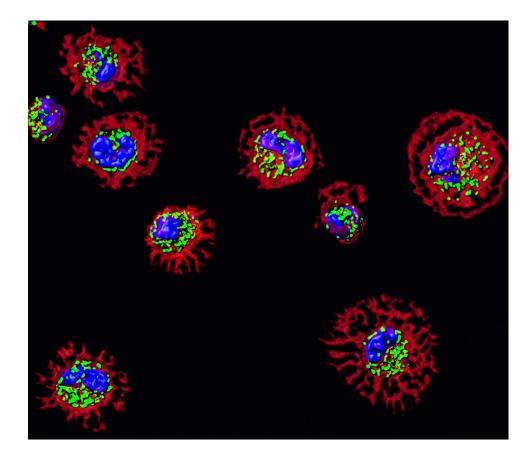
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE

CELL BIOLOGY



FY17 ANNUAL REPORT AND FY18 BUSINESS PLAN

Front Page

Cover figure by Dr. Claudette St. Croix. Surface rendered 3D reconstruction of the mitochondrial network in alveolar macrophages. Mitochondria (green), actin (red) and nuclei (blue). This is from work we published last year with Anuradha Ray (PACCM) (Khare A, Raundhal M, Chakraborty K, Das S, Corey C, Kamga CK, Quesnelle K, **St Croix C, Watkins SC**, Morse C, Oriss TB, Huff R, Hannum R, Ray P, Shiva S, Ray A. Mitochondrial H2O2 in Lung Antigen-Presenting Cells Blocks NF-κB Activation to Prevent Unwarranted Immune Activation. Cell Rep. 2016 May 24;15(8):1700-14. doi: 10.1016/j.celrep.2016.04.060. Epub 2016 May 12. PubMed PMID: 27184852; PubMed Central PMCID: PMC4880515.

Table of Contents of Cell Biology Annual Report Cell Biology General Program Description General Program Description 4 **Research Activities** Research Foci of Department 6 Centers of the Department 8 Faculty Data 10 CB Organizational Chart 11 **CB** Seminar Series 12 **Research and Other Scholarly Activities** Faculty Research Summaries 14 Faculty Study Sections 29 Faculty Advisory Committee Memberships 31 Faculty Sponsored Research Grants 35 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 52 **Teaching Activities** Cell Biology and Molecular Physiology Graduate Program 53 New CBMP Courses and CBMP Course Descriptions 55 **CB** Faculty Teaching Honors 60 **Faculty Teaching Activities** 61 Post Doctoral Personnel and Activities 65 **CBMP** Graduate Program Students 66 CBMP Students Graduated in 2017 67 **Teaching Ratings** 68 **Faculty Data** Current Cell Biology Faculty 69 New Cell Biology Faculty 70 Faculty Honors, Recognition and Professional Affiliations 71 **Faculty Presentations** 75 **Faculty Publications (2015-2017)** Peer Reviewed Publications 78 **Business Plan Executive Summary** 104 Initiatives and Implementation Strategies (SWOT Analysis) 105 Fiscal Issues 108 Budget 109p



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 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 nineteen primary faculty, eighteen 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 and direct (Dr. Hong) 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 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. Claudette St. Croix

Dr. St. Croix's independent research program utilizes a combination of advanced optical imaging technologies to dissect molecular signaling pathways controlling vascular function in rodent and zebrafish model systems of disease. An important facet of this work is the in vivo application of novel fluorescent molecular reporters to study the biology of reactive oxygen and nitrogen species (ROS and RNS, respectively). These approaches are central to my multi-PI efforts with Drs.



Marcel Bruchez and Alan Waggoner from Carnegie Mellon University. In addition, Dr. St. Croix expertise in the application of novel fluorescence-based probes and advanced in vivo imaging technologies have led to her appointment as an associate director of the Center of Biologic Imaging (CBI) at the University of Pittsburgh and invitations to present her work internationally and to take lead roles in well-respected courses such as Quantitative Fluorescence Microscopy (Mount Desert Island Biology Laboratory). In her leadership role at the CBI, Dr. St. Croix has well-established, active and productive collaborations with NIH funded investigators to study ROS based signaling, cell survival, and mitochondrial dynamics in living cells, tissue and animal models using an array of advanced, fluorescence based, optical imaging modalities. This is evidenced by her role as co-Investigator on federally funded projects, and as co-author on peerreviewed manuscripts, including a recent Cell paper.

Several images of the data from Dr. St. Croix research 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. The Department's major faculty groupings and research foci are summarized below.

Membrane trafficking and organelle biogenesis

Aridor Butterworth Devor Ford 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 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 Shi Stoltz St. Croix 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 all types of cellular junctions, mitochondria, nucleus, angiogenesis and vasculogenesis, and various routes of functional communication between dendritic cells.

Regulation of intracellular signaling and gene expression

Drain Hammond Leuba Sorkin St. Croix Thorne

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, ROS signaling and the mechanisms underlying virus replication. The particular focus is on the events leading to dysregylation of cellular signaling networks leading in the disease such as cancer.

Mass-spectrometry and proteomics

Shi Yates

These laboratories are focused on developing new methodologies of quantitative massspectrometric analyses of proteins including new approaches to data acquisition, analysis and storage.



Center for Biologic Imaging

Over the last several years, microscopy as a scientific tool has reinvented itself. It has changed from a group of principally descriptive methodologies, to a wide range of



Center for Biologic Imaging Imaging is Everything

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), 25 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. 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, STED) electron microscopes and multiphoton microscope through the NCRR. Furthermore, the Facility has supplemented its existing microscope and computer base with 2 new live cell imaging systems with microinjection capabilities. Currently the facility has 23 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 1.7 petabytes at 10 gigabit speed

Our current research themes are three fold. Very fast massive sample confocal imaging, Correlative Light and Electron Microscopy and probe development and application for reactive oxygen species imaging.

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



Distinguished Professor in the Department of Cell Biology and Professor of Immunology within the School of Medicine. His experience in microscopic methods covers most of the present light and electron microscopic methodologies.

The Associate Directors:

Dr. Donna Beer-Stolz is an Associate Professor in Cell Biology. Her funded research interests are in liver regeneration and vasculogenesis. 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.

Dr. Claudette St. Croix is an Associate Professor in Cell Biology. Dr. St. Croix's funded research interests focus primarily on the pulmonary system and vascular biology. She is also heavily involved in the living system (both animal and cell) components of the Center.

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 chargeback users, processing Center for Biologic Imaging purchase requisitions and other general administrative duties.





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Cell Biology Faculty Data [Current as of June, 2017]

Butterworth, Michael Kwiatkowski, Adam St. Croix, Claudette Hammond, Gerald Watkins, Simon C. Stolz, Donna Beer Sorkin, Alexander Thorne, Stephen Murray, Sandra Leuba, Sanford Duker, Georgia Traub, Linton Yates, Nathan Devor, Daniel Ford, Natalia Aridor, Meir Ford, Marijn Hong, Yang Drain, Peter Wan, Yong Shi, Yi Name

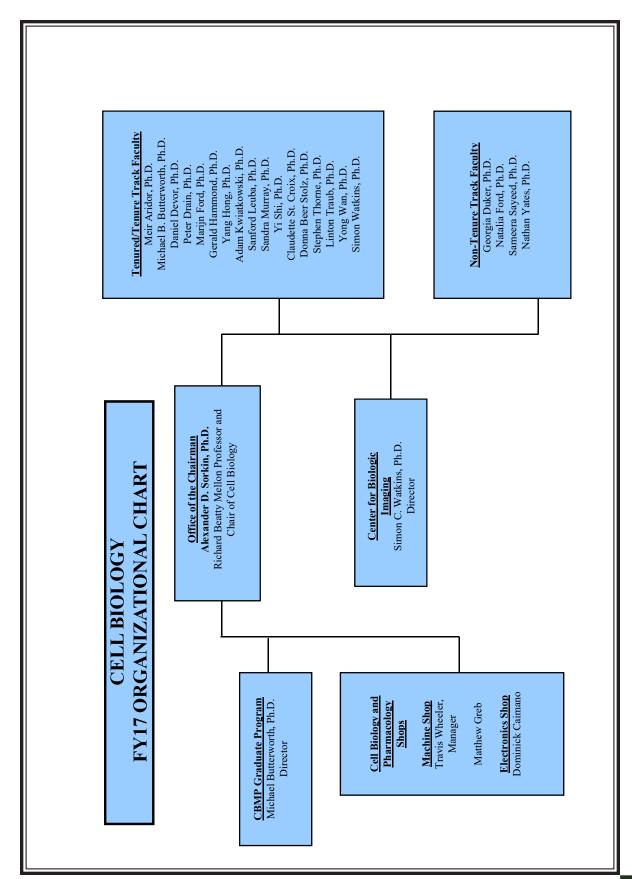
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Cell Biology Seminar Series Schedule 2016-2017

September 30, 2016 Suzanne Pfeffer, PhD Professor, Department of Biochemistry Stanford University "Structural surprises for vesicle tethering and cholesterol transport"

October 25, 2016 Alexandra Ainsztein, PhD Program Director, Division of Cell Biology & Biophysics NIH - NIGMS "Navigating the NIH and Peer Review Process"

<u>November 15, 2016</u> Umamaheswar Duvvuri, MD, PhD Associate Professor, Otolaryngology University of Pittsburgh Medical Center "Chloride Channels and Cancer – Please Pass the Salt"

<u>November 21, 2016</u> Marco Sardiello, PhD Assistant Professor, Molecular& Human Genetics Baylor College of Medicine "Clearage of Storage Material in Lysosomal Storage Disorders"

November 29, 2016 John York, PhD Professor & Chair, Biochemistry Vanderbilt University "Inositol Phosphates Act as Structural Cofactors to Regulate Biological Processes"

March 21, 2017 Roberto Botelho, PhD Associate Professor, Chemistry & Biology Ryerson University, Toronto "Having fun with lysosomes and phagosomes: how to adapt, expand and engorge them"

<u>March 28, 2017</u> Jianping Jin, PhD Associate Professor, Biochemistry and Molecular Biology University of Texas, Health Science Center of Houston "Control Cytokine-induced inflammation Responses by Ubiquitin and Ubiquitin-like Proteins"

<u>April 4, 2017</u> Brenton Hoffman, PhD Assistant Professor, Biomedical Engineering



Duke University "Visualizing Molecular Forces Across Specific Proteins in Living Cells"

<u>April 18, 2017</u> Adam Kwiatkowski, PhD Assistant Professor, Department of Cell Biology University of Pittsburgh "The actin connection: building adhesion complexes through alpha-catenin"

<u>April 25, 2017</u> Marijn Ford, PhD Assistant Professor, Department of Cell Biology University of Pittsburgh "A Structural characterization of Vps1"

May 2, 2017 Junying Yuan, PhD Professor, Cell Biology Harvard Medical School "RIPK1 and necroptosis: from basic cell biology to human clinical trials"

<u>May 9, 2017</u> Michael Butterworth, PhD Assistant Professor, Department of Cell Biology University of Pittsburgh "Regulation of renal transporters by non-coding RNAs"



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?

Michael B. Butterworth, Ph.D.

Assistant Professor

Dr. Butterworth's research interest is in the regulation of epithelial channels by vesicle trafficking and recycling. Research is focused into two broad areas. First, ongoing studies aim to characterize the mechanisms that underlie channel regulation by membrane trafficking in the mammalian kidney. Three renal transporters, namely the epithelial sodium channel (ENaC), potassium channel (ROMK) and aquaporin water channels are investigated. The work aims to map the intracellular itinerary of these channels and identify protein mediators that regulate channel surface density. In separate, but related studies, primary human bronchiolar epithelial cells are used to characterize ENaC regulation in the human distal airway, in particular mechanisms which may contribute to disease states like cystic fibrosis. By comparing ENaC regulation in two distinct systems, areas of common and divergent regulation have been established. The second research focus investigates the regulation of ENaC by microRNAs (miRNA). miRNAs are small RNAs that pair to the mRNA of protein coding genes to direct their post-transcriptional repression. Channel density in epithelial cells is determined to a large extent by steroid hormone signaling. The regulation of miRNAs by these hormones and impact of changes in miRNA expression on channel regulation is being studied.

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

Intermediate (KCa3.1 or IK) and small (KCa2.3 or SK3) conductance, calcium-activated potassium channels play critical roles in a host of physiological processes, including the endothelial derived hyperpolarizing factor (EDHF) response which is critical to the maintenance of vascular tone and hence blood pressure regulation, the maintenance of a hyperpolarized membrane potential across



the basolateral membrane of polarized epithelia required for transepithelial fluid secretion as well as being intimately involved in the afterhyperpolarization in nerves and a host of other processes. Thus, an understanding of the physiological and pharmacological regulation of these channels as well as their assembly, trafficking and gating is crucial to the development of novel therapies based on targeting these channels. The long-term goals of my lab are to obtain a detailed molecular understanding of these channels in order to unravel the mechanisms involved in their assembly, trafficking, regulation and gating as well as to define the physiological role these channels play using *C. elegans* as a model system. In light of these goals, we have several ongoing projects designed to further our understanding of these channels.

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

Second, as any physiological response is dictated by not only the likelihood that channels are in the open state (P₁), 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.



