Volume 2, Issue 1 Spring 2018

Weill Cornell Medicine
Graduate School
of Medical Sciences
A partnership with the Sloan Kettering Institute

WorthWEILL

HAPPY 2018 WEILL CORNELL!

ON behalf of myself and the Graduate Student Executive Council (GSEC), we hope you had a wonderful holiday season and wish you all the very best for your studies, happiness, and success in 2018. We would like to take this opportunity to welcome all of the interviewees to our campus. We are extremely excited to meet each and every one of you, and we, wish you success as you embark on your interview process. We certainly hope you enjoy your visit, and are able to get familiar with our outstanding community, premier training institution, and cutting-edge research.

The second half of 2017 was a busy time for us all. We had a fantastic Halloween Party, Thanksgiving Potluck, and we collected five full boxes of toys for Toys for Tots. In addition to these fun events, GSEC and the Weill Cornell community are also engaged in advocacy activities. On November 29th, GSEC and the Science & Education Policy Association (SEPA) held a "Tax Bill" phone rally to call Congress to have our voices heard regarding graduate student tuition waivers and other provisions in the proposed tax bill that would have affected higher education. We know that the increase in financial stress would have affected all graduate students and the tax hike would have deterred students with financial disadvantages from pursuing higher education. We are grateful for the support and participation of the Weill Cornell community and administration.

GSEC is full of energy and ready to make 2018 our best year yet! Our council aims to support graduate students' academic, personal, and professional development, as well as their well-being. We have added new clubs and subcommittee liaison positions to better represent and support the graduate student community; to increase leadership and service opportunities for graduate students; and to promote ethnic, cultural, and academic diversity within the biomedical community. We are fully aware that our journey through graduate school should not be faced alone. Thus, we are working closely with Graduate School leadership to best represent the interests of graduate students.

And 2018 is getting off to a great start! Our recruitment weekends and our annual ski trip to Killington are just around the corner. We hope you are able to take advantage of the numerous resources the council and Graduate School offer. If you ever have any concerns or suggestions, please reach out to us by email or stop by our monthly meeting.

We hope you have a great year full of success, pizza from GSEC meetings, and furry friend visitors at Wellness events. Stay tuned!

furry friend visitor Best, Kathryn Carnazza GSEC President



ONE THESIS. ONE SLIDE. THREE MINUTES ...







he 3rd Annual Three Minute Thesis (3MT[®]) Competition was held this past November featuring nine finalists chosen from a preliminary round consisting of 12 Ph.D. students from different research backgrounds. The 3MT[®] is an academic research communication competition designed to challenge graduate students to concisely explain their three-plus years of research in layman's terms in just three minutes using only one slide.

The 3MT[®] was developed by The University of Queensland in 2008, and is now held in more than 600 universities and institutions across 63 countries. This unique competition not only provides students the opportunity to develop their communication and presentation skills, but gives them the opportunity to showcase their research to researchers throughout the network, as well as open doors to new collaborations and networks for both researchers and PIs.

"I am highly motivated to make sure others communicate their science effectively. So, to be part of an event celebrating and rewarding graduate students who want to talk about their work was a delight to me," says Ushma S. Neill, Ph.D., Vice President, Scientific Education and Training at MSKCC, who served as one of the six judges. Neill has 16-plus years of experience in scientific communication as an editor and writer, and teaches a course entitled "The Art of Scientific Communication."

"This year, I was super impressed with the students who were able to fully explain complicated computational models, cell membrane biology and epigenetics. Over the years, I've learned so much about the diversity of research being done on our two campuses," adds Neill.

In fall 2015, Weill Cornell Graduate School in partnership with the Sloan Kettering Institute hosted the first 3MT[®] competition. The event has been an integral part of the institutions ever since. The \$500 prize itself is, of course, a great motivator, but the majority of the presenters aim to create a positive and friendly research environment. "I did not expect to win," says Shira Yomtoubian, first-prize winner and recipient of the People's Choice award as selected by the audience. "My goal was to actually try to get the People's Choice award because my priority was to entertain and ensure the audience enjoys themselves. As many of my friends know, I care about creating positive experiences for people."

