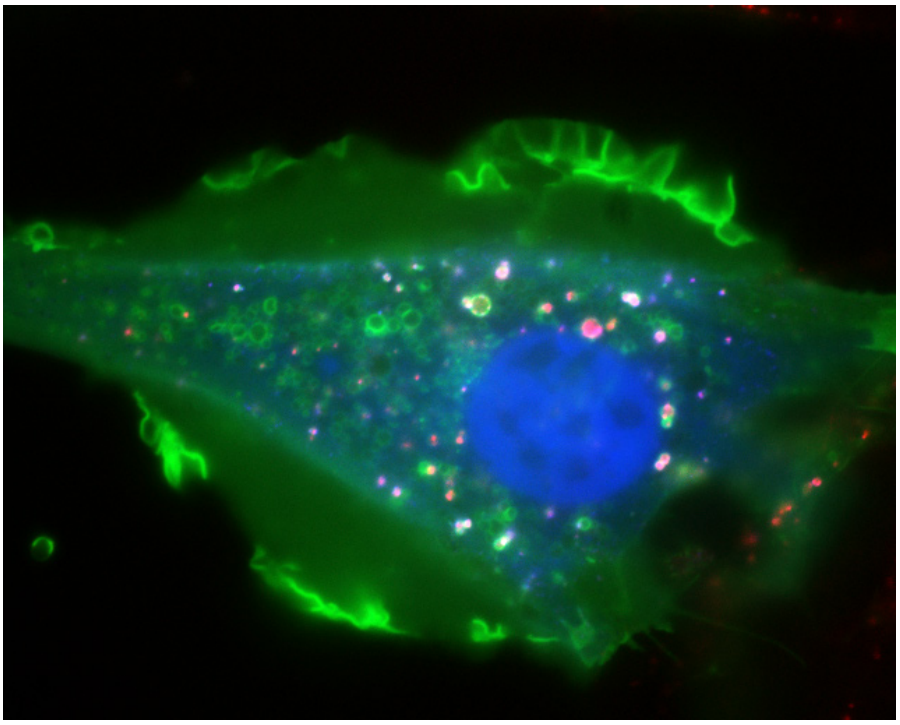
UNIVERSITY OF PITTSBURGH
SCHOOL OF MEDICINE

CELL BIOLOGY AND PHYSIOLOGY



FY11 ANNUAL REPORT
AND
FY12 BUSINESS PLAN

Front Page
Cover figure by Dr. Alexander Sorkin. Localization of Grb2-CFP, YFP-Ras and EGF-rhodamine in COS-1 cell.

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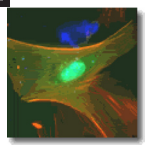
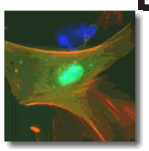


Department of Cell Biology and Physiology

In the cell, life is governed by a multitude of molecular systems that shape and sustain the organellar system of the cell, maintain cellular homeostasis and respond to extracellular cues. These systems are dynamic, multicomponent macromolecular complexes maintaining and regulating correct function of these complexes is essential for normal cell motility, growth, division, differentiation and programmed death. Dysregulation inevitably leads to an aberrant behavior and commonly disease. Understanding the structure, function and interactions of these complexes and the underlying mechanisms by which they regulate organelles and other cellular compartments lie at the core of Cell biology. The faculty in the Department of Cell Biology and Physiology employs an interdisciplinary approach to address a broad spectrum questions in Cell biology from the roles of single molecules to through complex multicomponent cellular mechanisms to integrated studies at the organismal level in the fly, fish and mouse. The research in the department involves translation of the fundamental cell functions to understanding the disease mechanisms and development of therapeutics.

The Department of Cell Biology and Physiology is one of eight basic science departments in the School of Medicine. Members of our Department benefit from close and collegial interactions with researchers in other Departments, and with basic scientists in the School of Arts and Sciences at the University of Pittsburgh and at Carnegie-Mellon University. The Department is comprised currently of fifteen faculty with federally funded research programs. Grant revenue to the Department has more than quadrupled during the last decade. Members of our faculty are active in both the medical and graduate school curricula, in curriculum development and student recruitment and mentoring. The graduate program in Cell Biology and Molecular Physiology is part of the Interdisciplinary Biomedical Graduate Program (IBGP) (http://www.gradbiomed.pitt.edu/) and led by our department faculty. We teach extensively in the Cell Biology Block, which comprises approximately one-third of the first year graduate course, Foundations of Biomedical Science. Our flagship course departmental offering, "Cell Biology of Normal and Disease States", is required of all students entering the program, and further information can be found at our departmental website (see: http://www.cbp.pitt.edu). The course has been recently revised to include exciting areas in modern cell biology as well as clinical conditions that arise from defects in these processes. Overall, the School of Medicine graduate program has more than 300 students currently working toward the PhD, and includes students in the newly formed HHMI-funded Computational Biology program, Neuroscience Program, the Program in Integrative Molecular Biology, and the Structural Biology/Molecular Biophysics graduate program. Several of our faculty are members of these newly formed programs as well.

The department is housed in administrative and research space in the South Wing of the Biomedical Science Tower (SBST). We also have satellite laboratories in the Childrens Hospital and the Hillman Cancer Institute. Our modern facilities and support cores provide the faculty with space designed to optimize their research efforts.

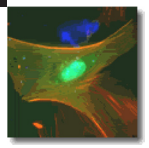


Faculty member featured in this Report: Dr. Alexander D. Sorkin, Ph.D.

The focus of the research in my laboratory is currently split into two major directions which are apparently distinct from each other with respect to the biological systems involved, their relation to the human disease, and experimental models used. However, the main ideas underlying both research directions are conceptually the same - to understand how endocytosis and post-endocytic trafficking regulates function(s) of the transmembrane proteins, such as receptors and transporters.

The elucidation of the molecular mechanisms of endocytosis of growth factor receptors using a prototypic member of the family, epidermal growth factor (EGF) receptor has been a long-term interest in the laboratory. More recently, this research expanded with the analysis of the role of endocytosis in spatial and temporal regulation of signal transduction by the EGF receptor. EGF receptor is the best studied receptor tyrosine kinase and a member of ErbB family implicated in regulation of key cellular functions in normal and neoplastic cells. EGF receptor is also important prognostic marker and therapeutics target in many types of human cancer. Despite that a number of EGF receptor inhibitors are already in clinical use, they currently benefit only a small pool of patients. Better understanding of EGF receptor regulation is necessary to develop new strategies of therapeutic intervention with EGF receptor dependent tumorigenesis. Studies of the mechanisms of EGF receptor endocytosis use of cutting-edge quantitative mass-spectrometry methods (collaboration with Dr. S. Gygi, Harvard Medical School), RNA interference screens in combination with measurements of the kinetics endocytosis using assays developed in our laboratory over the years. The role of endocytosis in spatial regulation of signaling is studied in conjunction with the development and application of a set of technologies allowing visualization of protein interaction and activities in living cells including various FRET methods. In addition, we have developed a new approach that enables analysis of the localization of fluorescently-tagged proteins expressed at physiological levels in living human cells. This is achieved by stable knock-down of the endogenous protein by RNA interference with concurrent constitutive expression of the same proteins tagged with fluorescent protein at the levels similar to that of an endogenous protein.

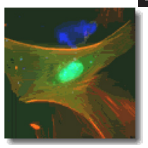
Studies of the role of trafficking processes in the regulation of dopaminergic neurotransmission by the plasma membrane dopamine transporter (DAT) is another major research focus in the laboratory. Dopamine (DA) plays an important role in brain reward, both to natural reinforcers and addictive drugs. Removal of DA from the extracellular space and its transport back into DA neurons is an important mechanism controlling DA neurotransmission. This removal occurs via the DAT. DAT plays important roles in psychomotor stimulant behavioral activation and reward. By understanding how DAT activity is regulated, we will better appreciate its contribution to normal neurotransmission and to brain diseases like drug addiction. Our current research is aimed at characterization of the mechanisms of endocytosis and intracellular trafficking of DAT. The first set of projects involves structure-function studies of heterologously-expressed human DAT. We have performed extensive analysis of the molecular mechanisms of DAT endocytosis and identified key players involved using DAT expressed in heterologous cells. The main focus in the next several years will be the analysis of trafficking of endogenous DAT in dopaminergic neurons in vivo and in vitro. We have recently



generated a knock-in mouse expressing epitope-tagged HA-DAT. We have also developed live-cell microscopy methods and endocytosis assays to follow HA-DAT trafficking in neurons. The data obtained using mechanistic analyses will be further developed in experiments with the intact animals to analyze how changes in DAT trafficking at the synapse correlate with the behavior patterns and response to the drugs of abuse, such as amphetamines and cocaine.

Several images of data acquired over the years from my work are included with this report.

Alexander D. Sorkin, Ph.D.
Chairman and Richard B. Mellon Professor
Cell Biology and Physiology



Department of Cell Biology and Physiology
2011 Research Activities

Biomedical research in the Department of Cell Biology and Physiology is directed at several major areas, as described below. The department is home of the School of Medicine's Center for Biological Imaging and the Cystic Fibrosis Research Center. The Department's major faculty groupings and research foci are summarized below.

Membrane trafficking and organelle biogenesis

Aridor
Butterworth
Devor
Frizzell
Murray
Sorkin
Traub

Scientists in this program are part of a larger "trafficking" community combining researchers from the School of Medicine, School of Arts and Sciences, and Carnegie Mellon University. The research is aimed at identifying the mechanisms of targeting of proteins and lipids to specific cellular compartments and at defining how these processes are disrupted in disease.

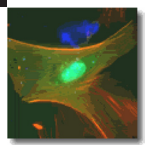
Regulation of channels and transporters

Butterworth
Devor
Sorkin
Thibodeau
Wu

Studies in this group aim at elucidating the physiological mechanisms underlying regulation of several ion channel and transporter proteins. Our approaches include biochemical, molecular, electrophysiologic, imaging, cell biologic and transgenic techniques. Inherited mutations in ion channels are responsible for many genetic diseases, including cystic fibrosis (CF). The department is home to a Translational Core Center in CF funded by the NIH and to a program grant from the CF Foundation.

Cellular organization and cell-cell communications

Hong
Murray
Stolz
Traub
Watkins

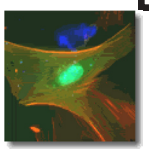


This group uses various state-of-the-art cell imaging, biochemical and genetic approaches to define the mechanisms involved in development and maintenance of epithelial cell polarity, regulation of gap junctions, angiogenesis and vasculogenesis, and various routes of functional communication between dendritic cells.

Regulation of intracellular signaling and gene expression

Drain
Leuba
Sorkin
Wan

Scientists in this group are examining signaling processes mediated by receptors for growth factors and hormones, mechanisms of hormone secretion, and processes involved in the regulation of cell cycle progression, DNA repair and transcription. The particular focus is on the events leading to dysregylation of cellular signaling networks leading in the disease such as cancer.



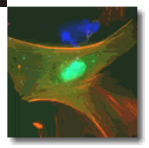
Center for Biologic Imaging

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), fifteen 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, by space, and by staff within the center. Over the last year, the Facility has continued to expand such that the base of imaging technologies has increased significantly, so that it now includes almost all cutting edge light microscopic, electron microscopic, and computer aided image analysis tools. The Center is split between the medical research facility of the UPSOM (in approximately 5500 sq ft. of space) and within the Hillman Cancer Center (700 sq ft). Both locations have been designed as dedicated, state of the art imaging facilities. The medical school location is the mainstay of the core and has fully equipped microscopy suites, computer labs, and wet and dry bench space for light and electron microscopic preparations. It incorporates a continuum of optical imaging technologies from routine histology to more exotic procedures such as EM, in situ hybridization and fluorescent imaging of live cells with multiple fluorochromes in 3 dimensions and time. The smaller Hillman Cancer Center location houses basic confocal and immunofluorescence imaging facilities. In the last 2 years the CBI has successfully competed for new instrumentation for live cell (2 new systems), multicolor imaging, spectral confocal imaging (2 new systems), high speed confocal (3 systems) and multiphoton microscopy through the NCRR.. Furthermore, the Facility has supplemented its existing microscope and computer base with 2 new live cell imaging systems with microinjection capabilities. Currently the facility has 19 confocal microscopes of different types (point scanners, spinning disks, etc) 6 live cell systems (two with micro injection, 1 new multiphoton system, 4 high end upright microscopes and 3 electron microscopes (SEM and TEM). We also have multipe (30) online image processing work stations equipped with Metamorph, Elements, Imaris and Photoshop. Real time storage is 150 terabytes at gigabit speed and a half



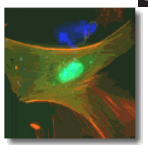
Petabyte tape library.

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.

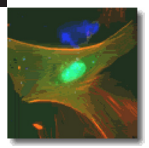
The Assistant Director: Dr. Donna Beer-Stolz is an Associate Professor in Cell Biology and Physiology. Her funded research interests are in liver regeneration and vasculogenesis. She has been the Assistant Director of the CBI for 12 years to this date. She was recruited specifically to facilitate interactions between the Cell and Tissue Imaging Core and its users. Dr. Beer-Stolz' primary role lies in the management and development of the electron microscopy component of the center.

Other Faculty
Dr. Katy Baty is another faculty in the Center for Biologic Imaging as director of live cell imaging; her expertise is in cardiac myocytes and RNA trafficking within these cells. Another faculty who has become closely involved in the Center is Dr. Claudette St. Croix. Dr. St. Croix has research interests focused around the application of live cell and tissue imaging to the lung and pulmonary physiology

Postdoctoral Research Associates:
Technical Specialists: The technical bases of the Center are all trained microscopists; in total 15 technical specialists work in the center. Furthermore we have a staff of three research assistants who provide general lab maintenance and digital imaging 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, book-keeping, 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.



Cystic Fibrosis Research Center

Center Director: Dr. Raymond A. Frizzell

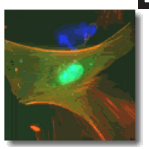
The Cystic Fibrosis Foundation established a Research Development Program Center for research in cystic fibrosis with a five-year, $2 million grant in 1997. It was renewed in 2002 and 2007 and 2011. The primary goal of the Center is to focus the attention of new and established investigators on multidisciplinary approaches to improve the understanding and treatment of cystic fibrosis (CF), the most common lethal genetic disease among Caucasians. 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 lung transplant activity. The University of Pittsburgh RDP Center is one of nine such Centers supported by the CF Foundation in North America.

In addition to the RDP award, the Center was the recipient, in 2004 and 2010, of a Core Center grant from the NIH (P30 entitled, "Basic and Clinical Studies of Cystic Fibrosis"). Three such Centers were awarded nationally in the last funding round. The CF Research Center is directed by Raymond A. Frizzell, Ph.D., with extensive interactions with clinical colleagues and co-Directors, Drs. Joseph Pilewski and Jay Kolls. The NIH Center supports pilot research projects and core facilities. The primary P30 award criterion was the presence of a significant research base of existing extramural grants, awarded to Center investigators, to justify its Research Cores. The current Center is a free-standing administrative unit and its primary cores are housed in the Rangos Research Center at the Children's Hospital of Pittsburgh, the Department of Cell Biology and Physiology, and the Adult Pulmonary Division of the Department of Medicine.

The Center's research efforts focus on several areas relevant to the understanding and treatment of CF: basic studies of the function, protein interactions, trafficking and processing of the CF gene product, CFTR and its disease-causing mutants; understanding the infection-inflammation issues that compromise the function of CF airways; the development of new therapies and diagnostic approaches for treating CF, and participation of Center investigators in clinical research. Our 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.

Research and Clinical Cores:

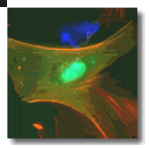
Human Airway Cell and Assays Core: This core provides access to patient materials obtained as a result of lung transplant activities in the Department of Surgery. This core offers well differentiated primary cultures of human bronchial epithelia to facilitate a variety of pre-clinical research investigations. It has supplied cells to various academic and industrial investigators involved in CF research. This core also provides functional assays of CFTR and other proteins. Its assay menu includes fluorescence assays for anion permeability, transepithelial current, conductance, impedance and current fluctuation analysis in polarized airway or other epithelial cell cultures, both established cell lines and primary HBE cultures (above). Facilities and

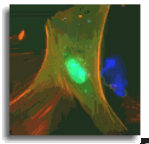


personnel for performing whole-cell and single channel patch clamp measurements are also available. The core also provides access to molecular reagents and techniques, to provide systems for gene expression, and standardized quality control. [Core Director: Raymond A. Frizzell, Ph.D. Department of Cell Biology and Physiology]

Cell 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. Its primary focus is immunocytochemistry; in addition, the core has been involved in the development of new methods for measurements of airway surface liquid volume, ciliary beat frequency, muco-ciliary clearance, water permeability and the development of novel methods for detecting this low abundance protein in collaboration with investigators at Carnegie Mellon University. [Core Director: Simon Watkins, Ph.D., Cell Biology and Physiology]

Clinical Studies Core: This core provides facilities and personnel for implementing clinical trials. It provides procedures for identifying functional outcomes, monitored in terms of lung function, radioisotope clearance, ion transport, inflammatory mediator levels or gene expression. It maintains patient records and procedures for enrolling patients in clinical studies, and it interfaces with the larger clinical studies effort of the Cystic Fibrosis Foundation. [Core Director: Joseph Pilewski, M.D. [Department of Medicine]





Cell Biology and Physiology Faculty Data

[Current as of June, 2011]

Name	Rank	Office Address	Email Address	Phone	Fax
Aridor, Meir	Associate Professor	S310 BST-South Wing	aridor@pitt.edu	412-624-1970	412-648-8330
Baty, Catherine	Res. Asst. Professor	S221 BST-South Wing	cjb16@pitt.edu	412-383-7264	412-383-8894
Bertrand, Carol	Res. Asst. Professor	S309 BST-South Wing	cbertra@pitt.edu	412-648-1044	412-648-8330
Butterworth, Michael	Assistant Professor	S314 BST-South Wing	michael7@pitt.edu	412-383-8591	412-648-8330
Devor, Daniel	Professor	S312 BST-South Wing	dd2@pitt.edu	412-383-8755	412-648-8330
Drain, Peter	Associate Professor	S323 BST-South Wing	drain@pitt.edu	412-648-9412	412-648-8792
Duker, Georgia	Assistant Professor	322 Scaife Hall	gduker1@pitt.edu	412-648-9409	412-648-8330
Frizzell, Raymond	Professor	7117 RANCH	frizzell@pitt.edu	412-692-9449	412-692-9724
Gay, Vernon	Associate Professor	S321 BST-South Wing	vlgay@pitt.edu	412-648-9422	412-781-8059
Hong, Yang	Assistant Professor	S325 BST-South Wing	yhong@pitt.edu	412-648-2845	412-648-8330
Leuba, Sanford	Associate Professor	2.26g Hillman Cancer Center	leuba@pitt.edu	412-623-7788	412-623-4840
Murray, Sandra	Professor	S324 BST-South Wing	smurray@pitt.edu	412-648-9566	412-648-8330
Peters, Kathryn	Res. Asst. Professor	S363 BST-South Wing	kathi@pitt.edu	412-383-7845	412-648-8330
Ryan, Kathleen	Associate Professor	M302 Scaife Hall	ryankath@pitt.edu	412-648-8859	412-648-8330
Schmidt, Bela	Res. Asst. Professor	S375 BST-South Wing	bes53@pitt.edu	412-383-7109	412-648-8330
Sorkin, Alexander	Professor and Chair	S368 BST-South Wing	sorkin@pitt.edu	412-624-3116	412-648-8330
Stolz, Donna Beer	Associate Professor	S221 BST-South Wing	dstolz@pitt.edu	412-383-7283	412-648-8330
Thibodeau, Patrick	Assistant Professor	S327 BST-South Wing	thibodeau.pitt.edu	412-383-8858	412-648-8330
Traub, Linton	Associate Professor	S325 BST-South Wing	traub@pitt.edu	412-648-9711	412-648-8330
Wan, Yong	Associate Professor	2.6 Hillman Cancer Center	yow4@pitt.edu	412-623-3275	412-623-7761
Watkins, Simon C.	Professor	S225 BST-South Wing	swatkins@pitt.edu	412-648-3051	412-383-8894
Wu, Christine	Associate Professor	S326 BST-South Wing	chriswu@pitt.edu	412-648-9260	412-648-8330

CELL BIOLOGY & PHYSIOLOGY
FY11 ORGANIZATIONAL CHART

Office of the Chairman
Alexander D. Sorkin, Ph.D.
Richard B. Mellon Professor and
Chair of Cell Biology & Physiology

CBP Graduate Program
William Walker, Ph.D.
Director

Cystic Fibrosis Research Center
Raymond A. Frizzell, Ph.D.
Director

Center for Biologic Imaging
Simon C. Watkins, Ph.D.
Director

Cell Biology & Physiology and Pharmacology Shops

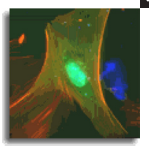
Machine Shop
Travis Wheeler,
Manager

Joshua Byler

Electronics Shop
Greg Szekeres

Tenured/Tenure Track Faculty
Meir Aridor, Ph.D.
Michael B. Butterworth, Ph.D.
Daniel Devor, Ph.D.
Peter Drain, Ph.D.
Raymond Frizzell, Ph.D.
Vernon Gay, Ph.D.
Yang Hong, Ph.D.
Sanford Leuba, Ph.D.
Sandra Murray, Ph.D.
Kathleen Ryan, Ph.D.
Guy Salama, Ph.D.
Donna Beer Stolz, Ph.D.
Patrick Thibodeau, Ph.D.
Linton Traub, Ph.D.
Yong Wan, Ph.D.
Simon Watkins, Ph.D.
Christine Wu, Ph.D.

Non-Tenure Track Faculty
Catherine Baty, Ph.D.
Carol Bertrand, Ph.D.
Georgia Duker, Ph.D.
Kathi Peters, Ph.D.



Cell Biology and Physiology
Research Seminar Schedule 2010-2011

September 7, 2010
Rama Mallampalli, Ph.D.
Professor, University of Pittsburgh School of Medicine
Acute Lung Injury Center of Excellence
"Novel Insights into the Pathobiology of Sepsis-Induced Acute Lung Injury"

September 14, 2010
Ben Glick, Ph.D.
Professor, University of Chicago
Molecular Genetics & Cell Biology
"A new layer of regulation in the secretory pathway"

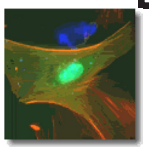
October 19, 2010
Ineke Braakman, Ph.D.
Professor, Utrecht University, The Netherlands
Cellular Protein Chemistry, Bijvoet Center for Biomolecular Research
"Protein folding in the Endoplasmic Reticulum"

November 16, 2010
Marcel Bruchez, Ph.D.
Research Professor/Program Manager, Carnegie Mellon University
Department of Chemistry, Technology Center for Networks
"Genetically targeted multichromophore structures for bright, sensitive, and responsive cellular imaging"

December 10, 2010
Mark Marsh, Ph.D.
Professor, University College of London
Cell Biology Unit
"Can better understanding of the cellular mechanisms of virus replication give novel opportunities for drug and vaccine development"

December 14, 2010
Duojia Pan, Ph.D.
Associate Professor, Johns Hopkins School of Medicine
Molecular Biology and Genetics
"Control of organ size and tumorigenesis by the Hippo signaling pathway"

January 18, 2011
Kris Dahl, Ph.D.
Assistant Professor, Carnegie Mellon University
Biomedical Engineering and Chemical Engineering
"Mechanical characterization of nuclear structural proteins"

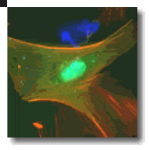


March 1, 2011
Wei Dai, Ph.D.
Professor, NYU
Environmental Medicine and Pharmacology
"Suppressing chromosomal instability & tumorigenesis by the spindle checkpoint"

March 29, 2011
Roberto Weigert, Ph.D.
Chief, Intracellular Membrane Trafficking, NIH
Oral and Pharyngeal Cancer Branch
"Intravital microscopy: a novel tool to study membrane trafficking in physiological conditions and during invasion and metastasis"

April 26, 2011
Tom Kirchhausen, Ph.D.
Professor, Harvard Medical School
Cell Biology, Program in Cellular and Molecular Medicine at Children's Hospital Boston;
Immune Disease Institute
"Dynamics of Endocytosis"

May 10, 2011
Frances Brodsky, Ph.D.
Professor, University of California, San Francisco
Biopharmaceutical Sciences
"Diversity of clathrin function in membrane traffic and beyond"



Faculty Research Interests

Meir Aridor, Ph.D.
Associate 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. Dr. Aridor is utilizing a variety of molecular biochemical, biophysical and cellular techniques to unravel the molecular basis of ER sorting.

