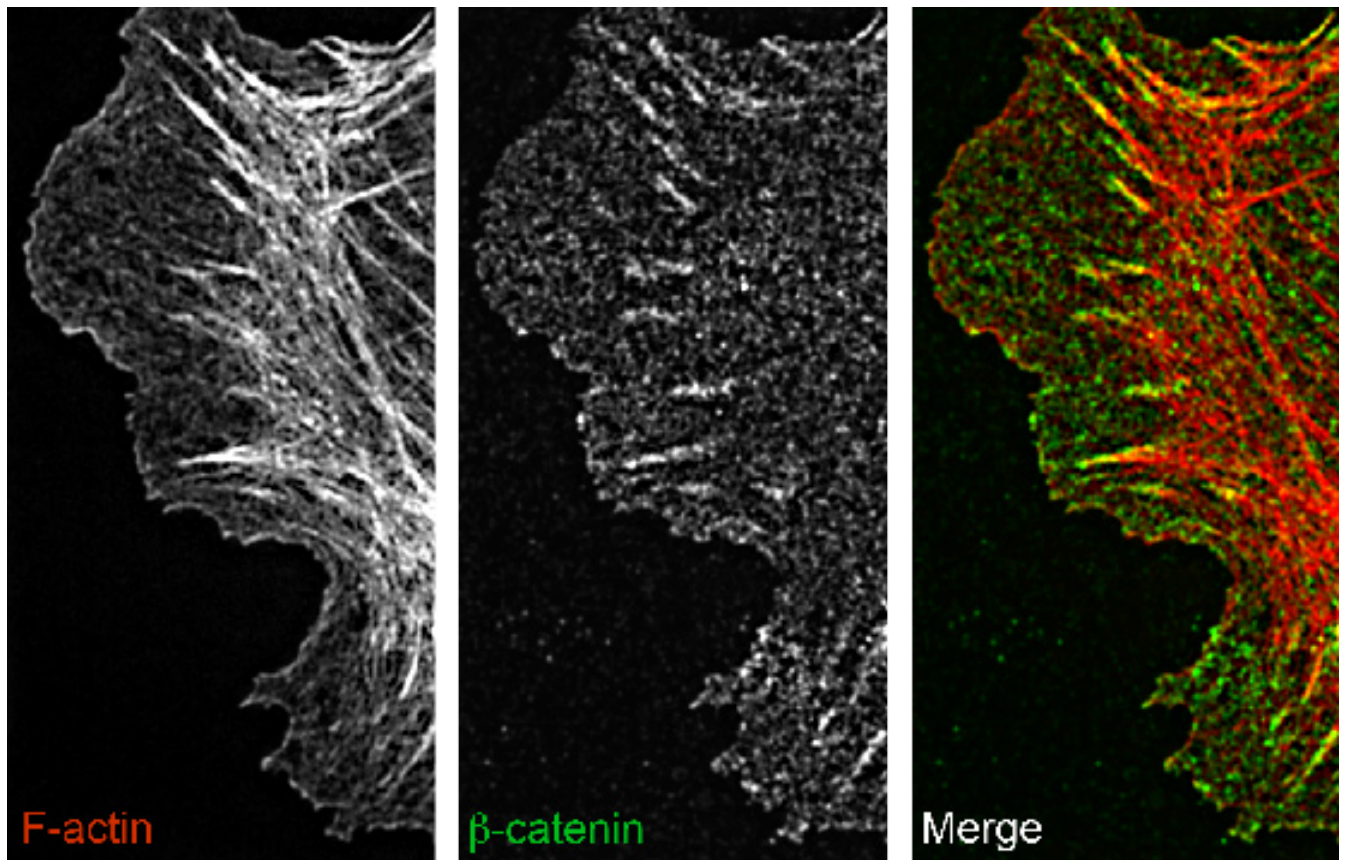


**UNIVERSITY OF PITTSBURGH
SCHOOL OF MEDICINE**

CELL BIOLOGY



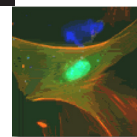
**FY13 ANNUAL REPORT
AND
FY14 BUSINESS PLAN**

Front Page

Cover figure by Dr. Adam Kwiatkowski. Structured Illumination Microscopy (SIM) images of MDCK epithelial cell plated on E-cadherin-coated functionalized substrate and stained for F-actin and β -catenin. Attachment to E-cadherin substrate drives cadherin-catenin adhesion complex formation on basal membrane of cell, as evidenced by β -catenin clustering. Notably, β -catenin localizes to F-actin-rich adhesions, reminiscent of focal adhesions.

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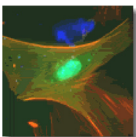
In the cell, life is governed by a multitude of molecular systems that shape and sustain the organellar system of the cell, maintain cellular homeostasis and respond to extracellular cues. These systems are dynamic, multicomponent macromolecular complexes. Maintaining and regulating the function of these 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 a broad spectrum questions in cell biology from the roles of single molecules to through complex multicomponent cellular mechanisms to integrated studies at the organismal level in the yeast, 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 other Schools of the University of Pittsburgh and 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 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. Adam Kwiatkowski

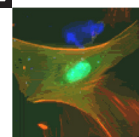
The regulated assembly and organization of the actin cytoskeleton is essential for cell migration and cell-cell adhesion in the developing embryo and adult organism. The spatial organization of filamentous actin (F-actin) differs between these cell behaviors: in motile cells, dynamic, highly-branched actin networks drive membrane protrusion, whereas in adherent cells, bundles of unbranched filaments are organized parallel to the plasma membrane to stabilize cell-cell contacts.



Multiple actin-binding proteins regulate the assembly, organization and disassembly of actin filaments within the cell. However, how these proteins cooperate to shape, and coordinate transitions between distinct actin network architectures remains unclear. A primary goal of the Kwiatkowski 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.

Most of our current efforts focus on understanding the function of α -catenin, an actin-binding component of the cadherin cell-cell adhesion complex. We have used a combination of biochemistry, cryo-electron microscopy (cryo-EM) and Total Internal Reflection Fluorescence microscopy (TIRF-M) to visualize α E-catenin binding to actin filaments and examine α E-catenin-mediated regulation of actin assembly and disassembly with single filament resolution. We find that α E-catenin binds specifically and cooperatively to actin filaments, and that binding promotes a conformational change in the actin protomer that has a long-range influence on filament structure. TIRF-M reveals that α E-catenin binding to actin filaments limits barbed-end elongation, inhibits filament branching by the Arp2/3 complex and blocks filament severing by cofilin, activities critical for actin dynamics and turnover. Thus, α E-catenin binding to actin favors assembly of stable, unbranched filament networks over more dynamic, branched filament arrays. These results provide a mechanistic and structural framework for how α E-catenin regulates actin organization and support a model in which transitions from branched to linear actin networks accompany changes between cellular migratory and adhesive states.

Several images of the data from Kwiatkowski lab are included with this report.



**Department of Cell Biology
2013 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

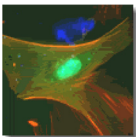
Aridor
Butterworth
Devor
Frizzell
Murray
Sorkin
Traub

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

Gay
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

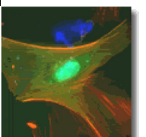
Drain
Leuba
Sorkin
Wan

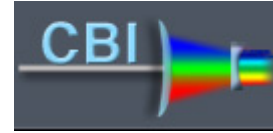
Scientists in this group are examining signaling processes mediated by receptors for growth factors and hormones, mechanisms of hormone secretion, and processes involved in the regulation of cell cycle progression, DNA repair and transcription. The particular focus is on the events leading to dysregulation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

Mass-spectrometry and proteomics

Wu
Yates

These two laboratories are focused on developing new methodologies of quantitative mass-spectrometric analyses of proteins including new approaches to sample preparations, data acquisition, analysis and storage.



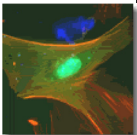
Center for Biologic Imaging

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 few 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) super resolutions systems (SIM, STORM, PALM) electron microscopes 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, 2 multiphoton systems, a SIM system a STORM system, 6 high end upright microscopes and 3 electron microscopes (SEM and



TEM). We also have multiple (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 Associate 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.

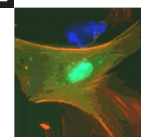
Other Faculty

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

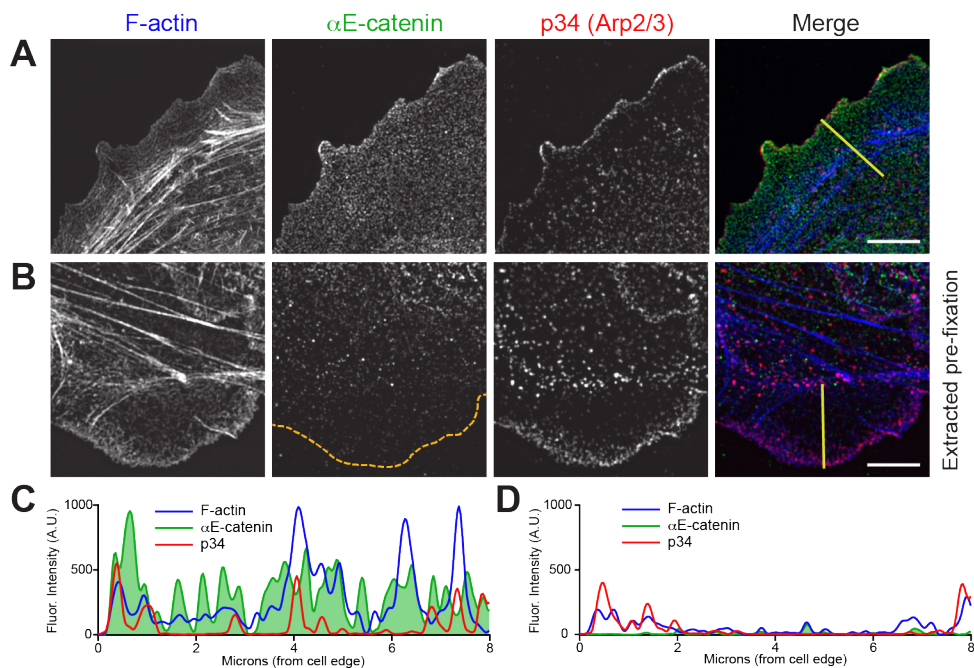
Associates:

Technical Specialists: The technical bases of the Center are all trained microscopists; in total 19 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.



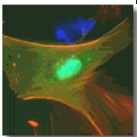
Adam Kwiatkowski. α E-catenin colocalizes with F-actin at developing cell-cell contacts.

3D-SIM images of MDCK epithelial cells stained for F-actin, α E-catenin and p34 (Arp2/3 complex). Scale bar is 5 microns.

(A) Without extraction, α E-catenin is distributed throughout the cell and p34 is enriched along the leading edge. Yellow line marks line scan in (C).

(B) Pre-extraction decreases α E-catenin signal in membrane protrusions, whereas the p34 signal is retained. Orange dashed line marks the cell boundary; yellow line marks the line scan in (D).

(C, D) Representative line scans of F-actin, α E-catenin and p34 signal intensities across the cell periphery in a control cell (C, yellow line in A) and a pre-extracted cell (D, yellow line in B). Pre-extraction removes the majority of the α E-catenin signal from the cell periphery, while the p34 signal is unperturbed. Note the presence of unlabeled phalloidin during extraction reduces the intensity of the F-actin signal in pre-extracted cells relative to control cells.



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.

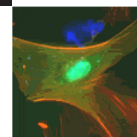
In 1998, this 'seed' funding from the CFF was supplemented by the award of NIH program funding in the form of a P50 SCOR. The P50 funding was renewed in the form of P30 Core Center grants in 2004 and 2010, each of which took decidedly more clinical turns. The latest P30 Core Center is entitled, "Basic 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, Pulmonary Allergy and Critical Care 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:

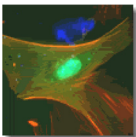
Human Airway Cell and Assays Core: This core provides access to patient materials obtained as a result of lung transplant activities in the Department of Surgery. This core offers well differentiated primary cultures of human bronchial epithelia to facilitate a variety of pre-clinical



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 Directors: Raymond A. Frizzell, Ph.D. and Joseph Pilewski, Departments of Cell Biology and Medicine]

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., Department of Cell Biology]

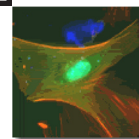
Clinical Studies Core: This core provides facilities and personnel for implementing clinical trials. It provides procedures for identifying functional outcomes, monitored in terms of lung function, radioisotope clearance, ion transport, inflammatory mediator levels or gene expression. It maintains patient 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]