Mridula Balakrishnan, third place winner, says she did not expect to win either. "I wanted to do my best and hoped to win, but winning was a surprise as there were so many good talks.

"The biggest challenge is to simplify your research and to find appropriate analogies that the audience can relate to. It's often easier to use scientific jargon, and avoiding that to use simple words is a challenge." The competitors weren't the only ones faced with a challenge. The judges had their work cut out for them as well, as they had to decide between nine well-prepared candidates—and, on top of that, order the top three. "We always wish we could give everyone an award," Neill says. "It takes a lot of guts to get up in front of a crowd, and we appreciate the effort every participant puts in to preparing. Since we do usually have to pick just one, it's often hard to criticize – they all do so well that the difference between 1st and 3rd place can be minuscule.

"We look for someone who is well practiced and who has an illuminating slide to accompany. For the last two years, we've picked the person who has the best metaphor for their work." For Yomtoubian, that meant using jeans as a metaphor for genes, in her presentation entitled "*Metastasis: Loosen Up Your Genes.*" "Once I found my analogy," she says, "I knew I had a fun direction to write about." Three years in, the hope is that even more students will be inspired to take part in future competitions. And while the prizes are compelling, it's what they can learn in preparing win or lose—where the real value lies. "I encourage students to participate in the future – it's a lot of fun and it helps them step outside the comfort zone," says fellow judge Jake Sneva, Ph.D., Director of Education Administration at Weill Cornell Medicine. "At the end of the day, all students are going to need this skill to be able present in front of all kind of different audiences. This is one more opportunity to help them develop this skill."

"The benefits of this competition are that it makes you take a step back and look at the bigger picture of your research," says Balakrishnan. "Questions such as how and why you research are important, but not thought about very often, and this competition makes you think about it."

Congratulations To All The 2017 Finalists!



From Left to Right:

Hannah Yun-Han Huang Xiaotong Yao Diana Acosta Coryandar Gilvary Mridula Balakrishnan R. Lea Sanford Shira Yomtoubian Ashlesha Odak Michael Crowley



From Left to Right:

Shira Yomtoubian First Prize & People's Choice Award "Metastasis: Loosen Up Your Genes"

R. Lea Stanford Second Prize "Membranes Matter: Predicting Drug Toxicity"

Mridula Balakrishnana Third Prize "Understanding Nemaline Myopathy (NM), a Fly's Perspective"

Carl F. Nathan, MD Dean, Graduate School of Medical Sciences

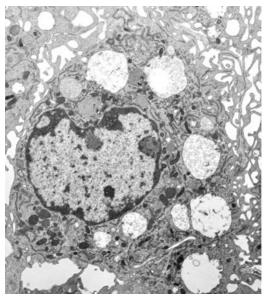
******Saving lives starts with research in the lab...*****

Born and raised in Bogota, Colombia as the son of two lawyers, Juan Cubillos-Ruiz, Ph.D., was always fascinated by biology, especially how genes were expressed and regulated.

After receiving his BS in Microbiology from University of Los Andes, Dr. Cubillos-Ruiz earned his Ph.D. in Immunology from Dartmouth Medical School in 2010 and spent four years of postdoctoral training under the tutelage of Dr. Laurie Glimcher. He joined Weill Cornell Medicine in 2015 as an Assistant Professor of Microbiology and Immunology in Obstetrics and Gynecology and a member of the Meyer Cancer Center.

Dr. Cubillos-Ruiz recently received the Pershing Square Sohn Prize for Young Investigators in Cancer Research, Schreiber Prize for Outstanding Mentored Investigators and the Jacquie Liggett Fellowship Award. The many prestigious awards for scientific achievement that he has earned come as no surprise and convey only part of the story of his outstanding career. Dr. Cubillos-Ruiz is also Co-Founder of Quentis Therapeutics, a New York-based biotechnology company focused on developing and commercializing unconventional immunotherapies for cancer.





Electron micrograph of dysfunctional tumorassociated dendritic cells accumulating lipid droplets.

