

CBP IN THE LOOP

THE LATEST NEWS AND UPDATES FROM CELL BIOLOGY AND
PHYSIOLOGY

Editors: Janice Warfford, Whitney Bell, Baggio Evangelista, Matthew Billard and Kathleen Caron

2022 Gottschalk Lecture



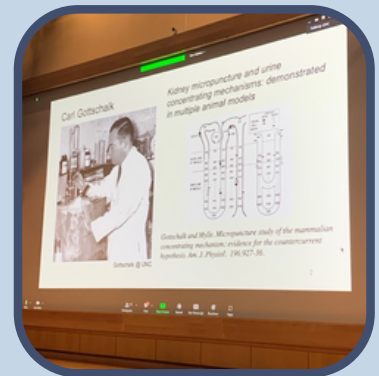
The UNC Department of Cell Biology and Physiology, UNC Kidney Center and Dr. Susan Fellner proudly hosted the well renowned kidney researcher, Iain Drummond, Ph.D, as this year's Prestigious Carl W. Gottschalk Lecturer. Dr. Drummond is the Director of the Kathryn W. Davis Center for Aging and Regeneration at MDI Biological Laboratory. As a researcher on the use of zebrafish as a model for human kidney development and repair, he delivered his lecture entitled "Kidney Development, Disease, and Regeneration: Lessons From the Fish" on Monday, October 24th at 4PM.

"Iain Drummond is a particularly deserving recipient of the Carl W. Gottschalk award. Because he explores mechanisms of kidney development and regeneration using the zebra fish as a model organism, his work has broad scientific appeal and would have been of special interest to Dr. Gottschalk."

-Dr. Susan Fellner*

Carl Gottschalk came to the University of North Carolina at Chapel Hill as a Cardiology fellow and instructor in 1952 and focused on using micropuncture to analyze kidney function. At the time, micropuncture had only been utilized in a limited way to study function of individual nephrons in the mammalian kidney. With only a small grant from the Edgecombe County (NC) Heart Association and a closet for a laboratory, he addressed how the kidney concentrated urine, pursuing the hypothesis that a countercurrent multiplier system of renal tubules and vasa rectae was responsible. Evidence confirming this hypothesis was published in Science in 1958. These remarkable studies were followed by other pioneering works on the mechanism of urine acidification, calcium excretion, potassium depletion, neural control of salt excretion and glomerular dynamics. Dr. Gottschalk's research group also made important observations on the pathology of acute and chronic renal failure. He served admirably on the national scene, leading a study on treatment of renal failure; his recommendations led to our current federal support of renal dialysis.

*Source: Dr. Fellner interview with MDIBL (featured on their website)



DEPARTMENTAL MISSION

The Department of Cell Biology and Physiology follows the guiding principles of our School of Medicine: to be nationally recognized for excellence in our discipline by leading, teaching, and caring.

- *Leading: to conduct cutting-edge, innovative research that advances the discipline of cell biology and physiology, with emphasis on topics that contribute to the improvement of human health*
- *Teaching: to provide a rigorous and competitive educational experience for a diverse population of graduate and professional trainees which enables them to succeed in their future careers*
- *Caring: to serve the people of North Carolina, the United States, and the international community, by excelling in our research and education missions which advance the discipline of cell biology and physiology*

CBP By the Numbers

2022

183

CBP Employees

\$25,655,286

CBP NIH Funding (2021)

**Ranking CBP #1 in the Nation in
NIH Funding 2021**

CBP Faculty

66

Grant Proposals Submitted by CBP Faculty

148

50

**CBP
Graduate
Students**

**CBP
32**

New Hires

**20 CBP
Postdocs**

Over

135

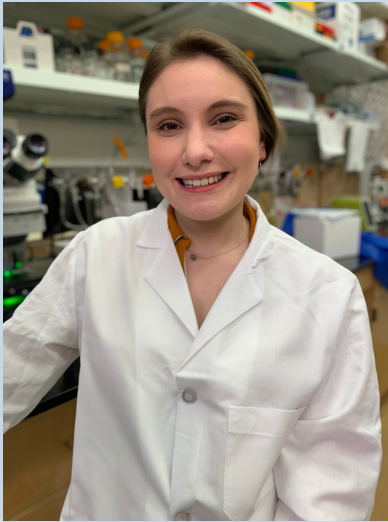
**CBP Publications
(Affiliated in PubMed)**

