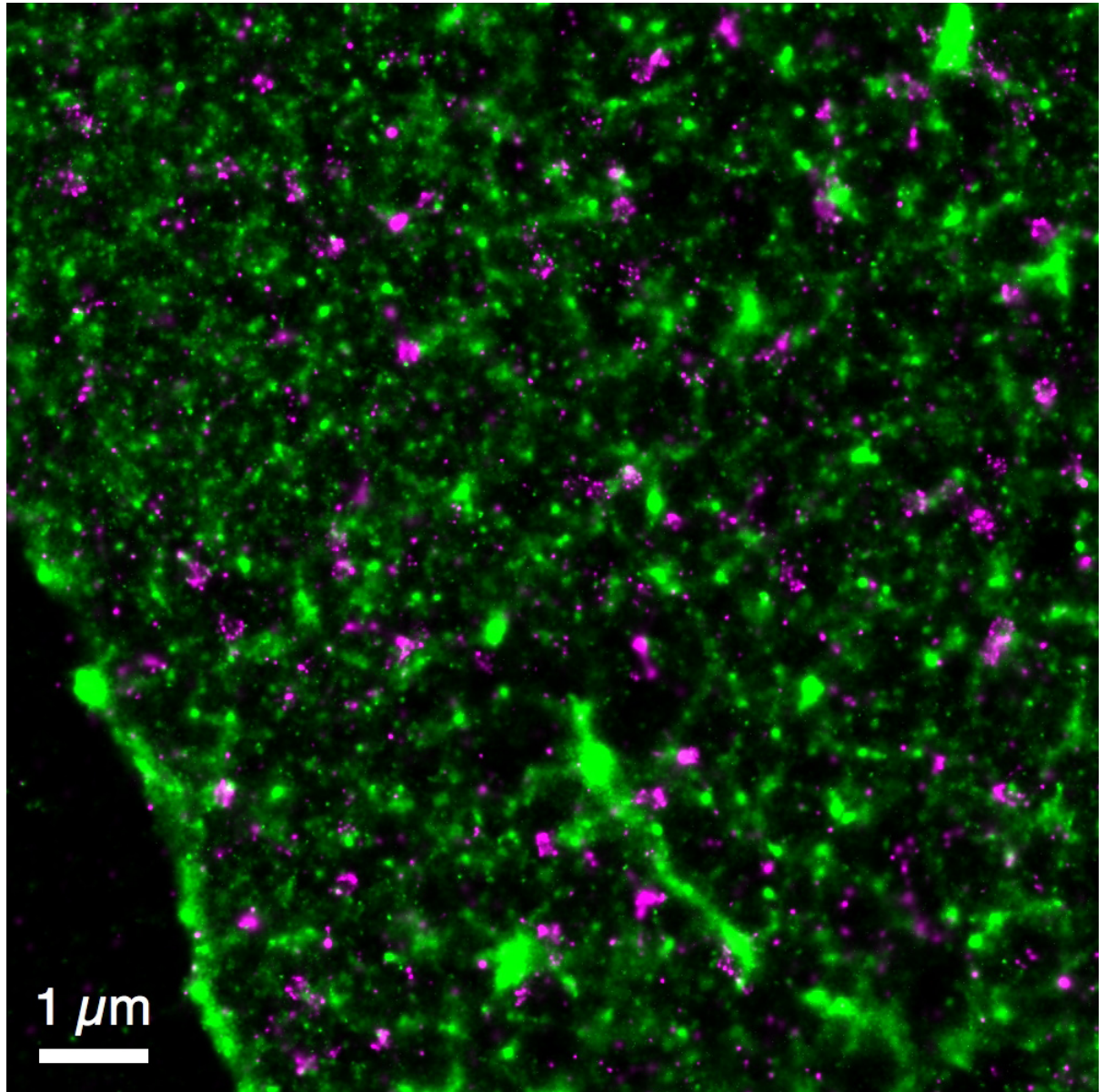


**UNIVERSITY OF PITTSBURGH  
SCHOOL OF MEDICINE  
CELL BIOLOGY**



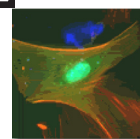
**FY15 ANNUAL REPORT  
AND  
FY16 BUSINESS PLAN**

## Front Page

**Cover figure by Dr. Gerald Hammond.** PIP2-CLC: super resolution image of clathrin-coated pits (purple) in a sea of the inositol lipid PIP2 in the plasma membrane (green).

## Table of Contents of CB Annual Report

<b>Cell Biology General Program Description</b>	
General Program Description	4
Research Activities	
Research Foci of Department	6
Centers of the Department	8
Faculty Data	13
CB Organizational Chart	14
CB Seminar Series	15
<b>Research and Other Scholarly Activities</b>	
Faculty Research Summaries	17
Faculty Study Sections	32
Faculty Advisory Committee Memberships	33
Faculty Sponsored Research Grants	37
Faculty Editorships	43
Charts - Trends in Research Support (Charts & Graphs)	45
Percent of Faculty Support on Grants	48
Students in Research	49
Training and Project Grants	50
New Research Recruits	54
<b>Teaching Activities</b>	
Cell Biology and Molecular Physiology Graduate Program	55
New CBMP Courses and CBMP Course Descriptions	59
CB Faculty Teaching Honors	64
Faculty Teaching Activities	65
Post Doctoral Personnel and Activities	70
CBMP Graduate Program Students	71
CBMP Students Graduated in 2015	72
Teaching Ratings	74
<b>Faculty Data</b>	
Current Cell Biology Faculty	75
New Cell Biology Faculty	76
Faculty Honors, Recognition and Professional Affiliations	78
Faculty Presentations	82
<b>Faculty Publications (2014-2015)</b>	
Peer Reviewed Publications	87
<b>Business Plan</b>	
Executive Summary	109
Initiatives and Implementation Strategies (SWOT Analysis)	110
Fiscal Issues	113
Budget	114



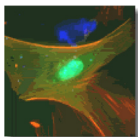
In the cell, life is governed by a multitude of molecular systems that shape and sustain the organellar system of the cell, maintain cellular homeostasis and respond to extracellular cues. These systems are dynamic, multicomponent macromolecular complexes. Maintaining and regulating the function of these 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 twenty primary faculty, sixteen of them with vigorous research programs. 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 ISB (Integrated Systems Biology) program, also HHMI-funded Computational Biology program, Center for Neuroscience Program (CNUP), the Program in Integrative Molecular Biology, and the Structural Biology/Molecular Biophysics graduate program. Several of our faculty are active members of these programs.

The Department is housed in administrative and research space in the South Wing of the Biomedical Science Tower (SBST). We also have laboratories in BST3, the Children's Hospital in Lawrenceville, 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. Gerald Hammond**

Membranes are sites of some of the most frantic cellular activity. As well as forming simple barriers that partition the cell and its internal compartments, membranes play host to thousands of proteins that carry out many of the incessant processes required for life. This partnership between lipid membranes and proteins provides a catalytic surface for cellular metabolism, controls the flux of materials and information across compartments, integrates these compartments with the

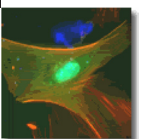


cell's cytoskeletal infrastructure and controls the budding and fusion of vesicles that transport materials between them. Malfunction of these pathways is associated with many diseases, from cancer to the common cold.

Although function is primarily associated with proteins, the cell needs a mechanisms to recruit, activate and co-ordinate the correct suite of proteins on a given membrane. Often relegated to simple inert building blocks of membranes, lipids are in fact increasingly recognized as key players in this process with one family - the inositol lipids - appearing to function as master regulators of this molecular choreography.

Our lab is particularly interested in the function of the plasma membrane, where one particular inositol lipid, commonly known as PIP2, is a key player in membrane protein recruitment and/or activation. Uniquely, this lipid is also a substrate to generate second messengers that transduce many of the signals from the cell's surroundings. As such, PIP2 regulates plasma membrane function in general, and failures in specific interactions of the lipid or its synthesis are contributors in cancer, hereditary and infectious diseases. Our goal is to understand how PIP2 is able to co-ordinate the plethora of cellular functions it regulates, as well as precisely how and why failures in specific elements of its synthesis or interactions lead to relatively subtle modifications of cellular function that cause disease, as opposed to a general collapse of plasma membrane function and cell death. Current areas of focus include: 1) using super-resolution fluorescence microscopy to probe the nanoscopic organization of the plasma membrane by PIP2, and 2) chemical genetic approaches to determine the subcellular sites of activity of inositol lipid phosphatases, and how these sites of activity regulate normal cellular homeostasis.

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



### Research foci

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*

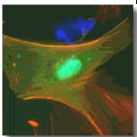
Aridor  
Butterworth  
Devor  
Ford  
Frizzell  
Hammond  
Murray  
Sorkin  
Traub  
Watkins

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 underlying the organization of the cellular membrane compartment system, targeting of proteins and lipids to specific organelles and compartments, and at defining how these processes are disrupted in disease.

#### *Regulation of channels and transporters*

Butterworth  
Devor  
Sorkin  
Thibodeau  
Watkins

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





***Cellular organization and cell-cell communications***

Hong  
Kwiatkowski  
Murray  
Stoltz  
Traub  
Watkins

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

***Regulation of intracellular signaling and gene expression***

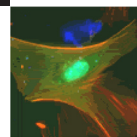
Drain  
Hammond  
Leuba  
Sorkin  
Thorne  
Wan

Scientists in this group are examining signaling processes mediated by receptors for growth factors and hormones, mechanisms of hormone secretion, processes involved in the regulation of cell cycle progression, DNA repair and transcription, and the mechanisms underlying virus replication. 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***

Yates

This laboratory is focused on developing new methodologies of quantitative mass-spectrometric analyses of proteins including new approaches to data acquisition, analysis and stor



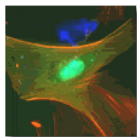
**Center for Biologic Imaging**

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 NCCR.. 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.

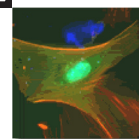
#### Other Faculty

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

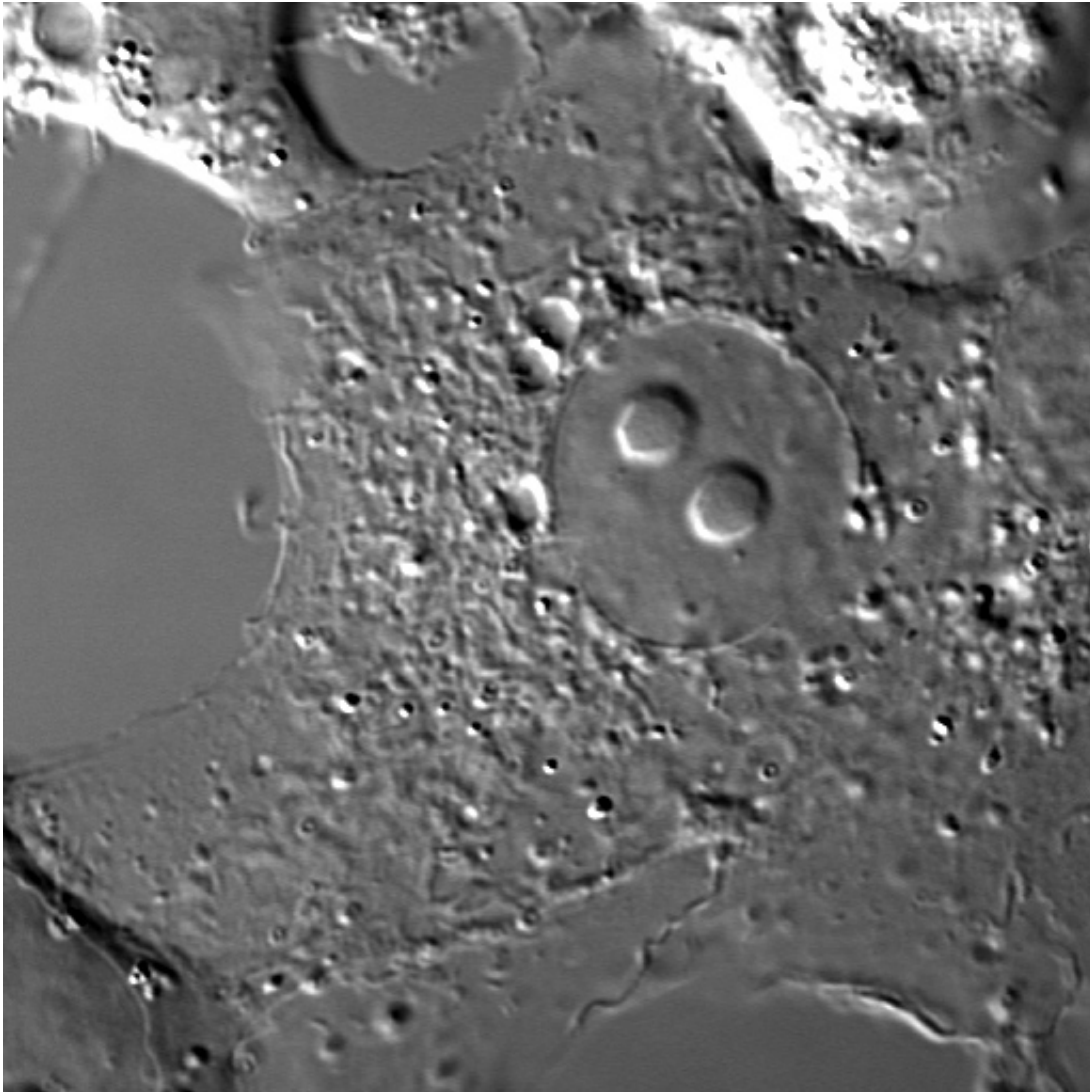
##### Associates:

**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,

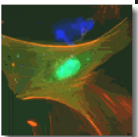


microscope maintenance, bookkeeping, solution preparation, etc.

**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.



**Gerald Hammond.** DIC: Differential interference contrast (DIC) image of a transformed COS-7 fibroblast.



**Cystic Fibrosis Research Center****Center Director:** *Dr. Raymond A. Frizzell*

*History:* 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.

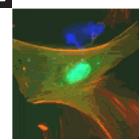
*Funding:* In 1998, this 'seed' funding from the CFF was supplemented by the award of NIH program funding in the form of a P50 SCOR. The P50 funding was renewed in the form of P30 Core Center grants in 2004 and 2010, each of which took decidedly more clinical turns. The latest P30 Core Center is entitled,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

*Structure:* 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).

*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:**

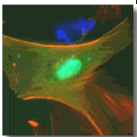
*Human Airway Cell and Assays Core:* This core provides access to patient materials obtained as a result of lung transplant activities in the Department of Surgery. This core offers well differentiated primary cultures of human bronchial epithelia to facilitate a variety of pre-clinical



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 and conductance 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 Center 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]

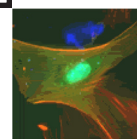
*Clinical Studies Core:* This core provides facilities and personnel for implementing clinical trials. It provides procedures for identifying functional outcomes, monitored in terms of lung function, *in vivo* radioisotope clearance, ion transport, inflammatory mediator levels or gene expression. It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



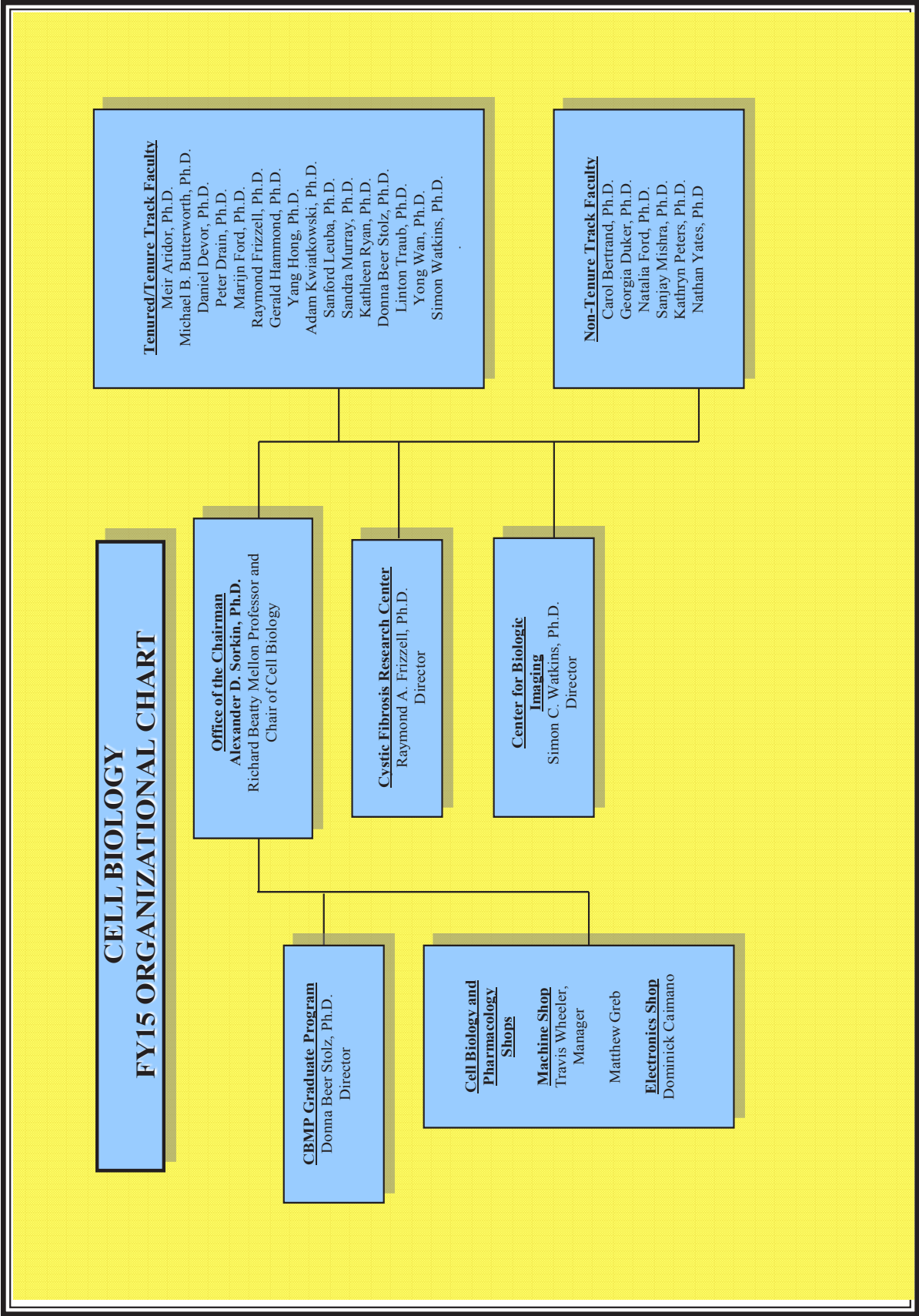
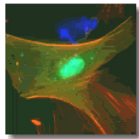
## Cell Biology Faculty Data

