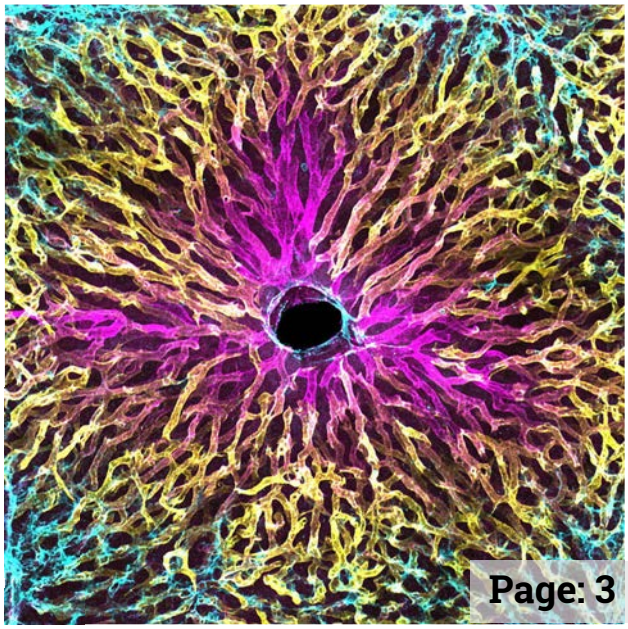
CBP In The Loop

Vol. 6, Fall 2024

Year in Review

#2 in the Nation for NIH Funding!



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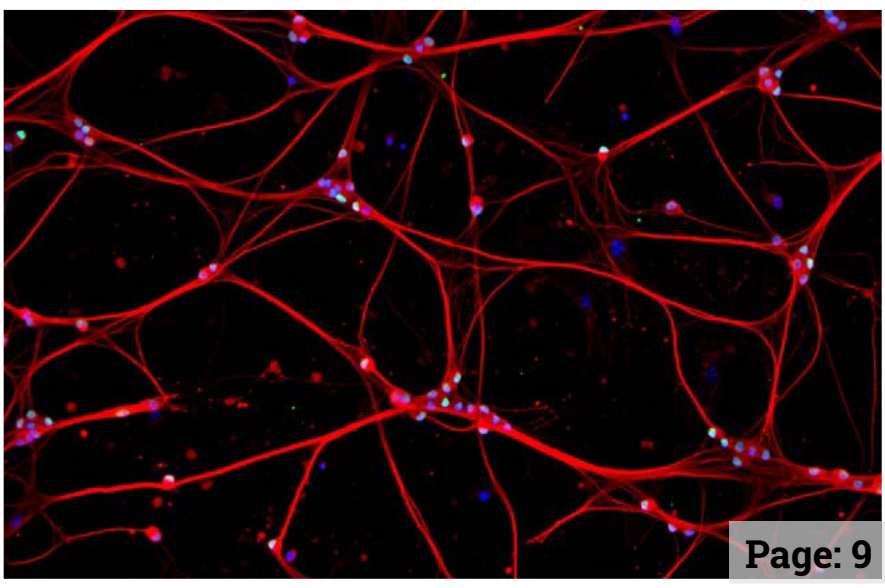

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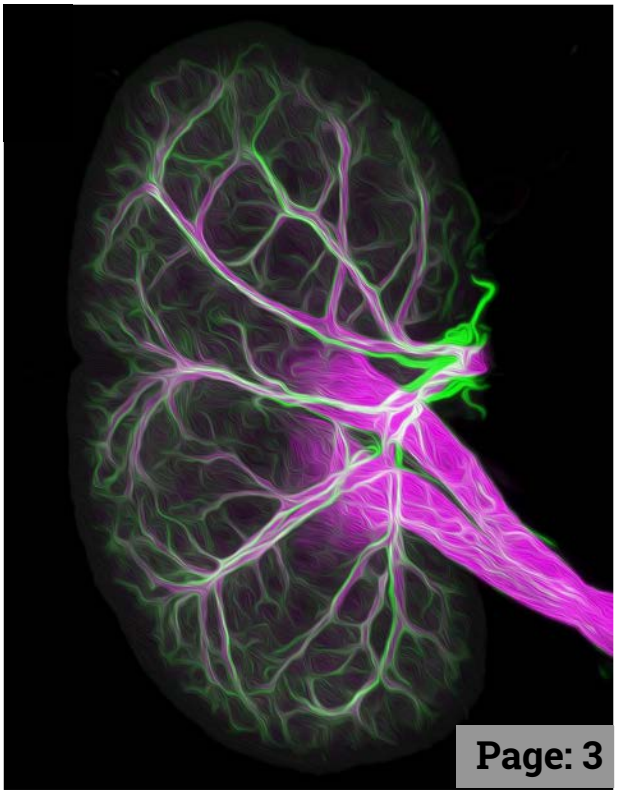

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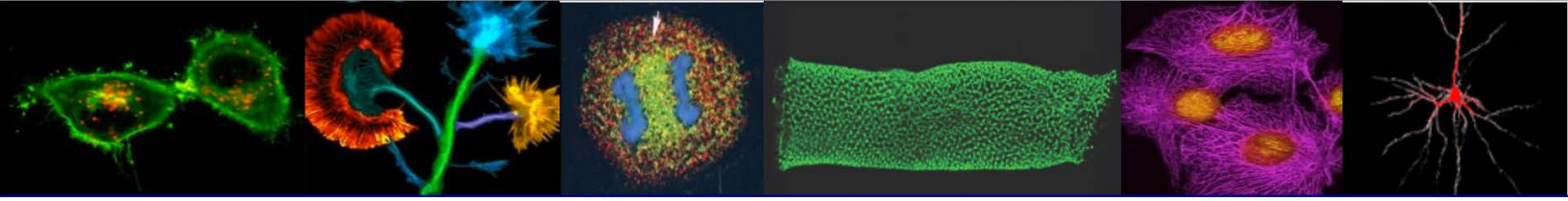
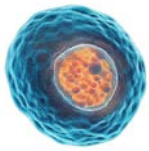
University of North Carolina at Chapel Hill

Department of Cell Biology and Physiology





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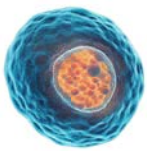
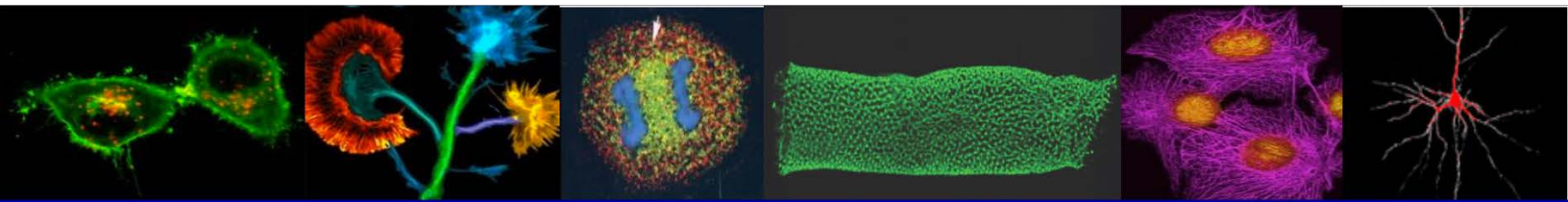


Cell Biology & Physiology



Under the microscope

Two CBP images win the School of Medicine's 2024 Art in Science Competition

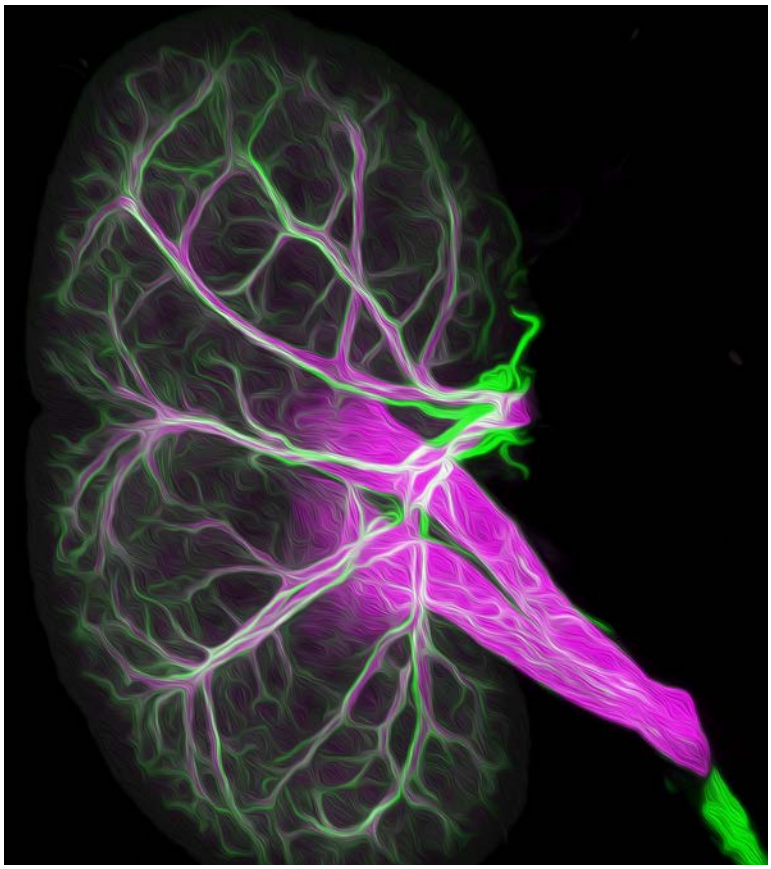
The black hole in the liver

Berfin Azizoglu, PhD Lab
Image credit: Aashita Rajput, Jack Bennett, and Berfin Azizoglu, PhD

What does this image show?
This image shows the three-dimensional vascular organization of the adult mouse liver. The liver has two lobes, each comprised of thousands of hexagonally shaped lobules containing liver cells. This image zooms into a single liver lobule. Blood enters the liver lobule through peripheral vessels, shown in a teal-like color at the edge of the image. It travels through irregularly shaped liver capillaries called sinusoids, shown in yellow, and tiny blood vessels called venules, shown in magenta. Finally, it drains through a central vein, seen in this image as a black hole in the lobule center. Blood drainage from the liver is essential for removing metabolic end products and detoxified substances from the body.