**PhD
Dissertations
Defended**

5

CBP POSTDOC SPOTLIGHT

Sophie Maiocchi
Bahnson Lab



Dr. Sophie Maiocchi is a recipient of a 2022 Postdoctoral Award for Research Excellence (PARE). One of five awardees, Sophie presented her research at the PARE Talks during UNC's University Research Week in October.

Originally from Sydney, Australia, Sophie completed her B.Sc. and Ph.D from the University of New South Wales. She completed her first postdoctoral training at the Heart Research Institute at the University of Sydney before joining Dr. Edward Bahnson's lab in 2018. Her research in the Bahnson lab focuses on the targeted vascular delivery of redox-based atherosclerosis treatments. Her recent publication in Biomaterials Science demonstrated that targeted delivery of Antioxidant Response Activating nanoParticles leads to the activation of genetic regulatory targets.

When not in the lab, Sophie enjoys hiking and kayaking at Saxapahaw and Jordan Lake.



Congratulations on the PARE!



As a part of the effort to increase underrepresented minorities in research, Scott Parnell has collaborated for the last six years with Dr. Fulton Crews, the Director of the Bowles Center for Alcohol Studies, and Dr. Leon Coleman, Assistant Professor of Pharmacology and the Center for Alcohol Studies, on an NIH-funded partnership grant with North Carolina Central University (NCCU), an HBCU located in Durham, NC. This recently refunded grant was designed to promote research at NCCU in order to give underrepresented individuals from NCCU more access to research experiences. Through this program, NCCU has trained numerous Master's and Ph.D. students that might not otherwise have gone into science. UNC's role in this process is to provide mentorship and access to scientific equipment and resources that would otherwise not be available to NCCU students. For this reason, numerous NCCU students have performed experiments in UNC labs, or with the Alcohol Center's support (particularly in terms of access to mouse resources) that were used to complete their Master's or Ph.D. thesis. Another aspect of this program is to provide undergraduates at NCCU access to greater research experiences. This research experience is critical for students who want get a Ph.D. in a scientific discipline as they are applying to graduate school, and many NCCU undergrads going through this program have gone on to excellent Ph.D. programs across the country. Overall, this program is designed to leverage the greater experience and resources of faculty here at UNC to enhance the pipeline of individuals from underrepresented groups going into scientific research and policy. One of the most exciting aspects of this grant is that it will include funds to be able to host NCCU undergraduate students in research labs here at UNC for summer research projects. This summer program should dramatically increase exposure to science and new research opportunities for NCCU students before they start applying to graduate schools.



FEATURE

Illuminating sub-cellular dynamics in human health and disease

Sarah Cohen and group awarded by Chan Zuckerberg Initiative, Neurodegenerative Challenge Network for multiplex live-cell imaging strategies.

By Baggio A. Evangelista

Dr. Sarah Cohen, Assistant Professor in the Department of Cell Biology and Physiology, was named co-recipient of the 1.6 Million dollar Chan Zuckerberg Initiative Collaborative Pairs Pilot Project Award, a funding extension of the CZI Neurodegeneration Challenge Network.

Founded in 2015, the Chan Zuckerberg Initiative (CZI) was established for global advancement in areas related to health, education, and scientific research. One of the CZI's first flagship programs was the Neurodegeneration Challenge Network (NDCN) which was launched in 2018 [1].

The NDCN's highly interdisciplinary research mission was established as a hub for biologists, computational scientists/bioinformaticians, engineers, and physicians, focused on tackling one of society's most mounting and incurable class of human diseases. This includes debilitating, often fatal, cognitive and/or movement disorders including Alzheimer's, Parkinson's, amyotrophic lateral sclerosis, and Huntington's disease. All of which are expected to increase in prevalence within the next three decades, bringing with them emotional and socioeconomic impacts on a global scale.



