

# 2022 School of Medicine Research Round-up

*To demonstrate the breadth of exceptional research done in the UNC School of Medicine, this publication is a compilation of the most noteworthy 1-2 research highlights over the past year provided by each Department.*

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## ***Department of Anesthesiology***

Anesthesiology Department faculty member, **Xinming An, PhD**, has been developing risk prediction tools, identifying objective biomarkers, and exploring homogeneous subtypes for acute posttraumatic neuropsychiatric sequelae (APNS). Along with his collaborators, Dr. An has published many high-impact research papers in top journals such as JAMA Psychiatry and Molecular Psychiatry. In one of his recent papers published in JAMA Psychiatry, they identified and validated several innovative trait and state biomarkers of APNS symptoms based on 24-hour activity patterns collected from the smartwatch. Simple biomarker/symptom change cut-offs suggest that these biomarkers might have utility as initial screening tools to identify individuals with potential good recovery in these domains who might not need further evaluation. In clinical practice, they could serve as ancillary data to help patients and physicians identify whether symptoms are improving or worsening post-trauma.

## ***Department of Biochemistry and Biophysics***

**Scientists uncover a new approach for treating aggressive cancer.** Researchers in **Greg Wang, PhD**'s lab have uncovered a new role of a chromatin-modulatory enzyme, termed EZH2, during cancer development. Certain subtypes of blood cancers, such as acute leukemias, rely on multiple mechanisms for sustaining growth of aggressive cancer cells. These mechanisms include those driven by EZH2 and cMyc, a prominent cancer-causing factor. The Wang lab has now shown that these two factors can directly associate with one another, modulating cancer-cell-specific programs of gene expression. To develop pharmacological means of targeting both EZH2 and cMyc, they teamed with the chemical biologists at Icahn School of Medicine at Mount Sinai and designed a new small-molecule, MS177, based on the proteolysis-targeting chimera (PROTAC) technology. MS177 targets both EZH2 and cMyc and thus inhibits cancer growth. Their findings were published in Nature Cell Biology (2022). [More about this finding can be found here.](#)



**Inside or out? Scientists discover new checkpoint for entry into cells.** **Rick Baker, PhD**'s laboratory uncovered key details about how cells decide which molecules to bring inside. In collaboration with the Gunther Hollopeter laboratory at Cornell University, they described the function of a family of proteins called Muniscins. Muniscins regulate a process called endocytosis, which is the main pathway external material enters cells, that is often misregulated in cancers and



heart disease. They showed that endocytosis has a “checkpoint” that allows for precise control of what molecules (“cargo”) are allowed inside. Muniscins act as gatekeepers by changing the shape of key endocytic protein AP2. This conformational change makes AP2 more likely to select one particular type of cargo for internalization. Understanding the determinants for entry into cells could lead to the design of better therapeutics that enter cells via endocytosis. Their findings were published in Nature Structural & Molecular Biology, [and you can read more about their discovery here.](#)

## Department of Biomedical Engineering

[An animal model study](#) published in *Nature* and led by **Yevgeny Brudno, PhD**, determined that treatment with an implantable biotechnology for CAR-T cell therapy that performs the steps of activation, reprogramming, and expansion in vivo in a single day, was faster and more effective than conventional CAR-T cell cancer treatment. To meet the traditional challenges with CAR-T cell therapy, the Brudno laboratory created Multifunctional Alginate Scaffolds for T cell Engineering and Release (MASTER), in partnership with **Gianpietro Dotti, MD**, and Frances Ligler, PhD, of Texas A&M University. MASTER is a biocompatible, sponge-like material where researchers pour a mixture of isolated patient T cells and non-activated T cells with an engineered virus. Mice that received CAR-T cell treatment via MASTER were far better at fighting off tumors than mice that received conventional CAR-T cell treatment. The improvement in anti-cancer efficacy was especially pronounced over the long term, when mice were faced with a recurrence of lymphoma.