Catherine J. Baty, D.V.M., Ph.D.
Research Assistant Professor

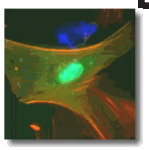
Our laboratory has begun focusing on lymphatic endothelial function. We have developed a 3 dimensional tissue culture system to study potential mechanisms of lymphatic failure. Despite the fact that the lymphatic vessels were identified hundreds of years ago, limited understanding exists of lymphatic development, function, and disease. Greater understanding of the structure and function of lymphatic endothelium will provide plausible new candidate genes for mutation screening in families with hereditary lymphedema. Such studies will ultimately reveal specific therapeutic targets appropriate both for those suffering from primary lymphedema and the greater population of patients with secondary lymphedema.

Carol A. Bertrand, Ph.D.
Research Assistant Professor

The primary research interests of the lab focus on the regulation of airway surface liquid (ASL) pH and mucin secretion in epithelia, and the involvement of ion channels in modulating the process. Both bicarbonate and mucin contribute to the pH of the ASL, which varies considerably in disease from acidic in CF to alkaline in chronic bronchitis. Current work centers on the biosynthesis and activity of chloride channels and anion exchangers that complement and may regulate the CFTR chloride channel, as well as the apical membrane permeability to bicarbonate. In addition, ongoing effort is devoted towards the development and refinement of methods for performing electrophysiology and live cell fluorescence microscopy.

Michael B. Butterworth, Ph.D.
Assistant Professor

Dr. Butterworth's research interest is in the regulation of epithelial channels by vesicle trafficking and recycling. Research is focused into two broad areas. First, ongoing studies aim to characterize the mechanisms that underlie channel regulation by membrane trafficking in the mammalian kidney. Three renal transporters, namely the epithelial sodium channel (ENaC), potassium channel (ROMK) and aquaporin water channels are investigated. The work aims to map the intracellular itinerary of these channels and identify protein mediators that regulate

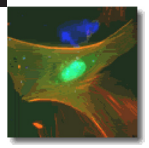


channel surface density. In separate, but related studies, primary human bronchiolar epithelial cells are used to characterize ENaC regulation in the human distal airway, in particular mechanisms which may contribute to disease states like cystic fibrosis. By comparing ENaC regulation in two distinct systems, areas of common and divergent regulation have been established. The second research focus investigates the regulation of ENaC by microRNAs (miRNA). miRNAs are small RNAs that pair to the mRNA of protein coding genes to direct their post–transcriptional repression. Channel density in epithelial cells is determined to a large extent by steroid hormone signaling. The regulation of miRNAs by these hormones and impact of changes in miRNA expression on channel regulation is being studied.

Daniel C. Devor, Ph.D.
Professor

Intermediate (KCa3.1 or IK) and small (KCa2.3 or SK3) conductance, calcium-activated potassium channels play critical roles in a host of physiological processes, including the endothelial derived hyperpolarizing factor (EDHF) response which is critical to the maintenance of vascular tone and hence blood pressure regulation, the maintenance of a hyperpolarized membrane potential across the basolateral membrane of polarized epithelia required for transepithelial fluid secretion as well as being intimately involved in the afterhyperpolarization in nerves and a host of other processes. Thus, an understanding of the physiological and pharmacological regulation of these channels as well as their assembly, trafficking and gating is crucial to the development of novel therapies based on targeting these channels. The long-term goals of my lab are to obtain a detailed molecular understanding of these channels in order to unravel the mechanisms involved in their assembly, trafficking, regulation and gating as well as to define the physiological role these channels play using C. elegans as a model system. In light of these goals, we have several ongoing projects designed to further our understanding of these channels.

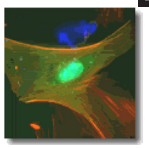
First, Mark Bailey, a graduate student in the lab, is carrying out patch-clamp studies designed to elucidate the role of S6 in the gating of KCa3.1. In these studies, we are employing PCMBS to probe the cysteines in S6 and evaluate their role in gating. PCMBS has advantages over MTS reagents in both the site of the reactive moiety as well as the size of the molecule such that a larger perturbation in local molecular space is achieved. By using PCMBS in combination with a mutagenesis approach we have demonstrated that side chains pointing away from the pore, and toward S5, are critical to the coupling between Ca2+ binding to the calmodulin binding domain and channel gating. In collaboration with Dr. Michael Grabe, of the Biological Sciences Department at the University of Pittsburgh, we are modeling the gating kinetics of KCa3.1 to extract the rate constants being affected by both PCMBs as well as mutations in this region of the channel. In the future, we plan to probe S5 by conducting a tryptophan scan of the region across from the cysteines in S6 to further our understanding of how S5-S6 interactions modulate the coupling between increasing Ca2+ and channel gating. We have also identified critical amino acids in the S4-S5 linker region of both KCa3.1 and the related family member KCa2.3 which, when mutated to increase side-chain volume, result in a shift in apparent Ca2+ affinity. These results suggest this region of the channel is similarly involved in the coupling between Ca2+ binding to calmodulin in the cytoplasmic C-terminus and subsequent gating. A combination of patch-clamping, mutagenesis and modeling will be employed to definitively define the role of this region of the channel in the coupling between Ca2+ and gating.



Second, as any physiological response is dictated by not only the likelihood that channels are in the open state (Po), i.e., gating, but also the number of actively gating channels (N), it is critical to understand how the number of KCa3.1 and KCa2.3 channels at the plasma membrane is maintained and regulated. To this end, Yajuan Gao and Corina Balut, two post-doctoral associates in the lab, recently developed novel biotin ligase acceptor peptide (BLAP)-tagged KCa2.3 and KCa3.1 constructs which allow us to evaluate, in real time, the endocytic fate of these channels. Using these constructs, we have developed three separate projects. In one project, our recent data demonstrates that KCa2.3 is rapidly endocytosed and enters the recycling pathway back to the plasma membrane in a Rab35/EPI64C (RabGAP)- and RME1-dependent manner. Indeed, our evidence points to the role of a 12 amino acid domain in the N-terminus of KCa2.3 as being critical in this process via an association with RME1. Future studies along these lines will be designed to elucidate the role of ubiquitination/de-ubiquitination in the recycling of this channel to the plasma membrane in addition to determining the role of agonists in regulating this process. We have also recently identified the Rab5 pathway as being critical to the endocytosis of KCa2.3, whereas endocytosis and recycling are independent of the Arf6 pathway. These results point to this being a dynamin and clathrin-dependent endocytic process, although Rab5 has also been shown to be important in clathrin-independent endocytosis. The mechanism by which KCa2.3 is endocytosed will be defined using a combination of imaging, protein biochemical mutagenesis and cell biological techniques.

In a related project to the one above, we have recently demonstrated that KCa3.1 is targeted to the lysosome via the ESCRT machinery. We have recently begun to utilize tandem ubiquitin binding entities (TUBES) to define the role of ubiquitinylation in this process. By combining BLAP tagging and TUBES we are able to rapidly assess the ubiquitination of plasma membrane channels and correlate ubiquitinylation with endocytosis. In this regard, we have now shown that the endocytosis of KCa3.1 is directly correlated with poly-ubiquitinylation of the channel. By inhibiting ubiquitinylation we are able to block the channels endocytosis. This was first identified using a 96-well plate assay to identify modulators of channel endocytosis and formed the basis of our upcoming publication in Future Medicinal Chemistry, detailing this approach. Future studies will continue to explore the role of ubiquitin in the endocytosis of KCa3.1 as well as determine whether this is a regulated process. For example, is this a classic K63-dependent ubiquitinylation process, or are other ubiquitin-linked side-chains involved? Can the endocytosis of KCa3.1 be modified by second messengers generated in response to agonist stimulation? Of course, we are also attempting to identify the deubquitinylating enzymes (DUBs) involved in ubiquitin removal as this is critical for both the proper degradation of KCa3.1 as well as the recycling of KCa2.3. In this regard, we have begun a collaboration with Dr. Christian Loch at LifeSensors. We have now screened KCa3.1 prior to and following endocytosis using a DUB CHIP and have identified USP8 and USP2 as being DUBs critical in the endocytosis of this channel. As both KCa2.3 and KCa3.1 enter dynamic endosomal compartments, modulation of the rate-limiting steps in these events will allow for the regulation of the number of channels present at the plasma membrane such that the physiological response to agonists may be modified.

Given that KCa3.1 is targeted to the basolateral membrane in polarized epithelia, where it plays a critical role in the generation of the electromotive driving force required for Ca2+-dependent agonists to stimulate Cl- and fluid secretion, an additional project, being undertaken in collaboration with Dr. Kirk Hamilton at the University of Otago in Dunedin, NZ, is designed to

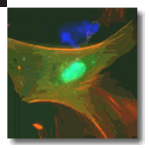


understand the mechanisms by which this channel is correctly targeted and endocytosed in various model systems, including FRT, MDCK and LLC-PK1 cells. In this regard, we have found that KCa3.1 is correctly targeted in each of these cell lines and that, similar to our studies on HEK cells and a microvascular endothelial cell line (HMEC-1), the channel is rapidly endocytosed. Further, we have generated chimeras between the C-terminal tail of KCa3.1 and the nerve growth factor receptor (NGFR, p75) and demonstrate that the C-terminus of KCa3.1 can redirect NGFR from its typical apical localization to the basolateral membrane in polarized epithelia. Future studies will be designed to elucidate the molecular motifs involved in the basolateral targeting of this channel as well as understanding the molecular mechanisms involved in the correct targeting of this channel to the basolateral membrane.

Fourth, in conjunction with our studies outlined above, we are using our BLAP-tagged channels to develop a 96-well plate assay to screen siRNA libraries to identify novel proteins involved in the endocytosis, recycling and lysosomal targeting of KCa2.3 and KCa3.1. By monitoring co-localization of these channels with a membrane marker over time we can determine whether knockdown of a specific protein influences the endocytic fate of these channels. Given the crucial role these channels play in a host of physiological processes it is anticipated that the identification of these novel proteins involved in maintaining plasma membrane localization will provide unique targets for therapeutic intervention.

While the majority of our studies are being carried out in HEK cells in order to facilitate an initial understanding of these processes which have not heretofore been studied in the context of KCa2.3 and KCa3.1, we similarly carry out crucial studies using the HMEC-1 microvascular endothelial cell line. One of our future aims is to develop a virus based infection system, such that the trafficking of these channels can be studied in confluent endothelial monolayers. This will not only allow us to gain a greater understanding of these channels in endothelial cells, but also afford us the opportunity to study the fate of these channels under more unique physiological situations, such as sheer stress.

Given our interest in understanding these channels at a tissue/model system level, Cavita Chotoo, a graduate student in the lab, in collaboration with Drs. Cliff Luke and Gary Silverman at Children's Hospital of Pittsburgh, is further defining the physiological role of one of these channels using C. elegans as a model system. A single C. elegans SK channel homologue was targeted for deletion and this KO animal displays a developmental delay phenotype. The exact nature of this phenotype is currently being studied. Cavita has also generated transgenic C. elegans lines expressing GFP- and RFP-tagged channels to determine both an expression pattern profile as well as to determine the effect of overexpression of this gene product on physiological function. Our data demonstrate that the C. elegans SK channel is expressed in both the gut as well as in numerous nerves, including the nerve ring, ventral nerve chord and ganglia in the tail. Future studies will elucidate the role of this SK channel in this model physiological system. Cavita has also begun to culture cells from her transgenic line which will allow us to define cells expressing the transgene and characterize these C. elegans channels by patch-clamping. We can then determine whether mutations at conserved amino acids to those identified by us in mammalian channels will produce similar phenotypes, including increased Ca2+ sensitivity; allowing us to evaluate the effect of a hyperactive phenotype on function at the level of an intact organism. Finally, we can utilize known endocytic/recycling phenotypes in C. elegans to probe the regulation of the number of channels (N) in a model system and determine



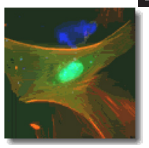
how perturbations in N alter physiological function. These studies will tie together our efforts on heterologously expressed channels to our proposed studies on channels within the microvasculature; providing us with a clear picture of how KCa2.3 and KCa3.1 are regulated at the plasma membrane. Given the role of these channels in multiple disease processes, an understanding of how the number of channels is regulated at the plasma membrane is critical to understanding how these channels can be manipulated for therapeutic gain.

Peter F. Drain, Ph.D.
Associate Professor

Our laboratory studies regulatory mechanisms underlying secretory vesicle cell biology in health and disease. Currently, the experimental focus is on the cell biology of mutations and binding partners of vesicle proteins that cause monogenic forms of diabetes and Parkinson's disease:

(1) We are continuing our ongoing investigations into the structure-mechanism relations underlying the ATP-inhibited potassium (KATP) channel response to physiologically important ligands, ATP, ADP, and anti-diabetic sulfonylureas. In pancreatic beta cells, the KATP channel brings insulin secretion under the control of blood glucose levels. Our major goal is to establish the cellular mechanisms underlying how interactions of the KATP channel with its small molecular ligands and with its protein binding partners changes with high and low glucose metabolism, and consequent changes in insulin granule transport and exocytosis. Normally, the fraction of time the KATP channel spends in the inhibited state determines insulin secretory rates. When this regulation goes awry, serious complications at the whole-organism level lead to diabetes and other diseases. The research has fundamental importance to pharmaco-genetics, in which certain diabetic subjects with certain mutations can be transferred from insulin replacement therapy injected multiple times a day to an oral sulfonyluea pill once a day.
(2) Another key molecule in insulin secretion is insulin itself. Mutations in human proinsulin, the propeptide precursor to insulin, have been shown to cause clinical diabetes. In studying the associated cellular mechanisms underlying insulin biogenesis, trafficking, and secretion, we have combined confocal fluorescence microscopy and a novel molecular strategy to visualize insulin secretion in live cells. The Ins-C-GFP reporter has exploded our ability to look inside live insulin-secreting cells to study glucose-stimulated insulin biogenesis, vesicle transport and exocytosis. Using this approach we have localized KATP channels to the beta cell's large dense core vesicle (LDCV) where we have shown they mediate ATP- and glibenclamide-stimulated insulin secretion. In this way, the proteins whose mutation causes diabetes, the KATP channel and insulin, have a more intimate cell biological relationship and clinical pertinence than previous thought. Diabetic mutations in human insulin are used to study the beta cell biology of proinsulin trafficking, biogenesis, ER stress and protein degradation, and the consequences on insulin secretion. These investigations provide mechanistic details of the relationships between how KATP channels and insulin work together properly and fail to do so in diabetes.
(3) More recently we have found that alpha-synuclein is expressed in pancreatic beta cells, where it localizes to secretory vesicles, in addition to its well established presence in dopaminergic and glutaminergic neurons of the brain. This has led to a new line of investigation studying the role of alpha-synuclein and how its interactions with other vesicle proteins changes under conditions of the stress leading to the hallmark degenerative cell biology that characterize these diseases.

Trainees in our laboratory have the opportunity to combine the techniques of molecular genetics



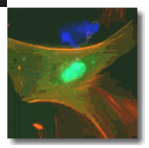
and confocal live-cell fluorescence imaging, with transgenic techniques to integrate understanding at the level of the molecule, organelle, whole cell, organ, and organism.

Georgia K. Duker, Ph.D.
Assistant Professor

My contributions to the University Of Pittsburgh School Of Medicine are primarily through teaching. I contribute as a faculty member to twelve separate courses throughout the first and second years of the medical students' education. My responsibilities include course director, lectures, problem based learning sessions, microscopy laboratories, designing and leading team-based learning and tutorial sessions. For seven of these courses, I direct the microscopy labs in normal histology. My photographs have been formed into slide-based lab sessions to cover many of the organ system studied. In resent years, a focus has been to contribute to the medical education web site: http://navigator.medschool.pitt.edu. Annotated image collections now guide students through the renal, gastrointestinal, pulmonary, endocrine, musculoskeletal, reproductive and nervous systems. The entire image collection is available to students in the Histology Resource Room adjacent to my office. Here, Kodachromes, glass slides, projectors, multiheaded microscopes, computer to view electronic versions and a variety of current texts are available for students to review material. In 2003, I served as the course director for the Cell Structure, Metabolism & Nutrition course. 2003-04 also saw my participation in both the Basic Science Task Force and the Organ Systems Task Force; these committees oversaw the restructuring of the first two years of the medical school curriculum. From 2004 through to 2011, I am a co-director for the second-year Digestion and Nutrition course.

Within the Department of Cell Biology and Molecular Physiology I am course director for the Graduate Histology course. This course is taken by the majority of our students. It is abroad survey of all the organ systems, focusing on structure/function correlations. For most students it is the only time they encounter a full body overview of systems beyond their own research. Graduate students within the Department of Cell Biology and Molecular Physiology may then serve as Teaching Fellows for the Histology labs within seven Medical School courses. One of my roles is coordinator of the Teaching Fellows, especially to oversee their training and preparation.

A third role has emerged for me as a School of Medicine Coordinator for the Undergraduate Honors College Program. In 2002, I created a new course, Biomedicine: Past, Present and Future. The course has been taught eight times. I examine 12 significant biotechnologies via their history and future applications. Twenty-eight faculty from the School of Medicine were recruited to contribute. This course is one of three from the School of Medicine to form the core requirements for a new Certificate in the History of Medicine. The Certificate program, coordinated by Dr. Johnathon Erlen, will be offered through the Undergraduate Honors College. It is an inter-university program with course offering from the University of Pittsburgh, Duquesne University and Carnegie Mellon University. Students from all three universities are permitted to cross register for the courses. This is the first inter-university certificate program in Pittsburgh.



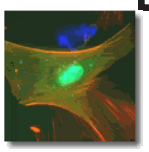
Raymond A. Frizzell, Ph.D.
Professor
Director of Cystic Fibrosis Research Center

Dr. Frizzell's interests concern the mechanisms of salt and water transport in secretory and absorptive epithelia and pathways that regulate these processes. Specifically, we are defining defects in ion transport regulation in the genetic disease, cystic fibrosis (CF), membrane trafficking of wild-type and mutant ion channel proteins, gene expression and therapeutic strategies. Since most CF is caused by the cellular destruction of misfolded mutant CF proteins, our main research efforts focus on defining the steps in the biogenesis of the CF protein (CFTR), and the quality control checkpoints where mutant CFTR proteins go 'off-pathway' and are degraded by the proteasome. CFTR processing can be viewed as a 'bucket brigade' in which protein is passed from checkpoint to checkpoint and some is lost at each step. Therefore, it is important to know quantitatively the contribution of each step to the loss of CFTR protein so that the major one(s) can be targeted for drug development. Recently, we have described novel interactions of CFTR with chaperones called small heat shock proteins, which we have found to catalyze the addition of SUMO, a ubiquitin related modifier, to selectively target mutant CFTR for degradation. The selectivity of this pathway for mutant CFTR appears to extend also to misfolded proteins that lead also to neurodegenerative diseases, and the results implicate the components of this pathway as therapeutic targets for correcting mutant protein biogenesis. Finally, we have identified an alternative anion channel at the apical membranes of airway epithelial cells, and we are examining its contribution to salt and water secretion in the formation of airway surface liquid. This channel interacts tightly with CFTR, regulates its activity, and their interaction influences the biogenesis of both proteins. The activation of this channel could provide an alternative to CFTR for regulation of airway liquid properties.
We also study the regulation of epithelial sodium transport in airway epithelia and the distal nephron of the kidney. Our interests lie in identifying the factors that control the apical membrane density of the sodium entry channel, ENaC, and how the mechanisms of apical insertion, retrieval and recycling influence sodium absorption. The role of 14-3-3 protein binding is a current interest in the regulation of both CFTR and ENaC trafficking, and 14-3-3 affinity capture methods are being used to identify new traffic proteins that are phosphorylated by regulators such as aldosterone and vasopressin. Defects in these processes influence the severity of both cystic fibrosis and hypertension.

Vernon L. Gay, Ph.D.
Associate Professor

Dr. Gay began his training in reproductive endocrinology as a graduate student at Indiana University in Bloomington. While there he devised a technique for rapid transauricular hypophysectomy of rats and used available bioassays to obtain the first measurements of the half lives of endogenous LH and FSH in the rat.

For his post-doctoral work Dr. Gay moved to the University of Michigan in Ann Arbor at a time when radio-immunoassays for gonadotropins (LH and FSH) were first available. In addition to describing hormone profiles throughout the reproductive cycle of the female rat, he was one of the first to describe the phenomenon of pulsatile pituitary hormone secretion in any species (specifically the castrated rat).



In the early 1970's, Dr Gay moved to the School of Medicine at the University of Pittsburgh where he described the mating induced secretion of LH in cats. More recently, he has used an excitatory amino acid that is structurally related to the artificial sweetener "Aspartame" to induce pulsatile LH secretion and resultant precocious puberty in the rhesus monkey.

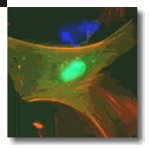
Dr. Gay's current interests are concerned with the neuronal networks that regulate pulsatile LH secretion in transgenic mice and in non-human primates. He has described a theoretical and highly speculative pattern of neuronal development that might serve to explain both the long delay and the rapid onset of sexual development (puberty) in primates (Rhesus monkey and human). In addition, he has recently participated in studies in which LH secretory patterns were monitored in transgenic mice expressing a green fluorescent protein in GnRH neurons. The failure of such female mice to exhibit pulsatile LH secretion suggests that the altered GnRH neuron may exhibit a reduced ability to modify synaptic connections following the removal of steroid negative feedback.

Yang Hong, Ph.D.
Assistant Professor

Establishing cell polarity is essential for cellular morphogenesis, function and tissue integrity. Using Drosophila epithelial cells as a model system, we aim to elucidate the fundamental mechanisms underlying the cell polarization by focusing on a group of so-called polarity proteins that play essential and conserved roles in regulating cell polarity. In order to systematically dissect their functions in Drosophila by genetic, cell biologic and proteomic approaches, we have developed a novel genetic tool termed "genomic engineering" that permits directed, efficient, and versatile modifications of a chosen genomic locus in Drosophila. Genomic engineering makes it possible for us to generate more than hundred novel knock-in alleles of polarity protein genes such as DE-Cadherin, Crumbs, Stardust and Lgl. These novel knock-in alleles include fluorescent protein knock-ins for live imaging assays, high-affinity epitope knock-ins for biochemical/proteomic assays, and mutant alleles carrying defined point mutations and/or deletions for structure-function analyses. These engineered alleles of selected polarity proteins already allowed us to identify novel molecular and cellular mechanisms of cell polarity, such as the regulation of adherens junction dynamics by polarity proteins during cell polarization. In addition, these alleles helped us to discover a novel regulatory mechanism of polarity proteins by hypoxia.

Sanford H. Leuba, Ph.D.
Associate Professor

Since the discovery of the nucleosome in the early 1970's, scientists have sought to correlate chromatin structure and dynamics with biological function. More recently, we have learned that nucleosomes and chromatin play a critical role in the regulation of transcription, replication, recombination, and repair (Zlatanova and Leuba, 2004). Our laboratory uses an interdisciplinary approach combining the disciplines of molecular biology, biochemistry, engineering, and physics to try to understand at the single nucleosome and single chromatin fiber level how chromatin structure and dynamics regulate biological processes that use DNA as a template. To this end, we are applying several single-molecule approaches such as atomic force microscopy



(AFM), magnetic tweezers, optical tweezers and single-pair fluorescence resonance energy transfer (spFRET) to native or reconstituted chromatin fibers of different protein compositions with the latter three methods using homebuilt instrumentation. Single-molecule techniques provide the sensitivity to detect and to elucidate small, yet physiologically relevant, changes in chromatin structure and dynamics. Recent examples of what we have been able to discover include the following:

- We have been able to use AFM to detect conformational changes in chromatin fiber structure due to the presence of 24 methyl groups per nucleosome (Karymov et al., 2001) implying that the combined action of the DNA methylation and linker histone binding required to compact chromatin may affect the transcription of large chromatin domains.

- We also used AFM to investigate the role of histone variants in chromatin fiber structure (Tomschik et al., 2001). Eukaryl and archaeal organisms have similar fiber structure with differences likely related to the more complex needs of eukaryl organisms to regulate transcription.

- We have used optical tweezers to determine the piconewton forces necessary to unravel individual nucleosomes in a fiber context (Bennink et al., 2001) and found that the measured forces for individual nucleosome disruptions are in the same range of forces reported to be exerted by RNA- and DNA-polymerases.

- We have used magnetic tweezers to observe a dynamic equilibrium between force dependent nucleosomal assembly and disassembly on a single DNA molecule in real time (Leuba et al., 2003) as a model of what happens to nucleosomes when a transcribing polymerase passes through the region where they are located.

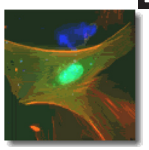
- We have used spFRET to demonstrate fast, long-range, reversible conformational fluctuations in nucleosomes between two states: fully folded (closed) with the DNA wrapped around the histone core, and open, with the DNA significantly unraveled from the histone octamer (Tomschik et al., 2005), implying that most of the DNA on the nucleosome can be sporadically accessible to regulatory proteins and proteins that track the DNA double helix.

- In collaboration with Saleem Khan (Molecular Genetics and Biochemistry), we have used spFRET to demonstrate that PcrA DNA helicase displaces RecA from both ssDNA as well as dsDNA (Anand et al., 2007), as a model for regulation of homologous recombination.

