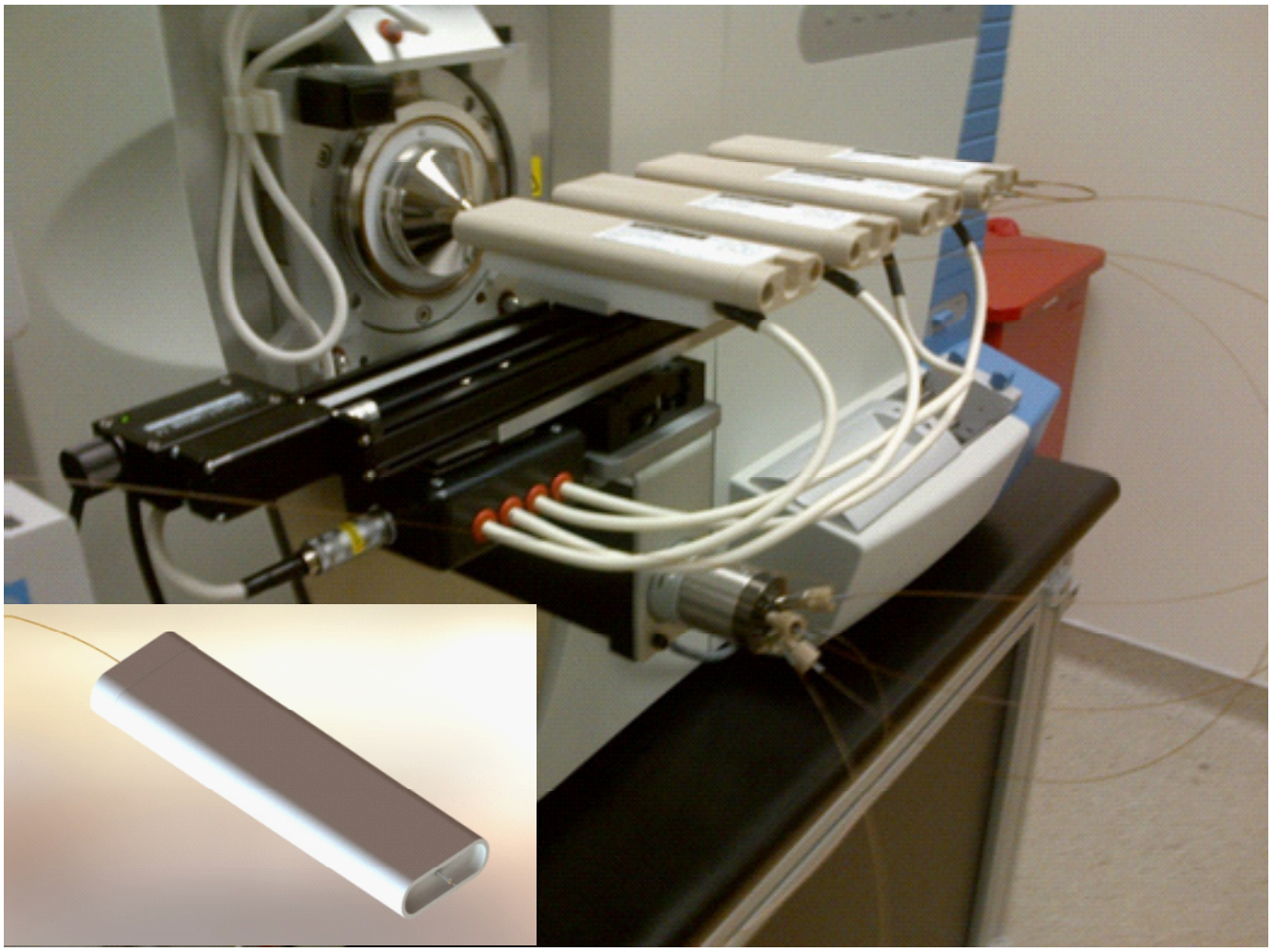
UNIVERSITY OF PITTSBURGH
SCHOOL OF MEDICINE

CELL BIOLOGY



FY12 ANNUAL REPORT
AND
FY13 BUSINESS PLAN

Front Page

Cover figure by Dr. Nathan Yates. In collaboration with industry, the Yates lab is developing modular electrospray “chips” that separate and ionize complex mixtures of peptides and proteins prior to mass spectrometry analysis (insert). Here, the modular nanoLC columns have been integrated into a proteomic assembly line that increases the throughput and reproducibility of analysis, while decreasing cost . The modular columns are an initial step towards the development of “plug and play” proteomics assays that have numerous basic and clinical applications.

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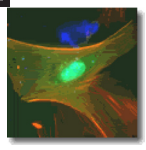


Department of Cell Biology

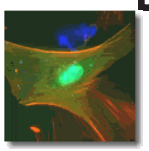
In the cell, life is governed by a multitude of molecular systems that shape and sustain the organellar system of the cell, maintain cellular homeostasis and respond to extracellular cues. These systems are dynamic, multicomponent macromolecular complexes. Maintaining and regulating the function of these complexes is essential for normal cell motility, growth, division, differentiation and programmed death. Dysregulation inevitably leads to an aberrant cell behavior and commonly disease. Understanding the structure, function and interactions of these macromolecular machineries 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 employs an interdisciplinary approach to address broad spectrum questions in cell biology from the roles of single molecules to through complex multi-component 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 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 seventeen primary faculty with extensive 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, Magee Women's Research Institute 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. Nathan Yates, Ph.D.

The systematic goal motivating our work is to develop and apply powerful mass spectrometry



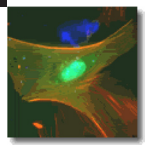
based tools that represent a new "microscope" for studying biology and advancing efforts to understand and treat disease. By integrating mass spectrometry, automation, and informatics, we are developing new analytical tools for the characterization and quantification of complex biological systems. These –omics tools provide exciting opportunities to probe biology with absolute molecular specificity, however, significant hurdles must be cleared before these tools have widespread impact in basic and clinical research. A specific aim of our research is to develop distributed informatics tools and mass spectrometry data analysis techniques. Prior to joining the University of Pittsburgh, Dr. Yates' work at Merck & Co. Inc. led to the invention and eventual the commercialization of Differential Mass Spectrometry (dMS). dMS is an efficient MS based method for comparing complex biological systems involving an un-biased analysis of all ions detected by full scan MS, not just ions that have corresponding MS/MS spectra.

The lab is also focused on the development of innovative technologies that are designed to improve the throughput and reliability of quantitative proteomics assays. In collaboration with several industry partners, the Yates lab is developing modular electrospray "chips" that separate and ionize complex mixtures of peptides and proteins prior to mass spectrometry analysis. Integration of modular nanoLC columns into a proteomic assembly line increases the throughput and reproducibility of analysis, while decreasing cost. The modular columns are an initial step towards the development of "plug and play" proteomics assays that have numerous basic and clinical applications.

A major emphasis of the laboratory is to develop distributed informatics tools that will enable biologists, clinicians, and ultimately patients to utilize proteomic data. In collaboration with academic and industrial partners, the Yates lab is creating a cloud based repository that can store and analyze large public and private proteomics data sets. New "unstructured" search algorithms are being developed that will help users find context relevant data amidst Petabytes of unrelated mass spectrometry data.

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



Department of Cell Biology
2012 Research Activities

Biomedical research in the Department of Cell Biology 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.

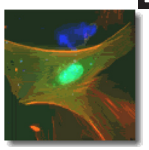
Regulation of Channels and Transporters

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
Kwiatkowski
Murray
Stoltz
Traub
Watkins

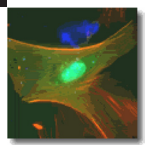


This group uses various state-of-the-art cell imaging, biochemical and genetic approaches to define the mechanisms involved in development and maintenance of epithelial cell polarity, regulation of gap junctions, angiogenesis and vasculogenesis, and various routes of functional communication between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

Regulation of Intracellular Signaling and Gene Expression

Drain
Leuba
Sorkin
Wan
Yates

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.



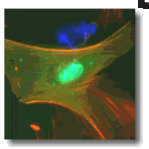
Center for Biologic Imaging

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



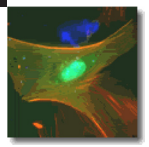
Petabyte tape library.

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 within the School of Medicine. His experience in microscopic methods covers most of the present light and electron microscopic methodologies.

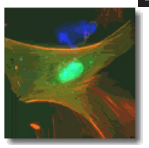
The Assistant Director: Dr. Donna Beer-Stolz is an Associate Professor in Cell Biology. Her funded research interests are in liver regeneration and vasculogenesis. She has been the Assistant Director of the CBI for 12 years to this date. She was recruited specifically to facilitate interactions between 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, bookkeeping, solution preparation, etc.



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



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 in 1997. It was renewed in 2002 and 2007 and 2011. 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.

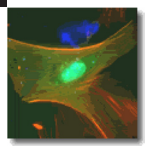
In 1998, this 'seed' funding from the CFF was supplemented by the award of NIH program funding in the form of a P50 SCOR. The P50 funding was renewed was renewed in the form of P30 Core Center grants in 2004 and 2010, each of which took decidedly more clinical turns. The latest P30 Core Center is entitled, "Basic and Clinical Studies of Cystic Fibrosis", and three such Centers were awarded nationally in the last funding round.

The primary goal of the CF Research 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. Thus, the CFRC 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 the Adult Pulmonary Division of the Department of Medicine. The CFRC is directed by Raymond A. Frizzell, Ph.D., with extensive interactions with clinical colleagues and co-Directors, Joseph Pilewski, M.D. (Dept of Medicine) and Jay Kolls, M.D. (Dept of Pediatrics and Director, Richard King Mellon Foundation Institute for Pediatric Research).

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:

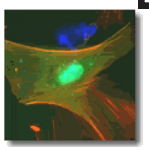
Human Airway Cell and Assays Core: This core provides access to patient materials obtained as a result of lung transplant activities in the Department of Surgery. This core offers well differentiated primary cultures of human bronchial epithelia to facilitate a variety of pre-clinical



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]

Cell Imaging Core: This core is housed within the Center for Biologic Imaging of the Department of Cell Biology. 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 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 at the cell surface, in collaboration with investigators at Carnegie Mellon University. [Core Director: Simon Watkins, Ph.D., Cell Biology]

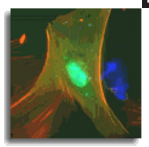
Clinical Studies Core: This core provides facilities and personnel for implementing clinical trials. It provides procedures for identifying functional outcomes, monitored in terms of lung function, radioisotope clearance, ion transport, inflammatory mediator levels or gene expression. It maintains patient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

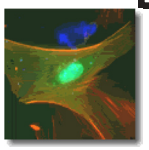


Cell Biology Faculty Data

[Current as of June, 2012]

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
Kwiatkowski, Adam	Assistant Professor	S324 BST-South Wing	adamkwi@pitt.edu	412-383-8139	412-648-8330
Leuba, Sanford	Associate Professor	2.26g Hillman Cancer Center	leuba@pitt.edu	412-623-7788	412-623-4840
Murray, Sandra	Professor	S313 BST-South Wing	smurray@pitt.edu	412-648-9566	412-648-8330
O'Donnell, Allyson	Res. Asst. Professor	321 Langly Hall	allyod@pitt.edu	412-624-8147	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
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
Yates, Nathan	Associate Professor	MWRIN B401	yatesn@pitt.edu	412-641-8148	412-641-2458





Cell Biology
Research Seminar Schedule 2011-2012

September 9, 2011
Gergely Lukacs, M.D.
Professor, Canada Research, Chair, Department of Physiology,
McGill University
"The Cell Biology of CFTR Folding"

September 13, 2011
John Yates, Ph.D.
Professor, Chemical Physiology
Scripps Research Institute
"Driving Biological Discovers using Quantitative Proteomics"

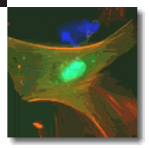
October 4, 2011
Robert Coffey Jr.,M.D.
Professor of Medicine & Cell and Developmental Biology
Vanderbilt University Medical Center
"New Ways of Thinking about the EGF Receptor in Colon Cancer"

October 18, 2011
Yi Sun, M.D., Ph.D.
Associate Prof, Director, Division of Cancer Biology, Department of Radiation Oncology,
University of Michigan School of Medicine
"SAG E3 ubiquitin ligase regulates angiogenesis and carcinogenesis"

December 6, 2011
Joerg Bewersdorf, Ph.D.
Assistant Professor, Department of Cell Biology and Biomedical Engineering
Yale University School of Medicine
"Towards Live Cell 3D Nanoscopy: Advances in Super-resolution Microscopy"

December 20, 2011
Arjumand Ghazi, Ph.D.
Assistant Professor, Pediatrics
Children's Hospital of Pittsburgh
"Sex, Worms & Aging"

February 16, 2012
Linda Van Aelst, Ph.D.
Professor, Cold Spring Harbor Laboratory
"Rho Regulators in Neuronal Development and Disease"

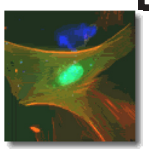


March 13, 2012
Richard Morimoto, Ph.D.
Professor of Biochemistry, Molecular Biology and Cell Biology
Northwestern University, Chicago
"The Stress of Misfolded Proteins in Biology, Aging and Disease"

April 17, 2012
Daniela Rotin, Ph.D.
Professor of Biochemistry, The Hospital for Sick Children
University of Toronto
Biological functions of the Nedd4 family of ubiquitin ligases"

April 24, 2012
Peter S. McPherson, Ph.D.
James McGill Professor, McGill University, Director, CBET Group
Montreal Neurological Institute
"The ins and outs of membrane trafficking: identification of a novel protein module controlling Rab GTPases"

May 1, 2012
Charlotte Vines, Ph.D.
Assistant Professor, Microbiology, Molecular Genetics and Immunology
University of Kansas Medical Center
"CCR7 Regulation of Signaling During Homeostasis and Disease"



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

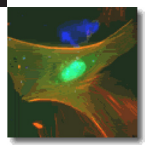
Our laboratory studies lymphatic endothelial function. We have developed a 3 dimensional tissue culture system to study potential mechanisms of lymphatic failure. Despite the fact that the lymphatic vessels were identified hundreds of years ago, limited understanding exists of lymphatic development, function, and disease. The breadth and significance of the roles of lymphatics in inflammation, immune response, metastasis, in addition to the generally accepted role of fluid transport, are beginning to be appreciated. 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 (e.g., women post breast cancer therapy).