My current research aims at understanding the regulation of immune responses to cancer. I am particularly interested in defining the molecular mechanisms that promote immune cell dysfunction in the tumor microenvironment. My lab is currently studying the role of Endoplasmic Reticulum (ER) Stress as a previously unappreciated driver of immunosuppression in cancer, and we are creating new cancer immunotherapies based on controlling the aberrant activation of ER stress sensors in tumor-infiltrating immune cells.

The Pershing Square Sohn award is an extraordinary funding mechanism that supports high risk or high reward research ideas by junior investigators interested in studying cancer. It enables junior faculty members like me to explore and develop unprecedented ideas that can revolutionize the treatment of cancer. My project aims at creating a new class of "armored" dendritic cells that can function under adverse conditions in the tumor microenvironment. With this approach, we hope to enhance the function of therapeutic vaccines to prevent the typical recurrence observed in lethal cancers such as ovarian carcinoma. We aim at training the immune system to be prepared if tumors come back after administration of standard treatments such as surgery and chemotherapy.

My first project as a graduate student has inspired me to continue with this research. I had to isolate and expand human tumor-infiltrating

T cells using genetically-engineered antigen-presenting cells. That was absolutely fascinating to me and I fell in love with this field. I am now convinced that harnessing the anti-tumor activity of our immune system is the only effective way to eliminate cancer. My main motivation in pursuing a career in cancer immunology is to bring hope to cancer patients using this approach. Saving lives starts with research in the lab.

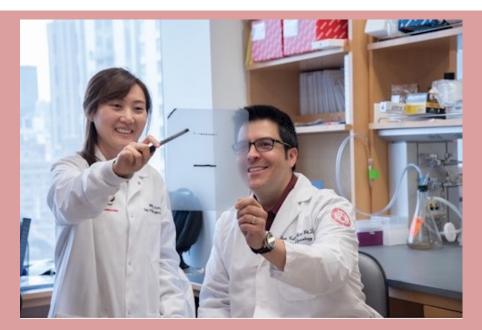
Quentis Therapeutics was created in April of 2016 based on our findings on the role of ER stress responses as key contributors of immunosuppression in cancer. It was founded in partnership between Weill Cornell Medicine and Versant Ventures. The current goal of Quentis is to develop potent small-molecule inhibitors that control ER stress responses in cancer hosts in order to re-activate anti-tumor immunity.

The biggest challenge I'm facing as a scientist and an entrepreneur is time management. Think about the amount of time you'll need to establish an academic lab, while simultaneously starting a biotech company. Finding time to create new technologies and attract investors is definitely very challenging in the face of major academic commitments like teaching, writing grants, training students and postdocs, as well as publishing papers.

Considering the growing biotech landscape and the competitive funding opportunities, I think it's critical to train our PhD students to strengthen their presentation and writing skills to ensure that they are better prepared to present their ideas or analysis more effectively and concisely.

My advice for Ph.D. students who want to pursue a non-traditional science career is be curious, creative and don't be afraid of taking risks! It is very important to think outside the box.

I enjoy spending time with my family and dogs, playing the classical guitar, as well as travelling and learning about other countries, cultures and traditions.



⁶⁶My advice for Ph.D. students is be curious, creative and don't be afraid of taking risks.⁹⁹ ¹¹Ultimately, it was an incredibly easy decision to choose Weill Cornell Graduate School," says Georgia Frost, a fourthyear Ph.D. candidate in the Neuroscience program. Frost is currently doing her thesis work in the lab of Dr. Yueming Li. The Li lab studies the enzyme gamma secretase, which plays a critical role in many cancers, as well as Alzheimer's disease. Frost's research focuses on the contribution of inflammation to amyloid beta production and Alzheimer's progression in both cell culture and mouse models. "My goal is to make a contribution to our understanding of what happens in the brain during Alzheimer's disease."

