UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE CELL BIOLOGY

FY19 ANNUAL REPORT AND FY20 BUSINESS PLAN

Front Page

Cover figure by Alan Watson. These images display Sox10 (green) and Hu C/D (Red) expression at subcellular resolution throughout a developing mouse embryo. On the left is a 3D reconstruction of the complete embryo, and on the right is a single high-resolution image which is a component of the 3D model on the left. The embryo was imaged with lateral resolution of 300 nanometers. These data were collected in collaboration with Dr. Michelle Southard-Smith at Vanderbilt University.

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In the cell, life is governed by a multitude of molecular systems that shape and sustain the organellar system of the cell, maintain cellular homeostasis and respond to extracellular cues. These systems are dynamic, multicomponent macromolecular complexes. Maintaining and regulating the function of these complexes is essential for normal cell motility, growth, division, differentiation and programmed death. Dysregulation inevitably leads to an aberrant cell behavior and commonly disease. Understanding the structure, function and interactions of these macromolecular compartments lie at the core of Cell Biology. The faculty in the Department of Cell Biology employs an interdisciplinary approach to address a broad-spectrum questions in cell biology from the roles of single molecules to through complex multicomponent cellular mechanisms to integrated studies at the organismal level in 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 eighteen primary faculty, seventeen of them with active 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 that departments offers, "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 also actively participating in teaching in new Biomedical Master Program (BMP) that was launched in 2017.

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: Alan Watson

Dr. Watson is an assistant director of the Center for Biologic Imaging (CBI) where his research program is focused around the development of platforms for rapid high-resolution imaging of whole tissues and biologic systems. Such platforms are multi-technology dependent, requiring integration of techniques and infrastructure to collect, store and process tera- even peta-scale



Cell Biology Annual Report imaging data. The resources that have been compiled at the CBI are unique, enabling the collection and processing of truly massive volumetric datasets. Dr. Watson's efforts include the development of tissue staining and clearing approaches, the refinement of confocal imaging technologies to accelerate acquisition of volumetric data, the design and maintenance of high-performance computing systems for image processing and the implementation of novel data analysis pipelines within the CBI and Pittsburgh Supercomputing Center. Several images displayed herein were generated by Dr. Watson in collaboration with researchers at the University of Pittsburgh and institutions nationally. The subject matter is interdisciplinary, including neurobiology, developmental biology, virology, ophthalmology and immunology.



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).

Cellular organization and cell-cell communications

Hong Kwiatkowski Murray Shi Stoltz St. Croix Traub Watkins

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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

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 dysregulation 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 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 microscopy through the NCRR. Furthermore, the Facility has supplemented its existing microscope and computer base with 2 new live cell imaging systems with microinjection capabilities. Currently the facility has 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.



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Dr. Alan Watson is an Assistant Professor in Cell Biology. Dr Watson's research program is directed towards the use and application of massive data methods including tissue clearing, very fast confocal and image analysis. His research focus is currently directed towards following rare events such as viral infectivity in entire tissues including brain, the ocular system, kidney, lung and bowel.

Technical Specialists: The technical bases of the Center are all trained microscopists; in total 19 technical specialists work in the center. Furthermore we have a staff of three research assistants who provide general lab maintenance and digital imaging services. These staff are responsible for the processing and experimental manipulation of materials for light and electron microscopy. They assist users directly in the application of microscopic techniques, though equally they perform complete procedures for users who are not sufficiently experienced to perform their own experiments. They are also responsible for the day-to-day running of the Center, including management of microscope usage, microscope maintenance, bookkeeping, solution preparation, etc.

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



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Cell Biology Facu [Current as of June, 2019]	llty Data	
Name	Rank	Office Address
Aridor, Meir	Associate Professor	S310 BST-South Wing
Butterworth, Michael	Associate Professor	S314 BST-South Wing

Name	Rank	Office Address	Email Address	Phone Fax	
Aridor, Meir	Associate Professor	S310 BST-South Wing	aridor@pitt.edu	412-624-1970	412-648-8330
Butterworth, Michael	Associate Professor	S314 BST-South Wing	michael7@pitt.edu	412-383-8591	412-648-8330
Devor, Daniel	Professor	S312 BST-South Wing	dd2@pitt.edu	412-383-8755	412-648-8330
Dong, Wei	Research Instructor	S333 BST-South Wing	wed16@pitt.edu	412-648-2846	412-648-8330
Drain, Peter	Associate Professor	S323 BST-South Wing	drain@pitt.edu	412-648-9412	412-648-8792
Duker, Georgia	Assistant Professor	322 Scaife Hall	gduker1@pitt.edu	412-648-9409	412-648-8330
Ford, Marijn	Assistant Professor	S326 BST-South Wing	marijn@pitt.edu	412-383-9025	412-648-8330
Ford, Natalia	Res. Asst. Professor	S355 BST-South Wing	nw@pitt.edu	412-383-9026	412-648-8330
Hammond, Gerald	Assistant Professor	S327 BST-South Wing	ghammond@pitt.edu	412-383-2215	412-648-8330
Hong, Yang	Associate Professor	S325 BST-South Wing	yhong@pitt.edu	412-648-2845	412-648-8330
Kwiatkowski, Adam	Assistant Professor	S324 BST-South Wing	adamkwi@pitt.edu	412-383-8139	412-648-8330
Leuba, Sanford	Associate Professor	2.26g Hillman Cancer Center	leuba@pitt.edu	412-623-7788	412-623-4840
Li, Yang	Research Instructor	S324 BST-South Wing	yangli@pitt.edu	412-383-7891	412-648-8330
Murray, Sandra	Professor	S313 BST-South Wing	smurray@pitt.edu	412-648-9566	412-648-8330
Pinilla Macua, Itziar	Research Instructor	S372 BST-South Wing	itp2@pitt.edu	412-624-8147	412-648-8330
Shi, Yi	Assistant Professor	9049 BST3	yi.shi@pitt.edu	412-383-3242	412-648-9009
St. Croix, Claudette	Associate Professor	S220.5 BST-South Wing	claudette.stcroix@pitt.edu	412-624-0180	412-383-8894
Sorkin, Alexander	Professor and Chair	S368 BST-South Wing	sorkin@pitt.edu	412-624-3116	412-648-8330
Stolz, Donna Beer	Associate Professor	S221 BST-South Wing	dstolz@pitt.edu	412-383-7283	412-648-8330
Surve, Sachin	Research Instructor	S372 BST-South Wing	svs23@pitt.edu	412-624-8147	412-648-8330
Tan, Xiaojun (Jay)	Res. Asst. Professor	550 Bridgeside Point Bldg.	xiaojun@pitt.edu	412-383-4405	412-648-8330
Traub, Linton	Professor	S325 BST-South Wing	traub@pitt.edu	412-648-9711	412-648-8330
Truschel, Steven	Assistant Professor	322 Scaife Hall	stt39@pitt.edu	412-648-9409	412-648-8330
Watkins, Simon C.	Distinguished Professor	S225 BST-South Wing	swatkins@pitt.edu	412-648-3051	412-383-8894
Watson, Alan	Res. Asst. Professor	S220.5 BST-South Wing	alan.watson@pitt.edu	412-648-9796	412-383-8894
Yates, Nathan	Associate Professor	9043B BST3	yatesn@pitt.edu	732-718-9739	412-648-9009



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Cell Biology Seminar Series Schedule (Fiscal Year 2018 – 2019)
<u>September 14, 2018</u> Juan Bonafacino, PhD NIH – NICHD Distinguished Investigator "AP-4 Autophagy and Hereditary Spastic Paraplegia"
<u>September 18, 2018</u> Tricia Serio, PhD Professor, Dean of the College of Natural Sciences University of Massachusetts, Amherst "Prion Biology: at the intersection of Protein Folding and Its Cellular Environment"
<u>October 2, 2018</u> Vladimir Gelfand, PhD Professor, Cell & Molecular Biology Northwestern University "Unconventional functions of conventional kinesin in ococytes and neurons"
<u>October 16, 2018</u> Ian Macara, PhD Professor and Chair, Cell & Developmental Biology Vanderbilt University "Watching Polarity Protein Dynamics in the Living Cell"
<u>October 23, 2018</u> Scott Hansen, PhD Assistant Professor, Chemistry & Biochemistry University of Oregon "Emergent properties and enzymology of membrane proximal signaling events"
<u>December 4, 2018</u> Joshua S. Chappie, PhD Assistant Professor, Molecular Medicine Cornell University "Structural characterization of nucleotide-powered molecular machines involved in bacterial defense and DNA repair"
<u>March 19, 2019</u> Aashish Manglik, MD, PhD Assistant Professor, Pharmaceutical Chemistry University of California, San Francisco "Molecular puzzles in transmembrane signaling"
<u>April 2, 2019</u> Gerald Hammond, PhD Assistant Professor, Cell Biology

University of Pittsburgh "Lipid Signals in Physiology & Cancer"

<u>April 9, 2019</u> Yi Shi, PhD Assistant Professor, Cell Biology University of Pittsburgh "Diving into the Dichotomous Humoral Immunity"

<u>April 16, 2019</u> Cara Gottardi, PhD Associate Professor, Pulmonary & Critical Care Northwestern University "Cell-cell adhesion and signaling in health and disease"

<u>April 23, 2019</u> Lan Huang, PhD Professor, Physiology & Biophysics University of California, Irvine "Cross-linking Mass Spectrometry for Interactomics and Structural Biology"

<u>April 30, 2019</u> Suzanne Hoppins, PhD Assistant Professor, Biochemistry University of Washington "Understanding the mitochondrial outer membrane fusion machine"

<u>May 7, 2019</u> Julie Brill, PhD Professor, Molecular Genetics & Director of Collaborative Program in Development Biology University of Toronto "Phosphoinositide signaling during sperm development: location, location, location"

<u>May 14,2019</u> Marijn Ford, PhD Assistant Professor, Cell Biology University of Pittsburgh "Structural insights into the SNX-BAR protein Mvp1"

<u>May 21, 2019</u> Adam Kwiatkowski, PhD Assistant Professor, Cell Biology University of Pittsburgh "Cardiomyocyte adhesion complexes and their linkage to the cytoskeleton"



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.

Associate Professor

Dr. Butterworth's research interest is in the regulation of epithelial ion transport, with a focus on the role of non-coding RNAs. Defective ion transport results in diseases such as hypertension and cystic fibrosis. To achieve plasma sodium homeostasis and modulate blood pressure, higher organisms rely on a complex signaling cascade which culminates in the release of steroid hormones that regulate sodium transport in kidney tubular epithelial cells. The role of non-coding RNAs in this regulation is being investigated by Dr. Butterworth. MicroRNAs (miRNAs) are small RNAs that pair to the mRNA of protein coding genes to direct their post-transcriptional repression. The regulation of miRNAs and other ncRNA species by steroid hormones and impact these changes have on ion channel function, sodium transport and blood pressure regulation is being studied.

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

Intermediate (KCa3.1 or IK) and small (KCa2.3 or SK3) conductance, calcium-activated potassium channels play critical roles in a host of physiological processes, including the endothelial derived hyperpolarizing factor (EDHF) response which is critical to the maintenance of vascular tone and hence blood pressure regulation, the maintenance of a hyperpolarized membrane potential across the basolateral membrane of polarized epithelia required for transepithelial fluid secretion as well as being intimately involved in the afterhyperpolarization in nerves and a host of other processes. Thus, an



understanding of the physiological and pharmacological regulation of these channels as well as their assembly, trafficking and gating is crucial to the development of novel therapies based on targeting these channels. The long-term goals of my lab are to obtain a detailed molecular understanding of these channels in order to unravel the mechanisms involved in their assembly, trafficking, regulation and gating as well as to define the physiological role these channels play using *C. elegans* as a model system. In light of these goals, we have several ongoing projects designed to further our understanding of these channels.

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

Second, as any physiological response is dictated by not only the likelihood that channels are in the open state (P₂), i.e., gating, but also the number of actively gating channels (N), it is critical to understand how the number of KCa3.1 and KCa2.3 channels at the plasma membrane is maintained and regulated. To this end, Yajuan Gao and Corina Balut, two post-doctoral associates in the lab, recently developed novel biotin ligase acceptor peptide (BLAP)-tagged KCa2.3 and KCa3.1 constructs which allow us to evaluate, in real time, the endocytic fate of these channels. Using these constructs, we have developed three separate projects. In one project, our recent data demonstrates that KCa2.3 is rapidly endocytosed and enters the recycling pathway back to the plasma membrane in a Rab35/ EPI64C (RabGAP)- and RME1-dependent manner. Indeed, our evidence points to the role of a 12 amino acid domain in the N-terminus of KCa2.3 as being critical in this process via an association with RME1. Future studies along these lines will be designed to elucidate the role of ubiquitination/ de-ubiquitination in the recycling of this channel to the plasma membrane in addition to determining the role of agonists in regulating this process. We have also recently identified the Rab5 pathway as being critical to the endocytosis of KCa2.3, whereas endocytosis and recycling are independent of the Arf6 pathway. These results point to this being a dynamin and clathrin-dependent endocytic process, although Rab5 has also been shown to be important in clathrin-independent endocytosis. The mechanism by which KCa2.3 is endocytosed will be defined using a combination of imaging, protein biochemical mutagenesis and cell biological techniques.