Cell Biology 4nnual Report

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

Given that KCa3.1 is targeted to the basolateral membrane in polarized epithelia, where it plays a critical role in the generation of the electromotive driving force required for Ca²⁺-dependent agonists to stimulate Cl⁻ and fluid secretion, an additional project, being undertaken in collaboration with Dr. Kirk Hamilton at the University of Otago in Dunedin, NZ, is designed to understand the mechanisms by which this channel is correctly targeted and endocytosed in various model systems, including FRT, MDCK and LLC-PK1 cells. In this regard, we have found that KCa3.1 is correctly targeted in each of these cell lines and that, similar to our studies on HEK cells and a microvascular endothelial cell line (HMEC-1), the channel is rapidly endocytosed. Further, we have generated chimeras between the C-terminal tail of KCa3.1 and the nerve growth factor receptor (NGFR, p75) and demonstrate that the C-terminus of KCa3.1 can redirect NGFR from its typical apical localization to the basolateral membrane in polarized epithelia. Future studies will be designed to elucidate the molecular motifs involved in the correct 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 GFPand RFP-tagged channels to determine both an expression pattern profile as well as to determine the effect of overexpression of this gene product on physiological function. Our data demonstrate that the C. elegans SK channel is expressed in both the gut as well as in numerous nerves, including the nerve ring, ventral nerve chord and ganglia in the tail. Future studies will elucidate the role of this SK channel in this model physiological system. Cavita has also begun to culture cells from her transgenic line which will allow us to define cells expressing the transgene and characterize these C. elegans channels by patch-clamping. We can then determine whether mutations at conserved amino acids to those identified by us in mammalian channels will produce similar phenotypes, including increased Ca^{2+} sensitivity; allowing us to evaluate the effect of a hyperactive phenotype on function at the level of an intact organism. Finally, we can utilize known endocytic/recycling phenotypes in *C. elegans* to probe the regulation of the number of channels (N) in a model system and determine how perturbations in N alter physiological function. These studies will tie together our efforts on heterologously expressed channels to our proposed studies on channels within the microvasculature; providing us with a clear picture of how KCa2.3 and KCa3.1 are regulated at the plasma membrane. Given the role of these channels in multiple disease processes, an understanding of how the number of channels is regulated at the plasma membrane is critical to understanding how these channels can be manipulated for therapeutic gain.

Peter F. Drain, Ph.D.

Associate Professor

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

(1) We are continuing our ongoing investigations into the structure-mechanism relations underlying the ATP-inhibited potassium (KATP) channel response to physiologically important ligands, ATP, ADP, and anti-diabetic sulfonylureas. In pancreatic beta cells, the KATP channel brings insulin secretion under the control of blood glucose levels. Our major goal is to establish the cellular mechanisms underlying how interactions of the KATP channel with its small molecular ligands and with its protein binding partners changes with high and low glucose metabolism, and consequent changes in insulin granule transport and exocytosis. Normally, the fraction of time the KATP channel spends in the inhibited state determines insulin secretory rates. When this regulation goes awry, serious complications at the whole-organism level lead to diabetes and other diseases. The research has fundamental importance to pharmaco-genetics, in which certain diabetic subjects with certain mutations can be transferred from insulin replacement therapy injected multiple times a day to an oral sulfonyluea pill once a day.

(2) Another key molecule in insulin secretion is insulin itself. Mutations in human proinsulin,

the propeptide precursor to insulin, have been shown to cause clinical diabetes. In studying the associated cellular mechanisms underlying insulin biogenesis, trafficking, and secretion, we have combined confocal fluorescence microscopy and a novel molecular strategy to visualize insulin secretion in live cells. The Ins-C-GFP reporter has exploded our ability to look inside live insulin-secreting cells to study glucose-stimulated insulin biogenesis, vesicle transport and exocytosis. Using this approach, we have localized KATP channels to the beta cell's large dense core vesicle (LDCV) where we have shown they mediate ATP- and glibenclamide-stimulated insulin, 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 medical students through the renal, gastrointestinal, pulmonary, endocrine, musculoskeletal, reproductive and nervous systems. The Normal Histology image collection for the entire body is available to students on the Navigator site. In 203, 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 2017, 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 (1995-2017). This course is taken by the majority of our students. It is abroad survey of all the organ systems, focusing on structure/function at the cellular, tissue and organ levels, with multiple clinical and pathological 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 Assistants for the Histology labs within seven Medical School courses. One of my roles is coordinator of the Teaching Assistants, 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, 2002-2017. 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 has two broad objectives: to understanding the molecular mechanism of membrane remodeling by members of the Dynamin-Related Protein (DRP) family, and to study the signaling pathways yeast use to respond to stress, particularly starvation stress.

The mechanism of membrane remodeling by the DRP family

DRPs are believed to remodel membranes by self-assembly into helices that concomitantly remodel the underlying membrane. We are interested in how this self-assembly is coupled to membrane deformation and also in exploring the biology of some of the pathways where DRP function is required. To this end, we have been focusing on a poorly characterized fungal-specific DRP known as Vps1, that was initially identified in a screen for yeast mutants defective in sorting of carboxypeptidase Y to the vacuole. We chose Vps1 for two reasons: first, it is a better model for a typical DRP than dynamin and second, as it is a fungal protein, we could leverage the genetic and imaging tractability of *Saccharomyces cerevisiae* for our studies.

Structural Studies:

Using crystallographic approaches, we have obtained insight into Vps1 assembly and helix formation by solving two novel structures of the GTPase domain of Vps1, the first in complex with GDP and the second in complex with the non-hydrolyzable GTP analog GMPPCP. Strikingly, the structure of the GDP-bound GTPase forms a dimer interface of 2,722 Å² with the GDP "trapped" in a deep pocket between the dimer partners. The switch I and II regions of the GTPase domains are unusually well ordered for a GDP-bound GTPase, due to partial stabilization by a loop contacting the GDP *in trans* from the dimerization partner. The structure bound to GMPPCP includes the full "Bundle Signaling Element" in an extended conformation. Comparison of the two structures has revealed new insight into the regulation of helix assembly by members of this family.

We have also determined the structure of a helical assembly of full-length Vps1 by cryo-electron microscopy, in collaboration with Frances Alvarez in the Zhang lab. The key enabling advance in this work was the ability to express and purify full length Vps1 for the first time. Extensive biochemical characterization resulted in optimized samples for cryo-preparation and data



collection. The structure of the Vps1 helix, determined to \sim 13 Å resolution, demonstrates a novel lateral interface between the GTPase domains in the assembled helix that may regulate the kinetics of helix assembly and disassembly and consequently its function in the cell.

Cell Biology:

We have identified a novel function for Vps1 in autophagic processes as well as other stress response pathways. In all these cases, Vps1 concentrates into puncta (presumably assembling) at sites of close endosomal/vacuolar juxtaposition that are the site of membrane remodeling in various vacuolar uptake processes, including microautophagy and piecemeal microautophagy of the nucleus. We demonstrated that Ivy1, a marker for microautophagic invaginations, and Vps1 segregate during the autophagic process. We have made extensive use of the imaging facilities in the Center for Biologic Imaging for this work.

Yeast Stress Response Pathways:

TORC1 is a multiprotein complex that couples external cues such as nutrients and other environmental stimuli to the pathways regulating cell growth. TORC1 deregulation is associated with variety of human cancers and metabolic disorders and has consequently been the object of intense study. In yeast, the amino acid availability signal is relayed to TORC1 via the conserved Rag GTPases Gtr1 and Gtr2, both components of the vacuolar-membrane-associated EGO complex (EGOC).

Cell Biology:

While studying the function of Vps1 in microautophagy, we identified the largely uncharacterized yeast protein Pib2 as an additional regulator of microautophagy and TORC1 signaling. Pib2 has a role in lysosomal membrane permeabilization and has two human homologues Phafin 1 and Phafin 2. Our work has demonstrated that Pib2, like the yeast EGO Complex, is required for TORC1 reactivation after exposure to the TORC1 inhibitor rapamycin.

Deletion of Pib2 phenocopies deletion of components of the EGO Complex in several assays: vacuolar morphology, TORC1 localization and activity, rapamycin sensitivity and inability to respond to amino acid supplementation after starvation.

The \Box Pib2 phenotype can be rescued by active form of TOR1, but not by the constitutively active forms of GTRs. Pib2 is required for EGO Complex-mediated activation of TORC1 by glutamine and leucine as well as for redistribution of Tor1 on the vacuolar membrane.

High-throughput Genetics:

A synthetic dose lethality screen, where Pib2 is overexpressed in each individual knockout in the yeast deletion collection, demonstrated strong genetic interactions with components of the EGO Complex, TORC1 and downstream components of the Protein Phosphatase 2A branch of TORC1 signaling.

Together, we show that Pib2 and EGO Complex are reciprocally required for TORC1 activation and function within the same molecular pathway. Our observations therefore demonstrate that Pib2 is a novel relay in the cell's signaling pathway from amino acid perception to a TORC1 signaling response post-starvation.



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:

<u>1) Control of plasma membrane targeting of polarity proteins:</u> 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 knockin 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 primary focus of work in the Kwiatkowski Lab is to gain a mechanistic understanding of cardiomyocyte adhesion and cytoskeletal organization. Our approach is to use to a combination of protein biochemistry, cell biology and microscopy to define mechanisms of cell-cell adhesion, and downstream regulation of actin and intermediate filament organization, by the cadherin-catenin adhesion complex. Our rationale is that understanding the molecular mechanisms of adherens junction adhesion in cardiomyocytes will provide fundamental insight into cardiomyocyte cell-cell adhesion and adherens junction biology.

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



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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 posttranslational 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).

Yi Shi, Ph.D.

Assistant Professor

The extraordinarily emergent properties of living cells have evolved largely as a consequence of the intricately ordered interactions of their biomolecular components. These cellular building blocks interact with each other to form a hierarchy of dynamic macromolecular assemblies that drive a plethora of important biological processes. Unfortunately, despite their central role in cell biology, many protein complexes identified to date remain refractory to structure-functional characterization.

We are interested in the development of integrative proteomic technologies to elucidate the structure and function of large, native protein complexes. We are interested in developing new proteomic tools to investigate the spatiotemporal regulations of mitochondria, as well as their roles in aging and neurodegenerative diseases.



Alexander D. Sorkin, Ph.D. *Professor, Chair 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 of the plasma membrane dopamine transporter (DAT) in the regulation of dopaminergic neurotransmission. In both these research areas we are using multidisciplinary methodological approach in *in vitro* and novel *in vivo* experimental models. Finally, we have recently engaged in a new collaborative project aimed at elucidating the mechanisms by which placenta-derived exosomes are internalized by target cells.

Claudette St. Croix, Ph.D.

Associate Professor Assistant Director of Center for Biologic Imaging

My independent research program utilizes a combination of advanced optical imaging technologies to dissect molecular signaling pathways controlling vascular function in rodent and zebrafish model systems of disease. An important facet of this work is the *in vivo* application of novel fluorescent molecular reporters to study the biology of reactive oxygen and nitrogen species (ROS and RNS, respectively). These approaches are central to my multi-PI efforts with Drs. Marcel Bruchez and Alan Waggoner from Carnegie Mellon University. In addition, my expertise in the application of novel fluorescence-based probes and advanced in vivo imaging technologies have led to my appointment as an associate director of the Center of Biologic Imaging (CBI) at the University of Pittsburgh and invitations to present my work internationally and to take lead roles in well-respected courses such as Quantitative Fluorescence Microscopy (Mount Desert Island Biology Laboratory). In my leadership role at the CBI, I have well-established, active and productive collaborations with NIH funded investigators to study ROS based signaling, cell survival, and mitochondrial dynamics in living cells, tissue and animal models using an array of advanced, fluorescence based, optical imaging modalities. This is evidenced by my role as co-Investigator on federally funded projects, and as co-author on peer-reviewed manuscripts, including a recent Cell paper.

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 coordinates 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.

Stephen Thorne, Ph.D.

Assistant Professor

It was first reported that viral infections, on occasion, result in tumor regressions over 100 years ago. This was further advanced 20 years ago with the development of viral vectors engineered to display tumor-selectivity in their replication (oncolytic viruses).

Although clinical responses were reported, it has become clear that directly lytic viral replication alone is rarely sufficient to eradicate large tumors or metastatic disease. However, in the last several years, the combination of faster replicating vectors and the expression of immuneactivating transgenes from the viruses themselves have resulted in improved clinical responses. This resulted in the first in class approval of the oncolytic virus IMLYGIC for the treatment of metastatic melanoma earlier this year and has led to extensive interest in the field.

Our interest has primarily focused on the pre-clinical and translational development of enhanced, next generation oncolytic virus vectors based on vaccinia virus. This has focused on several key areas that were determined to be of special interest;

We felt that the immune response raised against the virus in the tumor can play a critical role in the successful application of this platform. Tumor-selective viral replication leads to localized acute inflammation, helps direct the immune response towards the tumor and transiently overcomes tumor-mediated immunosuppression. Meanwhile, lysis of tumor cells releases relevant tumor antigens and associated danger molecules, resulting in priming of anti-tumor immunity and in situ vaccination. Previously this immunotherapeutic activity has relied on the viral vector's naturally evolved interactions with the host immune response, often boosted by the expression of a single cytokine transgene. We have successfully implemented a variety of strategies to enhance the immune interactions, including altering Toll Like Receptor signaling pathways, targeting of



immunosuppressive cells within the tumor, selectively activating anti-tumor CTL responses and altering trafficking patterns to direct activated immune cells into the tumor.

In addition, the limited ability to deliver oncolytic viral vectors intravenously to tumors in the clinic, especially in the face of anti-viral immunity, has seriously hampered the field. We have examined a variety of novel approaches to enhance this delivery, including altering the viral surface envelope, creating synthetic membranes to envelop the virus and delivering the virus within immune cell therapies.

Through combining these approaches, we are looking to develop novel therapies that can be produced at clinical grade for early Phase I clinical trials.

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 synapticvesicle membrane results in both morphological disruption of the nerve terminal and defective neurotransmission. Clathrin-coated vesicles also play an important role in controlling plasma LDL-cholesetrol levels in humans and yolk protein accumulation in Drosophila and mosquitoes by promoting the rapid internalization of a family of related lipoprotein receptors. We study the mechanisms and molecules involved in clathrin-coat assembly. We are interested how this complex process, involving a network of more than 25 discrete protein components, is temporally coordinated to prevent chaotic seizures or run-away coat assembly. We have found recently that some of these protein components display unexpected cargo sorting properties that expand the overall sorting repertoire of the forming clathrin-coated vesicle. To understand how these complex structures, assemble within only a minute or two, we use biochemical, cell biological, structural and live-cell imaging approaches to unravel the protein-protein interactions that orchestrate the formation of this elaborate protein-sorting machine.

Yong Wan, Ph.D.