Frost grew up in Surrey, a county just southwest of London and moved to the United States with her family in 2001. She knew that she wanted to pursue a Ph.D. in Neuroscience during her senior year at Allegheny College in Pennsylvania. "I really enjoyed working on my senior thesis using electrophysiology to find novel inhibitors of voltage gated calcium channels. From there I worked in a lab at the University of Pittsburgh and applied to graduate school," Frost says. She mostly applied to schools in NYC because she wanted to be closer to her family. "I felt so much more comfortable than at other schools and loved its location in the Upper East Side," she recalls of her interview at Weill Cornell. "Moreover, I was excited by the faculty I met, the world-class research facilities and the relationship with Sloan Kettering, Rockefeller and HSS."

Since joining Weill Cornell, Frost has held many roles in the Graduate School Executive Committee (GSEC)-from recruitment chair to orientation chair and GSEC secretary. She is also a member of the Student Life committee, which is comprised of students, faculty members and administration from both the graduate and medical schools. "Being involved with GSEC helped me build connections throughout the graduate school and develop a better understanding of the administrative organization of the institution. Additionally, GSEC funds many clubs and organizations for non-science activities such as the soccer club, which meets to play pick up in the Olin gym twice a week." Frost has also been an active participant in the Cornell and Rockefeller outreach programs. She says it's a great opportunity to interact with young students who are enthusiastic about science. "I have really enjoyed every outreach activity I have been a part of, and it has definitely improved my ability to communicate science."

It's amazing to walk up York Avenue and be surrounded by science and medicine for blocks and blocks.



In addition to her research and extracurricular activities, Frost still finds time to serve as a Teaching Assistant for several graduate school courses. "I am currently teaching the tutorial section of Next Generation Methods, an introductory course for first year Pharmacology and Neuroscience students. I have learned a lot from having to plan class meetings and answer student's questions."

According to Frost, this opportunity gives her direct experience interacting with and learning from faculty outside of her research niche, as well as improves her own teaching skills. "The experience has undoubtedly expanded my own scientific understanding and also my ability to logically present information," she explains.

Outside of Weill Cornell, Frost volunteers with the Carter Burden Center for the Aging, a non-profit agency that offers a variety of programs and services benefiting older New Yorkers. During her free time, she goes for a run or plays soccer.

Besides enjoying the Neuroscience retreat every spring, Frost's favorite part about Weill Cornell is the campus's location in the heart of a busy city. "It's amazing to walk up York Avenue and be surrounded by science and medicine for blocks and blocks. I can't imagine that there is a more concentrated area of medical research anywhere else in the world."



PUBLICATIONS

We would like to extend our congratulations to the following Ph.D. students who have successfully published their first and second author papers this past year. We are very proud of your accomplishments and looking forward to many more!

Jaclyn Bonner, Xiaolan Zhao Lab

Smc5/6 Mediated Sumoylation of the Sgs1-Top3-Rmi1 Complex Promotes Removal of Recombination Intermediates. Cell Reports *Replication-associated Recombinational Repair: Lessons from Budding Yeast.* Genes

Aaron Chang, David Scheneiberg Lab

A Therapeutic T Cell Receptor Mimic Antibody Targets Tumor-associated PRAME Peptide/HLA-I Antigens. The Journal of Clinical Investigation

Opportunities and Challenges for TCR Mimic Antibodies in Cancer Therapy. Expert Opinion on Biological Therapy

Lauren Fairchild, Christina Leslie Lab Prediction of Potent shRNAs with a Sequential Classification Algorithm.* Nature Biotechnology Chromatin States Define Tumour-specific T Cell Dysfunction and Reprogramming.** Nature

Taylor Floyd, Elizabeth Ross Lab

Characterization of Calbindin D28k Expressing Interneurons in the Ventral Horn of the Mouse Spinal Cord. Developmental Dynamics

Vanessa Gutzeit, Joshua Levitz Lab Perineuronal Nets in the Adult Sensory Cortex are Necessary for Fear Learning.** Neuron

David Kuo, Gunnar Rätsch Lab

Tumor Necrosis Factor Dynamically Regulates the mRNA Stabilome in Rheumatoid Arthritis Fibroblast-like Synoviocytes.** PLoS ONE