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

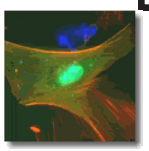


to characterize the mechanisms that underlie channel regulation by membrane trafficking in the mammalian kidney. Three renal transporters, namely the epithelial sodium channel (ENaC), potassium channel (ROMK) and aquaporin water channels are investigated. The work aims to map the intracellular itinerary 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.

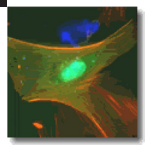
First, Mark Bailey, a graduate student in the lab, is carrying out patch-clamp studies designed to elucidate the role of S6 in the gating of KCa3.1. In these studies, we are employing PCMBS to probe the cysteines in S6 and evaluate their role in gating. PCMBS has advantages over MTS reagents in both 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.

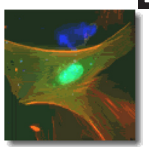


Given that KCa3.1 is targeted to the basolateral membrane in polarized epithelia, where it plays a critical role in the generation of the electromotive driving force required for Ca2+-dependent agonists to stimulate Cl- and fluid secretion, an additional project, being undertaken in collaboration with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

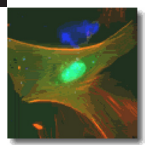


clamping. We can then determine whether mutations at conserved amino acids to those identified by us in mammalian channels will produce similar phenotypes, including increased Ca2+ sensitivity; allowing us to evaluate the effect of a hyperactive phenotype on function at the level of an intact organism. 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.

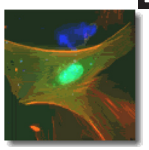
Trainees in our laboratory have the opportunity to combine the techniques of molecular genetics and confocal live-cell fluorescence imaging, with transgenic techniques to integrate understanding at the level of the molecule, organelle, whole cell, organ, and organism.

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, physiology workshops,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 2012, 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 nine 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

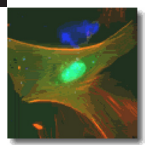
Dr. Frizzell's interests concern the mechanisms of salt and water transport in secretory and absorptive epithelia and pathways that regulate these processes. Specifically, we are defining defects in ion transport regulation in the genetic disease, cystic fibrosis (CF), membrane trafficking of wild-type 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.

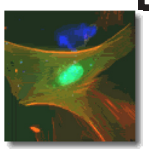
Dr. Gay's current interests are concerned with the neuronal networks that regulate pulsatile LH secretion in transgenic mice and in non-human primates. He has described a theoretical and highly speculative pattern of neuronal development that might serve to explain both the long delay and the rapid onset 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 amodel system, we aim to elucidate the fundamental mechanisms underlying the cell polarization by studying 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 first developed a novel genetic tool termed "genomic engineering" that allows targeted, 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. Taking advantage of the new and genetically validated fluorescent protein knock-in alleles of these key polarity proteins, a major research focus in the lab is to investigate the in vivo biosynthetic turnover and membrane redistribution dynamics of polarity proteins during apical-basal polarization. We are interested in elucidating how such dynamics regulates the polarity protein interactions to control the establishment and maintenance of apical-basal polarity. In addition, we recently discovered that cellular stresses directly regulate the subcellular relocalization process of certain polarity proteins, suggesting a previously unknown mechanism by which these proteins control cellular survival and tumorigenesis.

Adam Kwiatkowski, Ph.D.
Assistant Professor

The regulated assembly and organization of specific actin networks drive cell morphology, movement and adhesion. Changes in cell behavior are required to form complex tissue structures during development and must be accompanied by transitions in actin organization.



However, the molecular mechanisms governing actin network transitions are poorly understood. The goal of the lab is to understand how actin networks are assembled and organized to regulate cell morphology, movement and adhesion during development. We use a combination of protein biochemistry, cell biology, high-resolution microscopy and developmental biology to study actin dynamics at the molecular, cellular and organismal levels.

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:

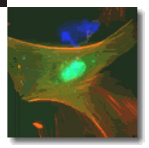
- We have been able to use AFM to detect conformational changes in chromatin fiber structure due to the presence of 24 methyl groups per nucleosome (Karymov et al., 2001) implying that the combined action of the DNA methylation and linker histone binding required to compact chromatin may affect the transcription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

- 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.

- 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.

- We have used spFRET to demonstrate the wrapping of DNA around the archaeal homohexameric MCM helicase from Sulfolobus solfataricus (Graham et al., NAR 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.

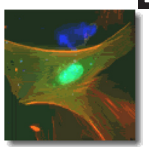
- In collaboration with Li Lan, Satoshi Nakajima and Vesna Rapic-Otrin (Molecular Genetics and Biochemistry), we have studied the ability of an E3 ligase to ubiquitinate histone H2a and destabilize nucleosomes with UV-damaged DNA (Li et al., JBC 2012).

- We have used spFRET to demonstrate that PcrA DNA helicase displaces RecA but not RecA mutants (Fagerburg et al., NAR 2012) 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.

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



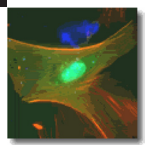
gap junction plaque endocytosis. Four different techniques (time-lapse video microscopy, immunocytochemistry, quantum dot immuno-electron microscopy, and western blot analysis) are being used to examine the role of clathrin and protein phosphorylation in gap junction protein (connexin) trafficking, including 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 cDNA antisense vectors, 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).

Allyson O'Donnell, Ph.D.
Research Assistant Professor

Nearly half of all prescription drugs alter G-protein coupled receptor (GPCR) signaling, including treatments for asthma, hypertension, neurodegenerative disorders and depression. β-arrestins are critical regulators of GPCRs: they act as trafficking adaptors to control GPCR endocytosis, impede G-protein signaling and are themselves therapeutic targets. However, β-arrestins are only a small branch of the larger arrestin family that includes the widely-conserved but functionally uncharacterized α-arrestins, the primary focus of my research. My work has shown that α-arrestins, like β-arrestins, regulate GPCR signaling, but also operate in unexpected trafficking pathways, including endosomal recycling and clathrin-independent endocytosis. Using Saccharomyces cerevisiae as a model, I've identified α-arrestin interactions with signaling regulators, cargos and vesicle coat proteins, and have begun to define the molecular mechanisms underlying α-arrestin-mediated trafficking. All of the α-arrestin-interacting partners identified in yeast are conserved. My research will apply insights gained in yeast to initiate studies on the relatively unstudied mammalian α-arrestins.

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

The cystic fibrosis transmembrane conductance regulator (CFTR) must reside in the apical plasma membrane to perform its primary function as a chloride channel that mediates cAMP-dependent salt and water secretion in epithelial cells. We investigate apical membrane CFTR trafficking in Calu-3 cells, an airway serous cell model that expresses endogenous CFTR because airway disease is the major cause of mortality and morbidity in CF. We see interactions between syntaxin 4 and CFTR as evidenced by co-immunoprecipitation experiments; biotinylation experiments show that cells subjected to cAMP stimulation by forskolin and 3-isobutyl-1-methylxanthine (IBMX) exhibit greater quantities of CFTR in the plasma membrane. Using adenovirus-mediated transduction of Calu-3 cells together with functional assays measuring 6-methoxy-N-(3-sulfopropyl) quinolinium (SPQ) fluorescence, we investigate the effects on CFTR of knocking down syntaxin 4. Our data suggest that syntaxin 4 mediates the insertion of CFTR into the apical membranes of Calu-3 cells to control its apical density and the magnitude of stimulated anion efflux.



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.

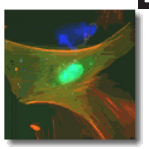
Alexander D. Sorkin, Ph.D.
Professor, Chairman of Department

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 tissue 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 incompletely understood. 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. Additional research concentrations include vascular and parenchymal changes in liver and kidney with normal aging and in mouse models of accelerated aging.

Dr. Stolz is Associate Director of the Center for Biologic Imaging and directs the electron microscopy facility of CBI. Her main role as Associate Director of CBI is to facilitate PI usage with the facility, as well as assist in design, execution and interpretation of experiments involving



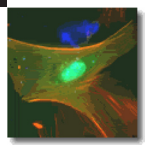
all types of imaging technologies in general. Additionally, she coordinate interactions of PIs and students with other arms of the CBI, including widefield and confocal microscopy as well as live cell imaging.

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

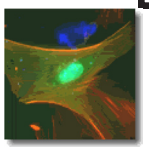
Research interests in my laboratory focus on the role of ubiquitin-dependent proteolysis in biological regulation. Currently, we are studying the control of cell cycle progression by proteolytic regulation. We are also interested in investigating the role of proteolysis in the regulation of the DNA damage-repair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

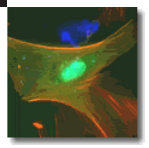
Christine Wu, Ph.D.
Associate Professor

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).



Nathan Yates, Ph.D.
Associate Professor

The systematic goal motivating our work is to develop and apply powerful mass spectrometry based tools that represent a new "microscope" for studying biology and advancing efforts to understand and treat disease. By integrating mass spectrometry, automation, and informatics, we are developing new analytical tools for the characterization and quantification of complex biological systems. These –omics tools provide exciting opportunities to probe biology with absolute molecular specificity, however, significant hurdles must be cleared before they tools have widespread impact in basic and clinical research. A specific aim of our research is to develop distributed informatics tools and mass spectrometry data analysis techniques. Prior to joining the University of Pittsburgh, Dr. Yates' work at Merck & Co. Inc. led to the invention and eventual the commercialization of Differential Mass Spectrometry; an unbiased quantitative proteomics method for comparing complex biological systems. The lab is also focused on the development of innovative technologies that are designed to improve the throughput and reliability of quantitative proteomics assays. In collaboration with several industry partners, the lab is developing "easy to use" assay platforms that will enable scientists in basic and clinical research.



Study Sections (Fiscal Year 2011-2012)

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

ASIRC - Italian Association for Cancer Research; Standing Member

Donna Beer Stolz, Ph.D.
Associate Professor

NIDDK GRB-8 (J1) December 2 –Digestive Diseases Core Centers Meeting Study Section (4 imaging core grants).

Yong Wan, Ph.D.
Associate Professor

Molecular Oncogenesis Study Section (MONC), NIH, Ad Hoc Reviewer (2011)

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

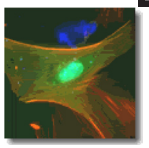
NIH Study Section NIH_IMST 16 SBIR-STTR, November 10th 2011 Chair
NIH study section: Feb 22nd 2012 Panelist
NIH study section SBIRs March 15 2012 Chair
NIH study section June 14th 15th 2012, P30's Panelist
ACS Study Section (Peer Review Committee on Clinical Cancer Research and Epidemiology) Atlanta GA), June 20th-21st 2012 Chair of Panel
NIH Study section (Washabagh) June 29thth 2012 Panelist
Canadian Foundation for Innovation, July 12th-14th Study section for Infrastructure. Chair of Panel
NIH study section, R03's (2012/10 ZAR1 EHB (M1) 1) July18th 2012 Panelist

Christine Wu, Ph.D.
Associate Professor

NIH/CSR U54 Roadmap Study Section: NIH/NCRR (S10 Shared Instrumentation Grants, PAR-09-118) (07/27/11-07/28/11)

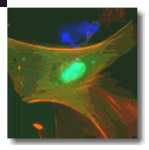
NIH/NIDDK (Nutrition Obesity Research Centers (P30) applications, NORC Program Announcement) (03/12/12-03/13/12); NIH/NCRR (S10 Shared Instrumentation Grants, PAR-012-017) (09/06/12-09/07/12)

NIH/CSR EBIT Study Section 2010 – 2014 (4 year appointment)



Nathan Yates, Ph.D.
Visiting Associate Professor

NIH CSR S10 Shares Instrumentation Grants (2010- 2011)
NIH CSR S10 High End Instrumentation Grants (2011)



Faculty Advisory Committee Memberships (Fiscal Year 2011-2012)

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 Space Committee
Cell Biology Faculty Recruitment Committee

Michael Butterworth, Ph.D.
Assistant Professor

Cell Biology Departmental Retreat Committee
Cell Biology Space Committee

Daniel Devor, Ph.D.
Professor

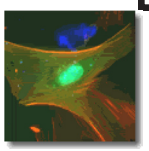
Cell Biology Departmental Tenure and Promotions Committee
Cell Biology Faculty Recruitment Committee
Chair, Interdisciplinary Biomedical Graduate Program Recruiting Committee