[Current as of June, 2015]

Name	Rank	Office Address	Email Address	Phone Fax
Aridor, Meir	Associate Professor	S310 BST-South Wing	aridor@pitt.edu	412-624-1970
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
Duker, Georgia	Assistant Professor	322 Scaife Hall	gduker1@pitt.edu	412-648-8792
Ford, Marijn	Assistant Professor	S326 BST-South Wing	marijn@pitt.edu	412-648-8330
Ford, Natalia	Res. Asst. Professor	S355 BST-South Wing	nw@pitt.edu	412-648-8330
Frizzell, Raymond	Professor	7117 RANCH	frizzell@pitt.edu	412-692-9724
Hammond, Gerald	Assistant Professor	S327 BST-South Wing	ghammond@pitt.edu	412-648-8330
Hong, Yang	Associate Professor	S325 BST-South Wing	yhong@pitt.edu	412-648-8330
Kwiatkowski, Adam	Assistant Professor	S324 BST-South Wing	adamkwi@pitt.edu	412-648-8330
Leuba, Sanford	Associate Professor	2.26g Hillman Cancer Center	leuba@pitt.edu	412-623-4840
Mishra, Sanjay	Res. Asst. Professor	7161 RANCH	skm25@pitt.edu	412-692-9724
Murray, Sandra	Professor	S313 BST-South Wing	smurray@pitt.edu	412-648-8330
Peters, Kathryn	Res. Asst. Professor	7161 RANCH	kathi@pitt.edu	412-692-9724
Ryan, Kathleen	Associate Professor	M302 Scaife Hall	ryankath@pitt.edu	412-648-8859
Sorkin, Alexander	Professor and Chair	S368 BST-South Wing	sorkin@pitt.edu	412-648-8330
Stolz, Donna Beer	Associate Professor	S221 BST-South Wing	dstolz@pitt.edu	412-383-7283
Traub, Linton	Associate Professor	S325 BST-South Wing	traub@pitt.edu	412-648-8330
Wan, Yong	Professor	2.6 Hillman Cancer Center	yow4@pitt.edu	412-623-3275
Watkins, Simon C.	Distinguished Professor	S225 BST-South Wing	swatkins@pitt.edu	412-648-3051
Yates, Nathan	Associate Professor	1719 BST3	yatesn@pitt.edu	732-718-9739









## **Cell Biology**

### **Research Seminar Schedule 2014 - 2015**

September 19, 2014

Steven P. Gygi, PhD

Professor, Department of Cell Biology

Harvard Medical School

“Towards a map of every protein’s social network”

October 7, 2014

Todd Lamitina, PhD

Associate Professor, Pediatrics

Children’s Hospital of Pittsburgh

“Bipartite control of cellular osmoregulation”

October 21, 2014

Ulrich Tepass, PhD

Professor, Cell and Systems Biology

University of Toronto

“Novel insights in epithelial cell adhesion and polarity”

October 28, 2014

Mark A. Lemmon, PhD

Professor and Chair of Biochemistry and Biophysics,

University of Pennsylvania

“Understanding Mechanisms of Receptor Tyrosine Kinase Regulation”

March 3, 2015

Holger Sondermann, PhD

Associate Professor, Graduate Field of Biophysics

Cornell University

“Molecular insights into membrane fusion”

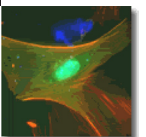
March 17, 2015

Stephen Thorne, PhD

Assistant Professor, Department of Surgery

University of Pittsburgh Cancer Institute

“Immuno-Oncolytic Viruses for Cancer Therapy”



April 7, 2015

Michael Butterworth, PhD

Assistant Professor, Department of Cell Biology

University of Pittsburgh

“MicroRNAs and the hormonal regulation of epithelial sodium transport: Small players with a large role”

April 14, 2015

Adam Kwiatkowski, PhD

Assistant Professor, Department of Cell Biology

University of Pittsburgh

“Cadherin/catenin function in cardiomyocyte adhesion and cytoskeletal organization”

April 21, 2015

Marijn Ford, PhD

Assistant Professor, Department of Cell Biology

University of Pittsburgh

“Stressed? You need dynamin to cope”

May 5, 2015

Bradley K. Yoder, PhD

Professor, Department of Cell, Developmental and Integrative Biology

University of Alabama, Birmingham

“Cilia in vivo functions and connections to disease”

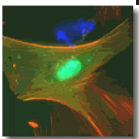
May 19, 2015

Michael Galko, PhD

Associate Professor, Department of Genetics

University of Texas MD Anderson Cancer Center

“Pinches and Pain: A Tour of Drosophila Tissue Repair Responses”



**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 that are being processed and sorted for vesicular transport in the ER. The development of a variety of human diseases, ranging from hemochromatosis, cystic fibrosis or hereditary emphysema to Pelizaeus-Merzbacher or ALS and Alzheimer's neurodegeneration can be derived from mistakes in ER sorting. Viruses such as coxsackie, polio, cytomegalovirus, HIV-1 Epstein-Barr and others manipulate sorting to self propagate and/or to evade immune surveillance.

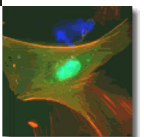
We take a multi disciplinary approach using a wide range of molecular, biochemical, biophysical and cellular techniques to unravel the molecular basis for protein and lipid sorting in the ER. Specifically, we use these approaches to address several related questions including the following: 1. What is the physical basis for membrane shaping and fission during ER exit? 2. What is the molecular basis for the assembly and organization of ER exit sites (ERES)? 3. How is the molecular machinery that organizes ERES regulated to couple ER sorting activities with physiological demands? 4. How are quality control activities in the ER coupled with cellular lipid homeostasis in normal and disease states?

**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.

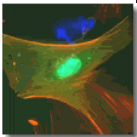
**Daniel C. Devor, Ph.D.**

*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  $\text{Ca}^{2+}$  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  $\text{Ca}^{2+}$  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  $\text{Ca}^{2+}$  affinity. These results suggest this region of the channel is similarly involved in the coupling between  $\text{Ca}^{2+}$  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  $\text{Ca}^{2+}$  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

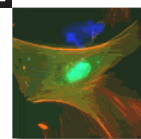


is rapidly endocytosed and enters the recycling pathway back to the plasma membrane in a Rab35/EPI64C (RabGAP)- and RME1-dependent manner. Indeed, our evidence points to the role of a 12 amino acid domain in the N-terminus of KCa2.3 as being critical in this process via an association with RME1. Future 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 ubiquitination of plasma membrane channels and correlate ubiquitinylation with endocytosis. In this regard, we have now shown that the endocytosis of KCa3.1 is directly correlated with poly-ubiquitinylation of the channel. By inhibiting ubiquitinylation we are able to block the channels endocytosis. This was first identified using a 96-well plate assay to identify modulators of channel endocytosis and formed the basis of our upcoming publication in *Future Medicinal Chemistry*, detailing this approach. Future studies will continue to explore the role of ubiquitin in the endocytosis of KCa3.1 as well as determine whether this is a regulated process. For example, is this a classic K63-dependent ubiquitinylation process, or are other ubiquitin-linked side-chains involved? Can the endocytosis of KCa3.1 be modified by second messengers generated in response to agonist stimulation? Of course, we are also attempting to identify the 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  $\text{Ca}^{2+}$ -dependent agonists to stimulate  $\text{Cl}^-$  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.

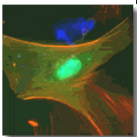
Given our interest in understanding these channels at a tissue/model system level, Cavita Chotoo, a graduate student in the lab, in collaboration with Drs. Cliff Luke and Gary Silverman at Children's Hospital of Pittsburgh, is further defining the physiological role of one of these channels using *C. 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  $\text{Ca}^{2+}$  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.

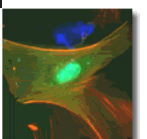
(3) More recently we have found that alpha-synuclein is expressed in pancreatic beta cells, where it localizes to secretory vesicles, in addition to its well established presence in dopaminergic and glutaminergic neurons of the brain. This has led to a new line of investigation studying the role of alpha-synuclein 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 2015, I am a co-director for the second-year Digestion and Nutrition course.

Within the Department of Cell Biology and Molecular Physiology I am course director for the Graduate Histology course (1995-2015). This course is taken by the majority of our students. It is abroad survey of all the organ systems, focusing on structure/function correlations. For most students it is the only time they encounter a full body overview of systems beyond their own research. Graduate students within the Department of Cell Biology and Molecular Physiology may then serve as Teaching Fellows for the Histology labs within seven Medical School courses. One of my roles is coordinator of the Teaching Fellows, especially to oversee their training and preparation.

A third role has emerged for me as a School of Medicine Coordinator for the Undergraduate Honors College Program. I created a new course, Biomedicine: Past, Present and Future, 2002-2015. We examine 12 significant biotechnologies via their history and future applications. Twenty-eight faculty from the School of Medicine 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.

### **Marijn Ford, Ph.D.**

*Assistant Professor*

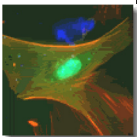
Our laboratory is interested in understanding the mechanism of action of the Dynamin-Related proteins, and, particularly, how they remodel membranes. To this end, we have been focusing on a poorly characterized fungal-specific DRP, Vps1 (Vacuolar Protein Sorting 1, initially identified in a screen for yeast mutants defective in sorting CPY).

We are approaching this problem in a number of ways:

#### **Cell Biology:**

We have made an comprehensive collection of yeast strains allowing us to monitor and dissect membrane remodeling in yeast under normal and stress conditions. We have identified novel functions of Vps1 in autophagic processes as well as other stress response pathways.

We extensively use the imaging facilities in the Center for Biologic Imaging for this purpose. In addition, we use other yeast cell biological techniques (processing assays etc.) as well as western blotting and RNA analysis to assay trafficking, autophagy and vacuolar responses in normal and stressed cells.



**Mass Spectrometry:**

Physical binding partners for Vps1 remain unknown, though some genetic interactors have been identified in the literature. A significant reason for this has been an inability to purify Vps1 to homogeneity in abundance. We have tried extensively to purify *S cerevisiae* Vps1 with limited success. However, we have succeeded in preparing Vps1 from closely related fungal sources (to the extent that heterologous expression of these Vps1 sequences under the control of native UTRs in *S cerevisiae* fully rescues the temperature-sensitive defect observed in  $\Delta$ vps1 cells. Consequently, we are doing mass spectrometry using these alternative Vps1 proteins as bait and probing *S cerevisiae* cytosol for interacting partners for identification by mass spectrometry.

**High-throughput genomics:**

We have conducted a screen using synthetic genetic array technology, where a yeast query strain, deleted in Vps1, is systematically crossed with a library containing yeast systematically deleted for every non-essential open reading frame in the yeast genome. A series of controlled replica-plating steps results in sporulation and selection for double mutant offspring. The readout is colony size, taken as a proxy for fitness of the double mutants. This allows rapid identification of genes that have a genetic interaction with the query (alleviating or synthetic sick/lethal). The screen with the  $\Delta$ vps1 query identified hits in multiple genes involved in endosome function, tethering and MVB formation.

As an extension, in collaboration with Kara Bernstein's lab, we have extended this approach to **synthetic dose lethality**, where we systematically heavily overexpress our query (Vps1) in a library of strains where each non-essential yeast gene has been deleted. We are looking for strains where the absence of a particular gene results in particular sensitivity to the presence of elevated levels of Vps1. This study will be followed by additional screens where assembly-deficient mutants of Vps1 and components of the nucleus-vacuole junction are overexpressed in turn.

**Biochemistry:**

We are purifying vacuoles from wild-type yeast and yeast deficient in several candidate proteins for *in vitro* reconstitution of microautophagic processes.

**Bioinformatics:**

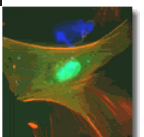
In collaboration with Nathan Clark's lab, we are using bioinformatic approaches to complement and strengthen our high-throughput genomic screening. To date, this work has suggested some connections between Vps1, TOR signaling and microautophagy which we have confirmed by experimental approaches.

**Structural Biology:**

We are screening carefully selected targets identified in our genetic screens with Vps1 for crystallization studies, as well as possible cryo-EM (which will be done in collaboration with Peijun Zhang's lab). To date we have focused extensively on VAC8, a peripheral membrane protein essential for nuclear-vacuolar junction formation, vacuole inheritance and micronucleophagy. Despite thousands of trials, suitable crystals have not yet been obtained and we are currently using bioinformatic and data-mining approaches to optimize the construct, as well as new tools developed in Pitt by the vanDemark lab.

**Summary of our results to date:**

- i) Purified functional Vps1 from several sources as well as *S. cerevisiae* proteins



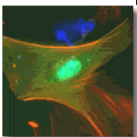
- involved in nuclear-vacuolar junction formation
- ii) Functionally tagged Vps1 *in vivo*, as well as numerous other trafficking, autophagy and vacuolar resident proteins
- iii) Identified a novel function of Vps1 in microautophagy and TOR signaling
- iv) Uncovered a link between ESCRT and Vps1 function on endosomes and vacuoles
- v) Identified a genetic interaction between Vps1 and GARP tethering complex responsible for endosomal-TGN trafficking which may be implicated in lipid transport or dissemination and ER homeostasis
- vi) Identified a role for Vps1 in the newly identified process of piecemeal microautophagy of the nucleus and its role in nuclear-vacuolar contact sites

**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. Recently, we have identified a component of the SUMO pathway that enhances CFTR biogenesis and allows the protein to escape degradation. 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 since it has been recently identified as a modifier of CF disease severity.

**Gerald Hammond, Ph.D.***Assistant Professor*

Healthy cellular function demands the co-ordination of assorted signals, molecular traffic and cytoskeletal attachment at membranes. Although protein function is usually the focus of research into these processes, inositol-containing phospholipids are absolutely crucial to membrane function in eukaryotes. They act as substrates in signaling reactions, recruit adaptors for membrane traffic, activate components of the cytoskeleton, as well as many other functions including the control of ion flux. How are these lipids and their protein ligands normally organized



and co-ordinated? What homeostatic mechanisms maintain a stable lipid and protein composition in the face of membrane turnover?

Answering these basic questions is crucial, because genetic diseases ranging from cancer to hereditary hearing loss are caused by disruption of membrane function resulting from mutations in inositol lipid metabolizing enzymes. Furthermore, many bacterial and viral pathogens re-model host cell membranes by actively disrupting inositol lipid distribution .

The overall aim of the lab is therefore to delineate the mechanisms of membrane organization and homeostasis, and how these mechanisms are altered in genetic and infectious disease. We use an array of state of the art methods, including live cell imaging, single molecule, super-resolution and chemical genetic approaches, supported by conventional molecular/cellular techniques, to probe the molecular scale organization of membranes. We interrogate specific protein-lipid complexes in both healthy cells and infectious or hereditary disease models.

### **Yang Hong, Ph.D.**

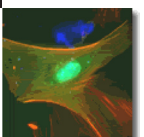
*Associate Professor*

Research in my lab focuses on the molecular mechanisms regulating the cell polarity. Specifically, epithelial cells develop so-called apical-basal polarity by partitioning the cell surface into distinct apical and basolateral domains through polarized formation of cell junctions. Establishing and maintaining apical-basal polarity is crucial for the function and structure of epithelia, while disruption of such polarity often accompanies the malignant transformation or stress-induced damage of epithelial cells.

To date a dozen of so-called “polarity proteins” have been identified for their conserved and essential roles in regulating the cell polarity in both vertebrates and invertebrates. A key feature of these polarity proteins is that they must localize to specific apical or basolateral membrane domains to regulate cell polarity, and it is generally assumed that their membrane targeting is achieved by physical interactions with other polarity proteins or cytoskeleton etc. However, we recently discovered that plasma membrane targeting of polarity protein Lgl is in fact mediated by direct binding between its positively charged polybasic domain and negatively charged inositol phospholipids PIP2 and PI4P on the plasma membrane. Using both *Drosophila* and cultured mammalian cells as model systems, we are investigating how direct interactions between polarity proteins and membrane lipids may act as a crucial molecular mechanism regulating the subcellular localization and functions of polarity proteins, such as:

1) Control of plasma membrane targeting of polarity proteins: direct binding to plasma membrane phospholipids likely targets proteins to all plasma membrane domains. We are identifying essential mechanisms that spatially restrict polarity proteins to specific membrane domains in polarized cells.

2) Role of phospholipids in regulating cell polarity: polybasic domain-mediated membrane targeting also highlights the critical role of inositol phospholipids such as PIP2 in establishing and maintaining cell polarity under cellular stress. Our discovery that hypoxia acutely and reversibly inhibits Lgl plasma membrane targeting through depleting membrane phospholipids suggests that phospholipid turn-over and homeostasis play significant role to conserve cell polarity and promote cell survival under cellular stress such as hypoxia/ischemia.





3) Regulation of membrane targeting of polarity proteins in tumorigenesis: many polarity proteins, such as Lgl, also function as tumor suppressors. Loss of Lgl membrane targeting is a hallmark in both *Drosophila* and human tumor cells. We are investigating the mechanism contribute to the compromised membrane targeting of polarity proteins and the progressive loss of cell polarity during tumorigenesis.

We have developed genomic engineering tools that allow efficient generation of knock-in alleles of *Drosophila* genes. We also developed comprehensive imaging tools for visualizing the dynamic subcellular localizations of polarity proteins under various physiological conditions including hypoxia.