How does this image help advance the research of the Azizoglu lab group?
Berfin Azizoglu's research team studies how the mammalian liver regenerates. They visualize the normal mouse liver at the organ scale with cellular resolution and compare it to injured livers to assess how the organization of the liver, its lobules, and vasculature change over time following injury and during recovery. Identifying these alterations sheds light on the mechanisms used by the liver to restore physiology and function in response to damage.

How was this image taken?
This maximum projection image was taken as a z-stack using a Leica SP8 confocal microscope at the Department of Cell Biology and Physiology.



Seeing double: a duplex kidney

Lori O'Brien, PhD Lab
Image credit: Jake Roetcisoender and Pierre-Emmanuel Yoan N'Guetta

What does this image show?
This image shows a postnatal mouse kidney immunostained for the renal arterial tree with alpha-smooth muscle actin (magenta) and for nerves with tubulin beta class-III (green). An oil filter overlay was added to the final image for artistic purposes. The image depicts a rare urinary tract congenital defect resulting in duplicated ureters in a mouse. Individuals with ureteral duplication use two ureters to drain urine from a single kidney.

How does this image help advance the research of the O'Brien lab group?
This image was taken as part of a larger cohort, where we look at the interplay between vascularization and innervation in the kidney at different developmental time points. The nerves and vasculature in the kidney are closely linked throughout development, and our goal is to understand how vascularization and innervation of the kidney help support proper organogenesis. We utilize this type of whole tissue imaging on genetic knockouts or ablations to assess impacts on the whole organ. The postnatal mouse kidney in this particular image has a duplicated ureter and mirrors a similar human congenital anomaly.

How was this image taken?
The kidney was imaged with the LaVision Ultramicroscope II LightSheet using an Olympus MVPLAPO 2X/0.5 objective at the University of North Carolina at Chapel Hill Microscopy Service Laboratory.

Research Awards
Postdocs

László Bálint, Ph.D

Award: UNC Peer Postdoc Award in Reserch Excellence

Focus: Exploring the structural and functional heterogeneity of the lymphatic system and broadening our understanding of the regulatory mechanisms determining organ-specific lymphatic function

Jessica Cote, Ph.D

Award: F32 postdoctoral fellowship from the National Institute of Arthritis and Musculoskeletal and Skin Diseases

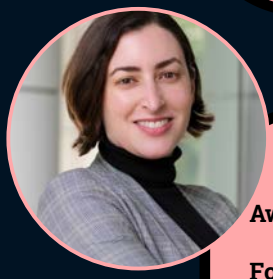
Focus: Studying the impact of specific alternative splicing events on skeletal muscle development

Research Awards
Faculty

Kathleen Caron, Ph.D.

Award: Advanced Research Projects Agency for Health (ARPA-H) Sprint for Women's Health award

Focus: Early-stage research investigating female lymphatic GPCR therapeutics for migraine treatment" (FLyGT)



Sarah Cohen, Ph.D.

Award: 2024 Allen Distinguished Investigator Award

Focus: Using machine learning and cell engineering to develop a new method for visualizing multiple organelle interations at a time and their influence on stem cell differentiation

Jimena Giudice, Ph.D.

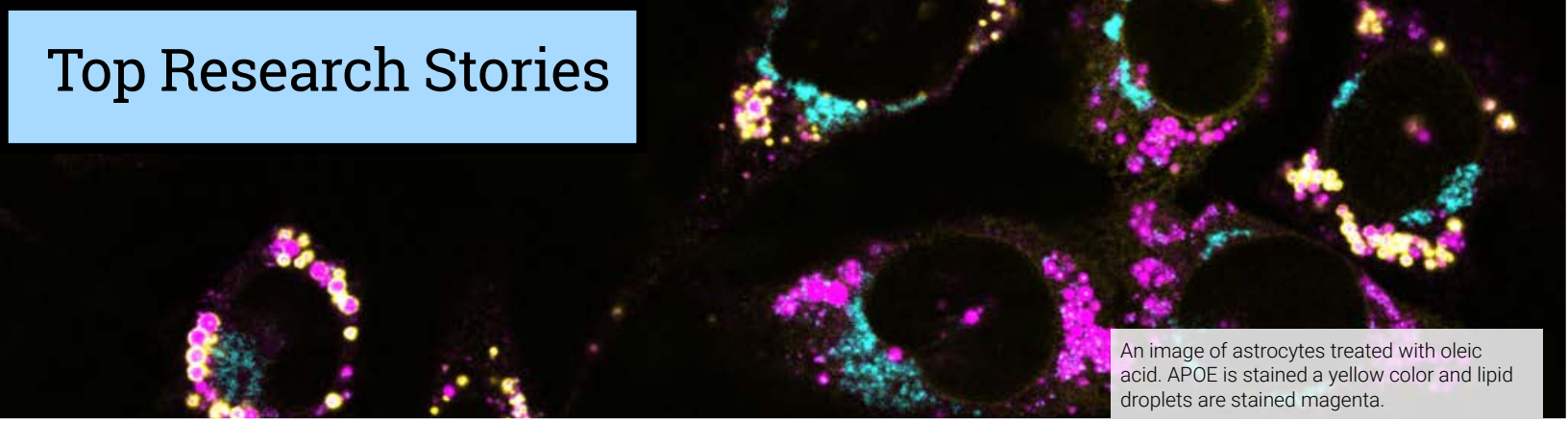
Award: MIRA/R35 grant for five years from the NIH/NIGMS

Focus: Investigating what happens when alternative splicing meets cytoskeleton organization, local translation, and transcription regulation

Shahzad Khan, Ph.D.

Award: 2024 Mentoring Institute for Neuroscience Diversity Scholars (MINDS) program

Focus: An NINDS-supported program that focuses attention on diversity individuals who are early in their careers as faculty members in the neurosciences



An image of astrocytes treated with oleic acid. APOE is stained a yellow color and lipid droplets are stained magenta.

Appeared in UNC Health and UNC School of Medicine Newsroom

Protein accumulation on fat droplets implicated in late-onset Alzheimer's disease

February 9, 2024

In an effort five years in the making, UNC School of Medicine cell biologist Sarah Cohen, PhD, and Rockefeller University's Ian Windham, PhD, describe the interplay between fats and proteins in brain cells and how their dysfunction contributes to the development of late-onset Alzheimer's disease.

UNC School of Medicine researcher Sarah Cohen, PhD, and Ian Windham, a former PhD student from the Cohen lab, have made a new discovery about apolipoprotein E (APOE) – the biggest genetic risk factor for late-onset Alzheimer's disease.

Older people who inherited a genetic variant called APOE4 from their parents have a two- or three-times greater risk of developing the late-onset neurodegenerative disease. If researchers can better understand how APOE4 is affecting brain cells, it may help them design effective therapeutics and target the mechanisms causing the enhanced disease risk.

Cohen and Windham performed an exceptionally thorough, five-year long study to better understand and visualize the relationship between APOE4, Alzheimer's Disease, and fat molecules called lipids in the brain.

"We discovered that brain cells known as astrocytes are more vulnerable to damage and may even go dysfunctional when APOE4 surrounds their lipid storage centers," said Cohen, assistant professor of cell biology and physiology and senior author on the paper published in the Journal of Cell Biology. "This mechanism could explain why exactly APOE4 increases one's risk of Alzheimer's on the cellular level."

The role of lipids in the brain

Sixty percent of the brain's dry mass is composed of lipids, which play important roles in the brain, such as storing cellular energy and forming myelin, the substance that surrounds and insulates neurons. Lipids can be found in specialized fat storage compartments known as lipid droplets within astrocytes.

Sarah Cohen, PhD

As helpful as they may be, lipids can also become toxic if the conditions are right. When excited or stressed, neurons release toxic lipids into the environment. Astrocytes are tasked with cleaning up the free-floating toxic lipids and preventing them from accumulating in the brain.

If astrocytes were to become damaged or dysfunctional in any way, they cannot perform their cleaning duties. As a result, other brain cells, called microglia, cannot clean up amyloid beta plaques in the brain either, another driving factor for Alzheimer's disease.

Seeing APOE in real time

APOE is produced by astrocytes. Much like a taxi or Uber, the protein oversees the releasing and transporting lipids between cell types in the brain. Windham and Cohen wanted to see what exactly happens with the lipids in the astrocytes. Windham led the charge, creating a labelling and tagging system that would allow them to see the innards of astrocytes in action under the microscope.

"Tagging APOE with green fluorescent protein allowed us to see the different places APOE goes while inside living cells," said Windham, now a postdoctoral fellow at The Rockefeller University and first author on the paper.

The team first fed astrocytes oleic acid, an omega-9 fatty acid naturally produced in the body. Using a microscope, the team observed the usual formation of lipid droplets. APOE4, surprisingly, zipped over to the lipid droplets like a magnet and changed the shape and size of the droplets.

It became abundantly clear to the researchers that APOE4 can escape secretion, lock itself inside astrocytes, and migrate to lipid droplets within astrocytes. Windham and Cohen hypothesize that the altered composition of the lipid droplets could be causing astrocyte dysfunction and affecting the microglia's ability to clear amyloid beta.

Lipids: the next frontier

However, more research needs to be done to know the specifics. Cohen hopes their findings will further emphasize the role of lipid droplets in Alzheimer's disease and other neurodegenerative diseases.

"In Alois Alzheimer's first paper, he described three characteristics of neurodegenerative disease: amyloid beta plaques, tau tangles, and accumulations of lipids," said Cohen. "The first two have gotten a lot of attention. The next frontier is lipids. With APOE being the biggest genetic risk factor, we think it holds the clues for how lipids fit into the story."