In a related project to the one above, we have recently demonstrated that KCa3.1 is targeted to the lysosome via the ESCRT machinery. We have recently begun to utilize tandem ubiquitin binding



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

Given that KCa3.1 is targeted to the basolateral membrane in polarized epithelia, where it plays a critical role in the generation of the electromotive driving force required for Ca²⁺-dependent agonists to stimulate Cl⁻ and fluid secretion, an additional project, being undertaken in collaboration with Dr. Kirk Hamilton at the University of Otago in Dunedin, NZ, is designed to understand the mechanisms by which this channel is correctly targeted and endocytosed in various model systems, including FRT, MDCK and LLC-PK1 cells. In this regard, we have found that KCa3.1 is correctly targeted in each of these cell lines and that, similar to our studies on HEK cells and a microvascular endothelial cell line (HMEC-1), the channel is rapidly endocytosed. Further, we have generated chimeras between the C-terminal tail of KCa3.1 and the nerve growth factor receptor (NGFR, p75) and demonstrate that the C-terminus of KCa3.1 can redirect NGFR from its typical apical localization to the basolateral membrane in polarized epithelia. Future studies will be designed to elucidate the molecular motifs involved in the basolateral targeting of this channel as well as understanding the molecular mechanisms involved in the correct targeting of this channel to the basolateral membrane.

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

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



to study the fate of these channels under more unique physiological situations, such as sheer stress.

Given our interest in understanding these channels at a tissue/model system level, Cavita Chotoo, a graduate student in the lab, in collaboration with Drs. Cliff Luke and Gary Silverman at Children's Hospital of Pittsburgh, is further defining the physiological role of one of these channels using C. *elegans* as a model system. A single *C. elegans* SK channel homologue was targeted for deletion and this KO animal displays a developmental delay phenotype. The exact nature of this phenotype is currently being studied. Cavita has also generated transgenic C. elegans lines expressing 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 secretion. In this way, the proteins whose mutation causes diabetes, the KATP channel and insulin, have a more intimate cell biological relationship and clinical pertinence than previous thought. Diabetic mutations in human insulin are used to study the beta cell biology of proinsulin trafficking, biogenesis, ER stress and protein degradation, and the consequences on insulin secretion. These investigations provide mechanistic details of the relationships between how KATP channels and insulin work together properly and fail to do so in diabetes.

(3) More recently we have found that alpha-synuclein is expressed in pancreatic beta cells, where it localizes to secretory vesicles, in addition to its well-established presence in dopaminergic and glutaminergic neurons of the brain. This has led to a new line of investigation studying the role of alpha-synuclein and how its interactions with other vesicle proteins changes under conditions of the stress leading to the hallmark degenerative cell biology that characterize these diseases.

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

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 ~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 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 Δ 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:

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

<u>2) Role of phospholipids in regulating cell polarity:</u> 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.

<u>3) Regulation of membrane targeting of polarity proteins in tumorigenesis:</u> 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 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.

Richard B. Mellon Professor and Chairman

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 wellrespected 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.

Linton M. Traub, Ph.D. 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.

Steve T. Truschel, Ph.D. Assistant Professor

My contributions to the University Of Pittsburgh School of Medicine are primarily through teaching. Since joining the department of Cell Biology and Physiology last year, I contribute as a faculty member to separate courses throughout the first year of the medical students' education. My responsibilities include lectures, problem-based learning sessions, team-based learning, microscopy laboratories, workshops, and curriculum design. I also contribute original electron micrographs to course manuals used by 1st year medical students.

Within the Department of Cell Biology and Physiology, I am the course director for the Graduate Histology course. This course is taken by the majority of our students and is a broad survey of all the organ systems, focusing on structure/function at the cellular, tissue and organ levels. Upon successful completion of this course, students may then serve as Teaching Fellows for the Histology labs within the Medical School courses. One of my roles is coordinator of the Teaching Fellows, especially to oversee their training and preparation.

Lastly, this year I have become course director for Histology and Cell Function in Health and Disease within the Biomedical Master's program. In collaboration with the Laboratory of Educational Technology, I am transforming the course curriculum by creating a virtual microscopy slide collection that will be added to the medical education Navigator website. The virtual slides are high resolution digital images that can be manipulated on a computer screen in a similar way as can be done on a microscope. Importantly, these virtual slides will be incorporated into the curricula of both the Biomedical Master's program as well as the University of Pittsburgh School of Medicine.

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.



Dr. Alan Watson. These images display brains from mice infected with Venezuelan Equine Encephalitis virus (green) via the aerosol route and perfused with microbeads (red) to display vasculature. Comparison of 72 (left) and 96 (right) hours post infection demonstrate the spread of virus from the olfactory bulbs and the breakdown of vascular flow within the brain. These data were collected in collaboration with Dr. William Klimstra from the Department of Immunology at the University of Pittsburgh.



Study Sections (Fiscal Year 2018 - 2019)
Michael Butterworth, Ph.D. Associate Professor
2019 NIH (Ad Hoc)
Adam Kwiatkowski, Ph.D. Assistant Professor
Ad hoc member, AHA Transformational Project Award Review Section
Alexander D. Sorkin, Ph.D. Richard B. Mellon Professor and Chairman
ASIRC - Italian Association for Cancer Research; Standing Member CSR Special Emphasis Panel ZRG1 CB-J (55) PAR-17-094: Maximizing Investigators' Research Award (R35) NIGMS
Claudette St. Croix, Ph.D. Associate Professor
American Heart Association Innovative Program Award Basic Sciences 2 Review Panel NIH CMT Standing Panel - Cellular and Molecular Technologies 2018/01 Temporary Member American Cancer Society - Clinical Cancer Research and Epidemiology (CCE), Standing Member
Donna B. Stolz, Ph.D. Associate Professor
NIDDK Training Grant Special Emphasis Panel, Member NIH ZGM1-RCB-9 NIGMS INBRE/COBRE grant reviews
Linton Traub, Ph.D. Professor
Ad hoc member of NIH ZRG, CSF and NRSA Study Sections
Simon C. Watkins, Ph.D. Distinguished Professor and Vice Chairman, Director of Center of Biologic Imaging
Israeli Ministry of Science and Technology grant review Invited reviewer.





Cell Biology Annual Report



Faculty Advisory Committee Memberships (Fiscal Year 2018 - 2019)

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 Committee University of Pittsburgh, School of Medicine, Integrated Systems Biology (ISB) Admission committee, PhD program.2014-2017 Biomedical Master Program (BMP) Admissions committee MSc program 2018-present Biomedical Master Program (BMP) Academic advising. 2018-present.

Michael Butterworth, Ph.D.

Associate 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

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

Marijn Ford, Ph.D. Assistant Professor

Organizer – Cell Biology Department Retreat Organizing Committee, Pittsburgh "Local Traffic" symposium Cell Biology Space Committee Institutional Biosafety Committee



Gerald Hammond, Ph.D.

Assistant Professor

Organizer – Cell Biology Department Retreat Organizing Committee, Pittsburgh "Local Traffic" symposium Cell Biology Space Committee Interdisciplinary Biomedical Graduate Program, Admissions Committee

Yang Hong, Ph.D. Associate Professor

Cell Biology Space Committee Cell Biology Faculty Recruitment Committee

Adam Kwiatkowski, Ph.D.

Assistant Professor

Cell Biology Space Committee Local Traffic Symposium Organizing Committee, Chair Associate Director, Cell Biology and Molecular Physiology Graduate Program UPSOM Student Promotions Committee

Sanford Leuba, Ph.D. Associate Professor

University Molecular Biophysics and Structural Biology Graduate Program Chair of Admissions Committee & Curriculum Committee

Sandra A. Murray, Ph.D.

Professor

Graduate School of Public Health Research Advisory Committee – Center for Minority Health Provost Advisory Committee for the Provost Development Fund Awards Morehouse College of Medicine Advisory Board Cell Biology Tenure and Promotions Committee Cell Biology Faculty Recruitment Committee Co-Chair of the Research Center of Excellence Committee, Graduate School of Public Health, University of Pittsburgh Graduate School of Public Health Community Engagement Research Core University Community Representative for Equipoise Junior Faculty Advancement – Panel Member



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 Masters Program Executive Committee
Claudette St. Croix, Ph.D. Associate Professor
Cell Biology Faculty Recruitment Committee
Donna Beer Stolz, Ph.D. Associate Professor
University of Pittsburgh School of Medicine Interdisciplinary Biomedical Graduate Program- Cell Biology and Molecular Physiology Program Admissions Committee Assistant Director - Cell Biology and Molecular Physiology Program School of Medicine Tenured Faculty Promotions and Appointments Committee
Linton M. Traub, Ph.D. Professor
University of Pittsburgh School of Medicine Health Sciences Research Advisory Committee Cell Biology Tenure and Promotions Committee Cell Biology Faculty Recruitment 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



Cell Biology Spo	insored Research Fund.	ing (FY19)		
Name	Agency Name	Title	Annual DC	Annual IDC
Michael Butterworth	National Institutes of Health	Role of MicroRNAs in kidney sodium regulation	216,384	116,848
Michael Butterworth	National Institutes of Health	Altered Biosynthesis and Function of ABCC6 in Systemix Mineralization Disorders	14,138	7,970
Marijn Ford	National Institutes of Health	The Roles of the Dynamin-Related Protein Vps1 and the ESCRT Complex in Microautophagy	193,752	99,936
Gerry Hammond	National Institutes of Health	Directing Membrane Function with Inositol Lipids in Health and Disease	242,237	136,685
Yang Hong	National Institutes of Health	Membrane Targeting and Retargeting of Polarity Proteins	196,500	106,228
Adam Kwiatkowski	National Institutes of Health	Alpha-Catenin Function in Cardiomyocyte Adhesion and Cytoskeletal Organization	236,158	125,503
Mads Larsen	National Institutes of Health	Cystic Fibrosis Foundation (Betrand)	30,491	
Mads Larsen	National Institutes of Health	Selective Steps in Wild-Type and F508del CFTR Processing (PI - Frizzell)	3,652	292
Sanford Leuba	National Institutes of Health	NNRTI Induced Conformational Changes in HIV 1 RT (Sluis-Cremer)	4,568	2,467
Sanford Leuba	National Institutes of Health	Novel Mechanisms of HIV Resistance to RTIS (Sluis-Cremer)	5,356	2,893
Sanford Leuba	National Institutes of Health	Evolved DNA Contacts Required for Hexameric Helicase Unwinding.	42,860	24,178
Chelsea Merkel	National Institutes of Health	The Role of Vinculin in Cardiomyocyte Adhesion and Mechanical Continuity	44,158	ı
Yi Shi	National Institutes of Health	Mechanisms of Signaling Protein Retention in the Primary Cilium	3,867	2,185
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer	63,898	36,102
Alexander Sorkin	US Dept of Veterans Affairs	Investigating the Role of TMEM16A/AN01 in SCCHN	5,801	ı
Alexander Sorkin	National Institutes of Health	Exosome Based Placental Maternal Communication	46,059	25,831
Alexander Sorkin	National Institutes of Health	Modeling Spatiotemporal Control of EGFR-ERK Signaling in Gene-Edited Cell Systems	116,895	65,945
Alexander Sorkin	National Institutes of Health	Signaling by them EGF Receptor from Endosomes	208,139	117,477
Alexander Sorkin	National Institutes of Health	Regulation of Dopamine Transporter by Trafficking	260,438	132,744
Claudette St. Croix	National Institutes of Health	In Vivo Localization and Mechanism of Regulatory B Cell Function in All immunity and Transplant Tolerance	8,846	4,777
Claudette St. Croix	National Institutes of Health	Pulmonary Arteriole Occlusion by Platelet Neutrohil micro emboli in acute chest syndrome	25,414	2,529
Claudette St. Croix	National Institutes of Health	Pathogenic Mechanisms of Gene-Environment Interactions in Parkinsons Disease	2,917	1,575
Claudette St. Croix	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lung Injury	5,314	2,870
Claudette St. Croix	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Preclinical Assessment Core	68,013	38,428
Claudette St. Croix	National Institutes of Health	Signaling Mechanisms by which Mitochondria Regulates Fibrosis in the Lung	4,496	2,428
Claudette St. Croix	National Institutes of Health	Reactive Oxygen Species in Vascular Disease	8,236	4,448
Claudette St. Croix	National Institutes of Health	Anti-Inflammatory Lipid Mediators in Asthma	8,575	4,845
Claudette St. Croix	National Institutes of Health	Vascular Smooth Muscle and Blood Pressure Regulation By cyb5R2	7,505	4,231
Claudette St. Croix	National Institutes of Health	Novel Role of Smooth Muscle B5 Reductase in Sickle Cell Disease	4,523	2,551
Claudette St. Croix	National Institutes of Health	Aging of Mesenchymal Stem cells Missing Link in IPF	6,984	3,771