**Adam Kwiatkowski, Ph.D.**

*Assistant Professor*

The regulated assembly and organization of specific actin networks drive cell morphology, movement and adhesion. Changes in cell behavior are required to form complex tissue structures during development and must be accompanied by transitions in actin organization. However, the molecular mechanisms governing actin network transitions are poorly understood. The goal of the lab is to understand how actin networks are assembled and organized to regulate cell morphology, movement and adhesion during development. We use a combination of protein biochemistry, cell biology, high-resolution microscopy and developmental biology to study actin dynamics at the molecular, cellular and organismal levels.

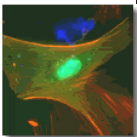
**Sanford H. Leuba, Ph.D.**

*Associate Professor*

Since the discovery of the nucleosome in the early 1970's, scientists have sought to correlate chromatin structure and dynamics with biological function. More recently, we have learned that nucleosomes and chromatin play a critical role in the regulation of transcription, replication, recombination, and repair (Zlatanova and Leuba, 2004). Our laboratory uses an interdisciplinary approach combining the disciplines of molecular biology, biochemistry, engineering, and physics to try to understand at the single nucleosome and single chromatin fiber level how chromatin structure and dynamics regulate biological processes that use DNA as a template. To this end, we are applying several single-molecule approaches such as atomic force microscopy (AFM), magnetic tweezers, optical tweezers and single-pair fluorescence resonance energy transfer (spFRET) to native or reconstituted chromatin fibers of different protein compositions with the latter three methods using homebuilt instrumentation. Single-molecule techniques provide the sensitivity to detect and to elucidate small, yet physiologically relevant, changes in chromatin structure and dynamics. Recent examples of what we have been able to discover include the following:

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

- We also used AFM to investigate the role of histone variants in chromatin fiber structure (Tomschik et al., 2001). Eukaryl and archaeal organisms have similar fiber structure with





differences likely related to the more complex needs of eukaryl organisms to regulate transcription.

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

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

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

- We have used spFRET to demonstrate that PcrA DNA helicase displaces RecA from both ssDNA as well as dsDNA (Anand et al., 2007), as a model for regulation of homologous recombination.

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

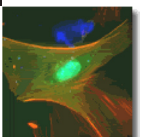
- We have used spFRET to demonstrate the wrapping of DNA around the archaeal homohexameric MCM helicase from *Sulfolobus solfataricus* (Graham et al., NAR 2011), protecting the displaced single-stranded DNA tail and preventing reannealing.

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

- We have used spFRET to demonstrate that PcrA DNA helicase displaces RecA but not RecA mutants (Fagerburg et al., NAR 2012) indicating that direct transduction of chemomechanical forces alone by translocating helicases, such as PcrA and Srs2, are insufficient to displace recombinases such as RecA and Rad51 that form large polymeric assemblies on ssDNA.

- We have used spFRET, single molecule protein induced fluorescence enhancement (PIFE), fluorescence anisotropy and modeling to demonstrate for the first time that allosteric inhibitors directly alter the mobility of HIV-1 reverse transcriptase on its DNA substrate by modulating its conformation, without changing the binding affinity of RT to DNA (Schauer et al., 2014).

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.**

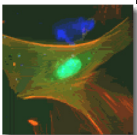
*Research Assistant Professor*

Nearly half of all prescription drugs alter G-protein coupled receptor (GPCR) signaling, including treatments for asthma, hypertension, neurodegenerative disorders and depression.  $\beta$ -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,  $\beta$ -arrestins are only a small branch of the larger arrestin family that includes the widely-conserved but functionally uncharacterized  $\alpha$ -arrestins, the primary focus of my research. My work has shown that  $\alpha$ -arrestins, like  $\beta$ -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  $\alpha$ -arrestin interactions with signaling regulators, cargos and vesicle coat proteins, and have begun to define the molecular mechanisms underlying  $\alpha$ -arrestin-mediated trafficking. All of the  $\alpha$ -arrestin-interacting partners identified in yeast are conserved. My research will apply insights gained in yeast to initiate studies on the relatively unstudied mammalian  $\alpha$ -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, from leaving the endoplasmic reticulum to assume residence in the apical plasma membrane, and from functioning in the cAMP regulated salt and water secretion in epithelial cells. We are identifying processes and proteins which modify any of a variety of mutant CFTRs 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*

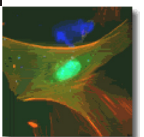
The focus of the research in the laboratory is currently split into two major directions which are distinct from each other with respect to the biological systems involved, their relation to the human disease, and experimental models used. However, the main idea underlying both directions is conceptually 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.

**Linton M. Traub, Ph.D.**

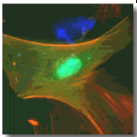
*Associate Professor*

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.**

*Professor*

Posttranslational modifications such as ubiquitylation, methylation, ADP-ribosylation as well as phosphorylation orchestrate genome stability, cell division, signal transduction, apoptosis and tumorigenesis. Posttranslational modifications act as critical molecular switches or fine-tune operators that determine the activation, deactivation or subcellular localization of functional proteins. Emerging evidence has drawn attention to the modulation of regulatory proteins in response to extrinsic/intrinsic signaling being executed simultaneously by multiple posttranslational modifications. Research interests in my laboratory seek to address how defects in the ubiquitin-proteasome system (E3 ligase/deubiquitinase), protein methyltransferase and



poly (ADP-ribose) polymerase 1 (PARP1) would result in genomic instability, abnormal cell cycle or apoptosis, and aberrant signal transductions (e.g., ER, TGF-beta and EGFR) that predispose otherwise normal cells to become cancerous tumor cells. The ultimate objective is to integrate our basic research with clinical translational studies that would allow the development of new anti-cancer therapy thereby fully exploiting our knowledge of posttranslational modifications. To achieve our goals, we have developed a multidisciplinary approach that includes biochemical, cell biological and genetic analyses as well as the use of animal models and analyses of clinical samples.

**Simon C. Watkins, Ph.D.**

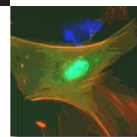
*Distinguished Professor, Vice Chairman of Department  
Director of Center for Biologic Imaging*

The application of advanced imaging tools to the field of cell biology is constantly revealing new facets of cellular and molecular behavior. 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 as well as the development and implementation of imaging tools for new multiparametric imaging probes.

**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 2014 - 2015)**

**Michael Butterworth, Ph.D.**

*Assistant Professor*

2014 AHA (National)

**Alexander D. Sorkin, Ph.D.**

*Richard B. Mellon Professor and Chairman*

ASIRC - Italian Association for Cancer Research; Standing Member

Association for International Cancer Research (mail)

NIH/NCI Omnibus Cancer Biology 3 ZCA1 RPRB-O (J1)

**Yong Wan, Ph.D.**

*Professor*

Molecular Oncogenesis Study Section (MONC), NIH

Special panel study section ZRG1 BCMB-A, NIH, Ad Hoc Reviewer (2014)

**Simon C. Watkins, Ph.D.**

*Distinguished Professor and Vice Chairman, Director of Center of Biologic Imaging*

ACS Study Section (Peer Review Committee on Clinical Cancer Research and Epidemiology),  
Chair of Panel, Atlanta, GA, Jan -21<sup>st</sup>-22<sup>nd</sup>, 2014

Expert Review Committee: Mt Sinai Medical Center, Chair of Panel April 17<sup>th</sup> 2014

NIH Study section High End Instrumentation Panel, NIH, Chair of Panel March 18<sup>th</sup> 2014

ACS Study Section (Peer Review Committee on Clinical Cancer Research and Epidemiology),  
Chair of Panel, Atlanta, GA, June -24<sup>th</sup> -25<sup>th</sup> 2014

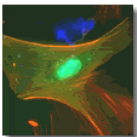
NIH Study Section Exceptionally Innovative tools and Technologies for Single Cell Analysis  
ZRG1 BST-A(50)R. Panelist June 30<sup>th</sup>-July 1<sup>st</sup> 2014

Mt Sinaii Research Resource Review: Invited reviewer, New York Sept 8<sup>th</sup> 2014

ACS Study Section (Peer Review Committee on Clinical Cancer Research and Epidemiology),  
Chair of Panel, Atlanta, GA, Jan -21<sup>st</sup>-22<sup>nd</sup>, 2015

ACS Study Section (Peer Review Committee on Clinical Cancer Research and Epidemiology),  
Chair of Panel, Atlanta, GA, June -26<sup>th</sup> -27<sup>th</sup> 2015

NIH Study section “the 4D Nucleome” Co-Chair of panel, 07/22/2015





**Faculty Advisory Committee Memberships (Fiscal Year 2014 - 2015)**

**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  
Integrated Systems Biology (ISB) Admission's Committee

**Michael Butterworth, Ph.D.**

*Assistant Professor*

Cell Biology Seminar Series  
Cell Biology Departmental Retreat Committee  
Cell Biology Space Committee  
University of Pittsburgh: Senate Council Member  
University of Pittsburgh: Faculty Assembly Member  
Organizer – Cell Biology Department Retreat  
Integrated Systems Biology (ISB) Course Director, Core Course (Imaging)  
Cell Biology and Molecular Physiology Graduate Program, Associate Director

**Daniel Devor, Ph.D.**

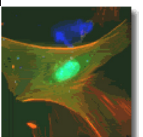
*Professor*

Cell Biology Departmental Tenure and Promotions 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

**Marijn Ford, Ph.D.**

*Assistant Professor*

Organizer – Cell Biology Department Retreat

**Raymond A. Frizzell, Ph.D.**

*Professor and Director, Cystic Fibrosis Research Center*

CFF Medical Advisory Council

**Yang Hong, Ph.D.**

*Associate Professor*

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

Cell Biology Space Committee

Cell Biology Faculty Recruitment Committee

**Adam Kwiatkowski, Ph.D.**

*Assistant Professor*

Organizer – Cell Biology Department Retreat

Local Traffic Symposium Organizing Committee

Integrative Systems Biology Admissions Committee

**Sanford Leuba, Ph.D.**

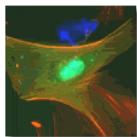
*Associate Professor*

University Molecular Biophysics and Structural Biology Graduate Program Chair of Admissions Committee & Curriculum 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  
Cell Biology and Physiology Tenure and Promotions Committee  
Advisory Board, NIH-R25 Vascular Medicine and Cell Biology Research A –  
Advisory Board Pittsburgh Undergraduate Research Diversity Program  
Member of Scientific Advisory Committee for the International Gap Junction Society Meeting

**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  
Dickson Prize Selection Committee - SOM

**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

**Linton M. Traub, Ph.D.**

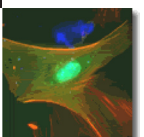
*Associate Professor*

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

**Simon C. Watkins, Ph.D.**

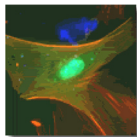
*Distinguished Professor and Vice Chairman, Director of Center of Biologic Imaging*

Cell Biology Tenure and Promotions Committee  
Cell Biology Student Advisory Committee  
Cell Biology Space Committee



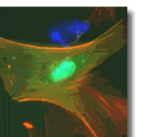
Cell Biology Faculty Recruitment Committee  
Graduate Program, Curriculum Committee  
University of Pittsburgh School of Medicine, Research Advisory Committee  
University of Pittsburgh Cancer Institute Core Resources Committee  
University of Pittsburgh Tenure and Promotions Committee  
Scientific Advisory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

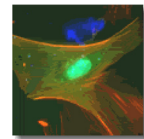
Cell Biology/Pharmacology Machine Shop



## Cell Biology Sponsored Research Funding (FY15)

Name	Agency Name	Title	Annual DC	Annual IDC
Catherine Baty	National Institutes of Health	IL-23 Stat3 drive oral immune responses to Candida albicans	765	403
Catherine Baty	National Institutes of Health	Apical protein sorting in renal epithelial cells	4,801	2,593
Carol Bertrand	Cystic Fibrosis Foundation	Role of SLC26A9 in biogenesis and anion secretion in airway	67,500	5,400
Ethan Block	National Institutes of Health	Regulation of protein kinase c-mediated dopamine transporter endocytosis in vivo	26,971	-
Michael Butterworth	Gilead	Regulation of the Epithelial Sodium (ENAC) in the Cystic Fibrosis Airway by Pseudomonas Eruginosa	25,097	2,008
Michael Butterworth	American Soc. for Nephrology	Aldosterone-Regulated microRNAs and sodium transport in distal kidney nephron	90,909	9,091
Peter Drain	JDRF	JDRF Live Alpha-Cell Glucagon Reporters Towards a T1D Cure	62,523	6,252
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	41,503	21,373
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	128,233	70,755
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	Research Training Core	70,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in Wild-Type and DF508 CFTR Processing	38,450	3,076
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in Wild-Type and DF508 CFTR Processing	192,018	15,361
Raymond Frizzell	National Institutes of Health	Traffic Regulatory Proteins and ENaC	16,454	8,474
Raymond Frizzell	National Institutes of Health	Trans-NIH-Research Support	4,148	2,178
Raymond Frizzell	National Institutes of Health	Chaperone Actions in CFTR Biogenesis	222,500	119,403
Raymond Frizzell	National Institutes of Health	Role of the sHsp-SUMO pathway in APP processing Pilot 31-1	20,825	10,724
Raymond Frizzell	Cystic Fibrosis Foundation	Fluorogen detection of ASL composition and mucin secretion	89,910	7,193
Yang Hong	National Institutes of Health	Regulation of Adherens Junction Dynamics by Polarity Proteins	137,550	27,510
Yang Hong	American Cancer Society	Regulation of a Tumor Suppressor and Cell Polarity Protein Lgl by Hypoxia	166,133	85,559
Adam Kwiatkowski	March of Dimes	Molecular coordination of cell movement and cell-cell adhesion during neural tube formation	39,750	3,975
Sanford Leuba	National Institutes of Health	NNRTI Induced Conformational Changes in HIV 1 RT (Sluis-Cremer)	63,443	27,574
Sanford Leuba	National Institutes of Health	Novel mechanisms of HIV resistance to RTIs	930	502
Sandra Murray	National Science Foundation	Regulation of annular gap junction processing	168,999	80,972
Sandra Murray	National Science Foundation	Regulation of annular gap junction processing	1,737	139
Sandra Murray	National Institutes of Health	National Institute of Mentoring Early Minority Faculty in Neuroscience	1,720	138
U. Perunthottathu	American Heart Association	Mechanistic Role of Clathrin Endocytosis	24,500	-
Alexander Sorkin	National Institutes of Health	The Influence of Gene-environment Interaction on Neuroan Mitochondrial Fission, Fusion and Transport in Chronic Parkinsons Disease-Relevant Environmental Toxins (Berman)	3,354	1,811
Alexander Sorkin	National Institutes of Health	Dopamine Transporter Regulation by Endocytosis	227,214	111,436

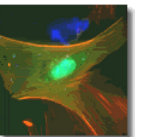


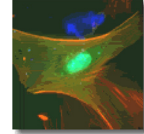


Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	228,539	99,580
Donna Beer Stolz	Massachusetts Institute of Tech.	Perfused 3D Tissue Surrogates for Complex Cell-Cell Communication Systems	6,891	3,549
Donna Beer Stolz	National Institutes of Health	Endogenous Regulators of Inflammation in Liver Ischemia/Reperfusion	10,731	5,525
Donna Beer Stolz	National Science Foundation	Engineering Research Center	23,916	12,317
Donna Beer Stolz	National Institutes of Health	Core A Cell and tissue Imaging Core	71,946	38,166
Donna Beer Stolz	National Institutes of Health	All Human Microphysical Model of Metastasis Therapy	87,780	40,834
Donna Beer Stolz	MWRI-NIH	Primary Human Trophoblasts and the Transfer of Viral Resistance	7,349	3,785
Donna Beer Stolz	National Institutes of Health	Bid-mediated killing of oncogenic stem cells in chemoprevention	4,640	2,493
Donna Beer Stolz	National Institutes of Health	Mechanisms of Arsenic-induced Muscle Morbidity and Reduced Regenerative Capacity	13,875	7,313
Donna Beer Stolz	National Institutes of Health	Local Expression of Alpha-1-Antitrypsin in Emphysema (Perlmutter)	2,372	1,281
Donna Beer Stolz	National Institutes of Health	Signaling pathways influencing liver disease phenotype in antitrypsin deficiency	31,175	16,051
Donna Beer Stolz	National Institutes of Health	Nitric Oxide and Hepatic Function in Sepsis and Trauma	11,010	4,098
Donna Beer Stolz	National Institutes of Health	Proteotoxicity in the Pathophysiology of Pancreatitis	6,445	2,770
Donna Beer Stolz	National Institutes of Health	Joel Freeze Fracture/Freeze Etch Device	300,180	-
Patriek Thibodeau	National Institutes of Health	Regulated Biosynthesis and Function of ABC-Transport Systems	125,000	64,375
Patriek Thibodeau	Cystic Fibrosis Foundation	Structural Interactions Regulating CFTR Channel Function	22,037	1,763
Linton Traub	National Institutes of Health	Clathrin-coated vesicles and endocytic function	233,970	123,681
Linton Traub	National Institutes of Health	Admin Supplement - Clathrin-coated vesicles and endocytic function	12,965	-
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)	80,348	41,379
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	15,000	7,092
Simon Watkins	National Institutes of Health	Amplification of IL-4/Ralpha Signaling Pathways in Human Airways Through I5 LOI	6,133	3,159
Simon Watkins	National Institutes of Health	Multiple Tumor Antigen-Loaded DC Vaccine for Hepatocellular Cancer	6,155	3,170
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	82,026	42,244
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	86,318	38,353
Simon Watkins	National Institutes of Health	Directing Tumor Specific T cells to Tumors	6,527	3,361
Simon Watkins	Mellon Pitt Corporation	Fluorescent Probes and Imaging for Networks and Pathways	12,450	5,770
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	8,715	4,488
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	20,634	9,083
Simon Watkins	National Institutes of Health	ROS Mechanisms in BAV Aortopathy	5,801	1,987
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Core B	5,799	1,981
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Project I	12,519	5,199