Researchers identify potential treatment for Angelman syndrome

Appeared in UNC Health and UNC School of Medicine Newsroom

July 8, 2024

Researchers in the lab of Ben Philpot, PhD, the Kenan Distinguished Professor of Cell Biology and Physiology at the UNC School of Medicine and associate director of the UNC Neuroscience Center, have identified a small molecule that could lead to a safe and effective treatment for the neurodevelopmental condition known as Angelman syndrome.

Angelman syndrome is a rare genetic disorder caused by mutations in the maternally-inherited UBE3A gene and characterized by poor muscle control, limited speech, epilepsy, and intellectual disabilities. Though there isn't a cure for the condition, new research at the UNC School of Medicine is setting the stage for one.

Ben Philpot, PhD, the Kenan Distinguished Professor of Cell Biology and Physiology at the UNC School of Medicine and associate director of the UNC Neuroscience Center, and his lab have identified a small molecule that could be safe, non-invasively delivered, and capable of "turning on" the dormant paternally-inherited UBE3A gene copy brain-wide, which would lead to proper protein and cell function, amounting to a kind of gene therapy for individuals with Angelman syndrome.

"This compound we identified has shown to have excellent uptake in the developing brains of animal models," said Philpot, who is a leading expert on Angelman syndrome and a member of UNC Lineberger Comprehensive Cancer Center. "We still have a lot of work to do before we could start a clinical trial, but this small molecule provides an excellent starting point for developing a safe and effective treatment for Angelman syndrome."

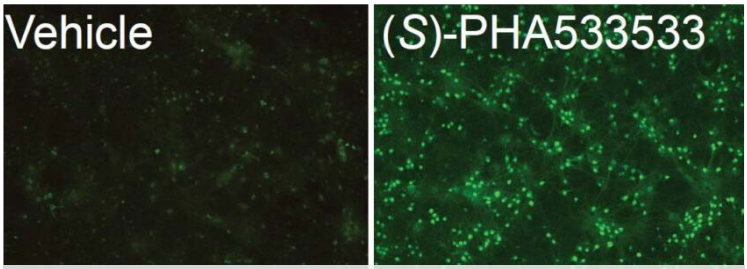
But these results, which were published in Nature Communications, mark a major milestone in the field, according to Mark Zylka, PhD, the W.R. Kenan Jr. Distinguished Professor of Cell Biology and Physiology at the UNC School of Medicine and Director of the UNC Neuroscience Center. No other small molecule compound has yet to show such promise for Angelman, he added.

Ben Philpot, PhD

Unlike other single-gene disorders such as cystic fibrosis and sickle-cell anemia, Angelman syndrome has a unique genetic profile. Researchers have found that children with the conditions are missing the maternally-inherited copy of the UBE3A gene, while the paternally-inherited copy of the UBE3A gene remains dormant in neurons, as it does in neurotypical individuals. Typically, UBE3A helps regulate the levels of important proteins; missing a working copy leads to severe disruptions in brain development.

For reasons that aren't fully clear, the paternal copy of UBE3A is normally "turned off" in neurons throughout the entire brain. Thus, when the maternal copy of the UBE3A gene is mutated, this leads to a loss of UBE3A protein in the brain. Philpot and other researchers have theorized that turning on the paternal copy of UBE3A could help treat the condition.

Hanna Vihma, PhD, a postdoctoral research fellow in the Philpot lab and first author on the study, and colleagues screened more than 2,800 small molecules from a Pfizer chemogenetic library to determine if one could potently turn on paternal UBE3A in mouse models with Angelman syndrome.



Neurons show a bright fluorescent glow when treated with (S)-PHA533533, indicating that the small molecule potently activated the dormant paternal allele of UBE3A. Credit: Vihma et al 2024.

Researchers genetically modified mouse neural cells with a fluorescent protein that glows when the paternal UBE3A gene is turned on. After treating the neurons with more than 2,800 small molecules for 72 hours, researchers compared their thousands of treated cells against those treated with topotecan, a known small molecule that can turn on paternal UBE3A but lacked therapeutic value in animal models of the condition.

(S)-PHA533533, a compound that was previously developed as an anti-tumor agent, caused neurons to express a fluorescent glow that rivaled that induced by topotecan, meaning that its effect was potent enough to successfully turn on paternal UBE3A. Researchers were able to confirm the same results using induced pluripotent stem cells derived from humans with Angelman syndrome, indicating that this compound has clinical potential.

Hanna Vihma, PhD

Additionally, researchers observed that (S)-PHA533533 has excellent bioavailability in the developing brain, meaning it travels to its target with ease and sticks around. This is notable in that previous genetic therapies for Angelman syndrome have had more limited bioavailability.

"We previously showed that topotecan, a topoisomerase inhibitor, had very poor bioavailability in mouse models," said Vihma. "We were able to show that (S)-PHA533533 had better uptake and that the same small molecule could be translated in human-derived neural cells, which is a huge finding. It means it, or a similar compound, has true potential as a treatment for children."

Although (S)-PHA533533 shows promise, researchers are still working to identify the precise target inside cells that causes the desired effects of the drug. Philpot and colleagues also need to conduct further studies to refine the medicinal chemistry of the drug to ensure that the compound – or another version of it – is safe and effective for future use in the clinical setting.

"This is unlikely to be the exact compound we would take forward to the clinic," said Philpot. Along with medicinal chemists in the lab of Jeff Aubé, PhD, the Philpot lab is working to identify similar molecules with improved drug properties and safety profiles. "However, this gives us a compound that we can work with to create an even better compound that could be moved forward to the clinic."

Diering's team uses a new noninvasive technique called the PiezoSleep Mouse Behavioral Tracking System to monitor subtle changes such as altered breathing or diaphragm movement that indicate the mouse has fallen asleep.

Making the connection between sleep and autism

October 24, 2024

Sleep disturbances during early development alter key synaptic proteins involved in autism spectrum disorder.

Appeared in UNC Health and UNC School of Medicine Newsroom in a different story

Anyone who has ever put a toddler to bed knows it's a struggle. While sleep might be the bane of a toddler's existence it is also an essential component for their brain development. Toddlers need an average of 11-14 hours of sleep a day (1). During that sleep, synaptic connections in toddlers' brains begin to mature.

Sean Gay, PhD

In a recent study published in the Proceeding of the National Academy of Sciences, Graham Diering, assistant professor in the Department of Cell Biology and Physiology at the University of North Carolina at Chapel Hill, and a team led by graduate student Sean Gay, found that sleep disturbances during development in young mice affect the regulation of key synaptic proteins implicated in autism (2). Synapses are small protein-filled spaces between neurons that allow them to communicate.

"Synapses are where memories are made and stored, and a lot of research has shown that synapses are part of the business end of what sleep is for," said Diering. Sleep and synaptic plasticity also play a role in learning and neurodevelopmental disorders. Many autism-associated genes encode synaptic proteins. People with autism spectrum disorder also experience significant sleep disturbances.

In a previous study in 2022, Diering and his team explored the effect of disrupting sleep in three-week old mice (roughly equivalent to age 1-2 in humans), that were genetically predisposed to develop autism. Disrupting sleep during early brain development caused long-lasting changes in the social behaviors of adult mice. However, if these mice experienced no sleep disturbances, then they developed behaviors more akin to their wildtype siblings (3), clearly implicating sleep in autism spectrum disorder development.

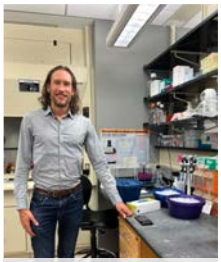
"It's clear that in most cases, [autism spectrum disorder] is not a purely genetic condition. It's really an interaction with other environmental factors," said Diering. In their recent study, Diering and Gay wanted to better understand the molecular cost of sleep loss during development and its interaction with autism risk genes. To do this they turned to wildtype mice. The team disturbed the sleep of wildtype three-week-old and adult mice for four hours by tapping on their cages any time the mice dozed off.

After the four hours of sleep disruption, the adult mice resumed sleeping and even slept more than usual during their normal wake times. "The way I like to phrase that for people to appreciate easily is that they stayed up past bedtime and slept in the next day. It's a very familiar behavior, and we see this across all different species," said Diering.

The big surprise for the team was that that the young mice who experienced disturbed sleep progressed through the day as normal without ever making up for the lost sleep. A lack of sleep also caused impaired memory function in young mice the next day.

To get at the molecular underpinnings of these observations, Diering's team extracted the mice's forebrains, including the cortex and hippocampus, key areas needed for higher cognitive function and memory. They isolated and molecularly analyzed synapses from these brain regions and found that sleep deprivation in juvenile, but not adult mice impacted important aspects of brain maturation such as synaptogenesis.

They also found that many known autism-risk proteins were upregulated in the synapses of sleep deprived young mice. Some of these proteins aid in forming the perineural net, an area located outside of cells that acts like a cell scaffold.



Graham Diering, PhD

"In the developing brain, these extracellular matrix proteins are what I call wet cement. They're basically forming as the brain is growing, and then once you exit development, these structures become hardened and last the rest of your life," said Diering. "It was kind of a surprise, but it really informs our thinking about how sleep disruption during development can contribute to lasting phenotypes."

One night of poor sleep though is unlikely to cause lasting effects. The mechanism underlying the link between sleep and autism is complex, cumulative, and influenced by both genetics and the environment. "Now, we know what are some key vulnerabilities that we can look to expand in our disease context, and hopefully make a bigger breakthrough on how sleep disruption in the autism context contributes to lasting behavior changes," said Diering.

His team is continuing to investigate the proteins that emerged from their recent study. They have also made some other intriguing findings of how sleep influences changes in adolescence and the aging brain. "The field has been after this holy grail for a long time of what's the function for sleep," said Diering. "Our research is really pushing this kind of new view that sleep doesn't just do one thing your whole life. There are actually different functions for sleep. To me that's one of the biggest wins."