- In collaboration with Pedro Rodriguez-Collazo (Cell Biology), we have developed a method to isolate in one-step histones containing their native post-translational modifications (Rodriguez-Collazo et al., 2009). This method has also been patented and licensed.

- In collaboration with Michael Trakselis (Chemistry), we have used spFRET to demonstrate the wrapping of DNA around the archaeal homohexameric MCM helicase from Sulfolobus solfataricus (Graham et al., 2011), protecting the displaced single-stranded DNA tail and preventing reannealing.

- In collaboration with Paul Sammak (Cell Biology) we have developed methods for



quantitation and differentiating human pluripotent stem cells to trophectoderm (placental stem cells) with BMP4 (Erb, et al., 2011). The process depends on heterochromatin assembly and histone deacetylase activity (HDAC3). Imaging techniques were developed to determine the epigenetic state of histones during development, and the process has been patented for use in drug toxicity testing and regenerative medicine.

- In collaboration with Li Lan, Satoshi Nakajima and Vesna Rapic-Otrin (Molecular Genetics and Biochemistry), we have studied the ability of an E3 ligase to ubiquitinate histone H2a and destabilize nucleosomes with UV-damaged DNA (Li et al., submitted 2011).

- More recently in collaboration with Saleem Khan and Syam Anand (Molecular Genetics and Biochemistry), we have used spFRET to demonstrate that PcrA DNA helicase displaces RecA but not RecA mutants (Fagerburg et al., to be submitted 2011) indicating that direct transduction of chemomechanical forces alone by translocating helicases, such as PcrA and Srs2, are insufficient to displace recombinases such as RecA and Rad51 that form large polymeric assemblies on ssDNA.

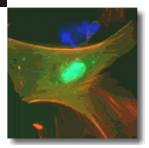
Our future goals are to build combination single-molecule instruments to image and manipulate intramolecular nanometer movements in submillisecond real-time with piconewton force sensitivity (e.g., we want to observe directly what happens to the histones in a nucleosome in the path of a transcribing polymerase). We want to observe what changes in superhelicity occur upon nucleosome formation, nucleosome by nucleosome. We hope to resolve whether the positive supercoils generated by a transcribing polymerase are sufficient to displace histone octamers. In addition to chromatin, we are studying the mechanism of action of individual helicases unwinding DNA. We are also working on the capability to observe in real time single nucleosome dynamics in living cells.

- We have been able to use AFM to detect conformational changes in chromatin fiber structure due to the presence of 24 methyl groups per nucleosome (Karymov et al., 2001) implying that the combined action of the DNA methylation and linker histone binding required to compact chromatin may affect the transcription of large chromatin domains.

- We also used AFM to investigate the role of histone variants in chromatin fiber structure (Tomschik et al., 2001). Eukaryl and archaeal organisms have similar fiber structure with differences likely related to the more complex needs of eukaryl organisms to regulate transcription.

- We have used optical tweezers to determine the piconewton forces necessary to unravel individual nucleosomes in a fiber context (Bennink et al., 2001) and found that the measured forces for individual nucleosome disruptions are in the same range of forces reported to be exerted by RNA- and DNA-polymerases.

- We have used magnetic tweezers to observe a dynamic equilibrium between force dependent nucleosomal assembly and disassembly on a single DNA molecule in real time (Leuba et al., 2003) as a model of what happens to nucleosomes when a transcribing polymerase passes through the region where they are located.



- We have used spFRET to demonstrate fast, long-range, reversible conformational fluctuations in nucleosomes between two states: fully folded (closed) with the DNA wrapped around the histone core, and open, with the DNA significantly unraveled from the histone octamer (Tomschik et al., 2005), implying that most of the DNA on the nucleosome can be sporadically accessible to regulatory proteins and proteins that track the DNA double helix.

- In collaboration with Saleem Khan (Molecular Genetics and Biochemistry), we have used spFRET to demonstrate that PcrA DNA helicase displaces RecA from both ssDNA as well as dsDNA (Anand et al., 2007), as a model for regulation of homologous recombination.

- In collaboration with Pedro Rodriguez-Collazo (Cell Biology), we have developed a method to isolate in one-step histones containing their native post-translational modifications (Rodriguez-Collazo et al., 2009). This method has also been patented and licensed.

- In collaboration with Michael Trakselis (Chemistry), we have used spFRET to demonstrate the wrapping of DNA around the archaeal homohexameric MCM helicase from Sulfolobus solfataricus (Graham et al., 2011), protecting the displaced single-stranded DNA tail and preventing reannealing.

- In collaboration with Paul Sammak (Cell Biology) we have developed methods for quantitation and differentiating human pluripotent stem cells to trophectoderm (placental stem cells) with BMP4 (Erb, et al., 2011). The process depends on heterochromatin assembly and histone deacetylase activity (HDAC3). Imaging techniques were developed to determine the epigenetic state of histones during development, and the process has been patented for use in drug toxicity testing and regenerative medicine.

- In collaboration with Li Lan, Satoshi Nakajima and Vesna Rapic-Otrin (Molecular Genetics and Biochemistry), we have studied the ability of an E3 ligase to ubiquitinate histone H2a and destabilize nucleosomes with UV-damaged DNA (Li et al., submitted 2011).

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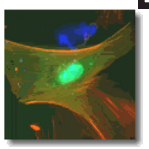


Sandra A. Murray, Ph.D.
Professor

In Dr. Murray's laboratory integrated approaches are being used in studies to assess the role of gap junctions and cell-to-cell communication in endocrine cell proliferation, migration, differentiation, and hormone production and to elucidate the molecular machinery that regulates gap junction plaque endocytosis. Four different techniques (time-lapse video microscopy, immunocytochemistry, quantum dot immuno-electron microscopy, and western blot analysis) are being used to examine the role of clathrin and protein phosphorylation in gap junction protein (connexin) trafficking, including gap junction plaque assembly and subsequent internalization. The effect of over expression and inhibition of gap junctions on adrenal cell function, are being studied with vectors containing cDNA antisense, dominant-negative constructs, siRNA approaches, and antibody directed against gap junction genes products. Together these studies are designed to elucidate the role of cell-cell communication in tissue function with particular interest in how endocytosis and post-endocytic trafficking of gap junction proteins is regulated to control cellular function(s).

Kathryn W. Peters, Ph.D.
Research Assistant Professor

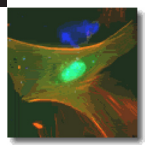
The cystic fibrosis transmembrane conductance regulator (CFTR) is a cAMP/PKA-regulated chloride channel; its phosphorylation controls both channel gating and trafficking at the plasma membrane. We are evaluating the distribution of CFTR and SNARE proteins in airway epithelial cells to determine their role in the trafficking process. Our data suggest that CFTR resides in lipid microdomains and that the cAMP-induced increase in apical membrane CFTR density involves regulation of CFTR trafficking to these domains through physical interactions with syntaxin 4. The presence of CFTR in lipid microdomains and increased amounts of CFTR in the plasma membrane after stimulation, suggest that CFTR is involved in trafficking in the human airway cell line, Calu-3.

Kathleen D. Ryan, Ph.D.
Associate Professor

Dr. Ryan's primary role is Associate Director of the Office of Medical Education in the School of Medicine.

Alexander D. Sorkin, Ph.D.
Professor, Chairman of Department

The focus of the research in the laboratory is currently split into two major directions which are apparently distinct from each other with respect to the biological systems involved, their relation to the human disease, and experimental models used. However, the main idea underlying both directions is conceptually the same - to understand how endocytosis and post-endocytic trafficking regulate function(s) of the transmembrane proteins, such as receptors and transporters. One major project aims at elucidating the molecular mechanisms of endocytosis of growth factor receptors using a prototypic member of the family, epidermal growth factor (EGF) receptor, and analyzing the role of endocytosis in spatial and temporal regulation of signal transduction by the



EGF receptor. Another major research direction is the study of the role of trafficking processes in the regulation of dopaminergic neurotransmission by the plasma membrane dopamine transporter (DAT). In both of these research areas we are using multidisciplinary methodological approach in in vitro and in vivo experimental models.

Donna Beer Stolz, Ph.D.
Associate Professor
Assistant Director of Center for Biologic Imaging

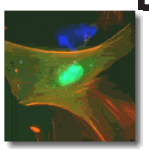
Overview: Angiogenesis is the process whereby new blood vessels sprout from existing vessels and requires that the specialized resident cells lining the vasculature, the endothelial cells (ECs), proliferate, migrate and differentiate spatially and temporally in response to specific signals. Vasculogenesis, on the other hand, has only recently emerged as an alternative mechanism of blood vessel growth in adult tissues and is the result of homing and engraftment of circulating EC precursors (ECPs) of bone marrow origin to sites of neovascularization. Both events are known to occur within the liver vasculature under very different conditions of growth, injury and repair, but the extent of each and the mechanisms by which they occur for each case is completely unknown. We evaluate various signaling events that accompany blood vessel growth and repair during liver regeneration following partial hepatectomy, the result of cold ischemia/warm reperfusion injury following liver transplantation or warm ischemia/warm reperfusion following surgical resections for cancer. Comparative analysis of these systems will elucidate both similar and dissimilar mechanisms that control these events and potentially lead to optimization of therapies that will reflect the specific requirements for injury based neovascularization in the liver.
Specific Projects: Compared to other organs, the liver is relatively hypoxic. We have shown that non-neoplastic hepatocytes do not respond through hypoxia Inducible factor-1 (Khan Z, Michalopoulos GK & Stolz DB, Peroxisomal localization of hypoxia-inducible factors and HIF regulatory hydroxylases in primary rat hepatocytes exposed to hypoxia-reoxygenation Am J Path 126(4):1251-1269. 2006), but still manage to upregulate expression of angiogenic factors like VEGF, PAI-1 and amphiregulin. How this occurs is unclear, but suggests alternative pathways to activate hypoxia-inducible angiogenic factors, which in the context of liver, will not mirror angiogenesis events in vascular beds with innately higher oxygen tensions.

Additional interests include novel subcellular localization patterns of specific signaling proteins such as peroxisomal iNOS, hypoxia inducible factor and its regulatory prolyl-hydroxylases in hepatocytes and other cell types.

Dr. Stolz is Assistant Director of the Center for Biologic Imaging and directs the electron microscopy facility of CBI.

Patrick Thibodeau, Ph.D.
Assistant Professor

The primary research interests of my lab relate to the structure and function of ABC-transporter systems. ABC transporters play key roles in a large number of cellular processes by facilitating the translocation of a variety of substrates, ranging in size from single ions and small molecules to peptides and large proteins. Ongoing lab research focuses on ABC transporter structure and



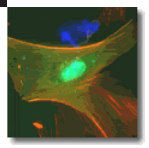
function, and how these structures are monitored and directed by cellular quality control machinery. The Pseudomonas aeruginosa Apr and Has protease-secreting ABC-transport systems are being used to probe the structural and mechanistic details associated with the translocation of large proteins implicated in the virulence of this, and other, human pathogens. Genetic and biochemical studies of these systems are directed towards understanding the recognition of substrate proteins and the mechanical details of their translocation. Second, recent work has led to the development of two assays, amenable to high throughput screening, which allow for the identification of cellular components that monitor and regulate the biosynthesis of mammalian ABC-transporter systems. Utilizing cytosolic domains from CFTR, we are currently working to identify the cellular machinery that facilitates the proper folding of wild-type CFTR and targets mutant forms of the protein for degradation. Finally, structural and biochemical studies of human ABC-transporters implicated in human disease (cystic fibrosis; cardiac calcification and pseudoxanthoma elasticum) are aimed at understanding defects associated with protein mutation and disease patho-physiology.

Linton M. Traub, Ph.D.
Associate Professor

Many molecules enter the cell interior within clathrin-coated vesicles, in process termed endocytosis. In the simplest sense, the clathrin-coated vesicle can be viewed as a nanomachine that temporally couples preferential retention of designated cargo with rapid vesicle assembly, invagination, and fission from the plasma membrane. In fact, this rapid process is critical to the way we move and think. At the tip of each axon, synaptic vesicles (packages of neurotransmitter) release their contents by fusing with the cell surface in response to stimulus-dependent calcium influx. Almost instantly, the membrane of the synaptic vesicle is then retrieved from the synapse within clathrin-coated vesicles. Clathrin-mediated 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 also play an important role in controlling plasma LDL-cholesetrol levels in humans and yolk protein accumulation in Drosophila and mosquitoes by promoting the rapid internalization of a family of related lipoprotein receptors. We study the mechanisms and molecules involved in clathrin-coat assembly. We are interested how this complex process, involving a network of more than 25 discrete protein components, is temporally coordinated to prevent chaotic seizures or run-away coat assembly. We have found recently that some of these protein components display unexpected cargo sorting properties that expand the overall sorting repertoire of the forming clathrin-coated vesicle. To understand how these complex structures assemble within only a minute or two, we use biochemical, cell biological, structural and live-cell imaging approaches to unravel the protein–protein interactions that orchestrate the formation of this elaborate protein-sorting machine.

Yong Wan, Ph.D.
Associate Professor

Research interests in my laboratory focus on the role of ubiquitin-dependent proteolysis in biological regulation. Currently, we are studying the control of cell cycle progression by proteolytic regulation. We are also interested in investigating the role of proteolysis in the regulation of the DNA damage-repair process, in the renewal and differentiation of stem cells, and



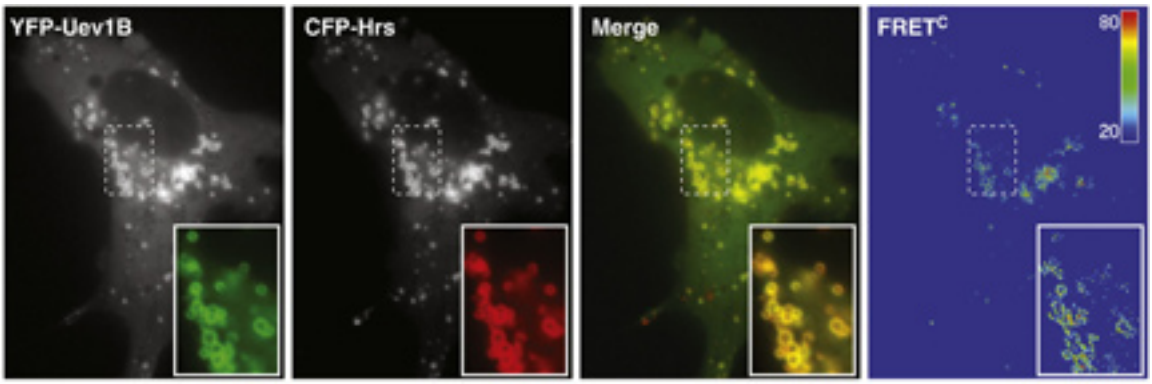
in the pathogenesis of tumor formation. The long-term goal is to understand the biochemistry of these protein degradation pathways and to develop new intervention strategies based on an understanding of proteolytic regulation to combat cancer and treat other human disease. To achieve this, we plan to develop mutidisciplinary approaches, including biochemical and genetic analyses as well as chemical genetic techniques. We will apply these methods using several systems including functional proteomics, mammalian tissue culture cells and mouse model system.

Simon C. Watkins, Ph.D.
Professor, Vice Chairman of Department
Director of Center for Biologic Imaging

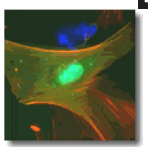
The application of advanced imaging tools to the field of immunology is constantly revealing new facets of cellular and molecular behavior within the immune system. The goals of my research program are two-fold. To develop novel quantitative fluorescent based assays using optical microscopy, and secondly to develop novel imaging platforms for use in health and disease. Recent accomplishments have been the development of multiple new high speed high resolution imaging platforms for multidimensional imaging of model systems. We are now applying these tools to high speed imaging of the physiology and cell biology of the regulation of vascular tone in the Zebra fish.

Christine Wu, Ph.D.
Associate Professor

During the past decade, biological mass spectrometry has expanded into a mainstream and indispensable analytical field. My lab is focused on the development of proteomic methods and technology for the characterization and quantification of proteins using mass spectrometry. In particular, we are interested in developing optimized proteomic strategies compatible with the analysis of integral membrane proteins. Recent experimental strategies utilize the use of global comparative bottom-up proteomic profiling (LC-MS/MS) followed by targeted hypothesis-driven strategies and the development of multiplexed SRM assays. These optimized workflows are then applied towards the identification of protein biomarkers of disease and the understanding of disease mechanisms (including breast cancer, liver disease, heart failure, and neural disorders).



Alexander Sorking. Colocalization and FRET between YFP-YEV-1B and CFP-Hrs in endosomes.



Study Sections (Fiscal Year 2010-11)

Sanford H. Leuba, Ph.D.
Associate Professor

NSF, Gene Regulation and Epigenetics October 2010

Sandra Murray, Ph.D.
Professor

NSF, Molecular Cell Biology, Membrane Trafficking, March 2011

Alexander D. Sorkin, Ph.D.
Professor and Chairman

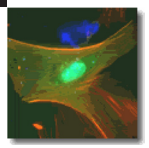
ASIRC (Italian Association for Cancer Research); Standing Member

Simon C. Watkins, Ph.D.
Professor and Vice Chairman, Director of Center of Biologic Imaging

NIH Study Section ICMICS March 2nd-3rd 2010 Panel Member
Canadian Foundation for Innovation Study Section: Toronto Canada January March 17th 2010 Panel Member
ACS study section (Peer Review Committee on Clinical Cancer Research and Epidemiology) Atlanta 2010 Panel Member
NIH study section, SBIRs, Washington DC June 30th 2010 Panel Member
NIH Study Section SBIR's San Francisco November 3rd 2010 Panel Member
NIH Study Section S10's November 17th-19th (Chair of Panel)
American Cancer Society Review Panelist Jan 25-27th 2011 Panel Member
NIH Study Section : RFA CA 11-005 ICMICS Panelist March 15th-16th 2011
NIH Study Section NIH_IMST 16 SBIR-STTR, March 23rd 2011 Co-Chair
NIH Study Section 2011/05 ZAR1 HL (M2) 1 March 24th 2011 Panelist
NCI study section (ZCA1 SRLB-9). Panel Member, June 14th-15th 2011
Study Section, (Peer Review Committee on Clinical Cancer Research and Epidemiology) Panel Member, Atlanta GA, June 22nd-23rd 2011
NIH study section ZRG1 IMST-J (15) B, Chair of Panel, June 29th- 30th 2011

Christine Wu, Ph.D.
Associate Professor

NIH/NCRR (S10 Shared Instrumentation Grants, PAR-09-118) (08/5/10-08/6/10)
NIH/CSR U54 Roadmap Study Section (RFA-RM010-018) (06/15/11)
NIH/CSR EBIT Study Section permanent member (3 study sections during this time period) (10/7/10-10/8/10, 1/28/11-1/29/11, 6/2/11-6/3/11)



Faculty Advisory Committee Memberships (Fiscal Year 2010-11)

Meir Aridor, Ph.D.
Associate Professor

University of Pittsburgh School of Medicine Interdisciplinary Biomedical Graduate Program-
Cell Biology and Molecular Physiology Program Committee
Local Traffic Symposium; Organizing Committee Member
Cell Biology and Physiology Space Committee
Cell Biology and Physiology Faculty Recruitment Committee

Michael Butterworth, Ph.D.
Assistant Professor

Cell Biology and Physiology Departmental Retreat Committee

Daniel Devor, Ph.D.
Professor

Cell Biology and Physiology Departmental Tenure and Promotions Committee
Cell Biology and Physiology Faculty Recruitment Committee
Chair, Interdisciplinary Biomedical Graduate Program Recruiting Committee: 2010-2011
Ad-hoc member, Interdisciplinary Biomedical Graduate Program Admissions Committee, 2010

Peter F. Drain, Ph.D.
Associate Professor

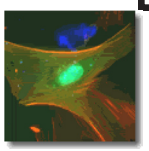
University of Pittsburgh School of Medicine Interdisciplinary Biomedical Graduate Program-
Cell Biology and Molecular Physiology Program Committee
Cell Biology and Physiology Representative, Graduate Student Recruitment Committee
Scholarly Project Executive Committee Member
University of Pittsburgh School of Medicine (UPSOM) Admissions Committee

Georgia K. Duker, Ph.D.
Assistant Professor

Vice-President of the C. F. Reynolds History of Medicine Society of the University of Pittsburgh
Honor Council Hearing Board – School of Medicine

Raymond A. Frizzell, Ph.D.
Professor and Director, Cystic Fibrosis Research Center

CFF Medical Advisory Council



NACFC Planning Committee
FoldRx (Pfizer) Collaborative Committee
Vertex Collaborative Committee

Vernon L. Gay, Ph.D.
Associate Professor

Institutional Review Board (IRB)
Institutional Animal Care and Use Committee (IACUC)

Yang Hong, Ph.D.
Assistant Professor

Cell Biology and Physiology Departmental Retreat Committee
Vice Director, Summer Undergraduate Research Program (SURP) in Cell Biology and Molecular Physiology

Sanford Leuba, Ph.D.
Associate Professor

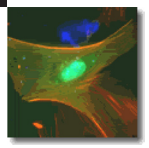
Nanoscale Biophysics Subgroup Meeting of the Biophysical Society

Sandra A. Murray, Ph.D.
Professor

Graduate School of Public Health Research Advisory Committee – Center for Minority Health
Provost Advisory Committee for the Provost Development Fund Awards
Annual Biomedical Conference for Minority Students Advisory Committee
American Society for Cell Biology – Chair of the National Visiting Professor Program
American Association of Cell Biology Nominating Committee
Morehouse College of Medicine Advisory Board
Norfolk State University Center for Biotechnology and Biomedical Sciences
University of Maryland Health Black Family Project Advisory Board
Cell Biology and Physiology Tenure and Promotions Committee

Kathleen D. Ryan, Ph.D.
Assistant Dean for Medical Education

Course Organizing Committee, Reproductive and Developmental Biology, University of Pittsburgh School of Medicine curriculum revision.
Chair, Institutional Animal Care and Use Committee, University of Pittsburgh
Promotions Committee, School of Medicine



Block Director, Basic Science Section, University of Pittsburgh, School of Medicine
Curriculum committee, University of Pittsburgh, School of Medicine
Retention committee (MS 1 & 2), University of Pittsburgh, School of Medicine
Retention committee (MS 2 & 3), University of Pittsburgh, School of Medicine

Alexander D. Sorkin, Ph.D.
Richard B. Mellon Professor and Chair

University of Pittsburgh Cell Biology and Molecular Physiology Program Committee
University of Pittsburgh Carnegie Mellon Medical Scientist Training Program Committee - CNUP
Cell Biology and Physiology Tenure and Promotions Committee
Cell Biology and Physiology Faculty Recruitment Committee
DIDARP External Advisory Board, Meharry Medical College, School of Medicine

Donna Beer Stolz, Ph.D.
Associate Professor

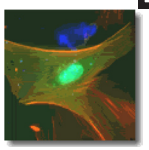
University of Pittsburgh School of Medicine Interdisciplinary Biomedical Graduate Program-Cell Biology and Molecular Physiology Program Admissions Committee
Assistant Director - Cell Biology and Molecular Physiology Program
Interdisciplinary Biomedical Graduate Program Admissions Committee Tour Guide
Summer Undergraduate Research Program Director – Cell Biology and Physiology

Linton M. Traub, Ph.D.
Associate Professor

University of Pittsburgh School of Medicine Health Sciences Research Advisory Committee
Cell Biology and Physiology Tenure and Promotions Committee
Cell Biology and Physiology Faculty Recruitment Committee
Cell Biology and Physiology Space Committee
Planning Committee of Local Traffic Symposium on intracellular membrane traffic
Ad hoc member of NCI Board of Scientific Councilors

Simon C. Watkins, Ph.D.
Professor and Vice Chairman, Director of Center of Biologic Imaging

Cell Biology and Physiology Tenure and Promotions Committee
Cell Biology and Physiology Student Advisory Committee
Cell Biology and Physiology Space Committee
Cell Biology and Physiology Faculty Recruitment Committee
Graduate Program, Curriculum Committee
University of Pittsburgh School of Medicine, Research Advisory Committee

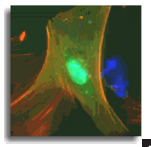


University of Pittsburgh Cancer Institute Core Resources Committee
University of Pittsburgh Tenure and Promotions Committee
Scientific Advisory Board: Lumencor
Scientific Advisory Board: Photometrics
Scientific Advisory Board: NIS Elements
Scientific Advisory Board: Metamorph
Member at Large, School of Medicine Executive Committee

Christine Wu, Ph.D.
Associate Professor

Cell Biology and Physiology Faculty Recruitment Committee

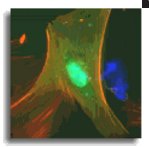
Cell Biology and Physiology/Pharmacology Machine Shop

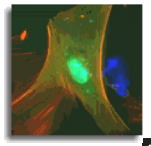


Cell Biology and Physiology Sponsored Research Funding (FY11)