Simon Watkins	National Institutes of Health	PINK1 Regulation of Neuronal and Mitochondrial Homeostasis	4,000	2,060
Simon Watkins	National Institutes of Health	Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging	10,892	5,609
Simon Watkins	National Institutes of Health	Combinatorial Immunotherapy targeting the Malonoma	22,406	10,389
Simon Watkins	National Institutes of Health	Cell Autonomous and Non-Autonomous Mechanisms of Again	124,217	60,775
Simon Watkins	National Institutes of Health	Targeted Fluorescent Indicators for Endothelial Physiology	23,880	7,287
Simon Watkins	National Institutes of Health	Biochemical and Spatial Regulation of IKKa/NEMO During T-Cell Activation	11,121	5,980
Simon Watkins	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lung Injury	102,412	48,203
Simon Watkins	National Institutes of Health	CYP 450 Mediated CBF Dysregulation and Neurotoxicity in Pediatric Cardiac Arrest	10,000	4,511
Simon Watkins	National Institutes of Health	Watkins/Saunders Aurora B-induced cytokinesis defects in malignant cells	13,340	-
Simon Watkins	National Institutes of Health	PQC2 Alteration of 3D nuclear organization at nanoscale in breast tumorigenesis	8,697	4,673
Simon Watkins	National Institutes of Health	Mechanisms of Perineural Invasion in head an neck cancer	10,000	5,400
Simon Watkins	National Institutes of Health	Mechanisms of Perineural Invasion in head and Neck cancer	5,006	1,207
Simon Watkins	National Institutes of Health	Mesoscale MR imaging of cellular connectivity in the ex vivo human hippocampus-	1,150	405
Simon Watkins	National Institutes of Health	ROS driven mitochondrial-telomere dysfunction during environmental stress-	2,229	529
Simon Watkins	National Institutes of Health	Request for a Nikon A1 Confocal Microscope -	357,942	-
Nathan Yates	National Institutes of Health	Cell Autonomous and Non-Autonomous Mechanism of Aging	162,549	56,975
Nathan Yates	National Institutes of Health	Plasticity of Auditory Cortical Circuits in Schizophrenia	11,151	5,978
Nathan Yates	National Institutes of Health	Bioengineering Tracheas through Targeting Activated Cell	16,908	9,078
Nathan Yates	National Institutes of Health	Request for triple quadrupole mass spectrometer for the University of Pittsburgh	487,268	-
			5,044,351	1,450,381

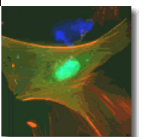


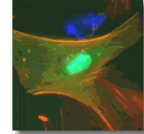


Cell Biology Sponsored Research Funding (FY16)

Name	Agency Name	Title	Annual DC	Annual IDC
Michael Butterworth	National Institutes of Health	Role of MicroRNAs in kidney sodium regulation	225,000	121,500
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Administrative Core	44,514	24,038
Raymond Frizzell	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core A	140,247	75,733
Raymond Frizzell	Cystic Fibrosis Foundation	Training Core	70,000	-
Raymond Frizzell	Cystic Fibrosis Foundation	Program Enrichment and Administration Core	32,000	-
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	38,450	3,076
Raymond Frizzell	Cystic Fibrosis Foundation	Selective Steps in Wild-Type and DF508 CFTR Processing	166,600	13,328
Raymond Frizzell	National Institutes of Health	Chaperone Actions in CFTR Biogenesis	222,500	120,151
Raymond Frizzell	Cystic Fibrosis Foundation	Fluorogen detection of ASL composition and mucin secretion	74,970	5,998
Christine Klemens	American Heart	Ankyrin G A Regulation of the Epithelial Sodium Channel after Adosterone Stimulation	26,000	-
Sanford Leuba	National Institutes of Health	NNRTI Induced Conformational Changes in HIV 1 RT (Sluis-Cremer)	62,973	24,346
Sanford Leuba	National Institutes of Health	Novel Mechanisms of HIV Resistance in RTIS (Sluis-Cremer)	5,629	3,040
Sandra Murray	National Science Foundation	Regulation of annular gap junction processing	163,027	88,035
Alexander Sorkin	National Institutes of Health	The Influence of Gene-environment Interaction on Neuroanal Mitochondrial Fission, Fusion and Transport in Chronic Parkinsons Disease-Relevant Environmental Toxins (Berman)	6,753	5,701
Alexander Sorkin	National Institutes of Health	Dopamine Transporter Regulation by Endocytosis	185,093	95,292
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	234,085	103,253
Alexander Sorkin	National Institutes of Health	Spatiotemporal regulation of GAB1-SHP2 complexes in response to EGFR activation	25,641	13,846
Donna Beer Stolz	National Institutes of Health	Endogenous Regulators of Inflammation in Liver Ischemia/Reperfusion	9,939	5,119
Donna Beer Stolz	National Science Foundation	Engineering Research Center	27,314	8,916
Donna Beer Stolz	National Institutes of Health	Core A Cell and tissue Imaging Core	70,644	38,148
Donna Beer Stolz	National Institutes of Health	All Human Microphysical Model of Metastasis Therapy	65,121	30,846
Donna Beer Stolz	MWRI-NIH	Primary Human Trophoblasts and the Transfer of Viral Resistance	7,268	3,743
Donna Beer Stolz	National Institutes of Health	Bid-mediated killing of oncogenic stem cells in chemoprevention	4,766	2,573
Donna Beer Stolz	National Institutes of Health	Mechanisms of Arsenic-induced Muscle Morbidity and Reduced Regenerative Capacity	12,775	6,829
Donna Beer Stolz	National Institutes of Health	Signaling pathways influencing liver disease phenotype in antitrypsin deficiency	29,330	14,488
Donna Beer Stolz	National Institutes of Health	Nitric Oxide and Hepatic Function in sepsis and Trauma	11,929	4,512
Donna Beer Stolz	National Institutes of Health	Proteotoxicity in the Pathophysiology of Pancreatitis	10,779	3,040
Donna Beer Stolz	National Institutes of Health	Mechanisms of Trabecular Meshwork Regeneration by stem cell	10,000	4,253
Donna Beer Stolz	National Institutes of Health	Critical Role for Fibroblast Growth Factor Receptors in Bladder Development	6,061	3,273

Donna Beer Stolz	National Institutes of Health	Role of autophagy in lung in a mouse model of alpha 1 antitrypsin proteotoxicity	43,020	21,881
Donna Beer Stolz	National Institutes of Health	Endogenous regulators of inflammation in liver ischemia	12,614	6,811
Donna Beer Stolz	National Institutes of Health	Endogenous regulators of inflammation in liver ischemia	22,670	12,252
Stephen Thorne	National Institutes of Health	Improving Vaccinia Ipr Peritoneal Tumors Enhanced Distribution and Immune Evasion	6,679	3,919
Stephen Thorne	National Institutes of Health	Combinational Immunotherapy Targeting Melanoma-Associated Vasculature	2,919	1,576
Stephen Thorne	National Institutes of Health	Exosomal Recombinase-a tool to dissect metastasis and the cancer microenviro	134	73
Stephen Thorne	National Institutes of Health	Creation of Immuno-Oncolytic Viruses for Cancer Therapy	125,809	67,937
Stephen Thorne	US Army	Real Time Visualization and Manipulation of the Metastatic Trajectory of Breast Cancer Cells	2,500	1,288
Stephen Thorne	Lustgarten	Novel oncolytic vaccinia strans for targeted pancreatic cancer therapy	104,025	20,803
Stephen Thorne	Devacell CRA	Silacate Coating of Oncolytic Vaccinia Virus to Enhance Delivery	11,777	1,177
Linton Traub	National Institutes of Health	Clathrin-coated vesicles and endocytic function	257,263	123,374
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)	80,347	41,378
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	15,000	7,020
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	82,258	44,245
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	83,805	39,422
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	25,388	5,559
Simon Watkins	National Institutes of Health	Adipose Triglyceride Lipases (ATGL) in Lipotoxicity and the Metabolic Syndrome	2,085	1,074
Simon Watkins	National Institutes of Health	ROS Mechanisms in BAV Aortopathy	5,301	2,730
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Core B	5,209	1,738
Simon Watkins	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Project 1	11,567	4,582
Simon Watkins	National Institutes of Health	Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging	11,284	5,811
Simon Watkins	National Institutes of Health	Combinational Immunotherapy targeting the Malonoma	20,718	9,820
Simon Watkins	National Institutes of Health	Cell Autonomous and Non-Autonomous Mechanisms of Again	100,079	48,640
Simon Watkins	National Institutes of Health	Targeted Fluorescent Indicators for Endothelial Physiology	22,944	7,098
Simon Watkins	National Institutes of Health	Biochemical and Spatial Regulation of IKKa/NEMO During T-Cell Activation	11,258	6,079
Simon Watkins	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lung Injury	108,518	50,330
Simon Watkins	National Institutes of Health	CYP450 Mediated CBF Dysregulation and Neurotoxicity in Pediatric Cardiac Arrest	10,324	4,603
Simon Watkins	National Institutes of Health	PQC2 Alteration of 3D nuclear organization at nanoscale in breast tumorigenesis	8,697	4,763
Simon Watkins	National Institutes of Health	Mechanisms of Perineural Invasion in head and neck cancer	9,993	5,396
Simon Watkins	National Institutes of Health	Mechanisms of Perineural Invasion in head and Neck cancer	5,006	1,207
Simon Watkins	National Institutes of Health	Mesoscale MR imaging of cellular connectivity in the ex vivo human hippocampus-	3,453	1,217
Simon Watkins	National Institutes of Health	ROS driven mitochondrial-telomere dysfunction during environmental stress-	8,918	2,115





Simon Watkins	National Institutes of Health	In vivo localization and mechanism of regulatory B cell function in alloimmunity and trasplant tolerance	11,225	6,078
Simon Watkins	National Institutes of Health	Pulmonary Arteriole Occlusion by Platelet Neutrophil Micro Emboli in acute chest syndrome	24,471	2,414
Simon Watkins	Department of Defense	Predictive understanding of the effects of encephalitic virus exposure on the blood brain barrier	50,000	21,600
Simon Watkins	National Institutes of Health	Mechanisms of sequential delivery of radiation mitogens	147,809	71,265
Simon Watkins	National Institutes of Health	Aging of MSCs missing Link in IPF	2,450	1,324
Simon Watkins	National Institutes of Health	Mechanisms of Trauma Induced immune dysregulation	90,019	41,715
Simon Watkins	National Institutes of Health	In vivo localization and mechanism of regulatory B cell function in alloimmunity and trasplant tolerance	10,003	4,403
Simon Watkins	National Institutes of Health	Adult stem cell based enhancement of nerve conduit for peripheral nerve repair	3,200	1,727
Simon Watkins	National Institutes of Health	Stem Cells for corneal engineering	59,497	32,129
Simon Watkins	National Institutes of Health	Countering the pro-inflammatory attributes of IL-33 during hematopoietic	4,373	1,417
Simon Watkins	National Institutes of Health	Exosomes as paracrine signal mediators in cardiac allograft rejection	8,853	3,431
Nathan Yates	National Institutes of Health	Cell Autonomous and Non-Autonomous Mechanism of Aging	132,562	48,821
Nathan Yates	National Institutes of Health	Plasticity of Auditory Cortical Circuits in Schizophrenia	11,264	6,056
Nathan Yates	National Institutes of Health	Bioengineering Tracheas through Targeting Activated Cell	17,891	9,660
Nathan Yates	National Institutes of Health	Request for triple quadrupole mass spectrometer for the University of Pittsburgh	5,328	3,039
			3,929,915	1,634,074

**Faculty Editorships (Fiscal Year 2014 - 2015)****Michael B. Butterworth, Ph.D.***Assistant Professor*

American Journal of Physiology – Renal Physiology  
 Frontiers in Renal and Epithelial Physiology  
 PLoS ONE  
 Physiological Genomics

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

Associate Editor/Reviewer, American Journal of Physiology: Cell Physiology

**Adam Kwiatkowski, Ph.D.***Assistant Professor*

Associate Editor, BMC Cell Biology

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

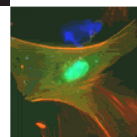
Section Editor, Biomed Central Biophysics

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

Molecular Biology of the Cell – Reviewing Editorial Board  
 Traffic, Associate Editor  
 Scientific Reports Editorial Board

**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.**

*Professor*

Member, Editorial Board, Journal of Biological Chemistry

**Simon C. Watkins, Ph.D.**

*Distinguished Professor and Vice Chairman, Director of Center of Biologic Imaging*

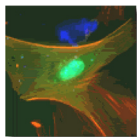
Member, Editorial Board, PittMed

Associate Editor, Experimental Biology and Medicine

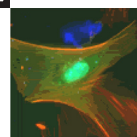
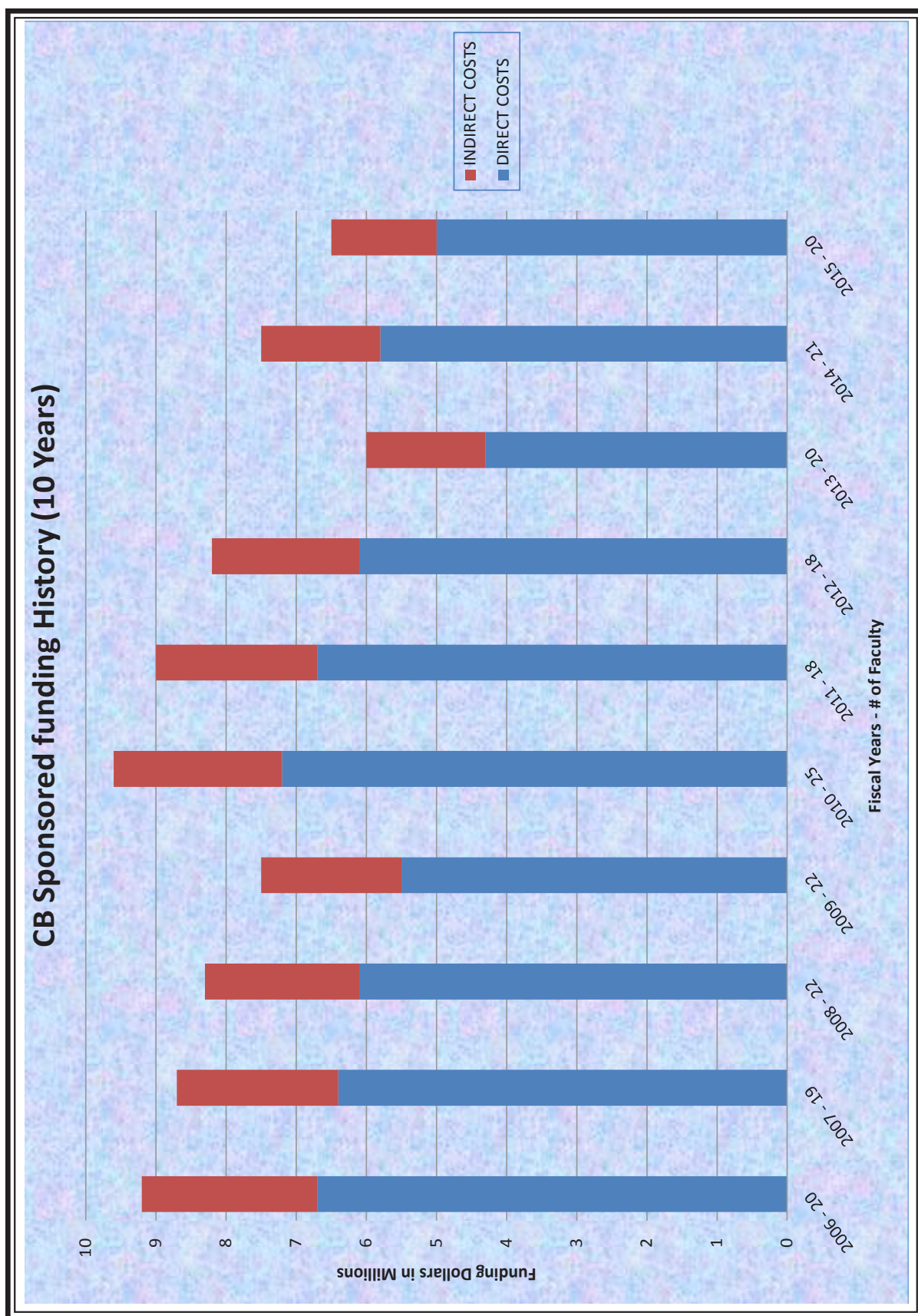
Editor, Current Protocols in Cytometry