Professor

Posttranslational modifications such as ubiugitylation, 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 2016-2017)

Adam Kwiatkowski, Ph.D. Assistant Professor

Ad hoc member, NIH Intercellular Interactions (ICI) Study Section

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

ASIRC - Italian Association for Cancer Research; Standing Member Breast Cancer Now / UK (mail) 2016 Springboard UK/Ireland (mail) 2016

Claudette St. Croix, Ph.D. Associate Professor

American Heart Association, Molecular Signaling 3 Study Section, Co-chair NIH/EBIT-A (90), Panel Member NIH CMT Standing Panel - Cellular and Molecular Technologies 2018/01

Donna B. Stolz, Ph.D. Associate Professor

ZDK1-GRB-8 J1 review of NIH NIDDK P01 grants, 4 meeting grants NIDDK P01 review. I grant, phone meeting. NIDDK Training Grant Special Emphasis Panel, Member

Linton Traub, Ph.D. Associate Professor

Ad hoc member of NIH ZRG, CSF and NRSA Study Sections

Yong Wan, Ph.D. *Professor*

Molecular Oncogenesis Study Section (MONC), NIH, Standing member (2013-2019)



Simon C. Watkins, Ph.D.

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

Canadian Foundation for Innovation Chair of Panel, July 6th -8th 2016 NIH review P41, New York Structural Biology Research Center Chair of Panel, October 26th-29th 2016 ACS Study Section (Peer Review Committee on Clinical Cancer Research and Epidemiology), Chair of Panel, Atlanta, GA, January 25st-27th 2017 NIH Common Fund's 4D Nucleome (4DN) program; Reviewer March 16th 2017 CFI Mac Grant Review Chair of Panel Ottawa CA April 5th-7th NIH Common Fund's 4D Nucleome (4DN) program Phase 2 reviewer April 8th 2017 ACS Study Section (Peer Review Committee on Clinical Cancer Research and Epidemiology), Chair of Panel, Atlanta, GA, June 29th-30th 2017 Dutch Research Council (NWO) National imaging resource, August 13th 2017 Reviewer

Cell Biology/Pharmacology Machine Shop





Faculty Advisory Committee Memberships (Fiscal Year 2016-2017)

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 Faculty Recruitment Committee Integrated Systems Biology (ISB) Admission's Committee

Michael Butterworth, Ph.D.

Assistant Professor

Cell Biology Space Committee Integrated Systems Biology (ISB) Program Committee Integrated Systems Biology (ISB) Course Director, Core Course (Imaging) Cell Biology and Molecular Physiology Graduate Program, Director

Daniel Devor, Ph.D. *Professor*

Cell Biology Departmental Tenure and Promotions Committee Chair, Interdisciplinary Biomedical Graduate Program Recruitment 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 Biomedical Masters Program Committee UPSOM Curriculum Committee

Georgia K. Duker, Ph.D. Assistant Professor

Honor Council Hearing Board - School of Medicine

Marijn Ford, Ph.D. Assistant Professor

Organizer – Cell Biology Department Retreat Cell Biology Space Committee



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Yi Shi, Ph.D. Assistant Professor Organizer - Cell Biology Department Retreat 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 Integrated Systems Biology Executive Committee **Biomedical Science Program Executive Committee** Claudette St. Croix, Ph.D. Associate Professor Cell Biology Faculty Recruitment Committee Graduate Student Mentoring Committee, EOH, Graduate School of Public Health Director of Student Recruitment and Admissions, EOH, Graduate School of Public Health Donna Beer Stolz, Ph.D. Associate Professor University of Pittsburgh School of Medicine Interdisciplinary Biomedical Graduate Program- Cell Biology and Molecular Physiology Program Admissions Committee Assistant Director - Cell Biology and Molecular Physiology Program Stephen Thorne, Ph.D. Assistant Professor University of Pittsburgh and University of Pittsburgh Cancer Institute, UPCI; Director, Small Animal Imaging Core, UPCI Leader, Viral Vector and Gene Delivery Section, Molecular Virology Program at UPCI

Steering Committee, UPCI Flow Cytometry Facility



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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
Yong Wan, Ph.D. Professor
Cell Biology Tenure and Promotions Committee Cell Biology Departmental Tenure and Promotions 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 Chair UPCI Luminex advisory committee Chair UPCI Proteomics advisory committee Chair UPCI flow cytometry advisory committee UPCI chemical biology advisory committee



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worth worth worth worth	Title aith Combing STAT3-Silencing and Oncolytic Vaccinia Virus to Enhance Anti-tumor Therapeutic Activity alth combing STAT3-Silencing and Oncolytic Vaccinia Virus to Enhance Anti-tumor Therapeutic Activity Role of MicroRNAs in kidney sodium regulation understanding Multiple Hormone Secretion Deficits in Prader-Willi Syndrome alth Understanding Multiple Hormone Secretion Deficits in Prader-Willi Syndrome alth The Roles of the Dynamin-Related Protein Vps1 and the ESCRT Complex in Microautophagy alth The Roles of the Dynamin-Related Protein Vps1 and the ESCRT Complex in Microautophagy alth Directing Membrane Function with Inositol Lipids in Health and Disease alth Membrane Targeting and Retargeting of Polarity Proteins Ankyrin G A Regulation of the Epithelial Sodium Channel after Adosterone Stimulation Alpha-Catenin Function in Cardiomyocyte Adhesion and Cytoskeletal Organization cystic Fibrosis Foundation (Betrand) NNRTI Induced Conformational Changes in HIV 1 RT (Sluis-Cremer) alth Novel Mechanisms of HIV Resistance ti RTIS (Sluis-Cremer) Novel Mechanisms of HIV Resistance ti RTIS (Sluis-Cremer) Evolved DNA Contacts Required for Hexameric Helicase Unwinding.	Annual DC A 16818 16818 221324 6188 197500 209890 49125 26000 247439 9727 62411 5734 51570 169553 36384	Annual IDC 119515 91932 113603 25997 0 126193 0 25923 3104 20870 88859
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Sanford Leuba National Institutes of Health		51570 169553 36384	20870 88859
Sanford Leuba National Institutes of Health		169553 36384	88859
Sandra Murray National Science Foundation	lation Regulation of annular gap junctionp rocessing	36384	
Chelsea Merkel National Institutes of Health	salth The Role of Vinculin in Cardiomyocyte Adhesion and Mechanical Continuity		0
Alexander Sorkin National Institutes of Health	salth Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	214656	94683
Alexander Sorkin National Institutes of Health	salth Supplement -Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	3924	2173
Alexander Sorkin US Dept of Veterans Affairs	fairs Investigating the Role of TMEM16A/AN01 in SCCHN	16578	0
Alexander Sorkin National Institutes of Health	ealth Exosome Based Placental Maternal Communication	25193	13819
Claudette St. Croix National Institutes of Health	salth Cardiolipin as a Novel Mediator of Acute Lung Injury	7970	4304
Claudette St. Croix National Institutes of Health	alth Aging of Mesenchymal Stem cells Missing Link in IPF	3024	1633
Claudette St. Croix National Institutes of Health	alth Implications and Stability of Clinical and Molecular Phenotypes of Severe asthma	5051	2601
Claudette St. Croix National Institutes of Health	alth Pathogenic Mechanisms of Gene-Environment Interactions in Parkinsons Disease	4058	2211
Claudette St. Croix National Institutes of Health	alth Core C: Cell Autonomous and Non-Autonomous mechanisms of Aging	41214	22379
Claudette St. Croix National Institutes of Health	alth ROS Mechanisms in BAV Aortopathy	3193	1644
Claudette St. Croix National Institutes of Health	alth Signaling Mechanisms by which Mitochondria Regulates Fibrosis in the Lung	2893	1562
Claudette St. Croix National Institutes of Health	salth Vascular Smooth Muscle and Blood Pressure Regulation By cyb5R2	7427	4027
Claudette St. Croix National Institutes of Health	salth Mesenchymal Stem Cell Secretome inLung Fibrosis: Mitochodria and RNA shuttle	27009	14585
Claudette St. Croix National Institutes of Health	salth Reactive Oxygen Species in Vascular Disease	7674	4144
Claudette St. Croix National Institutes of Health	salth Vascular Subphenotypes of Lung Disease - Preclinical Assesment Core	59205	32107
Claudette St. Croix National Institutes of Health	alth Novel Role of Smooth Muscle B5 Reductase in Sicle Cell Disease	3382	1827
Claudette St. Croix National Institutes of Health	alth Targeted Fluorescent Indicators for Endothelial Physiology	68606	37047



Cell Biology	4nnual Report
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Claudete St. Cock National institutes of Health Avti-Inflammatory Lipid Mediators in Asthma Claudete St. Cock National institutes of Health TSP-1 and RDS: CD47 and SIRP. applan as mediators of Vasalard Dyferditor Claudete St. Cock National institutes of Health TSP-1 and RDS: CD47 and SIRP. applan as mediators of Vasalard Dyferditor Doma Beer Stb2 National institutes of Health TSP-1 and RDS: CD47 and SIRP. applan as mediators of Vasalard Dyferditor Doma Beer Stb2 National institutes of Health TCF A Col and tssue imaging Core Doma Beer Stb2 National institutes of Health Primary Human Microphysical Model of Meatstasis Therapy Doma Beer Stb2 National institutes of Health Primary Human Thronocoperical Model of Meatafrasis and the Transfer of Viral Resistance Doma Beer Stb2 National institutes of Health Mechanisms of Asencin-induced Music Model Actor Regoneration by Stem Cole Doma Beer Stb2 National institutes of Health Mechanisms of Asencin-induced Music Recorders in Bidder Development Doma Beer Stb2 National institutes of Health Mechanisms of Asencin-induced Music Recorders in Bidder Development Doma Beer Stb2 National institutes of Health Mechanisms Provided In Larrin B1 Medied Development Doma Beer Stb2 National instit	equlation of Fuel Utilization by Lysine Acetylation in the Failing Heart	tion in the Failing Heart	2978	1616
National Institutes of Health National Institutes of Health National Science Foundation National Institutes of Health National	nti-Inflammatory Lipid Mediators in Asthma	1	6459	3488
 National Institutes of Health National Science Foundation National Institutes of Health National In	SP-1 and ROS: CD47 and SIRP-alpha as me	diators of Vascular Dysfunction	9376	5387
National Science Foundation National Institutes of Health National	eal Time Visualization and Manipulation of th	e Metastatic, Trajectory of Breast Cancer	1897	1025
National Institutes of Health National Institutes of Health M National Institutes of Health National Institutes of Health Nati	ngineering Research Center		8464	4359
National Institutes of Health National Institutes of Health	ore A Cell and tissue Imaging Core		59850	32463
National Institutes of Health National Institutes of Health	I Human Microphysical Model of Metastasis	herapy	59512	27816
National Institutes of Health National Institutes of Health	imary Human Trophoblasts and the Transfer	of Viral Resistance	6659	3429
National Institutes of Health National Institutes of Health	o-mediated killing of oncogenic stem cells in	chemoprevention	4791	2587
National Institutes of Health National Institutes of Health	echanisms of Arsenic-induced Muscle Morbi	ity and Reduced Regenerative Capacity	12226	6603
National Institutes of Health National Institutes of Health	litric Oxide and Hepatic Function in sepsis al	d Trauma	11517	4924
National Institutes of Health National Institutes of Health Lustgarten Stand Up 2 Cancer National Institutes of Health National Institutes of Health	echanisms of Trabecular Meshwork Regene	ation by stem cell	8330	3586
National Institutes of Health National Institutes of Health Luustgarten Stand Up 2 Cancer National Institutes of Health National Institutes of Health	itical Role for Fibroblast Growth Factor Rec	ptors in Bladder Development	6293	3398
National Institutes of Health National Institutes of Health Lustgarten Stand Up 2 Cancer National Institutes of Health National Institutes of Health	sfunctional Muscle remodeling and regener	tion in environmental disease	19890	10813
National Institutes of Health National Institutes of Health National Institutes of Health National Institutes of Health National Institutes of Health Lustgarten Stand Up 2 Cancer National Institutes of Health National Institutes of Health	ucidting Mechanisms Involved in Lamin B1 I	edited Demyelination	3947	2124
National Institutes of Health National Institutes of Health National Institutes of Health National Institutes of Health Lustgarten Stand Up 2 Cancer National Institutes of Health National Institutes of Health	ndogenous Regulators of Inflammation in Liv	r Ischemia/Reperfusion	12865	4247
National Institutes of Health National Institutes of Health National Institutes of Health Lustgarten Stand Up 2 Cancer National Institutes of Health National Institutes of Health C	uminal Epithelial Junctions, Polarity and Perr	eability in BPH	10801	3550
National Institutes of Health National Institutes of Health Lustgarten Stand Up 2 Cancer National Institutes of Health National Institutes of Health Ci	pha Catenin Function in Cardiomyocyte adh	sion and Cytoskeletal	1989	1074
National Institutes of Health Lustgarten Stand Up 2 Cancer M National Institutes of Health National Institutes of Health C	ombinational Immunotherapy Targeting Mela	ioma-Associated Vasculature	1201	649
Lustgarten N. Stand Up 2 Cancer M National Institutes of Health Vi National Institutes of Health C National Institutes of Health C National Institutes of Health P National Institutes of Health P National Institutes of Health P National Institutes of Health C National Institutes of Health C National Institutes of Health C National Institutes of Health C	eation of Immuno-Oncolytic Viruses for Can	er Therapy	168382	90399
Stand Up 2 Cancer M National Institutes of Health Vi National Institutes of Health Ci National Institutes of Health Ci National Institutes of Health Pi National Institutes of Health Pi National Institutes of Health Pi National Institutes of Health Ci National Institutes of Health Ci National Institutes of Health Ci National Institutes of Health Ci National Institutes of Health Ci	ovel oncolytic vaccinia strans for targeted pa	icreatic cancer therapy	68559	13712
National Institutes of Health Vi National Institutes of Health CI National Institutes of Health CI National Institutes of Health CI National Institutes of Health Pi National Institutes of Health Pi National Institutes of Health CI National Institutes of Health CI National Institutes of Health CI National Institutes of Health CI National Institutes of Health CI	etabolic reprogramming suing oncolytic virus	ss toimprove immunotherapy	25352	2536
National Institutes of Health National Institutes of Health	sualization of in vivo HIV-1 vaginal transmiss	on in the presence and absence of PrEP	23627	10057
National Institutes of Health National Institutes of Health	atherin-coated vesicles and endocytic functi	E	169258	91400
National Institutes of Health National Institutes of Health	ombinatioal Immunotherapy targeting the Ma	onoma	1721	817
National Institutes of Health National Institutes of Health National Institutes of Health National Institutes of Health National Institutes of Health	ombinatioal Immunotherapy targeting the Ma	onoma	19014	9030
National Institutes of Health National Institutes of Health National Institutes of Health National Institutes of Health	ttsburgh Center for Kidney Research		13755	6437
National Institutes of Health National Institutes of Health National Institutes of Health	ttsburgh Center for Kidney Research		1245	583
National Institutes of Health National Institutes of Health	YP 450 Mediated CBF Dysregulation and Ne	urotoxicity in Pediatric Cardiac Arrest	9467	4221
National Institutes of Health	YP 450 Mediated CBF Dysregulation and Ne	urotoxicity in Pediatric Cardiac Arrest	857	382
	ardiolipin as a Novel Mediator of Acute Lung	njury	105256	50908
Simon Watkins National Institutes of Health PQC2 Alteration of 3D nuclear organization at nanoscale in breast tumorigenesis	QC2 Alteration of 3D nuclear organization at	nanoscale in breast tumorigenesis	8087	3067
Simon Watkins National Institutes of Health Mechanisms of Perineural Invasion in Head and Neck Cancer	echanisms of Perineural Invasion in Head ar	d Neck Cancer	10056	5430