First Name	Agency Name	Title	Annual DC	Annual IDC
Meir Aridor	National Institutes of Health	The regulation of COPII coat mediated ER	20,875	10,751
Meir Aridor	Cystic Fibrosis Foundation	Selective Steps in Wild Type and DF508 CFTR Processing	52,311	4,185
Catherine Baty	National Institutes of Health	HGF and MET Mutations in Primary Lymphedema	88,243	45,445
Catherine Baty	National Institutes of Health	Structure-Function Relationships in the IL-17 Receptor	3,070	1,721
Catherine Baty	Army	The Blood Vessel-Associated Breast Cancer Invasion and Metastasis Mediated by Endothelial BDNF Release	2,785	1,434
Carol Bertrand	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Pilot # 3	62,475	32,175
Michael Butterworth	National Institutes of Health	EnaC regulation in the kidney by vesicle trafficking and recycling	176,934	72,066
Michael Butterworth	National Institutes of Health	EnaC Regulation in the Kidney by Vesicle Trafficking and Recycling (Stimulus)	20,850	462
Michael Butterworth	National Institutes of Health	Pittsburgh Center for Kidney Research	11,004	5,667
Daniel Devor	National Institutes of Health	Assembly and trafficking of IK1 and SK3 in Endothelia	248,559	122,187
Peter Drain	National Institutes of Health	Anesthetic Sites in Transmembrance Peptides by NMR	6,839	3,523
Peter Drain	Pittsburgh Foundation	Molecular Medicine in Shared Novel Secretory Mechanism Underlying Diabetes, Alzheimers Disease, and Parkinsons Disease	75,000	-
Peter Drain	Army	Towards a Possible Therapy for Diabetes Complications	30,850	15,887
Peter Drain	National Institutes of Health	Alzheimers Disease Research Center - Pilot	5,625	2,897
Wayne Ernst	Cystic Fibrosis Foundation	Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting	42,683	-
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	3,429	1,663
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	9,161	4,443
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	47,178	24,297
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	120,229	56,769
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Equipment Core	27,185	-
Raymond Frizzell	Cystic Fibrosis Foundation	Molecular Biology and Gene Expression	50,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Program Enrichment and Administration	27,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Functional Assays	55,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Research Training Core	70,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in WIld-Type and DF508 CFTR Processing	228,313	18,265
Raymond Frizzell	National Institute	Chaperone Actions in CFTR Biogenesis	210,730	108,526
Raymond Frizzell	Cystic Fibrosis Foundation	14-3-3 Proteins particiapate in the regulations of CFTR biogenesis	36,319	-
Raymond Frizzell	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	7,122	3,668
Raymond Frizzell	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	40,612	20,917
Raymond Frizzell	National Institutes of Health	Traffic Regulatory Proteins and ENaC	232,356	114,269
Yang Hong	National Institutes of Health	Genomic Engineering in Drosophila	52,125	26,844
Yang Hong	National Institutes of Health	Regulation of Adherens Junction Dynamics by Polarity Proteins	183,683	89,874
Sanford Leuba	National Institutes of Health	Development of Novel Single-molecule Approaches for Nanoscale Study of Helicases	147,578	42,909
Sanford Leuba	National Institutes of Health	Development of Novel Single-molecule Approaches for Nanoscale Study of Helicases	36,205	12,430
Sanford Leuba	National Institutes of Health	NNRTI induced conformational changes in HIV-1 RT	48,252	18,328
Xiubin Liang	National Institutes of Health	Phosphorylation-dependent regulation of epithelial sodium channel (ENaC) trafficking	31,250	2,450
Sandra Murray	National Science Foundation	Gap Junction Plaque Internalization	68,560	28,607
Pedro Rodriguez-Collazo	National Institute of Health	Regulation of Histone H3 Dephosphorylation	104,364	8,349
Paul Sammak	National Institutes of Health	Dynamic Image Analysis of Human Embryonic Stem Cells to Monitor Pluripotency	56,963	29,336
Alexander Sorkin	National Institutes of Health	Dopamine Transporter Regulation by Endocytosis	158,974	81,872
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	105,392	39,179
Alexander Sorkin	National Institutes of Health	EGF Receptor Signaling in Time and Space in Tumor Cells	172,848	89,017
Alexander Sorkin	National Institutes of Health	EGF Receptor Signaling in Time and Space in Tumor Cells	33,613	17,311
Donna Beer Stolz	National Institutes of Health	Post Traumatic Sepsis Regulation of LPS Binding Protein	6,160	2,987
Donna Beer Stolz	National Institutes of Health	Mechanisms for Arsenic-Induced Vascular Disease	8,448	4,350

Donna Beer Stolz	National Institutes of Health	Protective Role of Carbon Monoxide in Hepatic I/R Injury	7,948	3,855
Donna Beer Stolz	National Institutes of Health	Mediators of Fibrosis in Scleroderma Skin and Lung	4,221	2,174
Donna Beer Stolz	National Institutes of Health	Regulation of the Endcytic Trafficking of CFTR	15,679	8,075
Donna Beer Stolz	National Institutes of Health	Mechanisms for Arsenic-Induced Vascular Disease - ARRA Competitive Revision	26,031	13,407
Donna Beer Stolz	Massachusetts Institute of Technology	Perfused 3D Tissue Surrogates for Complex Cell-Cell Communication Systems	46,989	23,427
Donna Beer Stolz	National Institutes of Health	Pittsburgh Center for Kidney Research	1,660	855
Donna Beer Stolz	National Institutes of Health	Cell Imaging and Tissue Pathology (Core B)	96,090	49,486
Donna Beer Stolz	Army	Escape from Tumor Cell Dormancy	34,430	17,731
Donna Beer Stolz	National Institutes of Health	Ex Vivo Adipose Tissue as a Screening Tool	4,949	2,549
Donna Beer Stolz	National Institutes of Health	Pittsburgh Center for Kidney Research	11,004	5,667
Donna Beer Stolz	National Institutes of Health	Mechanism of Disc Proteoglycan Loss in a Mouse Model of Acelerated Aging	3,026	1,559
Donna Beer Stolz	National Science Foundation	Engineering Research Center	26,666	13,733
Fei Sun	National Institutes of Health	CFTR Degradation in its Early Biogenesis	208,500	107,377
Patrick Thibodeau	Cystic Fibrosis Foundation	Structural Interactions Regulating CFTR Channel Function	64,815	5,185
Patrick Thibodeau	National Institutes of Health	Biosynthesis and function of ABC transporter systems (Stimulus Bridge Funding)	124,950	64,349
Patrick Thibodeau	National Institutes of Health	Regulated Biosynthesis and Function of ABC-Transport Systems	36,323	18,706
Linton Traub	National Institutes of Health	Clatherin-coated vesicles and endocytic function	192,340	96,862
Linton Traub	National Institutes of Health	Pittsburgh Center for Kidney Research	1,660	855
Simon Watkins	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	40,000	-
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	6,692	3,246
Simon Watkins	National Institutes of Health	NO-Zinc Signaling in Intact Pulmonary Endothelium	38,257	18,555
Simon Watkins	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	17,571	8,522
Simon Watkins	National Institutes of Health	TLR4 Signaling in the Pathogenesis of Surgical Necrotizing Enterocolitis	13,348	6,800
Simon Watkins	National Institutes of Health	Interaction of Microvesicles and Bacterial Toxins With Immune Cells	24,750	12,004
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	79,100	40,736
Simon Watkins	National Institutes of Health	Duffy Antigen: Modifier of Systemic and Lung Chemoline Responses in Inflammation	21,071	10,220
Simon Watkins	National Institutes of Health	Novel Stategies for Brain Tumor Therapy	55,452	28,557
Simon Watkins	National Institutes of Health	Hepatocellular Carcinoma in Antitrypsin Deficiency	17,453	8,989
Simon Watkins	National Institutes of Health	High Throughput Genetic and Drug Screens for Alpha 1 Antitrypsin Deficiency	9,260	4,768
Simon Watkins	National Institutes of Health	Oxidation Lipidomics of Pulmonary Endothelial Apoptosis In Hyperoxia	27,731	14,281
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	23,104	11,899
Simon Watkins	National Institutes of Health	Improving Chromic Neural Recording Performances Through Biomaterial Strategies	8,580	4,419
Simon Watkins	National Institutes of Health	DC T Interactions in Pulmonary Immune Responses	17,840	9,188
Simon Watkins	National Institutes of Health	Divergent Pathways of Cell Death anfter Brain Injury	26,542	13,669
Simon Watkins	National Institutes of Health	Regulation of DC Activity by Memory and Effector CD8+ T Cells	8,582	4,420
Simon Watkins	National Institutes of Health	Intracellular Serpin Regulation of Intestinal Cell Necrosis	2,413	1,244
Simon Watkins	National Institutes of Health	Molecular Biology of Hemorrhagic Shock	99,148	51,061
Simon Watkins	National Institutes of Health	Directing Tumor Specific T cells to Tumors	56,296	28,992
Simon Watkins	National Institutes of Health	Amplification of IL-4Ralpha Signaling Pathways in Human Airways Through 15 LO1	5,000	2,575
Simon Watkins	National Institutes of Health	Multiple Tumor Antigen-Loaded DC Vaccine for Hepatocellular Cancer	7,308	3,664
Simon Watkins	National Institutes of Health	Request for Live Cell Confocal Microscope for BSL3 Facility (S10)	405,889	-
Simon Watkins	National Institutes of Health	Request for Live Cell Confocal TIRF Microscope	449,833	-
Simon Watkins	National Institutes of Health	Multi-Disciplinary Approaches to Driving Therapeutic Human Beta Cell Replication	11,191	5,763
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	75,862	39,069
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	79,896	41,146
Simon Watkins	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	138,119	71,132
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	4,684	2,412
Simon Watkins	National Institutes of Health	Adipose Triglyceride Lipases (ATGL) in Liptoxicity and the Metabolic Syndrome	2,086	1,075
Simon Watkins	National Institutes of Health	Stem Cells for Corneal Engineering	5,059	2,605
Christine Wu	National Institutes of Health	Proteomic Dissection of Withdrawal - Induced Excessive Drinking	135,223	69,637
Christine Wu	National Institutes of Health	Proteomic Dissection of Withdrawal - Induced Excessive Drinking - ARRA Supplement	120,414	62,013

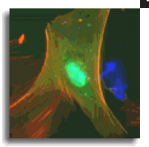


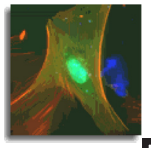


Christine Wu	National Institutes of Health	Quantitive Proteomic Analysis of Alcoholic Fatty Liver Biogenesis	168,680	86,870
Christine Wu	National Institutes of Health	Using Molecular Pathology to Predict Response in Heart Failure	69,038	35,554
Christine Wu	National Institutes of Health	A Triple Quadrupole Mass Spectrometer for the INIA-West Consortium	429,079	-
			6,834,984	2,305,997

Cell Biology and Physiology Sponsored Research Funding (FY12)

First Name	Agency Name	Title	Annual DC	Annual IDC
Meir Aridor	Cystic Fibrosis Foundation	Selective Steps in Wild Type and DF508 CFTR Processing	4342	347
Catherine Baty	National Institutes of Health	HGF and MET Mutations in Primary Lymphedema	14497	7466
Catherine Baty	National Institutes of Health	Structure-Function Relationships in the IL-17 Receptor	3070	1721
Catherine Baty	Army	The Blood Vessel-Associated Breast Cancer Invasion and Metastasis Mediated by Endothelial BDNF Release	928	478
Catherine Baty	National Institutes of Health	Obesity Related Pancreatic Fat Worsens Local Injury via Unsaturated Fatty Acids	13200	6800
Carol Bertrand	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Pilot # 3	12525	6450
Michael Butterworth	National Institutes of Health	EnaC regulation in the kidney by vesicle trafficking and recycling	167756	81244
Michael Butterworth	National Institutes of Health	Pittsburgh Center for Kidney Research	996	513
Daniel Devor	National Institutes of Health	Assembly and trafficking of IK1 and SK3 in Endothelia	245501	126432
Peter Drain	National Institutes of Health	Anesthetic Sites in Transmembrance Peptides by NMR	2313	1191
Peter Drain	Pittsburgh Foundation	Molecular Medicine in Shared Novel Secretory Mechanism Underlying Diabetes, Alzheimers Disease, and Parkinsons Disease	31275	0
Peter Drain	Army	Towards a Possible Therapy for Diabetes Complications	10283	5296
Peter Drain	National Institutes of Health	Alzheimers Disease Research Center - Pilot	16875	8691
Wayne Ernst	Cystic Fibrosis Foundation	Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting	36319	0
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	47178	24297
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	144330	68150
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Equipment Core	5450	0
Raymond Frizzell	Cystic Fibrosis Foundation	Program Enrichment and Administration Core	27000	0
Raymond Frizzell	Cystic Fibrosis Foundation	Molecular Biology and Gene Expression Core A	100000	0
Raymond Frizzell	Cystic Fibrosis Foundation	Research Training Core	70000	0
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in WIld-Type and DF508 CFTR Processing	230078	18406
Raymond Frizzell	National Institute	Chaperone Actions in CFTR Biogenesis	210375	108343
Raymond Frizzell	Cystic Fibrosis Foundation	14-3-3 Proteins particiapate in the regulations of CFTR biogenesis	35151	0
Raymond Frizzell	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	3676	1893
Raymond Frizzell	National Institutes of Health	Traffic Regulatory Proteins and ENaC	253387	124612
Yang Hong	National Institutes of Health	Regulation of Adherens Junction Dynamics by Polarity Proteins	181170	93303
Yang Hong	American Cancer Society	Regulation of aTumor Suppressor and Cell Polarity Protein Lgl by Hypoxia	150000	30000
Sanford Leuba	National Institutes of Health	NNRTI induced conformational changes in HIV-1 RT	48209	18290
Xiubin Liang	National Institutes of Health	Phosphorylation-dependent regulation of epithelial sodium channel (ENaC) trafficking	75860	6069
Sandra Murray	National Science Foundation	Gap Junction Plaque Internalization	113520	49863
Sandra Murray	National Science Foundation	Gap Junction Plaque Internalization - REI Supplement	11500	2500
Alexander Sorkin	National Institutes of Health	EGF Receptor Signaling in Time and Space in Tumor Cells	201274	103656
Alexander Sorkin	National Institutes of Health	Dopamine Transporter Regulation by Endocytosis	278488	124900
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis - Administrative Supplement	22000	11330
Donna Beer Stolz	National Institutes of Health	Mechanisms for Arsenic-Induced Vascular Disease	8581	4419
Donna Beer Stolz	National Institutes of Health	Mediators of Fibrosis in Scleroderma Skin and Lung	2937	1513
Donna Beer Stolz	National Institutes of Health	Regulation of the Endcytic Trafficking of CFTR	15945	8212
Donna Beer Stolz	National Institutes of Health	Mechanisms for Arsenic-Induced Vascular Disease - ARRA Competitive Revision	2941	1515
Donna Beer Stolz	Massachusetts Institute of Technology	Perfused 3D Tissue Surrogates for Complex Cell-Cell Communication Systems	45391	23376
Donna Beer Stolz	National Institutes of Health	Cell Imaging and Tissue Pathology (Core B)	16039	8260
Donna Beer Stolz	Army	Escape from Tumor Cell Dormancy	46804	24103
Donna Beer Stolz	National Institutes of Health	Ex Vivo Adipose Tissue as a Screening Tool	6491	3342
Donna Beer Stolz	National Institutes of Health	Pittsburgh Center for Kidney Research	996	513
Donna Beer Stolz	National Institutes of Health	Mechanism of Disc Proteoglycan Loss in a Mouse Model of Acelerated Aging	274	141
Donna Beer Stolz	National Science Foundation	Engineering Research Center	5346	2753





Patrick Thibodeau	Cystic Fibrosis Foundation	Structural Interactions Regulating CFTR Channel Function	53991	4319
Patrick Thibodeau	National Institutes of Health	Regulated Biosynthesis and Function of ABC-Transport Systems	217501	112013
Linton Traub	National Institutes of Health	Clatherin-coated vesicles and endocytic function	190185	95976
Simon Watkins	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	40000	0
Simon Watkins	National Institutes of Health	TLR4 Signaling in the Pathogenesis of Surgical Necrotizing Enterocolitis	2174	1120
Simon Watkins	National Institutes of Health	Interaction of Microvesicles and Bacterial Toxins With Immune Cells	24503	11884
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	79542	40965
Simon Watkins	National Institutes of Health	Duffy Antigen: Modifier of Systemic and Lung Chemoline Responses in Inflammation	19026	9228
Simon Watkins	National Institutes of Health	Novel Stategies for Brain Tumor Therapy	53209	27403
Simon Watkins	National Institutes of Health	Hepatocellular Carcinoma in Antitrypsin Deficiency	17535	9031
Simon Watkins	National Institutes of Health	High Throughput Genetic and Drug Screens for Alpha 1 Antitrypsin Deficiency	7007	3608
Simon Watkins	National Institutes of Health	Oxidation Lipidomics of Pulmonary Endothelial Apoptosis In Hyperoxia	25429	13096
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	23104	11899
Simon Watkins	National Institutes of Health	Improving Chromic Neural Recording Performances Through Biomaterial Strategies	8561	4409
Simon Watkins	National Institutes of Health	DC T Interactions in Pulmonary Immune Responses	13615	7012
Simon Watkins	National Institutes of Health	Intracellular Serpin Regulation of Intestinal Cell Necrosis	2313	1191
Simon Watkins	National Institutes of Health	Molecular Biology of Hemorrhagic Shock	96033	49458
Simon Watkins	National Institutes of Health	Directing Tumor Specific T cells to Tumors	46909	24159
Simon Watkins	National Institutes of Health	Amplification of IL-4Ralpha Signaling Pathways in Human Airways Through 15 LO1	5,734	2,953
Simon Watkins	National Institutes of Health	Multiple Tumor Antigen-Loaded DC Vaccine for Hepatocellular Cancer	7,333	3,776
Simon Watkins	National Institutes of Health	Multi-Disciplinary Approaches to Driving Therapeutic Human Beta Cell Replication	11,477	5,911
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	82,729	42,605
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	79,896	41,146
Simon Watkins	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	177,561	91,444
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	8,034	4,137
Simon Watkins	National Institutes of Health	Adipose Triglyceride Lipases (ATGL) in Liptoxicity and the Metabolic Syndrome	5,002	2,576
Simon Watkins	National Institutes of Health	Stem Cells for Corneal Engineering	20,234	10,421
Simon Watkins	Army	Molecular and Functional Characterization of the Lupus Platelet	15,945	8,212
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Core B	5,833	3,005
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Project 1	13,653	7,031
Simon Watkins	National Institutes of Health	Request for Zeiss 710 Multiphoton 5Live Duoscan Microscope	1,123,669	0
Simon Watkins	National Institutes of Health	PINK1 Regulation of Neuronal and Mitochondrial Homeostasis	4,000	2,060
Christine Wu	National Institutes of Health	Proteomic Dissection of Withdrawal - Induced Excessive Drinking	27,099	13,956
Christine Wu	National Institutes of Health	Proteomic Dissection of Withdrawal - Induced Excessive Drinking - ARRA Supplement	24,141	12,432
Christine Wu	National Institutes of Health	Quantitive Proteomic Analysis of Alcoholic Fatty Liver Biogenesis	479,868	247,132
Christine Wu	National Institutes of Health	Using Molecular Pathology to Predict Response in Heart Failure	32,566	16,772
			5,965,682	2,052,728

Faculty Editorships (Fiscal Year 2010-2011)

Michael B. Butterworth, Ph.D.
Assistant Professor
American Journal of Physiology – Renal Physiology
Frontiers in Renal and Epithelial Physiology
World Journal of Biological Chemistry

Vernon Gay, Ph.D.
Associate Professor
Member, Editorial Board, Endocrinology
Member, Editorial Board, Biology of Reproduction

Sanford Leuba, Ph.D.
Associate Professor
Section Editor, Biomed Central Biophysics

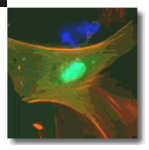
Alexander D. Sorkin, Ph.D.
Richard B. Mellon Professor and Chair
Molecular Biology of the Cell
Traffic
Frontiers in Physiology

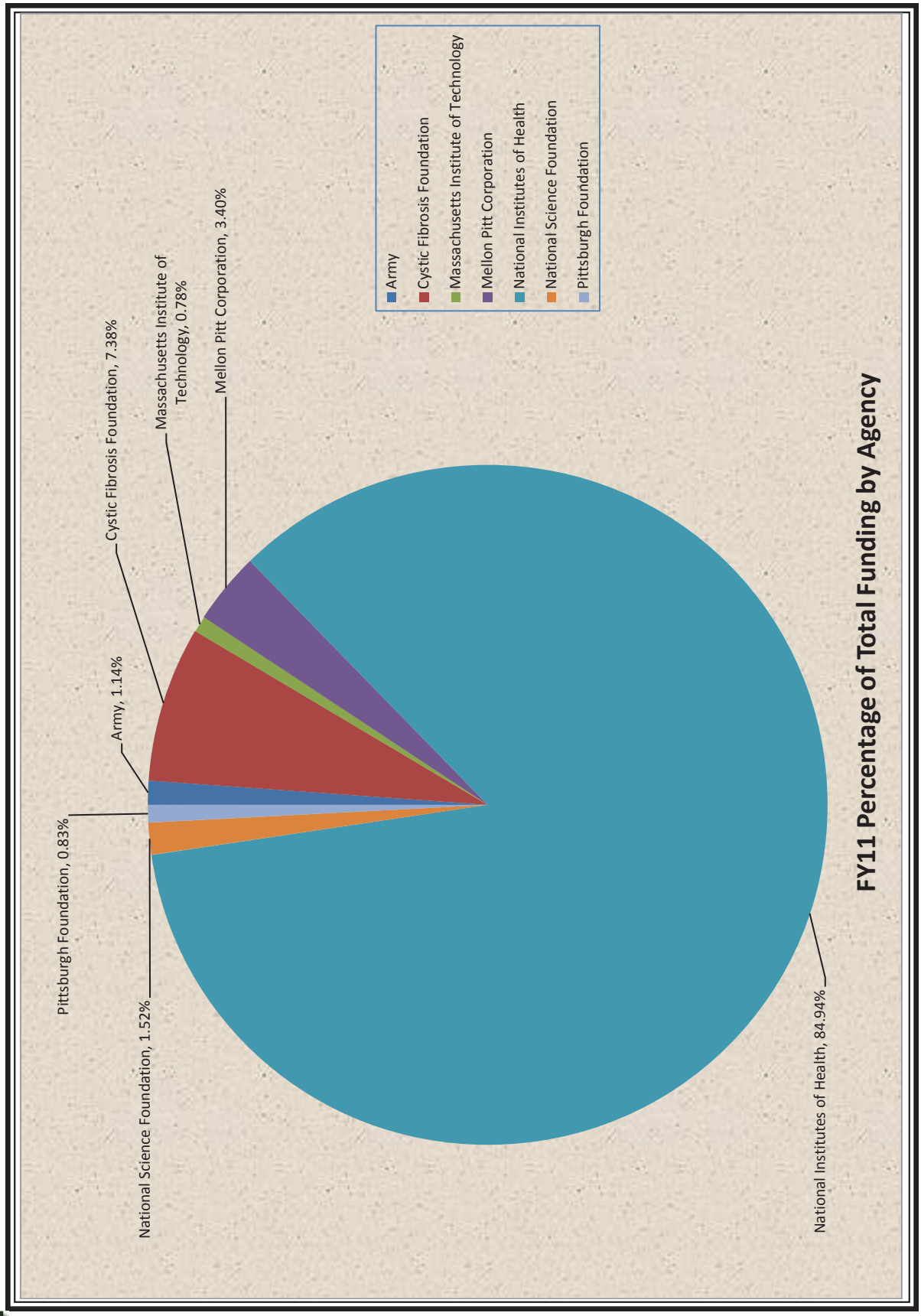
Donna Beer Stolz, Ph.D.
Associate Professor
Editorial Board, Cell Transplantation (Liver Section)

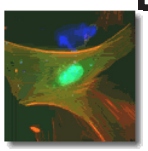
Yong Wan, Ph.D.
Associate Professor
Member, Editorial Board, Journal of Biological Chemistry