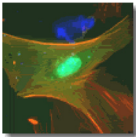
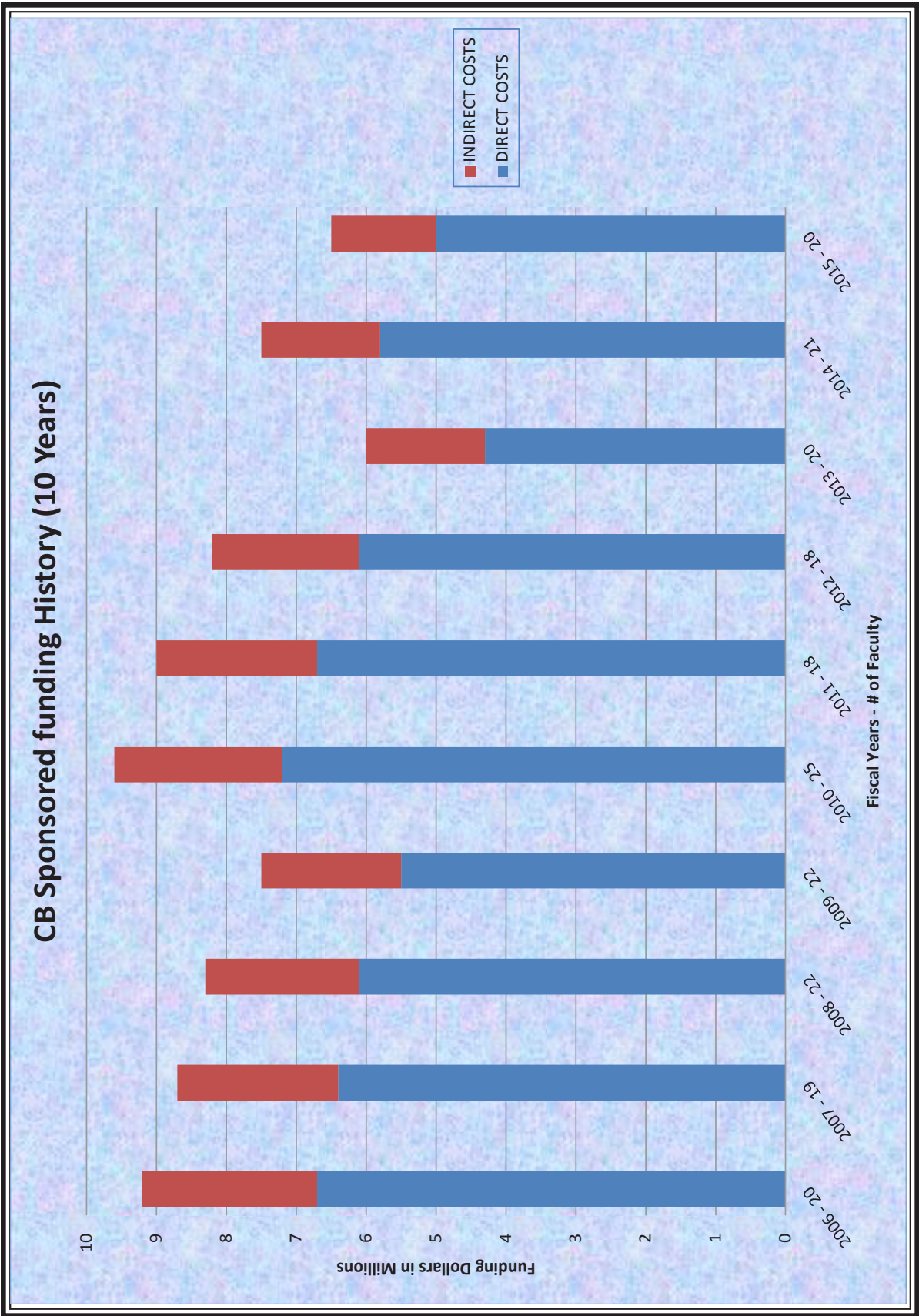
Editor, Experimental Science and Medicine

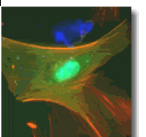
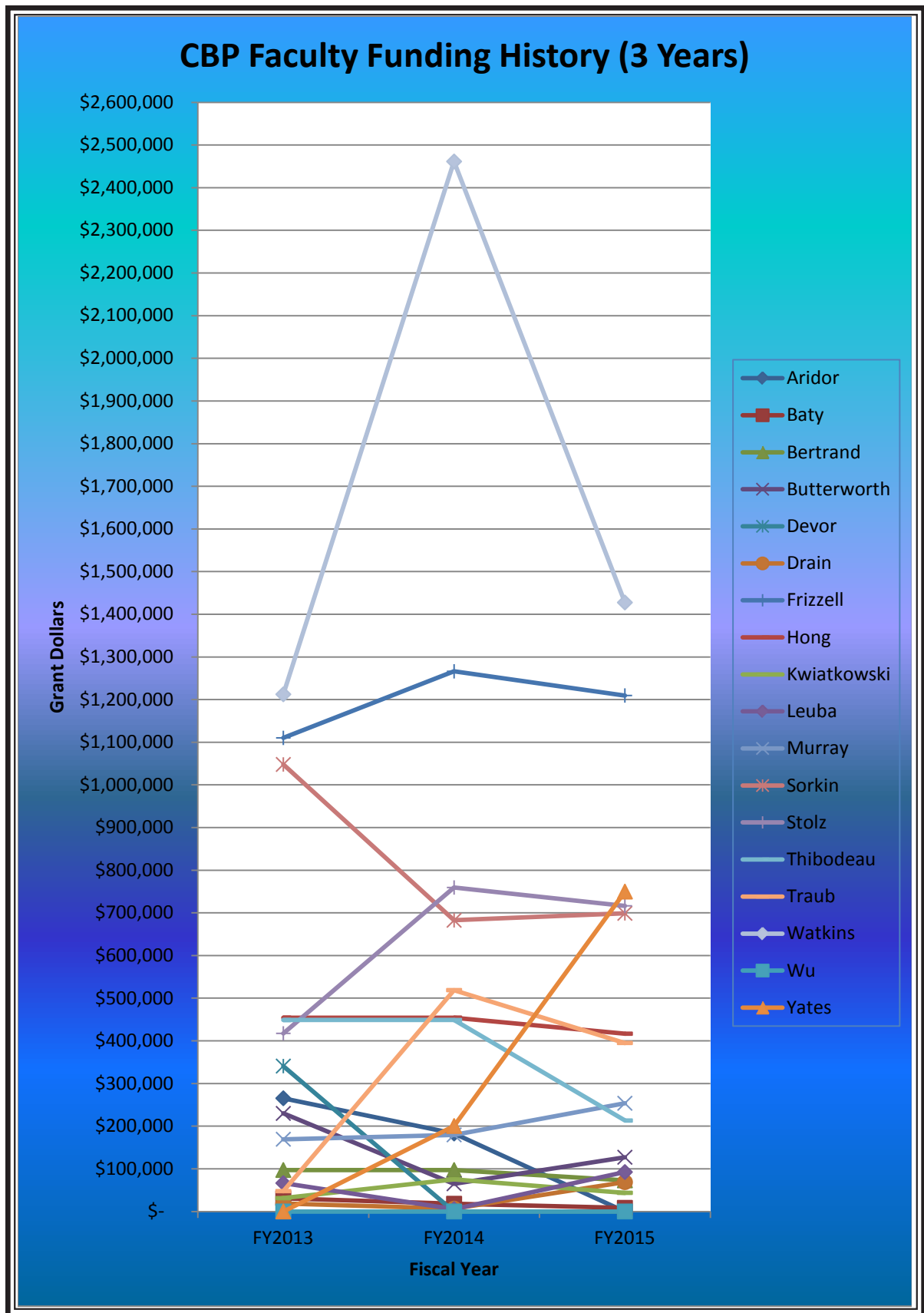
Editor, Microscopy Today







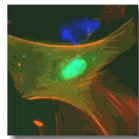




**CBP FACULTY ROSTER**  
**(Effective June, 2015)**

<b><u>Faculty Member</u></b>	<b><u>Salary Support on Grants</u></b>	<b><u>Rank</u></b>	<b><u>Status</u></b>
Bertrand, Carol	100.0%	Res. Assistant Professor	Non-tenure Track
Mishra, Sanjay	100.0%	Res. Assistant Professor	Non-tenure Track
Peters, Kathryn	100.0%	Res. Assistant Professor	Non-tenure Track
Stolz, Donna	78.7%	Associate Professor	Tenured
Watkins, Simon*	76.7%	Professor	Tenured
Frizzell, Raymond*	64.0%	Professor	Tenured
Traub, Linton	56.2%	Associate Professor	Tenured
Hong, Yang	56.0%	Associate Professor	Tenured
Sorkin, Alexander*	37.3%	Professor	Tenured
Yates, Nathan*	33.2%	Associate Professor	Non-tenure Track
Murray, Sandra	28.2%	Professor	Tenured
Butterworth, Michael	19.7%	Assistant Professor	Tenure Track
Leuba, Sanford	14.2%	Associate Professor	Tenured
Drain, Peter	10.1%	Associate Professor	Tenured
Aridor, Meir	0.0%	Associate Professor	Tenured
Devor, Daniel	0.0%	Associate Professor	Tenured
Duker, Georgia	0.0%	Assistant Professor	Non-tenure Track
Ford, Marijn	0.0%	Assistant Professor	Tenure Track
Ford, Natalia	0.0%	Res. Assistant Professor	Non-tenure Track
Hammond, Gerald	0.0%	Associate Professor	Tenured
Kwiatkowski, Adam	0.0%	Assistant Professor	Tenure Track

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

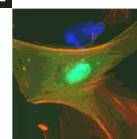


**STUDENTS INVOLVED IN RESEARCH IN CBP FACULTY LABS**

Snapshot as of June, 2015

**GRADUATE STUDENTS ENROLLED IN CBMP PROGRAM**

<b>STUDENT</b>	<b>LAB</b>	<b>SUPPORT</b>
Michael Calderon	Adam Kwiatkowski, Ph.D. Cell Biology	Adam Kwiatkowski, Ph.D. Cell Biology & Teaching Fellowship
Chelsea Merkel	Adam Kwiatkowski, Ph.D. Cell Biology	Adam Kwiatkowski, 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. Cell Biology & Teaching Fellowship
Kathryn Wack	Donna Stolz, Ph.D. Cell Biology	Donna Stolz, Ph.D. Cell Biology & ATP T32



**Cell Biology Training Grants  
FY14 and FY15**

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

**FY14 Projects**

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

Sorkin lab: *Regulation of Protein Kinase C-mediated Dopamine Transporter Endocytosis in Vivo*  
(National Institutes of Health)

The combined funding for this post doctoral fellowship grants is \$74,471 in FY14 (Total costs, annualized).

**FY15 Projects**

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

Sorkin lab: *Regulation of Protein Kinase C-mediated Dopamine Transporter Endocytosis in Vivo*  
(National Institutes of Health)

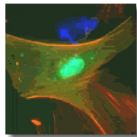
The combined funding for this post doctoral fellowship grants is \$51,471 in FY14 (Total costs, annualized).

**Program Grant Training Program:**

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

**FY14 Program Grant Training Funds - \$70,000**

**FY15 Program Grant Training Funds - \$70,000**





**Cell Biology Program Grants (Fiscal Year 2014-15)**

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

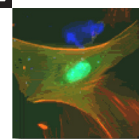
**National Institutes of Health Cystic Fibrosis Research and Translation Core Centers Program (Principal Investigator/Program Director - Raymond A. Frizzell, Ph.D.):**

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

This program grant totaled \$967,952 (total costs) in FY15.

**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

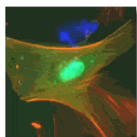


Development Program Center has existed at the University of Pittsburgh since 1997. The current center gathers over \$9.6M in external grants and contracts in support of CF-related research. It consists of 40 investigators in seven departments, whose research is focused in three major areas. The area 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 FY15. For more up to date information regarding the research conducted under this program grant, visit our website at: <http://www.cbp.pitt.edu/centers/cfrc.html>.

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

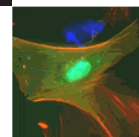
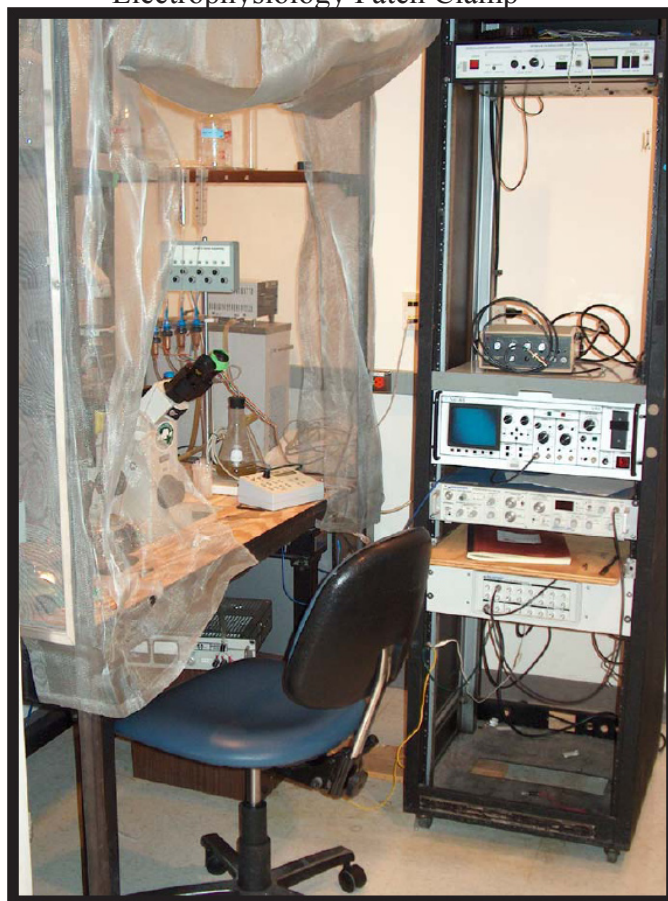
Over the last several years, microscopy as a scientific tool has reinvented itself. It has changed from a group of principally descriptive methodologies, to a wide range of quantitative tools and techniques to investigate the molecular organization of organs, tissues and cells. The University of Pittsburgh and Carnegie Mellon University (CMU) are homes to two of the leading imaging laboratories in the country; developing and applying novel fluorescent imaging tools to cutting edge biomedical research. At the Center for Biologic Imaging (CBI) of the University of Pittsburgh, we use commercially available and home built computer aided microscopic imaging tools to study these reporters within the context of living cells, tissues, and animals. The



Molecular Biosensor and Imaging Center (MBIC) at CMU has a long history of developing and applying innovative microscopy and imaging technologies. The ultimate goal of this Center will be to act as a catalyst to strengthen and expand the impact of the new probe developments by providing facilities and expertise to test and validate the probes in the context of the driving biological projects and ultimately the research community at large. In addition, this Core will provide the facilities and broad scope of knowledge and experience required to combine cells, reagents, imaging technologies, software and informatics to create high quality, robust applications for cellular analysis. These applications will be validated in the laboratories of the context of the driving biological projects, and then made available to the research community as a whole.

This program grant totaled \$18,220 (total costs) in FY15.

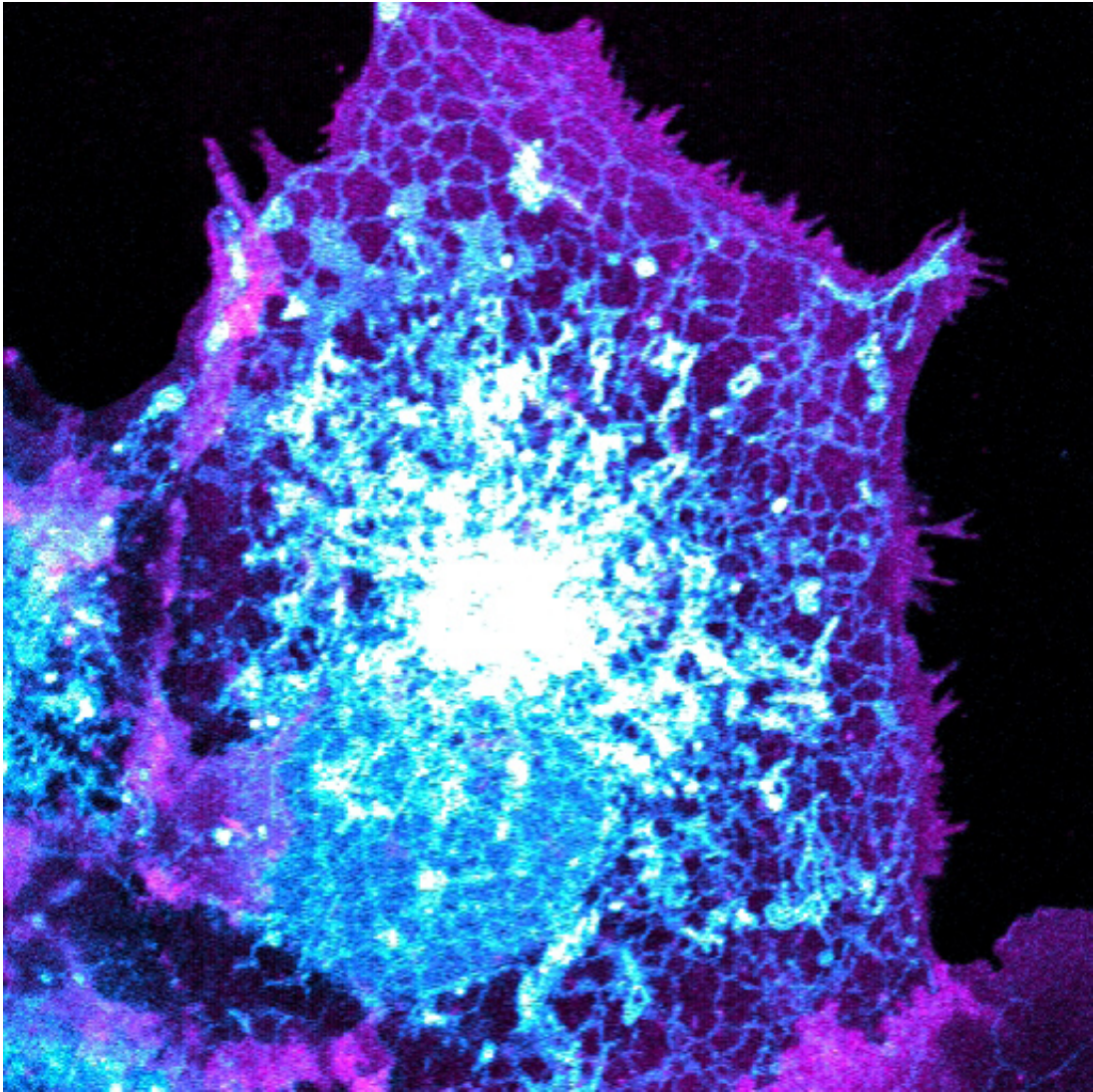
Electrophysiology Patch Clamp



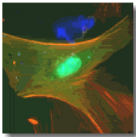


New CBP Research Recruits in FY15

Name	Rank	
Faculty Level		
Gerald Hammond	Assistant Professor	
Name	Rank	Lab Association
Post Doctoral Level		
Cheryl Bell	Post Doctoral Associate	Dr. Sandra Murray
Harris Bell-Temin	Post Doctoral Associate	Dr. Nathan Yates
Robert Edinger	Post Doctoral Associate	Dr. Butterworth



**Gerald Hammond.** ER-PM: The extensive endoplasmic reticulum (marked with ER tracker blue-white, shown in cyan) and plasma membrane (labelled with CellMask deep red, purple) at the bottom of a COS-7 cell



## 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, casual “work in progress” interactions with student peers, 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.