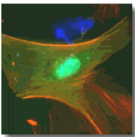
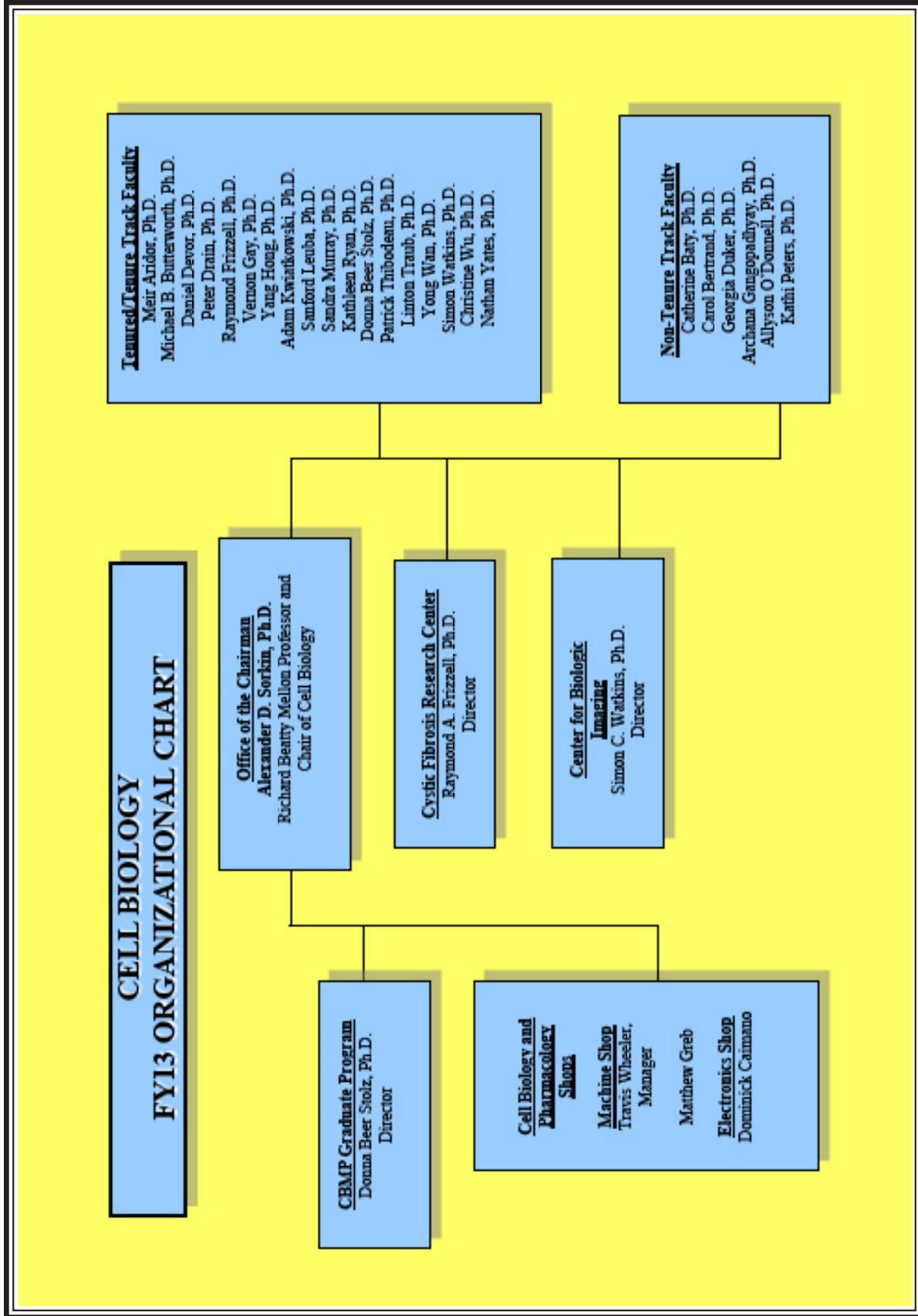


Cell Biology Faculty Data

[Current as of June, 2013]

Name	Rank	Office Address	Email Address	Phone Fax
Aridor, Meir	Associate Professor	S310 BST-South Wing	aridor@pitt.edu	412-624-1970
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Bertrand, Carol	Res. Asst. Professor	S309 BST-South Wing	cbertra@pitt.edu	412-648-1044
Butterworth, Michael	Assistant Professor	S314 BST-South Wing	michael7@pitt.edu	412-383-8591
Devor, Daniel	Professor	S312 BST-South Wing	dd2@pitt.edu	412-383-8755
Drain, Peter	Associate Professor	S323 BST-South Wing	drain@pitt.edu	412-648-9412
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Kwiatkowski, Adam	Assistant Professor	S324 BST-South Wing	adamkw1@pitt.edu	412-383-8139
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Stolz, Donna Beer	Associate Professor	S221 BST-South Wing	dstolz@pitt.edu	412-383-7283
Thibodeau, Patrick	Assistant Professor	S327 BST-South Wing	thibodeau.pitt.edu	412-383-8858
Traub, Linton	Associate Professor	S325 BST-South Wing	traub@pitt.edu	412-648-9711
Wan, Yong	Associate Professor	2.6 Hillman Cancer Center	yow4@pitt.edu	412-623-3275
Watkins, Simon C.	Professor	S225 BST-South Wing	swatkins@pitt.edu	412-648-3051
Wu, Christine	Associate Professor	S326 BST-South Wing	chriswu@pitt.edu	412-648-9260
Yates, Nathan	Associate Professor	1719 BST3	yatesn@pitt.edu	732-718-9739





Cell Biology**Research Seminar Schedule 2012–2013**

September 21, 2012

John Heuser, M.D.

Professor, Biophysics & Cell Biology

Washington University School of Medicine, St. Louis, MO

“Decipherine caveolar dynamics by “deep-etch” electron microscopy”

October 9, 2012

Kendra Bence, Ph.D.

Assistant Professor, Penn Veterinary Medicine

University of Pennsylvania

“Mind Over Matter? CNS Signaling Pathways in obesity and diabetes”

October 16, 2012

Sergio Grinstein, Ph.D.

Professor, Biochemistry

Hospital for Sick Children, University of Toronto

“Imaging phagocytosis: receptors, phosphoinositides and the cytoskeleton”

November 13, 2012

Jennifer Bomberger, Ph.D.

Assistant Professor, Microbiology & Molecular Genetics,

University of Pittsburgh School of Medicine

“Viral-bacterial synergy in the airway”

December 4, 2012

Sokol Todi, Ph.D.

Assistant Professor, Pharmacology & Neurology

Wayne State University School of Medicine

“Deubiquitinating Enzymes in Development, Normal Function and Disease”

March 5, 2013

Daniel Klionsky, Ph.D.

Professor, Molecular, Cellular and Developmental Biology

University of Michigan

“If you only have time to attend one talk on autophagy today, this is the one”

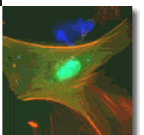
March 19, 2013

Michael S. Marks, Ph.D.

Professor, Pathology & Laboratory Medicine

University of Pennsylvania

“Functional amyloid formation and melanosome biogenesis”



March 26, 2013

Tanya Svitkina, Ph.D.

Associate Professor of Biology

University of Penn

“Actin cytoskeleton in cell migration and neuronal polarity”

April 16, 2013

Elias Spiliotis, Ph.D.

Assistant Professor, Director of Cell Imaging, Biology

Drexel University

“Spatial control of microtubule organization and dynamics by septin GTPases in polarizing epithelia”

April 30, 2013

Mark Peifer, Ph.D.

Professor, Biology

University of North Carolina, Chapel Hill

“Building the Body Plan: The Miracle of Morphogenesis”

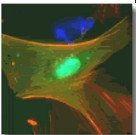
May 21, 2013

Beverly Wendland, Ph.D.

Professor and Chair, Biology

Johns Hopkins University

“Formin’ new ways to look at endocytosis”



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*

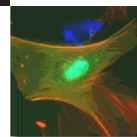
Our laboratory studies lymphatic endothelial function. We have developed a 3 dimensional tissue culture system to study potential mechanisms of lymphatic failure. Despite the fact that the lymphatic vessels were identified hundreds of years ago, limited understanding exists of lymphatic development, 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



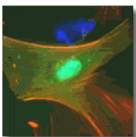
trafficking and recycling. Research is focused into two broad areas. First, ongoing studies aim to characterize the mechanisms that underlie channel regulation by membrane trafficking in the mammalian kidney. Three renal transporters, namely the epithelial sodium channel (ENaC), potassium channel (ROMK) 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,

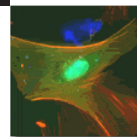


when mutated to increase side-chain volume, result in a shift in apparent Ca^{2+} affinity. These results suggest this region of the channel is similarly involved in the coupling between Ca^{2+} binding to calmodulin in the cytoplasmic C-terminus and subsequent gating. A combination of patch-clamping, mutagenesis and modeling will be employed to definitively define the role of this region of the channel in the coupling between Ca^{2+} and gating.

Second, as any physiological response is dictated by not only the likelihood that channels are in the open state (P_o), 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 ubiquitinylation 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 deubiquitinating 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



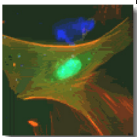
regulation of the number of channels present at the plasma membrane such that the physiological response to agonists may be modified.

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 Ca^{2+} -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



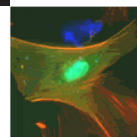
physiological system. Cavita has also begun to culture cells from her transgenic line which will allow us to define cells expressing the transgene and characterize these *C. elegans* channels by patch-clamping. We can then determine whether mutations at conserved amino acids to those identified by us in mammalian channels will produce similar phenotypes, including increased Ca^{2+} 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 sulfonylurea 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.

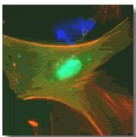
Georgia K. Duker, Ph.D.

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 recent 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 2013, I am a co-director for the second-year Digestion and Nutrition course.

Within the Department of Cell Biology I am course director for the Graduate Histology course. This course is taken by the majority of our students. It is a broad 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

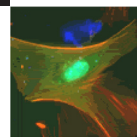
Dr. Frizzell's interests concern the mechanisms of salt and water transport in secretory and absorptive epithelia and pathways that regulate these processes. Specifically, we are defining defects in ion transport regulation in the genetic disease, cystic fibrosis (CF), membrane trafficking of wild-type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

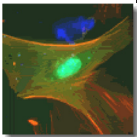
Associate Professor

Establishing cell polarity is essential for cellular morphogenesis, function and tissue integrity. Using *Drosophila* epithelial cells as a model system, we aim to elucidate the fundamental mechanisms underlying the cell polarization by 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 the actin cytoskeleton is essential for cell migra-



tion and cell-cell adhesion in the developing embryo and adult organism. The spatial organization of filamentous actin (F-actin) differs between these cell behaviors: in motile cells, dynamic, highly-branched actin networks drive membrane protrusion, whereas in adherent cells, bundles of unbranched filaments are organized parallel to the plasma membrane to stabilize cell-cell contacts. Multiple actin-binding proteins regulate the assembly, organization and disassembly of actin filaments within the cell. However, how these proteins cooperate to shape, and coordinate transitions between, distinct actin network architectures remains unclear. A primary goal of the Kwiatkowski 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.

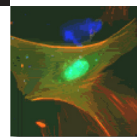
Most of our current efforts focus on understanding the function of α -catenin, an actin-binding component of the cadherin cell-cell adhesion complex. We have used a combination of biochemistry, cryo-electron microscopy (cryo-EM) and Total Internal Reflection Fluorescence microscopy (TIRF-M) to visualize α E-catenin binding to actin filaments and examine α E-catenin-mediated regulation of actin assembly and disassembly with single filament resolution. We find that α E-catenin binds specifically and cooperatively to actin filaments, and that binding promotes a conformational change in the actin protomer that has a long-range influence on filament structure. TIRF-M reveals that α E-catenin binding to actin filaments limits barbed-end elongation, inhibits filament branching by the Arp2/3 complex and blocks filament severing by cofilin, activities critical for actin dynamics and turnover. Thus, α E-catenin binding to actin favors assembly of stable, unbranched filament networks over more dynamic, branched filament arrays. These results provide a mechanistic and structural framework for how α E-catenin regulates actin organization and support a model in which transitions from branched to linear actin networks accompany changes between cellular migratory and adhesive states.

Sanford H. Leuba, Ph.D.

Associate Professor

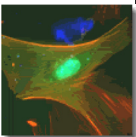
Since the discovery of the nucleosome in the early 1970's, scientists have sought to correlate chromatin structure and dynamics with biological function. More recently, we have learned that nucleosomes and chromatin play a critical role in the regulation of transcription, replication, recombination, 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). Eukaryal and archaeal organisms have similar fiber structure with differences likely related to the more complex needs of eukaryal 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 trophoblast (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 Ropic-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.

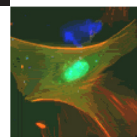
Professor

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*

Cystic fibrosis is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR); the most common is F508del which prevents CFTR from folding properly and from leaving the endoplasmic reticulum to assume residence in the apical plasma membrane to function in the cAMP regulated salt and water secretion in epithelial cells. We are identifying processes and proteins which modify mutant CFTR and send it along ubiquitylation or SUMOylation pathways for degradation or biosynthesis. It is important in this endeavor to analyze not only the impact of overexpression but to ask ultimately whether the pathway under study is significant in primary cultures of human bronchial epithelial cells as concerns ubiquitin-dependent and -independent F508del degradation. To this end, we are evaluating the localization of proteins through subcellular fractionation to relate their expression to interactions with CFTR domains in the cytoplasm. For example, we are asking if the nuclear SUMO regulator, PIAS4, is present also in the cytoplasm. As we identify other interactions, it will be necessary to validate their localization to authenticate their function.

Kathleen D. Ryan, Ph.D.*Associate Professor*

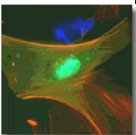
Dr. Ryan's primary role is Associate Director of the Office of Medical Education in the School of Medicine.

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.



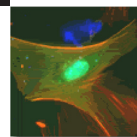
Vasculogenesis, on the other hand, has only recently emerged as an alternative mechanism of blood vessel growth in adult tissues and is the result of homing and engraftment of circulating EC precursors (ECPs) of bone marrow origin to sites of neovascularization. Both events are known to occur within 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. Dr. Stolz's research specialties involve vascular biology, liver regeneration and liver and kidney aging.