Kihyun Lee, Danwei Huangfu Lab

Genome Editing in hPSCs Reveals GATA6 Haploinsufficiency and a Genetic Interaction with GATA4 in Human Pancreatic Development.* Cell Stem Cell

Yuheng Lee, Christina Leslie Lab

Learning to Predict miRNA-mRNA Interactions from AGO CLIP Sequencing and CLASH Data. PLoS Computational Biology

Dmitrii Maleshko, Iman HajirasoulihaLab

metaSPAdes: A New Versatile Metagenomic Assembler.** Genome Research

Christopher Noetzel, Bjorn Kafsack Lab

Single-cell RNA Sequencing Reveals a Signature of Sexual Commitment in Malaria Parasites.* Nature

Asaf Poran, Olivier Elemento Lab,

Single-cell RNA Sequencing Reveals a Signature of Sexual Commitment in Malaria Parasites.* Nature

Jenny Xue, Piro Lito Lab

An Approach to Suppress the Evolution of Resistance in BRAFV600E-mutant Cancer. Nature Medicine

Zhaohui Yang, Alexandra Joyner Lab

Stromal Hedgehog Signaling Maintains Smooth Muscle and Hampers Micro-invasive Prostate Cancer. Disease Models and Mechanisms

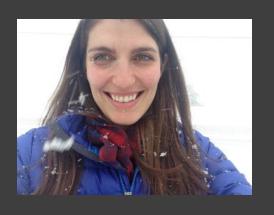
First co-author

** Second author

ennifer Oyler's love for science started in her senior year of high school with a few big dead sharks and an amazing biology teacher named Kate Hedeen. "I gave up a full scholarship playing college basketball so I could focus on undergraduate research and school," says Oyler, who grew up in rural Pennsylvania playing sports, reading, orchestrating epic Halloween costumes and hanging out with friends. After graduating from Saint Joseph's University, Oyler became a high school science teacher, but realized quickly that it wasn't for her. She then got a job at the University of Pennslyvania in the Microbiology department as a research specialist for two years.



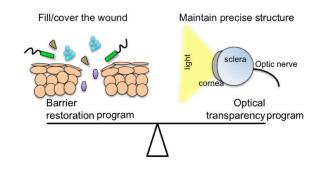
Dr. Oyler began her graduate training at Weill Cornell Graduate School in 2011 focusing on quantitative and computational biology, immunology, and cell signaling and earned her Ph.D. in 2016. She is currently a postdoctoral fellow at UCLA under the supervision of Dr. Roy Wollman.



⁴⁴I believe that most cutting edge basic science is still done in academia.⁷⁷

Can you please tell me about your current research?

I currently work on host-pathogen interactions in the context of wound healing in barrier tissues. We use the cornea as a model system because it is beautifully simple, yet has a stem cell niche, multiple different cell types, and, most importantly, it's optically clear so it's an ideal tissue for imaging. It's also easy to keep it alive in *ex vivo* culture. We also develop and use quantitative and computational tools for image analysis. In particular, we focus on how barrier tissues enable rapid re-establishment of the barrier (to avoid infection), while simultaneously maintaining the precise tissue structure required for vision.



What inspired you to get into this field of research?

I've always been interested in the dynamics of tissue responses to pathogens on long timescales. I'm also very interested in advanced microscopy techniques and computational tools for image processing. I knew that I wanted to develop imaging platforms to enable long time-scale analysis of biological processes in live organs or organisms. This project and lab gave me the perfect opportunity to do that.

Why did you choose Weill Cornell for your graduate training?

There were many investigators spread across Weill, MSKCC, NYP, and HSS whose work I found really interesting, so I knew there would be many options for me to do exciting science. During my interview, I was inspired by the program and graduate school leadership, and their interest in helping students mature intellectually. I also wanted to live in NYC and found the environment, including Rockefeller, to be very stimulating. The area definitely has a great vibe in terms of science and medicine.

What are the challenges, if any, are you facing as a female scientist?