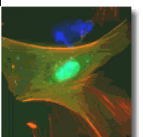
Matthew Nicotra, Ph.D. (Immunology)

Claudette St Croix, Ph.D. (EOH)

Donna Beer Stolz, Ph.D.

Stephen Thorne, Ph.D.

Simon C. Watkins, Ph.D.



### **Cellular Injury and Wound Healing**

James L. Funderburgh, Ph.D. (Ophthalmology)  
Todd Lamitina, Ph.D. (Children's Hospital)  
Rama K. Mallampalli, M.D. (Medicine)  
Sandra Murray, Ph.D.  
Gary Silverman, M.D., Ph.D. (Children's Hospital)  
Sunder Sims-Lucas, 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)  
Eric Goetzman, Ph.D. (Children's Hospital)  
Sanford Leuba, Ph.D.  
Shivalingappa Swamynathan, Ph.D. (Ophthalmology)  
William Walker, Ph.D. (MWRI)  
Yong Wan, Ph.D. (UPCI)  
Judith Yanowitz, Ph.D. (MWRI)

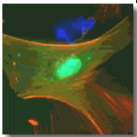
### **Ion Channel Biology**

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)  
Ossama Kashlan, 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)  
Michael Butterworth, Ph.D.  
Marcelo Carattino, Ph.D. (Medicine, Renal)  
Carolyn Coyne, Ph.D. (Microbiology and Molecular Genetics)  
Dan Devor, Ph.D.  
Marijn Ford, Ph.D.  
Ray Frizzell, Ph.D. (Children's Hospital)  
Eric Goetzman, Ph.D. (Children's Hospital)  
Gerry Hammond, Ph.D.  
Yang Hong, Ph.D.  
Rebecca Hughey, Ph.D. (Medicine, Renal)  
John Johnson, Ph.D. (Medicine, Renal)  
Tom Kleyman, M.D. (Medicine, Renal)  
Sandra Murray, Ph.D.  
Alexander Sorkin, Ph.D.  
Donna Stolz, Ph.D.  
Agnieszka Swiatecka-Urban, M.D. (Children's Hospital)  
Stephen Thorne, Ph.D.  
Linton Traub, Ph.D.  
Ora Weisz, Ph.D. (Medicine, Renal)

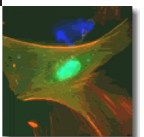
### **Regulation of Gene Expression during Development**

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.

Arjumand Ghazi, Ph.D. (Children's Hospital)

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)

### **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)

Eric Goetzman, Ph.D. (Children's Hospital)

David Whitcomb, M.D., Ph.D. (Medicine, Gastroenterology)

### **Center for Biological Imaging**

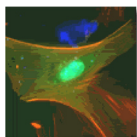
A state-of-the-art imaging center which is actively involved in the development and application of all aspects of cutting edge microscopic imaging. Through this unique facility, advances in laser confocal microscopy, live cell multicolor fluorescence microscopy, electron microscopy and computer-assisted 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](http://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-15**

#### **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*

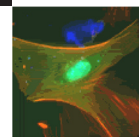
Course Director: Gerard Apodaca

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**

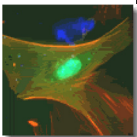
*Course Number:* 2870

*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: Daniel Devor

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

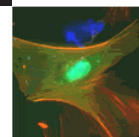
When: Spring Term

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%).

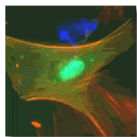
**Title: Reproductive Development from Model Organisms to Humans**

*Course Number: 3840*

Course Directors: Jennifer Condon-Jeysuria and Judith Yanowitz

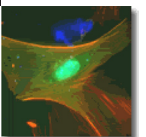
When: Fall Term

Prerequisites: None





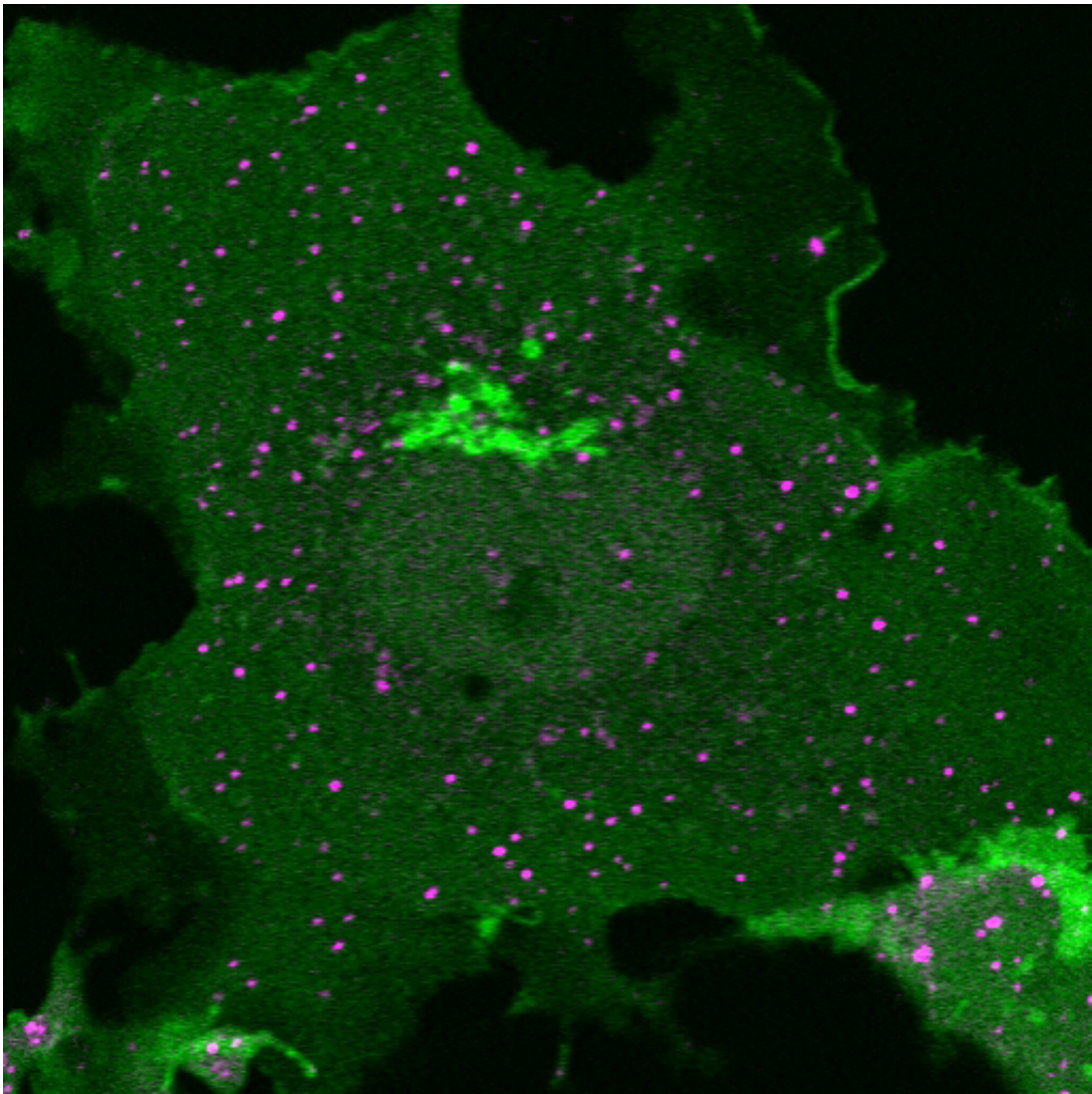
Description: This course focuses on the molecular aspects of the transition from gamete to a reproductive organism. The course progresses through the building of germ cells, fertilization and stem cell participation to sex determination, gonad morphogenesis, puberty, menopause and pregnancy. This course 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.



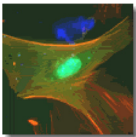
Faculty Teaching Honors (Fiscal Year 2014 - 2015)

**Georgia K. Duker, PhD**  
*Assistant Professor*

Excellence in Education Award (2014) – Basic Science Lecturer  
From the Medical Graduating Class of 2016

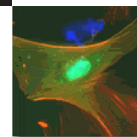


**Gerald Hammond.** PI3P-PI4P: distribution of two inositol lipids in cells, namely PI3P (purple) in early endosomes and PI4P (green) in the plasma membrane and Golgi.



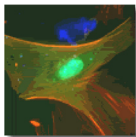
**University of Pittsburgh School of Medicine  
Educational Credit Units (AY 13-14)  
Department of Cell Biology  
Summary of Faculty ECU's**

Faculty Name	Activity	ECURV	Units	ECUs
<b>Aridor, Meir</b>				
	GS - Journal Club/Seminar Series Program Director	25.0	1.0	25.0
	GS - Lecture	2.0	10.0	20.0
	GS - Member: Program Steering Committee	40.0	1.0	40.0
	GS - Small group (e.g., PBL, conference, workshop)	2.0	26.0	52.0
	<b>Total ECUs:</b>			<b>137.0</b>
<b>Butterworth, Michael</b>				
	MS-1, MS-2 - Laboratory	2.0	8.0	16.0
	MS-1, MS-2 - Lecture	2.0	1.4	2.8
	MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	12.5	25.0
	GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
	<b>Total ECUs:</b>			<b>93.8</b>
<b>Devor, Daniel</b>				
	MS - AOC/LCP Lecture	2.0	3.0	6.0
	MS - AOC/LCP Small Group	2.0	55.5	111.0
	GS - Course Director	50.0	1.0	50.0
	GS - Member: Admissions Committee	75.0	1.0	75.0
	GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	1.0	5.0
	<b>Total ECUs:</b>			<b>247.0</b>
<b>Drain, Peter</b>				
	MS-1, MS-2 - Course Director	200.0	2.0	400.0
	MS-1, MS-2 - Lecture	2.0	1.3	2.5
	MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	19.8	39.5
	MS - Applicant Interviewer	1.0	27.0	27.0
	MS - Member, Admissions Committee	75.0	1.0	75.0
	MS - Member, Promotions Committee	5.0	1.0	5.0
	GS - Course Director	50.0	2.0	100.0
	GS - Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
	<b>Total ECUs:</b>			<b>651.0</b>
<b>Duker, Georgia</b>				
	MS-1, MS-2 - Course Director	200.0	1.0	200.0
	MS-1, MS-2 - Course Laboratory Segment/Session Coordinator	5.0	1.0	5.0
	MS-1, MS-2 - Course Segment Coordinator	5.0	1.0	5.0
	MS-1, MS-2 - Laboratory	2.0	19.2	38.5
	MS-1, MS-2 - Lecture	2.0	63.7	127.3



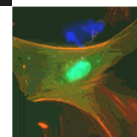
**University of Pittsburgh School of Medicine**  
**Educational Credit Units (AY 13-14)**  
**Department of Cell Biology**  
**Summary of Faculty ECU's**

Faculty Name	Activity	ECURV	Units	ECUs
MS-1, MS-2 - Other		2.0	3.0	6.0
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)		2.0	29.3	58.5
MS - Member, Promotions Committee		5.0	1.0	5.0
GS - Course Director		50.0	1.0	50.0
GS - Lecture		2.0	52.0	104.0
GS - Other		2.0	6.0	12.0
GS - Program Director		100.0	1.0	100.0
GS - Small group (e.g., PBL, conference, workshop)		2.0	28.0	56.0
Total ECUs:				767.3
Frizzell, Raymond				
MS-1, MS-2 - AOC/Longitudinal Curriculum Program Director		20.0	1.0	20.0
MS - AOC/LCP Lecture		2.0	3.0	6.0
MS - AOC/LCP Small Group		2.0	58.5	117.0
Total ECUs:				143.0
Hong, Yang				
GS - Lecture		2.0	4.0	8.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint		5.0	1.0	5.0
GS - Member: Curriculum, Recruiting, Program, or other SOM Committee		2.0	1.0	2.0
Total ECUs:				15.0
Kwiatkowski, Adam Vincent				
MS-1, MS-2 - Lecture		2.0	1.8	3.7
GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)		1.0	21.0	21.0
GS - Lecture		2.0	6.0	12.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint		5.0	2.0	10.0
GS - Ph.D. or M.Sc. Mentor		50.0	2.0	100.0
GS - Small group (e.g., PBL, conference, workshop)		2.0	22.5	45.0
Total ECUs:				191.7
Leuba, Sanford				
GS - Chair: Admissions Committee		100.0	1.0	100.0
GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee		5.0	1.0	5.0
GS - Course Director		50.0	1.0	50.0
GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)		1.0	20.0	20.0
GS - Lecture		2.0	2.0	4.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint		5.0	1.0	5.0
GS - Member: Curriculum, Recruiting, Program, or other SOM Committee		2.0	1.0	2.0
GS - Member: Program Steering Committee		40.0	1.0	40.0



**University of Pittsburgh School of Medicine  
Educational Credit Units (AY 13-14)  
Department of Cell Biology  
Summary of Faculty ECU's**

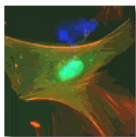
Faculty Name	Activity	ECURV	Units	ECUs
	GS - Ph.D. or M.Sc. Mentor	50.0	2.0	100.0
	GS - Small group (e.g., PBL, conference, workshop)	2.0	43.5	87.0
	Total ECUs:			413.0
Murray, Sandra				
	MS-1, MS-2 - Laboratory	2.0	78.0	156.0
	MS-1, MS-2 - Lecture	2.0	3.5	7.0
	MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	2.0	4.0
	MS - Member, Promotions Committee	5.0	1.0	5.0
	GS - Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
	Total ECUs:			174.0
Peters, Kathryn				
	MS - AOC/LCP Lecture	2.0	3.0	6.0
	MS - AOC/LCP Small Group	2.0	58.5	117.0
	Total ECUs:			123.0
Ryan, Kathleen				
	MS-1, MS-2 - Lecture	2.0	2.5	5.0
	MS-1, MS-2 - Simulator session	2.0	7.0	14.0
	MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	4.5	9.0
	MS - Applicant Interviewer	1.0	5.0	5.0
	MS - Member, Curriculum Committee	20.0	1.0	20.0
	MS - Member, Promotions Committee	5.0	1.0	5.0
	MS - Member, Retention Committee	5.0	1.0	5.0
	Total ECUs:			63.0
Sorkin, Alexander				
	GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	11.0	11.0
	GS - Lecture	2.0	6.0	12.0
	GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	4.0	20.0
	GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
	Total ECUs:			93.0
Stolz, Donna				
	MS-1, MS-2 - Laboratory	2.0	9.5	19.0
	MS-1, MS-2 - Lecture	2.0	2.3	4.5
	MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	8.5	17.0
	GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	4.0	20.0
	GS - Course Director	50.0	3.0	150.0
	GS - GS Academic Advisor	2.0	3.0	6.0





**University of Pittsburgh School of Medicine**  
**Educational Credit Units (AY 13-14)**  
**Department of Cell Biology**  
**Summary of Faculty ECU's**

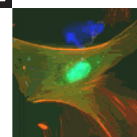
Faculty Name	Activity	ECURV	Units	ECUs
	GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	52.0	52.0
	GS - Lecture	2.0	17.0	34.0
	GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	7.0	35.0
	GS - Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
	GS - Member: Program Steering Committee	40.0	1.0	40.0
	GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
	GS - Program Director	100.0	1.0	100.0
	GS - Small group (e.g., PBL, conference, workshop)	2.0	10.0	20.0
	Total ECUs:			549.5
Thibodeau, Patrick				
	MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	6.8	13.5
	GS - Associate Director	75.0	1.0	75.0
	GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
	GS - Lecture	2.0	4.0	8.0
	GS - Member: Admissions Committee	75.0	1.0	75.0
	GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	7.0	35.0
	GS - Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
	GS - Member: Program Steering Committee	40.0	1.0	40.0
	GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
	GS - Small group (e.g., PBL, conference, workshop)	2.0	2.5	5.0
	Total ECUs:			308.5
Traub, Linton				
	GS - Associate Director	75.0	1.0	75.0
	GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
	GS - Course Director	50.0	2.0	100.0
	GS - Lecture	2.0	14.0	28.0
	GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	1.0	5.0
	GS - Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.0
	GS - Small group (e.g., PBL, conference, workshop)	2.0	31.0	62.0
	Total ECUs:			277.0
Wan, Yong				
	GS - Lecture	2.0	3.0	6.0
	GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	1.0	5.0
	Total ECUs:			11.0
Watkins, Simon				
	MS-1, MS-2 - AOC/Longitudinal Curriculum Program Director	20.0	1.0	20.0

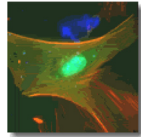




**University of Pittsburgh School of Medicine  
Educational Credit Units (AY 13-14)  
Department of Cell Biology  
Summary of Faculty ECU's**

Faculty Name	Activity	ECURV	Units	ECUs
	MS - AOC/LCP Lecture	2.0	3.0	6.0
	MS - AOC/LCP Small Group	2.0	85.5	171.0
	MS - Elective Course Research Mentor	4.0	1.0	4.0
	MS - Mentored Scholarly Project (MSP) Mentor	25.0	1.0	25.0
	GS - Course Director	50.0	2.0	100.0
	GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	8.0	8.0
	GS - Lecture	2.0	23.0	46.0
	GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	5.0	25.0
	GS - Other	2.0	4.0	8.0
	GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
	<b>Total ECUs:</b>			<b>463.0</b>
Yates, Nathan A.				
	GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	7.0	7.0
	GS - Lecture	2.0	6.7	13.3
	<b>Total ECUs:</b>			<b>20.3</b>
	<b>Subtotal:</b>			<b>4741.2</b>
<b>Total Faculty Reporting: 19</b>		<b>Total ECU's for Cell Biology:</b>		<b>4741.2</b>





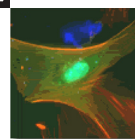
Post Doctoral Personnel Data

[Current as of June, 2015]