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*

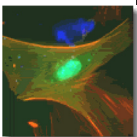
Many molecules enter the cell interior within clathrin-coated vesicles, in process termed endocytosis. In the simplest sense, the clathrin-coated vesicle can be viewed as a nanomachine that temporally couples preferential retention of designated cargo with rapid vesicle assembly, invagination, and fission 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-cholesterol 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 multidisciplinary 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.

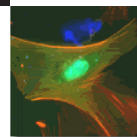
Associate Professor

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 2012 - 2013)

Alexander D. Sorkin, Ph.D.

Professor and Chairman

ASIRC - Italian Association for Cancer Research; Standing Member
NIH/NCI PAR12-144 "Cancer Biology-2"

Simon C. Watkins, Ph.D.

Professor and Vice Chairman, Director of Center of Biologic Imaging

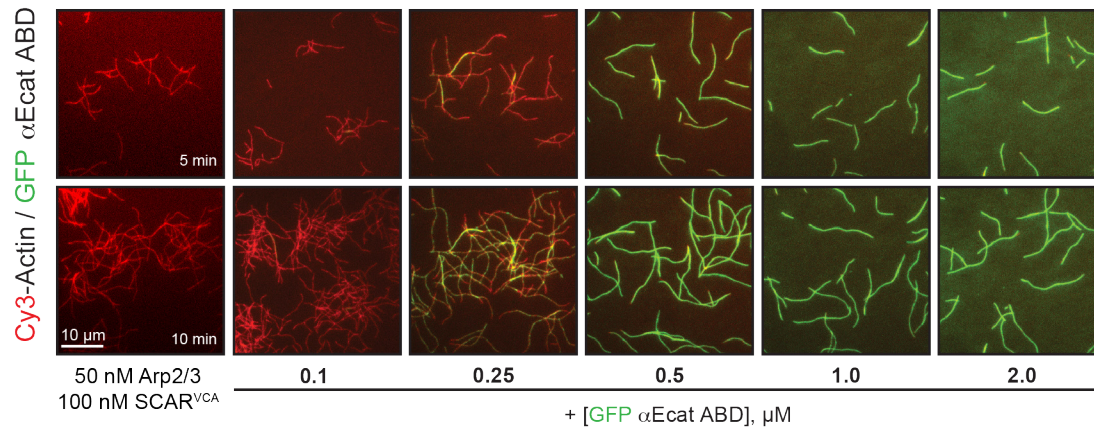
Canadian Foundation for Innovation, July 12-14 Study section for Infrastructure. Chair of Panel
NIH study section, R03's (2012/10 ZAR1 EHB (M1) 1) July 18, 2012 Panelist
American Cancer Society Review Panel Co-Chair Jan 22-23, 2013
NIH study section ZRG1 IMST-J (15) B Feb 14, 2013, Panelist
NIH study section ZRG1 IMST-K (14) B Feb 16, 2013 Panelist
NIH study section R03's March 18th Panelist

Christine Wu, Ph.D.

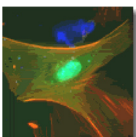
Associate Professor

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)



Adam Kwiatkowski. α E-catenin inhibits Arp2/3 complex branching of actin filaments. Images of 1 μ M Cy3-labeled Mg-ATP-actin polymerized with 50 nM Arp2/3 complex and 100 nM SCARVCA alone or in the presence of increasing concentrations of GFP α E-catenin actin binding domain (ABD). For each condition, all proteins were combined in TIRF buffer and flowed into the pegylated imaging chambers to initiate polymerization. The amount of spontaneous actin polymerization was not significantly affected by the presence of GFP α E-catenin.



Faculty Advisory Committee Memberships (Fiscal Year 2012 - 2013)

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 Seminar Series
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.

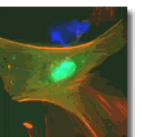
Associate Professor

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.

Associate Professor

Director, Summer Undergraduate Research Program (SURP) in Cell Biology and Molecular Physiology

Cell Biology Space Committee

Adam Kwiatkowski, Ph.D.

Assistant Professor

Organizer – Cell Biology Department Retreat

Local Traffic Symposium Organizing Committee

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

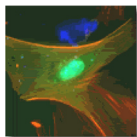
Cell Biology and Physiology Tenure and Promotions Committee

Kathleen D. Ryan, Ph.D.

Assistant Dean for Medical Education

Course Organizing Committee, Reproductive and Developmental Biology, University of Pittsburgh School of Medicine curriculum revision.

Chair, Institutional Animal Care and Use Committee, University of Pittsburgh Promotions



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

Alexander D. Sorkin, Ph.D.

Richard B. Mellon Professor and Chair

Executive Committee School of Medicine
 University of Pittsburgh and Carnegie Mellon Medical Scientist Training Program Committee
 MSTP
 Center for Neuroscience University of Pittsburgh – CNUP
 University of Pittsburgh Cell Biology and Molecular Physiology Program Committee
 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

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
 Director - Cell Biology and Molecular Physiology Program
 Interdisciplinary Biomedical Graduate Program Admissions Committee Tour Guide

Patrick H. Thibodeau, Ph.D.

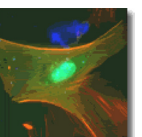
Assistant Professor

Associate Director, Cell Biology and Molecular Physiology Graduate Program
 Member, Interdisciplinary Biomedical Graduate Program Steering Committee
 Member, Cell Biology and Molecular Physiology Steering Committee
 Interdisciplinary Biomedical Graduate Program admissions committee, ad hoc member
 Interdisciplinary Biomedical Graduate Program admissions committee, CBMP representative

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

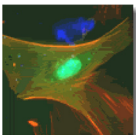
Cell Biology Tenure and Promotions Committee
Cell Biology Student Advisory Committee
Cell Biology Space Committee
Cell Biology Faculty Recruitment Committee
Graduate Program, Curriculum Committee
University of Pittsburgh School of Medicine, Research Advisory Committee
University of Pittsburgh Cancer Institute Core Resources Committee
University of Pittsburgh Tenure and Promotions Committee
Scientific Advisory Board: Roper Scientific
Member at Large, School of Medicine Executive Committee

Christine Wu, Ph.D.

Associate Professor

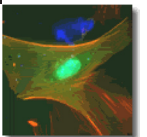
Cell Biology Faculty Recruitment Committee

Cell Biology/Pharmacology Machine Shop

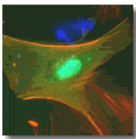


Cell Biology Sponsored Research Funding (FY13)

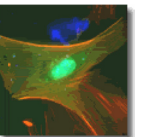
Name	Agency Name	Title	Annual DC	Annual IDC
Meir Aridor	National Institutes of Health	COPII Organization and Vesicle Formation at ER Exit Sites	150,000	77,250
Catherine Batty	National Institutes of Health	Structure-Function Relationships in the IL-17 Receptor	2,605	1,341
Catherine Batty	National Institutes of Health	Obesity Related Pancreatic Fat Worsens Local Injury via Unsaturated Fatty Acids	9,714	5,002
Catherine Batty	CTSI	The role of Placental Lymphatics in Preeclampsia and Intrauterine Growth Restriction	12,342	-
Carol Bertrand	Cystic Fibrosis Foundation	Role of SL C26A9 in biogenesis and anion secretion in airway	90,000	7,200
Michael Butterworth	National Institutes of Health	EnaC regulation in the kidney by vesicle trafficking and recycling	124,585	60,299
Michael Butterworth	National Institutes of Health	Pittsburgh Center for Kidney Research	1,038	534
Michael Butterworth	Gilead	Regulations of the epithelial sodium(ENaC)	40,200	3,226
Daniel Devor	National Institutes of Health	Assembly and trafficking of IK1 and SK3 in Endothelia	224,991	115,870
Peter Drain	National Institutes of Health	Anesthetic Sites in Transmembrane Peptides by NMR	1,453	748
Peter Drain	Army	Towards a Possible Therapy for Diabetes Complications	10,730	5,526
Wayne Ernst	Cystic Fibrosis Foundation	Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting	38,151	-
Raymond Frizzell	Cystic Fibrosis Foundation	Research Training Core	70,000	
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	45,260	23,308
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	132,974	77,158
Raymond Frizzell	Cystic Fibrosis Foundation	Program Enrichment and Administration Core	27,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Molecular Biology and Gene Expression Core A	100,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in Wild-Type and DF508 CFTR Processing	230,237	18,419
Raymond Frizzell	National Institutes of Health	Traffic Regulatory Proteins and ENaC	205,651	104,665
Raymond Frizzell	National Institutes of Health	Trans-NIH-Research Support	18,627	9,780
Yang Hong	National Institutes of Health	Regulation of Adherens Junction Dynamics by Polarity Proteins	183,508	90,964
Yang Hong	American Cancer Society	Regulation of a Tumor Suppressor and Cell Polarity Protein Lgl by Hypoxia	150,000	30,000
Adam Kwiatkowski	March of Dimes	Molecular coordination of cell movement and cell-cell adhesion during neural tube formation	28,432	2,843
Sanford Leuba	National Institutes of Health	NNRTI induced conformational changes in HIV-1 RT	48,209	18,290
Xiubin Liang	National Institutes of Health	Phosphorylation-dependent regulation of epithelial sodium channel (ENaC) trafficking	43,691	3,495
Sandra Murray	National Science Foundation	Gap Junction Plaques Internalization	110,602	50,422
Sandra Murray	National Science Foundation	Gap Junction Plaques Internalization	6,666	1,666
Uma Perunthottathu	American Heart	Mechanistic Role of Clathrin Endocytic Component, Fcho1 in Bmp Signaling (Postdoc Fellowshipship)	24,000	-
Alexander Sorkin	National Institutes of Health	The influence of gene-environment interactions on neuronal mitochondrial fission, fusion, and transport in chronic parkinson's disease-relevant environmental toxin models.	6,455	3,530



Alexander Sorokin	National Institutes of Health	EGF Receptor Signaling in Time and Space in Tumor Cells	167,661	86,345
Alexander Sorokin	National Institutes of Health	Dopamine Transporter Regulation by Endocytosis	249,590	105,715
Alexander Sorokin	National Institutes of Health	SPORE in Lung Cancer_DRP	35,000	18,025
Alexander Sorokin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	259,598	116,044
Donna Beer Stolz	National Institutes of Health	Mechanisms for Arsenite-Induced Vascular Disease	3,328	1,714
Donna Beer Stolz	National Institutes of Health	Mechanisms of Fibrosis in Scleroderma Skin and Lung	2,916	1,502
Donna Beer Stolz	National Institutes of Health	Regulation of the Endocytic Trafficking of CFTR	14,895	7,671
Donna Beer Stolz	Massachusetts Institute of Technology	Perfused 3D Tissue Surrogates for Complex Cell-Cell Communication Systems	41,993	21,625
Donna Beer Stolz	Army	Escape from Tumor Cell Dormancy	11,708	6,030
Donna Beer Stolz	National Institutes of Health	Ex Vivo Adipose Tissue as a Screening Tool	6,491	3,342
Donna Beer Stolz	National Institutes of Health	Endogenous Regulators of Inflammation in Liver Ischemia/Reperfusion	9,725	5,008
Donna Beer Stolz	MWRI-NIH	Primary Human Trophoblasts and the Transfer of Viral Resistance	9,560	4,923
Donna Beer Stolz	National Institutes of Health	All Human Microphysical Model of Metastasis Therapy	85,711	39,223
Donna Beer Stolz	National Institutes of Health	Core A Cell and tissue Imaging Core	61,725	32,406
Donna Beer Stolz	National Science Foundation	Engineering Research Center	27,859	14,000
Donna Beer Stolz	National Institutes of Health	Bid-mediated killing of oncogenic stem cells in chemoprevention	2,726	1,431
Patrick Thibodeau	National Institutes of Health	Regulated Biosynthesis and Function of ABC-Transport Systems	250,000	128,749
Patrick Thibodeau	Cystic Fibrosis Foundation	Structural Interactions Regulating CFTR Channel Function	53,991	4,319
Patrick Thibodeau	Cystic Fibrosis Foundation	BRIDGE FUNDING Structural Interactions Regulating CFTR Channel Function	10,803	864
Linton Traub	National Institutes of Health	Clathrin-coated vesicles and endocytic function	15,772	7,959
Simon Watkins	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	40,000	-
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	6,618	3,408
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	73,679	37,946
Simon Watkins	National Institutes of Health	Novel Strategies for Brain Tumor Therapy	42,048	21,655
Simon Watkins	National Institutes of Health	Hepatocellular Carcinoma in Antitrypsin Deficiency	13,428	6,915
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	22,727	11,704
Simon Watkins	National Institutes of Health	Improving Chronic Neural Recording Performances Through Biomaterial Strategies	711	366
Simon Watkins	National Institutes of Health	DC T Interactions in Pulmonary Immune Responses	5,878	3,027
Simon Watkins	National Institutes of Health	ROS Mechanisms in BAV Aortopathy	5,800	2,987
Simon Watkins	National Institutes of Health	Intracellular Serpin Regulation of Intestinal Cell Necrosis	1,909	559
Simon Watkins	National Institutes of Health	Molecular Biology of Hemorrhagic Shock	96,033	49,458
Simon Watkins	National Institutes of Health	Directing Tumor Specific T cells to Tumors	39,545	20,366
Simon Watkins	National Institutes of Health	Amplification of IL-4/Ralpha Signaling Pathways in Human Airways Through I15 LOI	5,982	2,248