CB Sponsored Research Funding

Claudette St. Croix	National Institutes of Health	Regulation of Fuel Utilization by Lysine Acetylation in the Failing Heart	3,625	2,043
Claudette St. Croix	National Institutes of Health	Exploring and Exploiting Metabolic Plasticity in Regulatory T Cells	8,925	5,031
Claudette St. Croix	National Institutes of Health	The Anti-Aging Role of Klotho in Skeletal Muscle Regeneration	27,601	9,932
Claudette St. Croix	National Institutes of Health	Host Control Mechanisms Against K. Pneumoniae Infection in the Lungs	25,943	14,610
Claudette St. Croix	National Institutes of Health	Mechanisms of Myocardial-Infarction Induced Insulin Resistance	12,166	6,846
Claudette St. Croix	National Institutes of Health	Mechanisms and Promotion of Immune Regulation by CD4+	14,232	5,209
Claudette St. Croix	National Institutes of Health	Mechanism-Directed Sequential Delivery of Radiation Mitigators Imaging Radiation Apathology Core	5,255	2,838
Claudette St. Croix	National Institutes of Health	Biological and Physical Mechanisms of Ultrasound/Microbubble-Mediated Therapeutic Gene Delivery Across the Endothelial Barrier	22,358	8,395
Claudette St. Croix	National Institutes of Health	Obesity-associated Mitophagy Resistance	16,181	9,143
Claudette St. Croix	National Institutes of Health	The Role of Telomerase in Valvular Calcification	3,312	1,871
Claudette St. Croix	American Heart Association	Reprogramming of the Vascular Matrisome and Matrix Cellularity as a Pathogenic Lynchpin for Pulmonary Hypertension	3,331	334
Claudette St. Croix	National Institutes of Health	The Function of EGFL6 in Ovarian Cancer Cell Biology, Tumor Initiation, and Therapy	3,347	1,891
Claudette St. Croix	Pitt Foundation	PET imaging of vaso-occlusion in sickle cell disease: from mice to humans	5,666	
Claudette St. Croix	National Institutes of Health	Mechanisms of platelet exosome-mediated acute chest syndrome in sickle cell disease	6,168	2,849
Claudette St. Croix	National Institutes of Health	Epigenetic Control of Smooth Muscle Cell Phenotype during Microvascular Remodeling	2,421	803
Donna Beer Stolz	National Institutes of Health	Mechanisms of Arsenic-induced Muscle Morbidity and Reduced Regenerative Capacity (PI - Bar- chowsky)	4,036	2,240
Donna Beer Stolz	National Institutes of Health	Mechanisms of Trabecular Meshwork Regeneration by Stem Cell (PI - Du)	10,040	3,884
Donna Beer Stolz	National Institutes of Health	Critical Role for Fibroblast Growth Factor Receptors in Bladder Development (PI - Bates)	6,638	3,585
Donna Beer Stolz	National Institutes of Health	Dysfunctional Muscle remodeling and regeneration in environmental disease (PI - Ambrosio/Bar- chowsky)	24,025	13,518
Donna Beer Stolz	National Institutes of Health	Elucidating Mechanisms Involved in Lamin B1 Mediated Demyelination (PI - Padiath)	4,405	2,380
Donna Beer Stolz	National Institutes of Health	Endogenous Regulators of Inflammation in Liver Ischemia/Reperfusion (PI - Tsung)	5,383	1,561
Donna Beer Stolz	National Institutes of Health	Luminal Epithelial Junctions, Polarity and Permeability in BPH (PI - Wang)	823	374
Donna Beer Stolz	National Institutes of Health	Luminal Epithelial Junctions, Polarity and Permeability in BPH (PI - Wang)	8,867	4,298
Donna Beer Stolz	National Institutes of Health	Alpha Catenin Function in Cardiomyocyte adhesion and Cytoskeletal (PI - Kwiatkowski)	8,264	4,463
Donna Beer Stolz	National Institutes of Health	Characterization of Meiotic Crossover Surveillance System (PI - Yanowitz)	7,243	4,092
Donna Beer Stolz	National Institutes of Health	Core G: Signature-Directed, Sequential Delivery of Radiation Mitigators (PI - Greenberger)	11,062	5,973
Donna Beer Stolz	National Institutes of Health	Melatonin Biosynthesis in Neuronal Mitochondria - (PI - Friedlander)	4,222	2,386

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Donna Beer Stolz	National Institutes of Health	Fox01 in Beta-Cell Compensation (PI - Dong)	3,483	1,968
Donna Beer Stolz	National Institutes of Health	Biological and Physical Mechanisms of Ultrasound/Microbubble-Mediated Therapeutic Gene Deliv- ery Across the Endothelial Barrier (PI - Villaneuva)	2,007	1,134
Donna Beer Stolz	National Institutes of Health	Correcting Pathogenic TGF beta Activity in the Airway	4,053	1,982
Donna Beer Stolz	National Institutes of Health	Progressive degenerative role of Nox and thrombospondin-1 in the aging vasculature	2,126	1,201
Linton Traub	National Institutes of Health	Clathrin-coated Vesicles and Endocytic Function	23,098	8,433
Steven Truschel	National Institutes of Health	Bladder Mucosal Dysfunction During Aging	29,190	16,492
Simon Watkins	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lung Injury	45,190	21,703
Simon Watkins	National Institutes of Health	Biomimetric surface for neural implants	5,447	2,941
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	81,261	43,882
Simon Watkins	National Institutes of Health	Inhibition of Neural Electrode-Mediated Inflammation and Neuronal Cell Death	9,351	4,753
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	9,315	5,103
Simon Watkins	National Institutes of Health	Exosomes as paracrine signal mediators in cardiac allograft rejection	17,157	7,511
Simon Watkins	National Institutes of Health	Inhibition of the ALT Pathway by Interfering with Poly-ADP-Ribose Metabolism	15,626	5,573
Simon Watkins	National Institutes of Health	T Cell Memory in Organ Transplantation	8,414	4,544
Simon Watkins	National Institutes of Health	Pittsburgh Center for Kidney Research	1,250	644
Simon Watkins	National Institutes of Health	BMP10 in Cardiovascular Development and Hereditary Hemorrhagic Telangiectasia.	10,207	3,705
Simon Watkins	National Institutes of Health	Regulated Activation of latent-TGfB Determines Leukocyte Occupancy of the Epidermal Niche	2,500	ı
Simon Watkins	National Institutes of Health	Mechanistic Elucidation and Targeted Therapy of Platelet Dysfunction After Trauma (Neal)	12,262	6,917
Simon Watkins	National Institutes of Health	B Cells in the Pathogenesis of Allograft Rejection (Chalasani)	7,007	3,912
Simon Watkins	National Institutes of Health	Improving cerebral aneurysm risk assessment through understanding wall vulnerability and failure models	17,218	8,863
Simon Watkins	National Institutes of Health	Blue Light Protects against Ischemia Induced Organ Injury (Rosengart)	1,864	1,053
Simon Watkins	National Institutes of Health	Genetics of Extracellular Matrix in Health and Disease (Urban)	6,311	1,968
Simon Watkins	National Institutes of Health	ROS driven mitochondrial-telomere dysfunction during environmental stress-	43,833	24,427
Simon Watkins	National Institutes of Health	Mechanisms of HMGB1 Release from Ischemic Muscle in Peripheral Arterial Disease (Hartman)	13,337	7,514
Simon Watkins	National Institutes of Health	Signaling by the EGF Receptor from Endosomes	11,860	6,686
Simon Watkins	National Institutes of Health	A Confocal fluorescence Microscopy Brain Data Archive	33,333	18,884
Simon Watkins	National Institutes of Health	Structure and Activation of Multiprotein Signaling Complex (PI Vignali)	13,434	4,199
Simon Watkins	National Institutes of Health	Benzodiazepine Treatment Induced Neuroplasticity	7,008	3,922
Simon Watkins	National Institutes of Health	Mechanisms of HMGB1 Release from Ischemic Muscle in Peripheral Arterial disease	8,847	3,264
Simon Watkins	National Institutes of Health	Surgery Triggered Immune Response and Liver Matastases	5,853	3,278
Simon Watkins	National Institutes of Health	Caspace-1 and Inflammasome Activation in Traumahemorrhagic Shock	20,068	7,913




Simon Watkins Simon Watkins	National Institutes of Health National Institutes of Health	Illuminating Metabolic Pathways Enabled by Early T Cell Activation Lipid Imaging in Traumatic Brain Injury by High Resolution GCIB-Secondary Ion Mass Spectrom- etry	11,893 9,999	6,710 5,649
Simon Watkins	National Institutes of Health	Core G: signature-directed sequential delivery	130,832	63,027
Simon Watkins	National Institutes of Health	Pittsburgh Center for HIV Protein Interactions (PCHPI) Gronenborn-	23,750	13,200
Simon Watkins	National Institutes of Health	Mechanisms of Immune Dysfunction After Trauma and Surgical Sepsis	20,240	9,726
Simon Watkins	National Institutes of Health	HIV-Reservoir in Naïve CD+T Cells	25,611	12,210
Simon Watkins	National Institutes of Health	Damage Sensor role of UV-DDB during base excision repair	9,778	5,524
Simon Watkins	National Institutes of Health	Lipid Imaging in Traumatic Brain Injury by High Resolution GCIB-Secondary Ion Mass Spectrom- etry	18,420	10,407
Simon Watkins	National Institutes of Health	Project 1 for SSC Cort	8,333	4,625
Simon Watkins	National Institutes of Health	IFITM-Mediated Virus Restriction	25,089	12,594
Simon Watkins	National Institutes of Health	Pgh Center for Kidney research	5,210	2,944
Simon Watkins	National Institutes of Health	Exploring Antisense Oligonucleotides as potential therapy for autosomal dominant	24,989	14,118
Simon Watkins	National Institutes of Health	Molecular Mechanisms of Eastern Equic Encephalitis Virus Pathogenesis	25,850	11,780
Simon Watkins	National Institutes of Health	Engineering Biologic Topography into Vascular Grafts	20,203	8,758
Simon Watkins	National Institutes of Health	Role of the Snail1-Twist-p21 axis on cell cycle arrest and renal fibrosis development	20,746	6,670
Simon Watkins	National Institutes of Health	Role of RAN peptides in polyQ-Independent Toxicity in a new C. Elgans Model	6,074	2,701
Simon Watkins	National Institutes of Health	Structure, Function and Mechanistic Analysis of LAG3	22,009	6,785
Simon Watkins	National Institutes of Health	Adult Stem Cell-Based Enhancement of Nerve Conduit for Peripheral Nerve Repair (McMann)	800	432
Simon Watkins	National Institutes of Health	Visualizing Synaptic Connection Between Distinct Cell types in Whole Mouse Brain (Bruchez)	79,762	39,326
Simon Watkins	National Institutes of Health	Targeting Host Responses to Prevent Virus Induced ARDS in the Nonhuman primate model	10,966	6,131
Simon Watkins	Cystic Fibrosis Foundation	Cell and Tissue Imaging Core C	38,014	ı
Simon Watkins	American Cancer Society	Epstein-Barr Virus Oncogenesis in Nasopharyngeal Carcinoma	11,256	2,251
Simon Watkins	National Institutes of Health	Center for Biological Imaging - Biogen - Gutstein	12,500	ı
Alan Watson	National Institutes of Health	Closed-Loop Neuroelectric Control of Meesis and Gastric Motility (supplement 1)	20,165	1,971
Alan Watson	National Institutes of Health	ENSMAP: Molecular and Functional Mapping of the Enteric Nervous System (Southard-Smith PI)	17,290	9,773
Nathan Yates	National Institutes of Health	Plasticity of Auditory Cortical Circuits in Schizophrenia	8,790	4,747
Nathan Yates	National Institutes of Health	Regulation of Fuel Utilization by Lysine Acetylation in the Falling Heart	17,744	9,998
Nathan Yates	National Institutes of Health	Alzheimer's Disease Research center-funding	11,772	6,356
Nathan Yates	National Institutes of Health	Novel Approaches to Enhance Tumor Cell Cytotoxicity of Alkylating Agents	33,957	10,690
Nathan Yates	National Institutes of Health	The Metabolic Evolution of Staphylococcus Aureus	11,860	6,685
Nathan Yates	American Heart Association	Defining the Systems Biology of the Vascular Matrix in Pulmonary Hypertension	2,237	224



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11,886	52,412	20,833	4,908	5,948	15,940	33,330	3,045,019			
Mechanisms by Which Cyanotriazoles Activate Latent HIV	Physiological Biomarkers of Resilience and Musculoskeletal Readiness	Chemokine CXCL 12/CXCR4 System and Synthetic Cathinones	Synaptic Resilience to Psychosis in Alzheimer Disease	Liver-enriched Transcription Factors as Prognostic markers and Therapeutic Targets in Alcoholic Hepatitis	A New Map to Recovery in Schizophrenia	Discovering the Protein Signature of Synapse Loss and Cognitive Decline During Aging				
National Institutes of Health	Department of Defense	National Institutes of Health	National Institutes of Health	National Institutes of Health	NARSAD	UPMC ITTC				
Nathan Yates	Nathan Yates	Nathan Yates	Nathan Yates	Nathan Yates	Nathan Yates	Nathan Yates				