Simon Watkins	National Institutes of Health	Mesoscale MR imaging of cellular connectivity in the ex vivo human hippocampus-	2168	811
Simon Watkins	National Institutes of Health	ROS driven mitochondrial-telomere dysfunction during environmental stress-	7910	2112
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	6366	3331
Simon Watkins	National Institutes of Health	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	71745	36807
Simon Watkins	National Institutes of Health	In vivo localization and mechanism of regultory B cell function in alloimmunity and trasplant toler- ance	11356	6128
Simon Watkins	National Institutes of Health	Pulmonary Arteriole Occlusion by Platelet Neutrophil Micro Emboll in acute chest syndrom	24472	2415
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	82294	44438
Simon Watkins	National Institutes of Health	Aging of MSCs missing Link in IPF	2450	1324
Simon Watkins	National Institutes of Health	Basic and Clinical Studies of Cystic Fibrosis - Core C	80270	39242
Simon Watkins	National Institutes of Health	Mechanima-directed sequential deliver of radiation mitgagors	24684	11887
Simon Watkins	National Institutes of Health	Mechanima-directed sequential deliver of radiation mitgagors	122745	59670
Simon Watkins	National Institutes of Health	Inhibition of Neural Electrode-Mediated Inflammation and Neuronal Cell Death	9666	4437
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	8168	4410
Simon Watkins	National Institutes of Health	Exosomes as paracrine signal mediators in cardiac allograft rejection	19020	7571
Simon Watkins	National Institutes of Health	Genetics of Extracellular Matrix in Health and Disease (Urban)	7497	1698
Simon Watkins	National Institutes of Health	Countering the Pro-Inflammatory Attributes of IL-33 During Hematopoietic Cell Tansplantation for Tolerance Induction	7552	2459
Simon Watkins	National Institutes of Health	Stem Cells for Corneal Engineering	5000	2700
Simon Watkins	National Institutes of Health	ROS Mechanisms in BAV Aortopathy	4816	2480
Simon Watkins	National Institutes of Health	Biochemical and Spatial Regulation of IKKg/NEMO During T Cell Activation	11449	6183
Simon Watkins	National Institutes of Health	T Cell Memory in Organ Transplantation	10000	5400
Simon Watkins	National Institutes of Health	Inhibition of the ALT Pathway by Interfering with Poly-ADP-Ribose Metabolism	15062	5434
Simon Watkins	National Institutes of Health	Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging	11284	5811
Simon Watkins	National Institutes of Health	PINK1 Regulation of Neuronal and Mitochondrial Homeostatis	2500	1353
Simon Watkins	National Institutes of Health	Center for Biological Imaging - Bakkenist	2500	0
Simon Watkins	National Institutes of Health	BMP10 in Cardiovascular Development and Hereditary Hemorrhagic Telangiectasia.	9969	5383
Simon Watkins	National Institutes of Health	Targeted Fluorescent Indicators for Endothelial Physiology	22944	7098
Simon Watkins	Department of Defense	Predictive understanding of the effects of encephalitic virus exposure on the blood brain barrier	00006	21600
Simon Watkins	National Institutes of Health	Cell Autonomous and Non-Autonomous Mechanisms of Aging	95650	46245
Simon Watkins	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	3199	1727
Simon Watkins	National Institutes of Health	Structure and Activation of a Multiprotein Signaling Complex (Vignali)	15049	4617
Simon Watkins	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	40000	0

American Cancer Society Epstein-Barr Virus C	Epstein-Barr Virus Oncogenesis in Nasopharyngeal Carcin	10047	2009
National Institutes of Health Mechanistic Elucida	Mechanistic Elucidation and Targeted Therapy of Platelet Dysfunction After Trauma	9403	5077
Improving Cerebral / National Institutes of Health Failure Models	Improving Cerebral Aneurysm risk Assessment Through Understanding Wall Vulnerability and Failure Models	23936	10047
National Institutes of Health The role of RTK Sig	The role of RTK Signaling in Opiod Tolerance	25974	14026
National Institutes of Health B Cells in the Patho	B Cells in the Pathogenesis of Allograft Rejection	5726	3106
National Institutes of Health Center for Biological	Center for Biological Imaging - Biogen - Gutstein	12500	0
National Institutes of Health Mechanisms of HMC	Mechanisms of HMGB1 Release from Ischemic Muscle in Peripheral Arterial Disease (Hartman)	436	241
National Institutes of Health Cell Autonomous an	Cell Autonomous and Non-Autonomous Mechanism of Aging	126548	54836
National Institutes of Health Plasticity of Auditory	Plasticity of Auditory Cortical Circuits in Schizophrenia	11434	6175
Novel and Robust M National Institutes of Health phrenia Research	Novel and Robust Methods for Differential Protein Network Analysis of Proteomics Data in Schizo- phrenia Research	16192	2475
National Institutes of Health Regulation of Fuel L	Regulation of Fuel Utilization by Lysine Acetylation in the Falling Heart	15840	8732
National Institutes of Health Implications of Proc.	Implications of Procaspase-8 mutations in oral	5706	3081
National Institutes of Health Alzheimer's Disease	Alzheimer's Disease Research center-funding	2852	1541
Novel and Robust M National Institutes of Health phrenia Research	Novel and Robust Methods for Differential Protein Network Analysis of Proteomics Data in Schizo- phrenia Research	6286	3158
		3785995	1728629

Cell Biology Sponsored Research Funding (FV18)	esearch Funding (FY18)			
Name	Agency Name	Title	Annual DC	Annual IDC
Michael Butterworth	National Institutes of Health	Role of MicroRNAs in kidney sodium regulation	216608	116968
Peter Drain	Prader-Willi Syndrome	Understanding Multiple Hormone Secretion Deficits in Prader-Willi Syndrome	2063	165
Marijn Ford	National Institutes of Health	The Roles of the Dynamin-Related Protein Vps1 and the ESCRT Complex in Microautophagy	197500	94486
Gerry Hammond	National Institutes of Health	Directing Membrane Function with Inositol Lipids in Health and Disease	235183	130445
Yang Hong	National Institutes of Health	Membrane Targeting and Retargeting of Polarity Proteins	196500	104518
Adam Kwiatkowski	National Institutes of Health	Alpha-Catenin Function in Cardiomyocyte Adhesion and Cytoskeletal Organization	242143	123196
Mads Larsen	National Institutes of Health	Cystic Fibrosis Foundation (Betrand)	29516	0
Sanford Leuba	National Institutes of Health	NNRTI Induced Conformational Changes in HIV 1 RT (Sluis-Cremer)	55424	29294
Sanford Leuba	National Institutes of Health	Novel Mechanisms of HIV Resistance ti RTIS (Sluis-Cremer)	6336	3422
Sanford Leuba	National Institutes of Health	Evolved DNA Contacts Required for Hexameric Helicase Unwinding.	56026	22971
Chelsea Merkel	National Institutes of Health	The Role of Vinculin in Cardiomyocyte Adhesion and Mechanical Continuity	40053	0
Alexander Sorkin	National Institutes of Health	Supplement -Pathogenesis of Cancer - Role of EGF Receptor Endocytosis	47277	26181
Alexander Sorkin	US Dept of Veterans Affairs	Investigating the Role of TMEM16A/AN01 in SCCHN	23855	0
Alexander Sorkin	National Institutes of Health	Exosome Based Placental Maternal Communication	60478	33188
Alexander Sorkin	National Institutes of Health	Modeling Spatiotemporal Control of EGFR-ERK Signaling in Gene-Edited Cell Systems	101008	56060
Alexander Sorkin	National Institutes of Health	Signaling by them EGF Receptor from Endosomes	208322	116966
Alexander Sorkin	National Institutes of Health	Regulation of Dopamine Transporter by Trafficking	259589	143715
Alexander Sorkin	National Institutes of Health	Coupling Between Dopamine Transporter Structural Dynamics, Oligomerization, Cellular Localization and Function	42753	24048
Claudette St. Croix	National Institutes of Health	In vivo localization and mechanism of regultory B cell function in alloimmunity and trasplant tolerance	11458	6186
Claudette St. Croix	National Institutes of Health	Pulmonary Arteriole Occlusion by Platelet Neutrohil micro emboli in acute chest syndrome	25356	2504
Claudette St. Croix	National Institutes of Health	Pathogenic Mechanisms of Gene-Environment Interactions in Parkinsons Disease	7864	4257
Claudette St. Croix	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lung Injury	10240	5530
Claudette St. Croix	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Preclinical Assesment Core	65672	36401
Claudette St. Croix	National Institutes of Health	Signaling Mechanisms by which Mitochondria Regulates Fibrosis in the Lung	4175	2324
Claudette St. Croix	National Institutes of Health	Regulation of Fuel Utilization by Lysine Acetylation in the Failing Heart	745	404
Claudette St. Croix	National Institutes of Health	Reactive Oxygen Species in Vascular Disease	8368	4519
Claudette St. Croix	National Institutes of Health	Anti-Inflammatory Lipid Mediators in Asthma	8575	4759
Claudette St. Croix	National Institutes of Health	Vascular Smooth Muscle and Blood Pressure Regulation By cyb5R2	7410	4098
Claudette St. Croix	National Institutes of Health	Novel Role of Smooth Muscle B5 Reductase in Sicle Cell Disease	4563	2525
Claudette St. Croix	National Institutes of Health	Aging of Mesenchymal Stem Cells Missing Link in IPF	9581	5174



Regulation of Fuel Utilization by Lysine Acetylation in the Failing Heart	Mechanisms oand Promotion of Immune Regulation by CD4+	Dissecting and breaking metabolic symbiosis between cancer cells and regulatory T cells	Core C: Cell Autonomous and Non-Autonomous mechanisms of Aging	The Anit-Aging Role of Klotho in Skeletal Muscle Regeneration	Engineering Research Center	Core A Cell and tissue Imaging Core	Bio-Mediated Killing of Oncogenic Stem Cells in chemoprevention	Mechanisms of Arsenic-induced Muscle Morbidity and Reduced Regenerative Capacity	Nitric Oxide and Hepatic Function in sepsis and Trauma	Mechanisms of Trabecular Meshwork Regeneration by stem cell	Critical Role for Fibroblast Growth Factor Receptors in Bladder Development	Dysfunctional Muscle remodeling and regeneration in environmental disease	Elucidting Mechanisms Involved in Lamin B1 Medited Demyelination	Endogenous Regulators of Inflammation in Liver Ischemia/Reperfusion	Luminal Epithelial Junctions, Polarity and Permeability in BPH	Alpha Catenin Function in Cardiomyocyte adhesion and Cytoskeletal	Characterization of Meiotic Crossover Surveillance System	Creation of Immuno-Oncolytic Viruses for Cancer Therapy	Metabolic reprogramming suing oncolytic viruses toimprove immunotherapy	Visualization of in vivo HIV-1 vaginal transmission in the presence and absence of PrEP	Pittsburgh Center for Kidney Research	CYP 450 Mediated CBF Dysregulation and Neurotoxicity in Pediatric Cardiac Arrest	Cardiolipin as a Novel Mediator of Acute Lung Injury	Biomimetric surface for neural implants	PQC2 Alteration of 3D nuclear organization at nanoscale in breast tumorigenesis	Regulated Activation of latent-TGfB Determines Leukocyte Occupany of the Epidermal Niche	ROS driven mitochondrial-telomere dysfunction during environmental stress-	University of Pittsburgh Center for HIV Protein Interactions (PCHPI)	Cancer Center Support Grant	Basic and Clinical Studies of Cystic Fibrosis - Core C	Core G: signature-directed sequential delivery of radiation mitigators
National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Science Foundation	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	Stand Up 2 Cancer	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health	National Institutes of Health
Claudette St. Croix	Claudette St. Croix	Claudette St. Croix	Claudette St. Croix	Claudette St. Croix	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Donna Beer Stolz	Stephen Thorne	Stephen Thorne	Stephen Thorne	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins	Simon Watkins