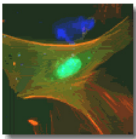


Simon Watkins	National Institutes of Health	Multiple Tumor Antigen-Loaded DC Vaccine for Hepatocellular Cancer	6,643	3,421
Simon Watkins	National Institutes of Health	Multi-Disciplinary Approaches to Driving Therapeutic Human Beta Cell Replication	3,792	1,953
Simon Watkins	National Institutes of Health	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	8,570	4,414
Simon Watkins	National Institutes of Health	Adipose Triglyceride Lipases (ATGL) in Lipotoxicity and the Metabolic Syndrome	5,240	3,951
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	18,115	7,183
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	21,727	11,189
Simon Watkins	National Institutes of Health	Imaging Mass Spectrometry for Oxidized Lipidomics in Acute Lung Injury	25,108	9,968
Simon Watkins	National Institutes of Health	Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging	11,289	5,814
Simon Watkins	National Institutes of Health	Combinational immunotherapy targeting the malonoma	19,833	10,412
Simon Watkins	Army	Molecular and Functional Characterization of the Lupus Platelet		
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Core B		
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Project 1	4,285,028	1,703,938

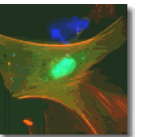


Cell Biology Sponsored Research Funding (FY13)

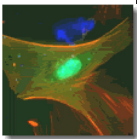
Name	Agency Name	Title	Annual DC	Annual IDC
Meir Aridor	National Institutes of Health	COPII Organization and Vesicle Formation at ER Exit Sites	124,995	64,349
Catherine Baty	CTSI	The Role of Placental Lymphatics in Preeclampsia and Intrauterine Growth Restriction	12,342	-
Carol Bertrand	Cystic Fibrosis Foundation	Role of SLC26A9 in biogenesis and anion secretion in airway	67,500	5,400
Michael Butterworth	Grilead	Regulations of the epithelial sodium(ENaC)	41,746	5,234
Peter Drain	National Institutes of Health	Anesthetic Sites in Transmembrane Peptides by NMR	1,220	628
Wayne Ernst	Cystic Fibrosis Foundation	Lipid Environments in the Endoplasmic Reticulum and CFTR Sorting	70,000	-
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	44,513	22,926
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	139,841	72,018
Raymond Frizzell	Cystic Fibrosis Foundation	Program Enrichment and Administration Core	27,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Molecular Biology and Gene Expression Core A	100,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in Wild-Type and DF508 CFTR Processing	19,109	1,529
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in Wild-Type and DF508 CFTR Processing-BRIDGE FUNDING	14,390	1,151
Raymond Frizzell	National Institutes of Health	Traffic Regulatory Proteins and ENaC	198,235	102,092
Raymond Frizzell	National Institutes of Health	Trans-NIH-Research Support	24,250	12,489
Yang Hong	National Institutes of Health	Regulation of Adherens Junction Dynamics by Polarity Proteins	183,721	90,753
Yang Hong	American Cancer Society	Regulation of a Tumor Suppressor and Cell Polarity Protein Lgl by Hypoxia	150,000	30,000
Adam Kwiatkowski	March of Dimes	Molecular coordination of cell movement and cell-cell adhesion during neural tube formation	68,182	6,818
Sandra Murray	National Science Foundation	Gap Junction Plaque Internalization	110,602	50,422
Sandra Murray	National Science Foundation	Gap Junction Plaque Internalization	13,334	3,334
Uma Perunthiathu	American Heart	Mechanistic Role of Clathrin-Endocytic Component, Fc β 1 in Bmp Signaling (Postdoc Fellowship)	48,000	-
Alexander Sorkin	National Institutes of Health	The influence of gene-environment interactions on neuronal mitochondrial fission, fusion, and transport in chronic parkinson's disease-relevant environmental toxin models. \	6,641	3,487
Alexander Sorkin	National Institutes of Health	Dopamine Transporter Regulation by Endocytosis	231,006	101,564
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	239,850	95,237
Donna Beer Stolz	Massachusetts Institute of Technology	Perfused 3D Tissue Surrogates for Complex Cell-Cell Communication Systems	41,604	21,426
Donna Beer Stolz	National Institutes of Health	Ex Vivo Adipose Tissue as a Screening Tool	1,102	568
Donna Beer Stolz	National Institutes of Health	Endogenous Regulators of Inflammation in Liver Ischemia/Reperfusion	8,698	4,479
Donna Beer Stolz	MWRENIH	Primary Human Trophoblasts and the Transfer of Viral Resistance	11,441	5,893
Donna Beer Stolz	National Institutes of Health	All Human Microphysical Model of Metastasis Therapy	90,960	41,192
Donna Beer Stolz	National Institutes of Health	Core A Cell and tissue Imaging Core	74,701	36,738
Donna Beer Stolz	National Science Foundation	Engineering Research Center	24,346	12,593



Donna Beer Stolz	National Institutes of Health	Bid-mediated killing of oncogenic stem cells in chemoprevention	4,712	2,474
Donna Beer Stolz	National Institutes of Health	Arginine/NO metabolism in HCC	24,990	-
Donna Beer Stolz	National Institutes of Health	Mechanisms of Arsenite-induced Muscle Morbidity and Reduced Regenerative Capacity	8,089	4,247
Donna Beer Stolz	National Institutes of Health	Signaling pathways influencing liver disease phenotype in antitrypsin deficiency	27,482	12,502
Patrick Thibodeau	National Institutes of Health	Regulated Biosynthesis and Function of ABC-Transport Systems	250,000	128,749
Patrick Thibodeau	Cystic Fibrosis Foundation	Structural Interactions Regulating CFTR Channel Function-BRIDGE FUNDING	10,803	864
Linton Traub	National Institutes of Health	Clathrin-coated vesicles and endocytic function	257,264	123,375
Simon Watkins	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	40,000	-
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	6,696	3,448
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	73,679	37,944
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	15,588	7,228
Simon Watkins	National Institutes of Health	ROS Mechanisms in BAV Aortopathy	5,407	2,784
Simon Watkins	National Institutes of Health	Intracellular Serpin Regulation of Intestinal Cell Necrosis	370	190
Simon Watkins	National Institutes of Health	Molecular Biology of Hemorrhagic Shock	95,343	41,892
Simon Watkins	National Institutes of Health	Directing Tumor Specific T cells to Tumors	29,659	15,275
Simon Watkins	National Institutes of Health	Amplification of IL-4/Ralpha Signaling Pathways in Human Airways Through 15 LO1	6,166	2,316
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	Cancer Center Support Grant	81,832	42,144
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	84,014	37,329
Simon Watkins	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	150,000	69,525
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	8,620	4,438
Simon Watkins	National Institutes of Health	Adipose Triglyceride Lipases (ATGL) in Lipotoxicity and the Metabolic Syndrome	5,000	2,575
Simon Watkins	National Institutes of Health	Stem Cells for Corneal Engineering	20,385	10,500
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Core B	5,114	2,466
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Project 1	11,757	6,056
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	5,844	3,010
Simon Watkins	National Institutes of Health	Imaging Mass Spectrometry for Oxidized Lipidomics in Acute Lung Injury	10,530	4,221
Simon Watkins	National Institutes of Health	Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging	11,628	5,988
Simon Watkins	National Institutes of Health	Biochemical and Spatial Regulation of IKKa/NEMO During T-Cell Activation	10,406	5,463
Simon Watkins	National Institutes of Health	Combinatorial Immunotherapy targeting the Malonoma	21,463	9,956
Simon Watkins	National Institutes of Health	Targeted Fluorescent Indicators for Endothelial Physiology	24,651	7,271
Simon Watkins	National Institutes of Health	Cell/Autonomous and Non-Autonomous Mechanisms of Aggravation	109,961	52,480



Simon Watkins	National Institutes of Health	CYP 450 Mediated CBF Dysregulation and Neurotoxicity in Pediatric Cardiac Arrest	9,943	4,254
Simon Watkins	National Institutes of Health	Dysfunctional Muscle Remodeling and Regeneration in Environmental disease	22,457	11,844
Simon Watkins	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lung Injury	104,312	55,024
			3,754,137	1,515,633



Faculty Editorships (Fiscal Year 2012 - 2013)**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*

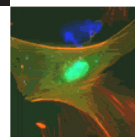
Member of board of reviewing editors, Molecular Biology of the Cell
 Traffic, Associate Editor
 Member of editorial board of Scientific Reports

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

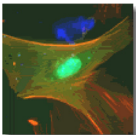
Editor, Experimental Science and Medicine

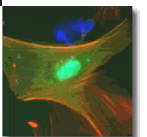
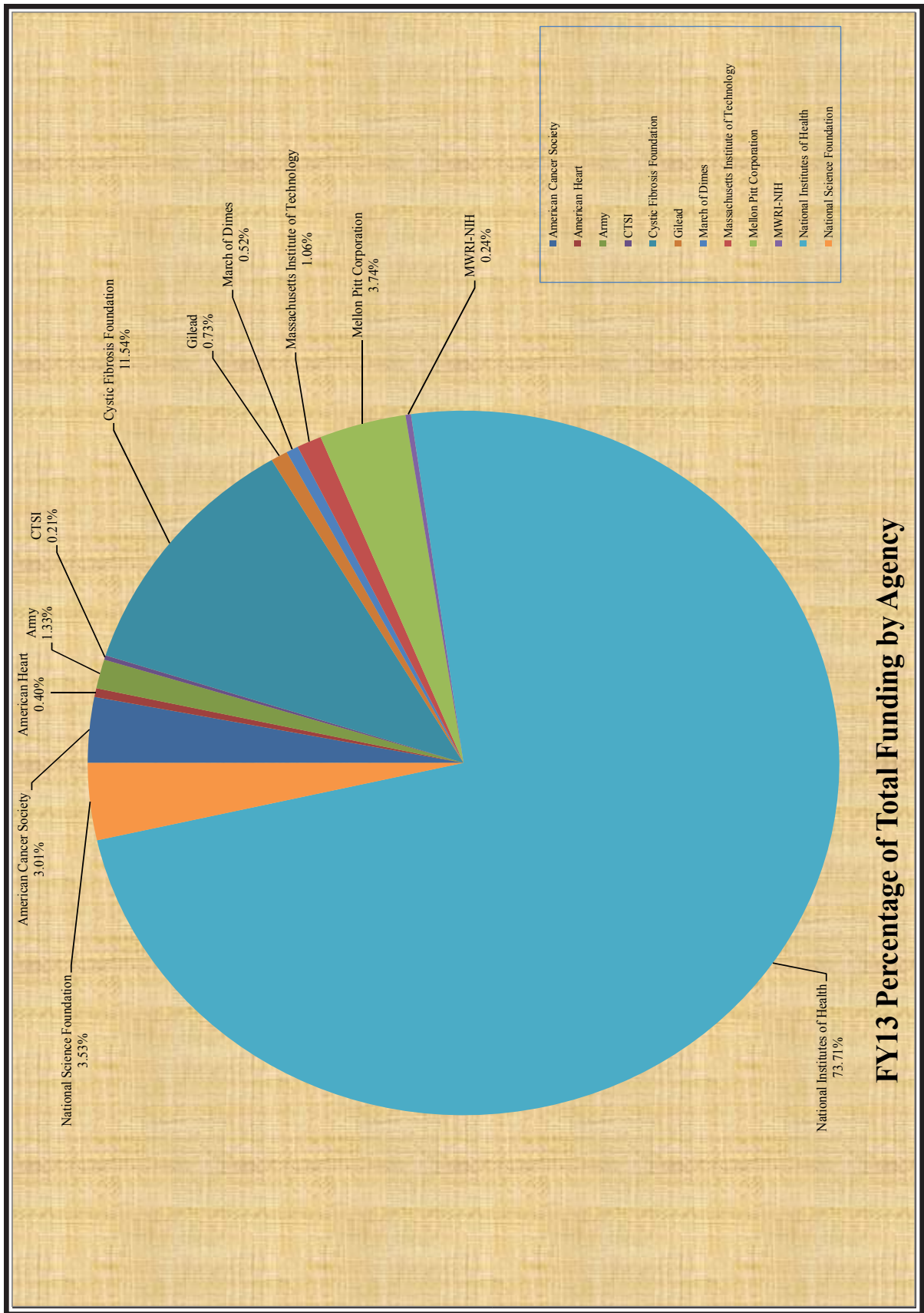
Christine C. Wu, Ph.D.