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Name	Agency Name	Title	Annual DC	Annual IDC
Michael Butterworth	National Institutes of Health	Role of MicroRNAs in kidney sodium regulation	179,404	96,878
Michael Butterworth	National Institutes of Health	Altered Biosynthesis and Function of ABCC6 in Systemix Mineralization Disorders	8,139	4,600
Marijn Ford	National Institutes of Health	The Roles of the Dynamin-Related Protein Vps1 and the ESCRT Complex in Microautophagy	193,752	99,936
Gerry Hammond	National Institutes of Health	Directing Membrane Function with Inositol Lipids in Health and Disease	249,404	140,914
Yang Hong	National Institutes of Health	Membrane Targeting and Retargeting of Polarity Proteins	196,500	106,582
Adam Kwiatkowski	National Institutes of Health	Alpha-Catenin Function in Cardiomyocyte Adhesion and Cytoskeletal Organization	233,866	124,235
Sanford Leuba	National Institutes of Health	Evolved DNA Contacts Required for Hexameric Helicase Unwinding.	42,141	23,810
Chelsea Merkel	National Institutes of Health	The Role of Vinculin in Cardiomyocyte Adhesion and Mechanical Continuity	8,181	
Yi Shi	National Institutes of Health	Mechanisms of Signaling Protein Retention in the Primary Cilium	15,586	8,055
Yi Shi	UPMC	Novel Tools to Study Mitochondria and Postsynaptic Densities in Aging	20,000	
Yi Shi	MJFF	Gaining Access to the Brain: Robust Integrative Proteomics to Produce Novel, Highly Potent Blood- Brain Barrier (BBB)	293,856	29,386
Alexander Sorkin	National Institutes of Health	Pathogenesis of Cancer	211,672	111,823
Alexander Sorkin	National Institutes of Health	Exosome Based Placental Maternal Communication	45,626	25,779
Alexander Sorkin	National Institutes of Health	Modeling Spatiotemporal Control of EGFR-ERK Signaling in Gene-Edited Cell Systems	116,400	65,767
Alexander Sorkin	National Institutes of Health	Signaling by them EGF Receptor from Endosomes	207,967	117,378
Alexander Sorkin	National Institutes of Health	Regulation of Dopamine Transporter by Trafficking	234,912	118,782
Claudette St. Croix	National Institutes of Health	In Vivo Localization and Mechanism of Regulatory B Cell Function in All immunity and Transplant Tolerance	4,483	2,421
Claudette St. Croix	National Institutes of Health	Pulmonary Arteriole Occlusion by Platelet Neutrohil micro emboli in acute chest syndrome	23,867	1,912
Claudette St. Croix	National Institutes of Health	Vascular Subphenotypes of Lung Disease - Preclinical Assessment Core	68,014	38,428
Claudette St. Croix	National Institutes of Health	Signaling Mechanisms by which Mitochondria Regulates Fibrosis in the Lung	4,623	2,496
Claudette St. Croix	National Institutes of Health	Anti-Inflammatory Lipid Mediators in Asthma	8,855	5,003
Claudette St. Croix	National Institutes of Health	Vascular Smooth Muscle and Blood Pressure Regulation By cyb5R2	7,632	4,312
Claudette St. Croix	National Institutes of Health	Novel Role of Smooth Muscle B5 Reductase in Sickle Cell Disease	4,517	2,552
Claudette St. Croix	National Institutes of Health	Regulation of Fuel Utilization by Lysine Acetylation in the Failing Heart	3,707	2,094
Claudette St. Croix	National Institutes of Health	Exploring and Exploiting Metabolic Plasticity in Regulatory T Cells	9,194	5,195
Claudette St. Croix	National Institutes of Health	The Anti-Aging Role of Klotho in Skeletal Muscle Regeneration	27,998	10,170
Claudette St. Croix	National Institutes of Health	Host Control Mechanisms Against K. Pneumoniae Infection in the Lungs	25,920	14,645
Claudette St. Croix	National Institutes of Health	Mechanisms of Myocardial-Infarction Induced Insulin Resistance	12,075	6,823
Claudette St. Croix	National Institutes of Health	Mechanisms and Promotion of Immune Regulation by CD4+	14,241	5,220
Claudette St. Croix	National Institutes of Health	Mechanism-Directed Sequential Delivery of Radiation Mitigators Imaging Radiation Apathology	6,429	3,472



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Claudette St. Croix	National Institutes of Health	Biological and Physical Mechanisms of Ultrasound/Microbubble-Mediated Therapeutic Gene Deliv- ery Across the Endothelial Barrier	29,830	11,768
Claudette St. Croix	National Institutes of Health	Obesity-associated Mitophagy Resistance	15,060	8,509
Claudette St. Croix	National Institutes of Health	The Role of Telomerase in Valvular Calcification	3,792	2,143
Claudette St. Croix	American Heart Association	Reprogramming of the Vascular Matrisome and Matrix Cellularity as a Pathogenic Lynchpin for Pulmonary Hypertension	3,334	334
Claudette St. Croix	National Institutes of Health	The Function of EGFL6 in Ovarian Cancer Cell Biology, Turnor Initiation, and Therapy	5,856	3,299
Claudette St. Croix	Pitt Foundation	PET imaging of vaso-occlusion in sickle cell disease: from mice to humans	11,672	,
Claudette St. Croix	National Institutes of Health	Mechanisms of platelet exosome-mediated acute chest syndrome in sickle cell disease	24,753	11,443
Claudette St. Croix	National Institutes of Health	Epigenetic Control of Smooth Muscle Cell Phenotype during Microvascular Remodeling	9,713	3,228
Claudette St. Croix	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lune Injury	74,824	39,451
Claudette St. Croix	National Institutes of Health	Role of Necroptosis in Colorectal Cancer Therapy	11,392	6,436
Claudette St. Croix	National Institutes of Health	Tead1 and Cardiac Adaptation	10,000	3,390
Claudette St. Croix	Department of Defense	Neomorphic cell-cell adhesive reprogramming facilitates metastasis of ESR1 mutant breast cancer	8,333	4,708
Claudette St. Croix	National Institutes of Health	Endothelial Reprogramming in Pulmonary Hypertension	9,955	3,930
Claudette St. Croix	National Institutes of Health	Role of extracellular matrix in age-related declines of muscle regeneration	25,969	10,151
Claudette St. Croix	National Institutes of Health	Inhibition of DNA double strand break repair in TNBC by nitro-fatty acids	7,697	4,348
Donna Beer Stolz	National Institutes of Health	Mechanisms of Trabecular Meshwork Regeneration by Stem Cell (PI - Du)	10,049	3,898
Donna Beer Stolz	National Institutes of Health	Dysfunctional Muscle remodeling and regeneration in environmental disease (PI - Ambrosio/Bar- chowsky)	24,786	13,744
Donna Beer Stolz	National Institutes of Health	Elucidating Mechanisms Involved in Lamin B1 Mediated Demyelination (PI - Padiath)	5,149	2,780
Donna Beer Stolz	National Institutes of Health	Luminal Epithelial Junctions, Polarity and Permeability in BPH (PI - Wang)	9,584	4,777
Donna Beer Stolz	National Institutes of Health	Alpha Catenin Function in Cardiomyocyte adhesion and Cytoskeletal (PI - Kwiatkowski)	8,523	4,602
Donna Beer Stolz	National Institutes of Health	Characterization of Meiotic Crossover Surveillance System (PI - Yanowitz)	8,952	5,058
Donna Beer Stolz	National Institutes of Health	Core G: Signature-Directed, Sequential Delivery of Radiation Mitigators (PI - Greenberger)	13,531	7,307
Donna Beer Stolz	National Institutes of Health	Melatonin Biosynthesis in Neuronal Mitochondria - (PI - Friedlander)	5,222	2,950
Donna Beer Stolz	National Institutes of Health	Fox01 in Beta-Cell Compensation (PI - Dong)	697	394
Donna Beer Stolz	National Institutes of Health	Biological and Physical Mechanisms of Ultrasound/Microbubble-Mediated Therapeutic Gene Deliv- ery Across the Endothelial Barrier (PI - Villaneuva)	2,971	1,682
Donna Beer Stolz	National Institutes of Health	Correcting Pathogenic TGF beta Activity in the Airway (PI - Swiatecka Urban)	9,872	4,831
Donna Beer Stolz	National Institutes of Health	Progressive degenerative role of Nox and thrombospondin-1 in the aging vasculature (PI - Pagano)	8,581	4,848
Donna Beer Stolz	National Institutes of Health	Cardiolipin as a Novel Mediator of Acute Lune Injury (PI- Mallampalli)	23,885	13,495
Donna Beer Stolz	National Institutes of Health	Mechanisms of hypersensitivity to sound-induced cochlear damage (Rubio)	9,419	4,418
Donna Beer Stolz	National Institutes of Health	Advanced Imaging Core A)	94,797	45,085

CB Sponsored Research Funding



Donna Beer Stolz	National Institutes of Health	Beta-catenin-driven hepatobiliary reprogramming as a therapeutic modality for cholangiopathies	5,716	3,229
Linton Traub	National Institutes of Health	Protein Mechanics Regulating Endocytic Clathrin Coat	167,795	85,825
Steven Truschel	National Institutes of Health	Bladder Mucosal Dysfunction During Aging	37,516	21,197
Simon Watkins	National Institutes of Health	Cancer Center Support Grant	82,665	43,946
Simon Watkins	National Institutes of Health	Inhibition of Neural Electrode-Mediated Inflammation and Neuronal Cell Death	9,840	4,331
Simon Watkins	National Institutes of Health	DNA Damage Recognition by Nucleotide Excision Repair Proteins	9,173	5,160
Simon Watkins	National Institutes of Health	Exosomes as paracrine signal mediators in cardiac allograft rejection	9,505	4,503
Simon Watkins	National Institutes of Health	Inhibition of the ALT Pathway by Interfering with Poly-ADP-Ribose Metabolism	15,720	5,624
Simon Watkins	National Institutes of Health	BMP10 in Cardiovascular Development and Hereditary Hemorrhagic Telangiectasia.	10,318	3,852
Simon Watkins	National Institutes of Health	Regulated Activation of latent-TGfB Determines Leukocyte Occupancy of the Epidermal Niche	2,500	
Simon Watkins	National Institutes of Health	Mechanistic Elucidation and Targeted Therapy of Platelet Dysfunction After Trauma (Neal)	12,262	6,917
Simon Watkins	National Institutes of Health	B Cells in the Pathogenesis of Allograft Rejection (Chalasani)	7,138	4,033
Simon Watkins	National Institutes of Health	Improving cerebral aneurysm risk assessment through understanding wall vulnerability and failure models	22,236	12,563
Simon Watkins	National Institutes of Health	ROS driven mitochondrial-telomere dysfunction during environmental stress-	44,578	25,187
Simon Watkins	National Institutes of Health	Mechanisms of HMGB1 Release from Ischemic Muscle in Peripheral Arterial Disease (Hartman)	13,322	7,527
Simon Watkins	National Institutes of Health	Signaling by the EGF Receptor from Endosomes	12,071	6,819
Simon Watkins	National Institutes of Health	A Confocal fluorescence Microscopy Brain Data Archive	40,000	22,660
Simon Watkins	National Institutes of Health	Structure and Activation of Multiprotein Signaling Complex (PI Vignali)	13,398	4,304
Simon Watkins	National Institutes of Health	Mechanisms of HMGB1 Release from Ischemic Muscle in Peripheral Arterial disease	8,942	3,360
Simon Watkins	National Institutes of Health	Caspace-1 and Inflammasome Activation in Traumahemorrhagic Shock	18,159	6,869
Simon Watkins	National Institutes of Health	Mechanisms of Immune Dysfunction After Trauma and Surgical Sepsis	21,307	10,344
Simon Watkins	National Institutes of Health	Illuminating Metabolic Pathways Enabled by Early T Cell Activation	11,893	6,711
Simon Watkins	National Institutes of Health	Damage Sensor role of UV-DDB during base excision repair	12,486	7,054
Simon Watkins	National Institutes of Health	Lipid Imaging in Traumatic Brain Injury by High Resolution GCIB-Secondary Ion Mass Spectrom- etry	17,776	10,043
Simon Watkins	National Institutes of Health	HIV-Reservoir in Naive CD4 + T Cells (PI - Sluis -Cremer)	2,134	1,018
Simon Watkins	National Institutes of Health	IFITM-Mediated Virus Restriction	26,688	11,152
Simon Watkins	National Institutes of Health	Pgh Center for Kidney research	5,237	2,959
Simon Watkins	National Institutes of Health	Exploring Antisense Oligonucleotides as potential therapy for autosomal dominant	4,867	2,750
Simon Watkins	National Institutes of Health	Visualization of Influenza Viral RNA Assembly (PI - Lakdowala)	10,187	4,344
Simon Watkins	National Institutes of Health	Engineering Biologic Topography into Vascular Grafts	24,244	10,510
Simon Watkins	National Institutes of Health	Molecular Mechanisms of Eastern Equic Encephalitis Virus Pathogenesis	26,173	11,962
Simon Watkins	National Institutes of Health	Project 1 for SSC Cort	10,000	5,566