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 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
FAST Advisor – First year medical students



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

CFF Medical Advisory Council

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

Sanford Leuba, Ph.D.
Associate Professor

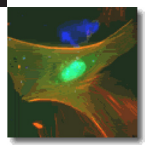
Nanoscale Biophysics Subgroup Meeting of the Biophysical Society

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
Cell Biology 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

Cell Biology Tenure and Promotions Committee
Cell Biology Faculty Recruitment Committee
External Advisory Committee for Nevada's Cell Biology COBRE Grant, University of Nevada School of Medicine, Reno, NV
Member at Large, School of Medicine Executive Committee

Donna Beer Stolz, Ph.D.
Associate Professor

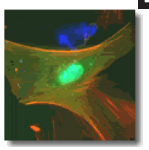
University of Pittsburgh School of Medicine Interdisciplinary Biomedical Graduate Program-Cell Biology and Molecular Physiology Program Admissions Committee
Assistant Director - Cell Biology and Molecular Physiology Program
Interdisciplinary Biomedical Graduate Program Admissions Committee Tour Guide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

Patrick H. Thibodeau, Ph.D.
Assistant Professor

Interdisciplinary biomedical graduate program admissions committee, ad hoc member, 2011-2012.
Interdisciplinary biomedical graduate program admissions committee, CBMP representative, 2012-2013
Cell Biology Retreat Committee

Linton M. Traub, Ph.D.
Associate Professor

University of Pittsburgh School of Medicine Health Sciences Research Advisory Committee
Cell Biology Tenure and Promotions Committee
Cell Biology Faculty Recruitment Committee
Cell Biology Space Committee
Planning Committee of Local Traffic Symposium on intracellular membrane traffic



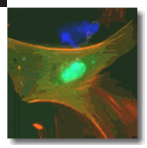
Simon C. Watkins, Ph.D.
Professor and Vice Chairman, Director of Center of Biologic Imaging

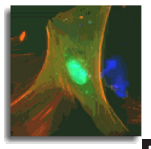
Cell Biology Tenure and Promotions Committee
Cell Biology Student Advisory Committee
Cell Biology Space Committee
Cell Biology Faculty Recruitment Committee
Graduate Program, Curriculum Committee
University of Pittsburgh School of Medicine, Research Advisory Committee
University of Pittsburgh Cancer Institute Core Resources 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 Faculty Recruitment Committee
Advising for Genomics and Proteomics Core laboratories (GPCL).

Cell Biology/Pharmacology Machine Shop

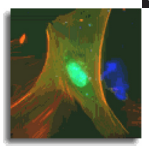


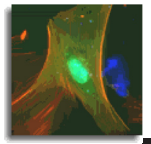


Cell Biology and Physiology Sponsored Research Funding (FY12)

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
Meir Aridor	National Institutes of Health	COPII Organization and Vesicle Formation at ER Exit Sites	25050	12901
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	4460	2296
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	13213	5969
Carol Bertrand	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Pilot # 3	12525	6450
Carol Bertrand	Cystic Fibrosis Foundation	Role of SLC26A9 in CFTR Biogenesis and Anion Secretion in Airway Epithelia	22500	1800
Michael Butterworth	National Institutes of Health	EnaC regulation in the kidney by vesicle trafficking and recycling	166951	80829
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	245298	126327
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	42474	21875
Peter Drain	National Institutes of Health	Alzheimers Disease Research Center - Pilot	17888	9212
Wayne Ernst	Cystic Fibrosis Foundation	Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting	43968	0
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	0	0
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	143959	68965
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	0	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 Institutes of Health	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	181382	93091
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	74941	5945
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	274881	127302
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis - Administrative Supplement	22000	11330
Alexander Sorkin	National Institutes of Health	SPORE in Lung Cancer_DRP	8750	4506
Alexander Sorkin	National Institutes of Health	Deubiquitination of EGF receptor: Target in Head and Neck Cancer	14583	0
Donna Beer Stolz	National Institutes of Health	Mechanisms for Arsenic-Induced Vascular Disease	8231	4239
Donna Beer Stolz	National Institutes of Health	Mediators of Fibrosis in Scleroderma Skin and Lung	2957	1523
Donna Beer Stolz	National Institutes of Health	Regulation of the Endcytic Trafficking of CFTR	15970	8224
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	44176	22751
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	46602	24000
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	32368	14524
Donna Beer Stolz	National Institutes of Health	Endogenous Regulators of Inflammaion in Liver Ischemia/Reperfusion	8991	4632
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	56482	29089
Simon Watkins	National Institutes of Health	Hepatocellular Carcinoma in Antitrypsin Deficiency	17823	9179
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	22727	11704

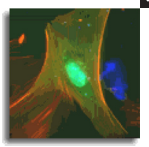


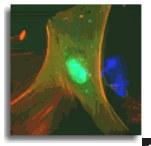


Simon Watkins	National Institutes of Health	Improving Chromic Neural Recording Performances Through Biomaterial Strategies	8561	4409
Simon Watkins	National Institutes of Health	DC T Interactions in Pulmonary Immune Responses	12016	6188
Simon Watkins	National Institutes of Health	Intracellular Serpin Regulation of Intestinal Cell Necrosis	2440	1257
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	46038	23710
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	7,328	3,774
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	84,754	43,648
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	80,221	40,822
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	8,426	4,339
Simon Watkins	National Institutes of Health	Adipose Triglyceride Lipases (ATGL) in Liptoxicity and the Metabolic Syndrome	5,086	2,619
Simon Watkins	National Institutes of Health	Stem Cells for Corneal Engineering	20,337	10,088
Simon Watkins	Army	Molecular and Functional Characterization of the Lupus Platelet	24,652	12,052
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Core B	5,949	2,891
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Project 1	13,823	6,861
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
Simon Watkins	National Institutes of Health	Identifying and Facilitating Ventricular Recovery on Mechanical Support	2,876	1,481
Simon Watkins	Army	Human Hepatocytes for Treatment of Life-Threatening Liver Injury	15,883	8,179
Simon Watkins	National Institutes of Health	Imaging Mass Spectrometry for Oxidized Lipidomics in Acute Lung Injury	12,146	5,396
Simon Watkins	National Institutes of Health	ROS Mechanims in BAV Aortopathy	983	507
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
			6,077,887	2,102,540

Cell Biology and Physiology Sponsored Research Funding (FY13)

First Name	Agency Name	Title	Annual DC	Annual IDC
Meir Aridor	National Institutes of Health	COPII Organization and Vesicle Formation at ER Exit Sites	150000	77250
Catherine Baty	National Institutes of Health	Structure-Function Relationships in the IL-17 Receptor	2605	1341
Catherine Baty	National Institutes of Health	Obesity Related Pancreatic Fat Worsens Local Injury via Unsaturated Fatty Acids	11710	6030
Carol Bertrand	Cystic Fibrosis Foundation	Role of SLC26A9 in CFTR Biogenesis and Anion Secretion in Airway Epithelia	90000	7200
Michael Butterworth	National Institutes of Health	EnaC regulation in the kidney by vesicle trafficking and recycling	124585	60299
Michael Butterworth	National Institutes of Health	Pittsburgh Center for Kidney Research	1038	534
Daniel Devor	National Institutes of Health	Assembly and trafficking of IK1 and SK3 in Endothelia	224991	115870
Peter Drain	National Institutes of Health	Anesthetic Sites in Transmembrance Peptides by NMR	1396	719
Peter Drain	Pittsburgh Foundation	Molecular Medicine in Shared Novel Secretory Mechanism Underlying Diabetes, Alzheimers Disease, and Parkinsons Disease	3663	0
Peter Drain	Army	Towards a Possible Therapy for Diabetes Complications	10730	5526
Wayne Ernst	Cystic Fibrosis Foundation	Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting	38151	0
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	0	0
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	132974	77158
Raymond Frizzell	Cystic Fibrosis Foundation	Program Enrichment and Administration Core	0	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	230237	18419
Raymond Frizzell	National Institutes of Health	Chaperone Actions in CFTR Biogenesis	35133	18093
Raymond Frizzell	National Institutes of Health	Traffic Regulatory Proteins and ENaC	208143	92187
Yang Hong	National Institutes of Health	Regulation of Adherens Junction Dynamics by Polarity Proteins	183508	90964
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	74941	5995
Sandra Murray	National Science Foundation	Gap Junction Plaque Internalization	110602	50422
Alexander Sorkin	National Institutes of Health	EGF Receptor Signaling in Time and Space in Tumor Cells	167661	86345
Alexander Sorkin	National Institutes of Health	Dopamine Transporter Regulation by Endocytosis	254552	106231
Alexander Sorkin	National Institutes of Health	SPORE in Lung Cancer_DRP	26250	13519
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	259598	116044
Alexander Sorkin	National Institutes of Health	Deubiquitination of EGF receptor: Target in Head and Neck Cancer	20417	0
Donna Beer Stolz	National Institutes of Health	Mechanisms for Arsenic-Induced Vascular Disease	3328	1714
Donna Beer Stolz	National Institutes of Health	Mediators of Fibrosis in Scleroderma Skin and Lung	2916	1502





Donna Beer Stolz	National Institutes of Health	Regulation of the Endcytic Trafficking of CFTR	14895	7671
Donna Beer Stolz	Massachusetts Institute of Tech.	Perfused 3D Tissue Surrogates for Complex Cell-Cell Communication Systems	43933	22625
Donna Beer Stolz	Army	Escape from Tumor Cell Dormancy	11708	6030
Donna Beer Stolz	National Institutes of Health	Ex Vivo Adipose Tissue as a Screening Tool	6491	3342
Donna Beer Stolz	National Institutes of Health	Endogenous Regulators of Inflammaion in Liver Ischemia/Reperfusion	9725	5008
Donna Beer Stolz	National Science Foundation	Engineering Research Center	5417	2360
Patrick Thibodeau	National Institutes of Health	Regulated Biosynthesis and Function of ABC-Transport Systems	250000	128749
Patrick Thibodeau	Cystic Fibrosis Foundation	Structural Interactions Regulating CFTR Channel Function	53991	4319
Linton Traub	National Institutes of Health	Clatherin-coated vesicles and endocytic function	15772	7959
Simon Watkins	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	40000	0
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	6618	3408
Simon Watkins	National Institutes of Health	Novel Stategies for Brain Tumor Therapy	42048	21655
Simon Watkins	National Institutes of Health	Hepatocellular Carcinoma in Antitrypsin Deficiency	13428	6915
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	22727	11704
Simon Watkins	National Institutes of Health	Improving Chromic Neural Recording Performances Through Biomaterial Strategies	711	366
Simon Watkins	National Institutes of Health	DC T Interactions in Pulmonary Immune Responses	5878	3027
Simon Watkins	National Institutes of Health	Intracellular Serpin Regulation of Intestinal Cell Necrosis	2466	1270
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	39545	20366
Simon Watkins	National Institutes of Health	Amplification of IL-4Ralpha Signaling Pathways in Human Airways Through 15 LO1	5,982	2,248
Simon Watkins	National Institutes of Health	Multiple Tumor Antigen-Loaded DC Vaccine for Hepatocellular Cancer	6,643	3,421
Simon Watkins	National Institutes of Health	Multi-Disciplinary Approaches to Driving Therapeutic Human Beta Cell Replication	11,354	5,847
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	82,634	42,557
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	83,805	37,237
Simon Watkins	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	152,490	71,448
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	8,707	4,484
Simon Watkins	National Institutes of Health	Adipose Triglyceride Lipases (ATGL) in Liptoxicity and the Metabolic Syndrome	5,117	2,636
Simon Watkins	National Institutes of Health	Stem Cells for Corneal Engineering	20,544	9,421
Simon Watkins	Army	Molecular and Functional Characterization of the Lupus Platelet	8,707	3,840
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Core B	5,566	2,008
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Project 1	12,549	5,175
Simon Watkins	National Institutes of Health	PINK1 Regulation of Neuronal and Mitochondrial Homeostasis	4,000	2,060
Simon Watkins	Army	Human Hepatocytes for Treatment of Life-Threatening Liver Injury	21,336	10,987

Simon Watkins	National Institutes of Health	Imaging Mass Spectrometry for Oxidized Lipidomics in Acute Lung Injury	24,513	10,563
Simon Watkins	National Institutes of Health	Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging	11,289	5,814
Christine Wu	National Institutes of Health	Quantitive Proteomic Analysis of Alcoholic Fatty Liver Biogenesis	245,665	126,518
			4,129,625	1,654,148

Faculty Editorships (Fiscal Year 2011-2012)

Michael B. Butterworth, Ph.D.
Assistant Professor

American Journal of Physiology – Renal Physiology
Frontiers in Renal and Epithelial Physiology
World Journal of Biological Chemistry
PLoS ONE

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

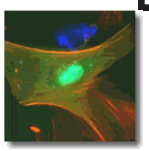
Molecular Biology of the Cell
Traffic
Current BioData Ltd

Donna Beer Stolz, Ph.D.
Associate Professor

Editorial Board: Cell Transplantation: The Regenerative Medicine Journal. Hepatocyte section.