Name	Title	Office Address	Email Address	Office Phone	Fax	Research
<b>Focus</b>						
Ahner, Annette	Vis. Research Associate	7161 RANCH	aschneid@pitt.edu	412-648-8162	412-648-8330	Frizzell Lab
Bell, Cheryl	Post Doctoral Associate	S346 BSTWR	clb206@pitt.edu	412-648-9565	412-648-8330	Murray Lab
Bell-Temin, Harris	Post Doctoral Associate	BST3-9th Fl	hbb16@pitt.edu	412-383-5937	412-641-2458	Yates 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
Dong, Wei	Post Doctoral Associate	S333 BSTWR	wed16@pitt.edu	412-648-2846	412-648-8330	Hong Lab
Edinger, Robert	Vis. Research Associate	S353 BSTWR	rse9@pitt.edu	412-383-5173	412-648-8330	Butterworth
Lab						
Gong, Xiaoyan	Research Associate	7161 RANCH	xig17@pitt.edu	412-692-9335	412-692-8906	Frizzell Lab
Larsen, Mads	Post Doctoral Associate	S234 BSTWR	mb16@pitt.edu	412-648-9796	412-648-8330	Frizzell/Wat-
kins Lab						
Long, Kimberly	Post Doctoral Associate	S307 BSTWR	kr134@pitt.edu	412-624-1971	412-648-8330	Aridor Lab
Mitra, Shalini	Post Doctoral Associate	S315 BSTWR	shm70@pitt.edu	412-624-8269	412-648-8330	Frizzell Lab
Perunthathu, Umasankar	Post Doctoral Associate	S306 BSTWR	ukp1@pitt.edu	412-624-9713	412-648-8330	Traub Lab
Pimilla-Macua, Itziar	Post Doctoral Associate	S372 BSTWR	itp2@pitt.edu	412-624-8147	412-648-8330	Sorkin Lab
Wang, Xiaohui	Post Doctoral Associate	S315 BSTWR	xiw68@pitt.edu	412-648-8620	412-648-8330	Frizzell Lab
Zhou, Zhuan	Post Doctoral Associate	HCCLB-2.6	zhou2@upmc.edu	412-623-7811	412-623-7761	Wan Lab

**Current Cell Biology and Molecular Physiology Graduate Program Students as of June 30, 2015**

<b><u>Student</u></b>	<b><u>Mentor</u></b>	<b><u>Year</u></b>
Christine Klemens	Dr. Mike Butterworth	3 <sup>nd</sup>
George Michael Preston	Dr. Jeff Brodsky	3 <sup>nd</sup>
Michael Calderon	Dr. Adam Kwiatkowski	1 <sup>st</sup>
Chelsea Merkel	Dr. Adam Kwiatkowski	1 <sup>st</sup>



**Prior Graduates of the Cell Biology and Molecular Physiology Program as of June 2015  
(Past five years)**

**Kathryn Wack, Ph.D.**

Defended July 23, 2014

Clinical Scientist, Omxyx, GE, Healthcare/UPMC Pittsburgh

**Arvind Suresh, M.S.**

Defended October 11, 2013

Scientist Consultant, Men's Mentis Consulting Service

**Christina Szalinski, Ph.D.**

Defended May 20, 2013

Science Writer, 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

Research Fellow, University of Michigan

**Xinxian Qiao, M.S.**

Defended December 17, 2012

Technician, Hillman Cancer Center, Pittsburgh, PA

**Anupma Jha, Ph.D.**

Defended December 8, 2011

Pos-Doc, Dept. Development Biology, University of Pittsburgh

**Siobhan Gregg, Ph.D.**

Defended November 4, 2011

New York Academy of Sciences Event Organizer

**Daniel Rho, Ph.D.**

Defended July 15, 2011

Clinical Fellow, Brigham Woman's Hospital

**James R. Thieman, Ph.D.**

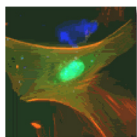
Defended June 9, 2011

Product Manager, Olympus Corporation

**ShanShan Cui, Ph.D.**

Defended December 7, 2010

Clinical Research Assoc., Medpace, Cincinnati, Ohio



**Mark A. Bailey, Ph.D.**

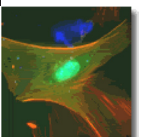
Defended September 23, 2010  
Student, UC Davis Law School

**Paula J. Bernal, PH.D.**

Defended August 12, 2010  
Post-Doc, Center for Vaccine Development, University of Maryland

**Ethan Block, Ph.D.**

Defended January 19, 2010  
Assistant Professor, Biology Dept., Chatham University



# CB Faculty Instructor Ratings

## Student Ratings of CBMP Faculty Teaching FY2015

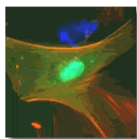
Name	Course	Type	Date	Rating	Ave
Butterworth	Methods and Logic in Medicine Part 2	SGCS	Fall-14	4.50	
Butterworth	Cellular and Pathological Basis of Disease	LAB	Spring-15	4.50	
Butterworth	Cellular and Pathological Basis of Disease	PBL	Spring-15	4.10	4.37
Devor	Methods and Logic in Medicine Part 2	SGCS	Fall-14	4.80	4.80
Drain	Methods and Logic in Medicine Part 2	SGCS	Fall-14	5.00	5.00
Duker	Introduction to Being a Physician	SGCS	Fall-14	4.40	
Duker	Body Fluid Homeostasis Cardiovascular	WKSP	Fall-14	4.40	
Duker	Body Fluid Homeostasis-Renal Segment	LEC	Fall-14	4.70	
Duker	Body Fluid Homeostasis-Pulmonary Segment	LEC	Fall-14	4.70	
Duker	Digestion and Nutrition	LEC	Fall-14	5.00	
Duker	Digestion and Nutrition	LAB	Fall-14	4.90	
Duker	Cellular and Pathological Basis of Disease	LEC	Spring-15	4.90	
Duker	Cellular and Pathological Basis of Disease	LAB	Spring-15	4.90	
Duker	Cellular and Pathological Basis of Disease	PBL	Spring-15	4.90	4.76
Kwiatkowski	Cellular and Pathological Basis of Disease	LEC	Spring-15	2.80	2.80
Murray	Medical Anatomy	LEC	Fall-14	3.60	
Murray	Medical Anatomy	LAB	Fall-14	4.20	3.90
Stolz	Cellular and Pathological Basis of Disease	LEC	Spring-15	3.70	
Stolz	Cellular and Pathological Basis of Disease	LAB	Spring-15	5.00	
Stolz	Cellular and Pathological Basis of Disease	PBL	Spring-15	4.70	
Stolz	Digestion and Nutrition	LAB	Fall-14	4.50	4.48

**Overall Teaching Average**

**4.49**

### Type codes:

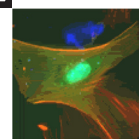
LEC	Lecture
PBL	Practice Based Learning
WKSP	Workshop
SGCS	Small Group Conference Session
AP	Applications Staff
LAB	Laboratory





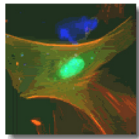
**CBP FACULTY ROSTER  
(Effective June, 2014)**

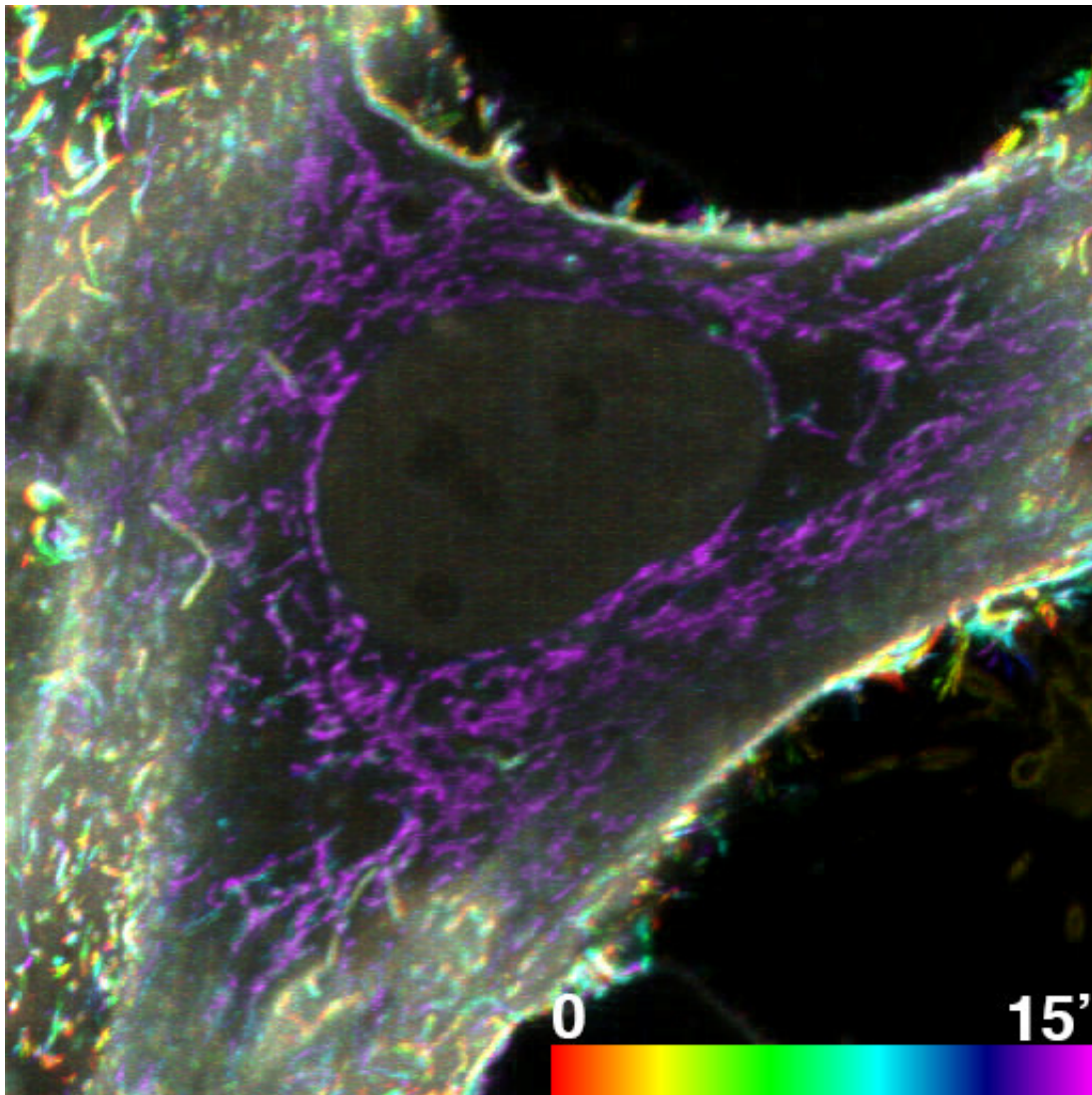
<b><u>Last Name</u></b>	<b><u>First</u></b>	<b><u>Rank</u></b>	<b><u>Status</u></b>
Sorkin	Alexander	Professor & Chair	Tenured
Devor	Daniel	Professor	Tenured
Frizzell	Raymond	Professor	Tenured
Murray	Sandra	Professor	Tenured
Wan	Yong	Professor	Tenured
Watkins	Simon	Professor	Tenured
Aridor	Meir	Associate Professor	Tenured
Drain	Peter	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
Yates	Nathan	Associate Professor	Non-tenure Track
Butterworth	Michael	Assistant Professor	Tenure Track
Ford	Marijn	Assistant Professor	Tenure Track
Hammond	Gerald	Assistant Professor	Tenure Track
Kwiatkowski	Adam	Assistant Professor	Tenure Track
Thibodeau	Patrick	Assistant Professor	Tenure Track
Duker	Georgia	Assistant Professor	Non-tenure Track
Bertrand	Carol	Res. Assistant Professor	Non-tenure Track
Ford	Natalia	Res. Assistant Professor	Non-tenure Track
Mishra	Sanjay	Res. Assistant Professor	Non-tenure Track
Peters	Kathryn	Res. Assistant Professor	Non-tenure Track



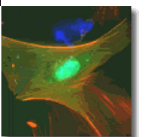
New CBP Faculty in FY15

<u>Name</u>	<u>Prior Institution /Rank</u>	<u>Current Rank</u>
Gerald Hammond	National Institutes of Health NICHD Bethesda, MD	Assistant Professor





**Gerald Hammond.** PIP2-mito: color-coded time lapse image showing accumulation of PIP2 in the mitochondria.



**Faculty Honors, Recognition and Professional Affiliations (Fiscal Year 2014 - 2015)**

**Michael Butterworth, Ph.D.**

*Assistant Professor*

Member, American Physiological Society  
Member, Elected Secretary, Salt and Water Club  
American Society of Nephrology  
American Heart Association  
Cell and Molecular Physiology New Investigator Award, American Physiological Society

**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  
Dean's Master Educator Award from Medical School, October 2014

**Georgia Duker, Ph.D.**

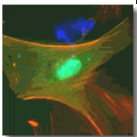
*Assistant Professor*

Excellence in Education Award - Basic Science Lecturer - Class of 2016

**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



**Gerry Hammond, Ph.D.**

*Assistant Professor*

Member, Biochemical Society

Member, American Association for the Advancement of Science

**Yang Hong, Ph.D.**

*Associate Professor*

Member of Faculty 1000

Research Scholar, American Cancer Society

**Adam Kwiatkowski, Ph.D.**

*Assistant Professor*

Member, American Society for Cell Biology

American Society for Biochemistry and Molecular Biology

American Heart Association

**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

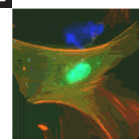
School of Medicine Summer "Minority" Work-Study Program

Member, Medical Student Promotions Committee

Member, Training Faculty Immunology Graduate Training Program

NIH - Biomedical Faces of Science Mentors

Co-Chair of the Research Center of Excellence Committee Graduate School of Public Health,



University of Pittsburgh  
Graduate School of Public Health Community Engagement Research Cor  
Graduate School of Public Health Research Advisory Committee- Center for Minority Health  
Provost Special Advisory Committee  
Provost Selection Committee for the Provost Development Fund Awards  
University Community Representative for Equipoise  
Junior Faculty Advancement – Panel Member

**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  
ASCB Science as Art Show, Philadelphia Airport, 2 pieces – 2014  
ASCB Science as Art Show, Washington Dulles Airport – 2014  
Nikon Small World Award (not yet ranked) - 2015

**Linton M. Traub, Ph.D.**

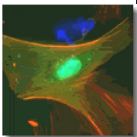
*Associate Professor*

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

**Yong Wan, Ph.D.**

*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.**

*Distinguished Professor and Vice Chairman, Director of Center of Biologic Imaging*

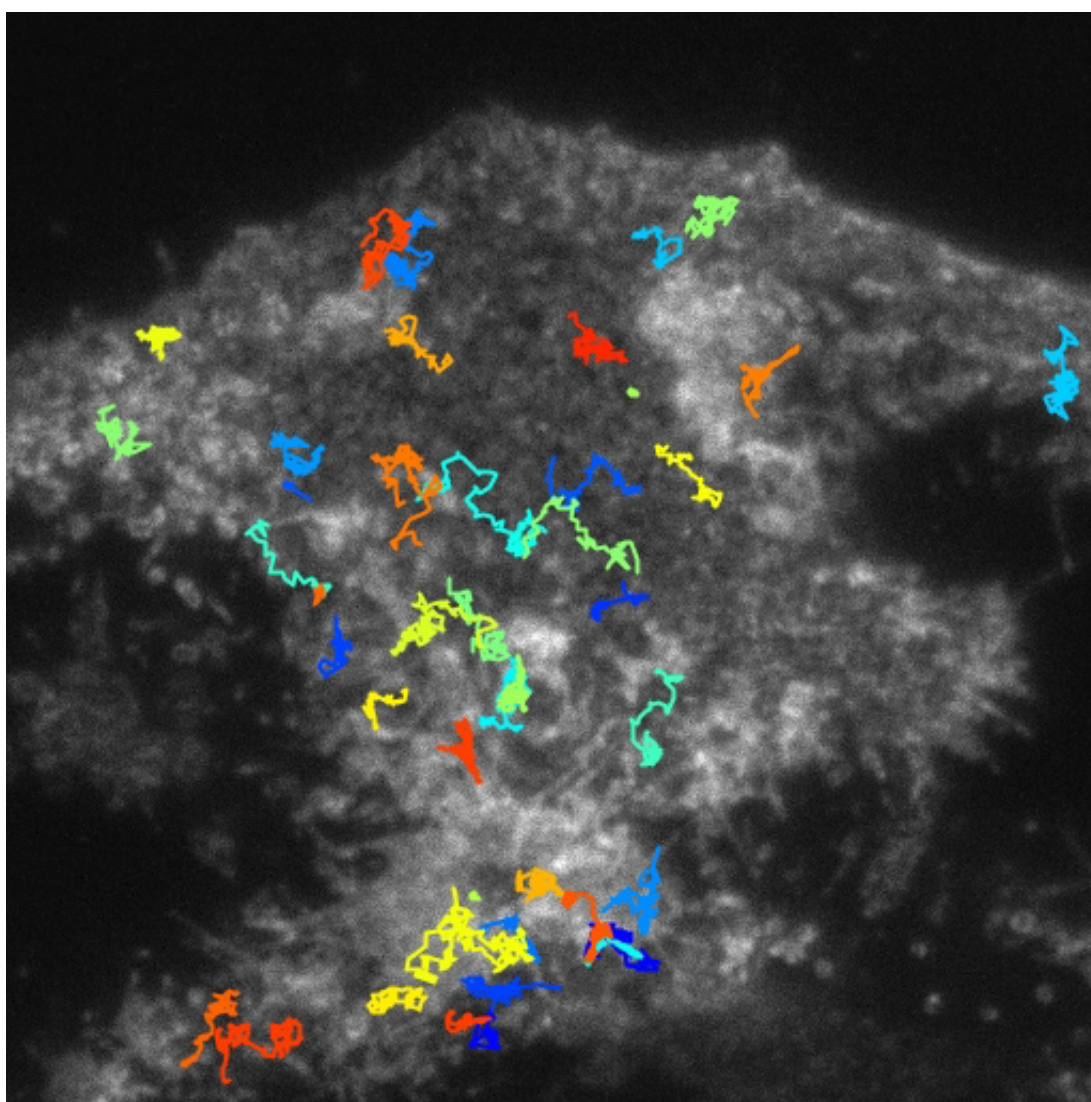
Member, The Pittsburgh Cancer Institute

**Nathan Yates, Ph.D.**

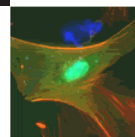
*Associate Professor*

American Chemical Society

American Society for Mass Spectrometry



**Gerald Hammond.** Tracks: single molecule trajectories for fluorescent protein labelled PIP2 lipids in the plasma membrane of a COS-7 cell.