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SIMON WALKINS	Nalional Insulutes of health	Kole of the Shall I-I Wis-PZT axis on cell cycle artest and rehal liprosis development	11,110
Simon Watkins	National Institutes of Health	Benzodiazepine Treatment Induced Neuroplasticity (PI - Jacob) 7,152	4,042
Simon Watkins	National Institutes of Health	Role of RAN peptides in polyQ-Independent Toxicity in a new C. Elgans Model 14,578	6,483
Simon Watkins	National Institutes of Health	Structure, Function and Mechanistic Analysis of LAG3 44,018	13,570
Simon Watkins	National Institutes of Health	Excision Repair of environmental Telomere Damage 34,880	19,707
Simon Watkins	National Institutes of Health	NitriteTherapy to Improve Mitochondrial Energetics 15,138	4,553
Simon Watkins	National Institutes of Health	Administrative Supplement to Bladder Mucosal Dysfunction during Aging (PI Birder) 18,460	10,430
Simon Watkins	National Institutes of Health	Immunity to Live Mosquito Probing and Flavivirus Infection in Human Skin (Barratt Boyes - PI) 2,387	1,349
Simon Watkins	National Institutes of Health	Pittsburgh Center for HIV Protein Interactions (PCHPI) Gronenborn-	13,201
Simon Watkins	National Institutes of Health	Core G: signature-directed sequential delivery 103,757	48,468
Simon Watkins	National Institutes of Health	Visualizing Synaptic Connection Between Distinct Cell types in Whole Mouse Brain (Bruchez - CMU subcontract)	40,228
Simon Watkins	National Institutes of Health	Targeting Host Responses to Prevent Virus-Induced ARDS in the Nonhuman primate model 11,023	6,228
Simon Watkins	National Institutes of Health	Seal r01 renewal 10,000	4,803
Simon Watkins	National Institutes of Health	Placental Extracellular vesicles 10,000	4,803
Simon Watkins	National Institutes of Health	DNA Damage Signaling 49,977	28,287
Simon Watkins	National Institutes of Health	Understanding & Countering Mechanisms Underlying IL-33_driven support of Graf vs host disease 14,678	3,208
Simon Watkins	National Institutes of Health	ROS Mechanisms in BAV Aortopathy 7,101	2,529
Simon Watkins	National Institutes of Health	Targeting the Chemokine System to Sensitize Tumors to Immunotherapy 50,249	28,391
Alan Watson	National Institutes of Health	Closed-Loop Neuroelectric Control of Meesis and Gastric Motility (supplement 1) 20,000	,
Alan Watson	National Institutes of Health	U54 Pilot Project - A comprehensive Approach to Imaging Benign rostatic Hyperplasia (BPH) 70,000 (Wang PI)	28,251
Alan Watson	National Institutes of Health	ENSMAP: Molecular and Functional Mapping of the Enteric Nervous System (Southard-Smith PI) 24,205	13,677
Alan Watson	National Institutes of Health	Atlas of Autonomic and Neuormodulatory Lineages in the Developing Lower Urinary Tract 29,952	16,923
Alan Watson	National Institutes of Health	Contribution of Sympathetic Nerves to Herpes Stromal Keratitis	12,340
Alan Watson	National Institutes of Health	Understanding Functional Connectivity of Sensory and Motor Pathways to Specific Regions of the 62,137 Lower Uninary Tract	35,107
Nathan Yates	National Institutes of Health	Regulation of Fuel Utilization by Lysine Acetylation in the Falling Heart	9,938
Nathan Yates	National Institutes of Health	Alzheimer's Disease Research center-funding 8,945	4,830
Nathan Yates	National Institutes of Health	Novel Approaches to Enhance Tumor Cell Cytotoxicity of Alkylating Agents 13,819	7,807
Nathan Yates	National Institutes of Health	The Metabolic Evolution of Staphylococcus Aureus 11,897	6,722
Nathan Yates	National Institutes of Health	Mechanisms by Which Cyanotriazoles Activate Latent HIV 8,945	5,054
Nathan Yates	Department of Defense	Physiological Biomarkers of Resilience and Musculoskeletal Readiness	17,183

28,736 4,071 224 223 - 2,227,553	Cell E Annu
50,861 7,205 397 50,995 4,675,130	tiology al Report
Synaptic Resilience to Psychools in Alzheimer Disease Liver-anriched Transcription Factors as Prognostic markers and Therapeutic Targets in Alcoholic Hepatits Omega-3. Isoflavones & Amyloid Deposition in Cognitively E R and post-ER quality control of integral membrane proteins Discovering the Protein Signature of Synapse Loss and Cognitive Decline During Aging	
National Institutes of Health National Institutes of Health National Institutes of Health UPMC	
Nathan Yates Nathan Yates Nathan Yates Nathan Yates	43

CB Sponsored Research Funding



Faculty Editorships (Fiscal Year 2018 - 2019)
Michael B. Butterworth, Ph.D. Associate Professor
American Journal of Physiology – Renal Physiology Frontiers in Renal and Epithelial Physiology PLoS ONE Physiological Genomics American Journal of Physiology – Cell Physiology
Adam Kwiatkowski, Ph.D. Assistant Professor
Associate Editor, BMC Cell Biology
Alexander D. Sorkin, Ph.D. Richard B. Mellon Professor and Chair
Traffic, Associate Editor Scientific Reports (Nature) Editorial Board
Linton Traub, Ph.D. 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
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







Dr. Alan Watson. Super resolution (~150 nanometer) reconstruction of neurofilament staining across the complete neuronal system of a 5 days post fertilization zebrafish embryo. Super resolution imagery was achieved by using novel tissue expansion techniques developed by Dr. Yongxin (Leon) Zhao at Carnegie Mellon University and imagery was captured using ribbon scanning confocal microscopy. Dr. Ed Burton from the Department of Neurology at the University of Pittsburgh provided the zebrafish embryo.













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CELL BIOLOGY FACULTY ROSTER (Effective June, 2019)

	<u>Salary</u>		
	<u>Support on</u>		
Faculty Member	<u>Grants</u>	<u>Rank</u>	<u>Status</u>
Dong, Wei	100%	Research Instructor	Non-tenure Track
Li, Yang	100%	Research Instructor	Non-tenure Track
Pinilla Macua, Itziar	100%	Research Instructor	Non-tenure Track
Surve, Sachin	100%	Research Instructor	Non-tenure Track
Tan, Xiaojun	100%	Res. Assistant Professor	Non-tenure Track
Watson, Alan	100%	Res. Assistant Professor	Non-tenure Track
Watkins, Simon*	80.63%	Professor	Tenured
St. Croix, Claudette	80.21%	Associate Professor	Tenured
Sorkin, Alexander*	74.57%	Professor	Tenured
Yates, Nathan*	61.14%	Associate Professor	Non-tenure Track
Hammond, Gerald	51.0%	Associate Professor	Tenured
Kwiatkowski, Adam	50.0%	Assistant Professor	Tenure Track
Butterworth, Michael	49.33%	Associate Professor	Tenured
Stolz, Donna	46.55%	Associate Professor	Tenured
Ford, Natalia	45.0%	Res. Assistant Professor	Non-tenure Track
Ford, Marijn	40.0%	Assistant Professor	Tenure Track
Hong, Yang	33.0%	Associate Professor	Tenured
Shi, Yi	20.0%	Assistant Professor	Tenure Track
Truschel, Steven	18.96%	Assistant Professor	Non-tenure Track
Murray, Sandra	16.7%	Professor	Tenured
Leuba, Sanford	15.4%	Associate Professor	Tenured
Traub, Linton	7.35%	Professor	Tenured
Drain, Peter	3.0%	Associate Professor	Tenured
Aridor, Meir	.21%	Associate Professor	Tenured
Devor, Daniel	0.02%	Associate Professor	Tenured

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



STUDENTS INVOLVED IN RESEARCH IN CELL BIOLOGY FACULTY LABS Snapshot as of June, 2019

STUDENT	LAB	SUPPORT
Sarel Urso	Todd Lamitina, Ph.D. Dept. Pediatrics	Todd Lamitina, Ph.D. Cell Biology & Teaching Fellowship
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 25% National Research Service Award (NRSA) NIH Trainee
Paige Rudich	Todd Lamitina, Ph.D. Dept. Pediatrics	Todd Lamitina, Ph.D. Children's Hospital Predoctoral Grant (RAC)
Chelsea Merkel	Adam Kwiatkowski, Ph.D. Cell Biology	Adam Kwiatkowski, Ph.D. National Research Service Award (NRSA) NIH Trainee

Cell Biology Annual Report





FY19 Projects

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

The combined funding for this post-doctoral fellowship grants is \$44,158 in FY19 (Total costs, annualized).

FY20 Projects

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

The combined funding for this post-doctoral fellowship grants is \$44,650 in FY20 (Total costs, annualized).



Cell Biology Program Grants (Fiscal Year 2018-19)

The Department of Cell Biology is funded by eight Program Grants and 4 by the National Institutes of Health, 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 2 currently funded program grants including

Cancer Center support Grant (PI Charleen Chu P30CA047904)

University of Pittsburgh Center for HIV Protein interactions (PCHPI, PI Gronenborn A 5P50GM082251)

Cardiolipin as a Novel Mediator of Acute Lung Injury (Mallampalli R. P01HL114453)

Vascular Subphenotypes of Lung Disease (PI Gladwin M. 5P01HL103455-09)

Pittsburgh Center for Kidney Research (PI Gerard Apodaca P30DK079307-09)

Mechanism-Directed Sequential Delivery of Radiation Mitigators Imaging Radiation Apathology Core (PI Joel Greenberger U19AI068021)

Alzheimer's Disease Research Center (PI Matthew MacDonald P30AG05133)

Project 1 for SSc Cort Novel Pathways in Systemic Sclerosis (PI Robert Lafyatis 2P50AR06078006)

Luminal Epithelial Junctions, Polarity and Permeabiility in BPH Pathogenesis (PI-Zhau Wang U54DK112079)

Pittsburgh Liver Research Center (PI - Satdarshan Singh Monga P30DK120531)

Mechanisms and Promotion of Immune Regulation by CD4 Regulatory T Cells within allografts (PI: Camirand U01AI132758)

Liver-enriched Transcription Factors as Prognostic markers and Therapeutic Targets in Alcoholic Hepatitis (PI: Bataller U01AA026972)





New Cell Biology Resea	arch Recruits in FY19		
Name	Rank		2 4
Faculty Level			nnua
Xiaojun (Jay) Tan	Research Assstant Professor		ology l Repo
Name	Rank	Lab Association	ort
Post Doctoral Level James Boslett	Post Doctoral Fellow	Dr. Nathan Yates	
			53



Graduate Program in Cell Biology and Molecular Physiology

The program in Cell Biology and Molecular Physiology has a strong track-record of scientific training and discovery. Graduates of the Ph.D. program undertake a range of careers in both academic and scientifically related fields. The department brings together basic and clinical research faculty who are dedicated to their research programs and to the training of graduate 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, imaging and systems biology to understand the integrated functions of cells, tissues, organs, organisms and humans.

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 beyond formal classroom training, including numerous journal clubs, "work in progress" interactions with student peers, research conferences and the opportunity to attend national and international meetings.

CBMP students can 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 by using virtual microscopy slides and presentations to identify tissues and cells and to understand the functions of the tissues and cells that they are observing. Teaching responsibilities 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 prepares them for their teaching responsibilities. Beyond the teaching experience, these fellowships also provide students with funding that covers much of their stipend and tuition for two years.

Courses

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 the foundations course, grant writing, scientific ethics and responsible research conduct, biostatistics and data analysis. 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 meets 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, Liu, Murray, Sorkin, Swiatecka-Urban, 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, Lamitina, Liu, Murray, Nicotra, Roy, Salama, Sims-Lucas, St. Croix, Stolz, Subramanya, Swiatecka-Urban, Thibodeau, Watkins, Weisz, Zhu.

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, Murray, Stolz, Swamynathan, Yanowitz, Zhu

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, 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, Devor, Drain, Goetzman, Hong, Kwiatkowski, Lamitina, Liu, Shi, Sims-Lucas, Sorkin, Swiatecka-Urban, Thibodeau, Weisz, Whitcomb, Zhu

Reproductive Biology

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

Ghazi, Schatten, Walker, Yanowitz.



Courses in the Cell Biology and Molecular Physiology Graduate Program

Courses in FY-19

Cell Biology

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Title: MS Thesis Research

Course Number: 2800 Course Director: Michael Butterworth 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: Steven Truschel 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: Michael Butterworth and Donna Beer Stolz When: Spring and Fall Term

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Annual Repor

Cell Biology

Prerequisites	INTRP 2000 Foundations of Biomedical Sciences
i icicquisites.	INTED 2005 Conferences
	IN I BP 2005 Conference

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

Title: Cellular Biology of Normal and Disease States

Course Number: 2880 Course Director: Daniel Devor When: Spring Term Prerequisites: INTBP 2000 Foundations of Biomedical Sciences INTBP 2005 Conference Core Course for: Cell Biology and Molecular Physiology Program

Description: This course will extend basic knowledge of cell and molecular biology obtained in Foundations of Biomedical science. The lectures will focus on four or five intensely active research areas of cell biology. Basic principles will be reinforced by considering disease states in which these processes are defective. Examples: cell growth and cancer, cell polarity and protein targeting, diseases of ion channels, cell biology of diabetes. Lectures and discussion groups.

<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: Michael Butterworth 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: Michael Butterworth 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%).

Title: Reproductive Development from Model Organisms to Humans

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.

Title: Graduate Student Writing Seminar

Course Number: INTBP 3240 Course Director: Daniel Devor When: Fall Term Prerequisites: None



Description: This Course teaches fundamental grantmanship skills using actual NIH training grant submissions. Students construct a competitive research training grant and are instructed on methods to identify funding sources. This course consists of introductory lectures followed by a series of workshops staffed by the IBGP training faculty. Workshops cover peer scientific review and study section operation, avoidance of common pitfalls in grant writing, grant writing ethics and scientific community service.



Dr. Alan Watson. Volumetric reconstruction of porcine limbal drainage system visualized as maximum intensity projections (MIPs) of the superior (A) limbus as seen from the anterior. A2 shows fine elements of the aqueous humor outflow tract distal to the trabecular meshwork (TM) as seen from the anterior chamber angle, viewed through the cornea and facing the z-plane. A3 shows the surface reconstruction and labeling of morphology with TM in yellow, collector channels in red, and scleral vascular plexus in blue. A4 shows a merged image with corresponding surfaces set to 50% transparency. Vertical, solid white lines demarcate boundaries within which representative sagittal subregions (A2.1, A3.1, A4.1) are segmented and positioned with the Z plane facing inward. These data were collected in collaboration with Dr. Nils Loewen from the from Department of Ophthalmology at the University of Pittsburgh. Adapted from: Susannah Waxman, Ralitsa T. Loewen, Yalong Dang, Simon C. Watkins, Alan M. Watson, Nils A. Loewen; High-Resolution, Three-Dimensional Reconstruction of the Outflow Tract Demonstrates Segmental Differences in Cleared Eyes. Invest. Ophthalmol. Vis. Sci. 2018;59(6):2371-2380. doi: 10.1167/iovs.17-23075.