Linton Traub, Ph.D.
Associate Professor

Member of editorial board of Traffic
Member of editorial board of Cellular Logistics
Member of editorial board of Scientific Reports
Member of editorial board of The Journal of Biological Chemistry
Member of board of reviewing editors, Molecular Biology of the Cell



Yong Wan, Ph.D.
Associate Professor

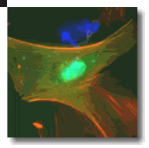
Member, Editorial Board, Journal of Biological Chemistry

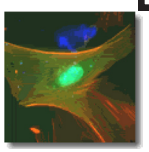
Simon C. Watkins, Ph.D.
Professor and Vice Chairman, Director of Center of Biologic Imaging

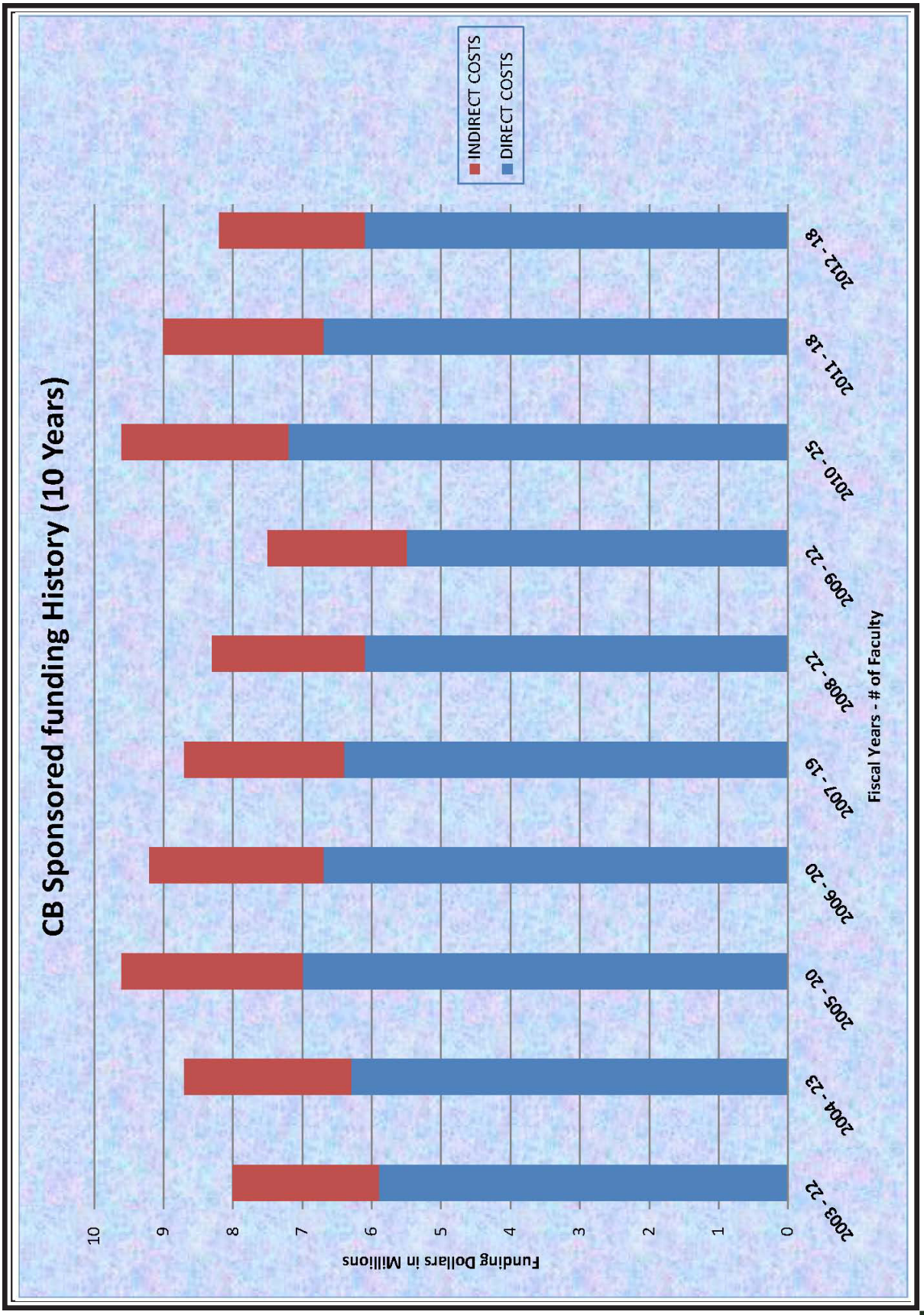
Member, Editorial Board, PittMed
Associate Editor, Experimental Biology and Medicine
Editor, Current Protocols in Cytometry
Editor, Experimental Science and Medicine

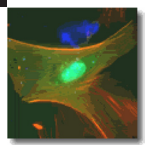
Christine C. Wu, Ph.D.
Associate Professor

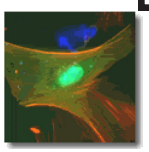
Editorial Board, Neurochemical Research
Editorial Board, Amino Acids (Proteomics Section)






CB Sponsored funding History (10 Years)
INDIRECT COSTS
DIRECT COSTS
Funding Dollars in Millions
0
1
2
3
4
5
6
7
8
9
10
2003 - 22
2004 - 23
2005 - 20
2006 - 20
2007 - 19
2008 - 22
2009 - 22
2010 - 25
2011 - 18
2012 - 18
Fiscal Years - # of Faculty

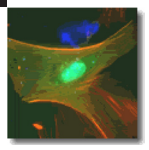




CB FACULTY ROSTER
(Effective June, 2012)

Faculty Member	Salary Support on Grants	Rank	Status
Baty, Catherine	100%	Res. Assistant Professor	Non-tenure Track
Bertrand, Carol	100%	Res. Assistant Professor	Non-tenure Track
Liang, Xiubin	100%	Res. Assistant Professor	Non-tenure Track
Peters, Kathryn	100%	Res. Assistant Professor	Non-tenure Track
Watkins, Simon*	89%	Professor	Tenured
Thibodeau, Patrick	70%	Assistant Professor	Tenure Track
Frizzell, Raymond*	69%	Professor	Tenured
Stolz, Donna	67%	Associate Professor	Tenured
Hong, Yang	56%	Assistant Professor	Tenure Track
Butterworth, Michael	51%	Assistant Professor	Tenure Track
Devor, Daniel	50%	Associate Professor	Tenured
Drain, Peter	45%	Associate Professor	Tenured
Wu, Christine	41%	Associate Professor	Tenured
Traub, Linton	40%	Associate Professor	Tenured
Sorkin, Alexander*	38%	Professor	Tenured
Murray, Sandra	16%	Professor	Tenured
Leuba, Sanford	8%	Associate Professor	Tenured
Aridor, Meir	0.2%	Associate Professor	Tenured

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

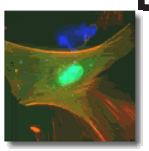


STUDENTS INVOLVED IN RESEARCH IN CB FACULTY LABS

Snapshot as of June, 2012

GRADUATE STUDENTS ENROLLED IN CBMP PROGRAM

STUDENT	LAB	SUPPORT
Cavita Chotoo	Dan Devor, Ph.D. Cell Biology	Dan Devor, Ph.D. Cell Biology
Elizabeth Delorme-Axford	Carolyn Coyne, Ph.D. MMG	Carolyn Coyne, Ph.D. MMG
Kathryn Wack	Donna Stolz, Ph.D. Cell Biology	Donna Stolz, Ph.D. Cell Biology
Xinxian Qiao	Peter Drain, Ph.D. Cell Biology	Peter Drain, Ph.D. Cell Biology
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



Cell Biology Training Grants
FY12 and FY13

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

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 $79,119 in FY12 (Total costs, annualized).

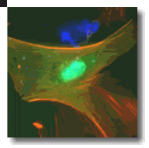
FY13 Projects

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

The combined funding for this post doctoral fellowship grants is $38,151 in FY13 (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:

FY12 Program Grant Training Funds - $70,000
FY13 Program Grant Training Funds - $70,000

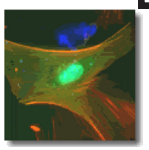


Cell Biology Program Grants (Fiscal Year 2011-12)

The Department of Cell Biology is funded for three Program Grants, two 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.

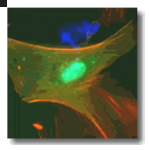
This program grant totaled $969,447 (total costs) in FY12.



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 $460,000 (total costs) in FY12. 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.

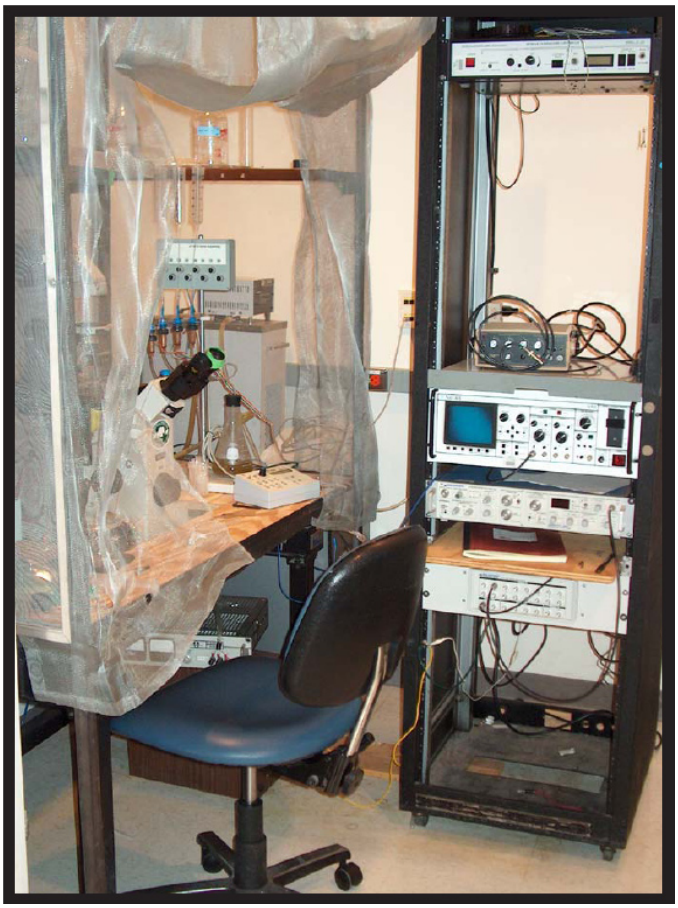
National Technology Centers for Networks and Pathways
(Principal Investigators –Simon Watkins, Ph.D.):
Over the last several years, microscopy as a scientific tool has reinvented itself. It has changed from a group of principally descriptive methodologies, to a wide range of quantitative tools and

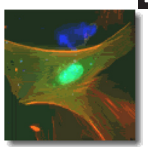


techniques to investigate the molecular organization of organs, tissues and cells. The University of Pittsburgh and Carnegie Mellon University (CMU) are homes to two of the leading imaging laboratories in the country; developing and applying novel fluorescent imaging tools to cutting edge biomedical 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 $219,525 (total costs) in FY12 .

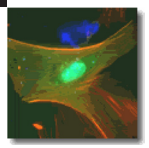
Electrophysiology Patch Clamp





New CB Research Recruits in FY12

Name	Rank	
Faculty Level		
Adam V. Kwiatkowski	Assistant Professor	
Allyson F. O'Donnell	Research Assistant Professor	
Nathan A. Yates	Associate Professor	
Name	**Rank**	**Lab Association**
Post Doctoral Level		
John P. Holleran	Post Doctoral Associate	Drs. R. Frizzell/S. Watkins
Itziar Pinilla-Macua	Post Doctoral Associate	Dr. Alexander D. Sorkin
Yanchao Ran	Post Doctoral Associate	Dr. Patrick Thibodeau
Xiaohui Wang	Post Doctoral Associate	Dr. Raymond Frizzell
Shouhui Yang	Post Doctoral Associate	Dr. Yong Wan
Xuejing Zhang	Post Doctoral Associate	Dr. Yang Hong
Zhuan Zhou	Post Doctoral Associate	Dr. Yong Wan



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, cellular and molecular biology to understand the integrated functions of cells, tissues, organs and model 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.

CBMP students have the opportunity to develop their teaching and mentoring skills by participating as instructors for the histology laboratory sections taught to first and second year medical students. Student instructors assist the medical students in using microscopes and presentations to identify tissues and cells as well as to understand the functions of the tissues and cells that they are observing. Teaching responsibilities normally require approximately 5 to 10 hours per month of preparation and teaching time. Prior to becoming instructors, the CMBP students are required to take the graduate level course in Histology (MSCBMP2870), which will prepare them for their teaching responsibilities. Senior students may have the opportunity to develop and present lectures in the graduate Histology Course. Beyond the teaching experience, these fellowships also provide students with funding for the majority of their stipend and tuition for two years.

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 metabolic, developmental and reproductive functions.

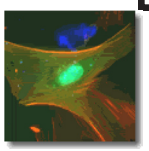
Cell Communication and Imaging

Controlled cell-cell communication is the basis of tissue homeostasis. Member faculty use a variety of techniques to study these phenomena.

Gerard Apodaca, Ph.D. (Medicine, Renal)
Yang Hong, Ph.D.
Jes Klarland, Ph.D. (Opthalmology)
Adam V. Kwiatkowski, Ph.D.
Sandra Murray, Ph.D.
Claudette St Croix, Ph.D. (EOH)
Donna Beer Stolz, Ph.D.
Simon C. Watkins, Ph.D.