 [@cohenlaboratory](https://twitter.com/cohenlaboratory)

Keeping in line with the collaborative mission of NDCN to best approach these often enigmatic diseases, Dr. Cohen received the Collaborative Pairs Pilot Project Award along with Dr. Mohanish Deshmukh, Full Professor, CBP and UNC Neuroscience Center.

Together with two senior post-doctoral scientists, Dr. Maria Clara Zanellati and Dr. Richa Basundra (of the Deshmukh lab), the investigators are carrying out cutting-edge techniques aimed at visualizing the dynamics of subcellular structures, called organelles, and how these dynamics change in diseased conditions.

“We are interested in how sub-cellular compartments called organelles reorganize in response to changing developmental or environmental cues.”
-S. Cohen, PhD

This approach combines expertise of both groups: human induced pluripotent stem cell neuron culture and modeling from the Deshmukh lab, and high resolution live-cell imaging of multiplexed organelle markers, an adaptation on multispectral imaging technology developed by Cohen during her post-doctoral training in the lab of Jennifer Lippincott-Schwartz (NIH Bethesda, MD).

With this funding, these groups will monitor changes to all major organelles in cultured human neurons when engineered to contain causative neurodegeneration-associated mutations. With this information, the group can begin to better understand deleterious changes in cellular processes related to neuronal survival and metabolism.

At large, this work will illuminate our mechanistic understanding of these devastating diseases, as well as paths toward more effective interventions.

Meet the scientists!

SARAH COHEN, PHD
PRINCIPAL INVESTIGATOR



Vancouver 🇨🇦

Hobbies: spending time outdoors, dancing.

Fun fact: dressed up as an endoplasmic reticulum for Halloween!

MARIA CLARA ZANELLATI, PHD
POST-DOCTORAL FELLOW



Milan 🇮🇹

Hobbies: houseplant aficionado

Fun fact: just started expanding her houseplant real estate to include aquatic plant aquariums!

How did your academic journey bring you to UNC?

"I was a graduate student at the University of British Columbia and a postdoc at the NIH Intramural Program in Bethesda. When I interviewed for faculty positions, it was immediately clear that UNC CBP would be a great fit – the Department has many research groups interested in membrane trafficking and neural cell biology. In addition, the campus has great resources for microscopy and microscope development." -Cohen

"I was a PhD at ETH Zurich when I fell in love with lipids, and I wanted to study organelle dynamics and metabolism. I came across the work of Sarah Cohen and decided the lab was a good fit for my research interests. I have been really happy to work with Sarah, and I am happy the UNC CBP department has many research labs that could be a good fit for my future research interests."
- M.C. Zanellati, PhD

What drew you to science?

"I grew up on the West Coast, spending a lot of time exploring the woods or intertidal zone. My mom was a biology teacher and would always tell me fun facts about the different plants and intertidal creatures. When I went to university, I remember a lab class where we looked at live plant cells under the microscope and saw cytoplasmic streaming of organelles. I was blown away by how dynamic the cell as a system was, and decided I wanted to focus on cell biology." -Cohen

"I always loved science since I was a child. We have a farm where I always spent my summers, and I think is this is where the magic happened. Nature and biology are intriguing and funny. I continued to study Biology and during my Master thesis I started to get attracted by mitochondria and neurodegeneration. However, only during my PhD did I mature an interest in how organelles can modulate metabolism, from neurodegeneration to diabetes." -Zanellati

What is one piece of career advice you feel applies to all stages?