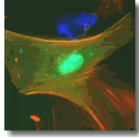
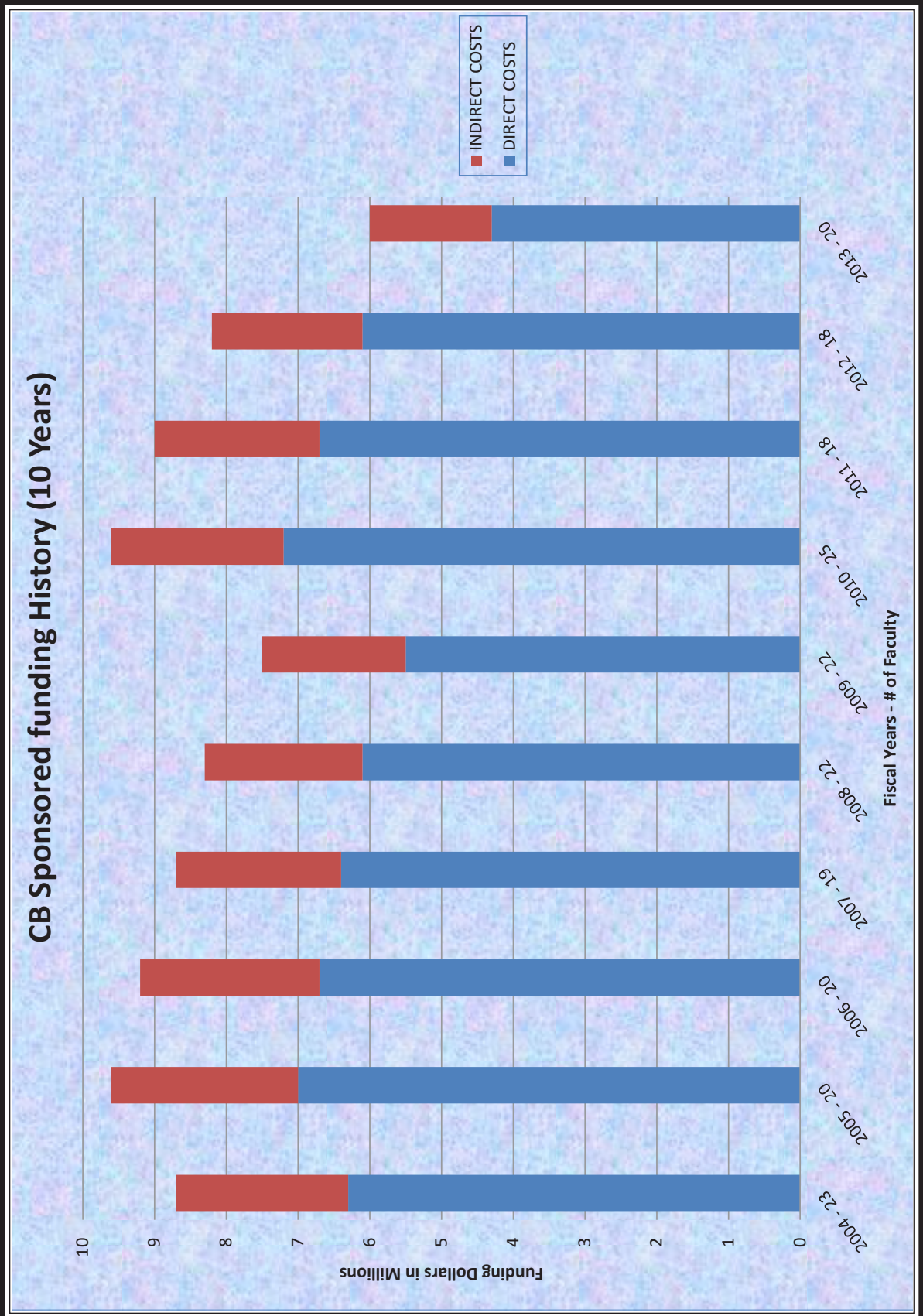
Associate Professor

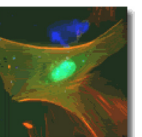
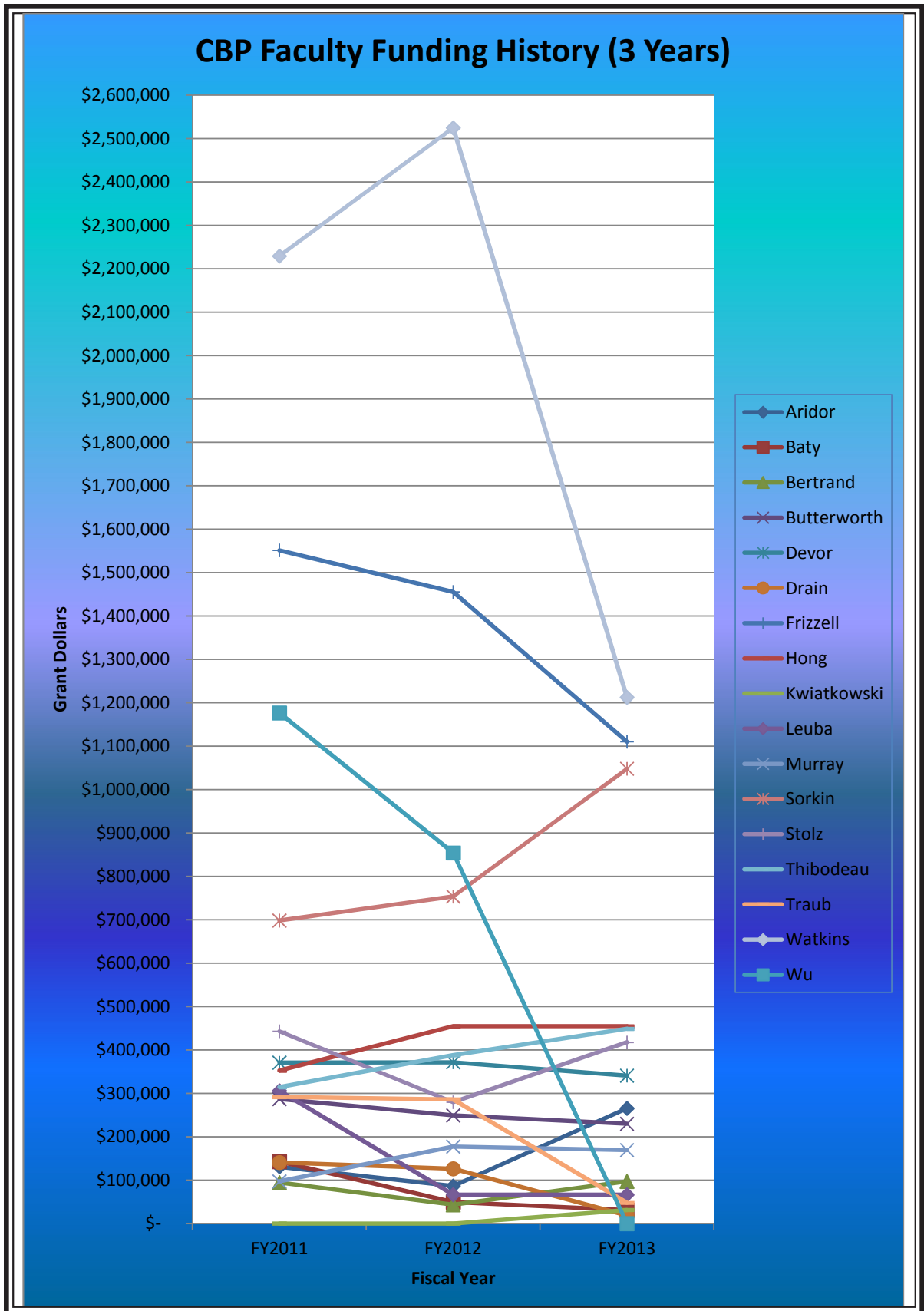
Editorial Board, Neurochemical Research

Editorial Board, Amino Acids (Proteomics Section)





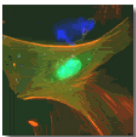




CBP FACULTY ROSTER
(Effective June, 2013)

<u>Faculty Member</u>	<u>Salary Support on Grants</u>	<u>Rank</u>	<u>Status</u>
Bertrand, Carol	100.0%	Res. Assistant Professor	Non-tenure Track
Gangopadhyay, Archana	100.0%	Res. Assistant Professor	Non-tenure Track
Liang, Xiubin	100.0%	Res. Assistant Professor	Non-tenure Track
O'Donnell, Allyson	100.0%	Res. Assistant Professor	Non-tenure Track
Peters, Kathryn	100.0%	Res. Assistant Professor	Non-tenure Track
Baty, Catherine	96.9%	Res. Assistant Professor	Non-tenure Track
Thibodeau, Patrick	71.6%	Assistant Professor	Tenure Track
Stolz, Donna	71.0%	Associate Professor	Tenured
Watkins, Simon*	70.8%	Professor	Tenured
Sorkin, Alexander*	59.4%	Professor	Tenured
Hong, Yang	56.0%	Associate Professor	Tenured
Frizzell, Raymond*	50.3%	Professor	Tenured
Devor, Daniel	45.8%	Associate Professor	Tenured
Aridor, Meir	40.1%	Associate Professor	Tenured
Butterworth, Michael	38.5%	Assistant Professor	Tenure Track
Wu, Christine	26.5%	Associate Professor	Tenured
Murray, Sandra	16.0%	Professor	Tenured
Drain, Peter	11.2%	Associate Professor	Tenured
Traub, Linton	7.8%	Associate Professor	Tenured
Leuba, Sanford	5.0%	Associate Professor	Tenured

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

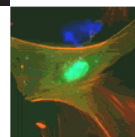


STUDENTS INVOLVED IN RESEARCH IN CBP FACULTY LABS

Snapshot as of June, 2013

GRADUATE STUDENTS ENROLLED IN CBMP PROGRAM

STUDENT	LAB	SUPPORT
Chelsea Crum	Patrick Thibodeau, Ph.D. Cell Biology	Patrick Thibodeau, Ph.D. Cell Biology & Teaching Fellowship
Christine Klemens	Michael Butterworth, Ph.D. Cell Biology	Michael Butterworth, Ph.D. Cell Biology & Teaching Fellowship
George Michael Preston	Jeffrey Brodsky, Ph.D. Biological Sciences	Jeffrey Brodsky, Ph.D. Biological Sciences & Renal T32
Kathryn Wack	Donna Stolz, Ph.D. Cell Biology	Donna Stolz, Ph.D. Cell Biology & ATP T32
Arvind Suresh	Jennifer Condon, Ph.D. OB/GYN	Jennifer Condon, Ph.D. OB/GYN & Teaching Fellowship
Christina Szalinski	Ora Weisz, Ph.D. Medicine/Renal	Ora Weisz, Ph.D. Medicine/Renal & Teaching Fellowship



**Cell Biology Training Grants
FY13 and FY14**

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

FY13 Projects

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

Traub lab: *Mechanistic Role of Clathrin Endocytosis*
(American Heart Association)

The combined funding for these post doctoral fellowship grants is \$62,151 in FY13 (Total costs, annualized).

FY14 Projects

Traub lab: *Mechanistic Role of Clathrin Endocytosis*
(American Heart Association)

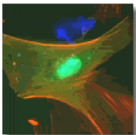
The combined funding for this post doctoral fellowship grants is \$48,000 in FY14 (Total costs, annualized).

Program Grant Training Program:

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

FY13 Program Grant Training Funds - \$70,000

FY14 Program Grant Training Funds - \$70,000



Cell Biology Program Grants (Fiscal Year 2012-13)

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

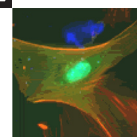
National Institutes of Health Cystic Fibrosis Research and Translation Core Centers Program (Principal Investigator/Program Director - Raymond A. Frizzell, Ph.D.):

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

This program grant totaled \$913,492 (total costs) in FY13.

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

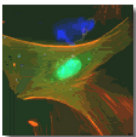


Development Program Center has existed at the University of Pittsburgh since 1997. The current center gathers over \$9.6M in external grants and contracts in support of CF-related research. It consists of 40 investigators in seven departments, whose research is focused in three major areas. The area 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 FY13. For more up to date information regarding the research conducted under this program grant, visit our website at: <http://www.cb.pitt.edu/centers/cfrc.html>.

National Technology Centers for Networks and Pathways (Principal Investigators –Simon Watkins, Ph.D.):

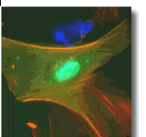
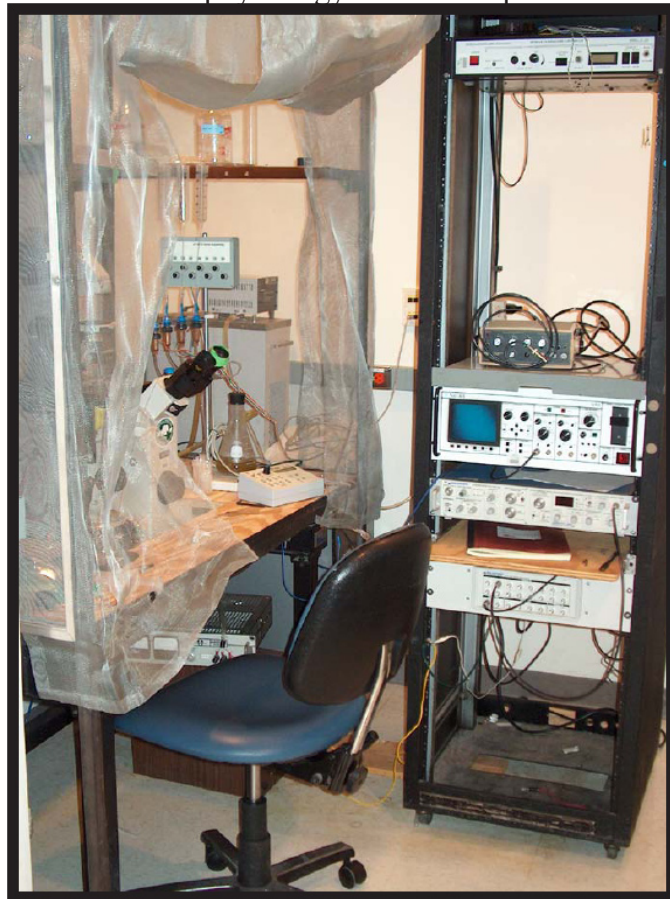
Over the last several years, microscopy as a scientific tool has reinvented itself. It has changed from a group of principally descriptive methodologies, to a wide range of quantitative tools and techniques to investigate the molecular organization of organs, tissues and cells. The University of Pittsburgh 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 FY13.