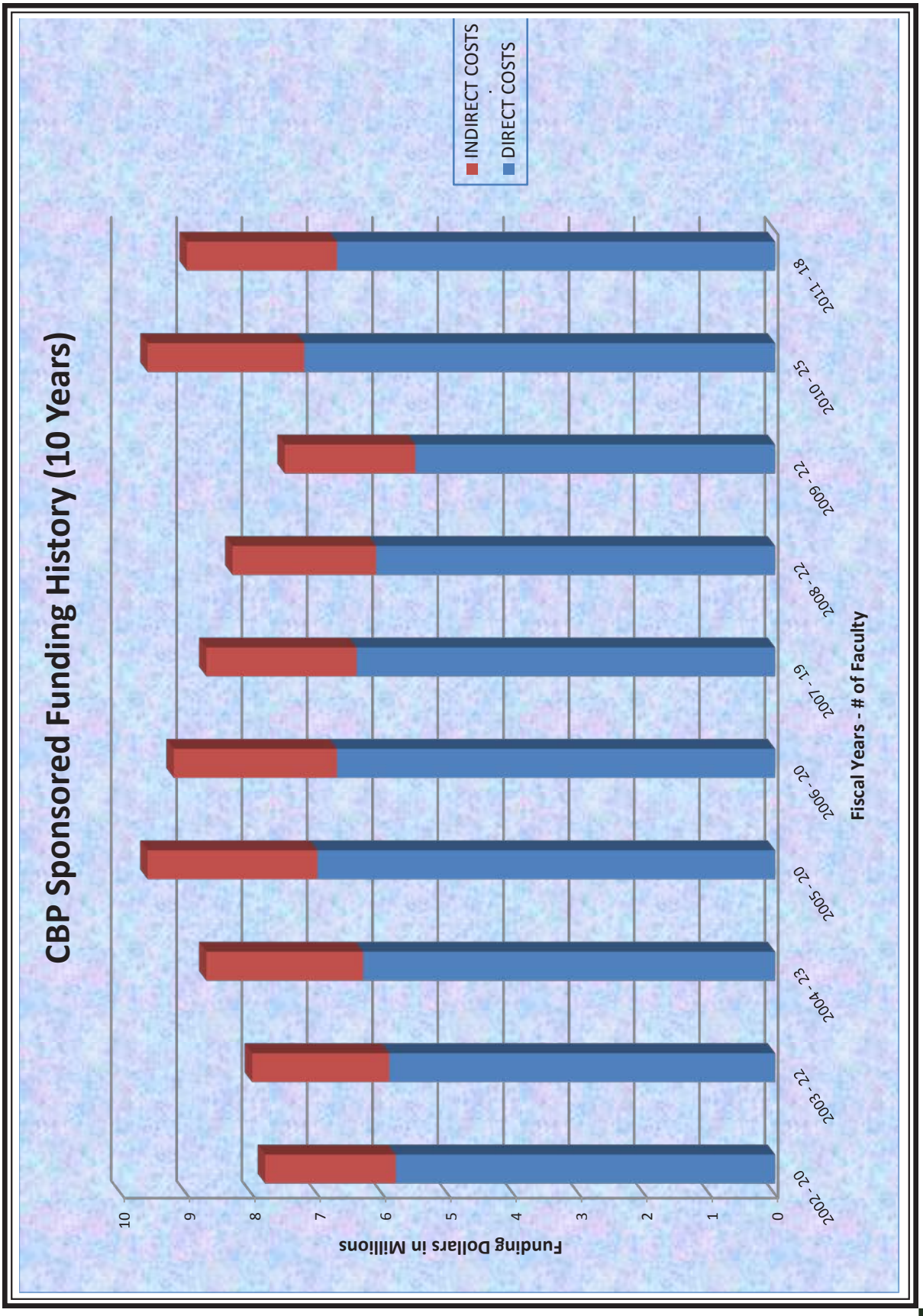
Simon C. Watkins, Ph.D.
Professor and Vice Chairman, Director of Center of Biologic Imaging
Member, Editorial Board, PittMed
Associate Editor, Experimental Biology and Medicine
Editor, Current Protocols in Cytometry
Editor, Experimental Science and Medicine

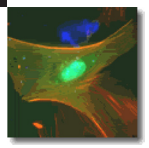
Christine C. Wu, Ph.D.
Associate Professor
Editorial Board, Neurochemical Research
Editorial Board, Amino Acids (Proteomics Section)

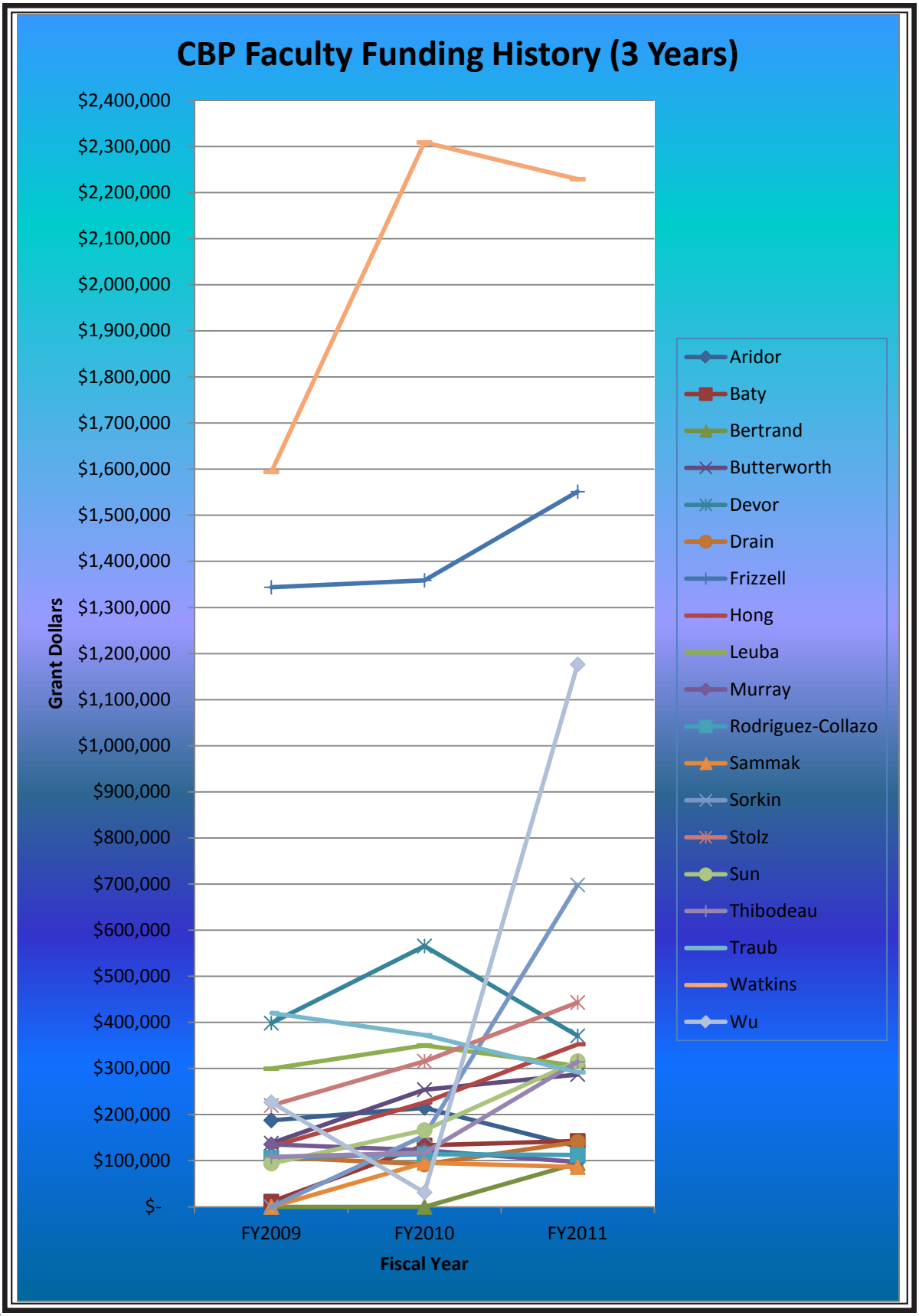



FY11 Percentage of Total Funding by Agency
Army
Cystic Fibrosis Foundation
Massachusetts Institute of Technology
Mellon Pitt Corporation
National Institutes of Health
National Science Foundation
Pittsburgh Foundation
Pittsburgh Foundation, 0.83%
Army, 1.14%
Cystic Fibrosis Foundation, 7.38%
Massachusetts Institute of Technology, 0.78%
Mellon Pitt Corporation, 3.40%
National Science Foundation, 1.52%
National Institutes of Health, 84.94%




CBP Sponsored Funding History (10 Years)
INDIRECT COSTS
DIRECT COSTS
Funding Dollars in Millions
0
1
2
3
4
5
6
7
8
9
10
2002 - 20
2003 - 22
2004 - 23
2005 - 20
2006 - 20
2007 - 19
2008 - 22
2009 - 22
2010 - 25
2011 - 18
Fiscal Years - # of Faculty




CBP Faculty Funding History (3 Years)
$2,400,000
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$2,100,000
$2,000,000
$1,900,000
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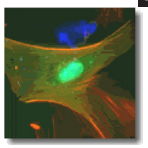
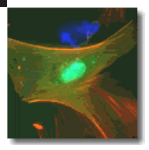
$1,700,000
$1,600,000
$1,500,000
$1,400,000
$1,300,000
$1,200,000
$1,100,000
$1,000,000
$900,000
$800,000
$700,000
$600,000
$500,000
$400,000
$300,000
$200,000
$100,000
$-
Grant Dollars
FY2009
FY2010
FY2011
Fiscal Year
Aridor
Baty
Bertrand
Butterworth
Devor
Drain
Frizzell
Hong
Leuba
Murray
Rodriguez-Collazo
Sammak
Sorkin
Stolz
Sun
Thibodeau
Traub
Watkins
Wu



CBP FACULTY ROSTER
(Effective June, 2011)

Faculty Member	Salary Support on Grants	Rank	Status
Baty, Catherine	100%	Res. Assistant Professor	Non-tenure Track
Liang, Xiubin	100%	Res. Assistant Professor	Non-tenure Track
Schmidt, Bela	100%	Res. Assistant Professor	Non-tenure Track
Bertrand, Carol	96%	Res. Assistant Professor	Non-tenure Track
Watkins, Simon*	88%	Professor	Tenured
Stolz, Donna	84%	Associate Professor	Tenure Track
Peters, Kathryn	80%	Res. Assistant Professor	Non-tenure Track
Frizzell, Raymond*	74%	Professor	Tenured
Devor, Daniel	73%	Professor	Tenured
Wu, Christine	65%	Associate Professor	Tenure Track
Thibodeau, Patrick	49%	Assistant Professor	Tenure Track
Drain, Peter	48%	Associate Professor	Tenure Track
Butterworth, Michael	47%	Assistant Professor	Tenure Track
Hong, Yang	46%	Assistant Professor	Tenure Track
Traub, Linton	41%	Associate Professor	Tenured
Sorkin, Alexander*	38%	Professor	Tenured
Leuba, Sanford	36%	Associate Professor	Track
Murray, Sandra	19%	Professor	Tenured
Aridor, Meir	9%	Associate Professor	Tenure Track

*Calculated using year appropriate NIH salary cap as upper limit for each grant

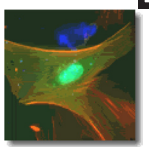


STUDENTS INVOLVED IN RESEARCH IN CBP FACULTY LABS

Snapshot as of June, 2011

GRADUATE STUDENTS ENROLLED IN CBMP PROGRAM

STUDENT	LAB	SUPPORT
Cavita Chotoo	Dan Devor, Ph.D. Cell Biology & Physiology	Dan Devor, Ph.D. Cell Biology & Physiology
Elizabeth Delorme-Axford	Carolyn Coyne, Ph.D. MMG	Carolyn Coyne, Ph.D. MMG
Siobhan Gregg	Laura Niedernhofer, M.D., Ph.D. MMG	Laura Niedernhofer, M.D., Ph.D. MMG
Anupma Jha	Linton Traub, Ph.D. Cell Biology & Physiology	Linton Traub, Ph.D. Cell Biology & Physiology
Xinxian Qiao	Peter Drain, Ph.D. Cell Biology & Physiology	Peter Drain, Ph.D. Cell Biology & Physiology
Daniel Roh	James Funderburgh, Ph.D. Ophthalmology	James Funderburgh, Ph.D. Ophthalmology
Arvind Suresh	Jennifer Condon, Ph.D. OB/GYN	Jennifer Condon, Ph.D. OB/GYN
Christina Szalinski	Ora Weisz, Ph.D. Medicine/Renal	Ora Weisz, Ph.D. Medicine/Renal
James Thieman	Linton Traub, Ph.D. Cell Biology & Physiology	Linton Traub, Ph.D. Cell Biology & Physiology



Cell Biology and Physiology Training Grants
FY11 and FY12

The Department of Cell Biology and Physiology has secured individual post-doctoral fellow sponsorship for a number of our research personnel.

FY11 Projects

Frizzell lab: 14-3-3 Proteins Participate in the Regulations of CFTR Biogenesis
(Cystic Fibrosis Foundation)

Aridor lab: Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting
(Cystic Fibrosis Foundation)

The combined funding for these post doctoral fellowship grants is $79,002 in FY11 (Total costs, annualized).

FY12 Projects

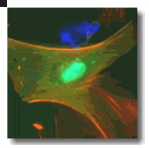
Frizzell lab: 14-3-3 Proteins Participate in the Regulations of CFTR Biogenesis
(Cystic Fibrosis Foundation)

Aridor lab: Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting
(Cystic Fibrosis Foundation)

The combined funding for these post doctoral fellowship grants is $71,470 in FY12 (Total costs, annualized).

Program Grant Training Program:
The Cystic Fibrosis Center funded Research Development Program (RDP) offer training funds to qualified post doctoral candidates, as follows:

FY11 Program Grant Training Funds - $70,000
FY12 Program Grant Training Funds - $70,000

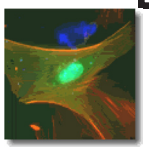


Cell Biology and Physiology Program Grants (Fiscal Year 2010-11)

The Department of Cell Biology and Physiology is funded for four Program Grants, three by the National Institutes of Health and one by the Cystic Fibrosis Foundation, as follows:

National Institutes of Health Cystic Fibrosis Research and Translation Core Centers Program (Principal Investigator/Program Director - Raymond A. Frizzell, Ph.D.):
(Abstract from the original application) A Cystic Fibrosis Research Center has existed at the University of Pittsburgh since 1997, although its structure and support mechanisms have, and continue to, change. The current center gathers over $9.6M in external grants and contracts in support of CF-related research. It consists of 39 investigators in 7 departments, whose research is focused in three major areas. The area of Cell and Molecular Biology of CF, directed at studies of CFTR in model systems and human airway cells, is led by Drs. Raymond Frizzell and Joseph Pilewski, and is supported largely through NIH R01 and Cystic Fibrosis Foundation (CFF) grants, as well as pharmaceutical industry contracts. This group studies mechanisms of CFTR biogenesis, trafficking and regulation, the role of CFTR in airway cell and pancreatic physiology, airway stem cells, and the epithelial sodium channel (ENaC), its regulation and its relation to the activity of CFTR. Therapeutic approaches evolving from several of these basic studies are being pursued as well. A second research area, Lung Infection and Inflammation, headed by Dr. Jay Kolls, focuses on the pulmonary inflammatory response to bacterial infection in human airway cell and animal models, defining the underlying mechanisms of these responses and how they can be modified therapeutically. This work is also supported primarily by NIH and CFF grants, and it represents a new and rapidly growing area within the Center. The third and also expanding area of focus is Clinical Research in CF, headed by Drs. Joseph Pilewski and David Orenstein. This group is pursuing several clinical studies that have emerged from the basic science initiatives of the Center, as well as projects within the Therapeutic Development Network (TDN) of the CFF; it is supported primarily by CFF grants at present. The proposed CF Research and Translation Core Center will be directed by Dr. Raymond Frizzell, who also directs the CFF-sponsored Research Development Program, a current NIH SCOR entitled 'CFTR in Airway Cell Function', is co-investigator on a T32-supported training program in epithelial cell biology, and participates in two other T32 training programs. Drs. Jay Kolls and Joseph Pilewski will serve as Associate Directors of the Center. The Center will be comprised of three cores other than the Administrative: Human Airway Cell Physiology (Raymond Frizzell and Joseph Pilewski, co-directors), Clinical Studies/Outcomes (Jay Kolls and Joseph Pilewski, co-directors), and Imaging (Simon Watkins, director). In addition, the Core Center will operate a Pilot and Feasibility Program to encourage new ideas and investigators in CF research. Of past P/F projects within the NIH SCOR application, 100% have received NIH R01 grant support and all continue to be involved in CF research. This Center emphasizes the translation of basic knowledge into applied therapeutics. The projected funding period should witness the clinical testing of several novel strategies originating at the Center in CF patients.

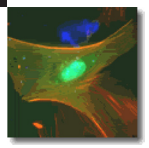
This program grant totaled $970,073 (total costs) in FY11.



Cystic Fibrosis Center funded Research Development Program (Principal Investigator/ Program Director - Raymond A. Frizzell, Ph.D.):
(Abstract from the original application) A Cystic Fibrosis Foundation sponsored Research Development Program Center has existed at the University of Pittsburgh since 1997. The current center gathers over $9.6M in external grants and contracts in support of CF-related research. It consists of 40 investigators in seven departments, whose research is focused in three major areas. The area of Cell and Molecular Biology of CF, directed at studies of CFTR in model systems and human airway cells, is led by Drs. Raymond Frizzell and is supported largely through NIH R01 and Cystic Fibrosis Foundation (CFF) research grants, as well as pharmaceutical industry contracts. This group studies mechanisms of CFTR biogenesis, trafficking and regulation, the role of CFTR in airway cell and pancreatic physiology, airway stem cells, and the epithelial sodium channel (ENaC), its regulation and its relation to the activity of CFTR. Therapeutic approaches evolving from several of these basic studies are being pursued as well. A second research area, Lung Infection and Inflammation, headed by Dr. Jay Kolls, focuses on the pulmonary inflammatory response to bacterial infection in human airway cell and animal models, defining the underlying mechanisms of these responses and how they can be modified therapeutically. This work is also supported primarily by NIH and CFF grants, and it represents a new and rapidly growing area within the Center. The third and also expanding area of focus is Clinical Research in CF, headed by Dr. Joseph Pilewski. This group is pursuing several clinical studies that have emerged from the basic science initiatives of the Center, as well as projects within the Therapeutic Development Network (TDN) of the CFF; it is supported primarily by CFF grants at present. The proposed RDP renewal will be directed by Dr. Raymond Frizzell, who directs the current RDP, a current NIH SCOR entitled 'CFTR in Airway Cell Function', and a recently reviewed is co-investigator on a T32-supported training program in epithelial cell biology, and participates in two other T32 training programs. Drs. Jay Kolls and Joseph Pilewski will serve as Associate Directors of the Center. The Center will be comprised of three cores other than the Administrative: Human Airway Cell Physiology (Raymond Frizzell and Joseph Pilewski, co-directors), Clinical Studies/Outcomes (Jay Kolls and Joseph Pilewski, co-directors), and Imaging (Simon Watkins, director). In addition, the Core Center will operate a Pilot and Feasibility Program to encourage new ideas and investigators in CF research. Of past P/F projects within the NIH SCOR application, 100% have received NIH R01 grant support and all continue to be involved in CF research. This Center emphasizes the translation of basic knowledge into applied therapeutics. The projected funding period should witness the clinical testing of several novel strategies originating at the Center in CF patients.

This program grant totaled $450,000 (total costs) in FY11. For more up to date information regarding the research conducted under this program grant, visit our website at: http://www.cbp.pitt.edu/centers/cfrc.html.

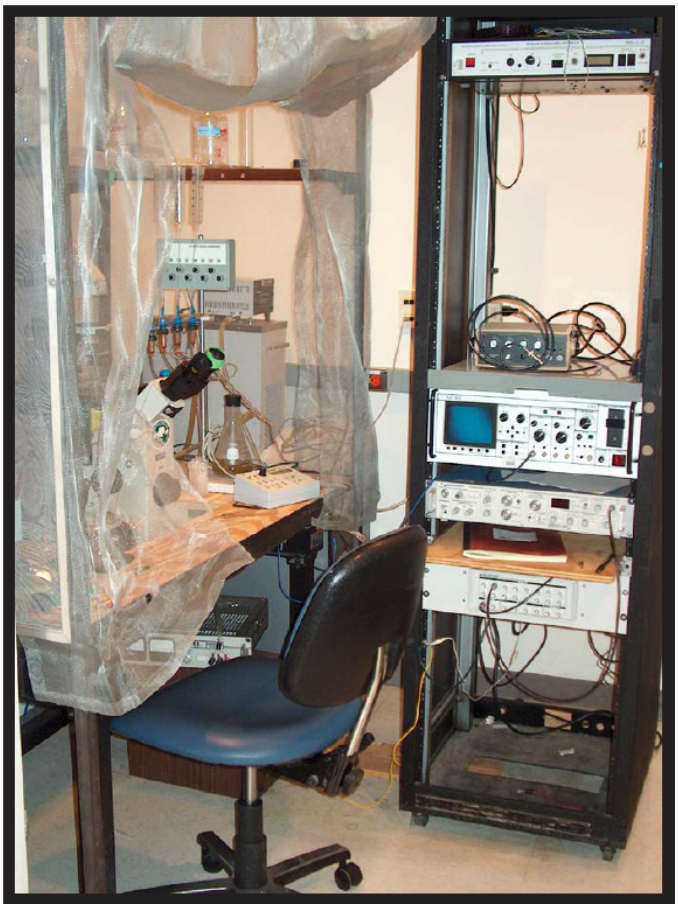
National Technology Centers for Networks and Pathways
(Principal Investigators –Simon Watkins, Ph.D.):
Over the last several years, microscopy as a scientific tool has reinvented itself. It has changed from a group of principally descriptive methodologies, to a wide range of quantitative tools and

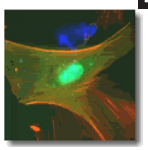


techniques to investigate the molecular organization of organs, tissues and cells. The University of Pittsburgh and Carnegie Mellon University (CMU) are homes to two of the leading imaging laboratories in the country; developing and applying novel fluorescent imaging tools to cutting edge biomedical research. At the Center for Biologic Imaging (CBI) of the University of Pittsburgh, we use commercially available and home built computer aided microscopic imaging tools to study these reporters within the context of living cells, tissues, and animals. The Molecular Biosensor and Imaging Center (MBIC) at CMU has a long history of developing and applying innovative microscopy and imaging technologies. The ultimate goal of this Center will be to act as a catalyst to strengthen and expand the impact of the new probe developments by providing facilities and expertise to test and validate the probes in the context of the driving biological projects and ultimately the research community at large. In addition, this Core will provide the facilities and broad scope of knowledge and experience required to combine cells, reagents, imaging technologies, software and informatics to create high quality, robust applications for cellular analysis. These applications will be validated in the laboratories of the context of the driving biological projects, and then made available to the research community as a whole.

This program grant totaled $228,191 (total costs) in FY11.

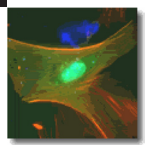
Electrophysiology Patch Clamp





New CBP Research Recruits in FY11

Name	Rank	Lab Association
Faculty Level		
Laurence R. Brewer	Visiting Assistant Professor	
Archana Gangopadhyay	Research Instructor	
Christine C. Wu	Associate Professor	
Post Doctoral Level		
Nicholas W. Bateman	Visiting Research Associate	Dr. Christine Wu
Claudia A. Bertuccio	Visiting Research Associate	Dr. Daniel Devor
Yi-Jiun Chen	Post Doctoral Fellow	Dr. Yang Hong
Ana C. Da Paula	Post Doctoral Fellow	Dr. Raymond Frizzell
Jason E. Duex	Visiting Research Associate	Dr. Alexander D. Sorkin
Arola Fortian-Bernabeu	Post Doctoral Fellow	Dr. Alexander D. Sorkin
Yong Liao	Visiting Research Associate	Dr. Raymond Frizzell
Jeyaganesh rajamanickm	Post Doctoral Fellow	Dr. Raymond Frizzell
Jaya Vatsyayan	Visiting Research Associate	Dr. Raymond Frizzell
Jingyu Wang	Post Doctoral Fellow	Dr. Fei Sun
Peng Xue	Post Doctoral Fellow	Dr. Patrick Thibodeau



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.

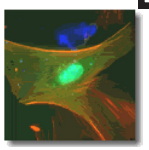
The educational component of the program offers students the opportunity to interact with multiple, well-supported faculty with international reputations. Stipends are provided for the students throughout their training. Students in the program enjoy a rich experience going far beyond formal classroom 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.

Genetic Disorders of Ion Channels
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.
Focus group Faculty:
Dan Devor, Ph.D.
Ray Frizzell, Ph.D.
Patrick Thibodeau, Ph.D.

Molecular Basis of Cardiac Arrhythmias
Molecular engineering of ion channels and high-speed imaging are being used to study the electrophysiology of the heart with the goal of identifying the mechanisms responsible for the initiation and termination of cardiac arrhythmias.
Focus group Faculty:
Guy Salama, Ph.D.

Regulation of Gene Expression during Development
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.
Focus group Faculty:
Pat Hebda, Ph.D. (Otolaryngology)
Nirmala Sundar-Raj, Ph.D. (Ophthalmology)
Donna Beer Stolz, Ph.D.
Simon C. Watkins, Ph.D.
Yang Hong, Ph.D.