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Cell Biology Annual Report

	National Institutes of Health	Inhibition of Neural Electrode-Mediated Inflammation and Neuronal Cell Death	9613	4478
Simon Watkins Ni	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	5242	7337
Simon Watkins N	National Institutes of Health	Exosomes as paracrine signal mediators in cardiac allograft rejection	19020	7571
Simon Watkins N	Vational Institutes of Health	Genetics of Extracellular Matrix in Health and Disease (Urban)	7497	1618
Simon Watkins Ni	Vational Institutes of Health	Mechanistic Elucidation and Targeted Therapy of Platelet Dysfunction After Trauma (Neal)	11255	6077
Simon Watkins Ni	National Institutes of Health	Stem Cells for Corneal Engineering	5000	2700
Simon Watkins Ni	National Institutes of Health	Improving cerebral aneurysm risk assessment rhrough understanding wall vulnerabilitya nd failure models	23936	10047
Simon Watkins Ni	Vational Institutes of Health	Biochemical and Spatial Regulation of IKKg/NEMO During T Cell Activation	11449	6184
Simon Watkins Ni	National Institutes of Health	T Cell Memory in Organ Transplantation	10000	5400
Simon Watkins Ni	National Institutes of Health	Predictive understanding of the effects of encephalitic virus exposure on the blood brain barrie	50091	21649
Simon Watkins Ni	National Institutes of Health	Inhibition of the ALT Pathway by Interfering with Poly-ADP-Ribose Metabolism	15062	5434
Simon Watkins N	National Institutes of Health	Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging	11284	5811
Simon Watkins Ni	National Institutes of Health	B Cells in the Pathogensis of Allograft Rejection (Chalasani)	6875	3729
Simon Watkins Ni	National Institutes of Health	BMP10 in Cardiovascular Development and Hereditary Hemorrhagic Telangiectasia.	9969	5383
Simon Watkins Ni	National Institutes of Health	Cell Autonomous and Non-Autonomous Mechanisms of Aging	79436	39286
Simon Watkins C	Cystic Fibrosis Foundation	Research Development Project - Imaging Core	40000	0
Simon Watkins A	American Cancer Society	Epstein-Barr Virus Oncogenesis in Nasopharyngeal Carcin	10047	2009
Simon Watkins Ni	National Institutes of Health	The role of RTK Signaling in Opiod Tolerance	25974	14026
Simon Watkins Ni	National Institutes of Health	Center for Biological Imaging - Biogen - Gutstein	12500	0
Simon Watkins Ni	National Institutes of Health	Blue Light Protects against Ischemia Induced Organ Injury (Rosengart)	3247	1753
Simon Watkins Ni	National Institutes of Health	Structural Analysis of the TCR-CD3 Complex and TCR Signaling	12538	3845
Simon Watkins Ni	National Institutes of Health	Adult Stem Cell-Based Enhancement of Nerve Conduit for Peripheral Nerve Repair (McMann)	3199	1727
Simon Watkins N	National Institutes of Health	ROS Driven Mitochondrial-Telomere Dysfunction During Environmental Stress. (Van Houten)	43473	24128
Simon Watkins Ni	National Institutes of Health	Mechanisms of HMGB1 Release from Ischemic Muscle in Peripheral Arterial Disease (Hartman)	5260	2910
Simon Watkins N.	National Institutes of Health	Visualizing Synaptic Connection Between Distinct Cell types in Whole Mouse Brain (Bruchez - CMU subcontract)	80000	38965
Simon Watkins Ni	National Institutes of Health	Pittsburgh Center for HIV Protein Interactions (PCHPI) Gronenborn-	25001	13870
Simon Watkins Ni	National Institutes of Health	Signaling by the EGF Receptor from Endosomes	9728	5415
Simon Watkins Ni	National Institutes of Health	Surgery Triggered Immune Response and Liver Matastases	9728	5415
Simon Watkins Ni	National Institutes of Health	A Conofcal fluorescence Microscoy Brain Data Archive	33320	18548
Simon Watkins N	National Institutes of Health	Illuminting Metabolic Pathways Enabled by Early T Cell Activation	6743	2708
Simon Watkins N	National Institutes of Health	Inflammasoome Acivation in Trauma Hemorrhagic shock	12616	5386
Simon Watkins N	National Institutes of Health	Mechanisms of HMGB1 Release from Ischemic Muscle in Peripheral Arterial disease	7362	2707



Faculty Editorships (Fiscal Year 2016-2017)

Michael B. Butterworth, Ph.D.

Assistant Professor

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

Adam Kwiatkowski, Ph.D.

Assistant Professor

Associate Editor, BMC Cell Biology

Sanford Leuba, Ph.D. Associate Professor

Section Editor, BMC 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 (Nature) Editorial Board

Donna Beer Stolz, Ph.D. Associate Professor

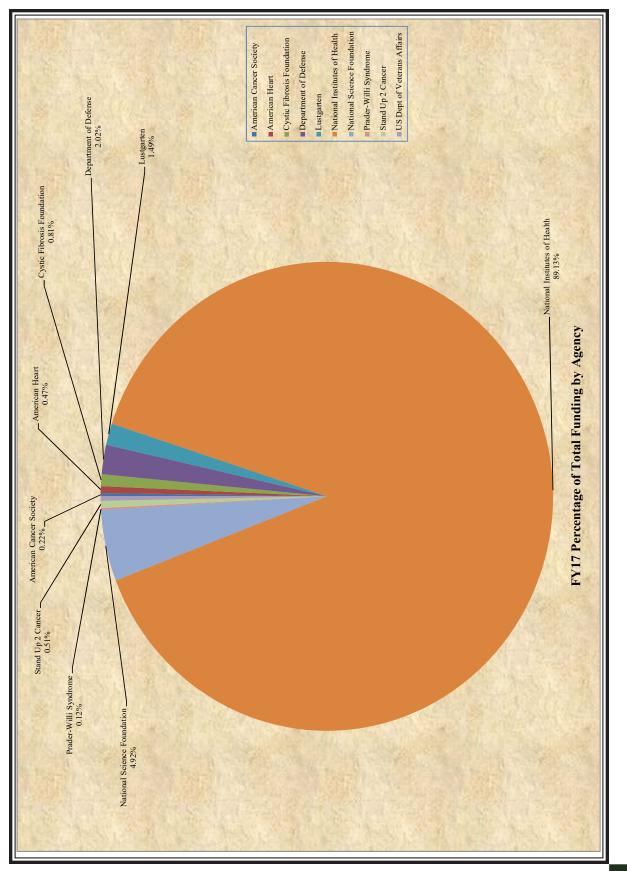
Editorial Board: Cell Transplantation: The Regenerative Medicine Journal. Hepatocyte section.

Stephen Thorne, Ph.D. Assistant Professor

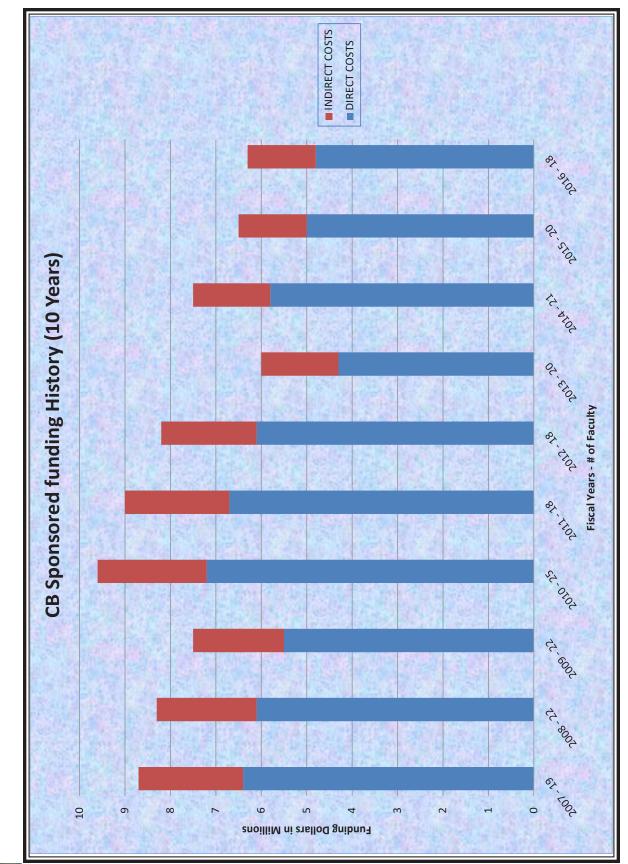
Journal of Clinical and Cellular Immunology American Journal of Cancer Research American Journal of Nuclear Medicine and Molecular Imaging Molecular Therapy - Oncolytics



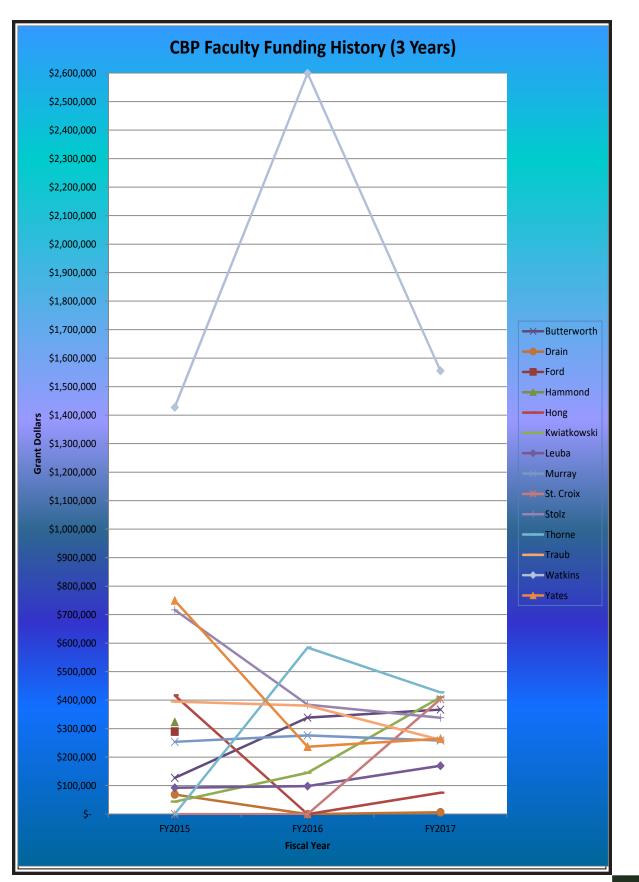
Linton Traub, Ph.D. Associate Professor
Member of editorial board of Traffic Member of editorial board of Cellular Logistics Member of editorial board of Scientific Reports Member of editorial board of The Journal of Biological Chemistry Member of board of reviewing editors, Molecular Biology of the 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, 2017)

	<u>Salary</u> <u>Support on</u>		
Faculty Member	Grants	<u>Rank</u>	<u>Status</u>
Stolz, Donna	87.5%	Associate Professor	Tenured
St. Croix, Claudette	85.9%	Associate Professor	Tenured
Watkins, Simon*	84.0%	Professor	Tenured
Thorne, Stephen	64.6%	Assistant Professor	Tenure Track
Kwiatkowski, Adam	50.0%	Assistant Professor	Tenure Track
Traub, Linton	48.5%	Associate Professor	Tenured
Hammond, Gerald	46.9%	Associate Professor	Tenured
Butterworth, Michael	40.0%	Assistant Professor	Tenure Track
Ford, Marijn	40.0%	Assistant Professor	Tenure Track
Yates, Nathan*	40.0%	Associate Professor	Non-tenure Track
Ford, Natalia	37.6%	Res. Assistant Professor	Non-tenure Track
Sorkin, Alexander*	23.2%	Professor	Tenured
Leuba, Sanford	27.4%	Associate Professor	Tenured
Murray, Sandra	16.4%	Professor	Tenured
Hong, Yang	9.8%	Associate Professor	Tenured
Drain, Peter	6.7%	Associate Professor	Tenured
Aridor, Meir	1.4%	Associate Professor	Tenured
Devor, Daniel	0.0%	Associate Professor	Tenured
Duker, Georgia	0.0%	Assistant Professor	Non-tenure Track
Shi, Yi	0.0%	Assistant Professor	Tenure Track

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

Cell Biology Annual Report





STUDENTS INVOLVED IN RESEARCH IN CBP FACULTY LABS Snapshot as of June, 2017

GRADUATE STUDENTS ENROLLED IN CBMP PROGRAM

STUDENT	LAB	SUPPORT
Rachel Wills	Gerald Hammond, Ph.D. Cell Biology	Gerald Hammond, Ph.D. Cell Biology & Teaching Fellowship
Jonathan Heier	Adam Kwiatkowski, Ph.D. Cell Biology	Adam Kwiatkowski, Ph.D. Cell Biology & Teaching Fellowship
Amity Eaton	Gerard Apodaca, Ph.D. Renal-Electrolyte Division	Gerard Apodaca, Ph.D. Cell Biology & Teaching Fellowship
Paige Rudich	Todd Lamitina, Ph.D. Dept. Pediatrics	Todd Lamitina, 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. AHA Training Grant &Teaching Fellowship
George Michael Preston	Jeffrey Brodsky, Ph.D. Biological Sciences	Jeffrey Brodsky, Ph.D. Biological Sciences



FY16 Projects

Butterworth lab: *Ankyrin G A Regulation of the Epithelial Sodium Channel after Adosterone Stimulation* (American Heart Association)

Thorne lab: *Combining STAT3-silencing and Oncolytic Vaccinia Virus to Enhance Anti-tumor Therapeutic Activity* (National Institutes of Health)

The combined funding for this post-doctoral fellowship grants is \$40,030 in FY16 (Total costs, annualized).

FY17 Projects

Butterworth lab: *Ankyrin G A Regulation of the Epithelial Sodium Channel after Adosterone Stimulation* (American Heart Association)

Kwiatkowski lab: *The Role of Vinculin in Cardiomyocyte Adhesion and Mechanical Continuity* (National Institutes of Health)

Thorne lab: *Combining STAT3-silencing and Oncolytic Vaccinia Virus to Enhance Anti-tumor Therapeutic Activity* (National Institutes of Health)

The combined funding for this post doctoral fellowship grants is \$85,111 in FY17 (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 in the amount of \$35,000.