I am thankful that all of the PI's I've ever worked with have been very supportive of efforts aimed at promoting women in science. That's not a coincidence, though. I chose PIs who I knew were progressive and valued diversity in science.

There are two areas that have stood as challenges for me personally. The first is that it has required a lot of self-encouragement to feel like I belong in quantitative and computational biology. I don't have a background in physics, math, or computer science and learned programming and computational tools on the fly during my PhD. Most members of computational biology departments are men with quantitative backgrounds, so I always feel like I have something to prove.

The other issue has been raising my son. Many universities do not offer childcare, or, if they do it is prohibitively expensive for postdocs. In addition, postdocs often rely on their advisor to grant time off after having a baby (i.e. there's no standard). Some PIs are great, but I do know of multiple advisors who demanded their postdoc return to lab after one or two weeks. That type of treatment is cruel and backwards.

My husband (also a postdoc) and I have been fortunate enough to have amazing mentorship and a lot of family support both in terms of time and money. I think universities have a lot of work to do to retain both men and women when the tech industry is sort of leading the way in terms of supporting families.

Considering the current funding climate, do you think PhD students are being discouraged from pursuing a postdoc position? Any advice for grad students who want a traditional science career or one in academia?

In my experience, I think Ph.D. students are actually being encouraged to pursue a postdoc, but only so that they can earn a higher wage in industry when they're done. The fact that only about 20 percent of postdocs end up with a position in academia partly reflects that attitude. I personally love the intellectual freedom of academia and I believe that most cutting edge basic science is still done in academia.

My advice is that if you want a career in academia, surround yourself with people who believe in you and support you both personally and professionally, and stick with it!

What do you like to do in your free time?

I like to spend time with my kid and husband, go to the beach (year-round in LA!), and read.

Any advice for incoming students?

Don't take your time there for granted. You are at an amazing research institution—let yourself be inspired and believe you're good enough to be there.

In Case You Missed It...

WELL AT WEILL

Wednesday Wellness Muffins

Griffis will provide muffins and coffee in Archbold Commons Wednesdays, 7:30am - 9:30am

Mindfulness Moments

Stop by for an evening of guided medidation, body work, massage, deep breathing aromatherapy, healing touch, Reiki and Mindful movements in Olin Lounge.

> Jan: Tuesdays & Thursdays, 4:00pm -6:00pm Feb: Tuesdays, 4:00pm - 6:00pm



The Rickman's lab research is focused on elucidating the role of proteins that drive prostate cancer progression, mechanisms of drug resistance and the transformation from castration resistant prostate adenocarcinoma to a neuroendocrine prostate cancer (NEPC). To this end, his lab has developed pre-clinical models that mimic this transformation. These models include isogenic cell lines, xenografts, genetically engineered mice and mouse prostate cancer organoid cultures. His lab combines phenotype data with genome-wide data of transcription factor binding, epigenetic and transcriptome alterations from these models and correlates this to patient-derived data.

Dr. Rickman maintains active collaborations with physician-scientists, computational biologists and medical oncologists at WCM and at other institutions within and outside the U.S. Active projects in Dr. Rickman's lab are characterizing the role of N-Myc in driving the NEPC phenotype, development of novel therapeutics for treatment of NEPC, identification of NEPCspecific antigens and characterizing the role of ERG in regulating gene expression and mediating taxane resistance.

David Rickman, Ph.D. Associate Professor Cell & Development Biology Program

The Guzman lab research focuses on the identification of novel therapeutic approaches for targeting cancer stem cells (CSCs) in hematologic malignancies without harming normal hematopoietic stem cells (HSCs) with the objective of clinical translation. Toward this goal, the laboratory aims to identify unique molecular features of AML that can be utilized as therapeutic targets.

The therapeutic strategies utilized in the laboratory include the use of plant derived compounds, novel small molecules design to target key pathways that CSCs rely upon, and engineered chimeric antigen receptor T-cells. The laboratory is highly collaborative with laboratories of diverse disciplines.