None



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University of Pittsburgh School of Medicine Educational Credit Units (2017-2018) Department of Cell Biology Summary of Faculty ECU's ECUs ECURV Units Faculty Name Activity Aridor, Meir GS - Journal Club/Seminar Series Program Director 25.0 25.0 1.0 GS - Lecture 2.0 9.0 18.0 GS - Small group (e.g., PBL, conference, workshop) 2.0 10.0 20.0 Total ECUs: 63.0 Butterworth, Michael GS - Course Director 50.0 2.0 100.0 GS - GS Academic Advisor 2.0 3.0 6.0 GS - Journal Club/Seminar Series Program Director 25.0 2.0 50.0 GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.) 1.0 12.0 12.0 2.0 GS - Lecture 4.0 8.0 GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint 5.0 2.0 10.0 GS - Member: Curriculum, Recruiting, Program, or other SOM Committee 2.0 3.0 6.0 GS - Member: Program Steering Committee 40.0 1.0 40.0 GS - Small group (e.g., PBL, conference, workshop) 37.5 2.0 18.8 Total ECUs: 269.5 Devor, Daniel MS-1, MS-2 - Small group (e.g., PBL, conference, workshop) 2.0 20.8 41.5 GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee 5.0 1.0 5.0 50.0 100.0 GS - Course Director 2.0 GS - Lecture 2.0 10.0 20.0 2.0 GS - Small group (e.g., PBL, conference, workshop) 12.0 24.0 Total ECUs: 190.5 Drain, Peter MS-1, MS-2 - Block Director 10.0 1.0 10.0 MS-1, MS-2 - Course Director 200.0 2.0 400.0 MS-1, MS-2 - Lecture 2.0 7.8 15.5 MS-1, MS-2 - Small group (e.g., PBL, conference, workshop) 2.0 11.3 22.5 16.0 MS - Applicant Interviewer 1.0 16.0 MS - Member, Admissions Committee 75.0 1.0 75.0 20.0 MS - Member, Curriculum Committee 20.0 1.0 MS - Member, Promotions Committee 5.0 1.0 5.0 MS - Member, Task Force/Work Group/Subcommittee/or other SOM Committee 5.0 1.0 5.0 Total ECUs: 569.0 Duker, Georgia

OFFICE OF MEDICAL EDUCATION 11/6/2018

DEPARTMENT OF Cell Biology Page 1 of 5



University of Pittsburgh School of Medicine Educational Credit Units (2017-2018) Department of Cell Biology Summary of Faculty ECU's			
Faculty Name Activity	ECURV	Units	ECUs
MS-1, MS-2 - Course Director	200.0	1.0	200.0
MS-1, MS-2 - Laboratory	2.0	14.1	28.2
MS-1, MS-2 - Lecture	2.0	19.6	39.2
MS-1, MS-2 - Other	2.0	8.0	16.0
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	27.1	54.2
MS - Course Design Group Member	5.0	1.0	5.0
MS - Member, Promotions Committee	5.0	1.0	5.0
GS - Course Director	50.0	1.0	50.0
GS - Lecture	2.0	27.0	54.0
GS - Other	2.0	6.0	12.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	46.0	92.0
	Total E	CUs:	555.5
Ford, Marijn			
GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS - Lecture	2.0	9.5	19.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	3.0	15.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	4.5	9.0
	Total E	CUs:	48.0
Hammond, Gerald			
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	11.3	22.5
GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	1.0	5.0
GS - Laboratory supervision (e.g., MSTP, Ph.D. & M.Sc.)	1.0	12.0	12.0
GS - Lecture	2.0	11.5	23.0
GS - Member: Admissions Committee	75.0	1.0	75.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	3.0	15.0
GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	4.5	9.0
	Total F		211 5
Hong Yang	i otai E		
GS - Course Director	50.0	10	50.0
GS - Lecture	50.0 2 A	10.0	20.0
GS - Member: Comprehensive Dissertation Thesis Preliminary or Denrint	2.0 5 0	20.0	10.0
GS - Small group (e.g PBL conference, workshop)	5.0 2.0	2.0	10.0 4 0
GS - Shiali group (e.g., PDL, contenence, workshop)	Z.U Total E	2.0 <u> </u>	94.0
Kuistlaudi Adam	i otal E	CUS:	ŏ4.U
MS-1, MS-2 - Laboratory	2.0	7.0	14.0
DFFICE OF MEDICAL EDUCATION 11/6/2018	DEPARTMENT OF Cell Biology Page 2 of 5		



Educational Credit Units (2017-2018) Department of Cell Biology Summary of Faculty ECU's			
Faculty Name Activity	ECURV	Units	ECU
MS-1, MS-2 - Lecture	2.0	2.3	4.
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	5.6	11.
MS - Course Design Group Member	5.0	1.0	5.
GS - Lecture	2.0	8.0	16.
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	6.0	30.
GS - Ph.D. or M.Sc. Mentor	50.0	2.0	100.
GS - Small group (e.g., PBL, conference, workshop)	2.0	3.0	6.
	Total E	CUs:	186.
Leuba, Sanford			
GS - Course Director	50.0	1.0	50.
GS - Lecture	2.0	11.0	22.
GS - Member: Curriculum, Recruiting, Program, or other SOM Committee	2.0	1.0	2.
GS - Member: Program Steering Committee	40.0	1.0	40.
GS - Small group (e.g., PBL, conference, workshop)	2.0	10.0	20.
	Total E	CUs:	134.
Murray, Sandra			
MS-1, MS-2 - Laboratory	2.0	31.8	63.
MS-1, MS-2 - Lecture	2.0	4.0	8.
MS-1, MS-2 - Other	2.0	21.0	42.
MS - Course Design Group Member	5.0	2.0	10.
MS - Member, Promotions Committee	5.0	1.0	5.
MS - Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	2.0	10.
GS - Lecture	2.0	1.0	2.
	Total E	CUs:	140.
Shi, Yi			
GS - Lecture	2.0	5.0	10.
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	1.0	5.
	Total E	CUs:	15.
Sorkin, Alexander			
GS - Lecture	2.0	6.0	12.
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	3.0	15.
GS - Ph.D. or M.Sc. Mentor	50.0	1.0	50.
GS - Small group (e.g., PBL, conference, workshop)	2.0	2.0	4.
	Total E	CUs:	81.
St Croix, Claudette			
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	9.5	19.
FICE OF MEDICAL EDUCATION 11/6/2018	DEP	PARTMENT OF	Cell Biolo Page 3 of



University of Pittsburgh School of Medicine Educational Credit Units (2017-2018) Department of Cell Biology Summary of Faculty ECU's			
Faculty Name Activity	ECURV	Units	ECUs
GS - Course Director	50.0	1.0	50.0
GS - Lecture	2.0	11.0	22.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	2.0	10.0
	Total E	CUs:	101.0
Stolz, Donna			
MS-1, MS-2 - Laboratory	2.0	8.7	17.3
MS-1, MS-2 - Lecture	2.0	0.8	1.7
MS-1, MS-2 - Small group (e.g., PBL, conference, workshop)	2.0	5.6	11.2
MS - Course Design Group Member	5.0	1.0	5.0
GS - Associate Director	75.0	1.0	75.0
GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	5.0	25.0
GS - Course Director	50.0	1.0	50.0
GS - Journal Club/Seminar Series Program Director	25.0	2.0	50.0
GS - Lecture	2.0	6.5	13.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	9.0	45.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	17.5	35.0
	Total E	CUs:	328.2
Thorne, Stephen			
GS - Lecture	2.0	1.5	3.0
	Total E	CUs:	3.0
Traub, Linton			
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	1.0	5.0
	Total E	CUs:	5.0
Watkins, Simon			
MS - Member, Task Force/Work Group/Subcommittee/or other SOM Committee	5.0	1.0	5.0
GS - Chair: Comprehensive, Dissertation, Thesis, Preliminary or Reprint Committee	5.0	2.0	10.0
GS - Course Director	50.0	1.0	50.0
GS - Lecture	2.0	9.5	19.0
GS - Member: Comprehensive, Dissertation, Thesis, Preliminary or Reprint	5.0	5.0	25.0
GS - Small group (e.g., PBL, conference, workshop)	2.0	8.0	16.0
	Total E	CUs:	125.0
Yates, Nathan			
GS - Lecture	2.0	3.0	6.0
	Total E	CUs:	6.0
	Subt	otal:	3116.5
FICE OF MEDICAL EDUCATION 11/6/2018	DEF	PARTMENT C	F Cell Biolog Page 4 of



CB Faculty Teaching Activities

2	University of Education Depa Sum	Pittsburgh School of Medicine Il Credit Units (2017-2018) rtment of Cell Biology mary of Faculty ECU's
ind.	Faculty Name Activity	ECURV Units ECUs
	Total Faculty Reporting: 19	Total ECU's for Cell Biology: 3116.5
	OFFICE OF MEDICAL EDUCATION 11/6/2018	DEPARTMENT OF Cell Biolog Page 5 of

	Research Focus Sorkin Lab fang Lab Hammond Lab Sorkin Lab Pord Lab
	Fax 412-648-8330 412-648-8330 412-648-8330 412-648-8330 412-648-8330 412-648-8330
	Office Phone 412-624-8147 412-648-3261 412-648-2846 412-383-1783 412-624-8147 412-383-9026
	Email Address tariqueb@pitt.edu jul105@pitt.edu jep160@pitt.edu mip85@pitt.edu das306@pitt.edu
	Office Address S372 BSTWR BST3-9th Fl S333 BSTWR S332 BSTWR S355 BSTWR S355 BSTWR
	Title Post Doctoral Associate Post Doctoral Associate Post Doctoral Associate Post Doctoral Associate Post Doctoral Associate
Post Doctoral Personnel Dat [Current as of June, 2019]	Name Bagalkot, Tarique Boslett, James Lu, Juan Pacheco, Jonathan Perez Verdaguer, Mireia Sun, Dapeng



<u>Current Cell Biology and Molecular Physiology Graduate Program Students as</u> of June 30, 2019

<u>Student</u>

<u>Student</u>	Mentor	<u>Year</u>
Chelsea Merkel	Dr. Adam Kwiatkowski	5th
Paige Rudich	Dr. Todd Lamitina	4th
Amity Eaton	Dr. Gerard Apodaca	4th
Jonathan Heier	Dr. Adam Kwiatkowski	3rd
Rachel Wills	Dr. Gerald Hammond	3rd
Sarel Urso	Dr. Lamitina	2nd





Prior Graduates of the Cell Biology and Molecular Physiology Program as of June 2019 (Past five years)

Chelsea DeAnn Merkel

Defended: 6/21/19 Industry

Paige Davison Rudich

Defended: 5/15/19 Post-Doc Canada

George Michael Preston, Ph.D.

Defended: April 13, 2017 Research Specialist Spark Therapeutics, Inc., Malvern, PA

Christine Klemens, Ph.D.

Defended April 11, 2017 Post-Doc Fellow, Medical College of Wisconsin

<u>Kathryn Wack, Ph.D.</u> Defended July 23, 2014 Vice President of Development, Western Oncolytics, Ltd.



Student Ratings of CBMP Faculty Teaching FY2019						
Name	Course	Туре	Date	Rating	Ave	
Devor	Investigation and Discovery	SGCS	Fall-18	4.40	4.40	
Butterworth	Tissues in Health and Disease	LAB	Spring-19	5.00	5.00	
Drain	Investigation and Discovery	SGCS	Fall-18	4.20	4.20	
Kwiatkowski Kwiatkowski	Tissues in Health and Disease Tissues in Health and Disease	LEC LAB	Spring-19 Spring-19	4.30 5.00	4.65	
Murray Murray	Medical Anatomy Medical Anatomy	LEC LAB	Fall-18 Fall-18	4.00 4.70	4.35	
Stolz Stolz	Tissues in Health and Disease Tissues in Health and Disease	LEC LAB	Spring-19 Spring-19	4.10 4.90	4.50	
	Overall Teaching Average			4.50		
Type codes: LEC PBL WKSP SGCS AP LAB	Lecture Practice Based Learning Workshop Small Group Conference Session Applications Staff Laboratory					





CELL BIOLOGY FACULTY ROSTER (Effective June, 2019)

<u>Last Name</u>	<u>First</u>	Rank	<u>Status</u>
Sorkin	Alexander	Professor & Chair	Tenured
Devor	Daniel	Professor	Tenured
Murray	Sandra	Professor	Tenured
Traub	Linton	Professor	Tenured
Watkins	Simon	Professor	Tenured
Aridor	Meir	Associate Professor	Tenured
Butterworth	Michael	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
Yates	Nathan	Associate Professor	Non-tenure Track
Ford	Mariin	Assistant Professor	Tenure Track
Hammond	Gerald	Assistant Professor	Tenure Track
Kwiatkowski	Adam	Assistant Professor	Tenure Track
Shi	Yi	Assistant Professor	Tenure Track
Truschel	Steven	Assistant Professor	Non-tenure Track
		1.0000001	
Ford	Natalia	Res. Assistant Professor	Non-tenure Track
Tan	Xiaojun (Jay)	Res. Assistant Professor	Non-tenure Track



Name	Prior Institution /Rank	Current Rank
ay (Xiaojun) Tan	UT Southwestern Medical Center Department of Molecular Biology Dallas, TX 75390 Postdoc	Res. Assstant Professor
Faculty Honors, Recognition and Professional Affiliations (Fiscal Year 2018 – 2019)

Michael Butterworth, Ph.D. Associate Professor

Member, American Physiological Society Member, 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

Marijn Ford, Ph.D.