FY16 Program Grant Training Funds - \$35.000 (Transferred to Pediatrics January 1. 2016) FY17 Program Grant Training Funds - \$0



Cell Biology Program Grants (Fiscal Year 2016-17)

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:

The CBI is funded to a large degree through multiple programmatic PHS grants, in which the CBI is listed as a core resource for the grant. There are 11 currently funded program grants including "Cancer Center support Grant" (PI Nancy Davidson P30 CA047904), "Basic and clinical studies of Cystic Fibrosis" (PI Ray Frizzell P30 DK072506) "Research studies in CF" (PI Ray Frizzell R8883-CR07), "Cell Autonomous and Non-Autonomous Mechanism of Aging" (PI Robbins P., 1P01AG043376-01A1); "DirectingTumor-specific T cells to Tumors" (PI Kalinski P, 5P01CA132714-05), "University of Pittsburgh Center for HIV Protein interactions" (PCHPI, PI Gronenborn A., 5P50GM082251-07), "Cardiolipin as a Novel Mediator of Acute Lung Injury" (Mallampalli R. P01 HL114453), "Vascular Subphenotypes of Lung Disease" (PI Gladwin M. 5P01HL103456-03), "Pittsburgh Center for Kidney Research" (PI Gerard Apodaca P30 DK079307-09), "Mechanism-Directed Sequential Delivery of Radition Mitigators Imaging Radiation Apathology Core" (PI Joel Greenberger U19 AI068021), and "Alzheimer's Disease Research Center" (PI Matthew MacDonald P30 AG05133)



New CBP Research Recruits in FY17

Name

Rank

Assistant Professor

Associate Professor

Faculty Level

Yi Shi Claudette St. Croix

Name

Rank

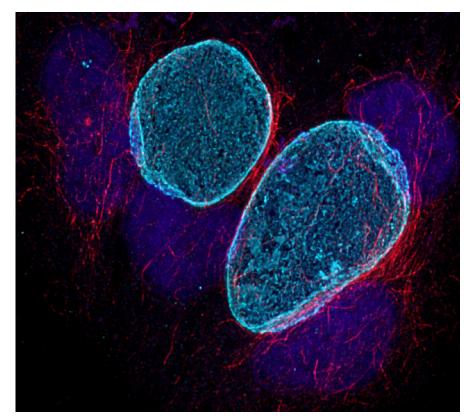
Post Doctoral Level

Changzhong Jin SM Ahasanul Kobir Yang Li Jonathan Pacheco Syed Raza

Post Doctoral Associate Post Doctoral Associate Vis. Research Associate Post Doctoral Associate Post Doctoral Associate

Lab Association

Dr. Yi Shi Dr. Sanford Leuba Dr. Adam Kwiatkowski Dr. Gerald Hammond Dr. Adam Kwiatkowski



Dr. Claudette St. Croix. An image of a chlamydial inclusion (cyan) inside a host cell that is labeled with DAPI (nuclei) and tubulin (red). This from work we published in collaboration with Fabienne Paumet from Thomas Jefferson University (Wesolowski J, Weber MM, Nawrotek A, Dooley CA, Calderon M, St Croix CM, Hackstadt T, Cherfils J, Paumet F. Chlamydia Hijacks ARF GTPases To Coordinate Microtubule Posttranslational Modifications and Golgi Complex Positioning. MBio. 2017 May 2;8(3). pii: e02280-16. doi: 10.1128/mBio.02280-16. PubMed PMID: 28465429; PubMed Central PMCID: PMC5414008.).



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. 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.

<u>Courses</u>

The CBMP program has 2 required courses and several electives available to students. Before entering the CBMP program, students successfully complete all the required first year IBGP courses including grant writing. After matriculating into the CBMP program all students are required to enroll in "Cell Biology of Normal and Disease States" (MSCBMP 2880) in the spring, and **one** of the imaging courses offered, either "Imaging Cell Biology in Living Systems" (MSCBMP 2885) in the spring or "Mutliparametric Microscopic Imaging" (MSCBMP 2860) in the summer. Students are encouraged to take the histology course (MSCBMP 2870) to be eligible to TA medical students. Ongoing classes include the work-in-progress class "Experiments and Logic in Cell Biology" (MSCBMP 2875) and a journal club that meet throughout the year.

Faculty

Faculty have a common interest in understanding the cellular basis of life and disease. As most human diseases arise from failures on a cellular level, our faculty investigate the cellular underpinnings of kidney, heart, lung and brain diseases, cancer, diabetes and inherited diseases of development and reproduction. Their research can be divided into the following broad categories:

Membrane Traffic of Proteins and Lipids Many of our faculty study how cells assemble the molecular machinery to coordinate membrane and organelle transport. Studies investigate how errors in cellular trafficking result in disease. Apodaca, Aridor, Brodsky, Butterworth, Ford, Goetzman, Hammond, Hong, Hughey, Murray, Sorkin, Swiatecka-Urban, Thorne, Traub, Weisz. *Cell Communication, Signaling and Ion Channel Biology* Studies aim to understand how cells receive, decode and transmit signals to establish complex signaling networks in the body. A breakdown in cellular communication leads to diseases like diabetes, neurodegenerative disease, cystic fibrosis, hypertension, heart disease and others, all under investigation by faculty. Brodsky, Butterworth, Carattino, Devor, Du, Dutta, Hammond, Hughey, Kashlan, Kleyman, Kwiatkowski, Murray, Nicotra, Roy, Salama, Lamitina, Sims-Lucas, St. Croix, Stolz, Swiatecka-Urban, Subramanya, Thibodeau, Thorne, Watkins, Weisz. Cellular Injury, Wound Healing, Aging and Tissue Regeneration Researchers are investigating responses to stress, cell or tissue damage to understand the cellular mechanisms that mediate repair and maintenance. This includes acute injury, chronic aging and new tissue growth. Du, Dutta, Funderburgh, Ghazi, Kwiatkowski, Lamitina, Mallampalli, Murray, Stolz, Swamynathan, Yanowitz. DNA Damage/Repair, Cell-Cycle Control and Gene Expression, Cancer An undamaged genome is essential to prevent cancer. Our faculty strive to identify defects associated with the cellular response to DNA damage/repair and cancer. Ghazi, Lamitina, Leuba, Swamynathan, Thorne, Walker, Yanowitz. Genomics, Proteomics and Metabolomics Faculty that aim to describe cellular function as a product of their genomic, proteomic or small molecule interactomes. Brodsky, Butterworth, Drain, Devor, Goetzman, Hong, Kwiatkowski, Lamitina, Rajkovic, Shi, Sims-Lucas, Sorkin, Swiatecka-Urban, Thibodeau, Thorne, Weisz, Whitcomb.

Reproductive Biology

Faculty specialize in the unique cellular processes associated with reproduction, and defects linked to reproductive disease and disorder.

Ghazi, Rajkovic, Schatten, Walker, Yanowitz.



Courses in the Cell Biology and Molecular Physiology Graduate Program

Courses in FY-17

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.

<u>Title: Cellular Biology of Normal and Disease States</u>

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.

<u>Title: Imaging Cell Biology in Living Systems</u>

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: Bennett Van Houten 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%).

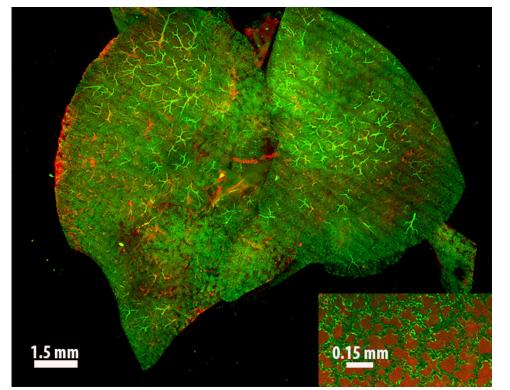
<u>Title: Reproductive Development from Model Organisms to Humans</u></u>

Course Number: 3840 Course Directors: 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.



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.



Dr. Claudette St. Croix. The lung image shows high resolution large area ribbon scanning confocal microscopy of lungs that have been perfused with green fluorescent beads and inflated with red fluorescent beads. The inset shows a zoomed in region of the image where you can clearly see the basket like structure of the capillary network (green) surrounding each alveolus (red). This new technology allows us to show the architecture of the vessels and the airways in the entire mouse lung and look for regional differences due to disease/damage. We recently published this method in Watson AM, Rose AH, Gibson GA, Gardner CL, Sun C, Reed DS, Lam LKM, St Croix CM, Strick PL, Klimstra WB, Watkins SC. Ribbon scanning confocal for high-speed high-resolution volume imaging of brain. PLoS One. 2017 Jul 7;12(7):e0180486. doi: 10.1371/journal.pone.0180486. eCollection 2017. PubMed PMID: 28686653;PubMed Central PMCID: PMC5501561.





Faculty Teaching Honors (Fiscal Year 2016-2017)

Georgia K. Duker, PhD Assistant Professor

Golden Apple Pre-Clinical Award for Excellence IN Teaching (2016) in MS-1 & MS-2 From the Medical Graduating Class of 2018



University of Pittsburgh School of Medicin Educational Credit Units (2015-2016) Department of Cell Biology Summary of Faculty ECU's	e		
Faculty Name Activity	ECURV	Units	ECUs
Aridor, Meir			
GS - Course Director	50.0	1.0	50.0
GS - Lecture	2.0	12.0	24.0
GS - Member: Admissions Committee	75.0	1.0	75.0
GS - Member: Program Steering Committee	40.0	1.0	40.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	28.0	56.0
	Total E	CUs:	245.0
Butterworth, Michael			
MS-1, MS-2 - Laboratory	2.0	8.4	16.8
MS-1, MS-2 - Lecture	2.0	1.3	2.7
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	13.3	26.7
GS - Course Director	50.0	3.0	150.0
GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	11.0	11.0
GS - Lecture	2.0	6.5	13.0
GS - Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	2.0	4.0
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 E	CUs:	434.2
Devor, Daniel			
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	16.8	33.5
GS - Chair: Admissions Committee	100.0	1.0	100.0
GS - Course Director	50.0	1.0	50.0
GS - Lecture	2.0	4.0	8.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	1.0	5.0
GS - Other	2.0	4.0	8.0
	Total E	CUs:	204.5
Drain, Peter			
MS-1, MS-2 - Course Director	200.0	2.0	400.0
MS-1, MS-2 - Lecture	2.0	1.5	3.0
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	16.8	33.5
MS - Applicant Interviewer	1.0	21.0	21.0
MS - Member, Admissions Committee	75.0	1.0	75.0
MS - Member, Curriculum Committee	20.0	1.0	20.0
MS - Member, Promotions Committee	5.0	1.0	5.0
FICE OF MEDICAL EDUCATION 12/19/2016	DEF	PARTMENT OF	Cell Biolog Page 1 of





	University of Pittsburgh School of Medicin Educational Credit Units (2015-2016) Department of Cell Biology Summary of Faculty ECU's	e		
Faculty Name	Activity	ECURV	Units	
GS - Course Direc	tor	50.0	2.0	1
		Total E	CUs:	6
Duker, Georgia				
MS-1, MS-2 - Cou	irse Director	200.0	1.0	2
MS-1, MS-2 - Cou	irse Segment Coordinator	5.0	1.0	
MS-1, MS-2 - Lab	oratory	2.0	18.2	
MS-1, MS-2 - Lec	ture	2.0	20.7	
MS-1, MS-2 - Oth	er	2.0	12.0	
MS-1, MS-2 - Sm	all group (e.g., PBL, conference, workshop)	2.0	27.3	
MS - Member, Pro	omotions Committee	5.0	1.0	
GS - Course Direc	tor	50.0	1.0	
GS - Lecture		2.0	43.0	
GS - Other		2.0	6.0	
GS - Small group	(e.g., PBL, conference, workshop)	2.0	34.0	
		Total E	CUs:	5
Ford, Marijn				
GS - Lecture		2.0	3.0	
GS - Small group	(e.g., PBL, conference, workshop)	2.0	10.0	
		Total E	CUs:	
Hammond, Gerald				
GS - Laboratory s	upervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	11.0	
GS - Lecture		2.0	9.0	
GS - Member: Co	mprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	3.0	
Total ECUs:		CUs:		
Hong, Yang				
GS - Lecture		2.0	7.0	
		Total E	CUs:	
Kwiatkowski, Adam				
MS-1, MS-2 - Lec	ture	2.0	1.8	
	upervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	20.0	
GS - Lecture		2.0	10.0	
GS - Member: Ad	missions Committee	75.0	1.0	
	mprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	2.0	
GS - Ph.D. or M.S		50.0	3.0	1
		Total E		2

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DEPARTMENT OF Cell Biology Page 2 of 4



University of Pittsburgh School of Medicine Educational Credit Units (2015-2016) Department of Cell Biology Summary of Faculty ECU's			
Faculty Name Activity	ECURV	Units	ECUs
Leuba, Sanford			
GS - Chair: Admissions Committee	100.0	1.0	100.0
GS - Course Director	50.0	2.0	100.0
GS - Lecture	2.0	2.3	4.7
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
GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	21.3	42.5
	Total E	CUs:	344.2
Murray, Sandra			
MS-1, MS-2 - Laboratory	2.0	41.5	83.0
MS-1, MS-2 - Lecture	2.0	4.0	8.0
MS-1, MS-2 - Other	2.0	21.0	42.0
MS - Member, Promotions Committee	5.0	1.0	5.0
GS - Lecture	2.0	1.0	2.0
	Total E	CUs:	140.0
Sorkin, Alexander			
GS - Lecture	2.0	6.0	12.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	4.0	20.0
GS - Member: Program Steering Committee	40.0	1.0	40.0
GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
	Total ECUs:		122.0
Stolz, Donna			
MS-1, MS-2 - Laboratory	2.0	14.3	28.7
MS-1, MS-2 - Lecture	2.0	2.3	4.7
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	11.1	22.2
MS - Mentored Scholarly Project (MSP) Mentor	25.0	1.0	25.0
GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	6.0	30.0
GS - Course Director	50.0	5.0	250.0
GS - Lecture	2.0	17.8	35.5
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	11.0	55.0
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
	100.0	1.0	100.0
GS - Program Director			

OFFICE OF MEDICAL EDUCATION 12/19/2016

DEPARTMENT OF Cell Biology Page 3 of 4



Summary of Faculty ECU's		
Faculty Name Activity	ECURV Units	ECI
Thorne, Stephen		
GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0 20.0) 20
GS - Lecture	2.0 5.5	5 11
GS - Small group (e.g., PBL, conference, workshop)	2.0 8.0) 16
	Total ECUs:	47
Traub, Linton		
GS - Course Director	50.0 2.0) 100
GS - Lecture	2.0 10.0) 20
	Total ECUs:	120
Wan, Yong		
GS - Lecture	2.0 6.0) 12
	Total ECUs:	12
Watkins, Simon		
MS - Mentored Scholarly Project (MSP) Mentor	25.0 1.0) 25
GS - Course Director	50.0 1.0) 50
GS - Lecture	2.0 16.5	5 33
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0 4.0) 20
	Total ECUs:	128
Yates, Nathan		
GS - Course Director	50.0 1.0) 50
GS - Lecture	2.0 4.3	8 8
	Total ECUs:	58
	Subtotal:	4051
Total Faculty Reporting: 18 Total	ECU's for Cell Biology:	4051
	DEPARTMENT	Γ OF Cell Biol Page 4 c