"Find something you are really excited to work on! It may take some exploration before you hit on the right thing. Science has its ups and downs, so it's important to find a question that motivates you to keep working on it." -Cohen

"Be curious and stay motivated! Because you never stop learning! how to do an experiment, how to teach to a person, how to write a grant, how to run a family and a lab!?...etc.... so try to have fun!" -Zanellati

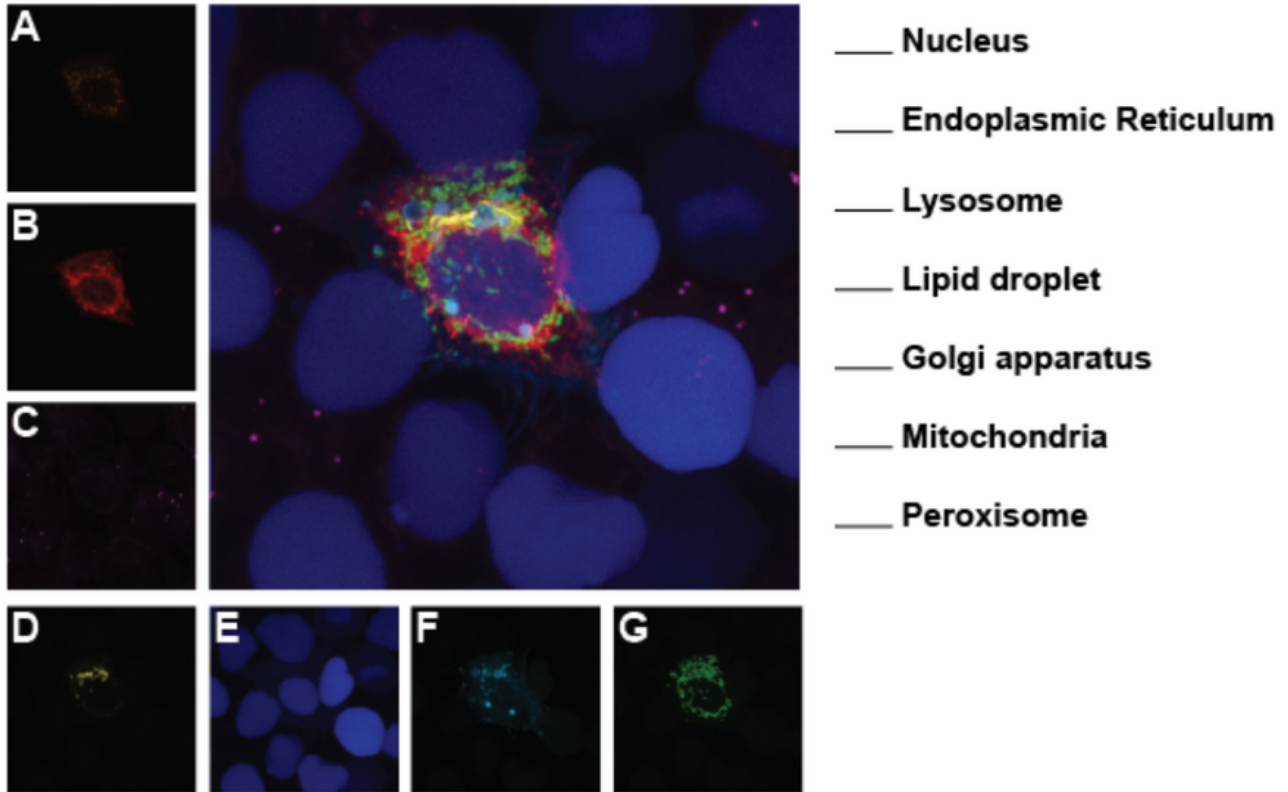


In the last edition of CBP in the Spotlight, we tested your knowledge of organelles using a crossword puzzle. Want to test your knowledge in practice like the Cohen Lab? Test yourself on page ____! Images courtesy of S. Cohen and M.C. Zanellati.



Test your knowledge of organelle signatures in iPSCs!

Each fluorescence channel shown in frames A-G mark unique cellular organelles imaged in a live, induced pluripotent stem-cell using a multispectral imaging platform developed by Cohen et al., 2017. Match each fluorescence channel with its respective organelle. Answers are listed on page ____.