> Monica L. Guzman, Ph.D. Associate Professor Pharmacology Program

The Orr lab focuses on glial-neuronal communication and mitochondrial signaling as therapeutic targets to ameliorate neurodegeneration. We investigate the effects of receptor signaling in astrocytes and microglia and the production of mitochondrial reactive oxygen species in health and disease.

Glial-neuronal communication

Glia, including astrocytes and microglia, are abundant brain cells that are critical for diverse brain functions including metabolic homeostasis. neuronal communication and responses to injury and disease. Our goal is to understand the underlying mechanisms and roles of glial-neuronal communication in normal and pathophysiological processes, including behavior and cognitive processes, neuroinflammatory signaling, and gene expression. We are particularly interested in how factors linked to frontotemporal dementia and Alzheimer's disease impair the functions of glial cells and disrupt glial-neuronal interactions that are critical for normal brain function and resilience to disease. Although the underlying causes of these disorders are not clear and no effective treatments are available, new research suggests that glial cells may hold the keys to prevention and effective treatment of these and related neurological disorders.

Mitochondrial signaling

Most cellular activities that go awry in neurodegenerative disease require proper mitochondrial signaling including neural transmission, immune responses and metabolism. Mitochondria in neurons and glia regulate how the brain responds to injury and play key roles in neurodegeneration. Our lab is currently investigating if and how mitochondrial production of reactive oxygen species contributes to aberrant glial and neuronal responses in experimental models of neurodegenerative disease.

The Orr lab uses diverse in vitro and in vivo approaches including chemogenetics, transcriptomics, biochemistry, behavioral assays, and transgenic mice which exhibit key neuropathological hallmarks of human disease. Findings obtained in experimental models are validated in human samples, such as human cell cultures and postmortem brain tissue. Insights gained from our studies are used to better understand the underlying causes of disease and help develop novel therapeutic interventions targeting key pathogenic cascades. These efforts may lead to the repurposing of known therapeutic agents and the discovery of new strategies to prevent neurological disease.

> Anna Orr, Ph.D. Assistant Professor Neuroscience Program

Dr. Zippin's research lab is focused on understanding the role of cAMP signaling in inflammatory skin disease, pigmentation and skin cancer. His lab has developed numerous cellular and mouse models for the investigation of cAMP in pigmentation, UV biology, skin cancer, and T cell mediated diseases. In addition, his lab is interested in the development of new diagnostic and therapeutic interventions for skin cancer. To accomplish these goals, Dr. Zippin maintains active collaborations with immunologists, cancer biologists, computational biologists, and pathologists at WCM and at numerous other institutions across the US and abroad.

Active projects include (1) establishing new mechanisms for organelle pH control important for normal pigmentation and melanoma risk; (2) determining the relevant cAMP microdomains in skin cancer and inflammatory diseases of the skin e.g., psoriasis and atopic dermaitits; (3) establishing the non-mutagenic role of UV radiation in carcinogenesis; and (4) employing UV radiation in the treatment of cancer.

> Jonathan Zippin, MD/Ph.D. Assistant Professor Pharmacology Program

The Finley lab investigates how cellular metabolic pathways regulate cell fate decisions in stem cells and cancer cells. We combine genetic and metabolomic approaches to investigate cell-type specific growth requirements and elucidate how flux through central metabolic pathways regulates key cellular activities, including self-renewal and differentiation. In particular, we are interested in understanding how changes in metabolite availability shape the chromatin landscape to influence gene expression programs that control cell survival, growth and differentiation.

Our work aims to answer fundamental questions about how cells regulate the commitment to differentiation and how failure to execute terminal differentiation can underlie diseases such as cancer.

Lydia Finley, Ph.D. Assistant Professor Cell & Development Biology Program **The Scheuring** laboratory is specialized in Atomic Force Microscopy (AFM) based technologies for the study of various membrane phenomena, such as membrane protein structure, assembly, diffusion and conformational dynamics. While the resolution of (membrane) protein structures becomes more common due to the impressive progresses in cryo-electron microscopy and X-ray crystallography, the characterization of protein dynamics and assembly into superstructures remains poorly understood and difficult to study.