Assistant Professor

Member, The Biochemical Society Member, American Society of Cell Biology

Gerry Hammond, Ph.D. Assistant Professor

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

Yang Hong, Ph.D. Associate Professor

Member of Faculty 1000



CB Faculty Honors, Recognition and Professional Affiliations

Adam Kwiatkowski, Ph.D. Assistant Professor Member, American Society for Cell Biology American Society for Biochemistry and Molecular Biology American Heart Association Sanford Leuba, Ph.D. Associate Professor Member, Biophysical Society Member, Spectroscopy Society of Pittsburgh Yang Li, Ph.D. Research Instructor Member, American Heart Association Member, American Society for Cell Biology Sandra A. Murray, Ph.D. Professor American Society for Cell Biology Lifetime Fellow Recognition for Distinguished Contributions to the Advancement of Cell Biology Member, American Society for Cell Biology - Council, Minority Affairs Member, Society for In Vitro Biology Member, The Pittsburgh Cancer Institute Member, Corporation of the Marine Biological Laboratory Member, Cell Transplant Society Member, Endocrine Society Member, American Physiological Society Member, International Society for Preventive Oncology University of Pittsburgh Helen Faison Council of Elders School of Medicine Summer "Minority" Work-Study Program Member, Medical Student Promotions Committee Member, Training Faculty Immunology Graduate Training Program NIH - Biomedical Faces of Science Mentors Co-Chair of the Research Center of Excellence Committee Graduate School of Public Health, University of Pittsburgh Graduate School of Public Health Community Engagement Research Cor Graduate School of Public Health Research Advisory Committee- Center for Minority Health Provost Special Advisory Committee Provost Selection Committee for the Provost Development Fund Awards



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Cell Biology Annual Report University Community Representative for Equipoise Junior Faculty Advancement – Panel Member

Itziar Pinilla-Macua, Ph.D. *Research Instructor*

Spanish Society of Biochemistry and Molecular Biology

Yi Shi, Ph.D. Assistant Professor

Member, American Society for Mass Spectrometry Member, New York Academy of Sciences

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

Member, 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

Jay Tan, Ph.D. Research Assistant Professor

Member, American Heart Association Member, American Society of Cell Biology Member, American Association for the Advancement of Science

Linton M. Traub, Ph.D. Professor

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



CB Faculty Honors, Recognition and Professional Affiliations

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

Member, The Pittsburgh Cancer Institute

Nathan Yates, Ph.D. Associate Professor American Chemical Society American Society for Mass Spectrometry



Dr. Alan Watson. Interferon lambda (IFN λ) is responsible for neutrophil sequestration into the eye. (a) Orthogonal projections from all three dimensions of a whole eye from a mouse injected with CMTPX-labeled WT neutrophils +IFN λ . Cells within the retina and Schlemm's canal are depicted as green spheres (b) with and (c) without the orthogonal projection. These data were collected in collaboration with Dr. Debasish Sinha from Department of Ophthalmology at the University of Pittsburgh. Adapted from article in press. https://doi.org/10.1038/s42003-019-0588-y



Faculty Presentations (Fiscal Year 2018 - 2019)

Marijn Ford, Ph.D. Assistant Professor

Department of Biological Sciences, Vanderbilt University, Nashville, Tennessee "Not all dynamin-related proteins are alike: the unique architecture of Vps1"

Midwest Yeast Meeting, Northwestern University "Ivyl is a negative regulator of Gtrdependent TORC1 activation"

Gerald Hammond, Ph.D. Assistant Professor

"SAC1 Degrades its Lipid Substrate PtdIns4P in the Endoplasmic Reticulum to Maintain a Steep Chemical Gradient with Donor Membranes" at Keystone Symposium: "Phosphoinositide Biology: New Therapeutic Targets Beyond Class I PI3K"

"SAC1 Degrades its Lipid Substrate PtdIns4P in the Endoplasmic Reticulum to Maintain a Steep Chemical Gradient with Donor Membranes" in "Molecular Basis of Signaling" symposium, American Society of Biochemistry and Molecular Biology 2018 Annual meeting, San Diego, CA.

"Reverse Engineering Lipid Signaling in Living Cells". Invited seminar, The Francis Crick Institute, London, UK.

"Dissecting the unique cellular functions driven by $PI(3,4)P_2$ ". FASEB conference "Phospholipids: Dynamic Lipid Signaling in Health and Disease". Steamboat Springs, CO.

"Reverse Engineering Lipid Signaling in Living Cells". Invited seminar, Department of Biological Sciences, University of Pittsburgh

"Reverse Engineering Lipid Signaling in Living Cells". Invited seminar, Department of Physiology, University of Texas Southwestern Medical Center, Dallas, TX.

"Reverse Engineering Lipid Signaling in Living Cells". Invited seminar, Department of Physiology, Albany Medical College, Albany, NY.

Yang Hong, Ph.D. Associate Professor

The 9th Jin Ling Conference of Development Biology, Nanjing, Jiangsu, China Gene Targeting 2011, Vienna, Austria.



Adam Kwiatkowski, Ph.D. Assistant Professor	
World Congress of Biomechanics, Dublin, Ireland.	
Molecular Medicine Research Seminar, Children's Hospital of Pittsburgh of UPMC, Pittsb PA.	ourgh,
Department of Regenerative Medicine and Cell Biology, Medical University of South Card Charleston, SC.	olina,
Cell and Developmental Biology Center, National Heart, Lung, and Blood Institute, Bethe MD.	sda,
Mechanobiology Institute, National University of Singapore, Singapore	
Sanford Leuba, Ph.D. Associate Professor	
Department of Chemistry and Biochemistry, Baylor University	
Yi Shi, Ph.D. Assistant Professor	
CPSA USA, Philadelphia	
Science 2018, Pittsburgh	
Shanghai Tech University, Shanghai, China	
CHUPO, Guangzhou, China	
Alexander D. Sorkin, Ph.D. <i>Richard B. Mellon Professor and Chairman</i>	
University of Arkansas Medical School, Little Rock, AK McGill University Health Center, Montreal, Canada	
Claudette St. Croix, Ph.D. Associate Professor	
Symposium Speaker, 19 th International Microscopy Congress, Sydney, Australia Invited Speaker: IDEX Corporation, National Sales Meeting, Las Vegas, NV	



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

Imaging Fast, Imaging Deep University of Melbourne, Invited seminar speaker

Exchange of Experience, Building, running and managing a truly large imaging center. Sydney Australia. Invited speaker

Imaging Futures: IDEX global meeting, Keynote speaker, Las Vegas NV

Imaging Fast Imaging Deep HUB-MAP annual meeting, Invited speaker

Alan Watson, Ph.D. *Research Assistant Professor*

How to Find a Single Neuron in the Brain: Technology for High-Speed High-Resolution Imaging of Whole Biologic Systems. Central Michigan University. Mt. Pleasant, MI.

Ribbon Scanning Confocal for High-Speed High-Resolution Imaging of Massive Volumes. University of Colorado Denver, Anschutz Medical Center. Aurora, CO.

Ribbon Scanning Confocal for High-Speed High-Resolution Imaging of Massive Volumes. University of Colorado Boulder. Boulder, CO.

Technologies for High-Speed High-Resolution Imaging of Whole Biologic Systems. Scripts. San Diego, CA.

Technologies for High-Speed High-Resolution Imaging of Whole Biologic Systems. Salk Institute. San Diego, CA

Technologies for High-Speed High-Resolution Imaging of Large Biologic Systems. GUDMAP Annual Meeting. Washington, DC.

Applying Technologies for High-Resolution Volumetric Imaging of Large Tissues to the Characterization of Benign Prostatic Hyperplasia. O'Brien Benign Urology Research Center Symposium. University of Pittsburgh, Pittsburgh, PA.

Nathan Yates, Ph.D. Associate Professor

"AD BioMarkers- Mass Spectrometry from Basic Research to the Clinic" GERO Talk, Santiago, Chile

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"Mass Spec. Technology, Protein Biomarkers and Protein Target" AAPS PharmSci 360 Conference, Washington DC





Peer Reviewed Publications (Fiscal Year 2017 - 2019)

Meir Aridor, Ph.D.

Associate Professor

Gang Yu; Yinan Liu; Shiyong Liu; **Meir Aridor**; Yuan Huang; Yushuang Hu; Longfeii Wang; Sisi Li; Hongbo Xiong; Bo Tang; Xia Li; Chen Cheng; Susmita Chakrabarti; Fan Wang; Qingyu Wu; Sadashiva Karnik; Chengqi Xu; Qiuyun Chen; Qing Wang (2018) Small GTPases SAR1A and SAR1B regulate the trafficking of the cardiac sodium channel Nav1.5. Biochim Biophys Acta Mol Basis Dis. 2018 Nov;1864(11):3672-3684. doi: 10.1016/j.bbadis.2018.09.003. Epub 2018 Sep

Michael Butterworth, Ph.D.

Assistant Professor

Mukherjee, A., Wang, Z., Kinlough, C.L., Poland, P.A., Marciszyn, A.L., Montalbetti, N., Carattino, M.D., Butterworth, M.B., Kleyman, T.R. and Hughey, R.P. (2017). Specific palmitoyltransferases associate with and activate the Epithelial Sodium Channel. Journal of Biological Chemistry. 292(10):4152-4163. PMID: 28154191

Klemens, C.A., Edinger, R.S, Kightlinger, L. Liu, X. and Butterworth, M.B. (2017). Ankyrin G expression regulates apical delivery of the epithelial sodium channel (ENaC). Journal of Biological Chemistry. 292(1):375-85. PMID: 27895120

Liu, X., Edinger, R.S., Klemens, C.A. Phua, Y.L., Bodnar, A.J., LaFramboise, W.A., Ho, J. and Butterworth, M.B. (2017). A microRNA cluster miR23~24~27 is upregulated in the distal kidney ephron where it alters sodium transport. Journal of Cellular Physiology. 232: 1306–1317. PMID: 27636893

Espiritu E.B., Crunk A.E., Bais A., Hochbaum D., Cervino A.S., Phua Y.L., Butterworth M.B., Goto T., Ho J., Hukriede N.A., Cirio M.C. (2018). The Lhx1-Ldb1 complex interacts with Furry to regulate microRNA expression during pronephric kidney development. Sci Rep. 8(1):16029. PMID: 30375416.

Phua Y.L., Chen K.H., Hemker S.L., Marrone A.K., Bodnar A.J., Liu X., Clugston A., Kostka D., Butterworth M.B., Ho J. (2019). Loss of miR-17~92 results in dysregulation of *Cftr* in nephron progenitors. Am J Physiol Renal Physiol. 316(5):F993-F1005. PMID: 30838872

Daniel Devor, Ph.D. *Professor*

Lee, S.L., D.C. Devor and K.L. Hamilton. Modulation of retrograde trafficking of KCa3.1 in polarized epithelium. Frontiers of Physiology, DOI: 10.3389/fphys.2017.00489, 2017.

Bertuccio, C.A., T. Wang, S.B. Condliffe and D.C. Devor. Plasma membrane insertion of KCa2.3 (SK3) is dependent upon the SNARE proteins, Syntaxin 4 and SNAP23. PLoS One.





13(5):e0196717. doi: 10.1371/journal.pone.0196717, 2018.

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

D. Brüning, K. Reckers, P. Drain, and I. Rustenbeck. 2017. Glucose Diminishes and KCl Increases Insulin Granule Turnover in the Submembrane Space of Primary Beta-Cells. J Mol Endocrinol Oct:59(3):311-324. PMID: 28765259.

Luppi, P., and P. Drain. 2017. Autocrine C-Peptide Mechanism Underlying INS1 Beta Cell Adaptation to Free Fatty Acid-Induced Oxidative Stress. In preparation.

Li Ma, Vytautas P. Bindokas, Christine Labno, Jie Wang, Andrey Kuznetsov, Manani Hara, Xuehui Geng, Peter Drain, Christopher J. Rhodes, Donald F. Steiner, and Louis H Philipson. 2017. Non-Crystallized Cargo Protein Shifts Insulin LDCV Exocytosis From Full to Transient Fusion, in revision

Marijn Ford, Ph.D.

Assistant Professor

Varlakhanova NV, Mihalevic MJ, Bernstein KA, **Ford MGJ**. Pib2 and the EGO complex are both required for activation of TORC1. J Cell Sci. 2017 Nov 15; 130(22):3878-3890. DOI: <u>10.1242/jcs.207910</u> PMID: <u>28993463</u>. PMCID: <u>PMC5702048</u>.

Varlakhanova NV, Tornabene BA, **Ford MGJ**. Feedback regulation of TORC1 by its downstream effectors Npr1 and Par32. 2018. Mol. Biol. Cell. DOI: <u>10.1091/mbc.E18-03-0158</u>. PMID: <u>30156471</u>.

Varlakhanova NV, Tornabene BA, **Ford MGJ**. Ivy1 is a negative regulator of Gtr-dependent TORC1 activation. 2018. J. Cell Sci. DOI: <u>10.1242/jcs.218305</u>. PMID: <u>30097557</u>.

Varlakhanova NV, Alvarez FJ, Brady TM, Tornabene BA, Hosford CJ, Chappie JS, Zhang P, **Ford MGJ**. Structures of the fungal dynamin related protein Vps1 reveal a unique, open helical architecture. J. Cell Biol. 2018. DOI: <u>10.1083/jcb.201712021</u>. PMID: <u>30087125</u>.

Natalia Varlakhanova Ford, Ph.D.

Research Assistant Professor

Varlakhanova NV, Mihalevic MJ, Bernstein KA, **Ford MGJ**. Pib2 and the EGO complex are both required for activation of TORC1. J Cell Sci. 2017 Nov 15; 130(22):3878-3890. DOI: <u>10.1242/jcs.207910</u> PMID: <u>28993463</u>. PMCID: <u>PMC5702048</u>.