Cellular Injury and Wound Healing

James L. Funderburgh, Ph.D. (Opthalmology)



David Hackam, M.D., Ph.D. (Children's Hospital)
Rama K. Mallampalli, M.D. (Medicine)
Sandra Murray, Ph.D.
Gary Silverman, M.D., Ph.D. (Children's Hospital)
Nirmala SunderRaj, Ph.D. (Opthalmology)
Shivalingappa Swamynathan, Ph.D. (Opthalmology)

Chromatin, DNA Repair, Cell Cycle Control, Gene expression and Cancer

Areas of study include the regulation of chromatin structure and repair 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.

Arjumand Ghazi. Ph.D. (Children's Hospital)
Sanford Leuba, Ph.D.
Laura Niedernhofer, M.D., Ph.D. (UPCI, adjunct Scripps Institute, Jupiter, FL)
Shivalingappa Swamynathan, Ph.D. (Opthalmology)
William Walker, Ph.D. (MWRI)
Yong Wan, Ph.D. (UPCI)
Judith Yanowitz, Ph.D. (MWRI)

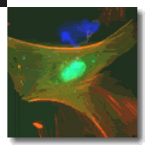
Ion Channel Biology

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.

Michael B. Butterworth, Ph.D.
Daniel C. Devor, Ph.D.
Raymond A. Frizzell, Ph.D. (Children's Hopsital)
Kenneth Hallows, M.D., Ph.D. (Medicine, Renal)
Thomas R. Kleyman, M.D. (Medicine, Renal)
Guy Salama, Ph.D. (Medicine, Cardiology)
Arohan Subramanya, M.D. (Medicine, Renal)
Patrick Thibodeau, Ph.D.

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.

Gerard Apodaca, Ph.D. (Medicine, Renal)
Meir Aridor, Ph.D.
Jeffrey Brodsky, Ph.D. (Biological Sciences)
Carolyn Coyne, Ph.D. (Microbiology and Molecular Genetics)
Yang Hong, Ph.D. (UPCI)
Rebecca Hughey, Ph.D. (Medicine, Renal)
John Johnson, Ph.D. (Medicine, Renal)
Tom Kleyman, M.D. (Medicine, Renal)
Sandra Murray, Ph.D.
David Perlmutter, M.D. (Children's Hospital)
Alexander Sorkin, Ph.D.
Agnieszka Swiatecka-Urban, M.D. (Children's Hospital)
Linton Traub, Ph.D.
Ora Weisz, Ph.D. (Medicine, Renal)

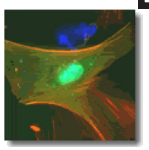
Regulation of Gene Expression during Development

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.

Arjumand Ghazi, Ph.D. (Children's Hospital)
Judith Yanowitz, Ph.D. (MWRI)
Donna Beer Stolz, Ph.D.
Simon C. Watkins, Ph.D.
Yang Hong, Ph.D.

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.



Jennifer Condon, Ph.D. (MWRI)
Arjumand Ghazi, Ph.D. (Children's Hopsital)
Nuria Pastor-Soler, M.D., Ph.D. (Medicine, Renal)
Tony Plant, Ph.D. (MWRI)
Aleksandar Rajkovic, M.D., Ph.D. (MWRI)
Abhirim Sahu, Ph.D. (MWRI)
Gerald P. Schatten, Ph.D. (MWRI)
William Walker, Ph.D. (MWRI)
Judith Yanowitz, Ph.D. (MWRI)
Anthony Zeleznik, Ph.D. (MWRI)

Signal Transduction in Diabetes and Metabolism

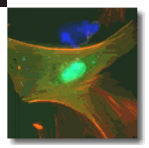
Regulated secretion of insulin by the pancreas and the actions of insulin and leptin in muscle, fat and liver cells are critical for controlling the body's energy metabolism. Disruption of these processes leads to diabetes or obesity. Researchers in this program are defining the cell signaling mechanisms 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.

Peter Drain, Ph.D.
Arjumand Ghazi, Ph.D. (Children's Hospital)
Abhiram Sahu, Ph.D. (MWRI)
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. See current resources at www.cbi.pitt.edu.
Additionally, Center faculty are active in teaching graduate courses in imaging technologies as well as their research specialties.

Director of CBI: Simon Watkins, Ph.D.
Associate Director: Donna Beer Stolz, Ph.D.
Assistant Director: Claudette M. St. Croix, Ph.D.



Courses in the Cell Biology and Molecular Physiology Graduate Program

New Courses in FY12

Title: Reproductive Development from Model Organisms to Humans
Course Number: 3840
Course Directors: Jennifer Condon-Jeysuria and Judith Yanowitz
When: Fall Term
Prerequisites: None

Description: This course focuses on the molecular aspects of the transition from gamete to a reproductive organism. The course progresses through the building of germ cells, fertilization and stem cell participation to sex determination, gonad morphogenesis, puberty, menopause and pregnancy. This course highlights both human and model organisms to bring together diverse aspects of the cell and developmental biology of reproductive tissues and their impact on disease pathology.

Title: Imaging Cell Biology in Living Systems
Course Number: 2885
Course Director: Simon Watkins
When: Fall Term
Prerequisites: None

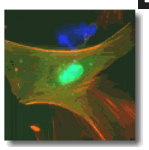
Description: The focus of this course is to study relevant problems in Cell Biology, Immunology, Developmental Biology and Neurobiology and how they have been solved using imaging approaches. The course will follow a Lecture/Demo/Journal Club format. Lectures will be interspersed with a journal club discussion of a relevant paper on each technology.

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 2011 – June 2012

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.

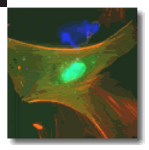
Title: Research Seminar in Cellular Biological Membrane Trafficking
Course Number: 2852
Course Director: Gerard Apodaca
When: Fall Term, Spring Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference
Core Course for: students in the Program in Cell Biology and Molecular 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

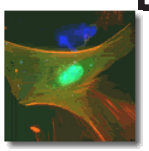
Description: a lecture/lab course that immerses students in the theory and practical aspects of modern microscopic imaging. The fields will cover the theory and implementation of all types of light and electron microscopy and computer aided imaging. Students will be expected to reach a functional capability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

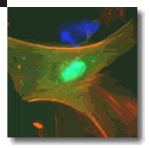
Title: Directed Study
Course Number: 2890
Course Director: William Walker
When: Fall Term, Spring Term, Summer Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

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

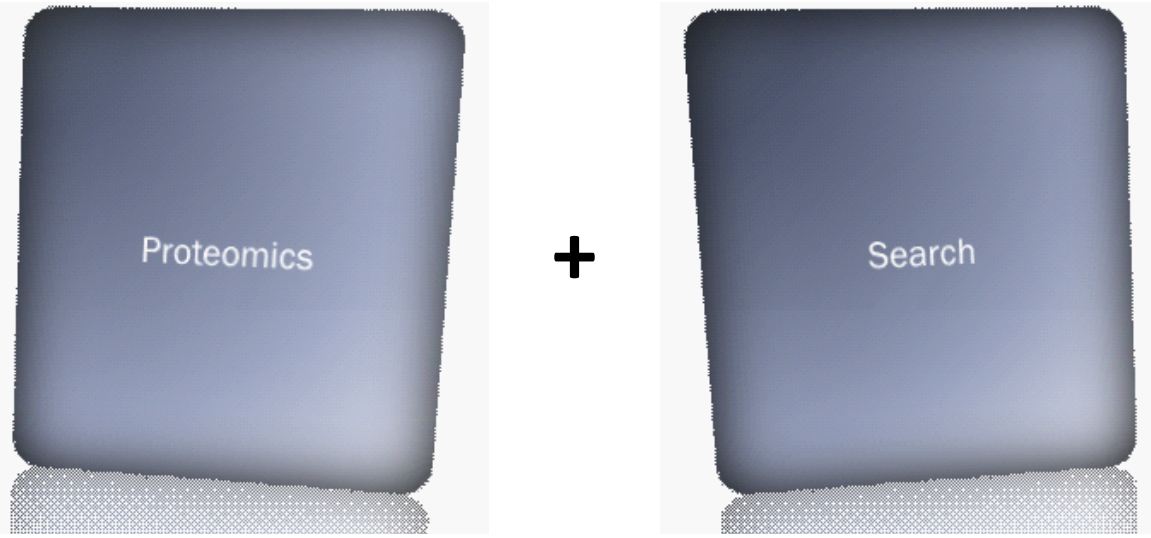


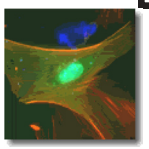
When: Fall Term, Spring Term
Prerequisites: INTBP 2000 Foundations of Biomedical Sciences
INTBP 2005 Conference

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%).

Proteomics@PITT

Nathan Yates. A major emphasis of the laboratory is to develop distributed informatics tools that will enable biologists, clinicians, and ultimately patients to utilize proteomic data. In collaboration with academic and industrial partners, the Yates lab is creating a cloud based repository that can store and analyze large public and private proteomics data sets. New "unstructured" search algorithms are being developed that will help users find context relevant data amidst Petabytes of unrelated mass spectrometry data .

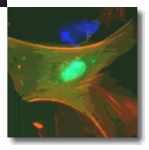




Faculty Teaching Honors (Fiscal Year 2011-2012))

Georgia K. Duker, Ph.D.
Assistant Professor

Excellence in Education Award (2011) - "Small Group Facilitator"
For first year Fundamentals of Basic Science - From the Medical Graduating Class of 2014



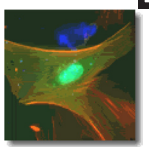
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE
EDUCATIONAL CREDIT UNIT REPORT (AY 2010 – 2011)

Department of Cell Biology

	# ECUs	% ECUs
Department of Cell Biology	**2397.8**	**13.3**
Combined Total for All Basic Science Departments	**18043**	**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	36.0	72.0
GS –Course Director	10.0	1.0	10.0
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	1.0	5.0
		Total ECU's:	105.0
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
Michael Butterworth, Ph.D.			
GS – Small group (e.g., PBL, conference, workshop)	2.0	4.0	8.0
		Total ECU's:	8.0
Daniel Devor, Ph.D.			
GS - Lecture	2.0	4.0	8.0
GS – Small group (e.g., PBL, conference, workshop)	2.0	2.0	4.0
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
		Total ECU's:	57.0
Peter Drain, Ph.D.			
MS 1, MS 2 – Lecture	2.0	1.3	2.5
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	18.5	37.0
MS 1 and MS 2 – 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 – Small group (e.g., PBL, conference, workshop)	2.0	4.0	8.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	3.0	15.0
		Total ECU's:	337.5

Georgia Duker, Ph.D.

MS 1, MS 2 – Lecture	2.0	18.5	37.0
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	85.5	171.0
MS 1, MS 2 – Laboratory	2.0	22.3	44.5
MS 1, MS 2 – Other	2.0	6.0	12.0
MS 1 and MS 2 – Course Director	100.0	1.0	100.0
MS 1 and MS 2 – TBL Designer	10.0	1.0	10.0
MS 1 and MS 2 – Course Segment Coordinator	5.0	2.0	10.0
MS –Coordinator, Undergraduate medical Education Teaching	5.0	1.0	5.0
MS – Chair, Task Force/Work Group/Subcommittee/or other SOM Committee	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	5.0	10.0
MS –Mentoring Scholarly Project (MSP) Mentor	25.0	1.0	25.0
MS –Elective Course Research Mentor	4.0	1.0	4.0
GS – Lecture	2.0	33.0	66.0
GS – Small group (e.g., PBL, conference, workshop)	2.0	12.0	24.0
GS – Other	2.0	6.0	12.0
GS – Course Director	10.0	1.0	10.0
		Total ECU's:	560.5

Raymond Frizzell, Ph.D.

MS 1 and MS 2 – AOC/Longitudinal Curriculum Program Director	20.0	1.0	20.0
MS – AOC/LCP activity (other than advising, e.g., teaching, precepting)	2.0	61.5	123.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	2.0	4.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	152.0

Vernon Gay, Ph.D.

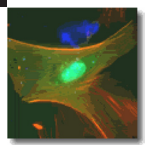
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	23.5	47.0
		Total ECU's:	47.0

Yong Hong, Ph.D.

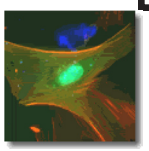
GS - Small group (e.g., PBL, conference, workshop)	2.0	6.0	12.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	3.0	15.0
		Total ECU's:	32.0

Sanford Leuba, Ph.D.