The Molecular Events Leading to Cancer

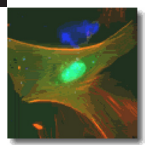
Areas of study include the regulation of chromatin structure that is essential for faithful function of the cell at the DNA level and the modifications of proteins that are required for the correct timing of cell division.
Focus group Faculty:
Sanford Leuba
Yong Wan

Membrane Traffic of Proteins and Lipids

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.
Focus group Faculty:
Gerard Apodaca, Ph.D. (Medicine, Renal)
Meir Aridor, Ph.D.
Carolyn Coyne, Ph.D.
Tom Kleyman, Ph.D. (Medicine, Renal)
Sandra Murray, Ph.D.
Alexander Sorkin, Ph.D.
Linton Traub, Ph.D.
Ora Weisz, Ph.D. (Medicine, Renal)

Reproductive Biology

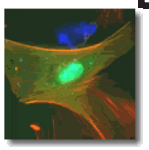
The neuroendocrine control of the hypothalamic-pituitary-gonadal axis is central to human sexual maturation and fertility. To better understand and replicate human reproductive processes, program members utilize rhesus monkeys as a model system. For this work, the Center for Research in Reproductive 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 signal transduction



pathways, stress, puberty, spermatogenesis, fertility preservation, ovarian function, parturition, aging and endocrine disruptors.
Focus group Faculty:
Jennifer Condon, Ph.D.
Tony Plant, Ph.D.
William Walker, Ph.D.
Anthony Zeleznik, Ph.D.

Signal Transduction in Diabetes
Regulated secretion of insulin by the pancreas and the actions of insulin and leptin in 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 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.
Focus group Faculty:
Peter Drain, Ph.D.
Abhiram Sahu, Ph.D.
David Whitcomb, M.D., Ph.D. (Medicine, Gastroenterology)

Center for Biological Imaging
A state-of-the-art imaging center, which is actively involved in the development and application of all aspects of cutting edge microscopic imaging. Through this unique facility, advances in laser confocal microscopy, live cell multicolor fluorescence microscopy, electron microscopy and computer-assisted image processing have facilitated program research efforts and collaborations. Currently the center is developing new methods for imaging multiparallel data sets both in vitro and in vivo.
Director of CBI:
Simon Watkins



Courses in the Cell Biology and Molecular Physiology Graduate Program

New Courses in FY11

Title: Experiments and Logic in Cell Biology
Course Number: 2875
Course Director: Peter Drain
When: Spring Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: The purpose of Experiments and Logic in Cell Biology (ELCB) is to engage the students of the Cell Biology and Molecular Physiology graduate program in a self-directed seminar structured to stimulate the students ability to think scientifically and critically as future scientists. The iterative, collaborative and collegial process of ELCB is the same used by teams of collaborating scientists to develop and solve biomedical projects.

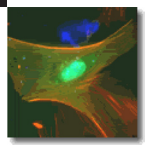
Course List July 2010 – June 2011

Title: MS Thesis Research
Course Number: 2800
Course Director: William Walker
When: Fall Term, Spring Term, Summer Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

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

Title: Regulation of Membrane Traffic
Course Number: 2840
Course Director: Gerard Apodaca and 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

Description: The focus of this course is to analyze membrane/protein traffic along both the biosynthetic and endocytic pathways. The general goal is to teach students how to read and interpret the literature. In particular, we emphasize the conclusions of the assigned papers, examine the experimental basis of these conclusions, and discuss their validity. The course is updated each year to include topics in which new and interesting developments have occurred. Emphasis is placed on how membrane traffic is regulated and how it is disrupted or subverted



during disease processes. The course is of general interest to students, fellows, and faculty interested in cell biology, immunology, neurobiology, pharmacology, and virology.

Title: Research Seminar in Cellular Biological 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 membrane traffic.

Title: Research Seminar in Reproductive Physiology
Course Number: 2853
Course Director: Tony Plant
When: Fall Term, Spring Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

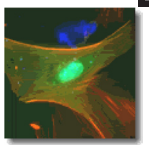
Description: Advanced research seminar with journal club format specializing in current aspects of reproductive physiology.

Title: Research Seminar in Molecular Physiology
Course Number: 2855
Course Director: Thomas Kleyman
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 molecular and cellular physiology.

Title: Multiparametric Microscopic Imaging
Course Number: 2860
Course Director: Claudette St. Croix and Donna Beer Stolz
When: Summer Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: a lecture/lab course that 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: Spring Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

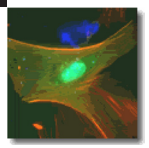
Description: The objective of this lecture/lab course is to comprehend the relationship between structure and function at the cell, organ and organ system levels. Focus is placed on the integration of cell biology, classical histology and basic physiology of each of the organ systems, with the exclusion of the central nervous system. This knowledge is applied by building skills in the interpretation of light and electron micrographic 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: Experiments and Logic in Cell Biology
Course Number: 2875
Course Director: Peter Drain
When: Spring Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: The purpose of Experiments and Logic in Cell Biology (ELCB) is to engage the students of the Cell Biology and Molecular Physiology graduate program in a self-directed seminar structured to stimulate the students ability to think scientifically and critically as future scientists. The iterative, collaborative and collegial process of ELCB is the same used by teams of collaborating scientists to develop and solve biomedical projects.

Title: Cellular Biology of Normal and Disease States
Course Number: 2880
Course Director: Gerard Apodaca
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 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: William Walker
When: Fall Term, Spring Term, Summer Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

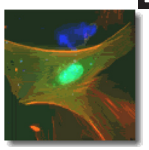
Description: This course provides the student an opportunity to carry out a specific laboratory project in any area of interest in Cell Biology or Physiology.

Title: Ph.D. Dissertation Research
Course Number: 3800
Course Director: William Walker
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.

Title: DNA Repair Journal
Course Number: 3835
Course Director: Robert Sobol
When: Fall Term, Spring Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

Description: The course is a journal club on current topics in DNA Repair as it relates to human disease, DNA damage processing, genome stability, telomere biology, cancer and aging. Primarily designed for students in the second year of their graduate program and beyond. Presentations will be held twice per month during the fall and spring semester. In order to receive credit for the course, students must attend a minimum of 80% of the sessions, present once per semester, participate in class discussion and complete anonymous peer-evaluations for each presenter. One week prior to presentation, presenters will identify a recent publication in the field and distribute it to their classmates. Presenters must define the hypothesis of the paper, provide background and significance, describe experimental methods used, interpret the data, conclude whether the data support the author's conclusions and propose future experiments. Grades will be determined by attendance (10%), class participation (20%) and quality of presentation (70%).



Faculty Teaching Honors (Fiscal Year 2010-2011)

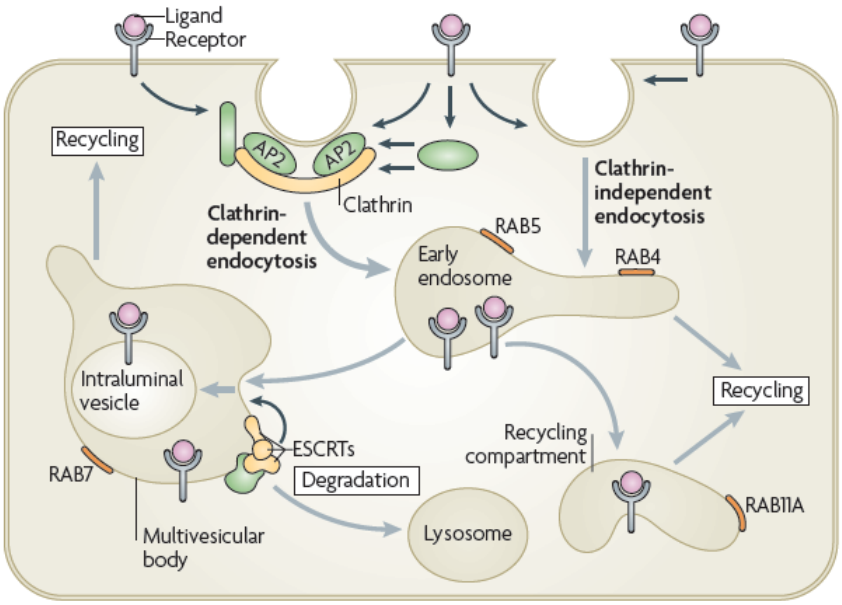
Georgia K. Duker, Ph.D.
Assistant Professor

Hooder, University of Pittsburgh Graduating Medical School Graduating Class of 2010

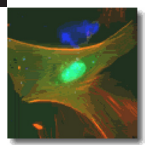
Student National Medical Association (SNMA) Open Door Award, 2010

Sandra Murray, Ph.D.
Professor

Academy of Master Educators (AME)



Alexander Sorkin. Schematic representation of endocytic trafficking pathways of the EGF receptor.



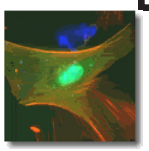
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE
EDUCATIONAL CREDIT UNIT REPORT (AY 2009 – 2010)

Department of Cell Biology and Physiology

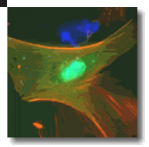
	# ECUs	% ECUs
Department of Cell Biology and Physiology	**2119.8**	**12.8**
Combined Total for All Basic Science Departments	**16613**	**100**

Summary of Faculty ECU's

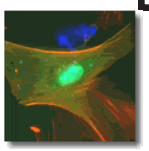
Faculty Name / Activity	ECURV	Units	ECU's
Meir Aridor, Ph.D.			
GS - Lecture	2.0	4.0	8.0
GS – Small group (e.g., PBL, conference, workshop)	2.0	28.0	56.0
GS –Journal Club/Seminar Series Program Director	3.0	2.0	6.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	80.0
Catherine Baty, Ph.D.			
MS – Mentored Scholarly Project IMSP) Mentor	25.0	1.0	25.0
MS – Elective Course Research mentor	4.0	1.0	4.0
		Total ECU's:	29.0
Daniel Devor, Ph.D.			
GS - Lecture	2.0	4.0	8.0
GS – Ph.D. or M.Sc. Mentor	20.0	2.0	40.0
GS –Chair: Curriculum, Recruiting, Program, or other SOM Committee	5.0	1.0	5.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	63.0
Peter Drain, Ph.D.			
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	10.8	21.5
MS – Course Director	100.0	2.0	200.0
MS –Member, Admissions Committee	50.0	1.0	50.0
MS –Member, Scholarly Project Executive Committee	20.0	1.0	20.0
MS –Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	10.0
		Total ECU's:	306.5



Georgia Duker, Ph.D.			
MS 1, MS 2 – Lecture	2.0	25.2	50.3
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	71.1	142.2
MS 1, MS 2 – Laboratory	2.0	39.3	78.5
MS 1, MS 2 – Other	2.0	8.0	16.0
MS 1 and MS 2 – Course Director	100.0	1.0	100.0
MS 1 and MS 2 – Course Segment Coordinator	5.0	2.0	10.0
MS –Member, Promotions Committee	5.0	1.0	5.0
MS –Coordinator, Undergraduate medical Education Teaching	5.0	1.0	5.0
MS – Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	3.0	15.0
MS –Mentoring medical students (e.g., FAST, AOC, or academic advising)	2.0	7.0	14.0
GS - Lecture	2.0	50.0	100.0
		Total ECU's:	536.0
Raymond Frizzell, Ph.D.			
MS 1 and MS 2 – AOC/Longitudinal Curriculum Program Director	20.0	1.0	20.0
GS - Lecture	2.0	33.0	66.0
GS –Journal Club/Seminar Series Program Director	3.0	1.0	3.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	99.0
Vernon Gay, Ph.D.			
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	22.3	44.5
		Total ECU's:	44.5
Yong Hong, Ph.D.			
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	10.0
		Total ECU's:	15.0
Sanford Leuba, Ph.D.			
GS - Lecture	2.0	16.7	33.3
GS – Ph.D. or M.Sc. Mentor	20.0	2.0	40.0
GS – Mentoring other SOM graduate students (e.g., MSTP, Ph.D. or M. Sc.)	2.0	1.0	2.0
GS – Course Director	10.0	1.0	10.0
GS –Journal Club/Seminar Series Program Director	3.0	2.0	6.0
GS – Member: Admissions Committee	5.0	1.0	5.0
GS –Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	103.3
Sandra Murray, Ph.D.			
MS 1, MS 2 – Lecture	2.0	3.0	6.0
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	2.0	4.0
MS 1, MS 2 – Laboratory	2.0	34.0	68.0
MS 1, MS 2 – Other	2.0	9.0	18.0
MS – Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	2.0	10.0
GS - Lecture	2.0	1.0	2.0
GS – Mentoring other SOM graduate students (e.g., MSTP, Ph.D. or M. Sc.)	2.0	1.0	2.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0



GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	10.0
		Total ECU's:	125.0
Kathryn Peters, Ph.D.			
MS – AOC/LCP activity (other than advising, e.g., teaching, precepting)	2.0	57.0	114.0
		Total ECU's:	114.0
Kathleen Ryan, Ph.D.			
MS 1, MS 2 – Lecture	2.0	7.3	14.5
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	30.9	61.8
MS 1, MS 2 – Other	2.0	2.0	4.0
MS 1 and MS 2 – Block Director	10.0	2.0	20.0
MS 3, MS 4 – Small group (e.g., PBL, conference, workshop)	2.0	5.5	11.0
MS –Member, Curriculum Committee	20.0	1.0	20.0
MS –Member, Promotions Committee	5.0	1.0	5.0
MS –Member, Retention Committee	5.0	1.0	5.0
MS –Applicant Interviewer	1.0	30.0	30.0
MS – Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	2.0	10.0
GS - Lecture	2.0	2.5	5.0
		Total ECU's:	186.3
Guy Salama, Ph.D.			
MS 1, MS 2 – Lecture	2.0	2.5	5.0
		Total ECU's:	5.0
Donna Stolz, Ph.D.			
MS 1, MS 2 – Lecture	2.0	1.0	2.0
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	4.2	8.3
MS 1, MS 2 – Laboratory	2.0	11.1	22.2
GS - Lecture	2.0	6.0	12.0
GS – Member: Admissions Committee	5.0	1.0	5.0
GS –Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	7.0	35.0
		Total ECU's:	91.5
Patrick Thibodeau, Ph.D.			
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	10.0
		Total ECU's:	10.0
Linton Traub, Ph.D.			
GS - Lecture	2.0	11.0	22.0
GS – Ph.D. or M.Sc. Mentor	20.0	2.0	40.0
GS – Course Director	10.0	2.0	20.0
GS –Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	6.0	30.0
		Total ECU's:	114.0
Yong Wan, Ph.D.			
MS – Mentored Scholarly Project IMSP) Mentor	25.0	1.0	25.0



GS - Lecture	2.0	2.0	4.0
GS – Mentoring other SOM graduate students (e.g., MSTP, Ph.D. or M. Sc.)	2.0	1.0	2.0
		Total ECU's:	31.0

Simon Watkins, Ph.D.

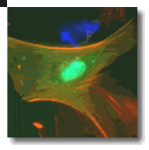
MS 1, MS 2 – Lecture	2.0	1.8	3.7
MS 1 and MS 2 – AOC/Longitudinal Curriculum Program Director	20.0	1.0	20.0
MS –Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	1.0	5.0
MS – AOC/LCP activity (other than advising, e.g., teaching, precepting)	2.0	54.0	108.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	10.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	4.0	20.0
		Total ECU's:	166.7

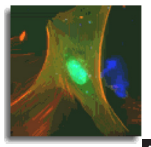
Total Faculty reporting	**18**	**Faculty ECU Subtotal:**	**2119.8**

Precetpting ECU's not attributed to individual faculty

Required clerkship AY 09-10	1.0	0.0	0.0
Acting internship clerkship AY 09-10	1.0	0.0	0.0
Elective clerkship(s) where enrollment = 1 or more students AY 09-10	1.0	0.0	0.0
		Precepting Subtotal:	**0.0**

Total ECU's for Cell Biology & Physiology:	**2119.8**



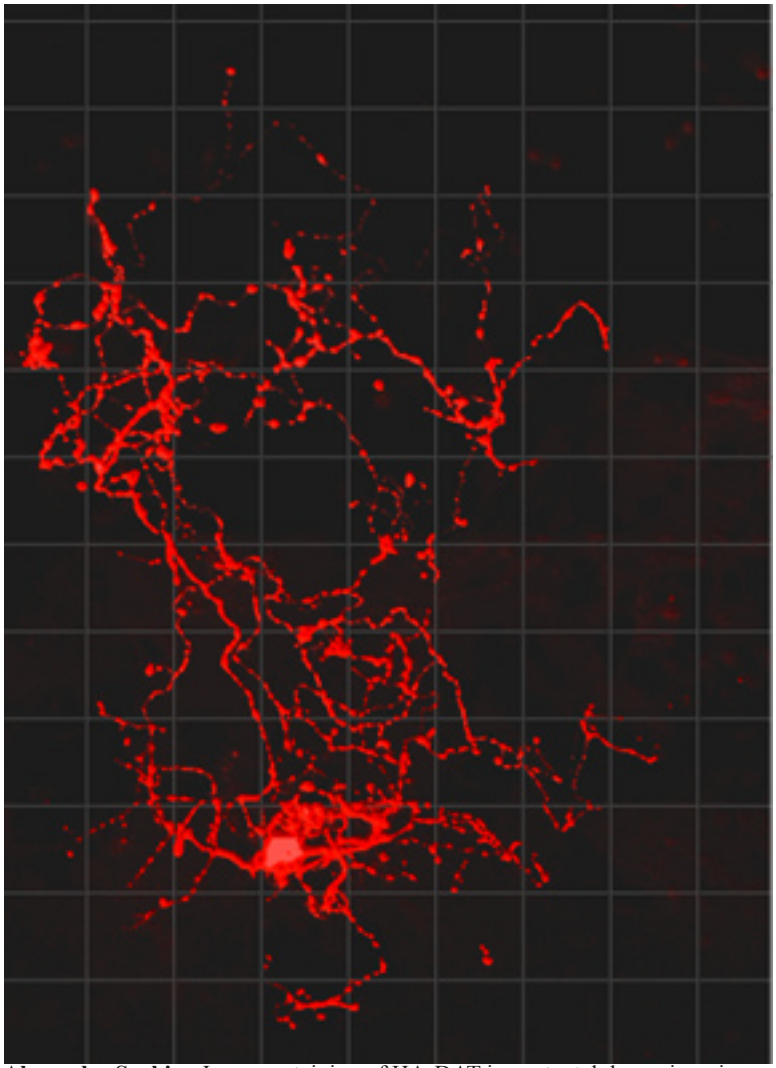


Post Doctoral Personnel Data
[Current as of June, 2011]

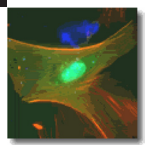
Name	Title	Office Address	Email Address	Office Phone	Fax	Research Focus
Ahner, Annette	Vis. Research Associate	7161 RANCH	aschneid@pitt.edu	412-648-8162	412-648-8330	Frizzell Lab
Balut Corina M.	Post Doctoral Associate	S331 BSTWR	cmb89@pitt.edu	412-383-7192	412-648-8330	Devor Lab
Bateman , Nicholas W.	Vis. Research Associate	S334 BSTWR	nwb5@pitt.edu	412-383-7891	412-648-8330	Wu Lab
Bertuccio, Claudia A.	Vis. Research Associate	S331 BSTWR	cab199@pitt.edu	412-383-7192	412-648-8330	Devor Lab
Caltagarone, John	Post Doctoral Associate	S372 BSTWR	jmcalt@pitt.edu	412-648-9260	412-648-8330	Sorkin Lab
Chen, Yi-Jiun	Post Doctoral Associate	S333 BSTWR	yic42@pitt.edu	412-648-2846	412-648-8330	Hong Lab
Da Paula, Ana C.	Post Doctoral Associate	7161 RANCH	acd36@pitt.edu	412-692-9326	412-692-8906	Frizzell Lab
Dong, Wei	Post Doctoral Associate	S333 BSTWR	wed16@pitt.edu	412-648-2846	412-648-8330	Hong Lab
Ernst, Wayne L.	Post Doctoral Associate	S307 BSTWR	wle3@pitt.edu	412-624-1971	412-648-8330	Aridor Lab
Fortian-Bernabeu, Arola	Post Doctoral Associate	S372 BSTWR	arf48@pitt.edu	412-624-8147	412-648-8330	Sorkin Lab
Gong, Xiaoyan	Research Associate	7161 RANCH	xig17@pitt.edu	412-692-9335	412-692-8906	Frizzell Lab
Hu, Dong	Post Doctoral Associate	2.7 Hillman Cancer	doh16@pitt.edu	412-623-7811	412-623-7761	Wan Lab
Liao, Yong	Vis. Research Associate	7161 RANCH	yol23@pitt.edu	412-692-9326	412-692-8906	Frizzell Lab
Liu, Weijie	Post Doctoral Associate	S333 BSTWR	wel51@pitt.edu	412-648-2846	412-648-8330	Hong Lab
Long, Kimberly	Post Doctoral Associate	S307 BSTWR	krl34@pitt.edu	412-624-1971	412-648-8330	Aridor Lab
Perunthathu, Umasankar	Post Doctoral Associate	S306 BSTWR	ukp1@pitt.edu	412-624-9713	412-648-8330	Traub Lab
Rajamanickam, Jeyaganesh	Post Doctoral Associate	S316 BSTWR	jer113@pitt.edu	412-648-8620	412-648-8330	Frizzell Lab
Sanker, Subramaniam	Vis. Research Associate	S306 BSTWR	sus48@pitt.edu	412-624-9713	412-648-8330	Traub Lab
Xue, Peng	Post Doctoral Associate	S332 BSTWR	pex3@pitt.edu	412-624-8933	412-648-8330	Thibodeau Lab
Zhang, Liang	Post Doctoral Associate	S332 BSTWR	liz46@pitt.edu	412-624-8933	412-648-8330	Thibodeau Lab
Zhang, Liyong	Research Associate	2.7 Hillman Cancer	zhangl5@upmc.edu	412-623-7811	412-623-7761	Wan Lab
Zhou, Wenke	Vis. Research Associate	S333 BSTWR	wez23@pitt.edu	412-648-2846	412-648-8330	Hong Lab

Current Cell Biology and Molecular Physiology Graduate Program Students as of June 2011

Student	Mentor	Year
Cavita Chotoo	Dr. Daniel Devor	6th
Elizabeth Delorme-Axford	Dr. Carolyn Coyne	3rd
Siobhan Gregg	Dr. Laura Niedernhofer	5th
Anupma Jha	Dr. Linton Traub	6th
Xinxian Qiao	Dr. Yong Wan	3rd
Daniel Roh	Dr. James Funderburgh	5th
Arvind Suresh	Dr. Jennifer Condon	3rd
Christina Szalinski	Dr. Ora Weisz	3rd
James Thieman	Dr. Linton Traub	6th



Alexander Sorkin. Immunostaining of HA-DAT in postnatal dopaminergic neurons of HA-DAT knock-in mouse.