Electrophysiology Patch Clamp



New CBP Research Recruits in FY13

Name

Rank

Faculty Level

None

Name

Rank

Lab Association

Post Doctoral Level

Nianhong Chen

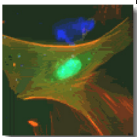
Post Doctoral Associate

Dr. Yong Wan

Emily Wickline

Post Doctoral Associate

Dr. Adam Kwiatkowski



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.

Adam V. Kwiatkowski, Ph.D.

Sandra Murray, Ph.D.

Claudette St Croix, Ph.D. (EOH)

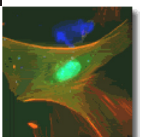
Donna Beer Stolz, Ph.D.

Simon C. Watkins, Ph.D.

Cellular Injury and Wound Healing

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

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)
Shivalingappa Swamynathan, Ph.D. (Ophthalmology)

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. (Ophthalmology)
William Walker, Ph.D. (MWRI)
Yong Wan, Ph.D. (UPCI)
Judith Yanowitz, Ph.D. (MWRI)

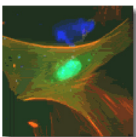
Ion Channel Biology

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 Hospital)
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.

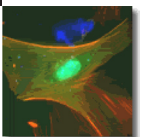
Yang Hong, Ph.D.

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 Hospital)



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

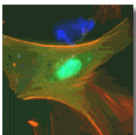
Regulated secretion of insulin by the pancreas and the actions of insulin and leptin in muscle, fat and liver cells are critical for controlling the body's energy metabolism. Disruption of these processes leads to diabetes or obesity. Researchers in this program are defining the cell signaling mechanisms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

Courses in FY-13

Title: MS Thesis Research

Course Number: 2800

Course Director: Donna Beer Stolz

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

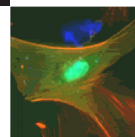
Course Director: Gerard Apodaca

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: William Walker

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

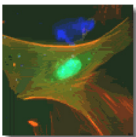
Course Number: 2870

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, and Donna Beer Stolz

When: Spring and Fall 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: Imaging Cell Biology in Living Systems

Course Number: 2885

Course Director: Simon Watkins

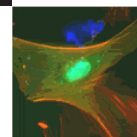
When: Spring Term

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: Directed Study

Course Number: 2890



Course Director: Donna Beer Stolz

When: Fall Term, Spring Term, Summer Term, and Fall 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: Donna Beer Stolz

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

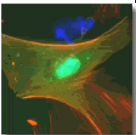
Course Number: 3835

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%).



Title: Reproductive Development from Model Organisms to Humans

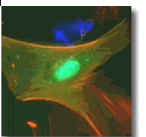
Course Number: 3840

Course Directors: Jennifer Condon-Jeysuria and Judith Yanowitz

When: Fall Term

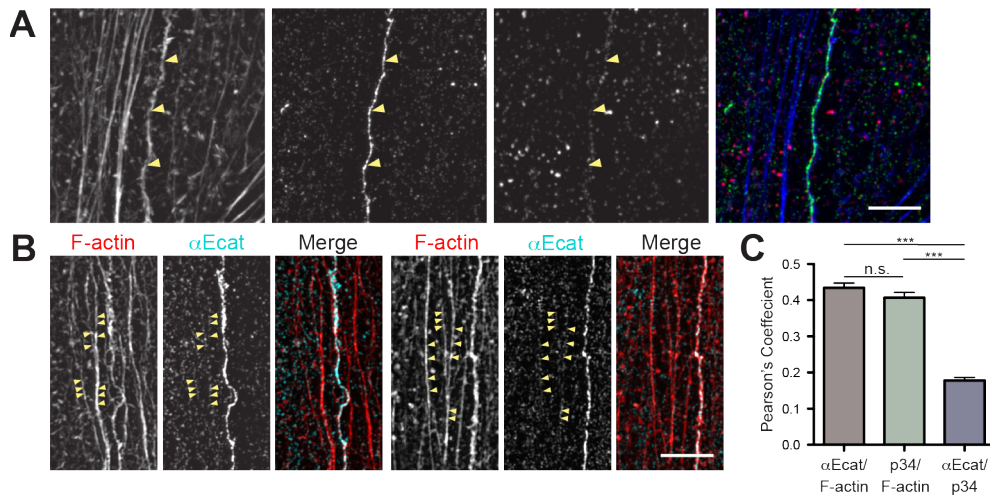
Prerequisites: None

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.

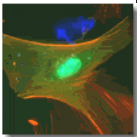


Faculty Teaching Honors (Fiscal Year 2012-2013)

NONE



Adam Kwiatkowski. α E-catenin colocalizes with F-actin at developing cell-cell contacts. 3D-SIM images of MDCK epithelial cells stained for F-actin, α E-catenin and p34 (Arp2/3 complex). Scale bar is 5 microns.
 (A) At 24 hour (E) cell-cell contacts, α E-catenin is enriched along the F-actin-rich adhesion, whereas p34 localization there is limited. Yellow arrows identify the cell-cell contact.
 (B) After pre-extraction, α E-catenin is occasionally observed along F-actin bundles, often adjacent to cell-cell contacts. Yellow arrows mark α E-catenin puncta along actin bundles.
 (C) Pearson's coefficient was calculated between individual channels along cell-cell contacts. Both α E-catenin and p34 displayed similar levels of colocalization with F-actin; however, there was little correlation between α E-catenin and p34 signals (***) $p < 0.0001$; one-way ANOVA with Tukey's range test). Errors bars indicate SEM (35 images, >40 contacts measured).



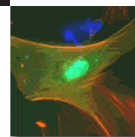
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE
EDUCATIONAL CREDIT UNIT REPORT (AY 2011 – 2012)

Department of Cell Biology and Physiology

	# ECUs	% ECUs
Department of Cell Biology and Physiology	2992.60	Not provided
Combined Total for All Basic Science Departments	Not provided	100

Summary of Faculty ECU's

Faculty Name	Activity	ECURV	Units	ECU's
Meir Aridor, Ph.D.				
	GS - Lecture	2.0	8.0	16.0
	GS – Small group (e.g., PBL, conference, workshop)	2.0	33.0	66.0
	GS –Course Director	10.0	1.0	10.0
	GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	3.0	15.0
	GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	2.0	1.0	<u>2.0</u>
				Total ECU's: 109.0
Catherine Baty, D.V.M., Ph.D.				
	MS – Mentored Scholarly Project (MSP) Mentor	25.0	1.0	25.0
	MS – Elective Course Research mentor	4.0	1.0	4.0
	GS – Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	3.0	<u>3.0</u>
				Total ECU's: 32.0
Michael Butterworth, 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 – Advising/Mentoring	20.0	1.0	20.0
	GS – Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	6.0	6.0
	MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	16.0	32.0
	MS 1, MS 2 – Laboratory	2.0	58.0	<u>116.0</u>
				Total ECU's: 186.0
Daniel Devor, Ph.D.				
	GS - Lecture	2.0	6.0	12.0
	GS – Advising/Mentoring	20.0	1.0	20.0
	GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	10.0
	GS –Chair: Curriculum, Recruiting, Program, or other SOM Committee	5.0	1.0	<u>5.0</u>
				Total ECU's: 47.0



Peter Drain, Ph.D.

MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	16.0	32.0
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, Course Design Group	5.0	1.0	5.0
MS –Member, Applicant Interviewer	1.0	10.0	10.0
GS – Lecture	2.0	3.0	6.0
GS – Small group (e.g., PBL, conference, workshop)	2.0	28.0	56.0
GS – Advising/Mentoring	20.0	1.0	20.0
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	2.0	2.0	<u>4.0</u>
			Total ECU's:403.0

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	85.6	171.0
MS 1, MS 2 – Laboratory	2.0	22.3	44.6
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 – Course Segment Coordinator	5.0	3.0	15.0
MS – Elective Course Director	10.0	1.0	10.0
MS – Chair or Member, subcommittee, task force, work group	5.0	4.0	20.0
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	<u>10.0</u>
			Total ECU's:560.6

Raymond Frizzell, Ph.D.

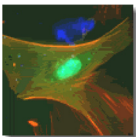
MS 1 and MS 2 – AOC/Longitudinal Curriculum Program Director	20.0	1.0	20.0
MS – AOC/LCP activity (other than advising, e.g., teaching, precepting)	2.0	61.5	123.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	2.0	<u>4.0</u>
			Total ECU's:147.0

Vernon Gay, Ph.D.

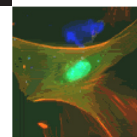
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	13.5	<u>27.0</u>
			Total ECU's: 27.0

Yong Hong, Ph.D.

GS – Lecture	2.0	4.0	8.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	4.0	8.0
GS – Exam proctoring	2.0	4.0	8.0
GS – Advising/Mentoring	2.0	3.0	6.0
GS –Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	3.0	<u>15.0</u>
			Total ECU's: 50.0

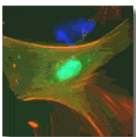


Sanford Leuba, Ph.D.			
GS - Lecture	2.0	2.0	4.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	8.0	16.0
GS – Other	2.0	10.0	20.0
GS – Ph.D. or M.Sc. Mentor	20.0	2.0	40.0
GS – Course Director	10.0	1.0	10.0
GS – Member: Admissions Committee	5.0	1.0	5.0
GS – Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	<u>5.0</u>
			Total ECU's:102.0
Sandra Murray, Ph.D.			
MS 1, MS 2 – Lecture	2.0	3.5	7.0
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	2.0	4.0
MS 1, MS 2 – Laboratory	2.0	40.0	80.0
MS – Exam proctoring	2.0	6.0	12.0
MS 1, MS 2 – Other	2.0	8.0	16.0
MS – Research Mentor	1.0	4.0	4.0
MS – Member of Medical Student Promotion or Retention Committee	5.0	1.0	5.0
GS - Lecture	2.0	1.0	2.0
GS – Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	3.0	3.0
GS – Member: all remaining committees and subcommittees	1.0	2.0	2.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	<u>10.0</u>
			Total ECU's:145.0
Kathryn Peters, Ph.D.			
MS – AOC/LCP activity (other than advising, e.g., teaching, precepting)	2.0	57.0	<u>114.0</u>
			Total ECU's:114.0
Kathleen Ryan, Ph.D.			
MS –Member, Curriculum Committee	20.0	1.0	20.0
MS –Member, Promotions Committee	5.0	2.0	10.0
MS –Applicant Interviewer	1.0	10.0	<u>10.0</u>
			Total ECU's: 40.0
Alexander Sorokin, Ph.D.			
GS - Lecture	2.0	4.0	8.0
GS – Lab Supervision	1.0	15.0	15.0
GS – Chair or Member, Comprehensive, Dissertation, Thesis, Preliminary, or Reprint	5.0	1.0	<u>5.0</u>
			Total ECU's: 28.0
Donna Stolz, Ph.D.			
MS 1, MS 2 – Lecture	2.0	1.	2.0
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	6.5	13.0
MS 1, MS 2 – Laboratory	2.0	20.5	41.0
MS – Exam proctoring	2.0	2.0	4.0
MS – Medical Student Applicant Interviewer	1.0	3.0	3.0
GS - Lecture	2.0	18.5	37.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	22.5	45.0

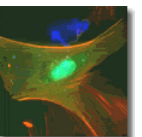


CB Faculty Teaching Activities

GS – Academic advisor	2.0	4.0	8.0
GS – PhD, MSTP, CSTP, PSTP MSc mentor	20.0	1.0	20.0
GS – Lab Supervision	1.0	20.0	20.0
GS – Course Director	10.0	2.0	20.0
GS – Program Director	30.0	1.0	30.0
GS – Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	15.0	75.0
GS – Chair: all remaining committees and subcommittees	5.0	5.0	25.0
GS – Member: all remaining committees and subcommittees	1.0	2.0	<u>2.0</u>
			Total ECU's:345.0
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Patrick Thibodeau, Ph.D.			
GS - Lecture	2.0	6.0	12.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	23.5	47.0
GS – PhD, MSTP, CSTP, PSTP MSc mentor	20.0	1.0	20.0
GS – Lab Supervision	1.0	15.0	15.0
GS – Member, Graduate Admissions Committee	5.0	1.0	5.0
GS –Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	3.0	15.0
MS 1, MS 2 – Small group (e.g., PBL, conference, workshop)	2.0	18.0	<u>36.0</u>
			Total ECU's:150.0
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Linton Traub, Ph.D.			
GS - Lecture	2.0	14.0	28.0
GS – Ph.D. or M.Sc. Mentor	20.0	1.0	20.0
GS – Chair or Member, Comprehensive, Dissertation, Thesis, Preliminary, or Reprint	5.0	5.0	25.0
GS – Chair: all remaining committees and subcommittees	5.0	1.0	<u>5.0</u>
			Total ECU's: 78.0
<hr/>			
Yong Wan, Ph.D.			
GS - Lecture	2.0	4.0	8.0
GS – Chair or Member, Comprehensive, Dissertation, Thesis, Preliminary, or Reprint	5.0	2.0	<u>10.0</u>
			Total ECU's: 18.0
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Simon Watkins, 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	101.0	202.0
GS – Lecture	2.0	25.5	51.0
GS – Exam proctoring	2.0	4.0	8.0
GS – Course Director	10.0	1.0	10.0
GS – Chair or Member, Comprehensive, Dissertation, Thesis, Preliminary, or Reprint	5.0	6.0	<u>30.0</u>
			Total ECU's:321.0
<hr/>			
Christine Wu, Ph.D.			
GS - Lecture	2.0	2.0	4.0
GS – Academic advisor	2.0	2.0	4.0
GS – Lab Supervision	1.0	4.0	<u>4.0</u>
			Total ECU's: 12.0
<hr/>			
Nathan Yates, Ph.D.			
GS - Lecture	2.0	4.0	8.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	20.0	40.0