GS - Lecture	2.0	2.0	4.0
GS – Ph.D. or M.Sc. Mentor	20.0	2.0	40.0
GS – Course Director	10.0	2.0	20.0
GS – Member: 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	2.0	10.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	86.0



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	33.5	67.0
MS 1, MS 2 – Other	2.0	6.0	12.0
MS – Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	3.0	15.0
GS - Lecture	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:	121.0
Kathleen Ryan, Ph.D.			
MS 1, MS 2 – Lecture	2.0	5.8	11.5
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	33.0	66.0
MS 1, MS 2 – Other	2.0	5.3	10.7
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	5.3	10.5
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	14.0
MS – Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	2.0	10.0
		Total ECU's:	172.7
Alexander Sorkin, Ph.D.			
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	5.0
Donna Stolz, Ph.D.			
MS 1, MS 2 – Lecture	2.0	0.5	1.0
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	7.6	15.2
MS 1, MS 2 – Laboratory	2.0	18.9	37.8
GS - Lecture	2.0	1.0	2.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	23.8	47.5
GS – Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	10.0	10.0
GS – Course Director	10.0	1.0	10.0
GS – Program Director	30.0	1.0	30.0
GS – Member: Admissions Committee	5.0	1.0	5.0
GS –Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	3.0	6.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	5.0	25.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	12.0	60.0
		Total ECU's:	249.5
Patrick Thibodeau, Ph.D.			
GS - Lecture	2.0	2.0	4.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	17.0	34.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	4.0	20.0
		Total ECU's:	58.0
Lin ton Traub, Ph.D.			
GS - Lecture	2.0	4.0	8.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	6.0	12.0



GS – Ph.D. or M.Sc. Mentor	20.0	2.0	40.0
GS –Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
GS –Chair: Curriculum, Recruiting, Program, 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:	77.0

Yong Wan, Ph.D.

MS – Mentored Scholarly Project IMSP) Mentor	25.0	1.0	25.0
GS – Ph.D. or M.Sc. Mentor	20.0	1.0	20.0
GS – Mentoring other SOM graduate students (e.g., MSTP, Ph.D. or M. Sc.)	5.0	2.0	10.0
		Total ECU's:	55.0

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	88.5	177.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	6.0	12.0
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	3.0	15.0
		Total ECU's:	237.7

Christine Wu, Ph.D.

MS 3, MS 4 – Small group (e.g., PBL, conference, workshop)	2.0	1.5	3.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
		Total ECU's:	8.0

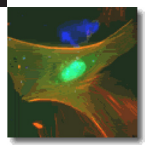
Total Faculty reporting 19 **Faculty ECU Subtotal: 2397.8**

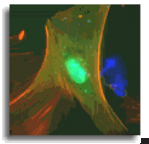
Precetpting ECU's not attributed to individual faculty

Required clerkship AY 10-11	1.0	0.0	0.0
Acting internship clerkship AY 10-11	1.0	0.0	0.0
Elective clerkship(s) where enrollment = 1 or more students AY 10-11	1.0	0.0	0.0

Precepting Subtotal: 0.0

Total ECU's for Cell Biology & Physiology: 2397.8





Post Doctoral Personnel Data
[Current as of June, 2012]

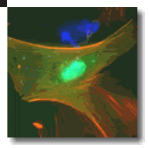
Name	Title	Office Address	Email Address	Office Phone	Fax	Research Focus
Ahner, Annette	Vis. Research Associate	7161 RANCH	aschneid@pitt.edu	412-648-8162	412-648-8330	Frizzell Lab
Balut Corina M.	Post Doctoral Associate	S331 BSTWR	cmb89@pitt.edu	412-383-7192	412-648-8330	Devor Lab
Bateman , Nicholas W.	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
Holleran, John P.	Post Doctoral Associate	S220 BSTWR	jph61@pitt.edu	412-648-9796	412-648-2797	Frizzell/Watkins 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
Pinilla-Macua, Itziar	Post Doctoral Associate	S372 BSTWR	itp2@pitt.edu	412-624-8147	412-648-8330	Sorkin Lab
Rajamanickam, Jeyaganesh	Post Doctoral Associate	S316 BSTWR	jer113@pitt.edu	412-648-8620	412-648-8330	Frizzell Lab
Ran, Yanchao	Post Doctoral Associate	S332 BSTWR	yar4@pitt.edu	412-624-0869	412-648-8330	Thibodeau Lab
Wang, Xiaohui	Post Doctoral Associate	S315 BSTWR	xiw68@pitt.edu	412-648-8620	412-648-8330	Frizzell Lab
Xue, Peng	Post Doctoral Associate	S332 BSTWR	pex3@pitt.edu	412-624-8933	412-648-8330	Thibodeau Lab
Yang, Shouhui	Post Doctoral Associate	2.7 Hillman Cancer	yangs5@upmc.edu	412-623-7811	412-623-7761	Wan Lab
Zhang, Liang	Post Doctoral Associate	S332 BSTWR	liz46@pitt.edu	412-624-8933	412-648-8330	Thibodeau Lab
Zhou, Wenke	Vis. Research Associate	S333 BSTWR	wez23@pitt.edu	412-648-2846	412-648-8330	Hong Lab
Zhou, Zhuan	Post Doctoral Associate	2.6 Hillman Cancer	zhouz2@upmc.edu	412-623-7811	412-623-7811	Wan Lab

STUDENTS INVOLVED IN RESEARCH IN CBP FACULTY LABS

Snapshot as of June, 2012

GRADUATE STUDENTS ENROLLED IN CBMP PROGRAM

STUDENT	LAB	SUPPORT
Cavita Chotoo	Dan Devor, Ph.D. Cell Biology	Dan Devor, Ph.D. Cell Biology
Elizabeth Delorme-Axford	Carolyn Coyne, Ph.D. MMG	Carolyn Coyne, Ph.D. MMG
Kathryn Wack	Donna Stolz, Ph.D. Cell Biology	Donna Stolz, Ph.D. Cell Biology
Xinxian Qiao	Peter Drain, Ph.D. Cell Biology	Peter Drain, Ph.D. Cell Biology
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



Graduates of the Cell Biology and Molecular Physiology Program as of June 2012
(Past five years)

Anupma Jha
Defended December 8, 2011

Siobhan Gregg
Defended November 4, 2011
Rockefeller University, New York City

Daniel Rho
Defended July 15, 2011
Medical Student

James R. Thieman
Defended June 9, 2011
Olympus Corporation

ShanShan Cui
Defended December 7, 2010
Cincinnati, Ohio

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

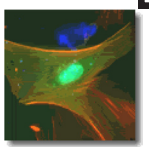
Paula J. Bernal
Defended August 12, 2010
Center for Vaccine Development, University of Maryland

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

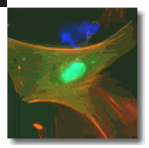
Mark Miedel
Defended August 27, 2008
University of Pittsburgh Medical School

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

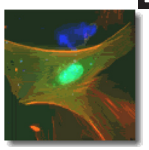


Student Ratings of CBMP Faculty Teaching FY2012

Name	Course	Type	Date	Rating	Ave
Butterworth	Methods and Logic in Medicine Part 2	SGCS	Fall-11	4.10	4.10
Drain	Methods and Logic in Medicine Part 2	SGCS	Fall-11	4.70	4.70
Duker	Introduction to Being a Physician	SGCS	Fall-11	4.40	
Duker	Body Fluid Homeostasis Cardiovascular	WKSP	Fall-11	4.80	
Duker	Body Fluid Homeostasis-Renal Segment	LEC	Fall-11	4.60	
Duker	Body Fluid Homeostasis-Pulmonary Segment	LEC	Fall-11	4.60	
Duker	Cellular and Pathological Basis of Disease	LEC	Spring-12	4.90	
Duker	Cellular and Pathological Basis of Disease	LAB	Spring-12	4.90	
Duker	Cellular and Pathological Basis of Disease	PBL	Spring-12	4.50	
Duker	Digestion and Nutrition	LEC	Fall-11	4.50	
Duker	Digestion and Nutrition	LAB	Fall-11	4.70	
Duker	Endocrine	LEC	Spring-12	4.90	4.68
Gay	Fuel Metabolism	PBL	Fall-11	4.80	4.80
Murray	Medical Anatomy	LAB	Fall-11	3.90	
Murray	Medical Anatomy	LEC	Fall-11	3.20	3.55
Ryan	Introduction to Being a Physician	SGCS	Fall-11	4.30	
Ryan	Body Fluid Homeostasis Cardiovascular	WKSP	Fall-11	4.40	
Ryan	Cellular and Pathological Basis of Disease	LEC	Spring-12	3.80	
Ryan	Digestion and Nutrition	LEC	Fall-11	3.80	4.08
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-12	4.40	
Stolz	Cellular and Pathological Basis of Disease	LAB	Spring-12	4.90	
Stolz	Cellular and Pathological Basis of Disease	PBL	Spring-12	5.00	
Stolz	Digestion and Nutrition	LAB	Fall-11	5.00	4.75
Thibodeau	Methods and Logic in Medicine Part 2	SGCS	Fall-11	4.80	4.80
Watkins	Cellular and Pathological Basis of Disease	LEC	Spring-12	4.00	4.00
	Overall Teaching Average			**4.48**	

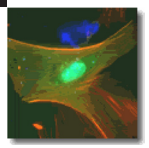
Type codes:

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



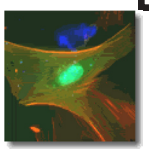
CB FACULTY ROSTER
(Effective June, 2012)

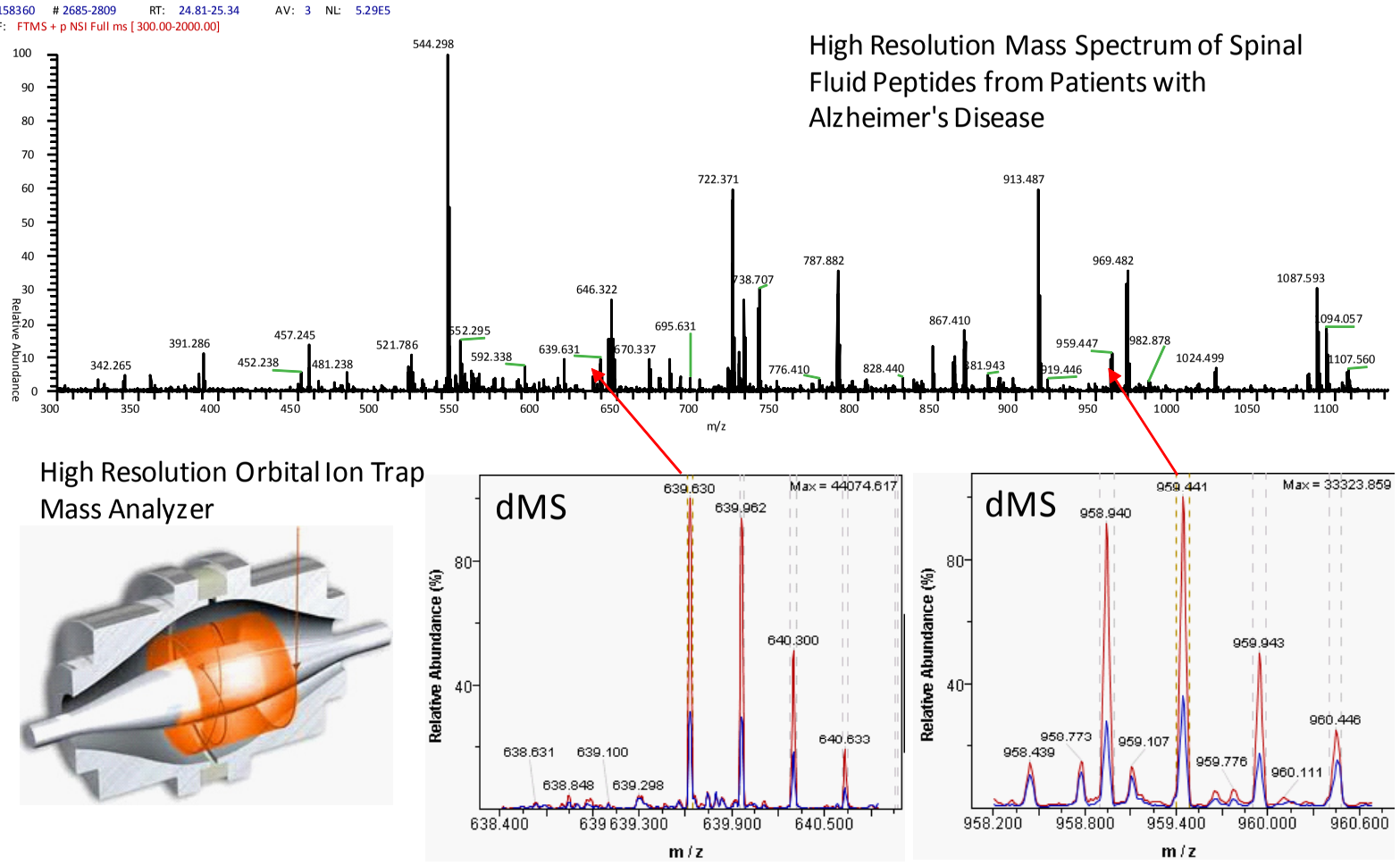
Last Name	First	Rank	Status
Sorkin	Alexander	Professor & Chair	Tenured
Devor	Daniel	Professor	Tenured
Frizzell	Raymond	Professor	Tenured
Murray	Sandra	Professor	Tenured
Watkins	Simon	Professor	Tenured
Aridor	Meir	Associate Professor	Tenured
Drain	Peter	Associate Professor	Tenured
Gay	Vernon	Associate 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
Yates	Nathan	Associate Professor	Non-tenure Track
Butterworth	Michael	Assistant Professor	Tenure Track
Hong	Yang	Assistant Professor	Tenure Track
Kwiatkowski	Adam	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
O'Donnell	Allyson	Res. Assistant Professor	Non-tenure Track
Peters	Kathryn	Res. Assistant Professor	Non-tenure Track



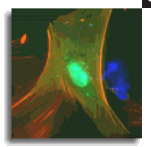
New CB Faculty in FY12

Name	Prior Institution /Rank	Current Rank
Adam V. Kwiatkowski	Stanford University Department of Biology Postdoctoral Fellow	Assistant Professor
Allyson F. O'Donnell	University of California At Berkeley Department of Molecular And Cell Biology Postdoctoral Fellow	Research Assistant Professor
Nathan A. Yates	Merck Research Laboratorries Exploratory and Translations Science Department Scientific Director	Associate Professor





Nathan Yates. Differential Mass Spectrometry (dMS) is an efficient MS based method for comparing complex biological systems. Un-biased analysis of all ions detected by full scan MS, not just ions that have corresponding MS/MS spectra. Here, the dMS method was used to discover candidate peptide biomarkers in archived cerebral spinal fluid samples from patients with and without Alzheimer's Disease.