Varlakhanova NV, Tornabene BA, **Ford MGJ**. Feedback regulation of TORC1 by its downstream effectors Npr1 and Par32. 2018. Mol. Biol. Cell. DOI: <u>10.1091/mbc.E18-03-0158</u>. PMID: 30156471.



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Varlakhanova NV, Tornabene BA, **Ford MGJ**. Ivy1 is a negative regulator of Gtr-dependent TORC1 activation. 2018. J. Cell Sci. DOI: <u>10.1242/jcs.218305</u>. PMID: <u>30097557</u>.

Varlakhanova NV, Alvarez FJ, Brady TM, Tornabene BA, Hosford CJ, Chappie JS, Zhang P, **Ford MGJ**. Structures of the fungal dynamin related protein Vps1 reveal a unique, open helical architecture. J. Cell Biol. 2018. DOI: <u>10.1083/jcb.201712021</u>. PMID: <u>30087125</u>.

Gerald Hammond, Ph.D.

Assistant Professor

Levin R, Hammond GRV, Balla T, DeCamillli P, Fairn, GD, Grinstein S. 2017. Multiphasic dynamics of phosphatidylinositol 4-phosphate during phagocytosis. Mol Biol Cell 28, 128-140.

Willett, R., Martina, J.A., Zewe, J.P., Wills, R., Hammond, G.R.V., and Puertollano, R. 2017. TFEB regulates lysosomal positioning by modulating TMEM55B expression and JIP4 recruitment to lysosomes. Nature Communications. doi:10.1038/s41467-017-01871-z. 8:1580.

Sohn, M., Korzeniowski, M., Zewe, J.P., Wills, R. C., Hammond, G., Humpolickova, J., et al. PI(4,5)P2 controls plasma membrane PI4P and PS levels via ORP5/8 recruitment to ER–PM contact sites. J Cell Biol. 2018;jcb.201710095.

Zewe J. P., Wills, C, Sangappa, Goulden, B. D., Hammond, G. R. V. SAC1 degrades its lipid substrate PtdIns4P in the endoplasmic reticulum to maintain a steep chemical gradient with donor membranes. eLife. 2018;7:e35588.

Chintaluri K., Goulden B.D., Celmenza C., Saffi G., Miraglia E., Hammond G.R., Botelho R.J. The PH domain from the Toxoplasma gondii PH-containing protein-1 (TgPH1) serves as an ectopic reporter of phosphatidylinositol 3-phosphate in mammalian cells. PLoS ONE. 2018;13(6):e0198454.

Goulden B, Pacheco J, Dull A, Zewe J, Deiters A, Hammond G. A High Avidity Biosensor Reveals PI(3,4)P2 is Predominantly a Class I PI3K Signaling Product. J Cell Biol. 2019;218(3): 1066-1079. Doi: 10.1083/jcb.201809026

Yang Hong, Ph.D. Associate Professor

Cao H, Xu R, Shi Q, Zhang D, Huang J and Hong Y. (2017) FERM Domain Phosphorylation and Endogenous 3'UTR are not Essential for Regulating the Function and Subcellular Localization of Polarity Protein Crumbs. J Genetics & Genomics 44(8):409-412. PMID: 28844685

Chen Y-J, Huang J, Huang L, Austin E and Hong Y. (2017) Phosphorylation Potential of Drosophila E-Cadherin Intracellular Domain is Essential for Development and Regulating Adherens Junction Biosynthetic Dynamics. Development 144(7):1242-1248. PMID: 28219947



Hong Y. (2018) aPKC: the Kinase that Phosphorylates Cell Polarity. *F1000Research* 2018, 7(F1000 Faculty Rev):903 (doi: 10.12688/f1000research.14427.1)

Raza Q, Choi JY, Li Y, O'Dowd RM, Watkins SC, Hong Y, Clark NL and Kwiatkowski AV. (2019) Evolutionary rate covariation identifies the GTPase activating protein Raskol as a signaling component of the cadherin adhesion network in *Drosophila*. *Plos Genetics* 15(2): e1007720. PMID: 30763317

Adam Kwiatkowski, Ph.D.

Assistant Professor

Kang H, Bang I, Jin KS, Lee B, Lee J, Shao X, Heier JA, Kwiatkowski AV, Nelson WJ, Hardin J, Weis WI, Choi HJ. Structural and Functional Characterization of Caenorhabditis elegans α -Catenin Reveals Constitutive Binding to β -catenin and F-actin. 2017 March 15 Epub. PMID: 28298447

Heier JA, Dickinson DJ, **Kwiatkowski AV**. Measuring Protein Binding to F-actin by Cosedimentation. J. Vis. Exp. 2017 May 18;(123). PMID: 28570520

Hager NA, Krasowski CJ, Mackie TD, Kolb AR, Needham PG, Augustine AA, Dempsey A, Szent-Gyorgyi C, Bruchez MP, Bain DJ, Kwiatkowski AV, O'Donnell AF, Brodsky JL. Select α-arrestins control cell-surface abundance of the mammalian Kir2.1 potassium channel in a yeast model. J Biol Chem. 2018 Jul 13;293(28):11006-11021. PMID: 29784874

Li Y, Merkel CD, Zeng X, Heier JA, Cantrell PS, Sun M, Stolz DB, Watkins SC, Yates NA, Kwiatkowski AV[†]. The N-cadherin interactome in cardiomyocytes as defined by quantitative proximity proteomics. J Cell Sci. 2019 Feb 11;132(3). PMID: 30630894 [†]Corresponding author; *a JCS Research Highlight and accompanied by JCS First Person interview with the first authors Yang Li and Chelsea Merkel*

Pang SM, Le S, **Kwiatkowski AV**, Yan J. Mechanical stability of α T-catenin and its activation by force for vinculin binding. Mol Biol Cell. 2019 Jul 22;30(16). PMID: 31318313

Raza Q, Choi JY, Li Y, O'Dowd RM, Watkins SC, Hong Y, Clark NL and Kwiatkowski AV. (2019) Evolutionary rate covariation identifies the GTPase activating protein Raskol as a signaling component of the cadherin adhesion network in *Drosophila*. *Plos Genetics* 15(2): e1007720. PMID: 30763317

Sanford Leuba, Ph.D. Associate Professor

Carney SM, Gomathinayagam S, Leuba SH, Trakselis MA. (2017) Bacterial DnaB helicase interacts with the excluded strand to regulate unwinding. J Biol Chem. Sep 22. pii: jbc.M117.814178. doi: 10.1074/jbc.M117.814178. [Epub ahead of print] PMID: 28939774

Chirico G*, Gansen A, Leuba SH*, Olins AL, Olins DE, Smith JC, Tóth K*. (2018) Jörg Langowski: his scientific legacy and the future it promises. BMC Biophysics (in press).



*Corresponding authors.

Yang Li, Ph.D.

Research Instructor

Liu, J., Li, Y., Lin, B., Sheng, Y., and L. Yang: HBL1 Is a Human Long Noncoding RNA that Modulates Cardiomyocyte Development from Pluripotent Stem Cells by Counteracting MIR1. Dev. Cell, 42(4):333-48, 2017.

Li Y, Merkel CD, Zeng X, Heier JA, Cantrell PS, Sun M, Stolz DB, Watkins SC, Yates NA, Kwiatkowski AV. The N-cadherin interactome in primary cardiomyocytes as defined using quantitative proximity proteomics. J Cell Sci. 132(3), 2019.

Raza Q, Choi JY, Li Y, O'Dowd RM, Watkins SC, Chikina M, Hong Y, Clark NL, Kwiatkowski AV. Evolutionary rate covariation analysis of E-cadherin identifies Raskol as a regulator of cell adhesion and actin dynamics in Drosophila. PLoS Genet. 15(2):e1007720, 2019. Sandra A. Murray, Ph.D.

Professor

Bell, C.L., Shakespeare, T.I. Smith, A. and **Murray, S.A**., Visualization of Annular Gap Junction Vesicle Processing: The Interplay Between Annular Gap Junctions and Mitochondria, International Journal of Molecular Sciences 20(1):44, 2018 doi: 10.3390/ ijms20010044

Itziar Pinilla Macua, Ph.D.

Research Instructor

Pinilla-Macua I, Grassart A, DuvvuriU, Watkins Simon C., Sorkin A, EGF receptor signaling, phosphorylation, ubiquitylation and endocytosis in tumors in vivo. Elife 2017; 6. piie31993

Yi Shi, Ph.D.

Assistant Professor

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Nathan Yates, Ph.D.

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Executive Summary for the Cell Biology FY2020 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 nine 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. 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 FY2020 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 FY20. 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 2020 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 transport regulation. The Faculty in the Department have made important contributions to these various areas of cell biology, and established themselves as leaders in their respective research fields. This is evident from recent publications in high-impact journals such as eLife (Sorkin, Traub), Journal of Cell Biology (Hammond), Molecular Biology of the Cell Journal of Cell Science (Ford, Kwiatkowsky), and others.

Membrane trafficking is a particular strength of the Department with the research covering the entire spectrum of traffic-related issues from general mechanisms of protein and lipid trafficking, endocytosis and membrane organelle biogenesis, to cargo-specific mechanisms of anterograde and endocytic trafficking of receptors, transporters and channels. Studies of the mechanisms of cell polarity, cell motility, and intracellular signaling have also been growing in the department. Our faculty continue to present their research at international and national meetings, participate in NIH and other grant review panels and other organizational and service activities, all reflecting their influence in the respective research areas.

The majority of the Cell Biology faculty maintains active, funded research programs. We have been especially successful in obtaining extramural research funding in multiple collaborative grants (Watkins, St. Croix, Stolz, Yates, Shi). All tenure-stream Assistant Professors, except Yi Shi who started two and a half ago, 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 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, CBI obtained a new lattice light sheet microscope system which is essential to the continued expansion of the CBI capabilities and departmental infrastructure. Dr. Yates, Director of the Biomedical Mass Spectrometry Center, SOM and U. Pitt, is also enhancing an infrastructure to implement modern methods of quantitative mass-spectrometric analyses.

Our faculty also participated in NIH funded program projects (Center for HIV Protein Interactions; Molecular Biology of Hemorrhagic Shock, and several others) and are 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. With the retirement of Dr. Duker, a new faculty member, Dr. Truschel replaced her in teaching extensively in the medical school.

Graduate Curriculum: We now have 6 students in the graduate Ph.D. program in Cell Biology and Molecular Physiology. Two students graduated in 2019; one is planning to graduate later in the year, and three new students joined the program. 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, CNUP among others. The major development this year has been the submission of the first application for the T32 training grant in cell biology which has been a joint effort of faculty in Cell Biology, School of Arts and CMU.

Biomedical Master's Program (BMP). Faculty in the Department together with the Department of Pharmacology launched a new BMP program in September 2017. Three faculty are teaching didactic courses, Dr. Peter Drain serves as the Director of Academic Affairs, and Dr. Sorkin is 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 large flood in the Department that occurred in January 2019. The fact that all post-flooding issues, such as dealing with cleaning and repair, supply an dequipment replacement and others, were successfully accomplished in a timely and efficient manner demonstrates the experience and strength of our administrative staff.

Weaknesses

Limited and poorly designed research space has become a weakness of the program, especially during our faculty recruitment efforts. We will commit major efforts to rearrange the space in BST South to allow for the growth of the research programs of new and current faculty located in this area.

One of the CBP faculty Dr. Leuba is located in the Hillman Cancer Center. There is clear separation from the rest of the Department leading to a lesser engagement of his laboratory 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 is to shape the future of the department, while achieving a healthy balance of junior and senior faculty members, and this 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 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 FY2019 Fiscal Issues

The main budgetary issue that faced the Department in the FY19 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 for FY20 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.



Department of Cell Biology Department of Cell Biology Schedule of Revenue and Expenses Fiscal Year	· 2020 B	udget				
_	University		UPP and Other		Total Budget FY 2019	
Revenue			<i>ф</i>		¢	
atient Care	\$	-	\$	-	\$	-
Jrant:	4.2	F 4 101			4.2	054 101
	4,554,101			-	4,3	054,101
Indirects	1,945,880			-	1,9	43,880
about of Madiaina	-			-	2	-
	3,4	80,424			3,4	100,424
ANIC	411.007			-		-
Detal D emonstra	411,097 \$ 10 105 502		¢	-	4 ¢ 10	105 502
Expenses						
alaries and Fringe Benefits:					.	
Faculty	\$ 3,634,200		\$	-	\$ 3,6	534,200
Non-Faculty	2,270,286			-	2,2	270,286
halpractice insurance		06 255		-		-
pace Kental	80,333			-		80,355
JPP Overneau	2.6	27.052		-	2.6	-
Oniversity Overnead	2,027,933				2,027,933	
The Operating Expenses	\$ 10 105 502		¢	-	\$ 10 195 502	
ona Operating Expenses	φ10 ,	195,502	φ	-	φ 10 ,	195,502
Excess Revenue over Expenses	\$	-	\$	-	\$	-
Capital Equipment/Improvements	\$	-	\$	-	\$	-
Fund Balances						
University Restricted Accounts as of 6/30/19	\$ 2,566,380		\$	-	\$ 2,5	566,380
University Endowments as of 6/30/19	403,036				4	03,036
UPP Fund Balance as of 6/30/19				-		-
UPMC Endowments as of 6/30/19				-		-
UPMC SPF Accounts as of 6/30/19				-		-
Total Fund Balances	\$ 2,	969,416	\$	-	\$ 2,9	969,416





Thank you for your kind attention.