Graduates of the Cell Biology and Molecular Physiology Program as of June 2011 (Past five years)

ShanShan Cui
Defended December 7, 2010
Cincinnati, Ohio

Mark A. Bailey
Defended September 23, 2010
University of Texas- Austin, Department of Neuroscience

Paula J. Bernal
Defended August 12, 2010
Center for Vaccine Development, University of Maryland

Ethan Block
Defended January 19, 2010
University of Pittsburgh, Department of Neurobiology

Bado Hewa DeFranco
Defended September 3, 2009
Pittsburgh, PA

Mark R. Silvis
Defended September 3, 2009
Fred Hutchinson Cancer Research Center, Seattle Washington

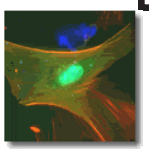
Roxana Teisanu
Defended April 30, 2009
Ecole Politechnique Federal de Lausanne (EPFL), Switzerland

Michelle Wood
Defended April 29, 2009
University of Michigan, Ann Arbor, MI

Dan Constantinescu
Defended December 8, 2008
Law School - California

Christopher Guerriero
Defended September 24, 2008
University of Pittsburgh Medical School

Mark Miedel
Defended August 27, 2008
University of Pittsburgh Medical School

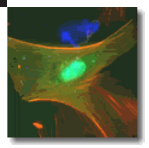


Christopher Lewarcick
Defended August 18, 2008
University of Pittsburgh Medical School

Asli Matos-Oztan
Defended November 20, 2007
Children's Hospital
Harvard Medical School, Boston, MA

Anna Zemke
Defended August 29, 2007
University of Pittsburgh Medical School

Elena Balestreire
Defended June 4, 2007
University of Pittsburgh Medical School

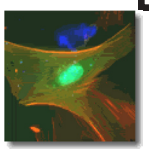


Student Ratings of CBMP Faculty Teaching
FY2011

Name	Course	Type	Date	Rating	Ave
Aridor	Foundations of Biomedical Science	LEC	Fall-10	2.82	
Aridor	Cell Biology of Normal and Disease States	LEC	Spring-11	3.50	3.16
Butterworth	Cell Biology of Normal and Disease States	LEC	Spring-11	3.80	3.80
Devor	Foundations of Biomedical Science	LEC	Fall-10	3.65	
Devor	Cell Biology of Normal and Disease States	LEC	Spring-11	4.17	3.91
Drain	Methods and Logic in Medicine Part 2	SGCS	Fall-10	4.60	
Drain	Cell Biology of Normal and Disease States	LEC	Spring-11	4.83	4.72
Duker	Introduction to Being a Physician	SGCS	Fall-10	5.00	
Duker	Body Fluid Homeostasis Cardiovascular	WKSP	Fall-10	4.70	
Duker	Body Fluid Homeostasis-Renal Segment	LEC	Fall-10	4.60	
Duker	Body Fluid Homeostasis-Pulmonary Segment	LEC	Fall-10	4.90	
Duker	Cell and Tissue Physiology	LEC	Spring-11	4.90	
Duker	Cell and Tissue Physiology	LAB	Spring-11	5.00	
Duker	Digestion and Nutrition	LEC	Fall-10	4.90	
Duker	Digestion and Nutrition	LAB	Fall-10	4.60	
Duker	Digestion and Nutrition	PBL	Fall-10	4.00	4.73
Frizzell	Cell Biology of Normal and Disease States	LEC	Spring-11	4.67	
Frizzell	Intensive Laboratory Research Experience	LEC	May-11	4.42	4.55
Gay	Fuel Metabolism	PBL	Fall-10	3.10	3.10
Hong	Cell Biology of Normal and Disease States	LEC	Spring-11	3.60	3.60
Murray	Medical Anatomy	LEC	Fall-10	4.10	
Murray	Medical Anatomy	SGCS	Fall-08	4.10	4.10
Ryan	Introduction to Being a Physician	SGCS	Fall-08	4.10	
Ryan	Body Fluid Homeostasis Cardiovascular	WKSP	Fall-10	4.40	
Ryan	Cellular and Pathological Basis of Disease	LEC	Spring-11	4.80	
Ryan	Digestion and Nutrition	LEC	Fall-10	4.00	4.33
Stolz	Scientific Ethics & the Responsible Conduct of Research	LEC	Summer-11	4.36	
Stolz	Cell Biology of Normal and Disease States	LEC	Spring-11	4.83	
Stolz	Cellular and Pathological Basis of Disease	LEC	Spring-11	3.60	
Stolz	Cellular and Pathological Basis of Disease	LAB	Spring-11	4.90	
Stolz	Digestion and Nutrition	LAB	Fall-10	4.30	4.40
Thibodeau	Cell Biology of Normal and Disease States	LEC	Spring-11	4.83	
Thibodeau	Scientific Ethics & the Responsible Conduct of Research	LEC	Summer-11	4.50	4.67
Traub	Foundations of Biomedical Science	LEC	Fall-10	3.58	
Traub	Cell Biology of Normal and Disease States	LEC	Spring-11	4.60	4.09
Watkins	Intensive Laboratory Research Experience	LEC	May-11	4.33	
Watkins	Cellular and Pathological Basis of Disease	LEC	Spring-11	4.60	
	Overall Teaching Average			**4.32**	

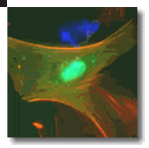
Type codes:

LEC	Lecture
PBL	Practice Based Learning
WKSP	Workshop
SGCS	Small Group Conference Session
AP	Applications Staff
LAB	Laboratory



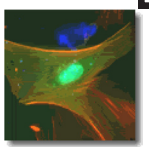
CBP FACULTY ROSTER
(Effective June, 2011)

Last Name	First	Rank	Status
Sorkin	Alexander	Professor & Chair	Tenured
Devor	Daniel	Professor	Tenured
Frizzell	Raymond	Professor	Tenured
Murray	Sandra	Professor	Tenured
Watkins	Simon	Professor	Tenured
Aridor	Meir	Associate Professor	Tenured
Drain	Peter	Associate Professor	Tenured
Gay	Vernon	Associate Professor	Tenured
Leuba	Sanford	Associate Professor	Tenured
Ryan	Kathleen	Associate Professor	Tenured
Stolz	Donna	Associate Professor	Tenured
Traub	Linton	Associate Professor	Tenured
Wan	Yong	Associate Professor	Tenured
Wu	Christine	Associate Professor	Tenured
Brewer	Laurence	Vis Res Assistant Professor	Non-Tenure Track
Butterworth	Michael	Assistant Professor	Tenure Track
Hong	Yang	Assistant Professor	Tenure Track
Thibodeau	Patrick	Assistant Professor	Tenure Track
Duker	Georgia	Assistant Professor	Non-tenure Track
Baty	Catherine	Res. Assistant Professor	Non-tenure Track
Bertrand	Carol	Res. Assistant Professor	Non-tenure Track
Gangopadhyay	Archana	Res. Assistant Professor	Non-tenure Track
Peters	Kathryn	Res. Assistant Professor	Non-tenure Track
Schmidt	Bela	Res. Assistant Professor	Non-tenure Track



New CBP Faculty in FY11

Name	Prior Institution /Rank	Current Rank
Laurence R. Brewer	Washington State University School of Chemical Engineering And Bioengineering Assistant Professor	Visiting Assistant Professor
Archana Gangopadhyay	University of Pittsburgh Department of Surgery Research Instructor	Research Instructor
Christine C. Wu	University of Colorado Health Sciences Department of Pharmacology Associate Professor	Associate Professor



Faculty Honors, Recognition and Professional Affiliations (Fiscal Year 2010-11)

Meir Aridor, Ph.D.
Associate Professor

Member, Society for Neuroscience

Catherine J. Baty, D.V.M., Ph.D.
Research Assistant Professor

Member, American College of Veterinary Internal Medicine
Member, American Heart Association

Carol A. Bertrand, Ph.D.
Research Assistant Professor

Member, Biophysical Society
Member, American Physiological Society

Michael Butterworth, Ph.D.
Assistant Professor

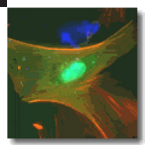
Member, American Physiological Society
Member, Salt and Water Club

Daniel C. Devor, Ph.D.
Professor

Member, American Physiological Society
Member, Biophysical Society
Member, Mount Desert Island Biological Laboratory

Peter F. Drain, Ph.D.
Associate Professor

Member, Biophysical Society
Member, American Association for the Advancement of Science
Member, Society of General Physiologists
Member, American Diabetes Association



Raymond A. Frizzell, Ph.D.
Professor and Director of Cystic Fibrosis Center

Member, American Physiological Society

Member, Society of General Physiologists

Member, Mount Desert Island Biological Laboratory
Member, American Society for Cell Biology
Member at Large, Medical Advisory Council, Cystic Fibrosis Foundation
Member, Salt and Water Club

Yang Hong, Ph.D.
Assistant Professor

Member of Faculty 1000

Vernon Gay, Ph.D.
Associate Professor

Member, Society for the Study of Reproduction (SSR)
Member, Endocrine Society
Member, International Society of Neuroendocrinology

Sanford Leuba, Ph.D.
Associate Professor

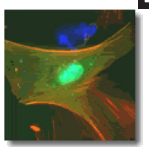
Member, Biophysical Society

Xiubin Liang, Ph.D.
Research Assistant Professor

Member, American Society of Nephrology
Member, American Heart Association

Sandra A. Murray, Ph.D.
Professor

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
Member, Endocrine Society
Member, American Physiological Society
Member, International Society for Preventive Oncology
University of Pittsburgh Helen Faison Council of Elders
School of Medicine Summer "Minority" Work-Study Program
Member, Medical Student Promotions Committee
Committee – Child Health Research Center Grant
Member, Training Faculty Immunology Graduate Training Program
Provost's Committee on Diversity

Kathleen D. Ryan, Ph.D.
Associate Professor

Member, Society for the Study of Reproduction (SSR)
Member, Endocrine Society
Member, Society for Neuroscience

Alexander D. Sorkin, Ph.D.
Richard B. Mellon Professor and Chairman

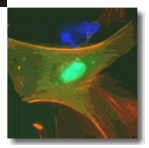
American Society for Cell Biology
ASPET
Society for Neuroscience

Donna B. Stolz, Ph.D.
Associate 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

Linton M. Traub, Ph.D.
Associate Professor

Member, American Society for Cell Biology
American Association for the Advancement of Science
American Society for Biochemistry and Molecular Biology



Yong Wan, Ph.D.
Associate Professor

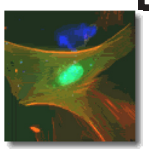
Member, American Association for Cancer Research
Member, American Association of Cell Biology
Member, American Association for The Advancement of Science

Simon C. Watkins, Ph.D.
Professor and Vice Chairman, Director of Center of Biologic Imaging

Member, The Pittsburgh Cancer Institute
Microscopy Society of America

Christine Wu, Ph.D.
Associate Professor

American Association for Cancer Research
American Association of Cell Biology
American Association for The Advancement of Science



Faculty Presentations (Fiscal Year 2010-2011)

Michael Butterworth, Ph.D.
Assistant Professor

Symposium Organizer & Chair: "Epithelial Ion Channel Trafficking". Experimental Biology 2011, Washington D.C.

Symposium Chair: "Regulation of distal ion transport :ENaC and ROMK". Experimental Biology 2011, Washington D.C.

Daniel C. Devor, Ph.D.
Professor

"Role of ubiquitination and UBPY-dependent deubiquitination in the endocytosis and lysosomal targeting of plasma membrane KCa3.1." Ubiquitin Drug Discovery and Diagnostics Conference 2010, Philadelphia, PA., August 23-25, 2010. Presented by Corina Balut, Postdoctoral Associate.

"DUB microarray as a tool for identifying DUBs involved in trafficking of KCa3.1" Ubiquitin Research and Discovery Conference, San Diego, CA, January 27-28, 2011. Presented by Corina Balut, Postdoctoral Associate.

"Using DUB Arrays and TUBEs to define the USP8-dependent lysosomal targeting of KCa3.1." Experimental Biology 2011, Washington, D.C., April 10-13, 2011.

Raymond A. Frizzell, Ph.D.
Professor, Director of Cystic Fibrosis Center

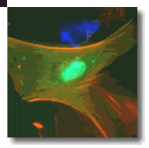
Molecular Medicine Research Seminar, Children's Hospital of Pittsburgh, "A new chloride channel contributes to anion secretion in cystic fibrosis", October 12, 2010.

European Cystic Fibrosis Society, Pisa, Italy, "Role of SLC26A9 in airway anion secretion", April 4, 2011.

Experimental Biology Symposium, American Physiological Society, "Rab Protein Regulators in Ion Channel Trafficking", April 13, 2011.

University of Toledo, Medicine Grand Rounds, "Role of 14-3-3 proteins in ion channel trafficking and biogenesis", April 14, 2011.

University of Utrecht, "Two modes of Ion Channel Regulation by phosphorylation and 14-3-3 proteins", April 24, 2011.



Yang Hong, Ph.D.
Assistant Professor

Department of Molecular Biosciences, Northwestern University, April 2011
Center for Metabolic Disease Research, Nanjing Medical University, March 2011
Speaker and co-chair of "Gene Targeting in Model Species" session, Gene Targeting, Vienna, Austria, February 2011
TriBeta, Allegheny College, November 2010

Sanford H. Leuba, Ph.D.
Associate Professor

Italian Institute of Technology, Genoa, Italy, July 2010.

Alexander D. Sorkin, Ph.D.
Richard B. Mellon Professor and Chairman

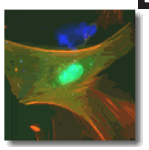
Science Transformations. University of Pittsburgh, October, 2010
Stony Brook University, November 2010
University of Barcelona, Spain, December 2010
Meharry Medical College, Tennessee, March 2011
ESCRTs in health and disease, ASBMB meeting, Utah, October 2010
Application of Microscopy Imaging, Wellington, New Zealand, February, 2011 (keynote speaker)
Molecular cell dynamics, SFB 629, Max Planck Inst., Muenster, Germany, June 2011

Donna Beer Stolz, Ph.D.
Associate Professor

Univ of Pittsburgh, Titusville, "Science and Art", October 2010
Univ of Pittsburgh, Titusville, "Microscopy-related Subjects", October 2010
Univ of Pittsburgh, Renal Seminar, Progeriod mouse model to study age-related kidney dysfunction, May 2011

Patrick H. Thibodeau, Ph.D.
Assistant Professor

Identifying novel targets to promote ΔF508folding, North American Cystic Fibrosis Conference, Baltimore, MD, 2010.
CFTR 2010, North American Cystic Fibrosis Conference, Baltimore, MD, 2010 (Symposium Chair).
Aberrant ABCC-family protein function as a mechanism of disease pathophysiology: Implications for PXE and DCC." PXE International Annual Conference, Bethesda, MD, 2010.



Linton Traub, Ph.D.
Associate Professor

The apoptotic engulfment protein Ced-6 participates in Clathrin-mediated yolk endocytosis in *Drosophila*' *Biological & Biophysical Basis of Membrane Dynamics and Organization* symposium, Carnegie Mellon University, Pittsburgh, PA., October 2010

Double duty: the apoptotic engulfment protein Ced-6 operates in yolk accumulation in flies' Department of Pharmacology and Chemical Biology, University of Pittsburgh School of Medicine, Pittsburgh, PA, February 2011

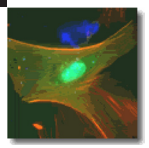
Double duty: the apoptotic engulfment protein Ced-6 operates in yolk accumulation in flies' Department of Physiology, University of Maryland School of Medicine, Baltimore, MD, April 2011

Yong Wan, Ph.D.
Associate Professor

Ubiquitin-proteasome in DNA damage response and cancer. The University of Hong Kong, 2011
Regulation of KLF4 Turnover Reveals an Unexpected Tissue Specific Role of pVHL in Tumorigenesis Bioscience for 21st Century: Emerging Frontiers and Evolving Concepts, 2011
APC pathway in cell cycle, genomic integrity and carcinogenesis. University of Pennsylvania, 2011
Regulation of genomic integrity by Cdh1/APC-Rad17 cascade in DNA damage checkpoint and melanomagenesis. Wistar Institute, 2010
Interplay between APC/Cdh1 and Rad17 in regulating DNA damage checkpoint and carcinogenesis, Science 2010, Pittsburgh, 2010
Regulation of stem cell division and differentiation by UPS. International Forum on Stem Cell. China, 2010
The role of proteolysis in cell cycle, genomic integrity and carcinogenesis. duPont Hospital for Children, Nemours Biomedical Research, 2010
The role of UPS in cell cycle control and carcinogenesis. Department of Urology, University of Pittsburgh, 2010

Simon C. Watkins, Ph.D.
Professor and Vice Chairman
Director of Center of Biologic Imaging

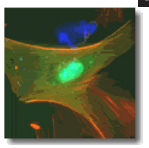
Intercellular Communication in the immune system: Networks or Chance. Invited speaker, Society for Industrial and Applied Mathematics, Annual meeting David Lawrence convention Center, Pittsburgh PA july 14th 2010



Live cell Imaging Workshop Director and lecturer Microscopy society of America annual meeting Portland Ore August 1st 2010
MAN Machine Microscope Symposium Organizer, Microscopy society of America annual meeting Portland Ore August 2st 2010
Imaging Mans Failures. Invited Speaker Microscopy society of America annual meeting Portland Ore August 2st 2010
Live Cell Imaging, building blocks. Technology Forum, Speaker Microscopy society of America annual meeting Portland Ore August 4st 2010
Camera futures and Camera Failures: the importance of modern camera technologies. Photometrics, Invited Speaker, August 27th 2010.
Long and short distance Communication in the Immune System: International Microscopy Meeting, Keynote Speaker Rio De Janiero Brazil, September 20th 2010
Optical possibililities in the 21st Century, Keynote Speaker, Imaging Symposium Penn State Hershey December 9th 2010
American Cancer Society Review Panelist Jan 25-27th 2011
Imaging Fast and Imaging Deep, UPCI basic sience seminar series, Invited speaker
Live cell imaging of FAP's in CF research NIH all hands meeting for TCNP's Invited Speaker, April 14-16th 2011
Imaging cellular communication in the Immune system, University of South Carolina April 21st 2011, Invited speaker
Designing imaging facilities for Level 4 containment National Biocontainment Laboratory, University of Texas, April 28th 2011, Invited Speaker
Long and short distance communication in the Immune system University of Texas Galveston, Invited Speaker April 29th 2011
Live cell imaging, Biotechniques Webinar, April 27th 2011
Course Director "Quantitative Fluorescence Microscopy", Mount Desert Island Biological Laboratories Maine May 19th-26th 2011
Intensive course in Physiology MDIBL Maine, May 29th-June 5th 20011 Invited Lecturer
Cancer Imaging Camp Invited Speaker and Director optical section, Washington University June 19th-23rd 2010
American Cancer Society Study Section, (Peer Review Committee on Clinical Cancer Research and Epidemiology) Panel Member, Atlanta GA, 22nd-23rd 2011

Christine C. Wu, Ph.D.
Associate Professor

Wu, CC. Using molecular pathology to predict response in heart failure. 9th Annual World HUPO Congress, Sydney, Australia. September 19-23, 2010.



Peer Reviewed Publications (Fiscal Year 2008-11)

Meir Aridor, Ph.D.
Associate Professor

Béla Z. Schmidt, Rebecca J. Watts, Meir Aridor and Raymond A. Frizzell (2009). Cysteine String Protein promotes proteasomal degradation of CFTR by increasing its interaction with CHIP and promoting CFTR ubiquitylation . *J Biol Chem.* 13; 284(7): 4168-78.

M. Aridor and K. N. Fish (2009) Selective Targeting and Regulation of ER Exit Sites Supports Axon Development*Traffic* 10(11):1669-84.

Kimberly R. Long, Yasunori Yamamoto, Adam L. Baker, David klinkenberg, Carolyn B.Coyne, Simon C. Watkins, James F. Conway and Meir Aridor (2010) Sar1 Assembly Regulates Membrane constriction and ER export. *J. Cell Biol.* 12;190(1):115-28.

Catherine J. Baty, D.V.M., Ph.D.
Research Assistant Professor

Finegold DN, Schacht V, Kimak MA, Lawrence EC, Foeldi E, Karlsson JM, Baty CJ, Ferrell RE. HGF and MET mutations in primary and secondary lymphedema. Lymph Res Biol, 2008; 6(2):69-76.

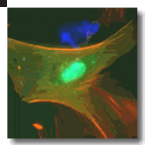
DeFranco BD, Nickel BM, Baty CJ, Martinez JS, Gay VL, Sandulache1 VC, Hackam DJ, and Murray SA. Migrating cells retain gap junction plaque structure and function. Cell Commun Adhes, 2008, 15(3):273-88.

Knickelbein JE, Khanna KM, Yee MB, Baty CJ, Kinchington PR, Hendricks RL. Noncytotoxic lytic granule-mediated CD8+ T cell inhibition of HSV-1 reactivation from neuronal latency. Science, 2008; 322(5899):268-71.

Wegiel B, Baty CJ, Gallo D, Csizmadia E, Scott JR, Akhavan A, Chin BY, Kaczmarek E, Alam J, Bach FH, Zuckerbraun BS, Otterbein LE. Cell surface biliverdin reductase mediates biliverdin-induced anti-inflammatory effects via phosphatidylinositol 3-kinase and Akt. J Biol Chem, 2009:284(32):21369-78.

Myerburg MM, King Jr JD, Oyster NM, Fitch AC, Magill A, Baty CJ, Watkins SC, Kolls JK, Pilewski JM, Hallows KR.AMPK Agonists Ameliorate Sodium and Fluid Transport and Inflammation in CF Airway Epithelial Cells. Am J Respir Cell Mol Biol. 2009: 42(6):676-84.

Wegiel B, Gallo DJ, Raman KG, Karlsson JM, Ozanich B, Chin BY, Tzeng E, Ahmad S, Ahmed A, Baty CJ, Otterbein LE.Nitric oxide-dependent bone marrow progenitor mobilization by carbon



monoxide enhance endothelial repair after vascular injury. Circulation. 2010;121(4):537-48.

Ferrell R.F., Baty CJ, Kimak M.A., Karlsson J.M., Lawrence E.C., Franke-Snyder, M., Meriney S.D., Feingold, E., and Finegold, D.N. GJC2 Missense mutations cause human lymphedema. Am J Human Genetics 2010; 86: (6):943-8.

Alzamora R, Thali RF, Gong F, Smolak C, Li H, **Baty CJ**, Bertrand CA, Auchli Y, Brunisholz RA, Neumann D, Hallows KR, Pastor-Soler NM. PKA regulates vacuolar H+-ATPase localization and activity via direct phosphorylation of the A subunit in kidney cells. J Biol Chem 2010; 285(32):24676-85.

Ni HM, Baty CJ, Li N, Ding WX, Gao W, Li M, ChenX, Ma J, Michalopoulos GK, Yin XM. Bid agonist regulates murine hepatocyte proliferation by controlling endoplasmic reticulum calcium homeostasis. Hepatology. 2010;52(1):338-48.

Gau D, Ding Z, **Baty C**, Roy P. Fluorescence resonance energy transfer (FRET)-based detection of profiling-VASP interaction. Cell Mol Bioeng. 2011;4(1):1-8.

Carol A. Bertrand, Ph.D.
Research Assistant Professor

Sun F, Mi Z, Condliffe SB, Bertrand CA, Gong X, Lu X, Zhang R, Latoche JD, Pilewski JM, Robbins PD, and Frizzell RA. (2008) Chaperone displacement from mutant cystic fibrosis transmembrane conductance regulator restores its function in human airway epithelia. FASEB J, 22(9):3255-63.

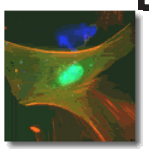
Kreindler JL, Bertrand CA, Lee RJ, Karasic T, Aujla S, Pilewski J, Frizzell R, and Kolls J. (2009) Interleukin-17A induces bicarbonate secretion in normal human bronchial epithelial cells. Am J Physiol Lung Cell Mol Physiol, 296(2):L257-66.

Silvis MR, Bertrand CA, Ameen N, Golin-Bisello F, Butterworth MB, Frizzell RA, and Bradbury NA. (2009) Rab11b Regulates the Apical Recycling of CFTR in Polarized Intestinal Epithelial Cells. Mol Biol Cell, 20:2337-2350.

Bertrand CA, Zhang R, Pilewski J, and Frizzell R. (2009) SLC26A9 is a constitutively active, CFTR-regulated anion conductance in human bronchial epithelia. J Gen Physiol, 133(4):421-438.

Alzamora R, Thali RF, Gong F, Smolak C, Li H, Baty CJ, **Bertrand CA**, Auchli Y, Brunisholz RA, Neumann D, Hallows KR, and Pastor-Soler NM. PKA Regulates Vacuolar H^+-ATPase Localization and Activity via Direct Phosphorylation of the A Subunit in Kidney Cells. J Biol Chem (2010), 285:24676.

Mo D, Potter BA, **Bertrand CA**, Hildebrand JD, Bruns JR, and Weisz OA. Nucleofection Disrupts Tight Junction Fence Function to Alter Membrane Polarity of Renal Epithelial Cells. Am J Phys (2010), doi:10.1152/ajprenal.00152.2010.



Michael Butterworth, Ph.D.
Assistant Professor

Liang, X.; Butterworth, M.B. ; Peters, K.W., Walker, W.H. and Frizzell, R.A. (2008). An obligatory heterodimer of 14-3-3β and 14-3-3ε is required for aldosterone regulation of the epithelial sodium channel. *Journal of Biological Chemistry.* **283:** 27418-27425

Hallows, K.R.; Edinger, R.S.; Butterworth, M.B.; Oyster, N.M.; Li, H.; Wang, H.; Buck, J.; Levin, L.R.; Johnson, J.P. and Pastor-Soler, N.M. (2009). Novel regulation of epithelial Na^+ transport by soluble adenylyl cyclase in kidney collecting duct cells. *Journal of Biological Chemistry.* **284(9):** 5774-83

Silvis, M.R.; Bertrand, C.A.; Ameen, N.; Golin-Bisello, F.; Butterworth, M.B., Frizzell, R.A. and Bradbury, N.A. (2009). Rab11b regulates the apical recycling of CFTR in polarized intestinal epithelial cells. *Mol.Biol.Cell*. **20(8):** 2337-50

Liang, X.; Peters, K.W.; Butterworth, M.B., Frizzell, R.A. (2010). AS160 modulates aldosterone stimulated epithelial sodium channel (ENaC) forward trafficking. Molecular Biology of the Cell. 21(12):2024-2033.

Myerburg M.M., Harvey P.R., Heidrich E.M., Pilewski J.M., Butterworth M.B. (2010). Acute regulation of ENaC in airway epithelia by proteases and trafficking. *American Journal of Respiratory Cell and Molecular Biology*. **43(6):** 712-9.

Hallows, K.R.; Edinger, R.S.; Butterworth, M.B.; Oyster, N.M.; Li, H.; Wang, H.; Buck, J.; Levin, L.R.; Johnson, J.P. and Pastor-Soler, N.M. (2009). Novel regulation of epithelial Na^+ transport by soluble adenylyl cyclase in kidney collecting duct cells. *Journal of Biological Chemistry.* **284(9):** 5774-83.

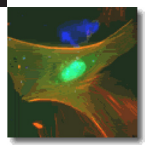
Daniel Devor, Ph.D.
Professor

Gao, Y., C.K. Chotoo, C.M. Balut, F. Sun, M.A. Bailey and **D.C. Devor**. Role of S3 and S4 transmembrane domain charged amino acids in channel biogenesis and gating of KCa2.3 and KCa3.1. J. Biol. Chem. 283(14): 9049-9059, 2008.