Faculty Honors, Recognition and Professional Affiliations (Fiscal Year 2011-2012)

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

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

Michael Butterworth, Ph.D.
Assistant Professor

Member, American Physiological Society
Member, Elected Secretary, Salt and Water Club
Research Recognition Award, Renal Section APS, Experimental Biology

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

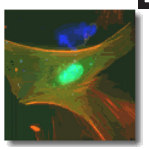
Member, Biophysical Society
Member, American Association for the Advancement of Science
Member, Society of General Physiologists
Member, American Diabetes Association
Academy of Master Educators (AME), University of Pittsburgh School of Medicine

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
Pitt Innovator Award

Yang Hong, Ph.D.
Assistant Professor

Member of Faculty 1000
Research Scholar, American Cancer Society



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

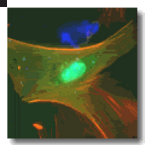
Member, American Society of Nephrology
Member, American Heart Association

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
Academy of Master Educators (AME), University of Pittsburgh School of Medicine
NIH - Biomedical Faces of Science Mentors

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
Member, American Physiological Society

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

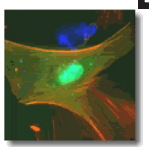
Member, American Association for Cancer Research
Member, American Association of Cell Biology
Member, American Association for The Advancement of Science

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

Member, The Pittsburgh Cancer Institute
Microscopy Society of America

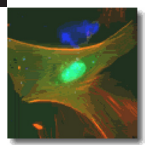
Christine Wu, Ph.D.
Associate Professor

American Society for Cell Biology (ASCB)
American Society for Mass Spectrometry (ASMS)
Research Society on Alcoholism (RSA)
American Chemical Society (ACS)
American Society for Pharmacology and Experimental Therapeutics (ASPET)



Nathan Yates, Ph.D.
Associate Professor

American Chemical Society
American Society for Mass Spectrometry
The Association for Biomolecular Resource Facilities
United States Human Proteomics Organization



Faculty Presentations (Fiscal Year 2011-2012)

Meir Aridor, Ph.D.
Associate Professor

"Cell Biology of CFTR Folding", CF Center, University of Pittsburgh, May, 2012

Carol Bertrand, Ph.D.
Research Assistant Professor

Ulrich Hopfer Symposium. Title: SLC26A9 interactions with wild type and mutant CFTR. 2012

Michael Butterworth, Ph.D.
Assistant Professor

"The regulation of microRNAs by aldosterone: Impact on ENaC". Physiology 2012. The Physiological Society Meeting, Edinburgh, UK.

"Regulation of the Epithelial Sodium Channel (ENaC): The Role of Protein Trafficking." Senior Vice Chancellor's Research Seminar 2012, University of Pittsburgh.

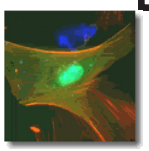
Daniel C. Devor, Ph.D.
Professor

"KCa2.3 and KCa3.1: Family members with unique trafficking itineraries" Georgia Health Sciences University, Department of Physiology, Augusta, GA

"Endocytosis, Recycling and Ubiquitylation of KCa2.3 and KCa3.1: Family members with unique endocytic itineraries" Wayne St. University School of Medicine, Department of Physiology, Detroit, MI

Yang Hong, Ph.D.
Assistant Professor

Invertebrate Neurobiology, Cold Spring Harbor Laboratory, Suzhou, China. June 2012
Molecular Medicine Research Seminar, Children's Hospital of Pittsburgh. May 2012
Department of Biology, John Hopkins University. November 2011
Program in Cell Dynamics, University of Massachusetts Medical School. October 2011
Spotlight Session "Imaging Systems for Imaging Systems", Science 2011, University of Pittsburgh. October 2012



Sanford H. Leuba, Ph.D.
Associate Professor

Pittcon, Orlando, Florida. March 2012.

Sandra Murray, Ph.D.
Professor

International Gap Junction Meeting, Ghent, Belgium, August 2011.

Allyson O'Donnell, Ph.D.
Research Assistant Professor

Arrestin Developments: New biological functions for the α-arrestin family of trafficking adaptors. Johns Hopkins University (2012), Baltimore, MD.

Yeast α-arrestins Aly1 and Aly2 regulate endosomal recycling in response to nutrient signaling. Pittsburgh Local Trafficking (2012), Pittsburgh, PA.

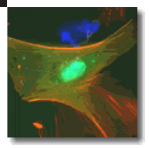
Alexander D. Sorkin, Ph.D.
Richard B. Mellon Professor and Chairman

University of Geneva (August 2011).
Department of Pharmacology, University of Pittsburgh (October 2011).
University of West Virginia (November 2011).
Department of Structural Biology, University of Pittsburgh (December 2011).
Department of Endocrinology, McGill University, Montreal, Canada (April, 2012)
EGF receptor, MD Anderson Center, September 2011
Membrane dynamics in cancer. Beatson International cancer conference, Glasgow, Scotland July, 2012

Donna Beer Stolz, Ph.D.
Associate Professor

Working your way through graduate school and your post-doc: making the most of the experience. Presentation to the Summer Undergraduate programs at Duquesne University. July 15, 2011.

Progeroid Mouse Model to Study Age-related Kidney Dysfunction. Cell Biology Retreat September 9, 2011.



Patrick H. Thibodeau, Ph.D.
Assistant Professor

"Basic cell biology of PXE: Understanding the molecular events underlying disease pathophysiology," European PXE Research Meeting, Budapest, Hungary, October, 2011.

"Conserved NBD-TMD interactions regulate the folding of ABC-transporter biosynthesis," European CF Basic science Conference, Ste Maxime, France, March, 2012.

"CFTR domain folding and domain-domain interactions." North American Cystic Fibrosis Conference, Anaheim, CA, 2011.

"The ABCs of cystic fibrosis: protein folding, misfolding and disease." Duquesne University, Pittsburgh, PA, March, 2012.

Linton Traub, Ph.D.
Associate Professor

"Clathrin-mediated endocytosis in developmental patterning" Dynamic endosomes: mechanisms controlling endocytosis EMBO meeting, Chania, Crete, Greece. September 2011

"Clathrin-mediated endocytosis in early development" 'Lysosomes and Endocytosis' Gordon Research Conference, Andover, NH. June 2012

Yong Wan, Ph.D.
Associate Professor

Proteolytic regulation of krupple like-factor 4 in the cell cycle control and carcinogenesis. Cold Spring Harbor Laboratory. Cell Cycle Conference 2012

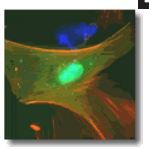
Post-translational modification of KLF4 in genomic integrity and cell cycle control. Emory University School of Medicine 2012

The role of UPS in DNA damage response and cancer formation. New York University 2012

CRS ubiquitin protein ligases and deubiquitinases in genome instability and tumorigenesis. George Washington University School of Medicine 2012

Ubiquitin-proteasome pathway in breast carcinogenesis, Western China Medical University 2012

Cross-talk between estrogen receptor and TGF-β signaling in carcinogenesis. University of Pittsburgh, Children's Hospital 2012



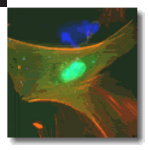
Simon C. Watkins, Ph.D.
Professor and Vice Chairman
Director of Center of Biologic Imaging

Novel Probes and Microscopies to study Cystic Fibrosis; Invited speaker, Woods Hole Marine Biology Laboratory, May 16th 2012

Intensive course in Physiology MDIBL Maine, May 28th-June 6th 2012 Invited Lecturer

Cancer Imaging Camp, Multiphoton practical aspects Vanderbilt University TN June 24th 2012 Invited Speaker

Cancer Imaging Camp June 24th-June 29th 2012 Course Faculty



Peer Reviewed Publications (Fiscal Year 2009-12)

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.

David Klinkenberg, Kimberly R. Long, Kuntala Shome, Simon C. Watkins and Meir Aridor (2012) Lipid Signals Direct p125A to Control an Ordered Assembly of Functional ER exit sites (submitted, in revision)

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

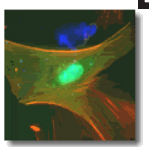
Wegiel B, Baty CJ, Gallo D, Csizmadia E, Scott JR, Akhavan A, Chin BY, Kaczmarek E, Alam J, Bach FH, Zuckerbraun BS, Otterbein LE. Cell surface biliverdin reductase mediates biliverdin-induced anti-inflammatory effects via phosphatidylinositol 3-kinase and Akt. J Biol Chem, 2009:284(32):21369-78.

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.

Jiang J, Maeda A, Ji J, Baty CJ, Watkins SC, Greenberger JS, Kagan VE. Are mitochondrial reactive oxygen species required for autophagy? Biochem Biophys Res Commun 2011; 412(1):55-60.

Navina S, Acharya C, DeLany JP, Orlichenko LS, Baty CJ Shiva SS, Durgampudi C, Karlsson JM, Lee K, Bae KT, Furlan A, Behari J, Liu S, McHale T, Nichols L, Papachristou GI, Yadav D, Singh VP. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. Sci Transl Med 2011; 3(107):107-10.

Sachdev U, Cui X, Hong G, Namkoong S, Karlsson JM, Baty CJ, Tzeng E. High mobility group box 1 promotes endothelial cell angiogenic behavior in vitro and improves muscle perfusion in vivo in response to ischemic injury. J Vasc Surg, 2012; 55(1):180-91.

Montecalvo A, Larregina AT, Shufesky WJ, Beer Stolz D, Sullivan ML, Karlsson JM, Baty CJ, Gibson GA, Erdos G, Wang Z, Milosevic J, Tkacheva OA, Divito SJ, Jordan R, Lyons-Weiler J, Watkins SC, Morelli AE. Mechanism of transfer of functional microRNAs between mouse dendritic cells via exosomes. Blood, 2012; 119(3):756-66

Finegold DN*, Baty CJ*, Knicklebein KZ, Persche S, Noon SE, Campbell D, Karlsson JM, Huang D, Kimak MA, Lawrence EC, Meriney SD, Brufsky A, Ferrell RE*. Connexin 47 mutations increase risk for secondary lymphedema following breast cancer treatment. Clinical Cancer Research 2012; 18(8):2382-90.

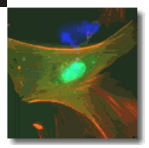
Carol A. Bertrand, Ph.D.
Research Assistant Professor

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.

Liang X, Da Paula AC, Bozóky Z, Zhang H, Bertrand CA, Peters KW, Forman-Kay JD, Frizzell RA. (2012) Phosphorylation-dependent 14-3-3 protein interactions regulate CFTR biogenesis. Mol Biol Cell, 23(6):996-1009.

Holleran JP, Glover ML, Peters KW, Bertrand CA, Watkins SC, Jarvik JW, Frizzell RA. (2012) Pharmacological rescue of the mutant CFTR detected by use of a novel fluorescence platform. Mol Med, 18(1):685-96.

Duvvuri U, Shiwarski DJ, Xiao D, Bertrand C, Huang X, Edinger RS, Rock JR, Harfe BD, Henson BJ, Kunzelmann K, Schreiber R, Seethala RS, Egloff AM, Chen X, Lui VW, Grandis JR, Gollin SM. (2012) TMEM16A induces MAPK and contributes directly to tumorigenesis and cancer progression. Cancer Res, 72(13):3270-3281.

Michael Butterworth, Ph.D.
Assistant Professor

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

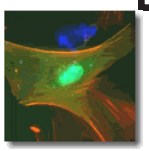
Silvis, M.R.; Bertrand, C.A.; Ameen, N.; Golin-Bisello, F.; Butterworth, M.B., Frizzell, R.A. and Bradbury, N.A. (2009). Rab11b regulates the apical recycling of CFTR in polarized intestinal epithelial cells. *Mol.Biol.Cell*. 20(8): 2337-50

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.

Butterworth M.B., Zhang L., Heidrich E., Myerburg M.M., Thibodeau P.H. (2012). Activation of the epithelial sodium channel (ENaC) by the alkaline protease from *Pseudomonas aeruginosa*.



Journal of Biological Chemistry. (In Press)

Butterworth, M.B.; Edinger, R.S.; Silvis, M.R.; Gallo, L.I.; Liang, X.; Apodaca, G.; Frizzell, R.A. and Johnson, J.P. (2012). Rab11b regulates the trafficking and recycling of the epithelium sodium channel (ENaC). *American Journal of Physiology – Renal.* 302:F581-90. (Highlighted as the featured article in the AJP-Renal Journal's March 2012 podcast)

Daniel Devor, Ph.D.
Professor

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.

