulation of ion transport across wild type and Δ F508 CFTR-expressing human bronchial epithelia. *Am. J. Physiol.* 279: C461-C479, 2000.

Singh, A.K., D.C. Devor, A.C. Gerlach, M. Gondor, J.M. Pilewski, and R.J. Bridges. Stimulation of Cl⁻ secretion by chlorzoxazone, an activator of basolateral membrane K_{ca} channels. *J. Pharm. Exp. Therap.* 292:778-787, 2000.

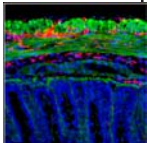
Singh, S., C.A. Syme, A.K. Singh, D.C. Devor and R.J. Bridges. Benzimidazolone activators of chloride secretion: Potential therapeutics for cystic fibrosis and chronic obstructive pulmonary disease. *J. Pharmacol. Exp. Therap.* 296:600-611, 2001.

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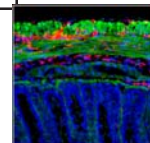
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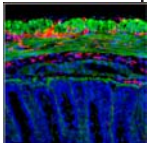
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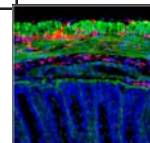
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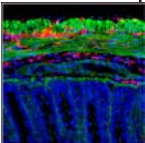
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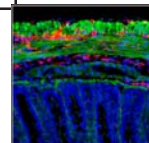
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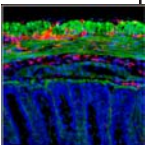
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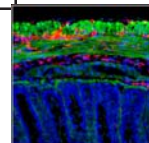
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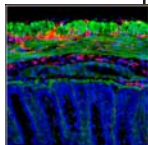
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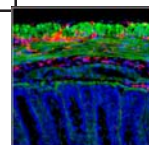
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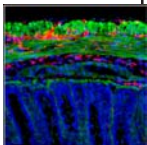
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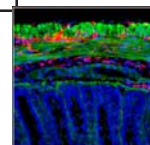
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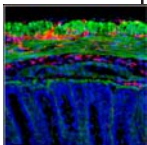
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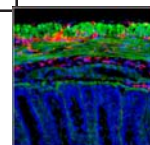
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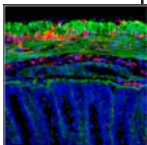
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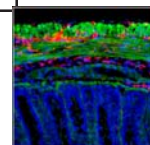
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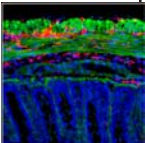
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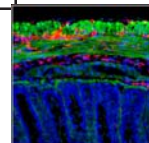
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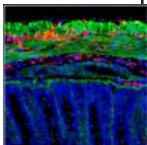
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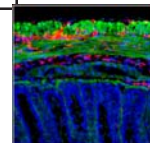
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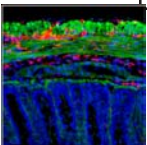
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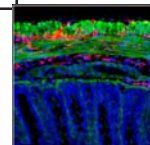
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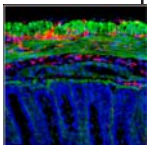
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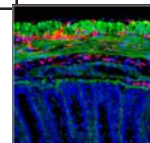
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William T. Ameredes, Ph.D. [Transferred to Department of Medicine, 12/31/01]
Visiting Research Assistant Professor

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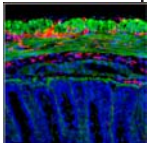
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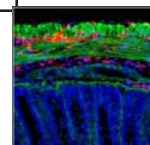
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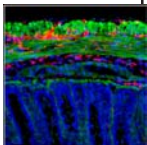
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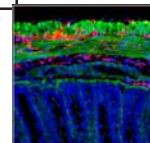
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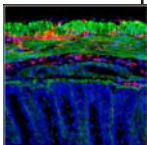
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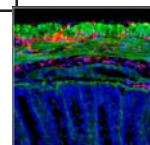
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Daniel C. Devor, Ph.D.

Assistant Professor

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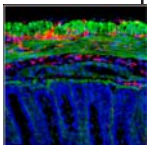
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Peter F. Drain, Ph.D.

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Georgia K. Duker, Ph.D.

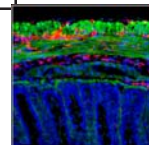
Assistant Professor

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Raymond A. Frizzell, Ph.D.

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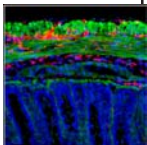
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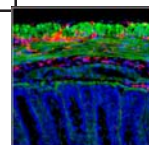
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Martin Ontell, Ph.D.

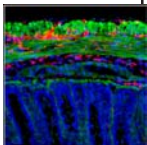
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Kathryn W. Peters, Ph.D.

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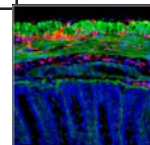
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Tony M. Plant, Ph.D.

Professor

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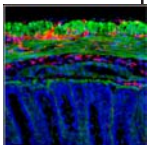
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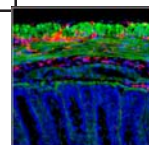
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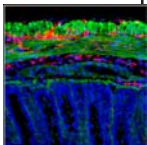
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Suresh Ramaswamy, Ph.D.



Research Assistant Professor

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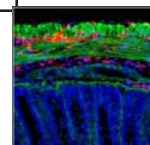
Abhiram Sahu, Ph.D.

Research Associate Professor

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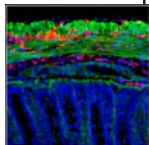
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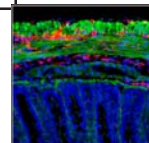
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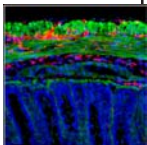
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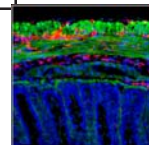
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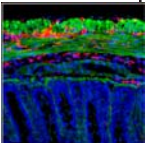
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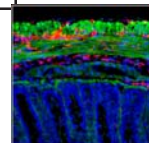
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