**Images courtesy of Cohen and Zanellati*

WELCOME NEW FACULTY

WE'D LIKE TO WELCOME OUR NEW CBP FACULTY THAT JOINED US IN 2022 AND WILL JOIN IN 2023!
PLEASE WELCOME THESE GREAT ADDITIONS TO OUR FACULTY RANKS!



**Heather McCauley,
PhD**

Welcome Dr. Heather McCauley, Ph.D. who recently joined us as an expert in mouse and human pluripotent stem cell-derived organoid model systems to investigate intestinal development, physiology and pathology. Dr. McCauley received her Bachelor of Arts in Biological Sciences and Bachelors of Science in Kinesiology from the University of Southern California in 2007, after which she spent two years at Medtronic Diabetes as a Therapy Associate. Dr. McCauley earned her Ph.D. in 2015 as a graduate student in the lab of Dr. Geraldine Guasch at the University of Cincinnati. Heather's thesis work focused on the signaling mechanisms that maintain epithelial homeostasis and become dysregulated during transformation into invasive tumor cells and metastases. Following her graduate school training, Dr. McCauley was recruited as a postdoctoral researcher to the laboratory of Dr. James Wells in the Department of Developmental Biology and Center for Stem Cell and Organoid Medicine at Cincinnati Children's Hospital Medical Center.

Dr. McCauley's independent research program centers around her creative and novel approaches to the study of enteroendocrine cells (EECs) in the intestine. EECs are emerging as powerful new therapeutic targets for the treatment of type 2 diabetes for their potent effects on pancreatic insulin secretion and as targets of anti-obesity drugs. The McCauley Lab research program seeks to bridge the fields of digestive health and metabolism and will focus on how EECs affect the function of the intestinal microenvironment and the broader implications of how these functions impact the body as a whole.



**Whitney Edwards,
PhD**

Welcome Dr. Whitney Edwards, Ph.D., an expert in the function of protein expression dynamics and protein-protein interactions in heart development and disease. Whitney received her Bachelor of Science in Biochemistry (cum laude) from St. Edward's University (Austin, TX) in 2012. Dr. Edwards then moved to the lab of Dr. Lori Raetzman at the University of Illinois at Urbana-Champaign as a graduate student where she earned a Master of Molecular and Integrative Physiology in 2015 and her Ph.D. in Molecular and Integrative Physiology in 2018. Whitney's thesis work focused on elucidating the molecular mechanisms that regulate pituitary gland development, making pioneering discoveries and using genetic mouse models, in vitro techniques, and primary cell culture to determine the role of the Notch signaling pathway during pituitary development. Following her graduate school training, Dr. Edwards was recruited as a postdoctoral researcher to the laboratory of Dr. Frank Conlon in the Departments of Biology and Genetics at UNC, Chapel Hill. As a postdoctoral fellow, Dr. Edwards' research focused on coupling cellular and molecular approaches to study cardiac development and disease.

In her most recent work, Dr. Edwards – in collaboration with the UNC Michael Hooker Proteomics Center -- has built a time-resolved proteomic atlas of the developing heart to identify novel pathways and proteins essential for cardiogenesis. This extensive proteomic dataset will be an invaluable resource for the field of cardiac development and for future studies in her independent research lab at UNC.

Congratulations



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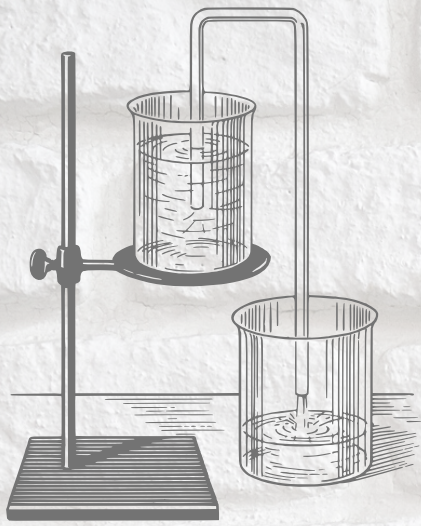
The Cell Biology and Physiology department has been a great scientific home, with its rich history in microscopy, neuroscience, the cytoskeleton, and membrane trafficking. I look forward to continued opportunities of learning and growth, to mentoring trainees, and to making our department and curriculum an inclusive community .