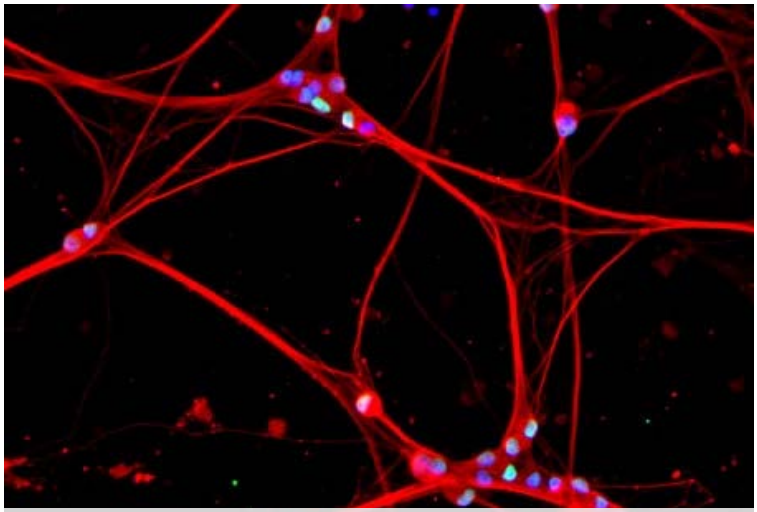
References

1. How much sleep is enough? National Heart Lung, and Blood Institute https://www.nhlbi.nih.gov/health/sleep/how-much-sleep (2022).
2. Gay, S.M. et al. Developing forebrain synapses are uniquely vulnerable to sleep loss. Proc Natl Acad Sci 121 (2024).
3. Lord, J. et al. Early life sleep disruption potentiates lasting sex-specific changes in behavior in genetically vulnerable Shank3 heterozygous autism model mice. Mol Autism 13(35) (2022).

Neuronal survival: from the brink of death

October 31, 2024

Neurons are among the few cells that can halt cell death and recover from apoptosis. Now scientists know why.



Spiess used fluorescent staining to identify p-c-Jun in neurons undergoing apoptosis. In this image, green indicates p-c-Jun, blue indicates cell nuclei, and red indicates alpha tubulin, a cytoskeletal protein.

"Neurons can reverse their decision to die from a point that's considered impossible in most other cells," said Mohanish Deshmukh, a neuroscientist in the Department of Cell Biology and Physiology. In a recent study published in Cell Death & Differentiation, Keeley Spiess, a graduate student in Deshmukh's lab found that even when neurons receive a persistent signal to die, they execute the steps of the apoptotic pathway transiently. This means they are always ready to reverse previously executed apoptotic steps for self-preservation.

The extraordinary ability of neurons to survive is not a surprise. Humans are born with most of the neurons they will ever have, which means that our neurons must last our entire lives for our brains to function properly. However, how neurons withstand environmental assaults, such as stress, and DNA damage to return from the brink of death was not known, until now.

In their recent paper, Spiess and Deshmukh asked if the molecular steps in the apoptotic pathway resulted in permanent changes, in which case neurons would have the herculean task of undoing numerous molecular steps to stop death, or if the molecular changes that happened during apoptosis were more transient. To activate apoptosis in neurons they removed nerve growth factor (NGF) and closely examined the molecular changes at each step in the apoptotic pathway.

Keeley Spiess

During the first 24-48 hours after receiving an apoptotic signal, cells phosphorylate c-Jun, a transcription regulator, which activates a family of proteins called the BH3 proteins. These proteins then bind to BAX proteins in the cytoplasm.

Conformationally changed BAX proteins then attach to mitochondrial surfaces, where they bore holes into mitochondrial membranes that allow cytochrome c to enter the cytoplasm and activate caspases that then begin the process of degrading cells. Once cell degradation happens, there's no turning back, but Spiess and Deshmukh found that every step up to that point is reversible.

Mohanish Deshmukh, PhD

"What people expected is that all those steps stay — c-Jun stays phosphorylated, BH3 proteins stay activated, etc. — and the game's over. It turns out in neurons, it's more like a relay, where one step tells the other to go ahead while it resets itself in case the neuron changes its mind," said Deshmukh. A neuron can even stop cell death after BAX has poked a few holes in mitochondrial membranes. BAX does its job of releasing cytochrome c and then stops. It doesn't stay bound to the mitochondria causing persistent pores, even though the apoptotic signal of depleted NGF is still present.

Spiess and Deshmukh found that to fully halt cell death and recover from initiating the apoptotic pathway after replenishing NGF, neurons need a protein called BCL-xL. BCL-xL was previously found by other research teams to be needed for preventing cell death in cancer cells, which hints that cancer cells may be able to recover from cell death in a similar manner as neurons. These findings may also provide insights into the molecular survival mechanisms of other post-mitotic cells such as cardiomyocytes that persist throughout an organism's lifespan.

For Deshmukh's research team though, these research findings contribute to a different, larger research goal of better understanding neurodegeneration and the healthy adult brain. "[Neuroscientists] have been studying how neurons die during injury and disease for the last 25 years. We're much more impressed with the ability of healthy neurons to survive," said Deshmukh. "Our approach to tackling neurodegeneration is very different from other labs that focus on what goes wrong in the degenerating brain. We're interested in what goes right in the healthy adult brain. What do healthy neurons do to survive long term and can we utilize that knowledge to fight

Reference
Spiess, K. et al. Apoptosis signaling is activated as a transient plus in neurons. Cell Death & Differentiation (2024).

Junior Faculty Spotlight

Shahzad Khan, Ph.D

Shahzad Khan, Ph.D. is an expert in the molecular properties of primary cilia in neurons and astrocytes in the brain. Dr. Khan received his Bachelor of Science in Chemical Sciences from Florida State University in 2011 and earned his Ph.D. in Neuroscience in 2018 in the lab of Dr. George S. Bloom at the University of Virginia. As a graduate student in the Bloom lab, Shahzad uncovered a molecular mechanism that is essential to both Alzheimer's disease (AD) and Parkinson's disease (PD) pathogenesis. His postdoc in the laboratory of Dr. Suzanne R. Pfeffer in the Department of Biochemistry at Stanford University focused on the LRRK2 signaling role in changes of primary cilia in neurons and astrocytes and showed how disruption contributed to the pathology of Parkinson's disease in rodent and human brains. Dr. Shahzad Khan was recruited to the Department of Cell Biology and Physiology in collaboration with Dr. Gwenn Garden in the Department of Neurology, where he received a secondary appointment. His independent research program focuses on the role of primary cilia in neurodegenerative diseases and integrates transgenic mouse models, neural cultures, single-cell transcriptomics, proteomics, and imaging to probe primary cilia function in the adult brain. Both Parkinson's and Alzheimer's are neurodegenerative diseases that impact racial and ethnic minorities with greater severity and earlier onset, so we also look forward to his research contributing to important questions regarding health disparities.

Berfin Azizoglu, Ph.D.

Berfin Azizoglu, Ph.D. investigates the mechanisms of how body-wide vascular and neural networks communicate distant signals to organ cells to influence local behaviors in cell growth and regeneration. Dr. Azizoglu received her Bachelor of Science in Molecular Biology and Genetics from Boğaziçi University (Istanbul, Turkey) in 2012. As an undergraduate, Berfin pursued research opportunities each year, obtaining training in the lab of Dr. Arzu Celik at Boğaziçi, as well as summer internships in Turkey and Germany. Dr. Azizoglu then moved to the lab of Dr. Ondine Cleaver at the University of Texas Southwestern Medical Center as a graduate student where she earned her Ph.D. in Molecular Biology in 2018. Berfin's thesis work focused the molecular mechanisms of biological tube formation and size determination during development. Following her graduate school training, Dr. Azizoglu was recruited as a postdoctoral researcher to the laboratory of Dr. Roel Nusse in the Department of Developmental Biology at Stanford University. At Stanford, Berfin's work focused on identifying mechanisms underlying determination of liver size as a way to also examine the more general question of how organs develop to the appropriate size. As faculty in CBP, her research program combines organ-wide volumetric imaging at cellular resolution with mouse genetics and transcriptomics to track, manipulate, and assess targeted cells in organs and gain insight into the signaling mechanisms from the molecular to the organ level.

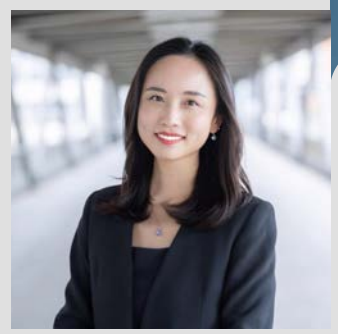
Ukrae Rae Cho, Ph.D.

Ukrae Rae Cho, Ph.D. focuses on how caspases and other proteases bring about rapid changes in cell morphology, behavior, and identity. Dr. Cho received his Bachelor of Science in Chemistry in 2010 from Seoul National University (Korea) where he contributed to the development of fluorescence based pH sensors as part of his undergraduate research. Rae then moved to the lab of Dr. James Chen at Stanford University as a graduate student where he earned his Ph.D. in Chemical and Systems Biology in 2016. Dr. Cho became an expert tool developer and built a time-resolved luminescence microscope that visualizes low-abundance biomolecules in highly autofluorescent samples. He was recruited as a postdoctoral researcher to the laboratory of Dr. Martin Hetzer at the Salk Institute for Biological Studies in La Jolla in 2017 where his work focused on how sublethal caspase activation facilitates cell differentiation. Rae is a scientist at the interface of chemistry and biology and he is also a skilled programmer, which contributes to his systems approach. His independent research program focuses on the non-apoptotic activation of caspases in myogenesis and explores how their aberrant activation backfires in disease conditions. Dr. Cho will also investigate spatiotemporal mapping of caspase activity in zebrafish embryos to improve our understanding of the developmental functions of proteases at the organismal level. Rae's ultimate goal is to identify a combination of protease inhibitors/activators that can modulate cell fate or cure human diseases.

Junior Faculty Spotlight

Phillip Clapp, Ph.D.