Over the past few years, our laboratory has been instrumental in the development and application of High-Speed Atomic Force Microscopy (HS-AFM), unique for the analysis of dynamics of unlabeled single molecules, allowing to bridge structure and function. Using HS-AFM, we reach lateral resolution of ~1nm, vertical resolution of ~0.1nm and temporal resolution of ~100ms. While we continuously push the technological limits, our state-of-the-art HS-AFM can readily resolve dynamics of single domains in transmembrane channels, transporters and membrane associated proteins in buffer solution and under ambient temperature and pressure.

We showcased the power of the technique through direct visualization of conformational changes in a cyclic nucleotide gated potassium channel exposed to cyclic nucleotides, the transport cycle of a glutamate transporter, and the compression of the ESCRT-III membrane fission machinery. Taking advantage of a microfluidic device coupled to the HS-AFM fluid chamber, we can stimulate membrane-proteins through real-time addition of ligand during imaging. Finally, we are currently developing HS-AFM sensing of fluctuations to characterize protein dynamics down to the microsecond time range.

Simon Scheuring, Ph.D. Professor Physiology, Biophysics & System Biology Program

Care. Discover. Teach.

The Josefowicz lab focuses on fundamental questions of genome organization and regulation, especially as it pertains to rapid cellular responses, including innate immune cell responses to pathogen sensing. Ongoing research in the lab is revealing links between aberrant activation of "signaling to chromatin" pathways, epigenetic alterations, and disease states, which include cancer, chronic inflammatory conditions, and accelerated aging.

Dr. Josefowicz and his group aim to identify mechanisms that enable cells to selectively, rapidly, and robustly induce expression of specific genes in response to environmental cues. Key to this process is what he calls "signaling-to-chromatin" pathways, a process by which these signals initiate transcription of a small number of select genes with speed and precision in the context of two-meters of "chromatinized" DNA compacted within a complex, micron-scale nuclear environment— a process well described by the metaphor of finding a needle in a haystack, and quickly. Factors in these signalingto-chromatin pathways are critical in rapid cellular responses, dysregulated in disease, and frequently co-opted in the process of oncogenesis. However, surprisingly little is known of how activation of kinase cascades transmits information directly to chromatincomposed of histone proteins complexed with DNA-for dynamic regulation of nuclear architecture and chromatin characteristics with consequences for transcription.

The Josefowicz lab is interested in understanding how cells address primary challenges that exist to accomplish this feat in health and disease and hope to gain insights into the process of transmission of information from outside the cell to chromatin that explain the speed, specificity, and robustness of signal-induced transcription. Beyond the potential for fundamental mechanistic insights into signaling-tochromatin pathways, the goal is to understand the role of dysregulation of these pathways in inflammatory disease, aging, and cancer.

Steven Josefowicz, Ph.D. Assistant Professor Immunology & Microbial Patogenesis Program Physiology, Biophysics & System Biology Program

The Pitt lab studies diseases and disorders of electrical activity in cells. We focus on ion channels and their regulatory proteins, and on the pathophysiology that results from abnormal ion channel function. We are especially interested in cardiac arrhythmias, epilepsies, ataxias, and neuropsychiatric disorders such as autism. Recently, the lab identified novel roles for ion channels in unexpected tissues and processes, including bone development and cardiac valve disease, and the lab is developing therapies based on these findings. The experimental approaches in the lab span from structural analyses and biochemistry through cellular and animal models, as well as investigations in patients.

Geoffrey Pitt, MD/Ph.D. Professor Pharmacology Program

Care. Discover. Teach.

Editor-in-Chief: Chrissie Kong

Speak your mind. Share your story. Show off your talent. Be a part of **WorthWEILL**. Contact us to get involved at <u>sok2016@med.cornell.edu</u>

FOLLOW ME



facebook.com/weillcornellgradschool



twitter.com/WeillCornellGS



instagram.com/weillcornellgs

Weill Cornell Medicine Graduate School of Medical Sciences

Weill Cornell Medicine Graduate School of Medical Sciences

> 1300 York Avenue New York, New York 212.736.6565

gradschool.weill.cornell.edu