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-Dr. Stephanie Gupton
Newly Appointed Professor/2022
Cell Biology and Physiology

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Graduate STUDENT CORNER

Ismael Gomez Research featured on Cover of cmgh



Dietary fat is absorbed by absorptive enterocytes, the main cell type of the small intestinal epithelium. The mechanisms by which these absorptive enterocytes take in dietary fat and export it to the rest of the body are still not completely understood. In this recent article published in Cellular and Molecular Gastroenterology and Hepatology (CMGH), UNC researchers developed a way to grow human absorptive enterocytes in the lab to study how these cells take in and

export fat. They discovered that they were able to control fat export by treating the cells with drugs that effect a process known as fatty acid oxidation. Drugs that inhibited fatty acid oxidation blocked fat export whereas drugs that increased fatty acid oxidation increased fat export. Interestingly, they found that metformin, which is the most commonly prescribed drug for type-2-diabetes, increased fat export by increasing fatty acid oxidation. The researchers were able to scale their platform to a 96-well format which could be applied for high-throughput drug screening and could be useful for identifying new drugs for metabolic diseases such as obesity and diabetes.

FUSION SEMINAR

Welcome to the Fall 2022 Semester



Cell Biology and Physiology

CBP Graduate Student Socials and Sweatshirts



Back to the Future of Science

Our CBP Graduate Students are so excited to be back planning and attending social events!

2022 CBP Halloween



CBP



CBP Pumpkin Carving Contest Winners



Parnell Lab



Bautch Lab



O'Brien Lab

Best Costume

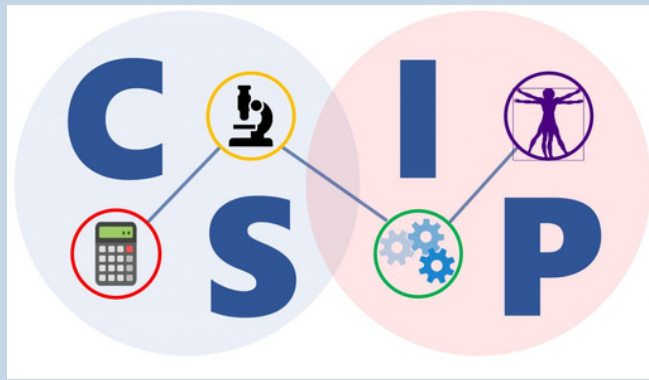


Bautch Lab



"What do you call an elevator full of organelles?"
a CELL-evator!
-Sarah Cohen, PhD





Cellular Systems and Integrative Physiology (CSIP) Training Program

The mission of the CSIP Training Program is to develop a diverse pool of responsible, rigorous scientists who have the skills to investigate the integrative, regulatory and developmental physiology of higher organisms and their organ systems by elucidating the functional cellular components of these processes and furthermore, can transition these skills into a wide variety of careers in the biomedical workforce and overall society.

This training grant is currently funding the following students:



Jocelyn Alvarado: (Mentor: Sharon Campbell, PhD)

Research: Investigate the coordination of vinculin and its splice isoform metavinculin in the regulation of cell morphology and force transmission at cellular adhesions of murine embryonic fibroblasts (MEFs) and the embryonic chick heart.



Amber Gomez: (Mentor: Justin Milner, PhD)

Research: Most recently we developed a new tumor model, a murine B cell leukemia (ALL) carrying the GP33M antigen. Using spectral flow cytometry we showed that P14 CD8s were able to specifically recognize and kill the ALL-GP33M, but not ALL. We are currently working on in vivo studies to characterize CD8 exhaustion subsets in the ALL model. In the future we will further manipulate the P14 CD8s by interfering with the NFkB pathway, an important signaling pathway in T cell function. By understanding the role NFkB plays in CD8 exhaustion we hope to identify manipulations that can improve exhausted T cells and lead to increased tumor clearance, therapy response, and survival.