Phillip Clapp, Ph.D. leverages his expertise on the creation of human lung cell models for basic and translational studies and development of novel technologies as part of the Marsico Lung Institute Tissue Procurement and Cell Culture Core. Dr. Clapp received his Bachelor of Science in Biology from the University of North Carolina at Chapel Hill in 2004 and his Ph.D. in Toxicology from UNC-CH in 2018. Phillip's thesis work in the lab of Dr. Ilona Jaspers focused on investigating the pulmonary effects of e-cigarette flavorants on normal cellular functions and innate defense responses. Dr. Clapp was then recruited as a postdoc to the lab of Dr. William Bennett, a leader in the field of aerosol science, to assess the effects of e-cigarette emissions on respiratory mucociliary clearance (MCC) in healthy adult vapers. Overall, Phillip has over 17 years of professional research experience in pulmonary biology, in vitro models, inhalation toxicology, and aerosol science at UNC and the Wake Forest Institute for Regenerative Medicine (WFIRM). His overarching research goals involve the characterization of airway epithelial cell growth and differentiation, the evaluation of innate defense responses to airborne toxicants, and the development of New Approach Methodologies (NAMs) that effectively link preclinical research with clinical outcomes. Ultimately, Dr. Clapp hopes to leverage these advancements to enhance equity in pulmonary medicine and reduce health disparities by focusing on inclusion of susceptible and vulnerable populations in basic scientific research.



Hokyung Kay Chung, Ph.D.

Hokyung Kay Chung, Ph.D. combines protein engineering and immunology expertise to focus on designer T cells and cancer-killing viruses. Dr. Chung received her Bachelor of Science in Pharmacy from Seoul National University (Korea) in 2011. As an undergraduate, Kay pursued research in the lab of Dr. Byung Woo Han, investigating conditions for truncation, expression, and crystallization of the calcium-activated chloride channel, Anoctamin-1. Dr. Chung earned her Ph.D. in Biology at Stanford University in the lab of Dr. Michael Z. Lin in 2018. As a graduate student, Kay developed new synthetic biology tools that respond to a chemical, light, or cancer signal to trigger biological responses. Furthermore, she generated synthetic oncolytic RNA virus of which replication can be controlled by drug or cancer signals. These platforms can enable safe and effective cell- or virus-based therapies. Kay was then recruited as a postdoc to the lab of Dr. Susan Kaech at the Salk Institute for Biological Studies in La Jolla. At Salk, Dr. Chung created a multi-omics pipeline that identifies transcription factors that direct CD8 T cell differentiation in an unbiased manner. She then used this platform to discover novel transcription factor perturbations that improve the efficacy of T cell cancer immunotherapy. As CBP and Lineberger Comprehensive Cancer Center joint faculty, Dr. Chung's research program seeks to maximize the anti-tumor potential of killer T cells by fully reprogramming their differentiation pathways and to remodel the tumor microenvironment to favor context-dependent T cell fates.

Tiffany Garbutt, Ph.D.

Tiffany Garbutt, Ph.D. is the Assistant Director of Communications and Media for the department. She is an expert in the field of science writing, with extensive experience as a freelance writer and consultant. Dr. Garbutt received her Bachelor of Arts in Biology from the University of the (US) Virgin Islands in 2010 and earned her PhD in Genetics from North Carolina State University in 2017. Tiffany was then recruited as a postdoctoral researcher to the lab of Dr. Li Qian, Professor in the UNC Department of Pathology and Laboratory Medicine at UNC. Her interdisciplinary research background spanned the field of pluripotent stem cells and included basic and translational research on cardiac maturation and regenerative medicine. Following her postdoc, Tiffany began her career as an assistant science editor at well-known science news and education journal, The Scientist. As a science writer and editor, she has worked with for-profit and non-profit organizations and medical and academic news publications. Tiffany joined the CBP faculty in 2024 following her successful time as the Senior Science Editor and Team Lead at Drug Discovery News.

The start of a new collaboration to share in the culture of science

November 26, 2024

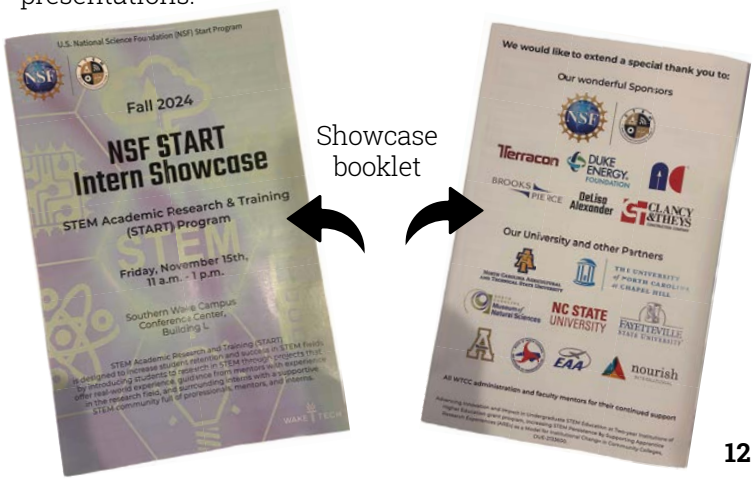
CBP students and faculty participate in the first of several planned events that span from 2024 to 2025 with Wake Tech Community College to foster scientific collaboration and community.

Students and faculty from the Department of Cell Biology and Physiology (CBP) kicked off an exciting new partnership with Wake Tech Community College on November 15, 2024. "This is the first event of what we hope will be a lasting and meaningful collaboration," said Natasha Snider, an associate professor in the Department of Cell Biology and Physiology at the University of North Carolina at Chapel Hill.

The new partnership aims to bring researchers and students from the two educational institutions together to share in the culture of science. Representatives from both universities, including several CBP students, Anna Beeson, Pierre N'Guetta, and Kayla Mason, gathered earlier this year to brainstorm opportunities for the two groups to collaborate. In the first of several planned activities, CBP students attended the STEM Academic Research & Training (START) Showcase at Wake Tech Community College on November 15th.

Natasha Snider, PhD

The START program is a National Science Foundation-funded program at Wake Tech Community College aimed at fostering student interest and retention in science, technology, engineering, and mathematics and improving scientific literacy. The program is designed for undergraduate students working towards a two-year associate degree. Students who participate in START commit to 60 hours of paid research per semester. The START Showcase is an opportunity for these students to share their research and grow their scientific research and communication skills. CBP graduate students and faculty attended the event to help support the START program and provide feedback on student projects, posters, and presentations.



Were there any posters or presentations that stuck out to you?

Two of the posters stood out! For the first poster, the student looked at the correlation between performance and growth mindset. She used self-reported survey data as well as demographic information from students taking biology at Wake Tech. She found that students with a growth mindset performed better in the class. I loved that along with this dataset she included some resources that Wake Tech provides for its students on her poster. The second poster stood out to me because the student presented it really well. She tested for antibiotic resistant microbes in soil samples with the goal of adding to our existing toolbox for fighting infections. She had a really comprehensive grasp of the project and the techniques she wanted to try in the future. She was waiting on admissions news from the Microbiology and Immunology Department at NCSU. She wants to do a PhD in virology. Fingers crossed she got good news from NC State!

—Katie Mulhern

There was a project on speed limit design that was quite interesting. I was unaware of the thought and math that goes into determining the speed. Next, a project on food insecurity research and environmental initiatives aiming to help those in the Orange County area seemed quite impactful. They were connecting local organizations to fight landfill waste and environmental damage. The students' goal was to specifically connect churches and environmental organizations in the Orange County area, and they had a strong idea of how to bridge this connection! Finally, a poster presentation describing sexual vs. asexual reproduction in plankton stuck out the most to me. The presenter explained how you can tell if the organism sexually or asexually reproduces by observing a round phenotype on their bottom. The presenter had interesting ideas for future directions of study including looking more into motility and organism density.

—Jack Bennett

What was the most enjoyable part of this experience?

The most enjoyable part of the Wake Tech visit, in my opinion, was chatting with the students, especially asking them questions about their projects, what they did, why they did it, and what they would do next if they continued the research project. It was nice to hear the students articulate what they had done and learned during the START program and to hear their excitement about their projects or potential future research.

—Frankie Marchan

Why did you choose to participate in this event?

For me, there are two angles to why I chose to participate in this event. I am passionate about making the scientific community inclusive and accessible and this was a great opportunity to reach out to students beyond UNC. I am always looking for chances to interact with other young scientists and help widen both of our circles of community. Secondly, it was an easy opportunity to take advantage of logistically speaking. Dr. Natasha Snider had already organized everything, and it didn't require me to take the entire day off from lab. This made it easy to move around my experiments to make volunteering possible.

—Ashlyn Laidman

I am passionate about this because I have participated in many science communication workshops as a participant and organizer. And through discussion with many people of different backgrounds, what came up was that young students and sometimes people with untraditional paths believe that it is impossible or too difficult for them to pursue higher education. This is my way to interact with young students and tell them that everyone has a different story but that does not mean you should sideline your dreams.

—Pierre-Emmanuel Yoann N'Guetta

Gottschalk: a collector and innovator

November 25, 2024

A tour of Carl W. Gottschalk's collection of historical books reveals the breadth of renal physiology's history and Gottschalk's place as a pioneering leader in the field.

As a child, Carl W. Gottschalk loved collecting. He collected stamps, coins, and most notably butterflies. At just 15 years old, he discovered a rare butterfly species that now bears his name, Stryman cecrops Gottschalki, and published his first scientific paper. His passion for collecting eventually took backstage to his interest in science. As an adult, Gottschalk made innovative advancements to kidney micropuncture and fundamental discoveries of kidney function that shape the field of renal physiology today. It wasn't until many years later that his passion for collecting was reignited by his friend and colleague, Jean Oliver, MD, a renal anatomist and pathologist.