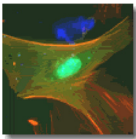
GS – PhD, MSTP, CSTP, PSTP MSc mentor		20.0	1.0	20.0
GS – Lab Supervision		1.0	10.0	10.0
		Total ECU's: 78.0		
<hr/>				
Total Faculty reporting	21		Faculty ECU Subtotal:	2992.6
<hr/>				
			Total ECU's for Cell Biolog:	2992.6



Post Doctoral Personnel Data

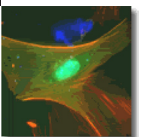
[Current as of June, 2013]

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
Bertuccio, Claudia A.	Vis. Research Associate	S331 BSTWR	cab199@pitt.edu	412-383-7192	412-648-8330	Devor Lab
Caltagarene, John	Post Doctoral Associate	S372 BSTWR	jmcalt@pitt.edu	412-648-9260	412-648-8330	Sorkin Lab
Chen, Nianhong	Post Doctoral Associate	HCCLB-2.7	nic40@pitt.edu	412-623-7811	412-623-7761	Wan 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, Atola	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
Liao, Yong	Vis. Research Associate	7161 RANCH	yol23@pitt.edu	412-692-9326	412-692-8906	Frizzell Lab
Long, Kimberly	Post Doctoral Associate	S307 BSTWR	kr134@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
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
Wickline, Emily	Post Doctoral Associate	S349 BSTWR	boyde@pitt.edu	412-383-7891	412-648-8330	Kwiatkowski Lab
Zhang, Liang	Post Doctoral Associate	S332 BSTWR	liz46@pitt.edu	412-624-8933	412-648-8330	Thibodeau Lab
Zhou, Zhuan	Post Doctoral Associate	HCCLB-2.6	zhouz2@upmc.edu	412-623-7811	412-623-7761	Wan Lab



Current Cell Biology and Molecular Physiology Graduate Program Students as of June 30, 2013

<u>Student</u>	<u>Mentor</u>	<u>Year</u>
Cavita Chotoo	Dr. Daniel Devor	7 th
Chelsea Crum	Dr. Patrick Thibodeau	1 st
Elizabeth Delorme-Axford	Dr. Carolyn Coyne	4 th
Christine Klemens	Dr. Mike Butterworth	1 st
George Michael Preston	Dr. Jeff Brodsky	1 st
Xinxian Qiao	Dr. Yong Wan	4 th
Arvind Suresh	Dr. Jennifer Condon	4 th
Christina Szalinski	Dr. Ora Weisz	4 th
Kathryn Wack	Dr. Donna Beer-Stolz	3 rd



**Prior Graduates of the Cell Biology and Molecular Physiology Program as of June 2013
(Past five years)**

Christina Szalinski, Ph.D.

Defended May 20, 2013
American Society for Cell Biology (ASCB), Bethesda, MD

Cavita Kitty Chotoo, Ph.D.

Defended March 26, 2013
Rutger's, Post-Doc

Elizabeth Delorme-Axford, Ph.D.

Defended March 14, 2013
Post-Doc University of Pittsburgh, Dept. Microbiology & Molecular Genetics

Xinxian Qiao, M.S.

Defended December 17, 2012
Technician, Hillman Cancer Center, Pittsburgh, PA

Anupma Jha, Ph.D.

Defended December 8, 2011

Siobhan Gregg, Ph.D.

Defended November 4, 2011
New York Academy of Sciences Event Organizer

Daniel Rho, Ph.D.

Defended July 15, 2011
Plastic Surgery Resident, Harvard U.

James R. Thieman, Ph.D.

Defended June 9, 2011
Olympus Corporation

ShanShan Cui, Ph.D.

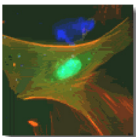
Defended December 7, 2010
Faculty, Galen College of Nursing, Cincinnati, Ohio

Mark A. Bailey, Ph.D.

Defended September 23, 2010
Post-Doc, Vollum Institute, Oregon

Paula J. Bernal, Ph.D.

Defended August 12, 2010
Staff, Center for Vaccine Development, University of Maryland



Ethan Block, Ph.D.

Defended January 19, 2010

Post-Doc, University of Pittsburgh, Department of Neurobiology

Bado Hewa DeFranco, Ph.D.

Defended September 3, 2009

Faculty, University of Pittsburgh at Greensburg, National Sciences, General Adm.

Mark R. Silvis, Ph.D.

Defended September 3, 2009

Post-Doc Fred Hutchinson Cancer Research Center, Seattle Washington

Roxana Teisanu, Ph.D.

Defended April 30, 2009

Post-Doc, Ecole Polytechnique Federal de Lausanne (EPFL), Switzerland

Michelle Wood, Ph.D.

Defended April 29, 2009

Post-Doc, University of Michigan, Ann Arbor, MI, Magee Women's Research Institute

Dan Constantinescu, Ph.D.

Defended December 8, 2008

Frommer, Lawrence, and Haug, LLP, New York, NY

Christopher Guerriero, Ph.D.

Defended September 24, 2008

University of Pittsburgh Medical School, Dept. of Biological Sciences

Mark Miedel, Ph.D.

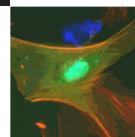
Defended August 27, 2008

Post-Doc University of Pittsburgh Medical School

Christopher Lewarcick, Ph.D.

Defended August 18, 2008

Post-Doc University of Pittsburgh Medical School



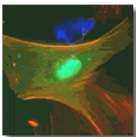
CB Faculty Instructor Ratings

Student Ratings of CBMP Faculty Teaching FY2013

Name	Course	Type	Date	Rating	Ave
Butterworth	Methods and Logic in Medicine Part 2	SGCS	Fall-12	4.20	
Butterworth	Cellular and Pathological Basis of Disease	LAB	Spring-13	4.60	
Butterworth	Cellular and Pathological Basis of Disease	PBL	Spring-13	4.50	4.43
Drain	Methods and Logic in Medicine Part 2	SGCS	Fall-12	4.20	4.20
Duker	Introduction to Being a Physician	SGCS	Fall-12	4.40	
Duker	Body Fluid Homeostasis Cardiovascular	WKSP	Fall-12	4.30	
Duker	Body Fluid Homeostasis-Renal Segment	LEC	Fall-12	4.50	
Duker	Body Fluid Homeostasis-Pulmonary Segment	LEC	Fall-12	4.80	
Duker	Cellular and Pathological Basis of Disease	LEC	Spring-13	4.70	
Duker	Cellular and Pathological Basis of Disease	LAB	Spring-13	4.90	
Duker	Cellular and Pathological Basis of Disease	PBL	Spring-13	4.60	
Duker	Digestion and Nutrition	LEC	Fall-12	4.70	
Duker	Digestion and Nutrition	LAB	Fall-12	4.90	
Duker	Endocrine	LEC	Spring-13	4.90	
Duker	Immunology in Health and Disease	LEC	Spring-13	4.70	
Duker	Immunology in Health and Disease	PBL	Spring-13	4.80	4.68
Kwiatkowski	Immunology in Health and Disease	LEC	Spring-13	4.50	
Kwiatkowski	Immunology in Health and Disease	PBL	Spring-13	4.00	4.25
Murray	Medical Anatomy	LEC	Fall-12	4.00	
Murray	Medical Anatomy	LAB	Fall-12	4.20	
Murray	Medical Anatomy	PBL	Fall-12	4.10	4.10
Ryan	Introduction to Being a Physician	SGCS	Fall-12	4.00	
Ryan	Body Fluid Homeostasis Cardiovascular	WKSP	Fall-12	4.40	
Ryan	Cellular and Pathological Basis of Disease	LEC	Spring-13	4.80	
Ryan	Digestion and Nutrition	PBL	Fall-12	4.80	
Ryan	Digestion and Nutrition	LEC	Fall-12	3.30	4.26
Stolz	Cell Biology of Normal and Disease States	LEC	Spring-11	4.83	
Stolz	Cellular and Pathological Basis of Disease	LEC	Spring-13	4.40	
Stolz	Cellular and Pathological Basis of Disease	LAB	Spring-13	4.90	
Stolz	Cellular and Pathological Basis of Disease	PBL	Spring-13	4.30	
Stolz	Digestion and Nutrition	LAB	Fall-12	4.70	4.63
Thibodeau	Methods and Logic in Medicine Part 2	SGCS	Fall-12	4.40	4.40
Watkins	Cellular and Pathological Basis of Disease	LEC	Spring-13	4.20	4.20
Overall Teaching Average				4.47	

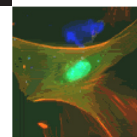
Type codes:

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



CBP FACULTY ROSTER
(Effective June, 2013)

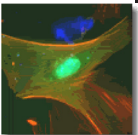
<u>Last Name</u>	<u>First</u>	<u>Rank</u>	<u>Status</u>
Sorkin	Alexander	Professor & Chair	Tenured
Devor	Daniel	Professor	Tenured
Frizzell	Raymond	Professor	Tenured
Murray	Sandra	Professor	Tenured
Watkins	Simon	Professor	Tenured
Aridor	Meir	Associate Professor	Tenured
Drain	Peter	Associate Professor	Tenured
Gay	Vernon	Associate Professor	Tenured
Hong	Yang	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
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

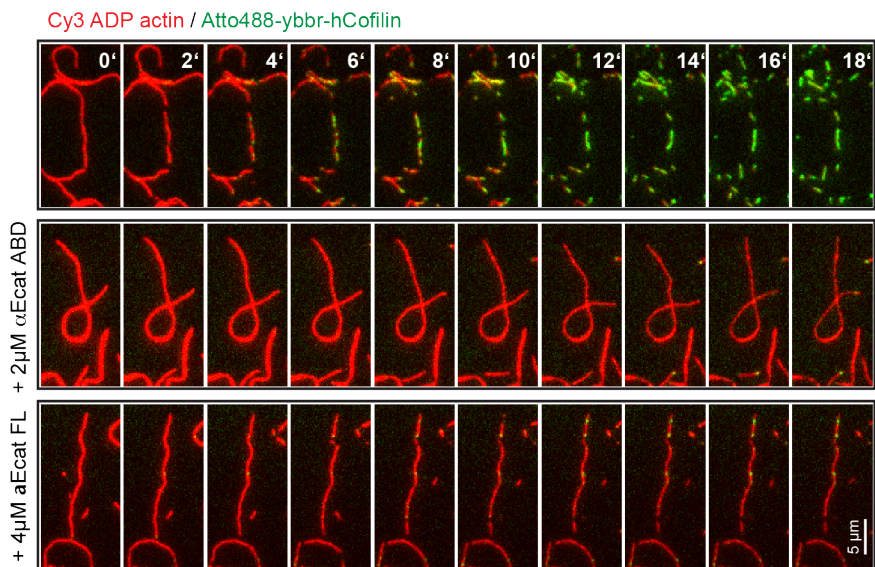


New CBP Faculty in FY13

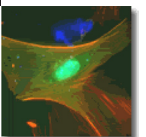
<u>Name</u>	<u>Prior Institution /Rank</u>	<u>Current Rank</u>
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None





Adam Kwiatkowski. α E-catenin inhibits cofilin severing of actin filaments. Montage of ADP actin filament (20% Cy3 labeled, red) disassembly in the presence of 75 nM Atto488-ybbr-hCofilin (green) alone or with α E-catenin ABD or full-length α E-catenin. Mixtures of Atto488-ybbr-hCofilin and α E-catenin (ABD and full-length protein) were flowed into the chamber simultaneously to initiate severing and actin filament binding, respectively.



Faculty Honors, Recognition and Professional Affiliations (Fiscal Year 2012-2013)

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

American Society of Nephrology

American Heart Association

Gilead Sciences Research Scholars Program in Cystic Fibrosis

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

Georgia Duker, Ph.D.

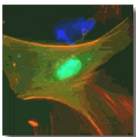
Assistant Professor

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

Yang Hong, Ph.D.

Associate 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

Adam Kwiatkowski, Ph.D.

Assistant Professor

Member, American Society for Cell Biology

Sanford Leuba, Ph.D.

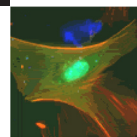
Associate Professor

Member, Biophysical Society

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
Society for Neuroscience

Donna B. Stolz, Ph.D.

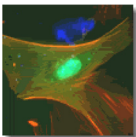
Associate Professor

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
Nikon Small World Honorable Mention photomicrograph
University of Pittsburgh Biomedical Graduate Student Association Distinguished Mentor Award

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.

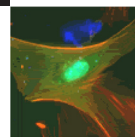
Associate Professor

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 2012-2013)

Carol Bertrand, Ph.D.

Research Assistant Professor

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

North American Cystic Fibrosis Conference, Symposium 15: CFTR: The Conductance Regulator. Title: CFTR and SLC26A9 exhibit coordinated regulation during protein maturation and functional activity. 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.