Current as of Jun. 2017] Confice Notice Email Address Email Address Email Address Email Address Confice Phone Fax Research Freeus Rell. Cheryl Pest Doctoral Associate S33 BSTWR rbb/6@pint.edu 412-643-833 Warry Lab Dong, Wei Rell. Cheryl Pest Doctoral Associate S33 BSTWR rbb/6@pint.edu 412-643-833 Warry Lab Dong, Wei Research Associate S33 BSTWR rbb/6@pint.edu 412-643-833 Warry Lab Dong, Wei Research Associate BST3-9hFT rbb/6@pint.edu 412-643-833 Warrs Lab Dong, Wei Research Associate BST3-9hFT rbb/6@pint.edu 412-643-833 Warrs Lab Dong, Wei Research Associate S33 BSTWR rbb/6@pint.edu 412-643-833 Warrs Lab Charge/Dong, Jin Post Doctoral Associate S33 BSTWR rbb/6@pint.edu 412-643-833 Warrs Lab Larsen, Mata Vis Research Associate S33 BSTWR rbb/6@pint.edu 412-643-833 Warrs Lab Larsen, Mata Vis Research Associate S33 BSTWR rbp/6@pint.edu 412-643-833 Warrs Lab Perton, Jana Vis Research Associate S33 BSTWR rbp/6@pint.edu 412-648-8330 Warts Lab Pert							
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Dest Doctoral AssociateBST3-9/h FIchj44@pitt.edu412-533-324212-641-2458Sin LabVis. Research AssociateH221B 2.26Ghobisming/itt.edu412-533-7829412-648-8330Matikus LabVis. Research AssociateS324 BSTWRyangli@pitt.edu412-548-8330Matikus LabVis. Research AssociateS323 BSTWRyangli@pitt.edu412-648-8330Matikus LabPost Doctoral AssociateS323 BSTWRspp10@pitt.edu412-648-3791Matikus LabPost Doctoral AssociateS322 BSTWRspp10@pitt.edu412-648-3791WatkowskiPost Doctoral AssociateS322 BSTWRspp10@pitt.edu412-648-3791WatkowskiPost Doctoral AssociateS322 BSTWRspp10@pitt.edu412-648-3791Watkins LabPost Doctoral AssociateS322 BSTWRspp10@pitt.edu412-648-330KwintkowskiPost Doctoral AssociateS322 BSTWRspp10@pitt.edu412-648-333Sorkin LabPost Doctoral AssociateS322 BSTWRsyr10@pitt.edu412-648-333Sorkin LabVis. Research AssociateS322 BSTWRsvs23@pitt.edu412-648-8333Sorkin LabVis. Research AssociateS372 BSTWRsvs23@pitt.edu412-648-8333Sorkin LabVis. Research AssociateS372 BSTWRsvs23@pitt.edu412-648-8333Sorkin LabVis. Research AssociateS372 BSTWRsvs23@pitt.edu412-648-8333Sorkin LabVis. Research AssociateS372 BSTWRsvs23@pitt.edu412-648-8333Sorkin LabVis. Research As		Research Associate	S333 BSTWR	wed16@pitt.edu	412-648-2846	412-648-8330	Hong Lab
 Wis. Research Associate HCCIB 2.26 kobinsm@pitt.edu 412.653-782 412.653-4840 Leuba.Lab Vis. Research Associate S234 BSTWR publ6@pitt.edu 412.353-789 412.648-330 Watkins.Lab Post Doctoral Associate S324 BSTWR papel@jitt.edu 412.353-789 412.648-330 Watkins.Lab Post Doctoral Associate S323 BSTWR papel@jitt.edu 412.333-789 412.648-330 Watkins.Lab Post Doctoral Associate S323 BSTWR papel@jitt.edu 412.333-789 412.648-330 Watkins.Lab Post Doctoral Associate S323 BSTWR papel@jitt.edu 412.333-789 412.648-330 Watkins.Lab Post Doctoral Associate S323 BSTWR papel@jitt.edu 412.333-789 412.648-330 Sovint.Lab Post Doctoral Associate S324 BSTWR syn06@pitt.edu 412.644-8147 412.648-8330 Sovint.Lab Vis. Research Associate S324 BSTWR sv23@pitt.edu 412.652-7701 Thorne Lab Vis. Research Associate HCCLB-2.6 zhouz2@upmc.edu 412.6623-7701 WatLab Vis. Research Associate HCCLB-2.6 zhouz2@upmc.edu 412.6623-7701 WatLab 		Post Doctoral Associate	BST3-9th Fl	chj44@pitt.edu	412-383-3242	412-641-2458	Shi Lab
 Vis. Research Associate S234 BSTWR mbl6@pitt.edu 412-648-8796 412-648-8330 Watkins Lab Vis. Research Associate S332 BSTWR pyapti@pitt.edu 412-638-7991 412-648-8330 Hammon Lab Post Doctoral Associate S220.5BSTWR kapena@pitt.edu 412-648-9796 412-648-8330 Sorkin Lab Post Doctoral Associate S320.5BSTWR kapena@pitt.edu 412-648-9796 412-648-8330 Sorkin Lab Post Doctoral Associate S372 BSTWR kapena@pitt.edu 412-648-9796 412-648-8330 Sorkin Lab Vis. Research Associate S372 BSTWR syn0@pitt.edu 412-648-9300 412-648-8330 Sorkin Lab Vis. Research Associate BTCLB-2.6 2000; pitt.edu 412-643-9796 412-648-8330 Sorkin Lab Vis. Research Associate HCCLB-2.6 2hout2@upmc.edu 412-623-1790 112-648-8330 Sorkin Lab Vis. Research Associate HCCLB-2.6 		Vis. Research Associate	HCCLB 2.26G	kobirsm@pitt.edu	412-623-7822	412-623-4840	Leuba Lab
Vis. Research Associate S324 BSTWR yangli@pitt.edu 412-383-7891 412-648-8330 Kwiatkowski Post Doctoral Associate S322 BSTWR jop100@pitt.edu 412-383-7783 412-648-8330 Mattins Lab Post Doctoral Associate S372 BSTWR syr10@pitt.edu 412-648-8330 Sorkin Lab Post Doctoral Associate S372 BSTWR syr10@pitt.edu 412-648-8330 Kwiatkowski Vis. Research Associate HCCLB 2.6 pas6@pitt.edu 412-648-8330 Sorkin Lab Vis. Research Associate HCCLB-2.6 zhou22@upmc.edu 412-623-7701 Want.ab Vis. Research Associate HCCLB-2.6 zhou22@upmc.edu 412-623-7701 Want.ab		Vis. Research Associate	S234 BSTWR	mb16@pitt.edu	412-648-9796	412-648-8330	Watkins Lab
Post Doctoral AssociateS332 BSTWRjep160@pitt.edu412-383-1783412-648-8330Post Doctoral AssociateS220.5BSTWRkapena@pitt.edu412-648-8330412-648-8330Post Doctoral AssociateS372 BSTWRinp2@pitt.edu412-648-8330412-648-8330Post Doctoral AssociateS324 BSTWRsyn0@pitt.edu412-63-1390412-648-8330Post Doctoral AssociateS324 BSTWRsyn0@pitt.edu412-623-1390412-648-8330Vis. Research AssociateS772 BSTWRsys32@pitt.edu412-623-1709412-63-8330Vis. Research AssociateHCCLB-2.6zhouz2@upmc.edu412-623-7761412-623-7761		Vis. Research Associate	S324 BSTWR	yangli@pitt.edu	412-383-7891	412-648-8330	Kwiatkowski Lab
Post Doctoral AssociateS220.5BSTWRkapena@pitt.edu412-648-9796412-648-330Post Doctoral AssociateS372 BSTWRip2@pitt.edu412-634-8147412-648-8330Post Doctoral AssociateS324 BSTWRsyr10@pitt.edu412-632-1390412-648-8330Vis. Research AssociateHCCLB G.16pas6@pitt.edu412-632-1390412-648-8330Vis. Research AssociateS372 BSTWRsvs23@pitt.edu412-623-1709412-648-8330Vis. Research AssociateHCCLB-2.6zhouz2@pitt.edu412-623-7701412-623-7701Vis. Research AssociateHCCLB-2.6zhouz2@pitt.edu412-623-7701412-623-7701		Post Doctoral Associate	S332 BSTWR	jep160@pitt.edu	412-383-1783	412-648-8330	Hammon Lab
Post Doctoral Associate S372 BSTWR ip2@pitt.edu 412-624-8147 412-648-8330 Post Doctoral Associate S324 BSTWR syr10@pitt.edu 412-333-7891 412-648-8330 Vis. Research Associate HCCLB G.16 pas6@pitt.edu 412-632-1390 412-632-7709 Vis. Research Associate HCCLB-2.6 zhouz2@upmc.edu 412-623-7701 412-623-7701 412-623-7701		Post Doctoral Associate	S220.5BSTWR	kapena@pitt.edu	412-648-9796	412-648-2797	Watkins Lab
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Vis. Research Associate HCCLB G.16 pas6@pitt.edu 412-623-1390 412-623-7709 Vis. Research Associate S372 BSTWR vs23@pitt.edu 412-624-8147 412-648-8330 Vis. Research Associate HCCLB-2.6 zhouz2@upmc.edu 412-623-7761 412-623-7761		Post Doctoral Associate	S324 BSTWR	syr10@pitt.edu	412-383-7891	412-648-8330	Kwiatkowski Lab
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HCCLB-2.6 zhouz2@upmc.edu 412-623-7811 412-623-7761		Vis. Research Associate	S372 BSTWR	svs23@pitt.edu	412-624-8147	412-648-8330	Sorkin Lab
		Vis. Research Associate	HCCLB-2.6	zhouz2@upmc.edu	412-623-7811	412-623-7761	Wan Lab



<u>Current Cell Biology and Molecular Physiology Graduate Program Students as of</u> <u>June 30, 2017</u>

<u>Student</u>

Christine Klemens George Michael Preston Chelsea Merkel Paige Rudich Amity Eaton Jonathan Heier Rachel Wills

	Mentor	<u>Year</u>
	Dr. Mike Butterworth	5th
n	Dr. Jeff Brodsky	5^{th}
	Dr. Adam Kwiatkowski	3 nd
	Dr. Todd Lamitina	2^{st}
	Dr. Gerard Apodaca	2^{st}
	Dr. Adam Kwiatkowski	1^{st}
	Dr. Gerald Hammond	1 st



Prior Graduates of the Cell Biology and Molecular Physiology Program as of June 2017 (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

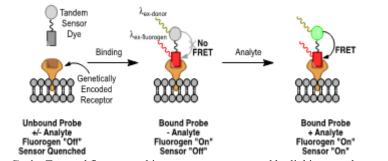
Christina Szalinski, Ph.D. Defended May 20, 2013 Science Writer, American Society for Cell Biology (ASCB), Bethesda, MD

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



Dr. Claudette St. Croix. Targeted fluorescent biosensors are constructed by linking together a sensitive optical sensor of ROS, with a fluorescent signaling moiety (FRET acceptor) that is activated upon binding to a genetically encoded receptor, called a fluorogen activating protein (FAP). The FAP-bound sensor is able to report (fluorescence signal) the physiology of the sensing at the site of interest.



Student Ratings of CBMP Faculty Teaching FY2017

Name	Course	Туре	Date	Rating	Ave
Butterworth	Investigation and Discovery	SGCS	Fall-16	4.60	4.60
Devor	Investigation and Discovery	SGCS	Fall-16	3.90	3.90
Drain	Investigation and Discovery	SGCS	Fall-16	4.60	4.60
Duker Duker Duker Duker Duker Kwiatkowski Kwiatkowski	Introduction to Being a Physician Body Fluid Homeostasis Cardiovascular Digestion and Nutrition Cellular and Pathological Basis of Disease Immunology in Health and Disease Cellular and Pathological Basis of Disease Cellular and Pathological Basis of Disease	SGCS LEC LAB LAB LAB LEC LAB	Fall-16 Fall-16 Fall-16 Spring-17 Spring-17 Spring-17	4.30 4.80 4.90 4.50 5.00 3.40 5.00	4.70 4.20
Murray Murray	Medical Anatomy Medical Anatomy	LEC LAB	Fall-16 Fall-16	3.90 4.60	4.25
Stolz Stolz	Cellular and Pathological Basis of Disease Digestion and Nutrition	LAB LAB	Spring-17 Fall-16	5.00 4.70	4.85

Overall Teaching Average

4.51

Type codes:LECLecturePBLPractice Based LearningWKSPWorkshopSGCSSmall Group Conference SessionAPApplications StaffLABLaboratory



CBP FACULTY ROSTER (Effective June, 2017)

<u>Last Name</u>	<u>First</u>	Rank	<u>Status</u>
Sorkin	Alexander	Professor & Chair	Tenured
Devor	Daniel	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
St. Croix	Claudette	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
Shi	Yi	Assistant Professor	Tenure Track
Thorne	Stephen	Assistant Professor	Tenure Track
Duker	Georgia	Assistant Professor	Non-tenure Track
Ford	Natalia	Res. Assistant Professor	Non-tenure Track



New CBP Faculty in FY17		
Name	Prior Institution /Rank	Current Rank
Yi Shi	The Rockerfeller University New York, NY Research Associate	Assistant Professor
Claudette St. Croix	University of Pittsburgh Department of Environmental and Occupational Health Pittsburgh, PA 15260 Associate Professor	Associate Professor
Dr. Claudette St.	. Croix. A pretty picture of a senescent cell sh	owing fragmented mitochon-

Dr. Claudette St. Croix. A pretty picture of a senescent cell showing fragmented mitochondria (green), tubulin (red) and nuclei (blue).