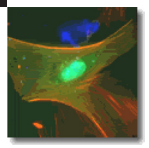
Balut, C.M., C. Loch and D.C. Devor. Role of ubiquitylation and USP8-dependent deubiquitylation in the endocytosis and lysosomal targeting of plasma membrane KCa3.1. FASEB J. 25(11): 3938-3948, 2011.

Gao, Y*., C.A. Bertuccio*, C.M. Balut, S.C. Watkins and D.C. Devor. Dynamin- and Rab5-dependent endocytosis of KCa2.3. PLoS ONE (in press). * These authors contributed equally.

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. 2012. 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

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.

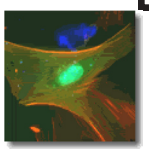
Schmidt, B.Z., R.J. Watts, M. Aridor, R.A. Frizzell. Cysteine string proteinpromotes proteasomal degradation of the cystic fibrosis transmembrane conductance regulator (CFTR) by increasing its interaction with the C-terminus of HSP 70-interacting protein (CHIP) and promoting CFTR ubiquitylation. J Biol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

K.W., T. Okiyoneda, W.E Balch, I. Braakman, J.L. Brodsky, W.B. Guggion, C.M. Penland, H.B. Pollard, E.J. Sorscher, W.R. Skach, P.J. Thomas, G.L. Lukacs, R.A. Frizzell. CFTR Folding Consortium: methods available for studies of CFTR folding and correction. Methods Mol Biol. 2011;742:335-53.

Butterworth, M.B., R.S. Edinger, M.R. Silvis, L.I. Gallo, X. Liang, G. Apodaca, R.A. Frizzell, J.P. Johnson. Rab11b regulates the trafficking and recycling of the epithelial sodium channel (ENaC). Am J Physiol Renal Physiol. 2012 Mar;302(5):F581-90.

Van Goor, F., S. Hadida, P.D. Grootenhuis, B. Burton, J.H. Stack, K.S. Straley, C.J. Decker, M. Miller,J. McCartney, E.R. Olson, J.J.Wine, R.A. Frizzell, M. Ashlock, P.A. Negulescu. Correction of the F508del-CFTR protein processing defect in vitro by the investigational drug VX-809. Proc Natl Acad Sci USA. 2011 Nov 15;108(46):18843-8.

Liang, X., A.C. Da Paula, Z. Bozóky, H. Zhang, C.A. Bertrand, K.W. Peters, J.D. Forman-Kay, R.A. Frizzell. Phosphorylation-dependent 14-3-3 protein interactions regulate CFTR biogenesis. Mol Biol Cell. 2012 Mar;23(6):996-1009.

Holleran, J.P., M.L. Glover, K.W. Peters, C.A. Bertrand, S.C. Watkins, J.W. Jarvik, R.A. Frizzell. Pharmacological Rescue of the Mutant Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Detected by Use of a Novel Fluorescence Platform. Mol Med. 2012 May 9;18(1):685-96.

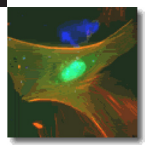
Saxena, A., Y.K. Banasavadi-Siddegowda, Y. Fan, S. Bhattacharya, G. Roy, D.R. Giovannucci, R.A. Frizzell, X. Wang. Human Heat Shock Protein 105/110 kDa (Hsp 105/110) Regulates Biogenesis and Quality Control of Misfolded Cystic Fibrosis Trnasmembrane Conductance Regulator at Multiple Levels. J Biol Chem. 2012 Jun 1;287(23):19158-70.

Archana Gangopahyay, Ph.D.
Visiting Research Instructor

Rodriguez AI, Gangopadhyay A, Kelley EE, Pagano PJ, Zuckerbraun BS, Bauer PM. HO-1 and CO decrease platelet-derived growth factor-induced vascular smooth muscle cell migration via inhibition of Nox1. Arterioscler Thromb Vasc Biol. 2010, 30(1):98-104.

Archana Gangopahyay, Max Oran, Eileen M. Bauer, Jeffrey W. Wertz, Suzy A. Comhair, Serpil C. Erzurum, and Philip M. Bauer. Bone Morphogenetic Protein Receptor II Is a Novel Mediator of Endothelial Nitric-oxide Synthase Activation. J Biol Chem. 2011, 286(38):33134-40.

Cruz JA, Bauer EM, Rodriguez AI, Gangopadhyay A, Zeineh NS, Wang Y, Shiva S, Champion HC, Bauer PM. Chronic hypoxia induces right heart failure in caveolin-1-/-mice. Am J Physiol Heart Circ Physiol. 2012, 302(12):H2518-27



Yang Hong, Ph.D.
Assistant Professor

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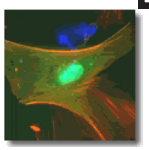

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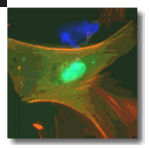

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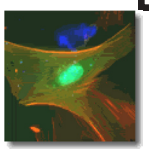

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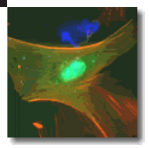

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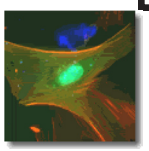

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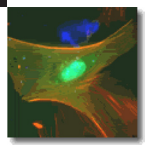

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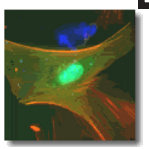

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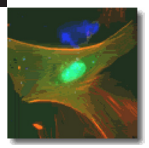

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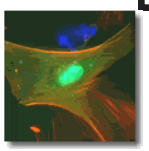

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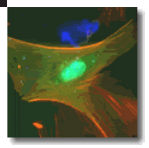

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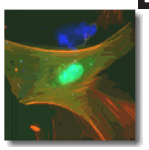

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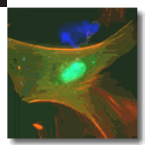

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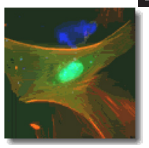

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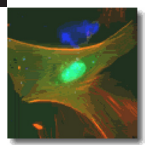

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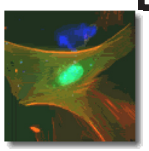

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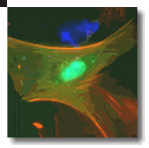

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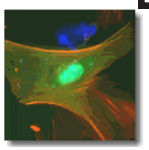

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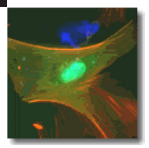

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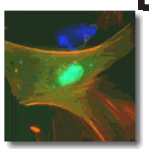

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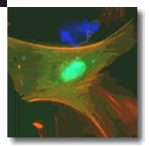

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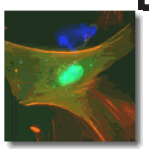

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Associate Professor

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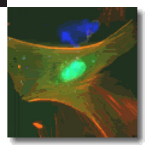

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Nathan Yates, Ph.D.
Associate Professor

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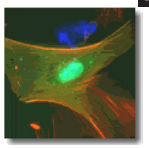

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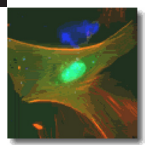
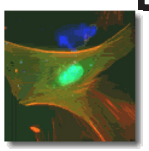


Executive Summary for the Cell Biology FY2013 Business Plan

One of the key issues in the FY2013 Business Plan will continue to 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. Two years ago significant changes in the Department took place with seven members of the primary faculty leaving the Department and two new members joining the faculty. This year two new primary faculty joined the Department. 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 FY2013 plan. This will be, in large part, achieved through the recruitment of one-two new faculty in the FY2013. We present the strengths, weaknesses, opportunities and threats to the success of the Department 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 2013 has been approved and is appended at the end of this analysis.



Strengths

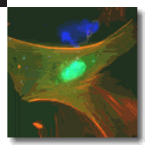
Research

The Department of Cell Biology has a strong research program aimed at addressing fundamental questions of cell biology, including mechanisms controlling membrane trafficking, cell polarity, actin cytoskeleton, signal transduction, 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 Nature Cell Biology (Umasankar et al., 2012, 14: 488–501), Molecular Cell (Gamper A. et al., 2012, 45: 233-43), 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 (Liang et al. 2010, 21: 2024-2033), and Journal of Cell Science (Huang et al., 124:4001-3).

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. Studies of the mechanisms of cell polarity, cell motility, and intracellular signaling have also been growing in the department. Our 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 Cell Biology faculty 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 Center for HIV Protein Interactions (Watkins) grant, and the competitive renewal of RO1 funding (Aridor, Sorkin). Three senior faculty, Drs. Frizzell, Sorkin, and Watkins, have multiple NIH grants. Three junior faculty, Drs. Butterworth, Hong and Thibodeau are 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 new recruits, Dr. Yates (Associate Professor) and Kwiatkowski (Assistant Professor) have joined the Department in November 2011 and April 2012, respectively. Nathan is an expert in mass-spectrometry and proteomics, and will be developing new approaches to systematic, quantitative analysis of proteins in cells and tissues. He will be working with many investigators in Cell Biology and other departments on implementing high-end proteomics analysis in their research. Dr. Kwiatkowski is an expert in the function and regulation of actin cytoskeleton. He conducts mutildisciplinary research of the mechanisms of actin cytoskeleton regulation *in vitro* and the role of actin dynamics during development in *in vivo* animal models.



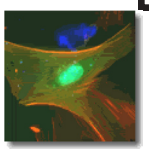
Two Centers associated with the Department represent particular strengths of the Department and the School. The Center for Biologic Imaging (CBI) is one of the largest imaging facilities in the country and provides state-of-the-art equipment and indispensible expertise in all types of cellular imaging 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 multiphoton 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 CB 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 8 students in the graduate Ph.D. program in Cell Biology and Molecular Physiology. Thanks to the efforts of the former program director, Dr. Walker, and a new director Dr. Stolz, as well as newly formed CBMP program committee, we were successful in attracting several new students to the program. Several students graduated in the last year, taking positions as postdoctoral fellows. In addition, CB 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, Neuroscience among others.

Administration: All of the committees in the Department have undergone restructuring. Vice-chair, Dr. Watkins, has assumed leadership in the Promotion and Space committees. 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, recruitment of new faculty, 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; 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 CB faculty members operate on different campuses. Dr. Frizzell's laboratory is located in the Children's Hospital in Lawrenceville, Dr. Yates's group is at Magee Womens Hospital, 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 four laboratories in the main activities of the Department at Oakland campus.

Opportunities

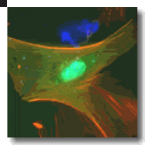
The vision of the new chair, and the leadership of the School, is to focus our research program towards basic cell biology and build a premier Department of Cell Biology. The key to accomplishing this task is the recruitment of focused and creative new faculty. We plan to recruit two additional faculty 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.

Cohesiveness of the faculty research expertise in the Department creates exceptional opportunities for collaborative research, which should open doors to building new program projects and centers. The Department is now in the position to lead the assembly of new interdisciplinary research programs that would be competitive in obtaining the extramural funding.

Threats

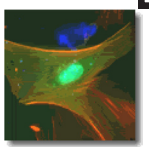
The steady decrease in federal and private funding opportunities will continue to be the most significant threat during next several years. Yet, in order for the Department to become one of the elite cell biology departments, total funding of the Department must increase 2-fold above the current level.

Another difficult challenge 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.



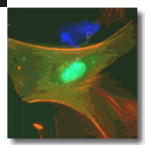
Cell Biology FY2013 Fiscal Issues

The main budgetary issue that face the Department in the FY13 budget will be maintaining the level of extramural funding of the faculty at the level necessary to support their research program. In light of the continuing drought of NIH funding this is expected to be a major challenge. Main efforts will be devoted to ensure that the departmental infrastructure continues to improve.



University of Pittsburgh School of Medicine
University of Pittsburgh Physicians
DEPARTMENT OF Cell Biology
Schedule of Revenue and Expenses Fiscal Year 2012 Budget

	University	UPP and Other	Total Budget FY 2011
Revenue			
Patient Care	$ -	$ -	$ -
Grant:			
Directs	3,488,991	-	3,488,991
Indirects	1,502,167	-	1,502,167
Hospital Contract	-	-	-
School of Medicine	3,055,311		3,055,311
VAMC		-	-
Other	351,747	-	351,747
Total Revenue	$ 8,398,216	$ -	$ 8,398,216
Expenses			
Salaries and Fringe Benefits:			
Faculty	$ 2,445,833	$ -	$ 2,445,833
Non-Faculty	2,530,234	-	2,530,234
Malpractice Insurance		-	-
Space Rental	87,894	-	87,894
UPP Overhead		-	-
University Overhead	2,227,111		2,227,111
Other Operating Expenses	1,107,144	-	1,107,144
Total Operating Expenses	$ 8,398,216	$ -	$ 8,398,216
Excess Revenue over Expenses	$ -	$ -	$ -
Capital Equipment/Improvements	$ -	$ -	$ -
Fund Balances			
University Restricted Accounts as of 6/30/12	$ 4,987,174	$ -	$ 4,987,174
University Endowments as of 6/30/12	351,747		351,747
UPP Fund Balance as of 6/30/12		-	-
UPMC Endowments as of 6/30/12		-	-
UPMC SPF Accounts as of 6/30/12		-	-
Total Fund Balances	$ 5,338,921	$ -	$ 5,338,921



Thank you for your kind attention.