This time though, instead of butterflies, Gottschalk collected historic texts containing hand-drawn illustrations from ancient anatomists dating as far back as the 1500s. On November 25, 2024, students, postdocs, and faculty from the Department of Cell Biology and Physiology, and the invited speaker for the 24th annual Gottschalk Lecture, Samir Parikh, MD, from the University of Texas Southwestern Medical Center, got a peek inside Gottschalk's historic collection of books in the Wilson Library at the University of North Carolina at Chapel Hill (UNC-CH).

Some books within the collection, including one from Bartolomeo Eustachii, an Italian anatomist from the 1500s, boasted realistic illustrations of the human kidney. Other books, such as one from Andreas Vesalius, an anatomist from the 1500s, who is often referred to as the father of human anatomy, took more creative liberties in depicting a surgical procedure as a show. Nestled among these 16th century texts are more recent manuscripts from the 1940s, including one from Jean Oliver on the architecture of the kidney in chronic Bright's disease and another from W.J. Kolff, PhD, on the artificial kidney.

The collection was donated to the library by Susan Fellner, MD, a nephrologist and Gottschalk's wife. Fellner attended the tour and shared anecdotes about the collection, including a touching story about one of the texts on display, a copy of the 1967 report from the Committee on Chronic Kidney Disease chaired by Gottschalk. "Carl was chosen [to lead the committee] because he was so fair and softspoken and could make things happen," said Fellner. In the document, the committee concluded that people with chronic kidney disease could be treated successfully with dialysis and that no one should be denied this treatment for financial reasons. This document proved critical in later efforts passed into law in 1972 entitling individuals with end-stage chronic kidney disease to dialysis under Medicare.

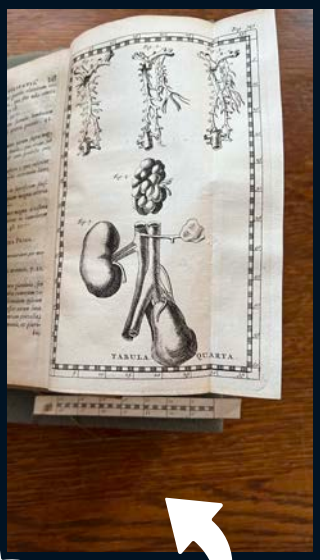
Susan Fellner, MD (left) and Samir Parikh, MD (right)

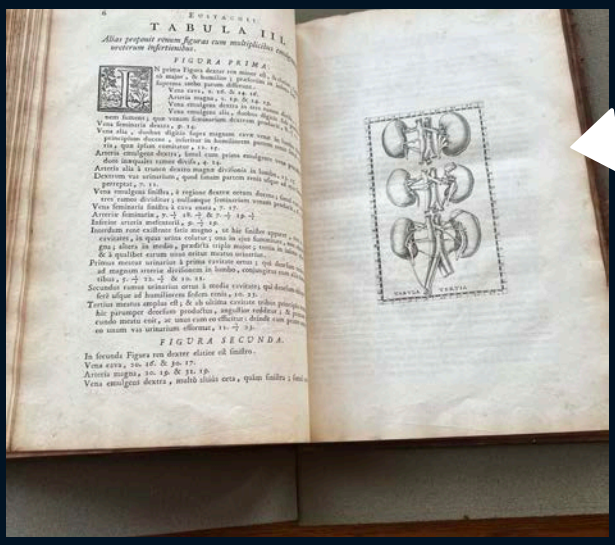
"I met Carl at the Mont Desert Island Biological Laboratory at Homer Schmitt's Symposium. A week later, at the University of Chicago, I received a copy of this [report] from Carl. It was my first love note," said Fellner. "Written across the front was, 'You will be interested in this, fondly.' I think that is as unique a correspondence between people newly met that you could imagine," continued Fellner. The story personifies their meeting of minds and shared passion for renal physiology. Researchers can explore more historical books and illustrations from Gottschalk's collection at the Wilson Library. Also on display in the library is Gottschalk's unique kidney-shaped desk.

Gottschalk started his lab at UNC-CH in 1952, where he made many of his foundational discoveries. Every year the Department of Cell Biology and Physiology and the UNC Kidney Center invite a notable leader in kidney research to talk about their research. This year Samir Parikh, MD, discussed ways to turn back kidney frailty by targeting metabolism and made several references to Gottschalk. In one such reference, he mentioned he follows Gottschalk's approach of testing multiple insults in different animal models to understand kidney function and dysfunction. Parikh's research team found that transient insults cause mitochondrial DNA mutations in the kidney that exaggerate kidney stress responses. Parikh shared research from his team that suggests that augmentation with the coenzyme, nicotinamide adenine dinucleotide may enhance kidney resilience to transient stressors and that restoring ATP building blocks may counteract kidney frailty caused by mitochondrial DNA mutations. "Carl Gottschalk painstakingly demonstrated how urine can be concentrated relative to plasma. This is fundamental to terrestrial life," wrote Parikh in a social post prior to the event. "What an honor and privilege to be connected with Dr. Gottschalk."

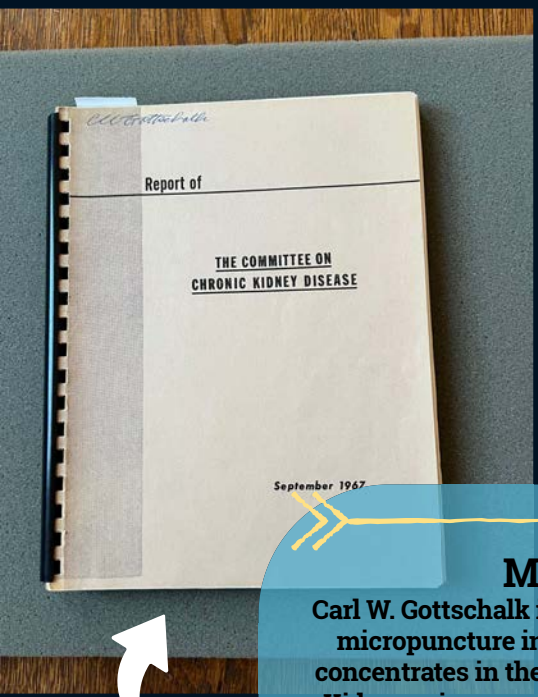
Reference
Burg, M.B. Carl W. Gottschalk. National Academies of Sciences, Engineering, and Medicine. Biographical Memoirs: Volume 77. Washington, DC: The National Academies Press (1999).

Andreas Vesalius (1500s) and Frederik Ruysch (1700s) took more creative liberties in their scientific illustrations.

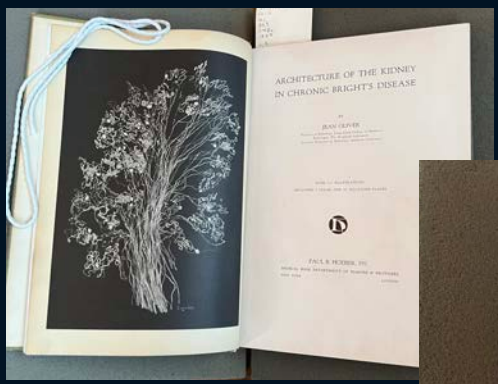




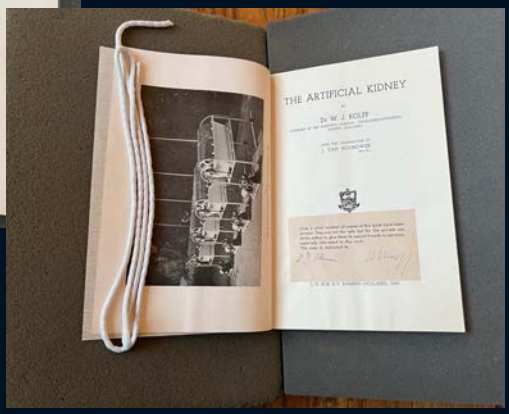
Bartolomeo Eustachii tooks a more realistic approch to his scientific illustrations. He even included a scale bar in the form of a bookmark in the above drawing.



This report adided in the passing of the amendment to Public Law 92-603, which entitlted people with end-stage chronic kidney disease to treatment under Medicare.



The collection also included mroe resent texts from the 1940s from Jean Oliver and W.J. Kolff.



More on Gottschalk

Carl W. Gottschalk is best known for his innovations to kidney micropuncture in the 1950s and for discovering how urine concentrates in the kidney by countercurrrent multiplication. Kidney micropuncture was initially developed by A. Newton Richards and Joseph T. Wearn at the University of Pennsylvania in the 1920s but fell out of favor after World War II for being too difficult. Gottschalk's innovations to micropuncture revived the technique and cemented its utility for kidney research. Kidney micropuncture allows researchers to access distinct kidney nephrons, tiny but key functional units of the kidney, in vivo. This technique helps researchers to better understand kidney function and reveals how the kidney filters and transports drugs and chemicals out of the body.

Eileen Dewitya and Dawne Lucas lead the care of the Gottschalk collection at the Wilson Library.

Appeared in Vital Signs

Five questions with Andrew Scott Kennedy, Jr.

In this new Vital Signs series, we feature graduate student Andrew Scott Kennedy Jr., in the Thaxton lab. He's a budding microscopist who plans to dedicate his research career to understanding health and disease to help patients.

January 22, 2024

Andrew Scott Kennedy Jr. is a 4th year PhD Candidate in the lab of Jessica Thaxton, PhD, associate professor of cell biology and physiology and member of UNC Lineberger Comprehensive Cancer Center. In the lab, Kennedy Jr. uses super-resolution microscopy techniques to visualize and better understand how CAR-T cells, a specialized type of immunotherapy, battle solid cancers like sarcoma to help patients overcome the disease.

Q: What were your interests when young, and how did you get into biomedical science?

A: When I was in elementary school, I looked forward to the yearly science fair experiments. At first, I wanted to play around with baking soda and vinegar "volcanos", but science quickly became my favorite subject. Clinical science was the only field I knew about because both my father and grandmother worked in healthcare.