**Faculty Presentations (Fiscal Year 2014- 2015)**

**Meir Aridor, Ph.D.**

*Associate Professor*

“A molecular cascade for exit from the ER” Molecular Medicine Seminar, Children’s Hospital of Pittsburgh, November, 2014

“Super-Resolution Microscopy is Dynamite: It’s Beginning, Present, and Future”, School of Medicine, University of Pittsburgh, November, 2014

**Michael Butterworth, Ph.D.**

*Assistant Professor*

“Kidney microRNAs: Central players in sodium regulation or innocent bystanders?” Department of Human Biology, University of Cape Town, South Africa. 2015

“More than Just a Pinch of Salt: Regulation of Sodium Transport in the Kidney”. Division of Nephrology, University of the Witwatersrand, South Africa. 2015

**Daniel Devor, Ph.D.**

*Professor*

“Regulation of KCa3.1 and KCa2.3 trafficking in epithelia and endothelia” Cystic Fibrosis Research Center, University of Pittsburgh

**Raymond A. Frizzell, Ph.D.**

*Professor, Director of Cystic Fibrosis Research Center*

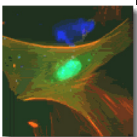
Microbiology and Molecular Genetics, Univ. of Pittsburgh, Wrestling with CFTR folding: “Two sides to SUMO”, September 24, 2014

**Yang Hong, Ph.D.**

*Associate Professor*

Annual *Drosophila* Research Conference, Chicago, 2015

Dynamics of Cellular Behavior During Development and Disease, Cold Spring Harbor Asia Conference, Suzhou, China, 2014



**Adam Kwiatkowski, Ph.D.**  
*Assistant Professor*

Seminar, Vascular Medicine Institute, University of Pittsburgh School of Medicine, Pittsburgh, PA. October 20, 2014.

Presentation, March of Dimes Board Meeting, Pittsburgh, PA. October 21, 2014.

Special seminar on the 2014 Noble Prize in Chemistry, University of Pittsburgh School of Medicine, Pittsburgh, PA. November 20, 2014.

**Sandra Murray, Ph.D.**  
*Professor*

Speaker- Faculty Research and Education Development (FRED) Program, Funded by the NSF (San Juan, Puerto Rico, 2014, Houston, Texas, 2015).

Discussion Leader- American Society for Cell Biology Meeting, Table Topic, Endoexocytosis, Philadelphia, PA 2014

Session Chair- International Adrenal Conference (Receptors and Signaling Session), Charleston NC, 2014

Invited Speaker- Albany State University, Albany, GA. April 2015.

Presenter International Gap Junction Meeting, Valparaiso, Chile 2015.

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

Science Transformations. University of Pittsburgh (October, 2014)

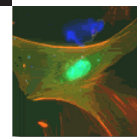
Boston University, Biochemistry Department “EGF receptor endocytosis: mechanisms and role in signaling”, Boston MA (November, 2014)

Drug Discovery Institute, “Endocytosis of the EGF receptor and dopamine transporter: potential drug targets?” University of Pittsburgh (December, 2014)

**Donna B. Stolz, Ph.D.**  
*Associate Professor*

Chronic Kidney Disease in the ERCC-1 deficient mouse model of accelerated aging. Cell Biology Department Retreat, University of Pittsburgh. September 19, 2014

Imaging Alpha-1 antitrypsin Disease. Albert Einstein College of Medicine. Bronx, NY. Nov. 5, 2014.



Career Choices with a Biochemistry degree. University of Massachusetts, Amherst. Nov 14, 2014.

**Linton Traub, Ph.D.**  
*Associate Professor*

‘Endocytic cargo selection and clathrin coat assembly’ *The Dynamic Cell*. The Biochemical Society Conference. Robinson College, Cambridge, UK.

So why study clathrin-mediated endocytosis anyway? Department of Cellular Biology and Anatomy, Georgia Regents University, Augusta,

**Yong Wan, Ph.D.**  
*Associate Professor*

Impact of posttranslational modification in DNA damage response and tumorigenesis. MD Anderson Cancer Center, 2014

Ubiquitin-proteasome system in signaling and carcinogenesis. Purdue University, 2014

Impact of UPS: from Kruppling development to tumorigenesis. Symposium of frontier cell biology and human disease, Harvard Medical School, 2015

Posttranslational modification in genome stability and carcinogenesis. South University of Science and Technology of China, 2015

Impact of posttranslational modification in human diseases. Sun Yat-sen University School of Medicine. China, 2015

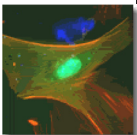
Crosstalk between ubiquitylation and protein methylation in tumorigenesis. University of Florida, 2015

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

Society for Biomolecular Imaging and Informatics Conference “Novel imaging approaches, probes and microscopies for HTS screening of CF correction” Invited Speaker, Harvard University September 12<sup>th</sup> 2014

Society for Biomolecular Imaging and Informatics Conference Emerging Frontiers symposium organizer and chair, Harvard University September 12<sup>th</sup> 2014

Cutting edge imaging approaches and probes for high speed multidimensional imaging. Keynote



speaker, Cincinnati Children's Hospital Medical Center, Annual research Day. September 17<sup>th</sup> 2014

Novel Probes and Novel Microscopies: Invited speaker, University of Akron, Akron Ohio October 14<sup>th</sup> 2014

Microscopies: Future Facts. Invited Speaker, Nikon Corporation Tokyo Japan October 21<sup>st</sup> 2014  
2014 Nobel in Chemistry, Presenter, Nov 15 2014 University of Pittsburgh

Imaging single molecules in living systems, PittCon 2015 Chair of Symposium, New Orleans, March 2015

Novel probes and novel microscopies to study cystic fibrosis PittCon 2015 Invited Speaker New Orleans March, 2015

Novel probes and novel microscopies to study cystic fibrosis ABRF annual meeting Invited speaker March, 2015.

Imaging Futures: Round table chair, ABRF annual meeting March 30, 2015

Invited Speaker, Healthy Aging Advances University of Pittsburgh June, 2015

**Nathan Yates, Ph.D.**  
*Associate Professor*

"MS in the Cloud" International Mass Spectrometry Conference, Geneva, Switzerland, August 2014

"Automated Multi-dimensional Multi-channel LC/LC-MS/MS For Increased Dynamic Range" CPSA 2014 USA Innovators Lecture, Langhorne, PA, October 2014

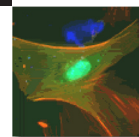
"Re-Thinking and Re-Creating the Modern Scientific Data Analysis Paradigm: Mass Spectrometry Moves Big Data to the Cloud" CPSA 2014 USA Thermo Fisher Lunch and Roundtable, Langhorne, PA, October, 2014

"ReThinking and ReCreating Scientific Data Analysis: Mass Spectrometry Moves Big Data to the Cloud" Magee Women's Research Institute, Pittsburgh PA, October 2014

"CHORUS: A Community-based Solution for the Storage, Analysis, and Exchange of Mass Spectrometry Data and Information" Presentation at Thermo Fisher, San Jose CA, October 2014

"Re-Thinking and Re-Creating the Modern Scientific Data Analysis Paradigm: Mass Spectrometry Moves Big Data to the Cloud" ACS Central Eastern Regional Meeting, Pittsburgh, October 2014

"Proteomic Applications of Differential Mass Spectrometry From Basic Research to the Clinic" Presentation to Novartis Analytical Science Institute, Basel Switzerland, February 2015



“CHORUS - a Community Solution for the Storage, Visualization, Sharing, and Analysis of Mass Spectrometry Data” Presentation to Novartis Analytical Science Institute, Basel Switzerland, February 2015

“Software and Cloud-Based Applications for the Clinical Laboratory” Pittcon 2015, New Orleans, LA, February 2015

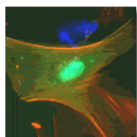
“Breaking the Megapixel Boundary with Multi-Dimensional Proteomic Analysis” Multi-Chromatographic Separation and Identification for Glyco-proteomics Tsinghua University, Shanghai, China, April 2015

“Continuous MUDPIT – Automated and Flexible Multi-Dimensional LC System for Comprehensive Proteomic Analysis” National Facility for Protein Science Shanghai (NCPSS), Shanghai, China, April 2015

“Mass Spectrometry Looks to Cloud Computing for Data Permanence and Re-Analysis” Pharmaceutical Structure Analysis Meeting, Shanghai, China, June 2015

“Identifying Proteins to which Small-Molecule Probes and Drugs Bind” Presentation to Merck Research Laboratories, Rahway NJ, June 2015

“The Proteomics Telescope - How Differential Mass Spectrometry Is Changing Our View of the Proteome” Senior Vice Chancellor’s Research Seminar, Pittsburgh, PA, June 2015





**Peer Reviewed Publications (Fiscal Year 2014-2015)****Meir Aridor, Ph.D.***Associate Professor*

Klinkenberg D, Long KR, Shome K, Watkins SC, Aridor M. (2014) A cascade of ER exit site assembly that is regulated by p125A and lipid signals. *J. Cell Sci.* 127:1765-78.

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

Shiwerski DJ, Shao C, Bill A, Kim J, Xiao D, **Bertrand CA**, Seethala RS, Sano D, Myers JN, Ha P, Grandis J, Gaither LA, Puthenveedu MA, Duvvuri U. (2014) To “Grow” or “Go”: TMEM16A Expression as a Switch between Tumor Growth and Metastasis in SCCHN. *Clin Cancer Res*, 20(17):4673-4688.

**Michael Butterworth, Ph.D.***Assistant Professor*

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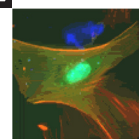
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**Daniel Devor, Ph.D.***Professor*

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**Peter F. Drain, Ph.D.**

*Associate Professor*

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**Marijn Ford, Ph.D.**

*Assistant Professor*

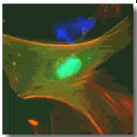
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*Research Assistant Professor*

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**Raymond A. Frizzell, Ph.D.**

*Professor, Director of Cystic Fibrosis Research Center*

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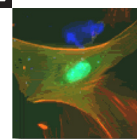
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*Assistant Professor*

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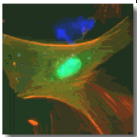
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**Adam Kwiatkowski, Ph.D.***Assistant Professor*

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**Sanford Leuba, Ph.D.**

*Associate Professor*

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**Sandra A. Murray, Ph.D.**

*Professor*

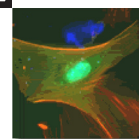
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**Kathryn Peters, Ph.D.**

*Research Assistant Professor*

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**Alexander D. Sorkin, Ph.D.**

*Richard B. Mellon Professor and Chairman*

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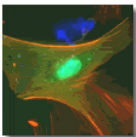
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### **Donna B. Stolz, Ph.D.**

*Associate Professor*

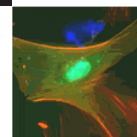
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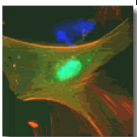
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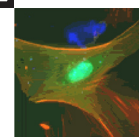
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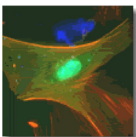
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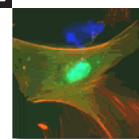
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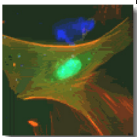
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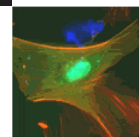
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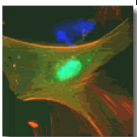
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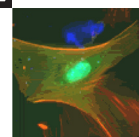
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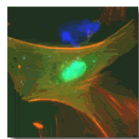
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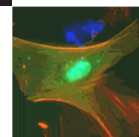
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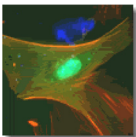
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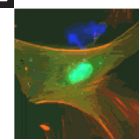
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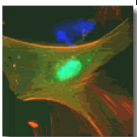
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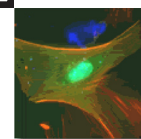
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**Nathan Yates, Ph.D.**

*Associate Professor*

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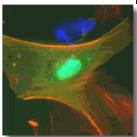
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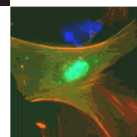


**Executive Summary for the Cell Biology FY2016 Business Plan**

The department has developed a diverse group of well funded investigators who contribute on many levels to the research and educational programs of the School of Medicine. During last five years significant changes in the Department took place with eight members of the primary faculty leaving the Department and seven new members joining the faculty. This year two new primary faculty, Drs. G. Hammond and S. Thorne, joined 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 FY2016 plan. To this end, we hope that a new mid-career faculty will join the Department in the FY2016. 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 2016 has been approved and is appended at the end of this analysis.



**Strengths**

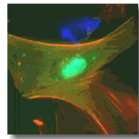
*Research*

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 Journal of Cell Biology (Yang Hong’s group), eLife (Linton Traub’s group), Journal of Neuroscience (Alexander Sorkin’s group) and Nature Communications (Yong Wan’s group). 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 maintains active, funded research programs. We have been moderately successful in obtaining extramural research funding in the past cycle, as evidenced by the renewal of the P30 grant (Watkins), the competitive renewal of NIH and NSF grants (Frizzell, Murray). Two senior faculty, Drs. Sorkin, and Watkins, have multiple NIH grants. Submission of new grant applications remains to be at a high rate which ensures relative fiscal stability of the Department.

The new recruit, Dr. Gerald Hammond, joined the Department in February, 2015. His research is focused on elucidating the mechanisms of phosphoinositide lipid regulation. Two Centers associated with the Department represent particular strengths of the Department and the School of medicine. 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, Drs. Watkins and Stolz were awarded multiple NIH shared instrumentation grants including two confocal microscopes which are essential to the continued growth of the CBI and departmental infrastructure. Dr. Yates, Director of the Biomedical Mass Spectrometry Center, SOM and UP, is currently building an infrastructure of a new facility to study metabolomics.

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 also participated 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 various 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 participate 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 6 students in the graduate Ph.D. program in Cell Biology and Molecular Physiology. One student graduated in 2014, taking position as a postdoctoral fellow. 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 all these tasks were successfully accomplished in a timely and efficient manner attests to the experience and strength of our administrative staff.

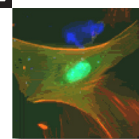
**Weaknesses**

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. This space will be temporarily rented to another department. Hopefully, more space will be required to allow for growth of the research programs of the current faculty located at BST South. Several of the CBP faculty members operate on different campuses. Dr. Frizzell's laboratory is located in the Children's Hospital in Lawrenceville, and Drs. Thorne, Wan and Leuba are in the Hillman Cancer Center. There is clear separation from the rest of the Department leading to a lesser engagement of these three laboratories in the main activities of the Department.

**Opportunities**

The vision of the 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 new dynamic and creative faculty. We plan to continue recruiting faculty whose research programs focus on fundamental questions of cell biology, and in particular, who is using state-of-the-art mass-spectrometry methodologies. 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.

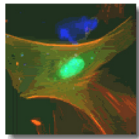
Cohesiveness of the faculty research expertise in the Department creates exceptional opportunities for collaborative research, which should open doors to building new program projects and centers. The Department is now in the position to lead the assembly of new interdisciplinary research programs that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



**Threats**

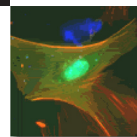
The steady decrease in federal and private funding opportunities will continue to be the most significant threat during next several years. Several faculty are currently struggling with obtaining funding for their research programs. Yet, in order for the Department to become one of the elite cell biology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

Another difficult challenge we face is to strengthen 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.



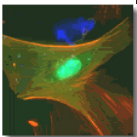
**Cell Biology FY2016 Fiscal Issues**

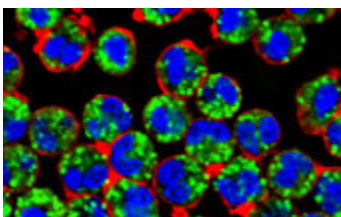
The main budgetary issue that faced the Department in the FY15 budget was maintaining the extramural funding of the faculty at the level necessary to support their research program and as required by the SOM Policies. Our goal is to maintain the funding level of previous years; however, all efforts must 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 2016 Budget**

	University	UPP and Other	Total Budget FY 2016
<b><u>Revenue</u></b>			
Patient Care	\$ -	\$ -	\$ -
Grant:			
Directs	3,313,199	-	3,313,199
Indirects	1,274,880	-	1,274,880
Hospital Contract	-	-	-
School of Medicine	3,430,578		3,430,578
VAMC		-	-
Other	395,134	-	395,134
<b>Total Revenue</b>	<b>\$ 8,413,791</b>	<b>\$ -</b>	<b>\$ 8,413,791</b>
<b><u>Expenses</u></b>			
Salaries and Fringe Benefits:			
Faculty	\$ 2,543,717	\$ -	\$ 2,543,717
Non-Faculty	2,006,833	-	2,006,833
Malpractice Insurance		-	-
Space Rental	60,443	-	60,443
UPP Overhead		-	-
University Overhead	2,401,465		2,401,465
Other Operating Expenses	1,401,333	-	1,401,333
<b>Total Operating Expenses</b>	<b>\$ 8,413,791</b>	<b>\$ -</b>	<b>\$ 8,413,791</b>
<b>Excess Revenue over Expenses</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ -</b>
<b>Capital Equipment/Improvements</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ -</b>
<b><u>Fund Balances</u></b>			
University Restricted Accounts as of 6/30/15	\$ 4,603,150	\$ -	\$ 4,603,150
University Endowments as of 6/30/15	371,192		371,192
UPP Fund Balance as of 6/30/15		-	-
UPMC Endowments as of 6/30/15		-	-
UPMC SPF Accounts as of 6/30/15		-	-
<b>Total Fund Balances</b>	<b>\$ 4,974,342</b>	<b>\$ -</b>	<b>\$ 4,974,342</b>





Thank you for your kind attention.