Faculty Honors, Recognition and Professional Affiliations (Fiscal Year 2016-2017)

Michael Butterworth, Ph.D. Assistant Professor

Member, American Physiological Society Member, Elected Secretary, Salt and Water Club American Society of Nephrology American Heart Association

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

Gerry Hammond, Ph.D. Assistant Professor

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

Yang Hong, Ph.D. Associate Professor

Member of Faculty 1000



Assisi	tant Professor
Amer	ber, American Society for Cell Biology ican Society for Biochemistry and Molecular Biology rican Heart Association
	ord Leuba, Ph.D. siate Professor
	ber, Biophysical Society ber, Spectroscopy Society of Pittsburgh
Sand Profe	ra A. Murray, Ph.D. ssor
Memi Memi Memi Memi Memi Unive Schoo Memi Memi NIH - Co-C Unive Gradu Gradu Provo	ber, American Society for Cell Biology ber, Society for In Vitro Biology ber, The Pittsburgh Cancer Institute ber, Corporation of the Marine Biological Laboratory ber, Cell Transplant Society ber, Endocrine Society ber, American Physiological Society ber, International Society for Preventive Oncology ersity of Pittsburgh Helen Faison Council of Elders ol of Medicine Summer "Minority" Work-Study Program ber, Medical Student Promotions Committee ber, Training Faculty Immunology Graduate Training Program - Biomedical Faces of Science Mentors hair of the Research Center of Excellence Committee Graduate School of Public Heal ersity of Pittsburgh uate School of Public Health Community Engagement Research Cor uate School of Public Health Research Advisory Committee- center for Minority Health best Special Advisory Committee best Selection Committee for the Provost Development Fund Awards
Junio	ersity Community Representative for Equipoise r Faculty Advancement – Panel Member ii, Ph.D.
	tant Professor
	ber, American Society for Mass Spectrometry ber, New York Academy of Sciences





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 Investigative Pathology Member, American Physiological Society

Stephen Thorne, Ph.D. Assistant Professor

American Association of Cancer Research American Society of Cellular and Gene Therapy Society of Nuclear Medicine and Molecular Imaging

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*

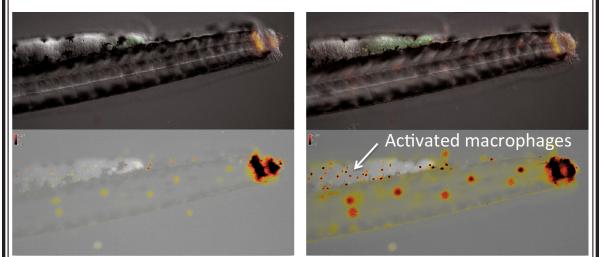
Member, The Pittsburgh Cancer Institute



CB Faculty Honors, Recognition and Professional Affiliations

Cell Biology Annual Report Nathan Yates, Ph.D. Associate Professor

American Chemical Society American Society for Mass Spectrometry



Dr. Claudette St. Croix. The activation of the ROS sensor in an embryonic zebrafish after tail injury are consistent with expected biological responses (activation of macrophages, wound-site activation).Representative Publication: He J, Wang Y, Missinato MA, Onuoha E, Perkins LA, Watkins SC, St Croix CM, Tsang M, Bruchez MP. Nat Methods. 2016 PubMed PMID: 26808669.



Faculty Presentations (Fiscal Year 2016-2017)

Michael Butterworth, Ph.D. Assistant Professor

"MicroRNAs and the Regulation of Epithelial Ion Transport". Experimental Biology (FASEB) Chicago, IL, 2017

Gerald Hammond, Ph.D. Assistant Professor

"It's all about the middle man: new insights into the metabolism and function of the phosphoinositides", Upstate Medical University, Syracuse, NY, 2017.

"Multitasking Molecules: new insights into the metabolism and function of the phosphoinositides" Penn State University, State College, PA, 2017.

"An inositol lipid conductor and the membrane orchestra", Senior Vice Chancellor's Seminar Series, University of Pittsburgh, 2017.

"Sac1 degrades its lipid substrate P14P in the ER to maintain a steep electrochemical gradient on donor membranes", in "Regulation of Intracellular Cholesterol Transport", American Society of Biochemistry and Molecular Biology 2017 Annual Meeting, Chicago, IL, 2017.

Yang Hong, Ph.D. Associate Professor

Annual Drosophila Research Conference, San Diego, March, 2017 PGH Translational Medicine Research Conference, Guangzhou, China, November 2016

Adam Kwiatkowski, Ph.D. Assistant Professor

"Talk, Cell Contact & Adhesion", Gordon Research Conference, Andover, NH. June, 2017.

Yi Shi, Ph.D. Assistant Professor

Magee Women's Research Institute, Pittsburgh, PA, May 2017. 65th American Society of Mass Spectrometry (ASMS) Conference on Mass Spectrometry and Allied Topics, Indianapolis, IN, June, 2017



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

Regeneron Pharmaceuticals, Inc., Teddytown, NY, November 2016 University of Nebraska, December 2016 Ryerson University, Toronto, Canada, February 2017 Genentech, Inc., San Francisco, CA, April 2017 University of San Francisco, CA, April 2017 Stanford University, Palo Alto, CA, April 2017

Donna B. Stolz, Ph.D. Associate Professor

Keynote Speaker, Duquesne University of Biological Sciences Retreat "Not all who wander are lost: My story of navigating the world of Biomedical Science as a Cell Biologist", August 2016. Nobel Autophagy: "A Lot to Digest". University of Pittsburgh Medical School Nobel Lectures, December 2016.

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

Inaugural lecture, Distinguished Professor, "From Little Animals to Moving Molecules". University of Pittsburgh, September 15th 2016 Opportunities in Correlative EM, JEOL USA, September 28th, 2016 Ohio State University, Department of Physics, Invited Colloquim speaker "From Little Animals to Moving Molecules", February 1 2017 Canadian Microscopy and Cytometry Symposium Montreal Quebec: May 9th 2017 Round Table Leader: Choices and Imperatives for facility management Canadian Microscopy and Cytometry Symposium Montreal Quebec: May 11th 2017 Super-Resolution imaging past, present and future. Invited speaker.

Nathan Yates, Ph.D. Associate Professor

"Rapid Identification of Proteins that Bind Small Molecule Drugs by <u>D</u>ifferential <u>Intensity</u> <u>Screening and Ranking of Unknown Protein Targets (DISRUPT)</u>" Cell Biology Retreat, Pittsburgh, PA, September 2016

"Precision Proteomics-New Tech Reveals Novel Drug Targets" Science 2016 –Game Changers, Pittsburgh, PA, October 2016

"Introduction to the Biomedical Mass Spectrometry Center" Immunology Department Meeting, Pittsburgh, PA, December 2016

"Introduction to Proteomics at the University of Pittsburgh" Kallyope, New York, NY, December 2016

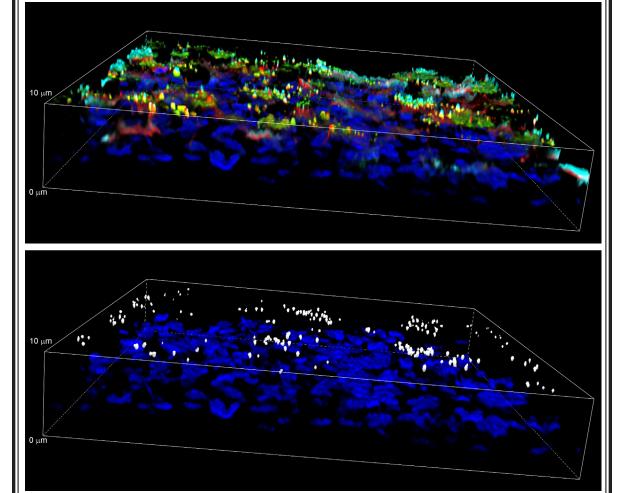


"Application of Differential Mass Spectrometry for the Unbiased Identification of CSF Biomarkers and Novel Protein Targets" Center of Excellence for Computational Chemogenomics Drug Abuse Research (CDAR), Pittsburgh, PA, December 2016

"Performance Proteomics – Next Generation Technology Needs for Precision Medicine" Mozaic Solutions Annual Meeting, Pittsburgh, PA, May 2017

"Modular Design and Independent Control: Two Important Features For Prototyping Innovative Nanoflow Chromatography Systems" CPSA Analytics, Pittsburgh, PA, May 2017

"Benefits of Larger Studies in Discovery Proteomics" New Objective ASMS Users Meeting, Indianapolis, IN, June 2017



Dr. Claudette St. Croix. 3D confocal reconstruction of human airway endothelial cells stimulated with IL-13 showing immuno-localization of 15LO1 (green), PEBP1 (red) and GPX(4) (cyan). The white puncta in the bottom panel identify regions where the three proteins co-localize. These three proteins (15LO1, PEBP1 and GPX4) through their interactions with each other and with phospholipids in a complex termed "a redox phospholipoxysome" (RPL), are purported to play a fundamental role in determining the episodic nature asthma. This work will appear in the October 19th, 2017 issue of Cell ("PEBP1 Wardens Ferroptosis by Enabling Lipoxygenase Generation of Lipid Death Signals" by SE Wenzel, YY Tyurina, J Zhao, CM St. Croix, G Mao, VA Tyurin, TS Anthonymuthu, AA Kapralov, K Mikulska-Ruminska, IH Shrivastava, E Kenny, Q Yang, HH Dar, F Qu, AA Amoscato, LJ Sparvero, DR Emlet, JC Rosenbaum, SC Watkins, AP VanDemark, JA Kellum, Y Minami, I Bahar, H Bayir, VE Kagan.)



Peer Reviewed Publications (Fiscal Year 2018-2017)

Meir Aridor, Ph.D. Associate Professor

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Michael Butterworth, Ph.D.

Assistant Professor

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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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Gerald Hammond, Ph.D.

Assistant Professor

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Adam Kwiatkowski, Ph.D.

Assistant Professor

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Sandra A. Murray, Ph.D.

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Yi Shi, Ph.D.

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Claudette St. Croix, Ph.D. Associate Professor

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Executive Summary for the Cell Biology FY2017 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 seven years significant changes in the Department took place with ten members of the primary faculty leaving the Department and eight new members joining the faculty. This year two new primary faculty, Drs. Yi Shi and St. Croix, 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 FY2018 plan. To this end, we hope that one Assistant professor will be promoted and we will recruit one more tenure-track faculty in the Department in FY18. We plan to recruit a scientist who studies fundamental aspects of cell biology, in particular, in the area of protein folding and protein conformational diseases, 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 2018 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, intercellular interactions, and membrane channel and transportr 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 such as Journal of cell Science (Ford), Scientific Reports (Sorkin), Development (Hong), Current Opinions in cell Biology (Hammond and Hong) and others.

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 cargospecific 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 successful in obtaining extramural research funding in the past cycle, as evidenced by, obtaining funding in multiple collaborative grants (Watkins, Yates, Stolz, St. Croix), and the competitive renewal of NIH grants (Hong, Sorkin). All tenure-stream Assistant Professors, except Yi Shi who just arrived, are currently funded by NIH. Submission of new grant applications remains to be at a high rate which ensures relative fiscal stability of the Department.

The new recruit, Dr. Yi Shi joined the Department in January 2017. His research is focused on structure-Ofunctional analysis of macromolecular complexes using crosslinking mass-spectrometry.

The Center for Biologic Imaging (CBI) associated with the Department 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, St. Croix and Stolz were awarded NIH shared instrumentation grant to fund a new confocal microscope which is 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 enhancing an infrastructure to implement modern methods of quantitative mass-spectrometric analyses.

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. Two students graduated in 2016, taking position as postdoctoral fellows. In addition, CB faculty participate in other graduate programs under umbrella of the Medical School Interdisciplinary Biomedical Graduate Program, as well as in the Departments of Bioengineering, Biological Sciences, ISB, Neuroscience among others.

New Biomedical master's Program (BMP). Faculty in the Department together with the Department of Pharmacology launched a new BMP program in September 2017. At least four faculty will be teaching didactic courses, Dr. Peter Drain will serve as the Director of Academic Affairs, and Dr. Sorkin will be a member of the Executive Committee.

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 demonstrates 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. Because of budgetary issues some space in BST South was temporarily rented to another department. We will commit major efforts to rearrange the space in BST South to allow for growth of the research programs of the new and current faculty located in this area.



Two of the CBP faculty Drs. Thorne and Leuba are located 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, and continue to support productive mid-career and senior faculty. We hope to continue recruiting faculty whose research programs focus on fundamental questions of cell biology. The importance of the successful recruitment of a strong faculty to shape the future of the department, while achieving a healthy balance of junior and senior faculty members, is difficult to overemphasize.

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

Threats

The steady decrease in federal and private funding opportunities to support <u>basic</u> cell biology research will continue to be the most significant threat during next several years. Several senior faculty are currently struggling with sustaining level of funding necessary to support 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 FY2018 Fiscal Issues

The main budgetary issue that faced the Department in the FY17 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 increase the funding level of previous years. Main efforts will be devoted to ensuring that the departmental infrastructure necessary for advancing research programs of the faculty continues to improve.

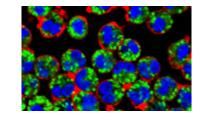




University of Pittsburgh School of Medicine					
University of Pittsburgh Physicians					
Department of Cell Biology					
Schedule of Revenue and Expenses Fiscal Year	2017 Budget				
<i>y i</i>	8				
				Total	
		LIDD	UPP and Other		,
	T T				Budget FY 2017
Revenue	University	Other		1 1 2017	
Patient Care	\$	\$	_	\$	_
Grant:	Ψ	Ψ		Ψ	
Directs	3,278,854		_	3.2	78,854
Indirects	1,314,065		-		14,065
Hospital Contract	-		-)-	-
School of Medicine	3,563,049			3,5	63,049
VAMC			-		-
Other	395,134		-	3	95,134
Total Revenue	\$ 8,551,102	\$	-	\$ 8,5	51,102
Expenses					
Salaries and Fringe Benefits:	¢ 20(0.210	¢		¢ 2 0	(0.210
Faculty New Faculty	\$ 3,068,319	\$	-		68,319
Non-Faculty Malarastics Insurance	2,592,779		-	2,5	92,779
Malpractice Insurance Space Rental	195,682		-	1	- 95,682
UPP Overhead	195,082		-	1	95,082
University Overhead	2,346,558		-	23	46,558
Other Operating Expenses	347,764		_	,	47,764
Total Operating Expenses	\$ 8,551,102	\$	-		51,102
	\$ 0,001,102	Ψ		\$ 0,5	
Excess Revenue over Expenses	\$ -	\$	-	\$	-
	•	.		<i>.</i>	
Capital Equipment/Improvements	\$ -	\$	-	\$	-
Fund Balances					
University Restricted Accounts as of 6/30/17	\$ 3,525,780	\$	-	\$ 3.5	25,780
University Endowments as of 6/30/17	395,134	*			95,134
UPP Fund Balance as of 6/30/17	,		-	-	-
UPMC Endowments as of 6/30/17			-		-
UPMC SPF Accounts as of 6/30/17			-		-
Total Fund Balances	\$ 3,565,314	\$	-	\$ 3,5	65,314

Cell Biology Annual Report





Thank you for your kind attention.