Jennifer Nwako: (Mentor: Frank Conlon, PhD)

Research: Investigates sex differences in the role of GATA4, a core cardiac transcription factor required for cardiac development. When mutated, GATA4 causes human heart disease in adults and children.



Alex Powers: (Mentor: Sarah Cohen, PhD)

Research: Investigating the function of apolipoprotein E on the regulation of lipid droplets in astrocytes and its implications in Alzheimer's disease.

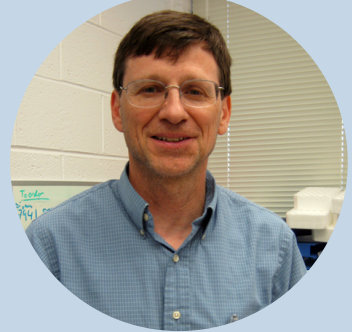
Employee Spotlight

2022

Congratulations to these
outstanding employees as they
celebrate their milestone
anniversaries this year!



Bonnie Blake: 35 Years



Larry Ostrowski: 25 Years

Celebrating 20 years!!!



Jay Brenman



Edward Kernick



Hongyu Ren



Maryna Kapustina, 15 Years



Guendalina Rossi, 10 Years

Celebrating 5 Years!!



Sarah Cohen



Graham Diering



John Ikonmidis



Michelle Itano



Ellen O'Shaughnessy



Wendy Salmon



Julia Lord



2022

CBP Departmental Awards

Faculty Mentoring Award

Recognition of outstanding mentoring to any of the following groups: Jr Faculty, postdocs, graduate students, undergraduate students.



Alain Burette



Lori O'Brien

Innovation in Teaching Award

Recognition of new & innovative teaching techniques proven to be useful in achieving the department's teaching mission.



Emily Moorefield

Extra Mile Award for CBP Curriculum Graduate Student

Recognition of outstanding research endeavors, outstanding leadership abilities and/or outstanding service to fellow students and curriculum.



Natalie Harris



Baggio Evangelista

Extra Mile Award for Postdocs and EHRA Non-Faculty Ranked Positions

Recognition of outstanding research endeavors, outstanding leadership abilities and/or outstanding service to lab and department.



Greg Miner

Staff Excellence Award

Recognition of outstanding work performance & customer service skills; demonstrating dedication, cooperation and a positive attitude.



Julia Lord



Tonya Murrell

Cell Biology and Physiology Service Award

Recognition of exceptional service to the CBP department or curriculum, to the University and /or to the surrounding community.



Rebecca Hirsch



**Nicole
Hondrogiannis**

Cell Biology and Physiology Publication of the Year Award

Recognition of best scientific
publication.

Jess Thaxton
Lab

CANCER RESEARCH | TUMOR BIOLOGY AND IMMUNOLOGY

Stress-Mediated Attenuation of Translation Undermines T-cell Activity in Cancer

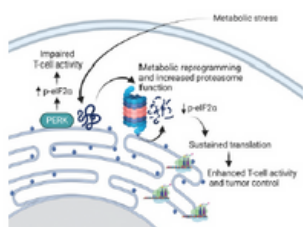
Brian P. Risenberg¹, Elizabeth G. Hunt^{1,2}, Megan D. Tennant³, Katie E. Hurst¹, Alex M. Andrews⁴,
Lee R. Leddy⁵, David M. Neskey⁶, Elizabeth G. Hill^{4,5}, Guillermo O. Rangel Rivera^{1,6}, Chrystal M. Paulos^{1,6},
Peng Gao⁷, and Jessica E. Thaxton^{1,2}

ABSTRACT

Protein synthesis supports robust immune responses. Nutrient competition and global cell stressors in the tumor microenvironment (TME) may impact protein translation in T cells and antitumor immunity. Using human and mouse tumors, we demonstrated here that protein translation in T cells is repressed in solid tumors. Reduced glucose availability to T cells in the TME led to activation of the unfolded protein response (UPR) element eIF2 α (eukaryotic translation initiation factor 2 alpha). Genetic mouse models revealed that translation attenuation mediated by activated p-eIF2 α undermines the ability of T cells to suppress tumor growth. Reprogramming T-cell metabolism was able to alleviate p-eIF2 α accumulation and translational attenuation in the TME, allowing for sustained protein translation. Metabolic and pharmacological approaches showed that proteasome activity mitigates induction of p-eIF2 α to support optimal antitumor T-cell function, protecting from translation attenuation and enabling prolonged cytokine synthesis in solid tumors. Together, these data identify a new therapeutic avenue to fuel the efficacy of tumor immunotherapy.