Balut, C.M., Y. Gao, C. Luke and **D.C. Devor**. An immunofluorescence-based assay to identify modulators of the number of plasma membrane KCa3.1 channels. Future Med. Chem. 2(5): 707-713, 2010.

Gao, Y., C.M. Balut, M.A. Bailey, G. Patino-Lopez, S. Shaw and **D.C. Devor**. Recycling of the Ca^{2+}-activated K^+ channel, KCa2.3 is dependent upon RME-1, Rab35/EPI64C and an N-terminal domain. J. Biol. Chem. 285(23): 17938-17953, 2010.

Balut, C.M., Y. Gao, S.A. Murray, P.H. Thibodeau and **D.C. Devor**. ESCRT-dependent targeting of plasma membrane localized KCa3.1 to the lysosomes. Am. J. Physiol.: Cell Physiology. 299(5): C1015-1027, 2010.



Bailey, M.A., M. Grabe and **D.C. Devor**. Characterization of the PCMBS-dependent modification of KCa3.1 Ca^{2+}-dependent channel gating. J. General Physiology. 136(4): 367-387, 2010.

Millership, J.E., **D.C. Devor,** K.L. Hamilton, C.M. Balut, J.I. Bruce and I.M. Fearon. Calcium-activated K^+ channels increase cell proliferation independent of K^+ conductance. Am. J. Physiol.: Cell Physiology. 300(4): C792-802, 2011.

Balut, C.M., C. Loch and **D.C. Devor**. Role of ubiquitylation and USP8-dependent deubiquitylation in the endocytosis and lysosomal targeting of plasma membrane KCa3.1. FASEB J. Aug. 9, 2011 (Epub ahead of print).

Peter F. Drain, Ph.D.
Associate Professor

Luppi P, Geng X, Cifarelli V, Drain P, Trucco M. 2009. C-peptide is internalised in human endothelial and vascular smooth muscle cells via early endosomes. Diabetologia 52(10):2218-28.

X. Geng, H. Lou, J. Wang, L. Li, R. G. Perez, and **P. Drain**. 2011. Alpha-Synuclein Binds the KATP Channel at Insulin Secretory Granules and Inhibits Insulin Secretion. **Am. J. Physiol. Endocrinol. Metab.** 300(2): E276-86.

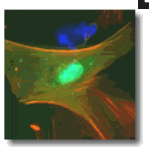
Mihaela Stefan, Rebecca A. Simmons, Suzanne Bertera, Massimo Trucco, Farzad Esni, **Peter Drain**, Robert D. Nicholls. 2011. Global deficits in development, function, and gene expression in the endocrine pancreas in a deletion mouse model of Prader-Willi syndrome. **Am. J. Physiol. Endocrinol. Metab:** 300(5): E909-22.

Chu KY, Briggs MJ, Albrecht T, **Drain PF**, Johnson JD. 2011. Differential regulation and localization of carboxypeptidase D and carboxypeptidase E in human and mouse β-cells. **Islets** 3(4): 155-65.

Li Ma, Vytautas P. Bindokas, Christine Labno, Jie Wang, Andrey Kuznetsov, Manani Hara, Xuehui Geng, **Peter Drain**, Christopher J. Rhodes, Donald F. Steiner, and Louis H Philipson. 2011. Non-Crystallized Cargo Protein Shifts Insulin LDCV Exocytosis From Full to Transient Fusion, Traffic, in revision.

Raymond A. Frizzell, Ph.D.
Professor, Director of Cystic Fibrosis Research Center

Myerburg, M.M., E.E. McKenna, C.J. Luke, R.A. Frizzell, T.R. Kleyman, J.M. Pilewski. Prostasin expression is regulated by airway surface liquid volume and is increased in cystic fibrosis. Am J Physiol Lung Cell Mol Physiol. 2008 May; 294-(5):L932-41.



Sun F., Z. Mi, S.B. Condliffe, C. Bertrand, X. Gong, X. Lu, R. Zhang, J.D. Latoche, J.M. Pilewski, P.D. Robbins, R.A. Frizzell. Chaperone displacement from mutant cystic fibrosis transmembrane conductance regulator restores its function in human airway epithelia. Faseb J. 2008 Sep;22(9):3255-63.

Butterworth, M.B., R.S. Edinger, R.A. Frizzell, J.P. Johnson. Regulation of epithelial sodium channel (ENaC) by membrane trafficking. Am J Physiol Renal Physiol. 2008 May 28. (Epub ahead of print)

Liang, X., M.B. Butterworth, K.W. Peters, W.H. Walker, R.A. Frizzell. An obligatory heterodimer of 14-3-3beta and 14-3-3episilon is required for aldosterone regulation of the epithelial sodium channel. J Biol Chem. 2008 Oct 10;283(41):27418-25.

Lewarchik, C.M., K.W. Peters, J. Qi, R.A. Frizzell. Regulation of CFTR trafficking by its R domain. J Biol Chem. 2008 Oct 17:283(42):28401-28412.

Kreindler, J.L., C.A. Bertrand, R.J. Lee, T. Karasic, S. Aujla, J.M. Pilewski, R.A. Frizzell, J.K. Kolls. Interleukin-17A induces bicarbonate secretion in normal human bronchial epithelial cells. Am J Physiol Lung Cell Mol Physiol. 2009 Feb;296(2):L257-66.

Schmidt, B.Z., R.J. Watts, M. Aridor, R.A. Frizzell. Cysteine string proteinpromotes proteasomal degradation of the cystic fibrosis transmembrane conductance regulator (CFTR) by increasing its interaction with the C-terminus of HSP 70-interacting protein (CHIP) and promoting CFTR ubiquitylation. J Biol Chem. 2008 Dec 20. (Epub ahead of print).

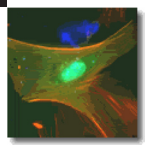
Silvis, M.R., C.A. Bertrand, N. Ameen, F. Golin-Bisello, M.B. Butterworth, R.A. Frizzell, N.A. Bradbury. Rab11b Regulates the Apical Recycling of CFTR in Polarized Intestinal Epithelial Cells. Mol Biol Cell. 2009 Feb 25. {Epub ahead of print]

Bertrand, C.A., R. Zhang, J.M. Pilewski, R.A. Frizzell. SLC26A9 is a constitutively active, CFTR-regulated anion conductance in human bronchial epithelia. J Gen Physiol. 2009 Apr; 133(4):421-38.

Hutt DM, D. Herman, A.P. Rodrigues, S. Noel, J.M. Pilewski, J. Matteson, B. Hoch, W. Kellner, J.W.Kelly, A. Schmidt, P.J. Thomas, Y. Matsumura, W.R. Skach, M. Gentzsch, J.R. Riordan, E.J. Sorscher, T. Okiyoneda, J.R. Yates 3rd, G.L. Lukacs, **R.A. Frizzell**, G. Mannin, J.M. Gottesfeld, W.E. Balch. Reduced histone deacetylase 7 activity restores function to misfolded CFTR in cystic fibrosis. Nat Chem Biol. 2010 Jan;6(1):25-33.

VanGoor F., S. Hadida, P.D. Grootenhuis, B. Burton, D. Cao, T. Neuberger, A. Turnbull, A. Singh, J. Joubran, A. Hazlewood, J. Zhou, J. McCartney, V. Arumugam, C. Decker, J. Yang, C. Young, E.R. Olson, J.J. Wine, **R.A. Frizzell**, M. Ashlock, P. Negulescu. Rescue of CF airway epithelial cell function in vitro by a CFTR potentiator, VX-770. Proc Natl Acad Sci USA, 2009 Nov 3;106(44):18825-30.

Liang X., M.B. Butterworth, K.W. Peters, R.A. Frizzell. AS160 modulates aldosterone-stimulated epithelial sodium channel forward trafficking. Mol Biol Cell. 2010 June 15:21(12:2024-33.



Vernon L. Gay, Ph.D.
Associate Professor

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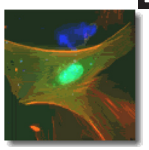

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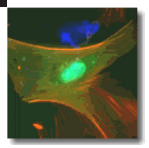

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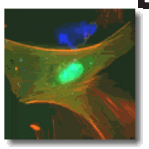

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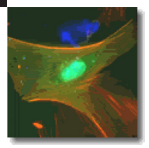

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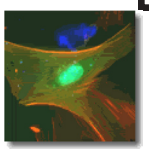

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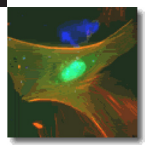

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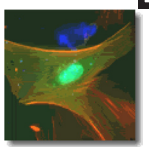

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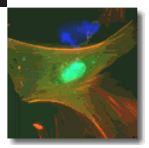

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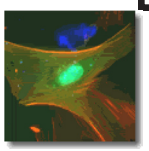

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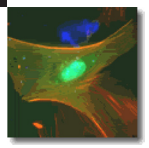

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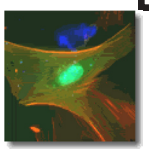

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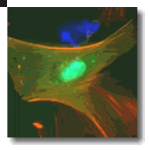

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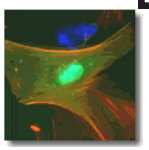

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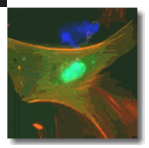

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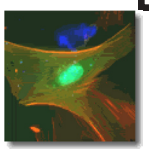

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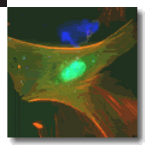

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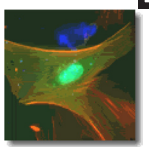

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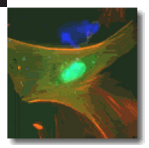

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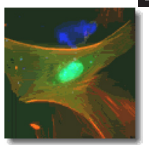

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Christine Wu, Ph.D.
Associate Professor

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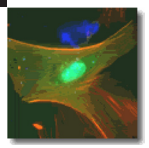

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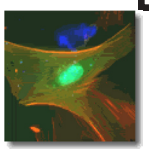
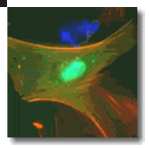


Executive Summary for the Cell Biology and Physiology FY2011 Business Plan

One of the key issues in the FY2012 Business Plan will be recruitment of new faculty. In the past fifteen years, the department has developed a diverse group of well funded investigators who contribute on many levels to the School of Medicine and its research and educational programs. Last year significant changes in the Department took place with seven members of the primary faculty leaving the Department and two new members joining the faculty. Achievement of the balanced distribution of the junior and senior faculty and strong integration of all activities of the remaining faculty is an important topic of our FY2012 plan. This will be, in large part, achieved through the recruitment of one-two new faculty in the FY2012. We present the strengths, weaknesses, opportunities and threats to the success of the Department in its current configuration in this section of the Annual Report. This analysis incorporates also the implementation strategy of the current recruitment of a new faculty to the Department. We plan to recruit scientists who study fundamental aspects of cell biology and who can interface with our faculty, researchers in other departments in the School of Medicine and the entire
Pittsburgh scientific community.

The outlook for the future of the Department is optimistic. New research themes and resources are integrated into the Department, which should lead to the overall increase in the research productivity and funding, new scientific interactions and development of new joint funding opportunities. There is also a strong confidence in continuing excellence of the established programs in the Department.

The Department's operating budget for fiscal year 2012 has been approved and is appended at the end of this analysis.



Strengths

Research

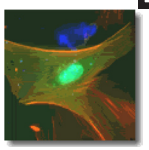
The Department of Cell Biology and Physiology has a strong research program aimed at addressing fundamental questions of cell biology, including mechanisms controlling membrane trafficking, cell polarity, signal transduction and cell cycle, transcription, intercellular interactions and channel regulation. The Faculty in the Department have made important contributions to these various areas of cell biology, and established themselves as leaders in their respective research fields. This is evident from recent publications in top tier cell biology journals such as the Journal of Cell Biology (Goh et al., 189:871-883; Long et al., 2010 190:115-128), Proceedings of National Academy of Sciences USA (Liang et al., 2010 107: 0532-7), Molecular Biology of the Cell (Collette et al., 2009 20: 3401-3413; Duex and Sorkin, 2009 20: 1833-1844; Liang et al. 2010 21: 2024-2033; Silvis et al. 2009 20: 2337-2350), and Journal of Cell Science (Huang et al., 2011).

Membrane trafficking is a particular strength of the Department with research covering the entire spectrum of traffic-related issues from general mechanisms of protein and lipid trafficking, endocytosis and membrane organelle biogenesis, to cargo-specific mechanisms of anterograde and endocytic trafficking of receptors, transporters and channels. An example of the recognition and leadership of our faculty in the trafficking field is apparent in the content of a recent issue of *Nature Reviews in Molecular and Cell Biology* that was entirely dedicated to endocytosis. Among four full scholarly reviews in this issue, two were from the CBP Department, written by Drs. Traub and Sorkin. Furthermore, CBP faculty continue to present their research at international and national meetings, participate in NIH and other grant review panels and other organizational and service activities, all reflecting their influence in the respective research areas.

The majority of the CBP faculty continue to maintain active, funded research programs and have had remarkable success in obtaining new extramural research funding in the past cycle, as evidenced by the renewal of both the Cystic Fibrosis (Frizzell) and Networks and Pathways (Watkins) Center grants, and the competitive renewal of RO1 funding (Devor, Frizzell, Sorkin, Walker). Four senior faculty, Drs. Frizzell, Sorkin, Wu and Watkins, have multiple NIH grants. All three junior faculty, Drs. Butterworth, Hong and Thibodeau are now principal investigators on NIH funded grants. This is an impressive achievement in the current funding environment. Submission of new grant applications remains to be at high rate which ensures relative fiscal stability of the Department.

The first new recruit, Dr. Christine Wu, has joined the Department in September 2010. Christine plans to combine her interest in membrane proteomics and expertise in mass-spectrometry, with the existing expertise in cell biology and structure-function analysis of membrane proteins of the faculty in the CBP Department.

Two Centers associated with the Department represent particular strengths of the Department and the School. The Center for Biologic Imaging (CBI) is one of the largest imaging facilities in the country and provides state-of-the-art equipment and indispensible expertise in all types of cellular imaging to faculty of the Department and the entire School of Medicine. In the last year, the CBI was awarded multiple shared instrumentation grants from the NIH for live cell and confocal microscopes, which are essential to the continued growth of departmental infrastructure. The Center for Cystic Fibrosis is an example of a successful and well established program based on a coherent mix of the basic and translational science. Our faculty participates in NIH funded program projects (Fluorescent Probes and Imaging for Networks and Pathways;



Center for HIV Protein Interactions; Molecular Biology of Hemorrhagic Shock) and is involved in multiple collaborations with basic science faculty and divisions of the Departments of Medicine and Pediatrics, as well as with the researchers at Carnegie Mellon University. Individual CBP Faculty hold major roles in organization of the annual "Local Traffic" symposium, running the Membrane Trafficking journal club and in various School committees.

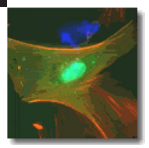
Teaching
Medical Curriculum: The department contributes extensively to the teaching of medical and graduate students in the School of Medicine. Our faculty has been actively participating in the remodeling of the first year curriculum, particularly in the area of biochemistry and cell biology, involving formal lectures in these areas and contributing to small group PBLs.

Graduate Curriculum: We now have 9 students in the graduate Ph.D. program in Cell Biology and Molecular Physiology. Thanks to the efforts of the program director, Dr. Walker, and newly formed CBMP program committee we were successful in attracting several new students to the program. Multiple students graduated in the last year, returning to medical school as MD/PhD students, or taking positions as postdoctoral fellows. In addition, CBP faculty participate in other graduate programs under umbrella of the Medical School Interdisciplinary Biomedical Graduate Program, as well as in the Departments of Bioengineering, Biological Sciences, Neurobiology among others.

Administration: FY2010-11 was the first full year since the new chair, Dr. Sorkin, joined the Department. All of the committees in the Department have undergone restructuring. Vice-chair, Dr. Watkins, has assumed leadership in both the Promotion and Space committees, and also carries a significant amount of other administrative duties in helping Dr. Sorkin with the transition to his new administrative role. The administrative staff, headed by Susan Conway, has done an excellent job in providing various levels of support to the research, teaching and service activities. There have been additional and substantial loads placed on the administration due to extensive changes in the faculty and the associated transfer of multiple grants to and from the Department, as well as with changes in the administrative staff. The fact that the transition was successfully accomplished in a timely and efficient manner attests to the experience and strength of our administrative staff.

Weaknesses
While not a problem at the present time, limited research space will likely become a weakness of the program in the future. There is presently unoccupied space in BST South due to the departures of Drs. Coyne and Zhao, and the relocation of Dr. Salama to Cardiology. However, this space may not be sufficient in order to recruit new faculty. In addition, more space will be required to allow for growth of the research programs of the current faculty located at BST South. Several of the CBP faculty members operate on different campuses. Dr. Frizzell's laboratory is located in the Children's Hospital in Lawrenceville, and Drs. Wan and Leuba are at the Hillman Cancer Center. There is clear separation from the rest of the Department leading to a lesser engagement of these three laboratories in the main activities of the Department at Oakland campus.

Opportunities
The vision of the new chair, and the leadership of the School, is to focus our research program



towards basic cell biology and build a premier Department of Cell Biology. The key to accomplishing this task is the recruitment of focused and creative new faculty. We plan to recruit three additional faculty whose research programs focus on fundamental questions of cell biology. The importance of the successful recruitment of strong faculty to shape the future of the department, while achieving a healthy balance of junior and senior faculty members, is difficult to overemphasize.

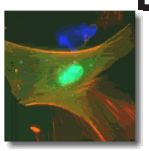
The influx of discretional funds with arrival of new chair has made it possible to re-vitalize important departmental activities that were stalled due to the lack of funding in the past. These functions include the annual departmental retreat and the weekly seminar series. There is also an opportunity to improve the departmental infrastructure including the needs for common equipment and a well designed web page. A new post-doctoral seminar series will allow better engagement of post-doctoral fellows in departmental activities, promote the establishment of new collaborations, and aid in preparing post-doctoral trainees to independent careers.

Threats

The steady decrease in federal and private funding opportunities will continue to be the most significant threat during next several years. Yet, in order for the Department to become one of the elite cell biology departments, total funding of the Department must increase 2-fold above the current level.

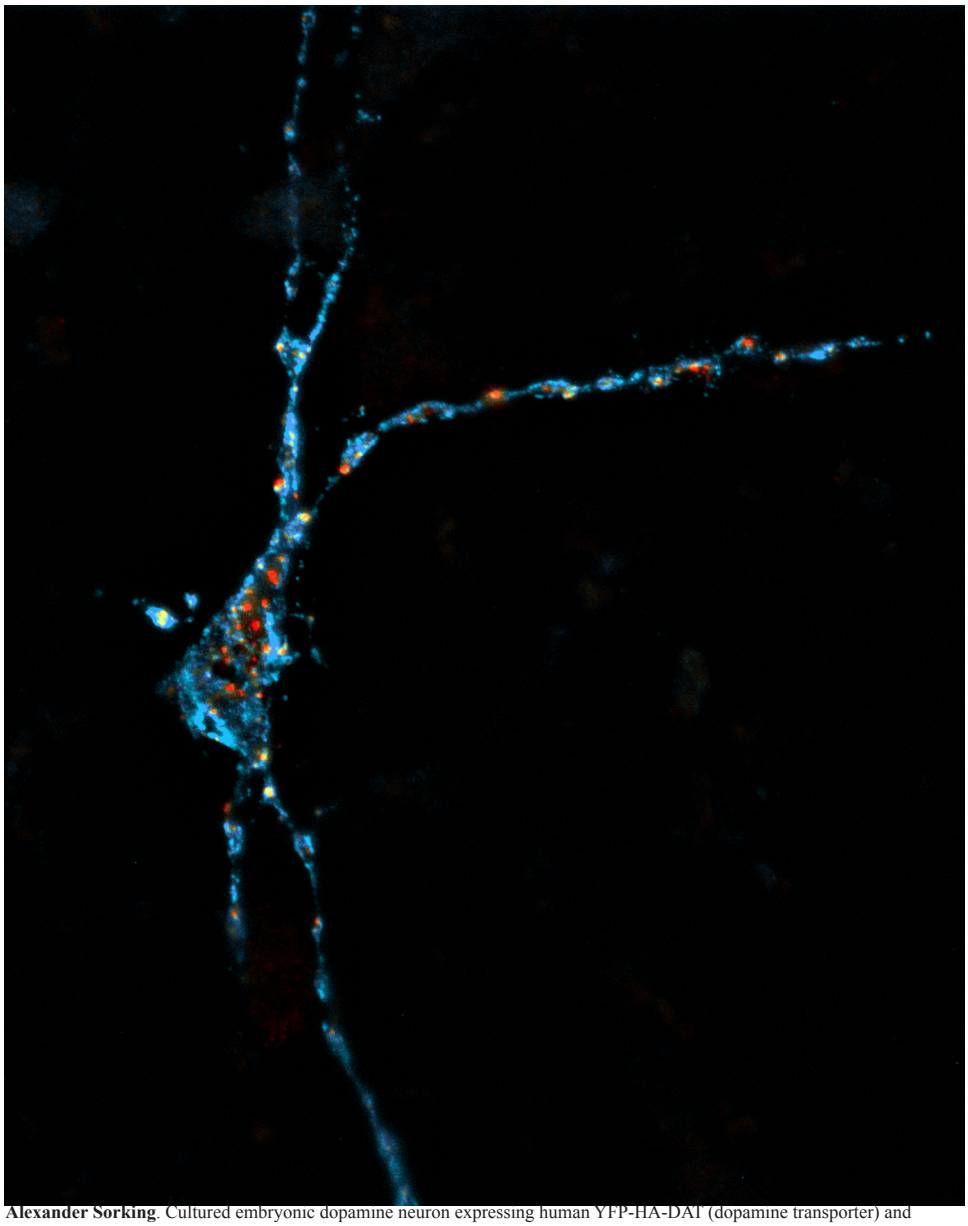
Another problem, though temporary, is the reduction in the number of the primary faculty in the Department, resulting in increased individual loads in service and teaching.

One of the biggest and difficult challenges we face is the strengthening of the Cell Biology and Molecular Physiology Graduate Program through the recruitment of top-tier students and provision of the best possible training environment in the laboratories of the Department. In this regard, a significant threat to student recruitment and training is the significant cost of maintaining graduate students in investigator laboratories at a time when research funding is in jeopardy.

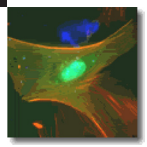


Cell Biology and Physiology FY2012 Fiscal Issues

There are no serious budgetary issues that face the Department in the FY12 budget. Main efforts will be devoted to ensure that every primary faculty has sufficient external funding to support their research program, and that the departmental infrastructure continues to improve.

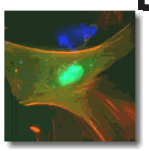


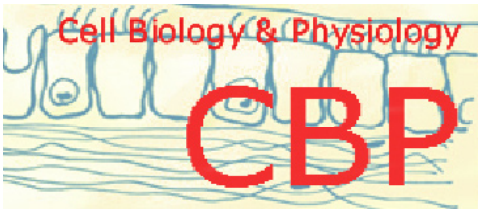
Alexander Sorking. Cultured embryonic dopamine neuron expressing human YFP-HA-DAT (dopamine transporter) and stained with Cy5 (blue, plasma membrane) and Cy3 (red, endosomes) conjugated antibodies.



University of Pittsburgh School of Medicine
University of Pittsburgh Physicians
DEPARTMENT OF CELL BIOLOGY AND PHYSIOLOGY
Schedule of Revenue and Expenses Fiscal Year 2011 Budget

	University	UPP and Other	Total Budget FY 2011
Revenue			
Patient Care	$ -	$ -	$ -
Grant:			
Directs	4,614,214	-	4,614,214
Indirects	1,798,823	-	1,798,823
Hospital Contract	-	-	-
School of Medicine	3,170,766		3,170,766
VAMC		-	-
Other	351,747	-	351,747
Total Revenue	$ 9,935,550	$ -	$ 9,935,550
Expenses			
Salaries and Fringe Benefits:			
Faculty	$ 3,152,282	$ -	$ 3,152,282
Non-Faculty	2,881,517	-	2,881,517
Malpractice Insurance		-	-
Space Rental	365,696	-	365,696
UPP Overhead		-	-
University Overhead	2,184,893		2,184,893
Other Operating Expenses	1,351,162	-	1,351,162
Total Operating Expenses	$ 9,935,550	$ -	$ 9,935,550
Excess Revenue over Expenses	$ -	$ -	$ -
Capital Equipment/Improvements	$ -	$ -	$ -
Fund Balances			
University Restricted Accounts as of 6/30/10	$ 4,773,725	$ -	$ 4,773,725
University Endowments as of 6/30/10	351,747		351,747
UPP Fund Balance as of 6/30/10		-	-
UPMC Endowments as of 6/30/10		-	-
UPMC SPF Accounts as of 6/30/10		-	-
Total Fund Balances	$ 5,125,472	$ -	$ 5,125,472





Thank you for your kind attention.