“Regulation of the Epithelial Sodium Channel by microRNAs”. Division of Nephrology, University of New Mexico School of Medicine. 2013

Daniel C. Devor, Ph.D.

Professor

“Trafficking of IK1 and SK3 in Endothelia” 10th Annual Ion Channel Symposium, May 23-24, 2013, Copenhagen, Denmark.

Raymond A. Frizzell, Ph.D.

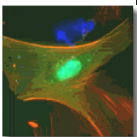
Professor, Director of Cystic Fibrosis Research Center

University of Otago, Department of Physiology, Dunedin, New Zealand. “Role of SLC26A9 in Cystic Fibrosis” November 2012.

University of Otago, Department of Pediatrics, Dunedin, New Zealand. “Strategies and Outcomes: Treating the Core Defect in Cystic Fibrosis” November 2012.

Australian-New Zealand Physiological Society Meeting, Sydney, Australia. “Fluorogen activating proteins report corrector-mediated restoration of mutant CFTR trafficking to the cell surface and its regulated peripheral recycling” December 2012.

Wayne State University Seminar Series, “Small heat shock proteins target mutant CFTR for degradation: SUMO enter the ring”, March 2013.



Adam Kwiatkowski, Ph.D.*Assistant Professor*

Regulation of Actin Network Organization at Cell-Cell Contacts. Seminar, Department of Cell Biology and Physiology, University of North Carolina – Chapel Hill, Chapel Hill, NC. May, 2013.

Regulation of Actin Network Organization at Cell-Cell Contacts. Seminar, Department of Biological Sciences, Duquesne University, Pittsburgh, PA. January, 2013.

Promoting Change From Within: A Mechanistic Framework for Actin Network Reorganization by Alpha-Catenin at Cell-Cell Contacts. Seminar, Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA. October, 2012.

Sanford H. Leuba, Ph.D.*Associate Professor*

International Plasmid Biology Meeting, Santander, Spain 12-16 September 2012.
CSIC, Madrid, Spain 18 September 2012.

Monie Ferst Award Symposium of Sigma Xi at Georgia Tech University in Honor of Ken van Holde in Atlanta 9 November 2012.

Guoliang Yang Memorial Symposium, Drexel University, 1 February 2013.

DKFZ, German Cancer Research Foundation, Heidelberg, Germany 19 April 2013.

IX International Interdisciplinary Scientific Research Congress (IX CIC), Santo Domingo, Dominican Republic, 13-14 June 2013.

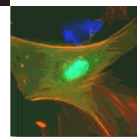
Sandra Murray, Ph.D.*Professor*

Scientific Boot Camp at Savannah State University 2012

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.

Arrestin' Developments: New biological functions for the α -arrestin family of trafficking adaptors. Carnegie Mellon University (2013), Pittsburgh



Arrestin' Developments: New biological functions for the α -arrestin family of trafficking adaptors. Duquesne University (2012), Pittsburgh

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

Membrane dynamics in cancer. Beatson International cancer conference, Glasgow, Scotland July, 2012

Life Sciences, BioConference Live September 12, 2012

Endocytosis and signaling. ASCB Annual meeting, San Francisco, December, 2012.

NCI-sponsored workshop "Dysregulated endocytosis in cancer", January 10-11, 2013.

Department of Biochemistry, Lexington, Kentucky, November, (2012).

Department of Biochemistry, Wright State University, February, (2013).

Patrick H. Thibodeau, Ph.D.
Assistant Professor

"The CFTR3D structural consortium." North American Cystic Fibrosis Conference, Orlando, FL, 2012

Yong Wan, Ph.D.
Associate Professor

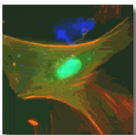
Proteolytic regulation of kruppel like-factor 4 in the cell cycle control and carcinogenesis. Cold Spring Harbor Laboratory. Cell Cycle Conference 2012

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

AAAS, Science webinar: "live cell imaging at speed" July 18, 2012, Invited Speaker

Novel Probes and Microscopies to study Cystic Fibrosis; University of Wisconsin, Madison WI, July 27, 2012 Invited Speaker

Quantitative Fluorescence Imaging: Biophotonics Optics World Webinar, Invited Speaker September 11, 2012

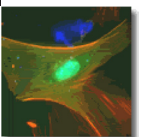
Optical Solutions in Multiple Dimensions: University of Madison, Madison WI, September 14, 2012 Invited Speaker

Novel Probes and Microscopies to study Cystic Fibrosis Children's Hospital, University of Pittsburgh September 18, 2012 Invited Speaker

Novel Probes and Microscopies to study Cystic Fibrosis; Vanderbilt University Nashville TN, November 30, 2012 Invited Speaker

Enabling Technologies Workshop, Invited Speaker, "Imaging Molecular Structure in situ" University of Pittsburgh February 4, 2013

Novel Probes and Microscopies to study Cystic Fibrosis, Invited Speaker, McGee Womens Institute March 12, 2013



Peer Reviewed Publications (Fiscal Year 2010-13)**Meir Aridor, Ph.D.***Associate Professor*

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, Gallo DJ, Raman KG, Karlsson JM, Ozanich B, Chin BY, Tzeng E, Ahma 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.

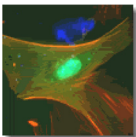
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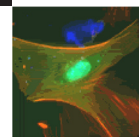
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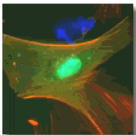
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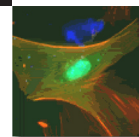
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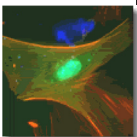
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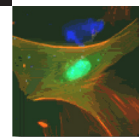
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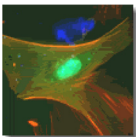
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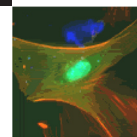
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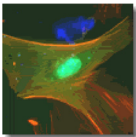
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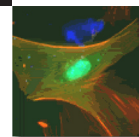
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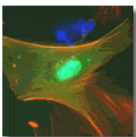
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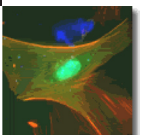
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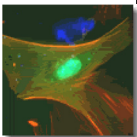
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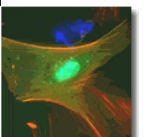
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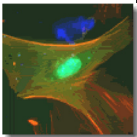
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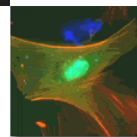
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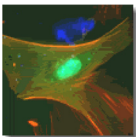
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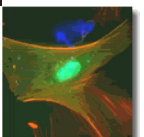
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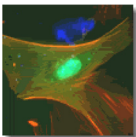
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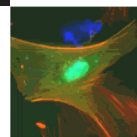
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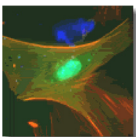
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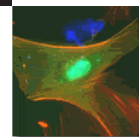
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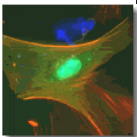
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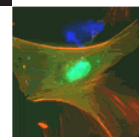
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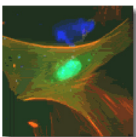
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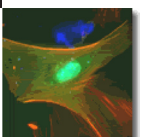
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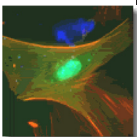
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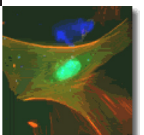
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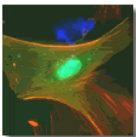
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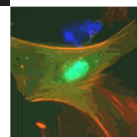


Executive Summary for the Cell Biology FY2013 Business Plan

In the past sixteen 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. During last three years significant changes in the Department took place with seven members of the primary faculty leaving the Department and four new members joining the faculty. This year one new primary faculty will join the Department. Achievement of the balanced distribution of the junior and senior faculty and strong integration of all activities of the faculty remains the important goal of our FY2013 plan. To this end, we will continue search for a senior faculty to join the Department in FY2013. We plan to recruit a scientist who studies 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

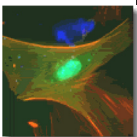
The Department of Cell Biology has a strong research program aimed at addressing fundamental questions of cell biology, including mechanisms controlling membrane trafficking, cell polarity, actin cytoskeleton, signal transduction, cell cycle, transcription, intercellular interactions and channel regulation. 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 general and cell biology journals such as the Proceedings of National Academy of Sciences USA (Huang et al. et al., 2013), Molecular Biology of the Cell (Ahner et al, 2012), Journal of Cell Science (Holleran et al., 2013), Development (Zhou and Hong, 2012) and Traffic (Sorkina et al., 2013). The department was selected as one of 13 cell biology departments to be featured at the Annual Meeting of the American Society of Cell Biology (December, 2012) in a video presentation.

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. We have been successful in obtaining new extramural research funding in the past cycle, as evidenced by the renewal of the P30 grant (Watkins and Yates), and the competitive renewal of an RO1 (Traub). Two senior faculty, Drs. Sorkin, and Watkins, have multiple NIH grants. Two junior faculty, Drs. Butterworth and Thibodeau are principal investigators on NIH funded grants. The most recent recruit, Dr. Kwiatkowski was awarded the March of Dimes grant. Dr. Hong was promoted to the position of Associate professor with tenure and continues to run the well-funded program. Submission of new grant applications remains to be at a high rate which ensures relative fiscal stability of the Department.

The new recruit, Dr. Marijn Ford, will join Department in December, 2013. He is a structural biologist who recently solved the crystal structure of a membrane fission protein, dynamin. His research is focused on elucidating the mechanisms of fusion and fission of mitochondria.

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 indispensable expertise in all types of cellular imaging to the faculty of the Department and the entire School of Medicine and University of Pittsburgh. In the last year, the CBI



expanded to include six more imaging systems. Drs. Watkins and Stolz were awarded multiple NIH shared instrumentation grants including new electron microscope, SIM super-resolution system and ultracryotom which are essential to the continued growth of the CBI and 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” and “Ubiquitin” symposiums, running the Membrane Trafficking journal club and in various School committees.

Teaching

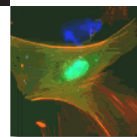
Medical Curriculum: The department contributes extensively to the teaching of medical and graduate students in the School of Medicine. Our faculty has been actively participating in the remodeling of the first year curriculum, particularly in the area of biochemistry and cell biology, involving formal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

Graduate Curriculum: We now have 4 students in the graduate Ph.D. program in Cell Biology and Molecular Physiology. 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: 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 senior faculty. In addition, more space will be required to allow for growth of the research programs of the current faculty located at BST South.



Several of the CBP faculty members operate on different campuses. Dr. Frizzell's laboratory is located in the Children's Hospital in Lawrenceville, Dr. Yates's group is at BST3, 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

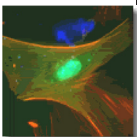
The vision of the new chair, and the leadership of the School, is to focus our research program towards basic cell biology and build a premier Department of Cell Biology. The key to accomplishing this task is the recruitment of focused and creative new faculty. We plan to continue recruiting senior faculty whose research programs focus on fundamental questions of cell biology. The importance of the successful recruitment of a 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

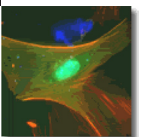
The steady decrease in federal and private funding opportunities will continue to be the most significant threat during next several years. Yet, in order for the Department to become one of the elite cell biology departments, total funding of the Department must increase 2-fold above the current level.

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.



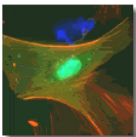
Cell Biology FY2013 Fiscal Issues

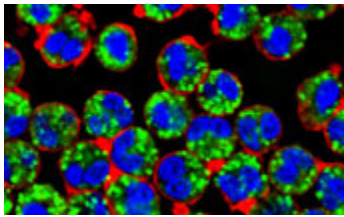
The main budgetary issue that face the Department in the FY13 budget will be maintaining the extramural funding of the faculty at the level necessary to support their research program and as required by the SOM Policies. This means that not only we would have to maintain current funded project and all efforts must be made to obtain additional funding. 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 2014 Budget*

	University	UPP and Other	Total Budget FY 2014
<u>Revenue</u>			
Patient Care	\$ -	\$ -	\$ -
Grant:			
Directs	4,954,856	-	4,954,856
Indirects	1,502,496	-	1,502,496
Hospital Contract	-	-	-
School of Medicine	3,230,578		3,230,578
VAMC		-	-
Other	351,747	-	351,747
Total Revenue	\$ 10,039,677	\$ -	\$ 10,039,677
<u>Expenses</u>			
Salaries and Fringe Benefits:			
Faculty	\$ 2,688,259	\$ -	\$ 2,688,259
Non-Faculty	2,546,844	-	2,546,844
Malpractice Insurance		-	-
Space Rental	87,894	-	87,894
UPP Overhead		-	-
University Overhead	2,238,413		2,238,413
Other Operating Expenses	2,478,267	-	2,478,267
Total Operating Expenses	\$ 10,039,677	\$ -	\$ 10,039,677
Excess Revenue over Expenses	\$ -	\$ -	\$ -
Capital Equipment/Improvements	\$ -	\$ -	\$ -
<u>Fund Balances</u>			
University Restricted Accounts as of 6/30/13	\$ 4,837,451	\$ -	\$ 4,837,451
University Endowments as of 6/30/13	351,747		351,747
UPP Fund Balance as of 6/30/13		-	-
UPMC Endowments as of 6/30/13		-	-
UPMC SPF Accounts as of 6/30/13		-	-
Total Fund Balances	\$ 5,189,198	\$ -	\$ 5,189,198





Thank you for your kind attention.