Significance: Proteasome function is a necessary cellular component for enduring T cells with tumor killing capacity by mitigating translation attenuation resulting from the unfolded

protein response induced by stress in the tumor microenvironment.



Metabolic reprogramming results in heightened protein degradation in T cells exposed to tumor stress, enabling sustained translation and tumor control.

Introduction

Activation of protein synthesis is a requirement for T-cell growth and effector function (1). Eukaryotic translation initiation factor 2 (eIF2) controls cap-dependent protein translation efficiency by bridging Met-tRNA_i and the ribosomal subunit (2). However, endoplasmic

reticulum (ER) stress, catalyzed by accrual of unfolded proteins in the ER lumen, undermines the competency of the process. In response to ER stress, the unfolded protein response (UPR) is initiated via phosphorylation of the α subunit of eIF2 causing translation attenuation as a means to restore proteostasis (3). The tumor microenvironment (TME) is replete with metabolic stressors known to activate the UPR (4–7). We and others have shown that PERK, ER-like kinase (PERK), a stress sensor responsible for eIF2 α phosphorylation (8, 9), undermines T-cell antitumor efficacy (10, 11). Although these studies implicate the UPR-mediated translational machinery as a potential molecular checkpoint prompted by TME stress, the extent to which translational regulation influences outcomes in the context of antitumor immunity is unknown.

Glycolysis is the critical energy requirement for T cells to undergo protein translation (12). However, upon entering the TME, CD8 T cells encounter competition for exogenous glucose, resulting in a significant reduction in effector function (5). In contrast, T cells that depend on metabolic pathways apt for cell survival in nutrient stress, such as gluconeogenesis (13) or fatty acid oxidation (14), demonstrate heightened tumor control (15, 16). Metabolic reprogramming through cytokine conditioning (17) or chronic glucose deprivation (15) generates T cells enriched for such pathways that fuel resistance in nutrient-deplete settings. Although we previously demonstrated that metabolic reprogramming through cytokine conditioning generates T cells capable of sustaining protein translation

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Corresponding Author: Jessica E. Thaxton, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, 225 Mason Farm Road, Chapel Hill, NC 27594. Phone: 919-966-4970; E-mail: jess_thaxton@med.unc.edu

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AACR American Association
for Cancer Research

AACRJournals.org | 4386

Pictured (Top to Bottom):

Jess Thaxton
Brian P. Risenberg
Elizabeth G. Hunt
Megan Tennant
Katie E. Hurst
Alex Andrews



Save
the Date



CBP DEPARTMENTAL RETREAT

Friday
April
21
2023

Please visit our **Make a Gift** website to give:

<https://www.med.unc.edu/cellbiophysio/make-a-gift/funding-opportunities>

Current opportunities to support the Department of Cell Biology and Physiology:

CELL BIOLOGY AND PHYSIOLOGY GIFT TRUST

This fund is a general fund to help support invited experts, informative speakers, and events that foster collaboration, professional development, and scientific growth.

MAREN TRUST FOR GRADUATE STUDENTS

The Thomas P. Maren Graduate Student Fund is intended to provide CBP Curriculum graduate students with opportunities to learn new skills and gain experience with emerging technologies.

CELL BIOLOGY AND PHYSIOLOGY POST-DOC FUND

This fund is intended to provide CBP postdoctoral trainees with funds to support travel expenses and registration fees for scientific conferences and specialized training opportunities or workshops.



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Physiology**

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