When I attended UNC-Chapel Hill as an undergraduate, I volunteered in Robert Tarran's laboratory at the Marsico Lung Institute/UNC Cystic Fibrosis Center studying lung disease just to get experience for medical school applications. I immediately decided to switch to a career in research because I fell in love with the creative puzzle-solving and seeing how the discoveries researchers made at UNC were advancing our understanding of medicine and biology.

Q: Why did you choose UNC and the lab you are in?

A: I chose UNC because of the amazing accessible technology we have here, and the fact that there is an abundance of world-class experts we can connect and work with. I joined my current group, the Thaxton lab, because they were using cool techniques to study immune cells, and at the same time studying a subject that would influence cancer treatment.

Andrew Scott Kennedy, Jr.

Q: What are you working on right now?

A: I'm studying CAR-T cells, an immunotherapy that uses a patient's own immune cells to treat their cancer. CAR-T cells have shown amazing results in patients with some blood cancers, but unfortunately, it hasn't been as successful in solid tumors like sarcomas. I use super-resolution microscopy techniques, in collaboration with other experts at UNC, to study how changes made to these CAR-T cells can improve the treatment of solid cancers. Right now, I am developing a way to get extremely magnified pictures of these cancer-killing cells so we can better understand how they work in patients.

Q: What are your goals after earning your PhD?

A: I would love to continue to work on CAR-T cell research. Some groups are expanding this therapy to other diseases, like autoimmune disorders or viral infections. Regardless of whatever subject it happens to be, I want to be close to a microscope in my next work.

Q: What inspires you the most about working in your field?

I love microscopes, so I always get curious to try new imaging techniques when they are published. But when I read the latest research in immunotherapy, the bottom line for this work is if it improves survival of patients. When you're at the lab bench you can get lost in the specifics and forget what the end goal of your work is, so it's really exciting to see when new developments are directly helping patients.

Five questions with Max Hockenberry

March 6, 2024

Appeared in Vital Signs

In this new Vital Signs series, we feature graduate student Max Hockenberry, who performs research in the labs of Wes Legant, PhD, and Jim Bear, PhD. Hockenberry is developing new microscopy methods so researchers can measure the mechanisms cells use to maneuver through tight spaces in the body.

Max Hockenberry is a joint PhD student in the labs of Wes Legant, PhD, assistant professor of pharmacology, and James Bear, professor of cell biology and physiology, with a joint appointment in pharmacology, at the UNC School of Medicine. Both are UNC Lineberger members. In the lab, Hockenberry is developing a new microscopy method so that researchers can how cells exert force to squeeze through small spaces as they migrate within the body.

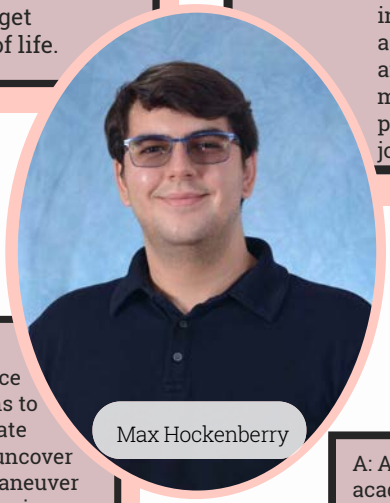
Q: What were your interests when young, and how did you get into biomedical science?

A: Growing up, I was all about astronomy – obsessed with the mysteries of space and always lost in a sci-fi novel. But I reached a turning point during a senior research project in high school. That first time peering through a microscope at a sample of pond water was a game-changer. It was like discovering a whole new universe right in front of me, just as mind-blowing as anything in space. But this time, I could interact with it directly. That moment fueled a new passion, guiding me toward a path in biomedical science where I could get hands-on with the incredible intricacies of life.

Q: Why did you choose UNC and the lab you are in?

A: I have been involved in research at UNC for many years. I attended UNC for my undergraduate degrees and became involved in the research community almost immediately. What drew me back to UNC for graduate school was the impressive array of multidisciplinary research opportunities, the genuinely collaborative atmosphere, and the cytoskeleton research community. This atmosphere fueled my curiosity and set the stage for my academic journey.

Joining the labs of Wes Legant and Jim Bear was a natural choice for me. Their focus on molecular biology, cutting-edge microscopy techniques, and the intricacies of the cytoskeleton resonated with my scientific interests. What stood out was the chance to amalgamate advanced microscopy, material and microdevice engineering, and molecular biology under the guidance of experienced mentors. This dynamic combination of expertise and the prospect of pushing boundaries in scientific exploration made joining their labs a compelling decision for me.



Max Hockenberry

Q: What are you working on right now?

A: I am focused on developing a novel traction force microscopy protocol. This innovative method aims to measure the forces exerted by cells as they navigate through micron-scale confinements. We want to uncover the physical mechanisms employed by cells to maneuver through tight spaces, which mirrors real-life scenarios encountered during migration within the body or in disease states such as cancer metastasis. The insights gained from this protocol not only enhance our understanding of cellular behavior but also hold potential implications for addressing challenges in various pathological conditions.

Q: What are your goals after earning your PhD?

A: After completing my PhD, I hope to embark on a career in academia, where I can seamlessly blend my passion for research with a focus on the multi-scale interactions of the cytoskeleton. Unraveling the intricacies that underlie cellular functions like migration and cell division continues to captivate my interest. In the long term, I envision leading my own research laboratory, leveraging the diverse skills I've acquired.

My goal is to contribute to the field by addressing challenging biological questions, particularly in areas such as cancer metastasis or immune response. I am enthusiastic about the prospect of integrating cutting-edge technology with these complex biological inquiries to make meaningful contributions to our understanding of cellular processes and their implications in health and disease.

Q: What inspires you the most about working in your field?

A: What inspires me most about working in my field is the constant innovation and pushing of boundaries by my colleagues. Witnessing the relentless pursuit of understanding living cells through cutting-edge technology is truly motivating. The field is dynamic, with advancements like super-resolution microscopy and sophisticated computational techniques providing unprecedented insights into the nature of single molecules.

The genetic engineering of optogenetic tools has opened up new frontiers, reshaping our understanding of cellular processes. It's a thrilling journey, as I find myself regularly astounded by articles that challenge my preconceptions and reshape my perspectives on seemingly solved problems. This continuous evolution and the collaborative spirit within the scientific community make every day in this field an exciting exploration of the unknown.

Paving a path in cancer research for CBP graduate students

December 5, 2024

CBP graduate student, Kimberly Lukasik received a National Cancer Institute F99/K00 predoctoral to postdoctoral fellow transition award.

Kimberly Lukasik

Kimberly Lukasik, a graduate student in Stephanie Gupton's laboratory is the first student from the Department of Cell Biology and Physiology to win a F99/K00 award from the National Cancer Institute. The award supports outstanding doctoral candidates and aids in their transition to career-building postdoctoral positions. It funds up to two years of graduate work and four years of postdoctoral research.

The award entailed a competitive internal selection process in which leaders at the University of North Carolina at Chapel Hill could only select one candidate from the entire university to compete for the award at a national level. "To be honest, I just assumed I wasn't going to get it," said Lukasik. She received notice near the beginning of October last year that she had been selected as UNC's candidate.

"I was really excited and thought, this is real. Okay, what do we do now," said Lukasik. The internal application process for UNC only required a broad description of her research, a biography, and recommendation letters. Now, Lukasik had to propose an F31/32-type grant that detailed her specific research aims for her graduate work, her broad research aims for her postdoctoral research, and how these projects would help establish the eventual direction of her own research laboratory, and she only had a little over a month to prepare.

A standout project

Lukasik's research project in Gupton's laboratory is a bit unique. The lab group focuses on how neuronal development occurs, including the proteins and cytoskeletal dynamics involved. Lukasik found that one of these proteins, TRIM9, enriched in the brain and nervous system but not anywhere else in the body was expressed in melanoma (skin cancer) cells. Interestingly, TRIM9 is also not expressed in normal melanocytes, and patients with high levels of TRIM9 often have more aggressive forms of melanoma.

During her graduate work, Lukasik found that TRIM9 negatively regulates exocytosis, or the release of molecules into the extracellular environment. It also negatively regulates focal adhesion size and number. Focal adhesions are proteins that connect the cytoskeleton of a cell to the extracellular matrix. When Ludkasik knocked out TRIM9 expression in human melanoma cells, she saw that the cells migrated faster, had different focal adhesions, and reduced proliferation.

For the specific aims linked to her graduate research, she proposed piecing together how TRIM9's effects on migration, proliferation, and exocytosis affect cancer metastasis in a melanoma mouse model. For her postdoctoral work and future career, she proposed looking at the interactions between cancer and the nervous system. "I thought about not only what I would do for my postdoc, but how I could make my own lab," said Lukasik. "It's a new field from what I understand that is about 10 years old, the neuroscience of cancer, seeing how cancer exploits the nervous system to metastasize or proliferate."

With a little help

To assemble her application and write her aims, Lukasik reached out to a previous NCI F99/K00 winner from a different department at UNC who had since graduated and was nearing the end of her postdoctoral research. Although the two did not know each other, Lukasik found a comrade in her fellow UNC alum and received helpful advice and guidance. Lukasik also had the unwavering support of her mentor.

"Stephanie has always been 100% supportive and has encouraged me to write all the fellowships that I've been interested in," said Lukasik. "She's never really told me no. That's important, having the support of your PI." Lukasik also found support from CBP at large. After winning the award, she received help and guidance from the CBP admin team on budgeting and planning. She also credited her committee and CBP core imaging services.

"CBP has been very helpful in helping me do good science. My co-sponsor for the application is James Bear. He's part of CBP and on my committee. Most of my committee is CBP, including Pat Brennwald, who has been a great resource and completely supportive of me throughout my graduate career in multiple ways. I've never had any of them tell me no when I've asked for help," said Lukasik. "And the Hooker Imaging Core led by Wendy Salmon is incredible. Multiphoton imaging is difficult. Nobody else in our lab does multiphoton imaging or uses this mouse model. Without having people to consult on campus, all of them in CBP, I wouldn't know what to do."

Some students may feel discouraged from applying for this award because they feel the process is too competitive or that their project doesn't have enough of a cancer focus. Lukasik's advice is to apply anyway. "The worst they can do is tell you no. Just apply and show that you are really interested in how you could gain the skills to conduct a successful cancer-focused project. And reach out to people because a lot of people at UNC are very helpful," said Lukasik.

Applications for the NCI F99/K00 are due in November every year.

Programming a bioinformatic housekeeping helper

December 5, 2024

Danica Dy stepped out of her comfort zone to build new bioinformatic tools in the biopharmaceutical industry.

Danica Dy

This summer Danica Dy made a bold but strategic move to enhance her skillset and prepare for her future career. She completed a bioinformatics internship focused on cancer research with IQVIA. Dy, a graduate student in Robert Wirka's lab in the Department of Cell Biology and Physiology, specializes in cardiovascular research. She investigates the molecular drivers of cardiovascular disease and mostly uses classic wet lab cell biology methods such as cell culture, protein overexpression, and histology.

"Coming into it, one of the concerns I had was, do I have enough of the bioinformatic background to be successful in this internship," said Dy. The internship was organized through the University of North Carolina at Chapel Hill's Training Initiatives in Biomedical and Biological Sciences (TIBBS) ImPACT program, which offers graduate students an opportunity to complete a one-month full time or two-month part time internship in a career area of their choice. The program partners with a range of organizations in the biopharmaceutical, scientific communication, and higher education fields.

Most students who participate in the internship use it to explore careers that they already have some training in to transition into a full-time job after graduation. Dy saw it as an opportunity to enhance her skills in an area where she had limited experience. She reached out to IQVIA and interviewed. Ultimately her ability to dissect a problem and her enthusiasm to learn earned her the position.

Building something new using old skills

"The partnership worked out and I was able to actually leverage my background in cell biology in a bioinformatics context," said Dy. At IQVIA, she was tasked with developing a bioinformatic program to filter large RNA datasets from patients with cancer and pull-out genes in hopes of identifying a pan housekeeping gene for all cancers. The challenge for Dy was slicing and organizing this real world data in a way that made sense biologically.

"For me, coming from the angle of having worked in molecular and cellular biology, I have an idea of what we know are housekeeping genes, what we should consider, and what are the important conditions for how genes are differentially expressed. Introducing that piece of how we approach building the program was what I brought to the internship," said Dy.

Ultimately, Dy's approach found a few genes that could potentially qualify as pan cancer housekeeping genes in solid tumor samples. Interestingly, some of the typical culprits that scientists tend to think about as reliable housekeeping genes such as GAPDH performed poorly. Instead, her program found different groups of more reliable housekeeping genes based on solid vs. liquid tumors and originating tissue type.

"Danica has gone above and beyond in giving her time and effort to wrap up the project and create a script that is ready to go for detecting housekeeping genes. She incorporated her own research and knowledge to the project, adding new perspective and value," wrote Douglas Wilson, Dy's manager at IQVIA.

Leaving an impact

Next, the team at IQVIA will pass the Dy's script to their assay development team. The plan is for the team to eventually feed RNA sequencing data from IQVIA clinical trials into the program to see what housekeeping genes it suggests for developing better, more robust assays.

Danica Dy posed with her line manager, Dr. Gunjan Hariani and manger, Douglas Wilson outside IQVIA

"In academia, we focus on novelty, we're often chasing our curiosity, which is great," said Dy. Her manager at IQVIA explained that in industry the focus is more on optimizing and tool building. Dy also noted that industry research required more collaboration across departments and sectors to bring a tool or discovery to reality.

"Just having the exposure to an industry environment was immensely beneficial. It felt like a black box before having this internship because all I've known is lab academia," said Dy. "It also helped me figure out that I have skills that are transferable. The way a PhD program teaches you how to think and approach a problem is the core of what you get out of it because I can take off my cardiovascular biology hat and switch over to cancer informatics. That was surprising, which was really great. I didn't realize I could do that."

Dy would encourage other students to apply for the ImPACT program. She believes that stepping out of the lab environment helps shift students' focus and helps them execute tasks for their PhD research with a new set of eyes and a better idea of the future ahead.

"For students concerned about having a skill or knowledge gap, that's healthy," said Dy. "The reality is, and my manager said this too, you always want to use the next opportunity, whether it's a job or an internship to fill a new skill or to learn something you don't 100% know. It's a learning experience. Just take the jump and trust that your skills will translate."

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Current supported students

Leo Blondel

Mentor: Mark Zylka, PhD

Focus: Using computational, genetic, and mouse models to safely and effectively unsilence UBE3A in Angelman Syndrome

Shanice Harrison

Mentor: Whitney Edwards, PhD

Focus: Investigation of N-myristoyltransferase 1 (NMT1)-mediated myristoylization in sarcomere formation during cardiac develoment.

Frankie Marchan

Mentor: James Bear, PhD

Focus: Investigating how actin network dynamics and force production contribute to homeostatic balance during cellular membrane trafficking

Samantha Ryken

Mentor: Stephanie Gupton, PhD

Focus: : The role of focal adhesion kinase and calcium dynamics in the regulation of exocytosis and membrane expansion during neuronal morphogenesis.

Past recipients

Jocelyn Alvarado
Keith Breau
Amber Gomez
Anna Kim
Juliet King
Rhianna Lee (Graduated)
Julie Necarsulmer (Graduated)
Nate Nelson-Maney (Graduated)
Jennifer Nwako
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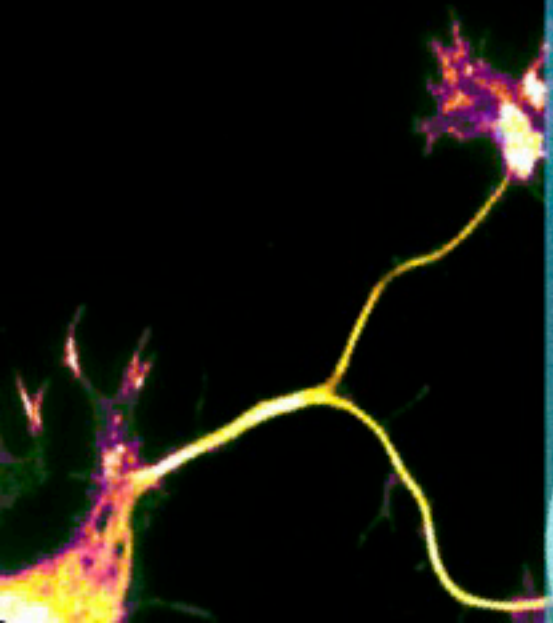

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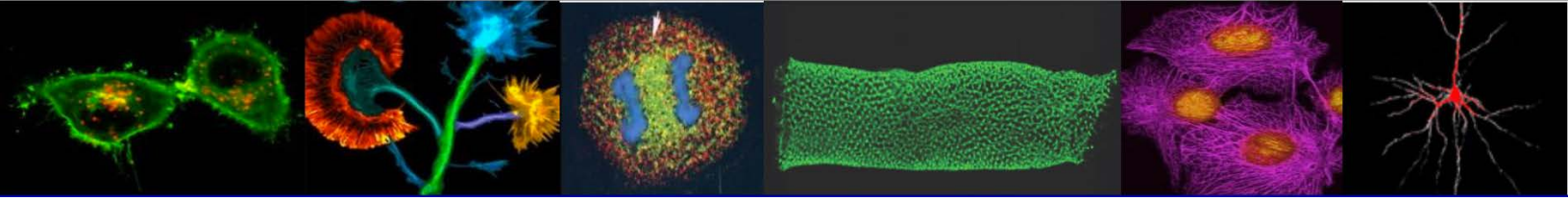

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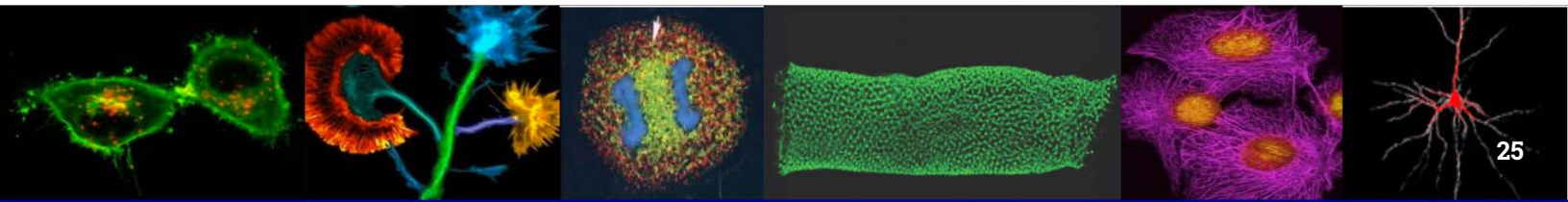

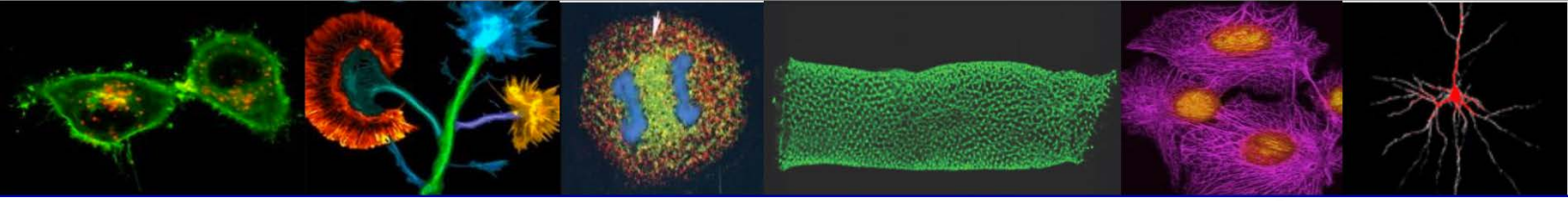

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