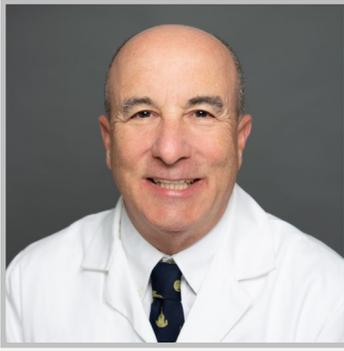
**Scott Magness, PhD**, along with postdoctoral researcher **Joseph Burclaff, PhD**, graduate student **Jarrett Bliton**, and colleagues mapped the entire human gut at single cell resolution. The Magness laboratory used human gastrointestinal tracts from three organ donors to show how cell types differ across all regions of the intestines. “As far as we know, we’re the first to do this kind of analysis across the length of the human gut from three full donors,” said Bliton. [Published here](#) in *Cellular and Molecular Gastroenterology and Hepatology*, their work explored cellular functions and how gene expression differs between cells and individuals. Researchers could see which receptors were expressed the most and in which type of cell, painting a new picture of how cells might interact with gut contents such as nutrients, microbes, toxins, and drugs. The lab hopes this will help researchers understand why some people experience toxicity to certain foods or drugs, while others do not.

## Department of Cell Biology and Physiology

Sleep during early development of humans and other mammals is believed to be critical for postnatal brain development. Sleep disruption is an early symptom in autism spectrum disorder (ASD) and a potential driver of future symptoms. The lab of **Graham Diering, PhD**, assistant professor of Cell Biology and Physiology, used a clinically relevant heterozygous *Shank3* ASD mouse model to examine the potential causal role of developmental sleep disruption in altered brain function and behavioral phenotypes in adults. This work, published in [Molecular Autism](#), concludes that early life sleep disruption contributes to long-lasting and sex-specific changes in adult behavior in the genetically vulnerable *Shank3* heterozygous mice. These findings by the Diering lab place emphasis on the importance of understanding and treating sleep disruption in ASD and other neurodevelopmental conditions.



Cystic Fibrosis (CF) is a genetic disorder where absent or dysfunctional CF Transmembrane Regulator (CFTR) leads to severe pathology in the lungs. CFTR modulators treat CF by directly acting on the CFTR protein to correct folding, trafficking, function or stability, extending the lives of eligible patients. Treatment options for individuals who express rare CFTR variants are limited and new drug discovery is impeded by the scarcity of relevant cellular resources. **Scott Randell, PhD**,



professor of Cell Biology and Physiology, and his team generated primary airway epithelial cell lines that recapitulate clinical responses to CFTR modulators and can be used to evaluate novel treatment approaches for patients expressing rare CFTR variants *in vitro*. This impactful work, published in the [\*Journal of Clinical Investigation\*](#), describes the creation of patient-derived primary cell lines and illustrates their utility for testing novel therapies that target rare genetic variants in patients with CF.

## **Department of Dermatology**

Linear IgA bullous dermatosis (LABD) is an autoimmune skin blistering disease affecting both children and adults. Our research team, including **Ning Li, PhD**, **Paul Googe, MD**, **Luis Diaz, MD**, **Nancy Thomas, MD, PhD**, and **Zhi Liu PhD**, developed the first clinically relevant mouse model of LABD which is suitable for systematically dissecting the immunopathogenesis of the disease. This study will be published in *The Journal of Investigative Dermatology*.

**Ash Sampath MD**, **Christopher Sayed, MD**, **Franklin Blum**, **Paul Googe, MD**, and **Jayson Miedema, MD** led a group of international experts in the development of a standardized reporting tool for histologic findings in hidradenitis suppurativa (HS), which was presented at the American Society of Dermatopathology Annual meeting. **Christopher Sayed, MD**, along with clinical research fellow, **Helen Bui, MD**, also led a Delphi consensus effort standardizing definitions for HS surgery with the results accepted for publication in *JAMA Dermatology*. Additional high impact HS original research articles were published characterizing pediatric HS patient cohorts (**Christopher Sayed, MD** and **Helen Bui, MD**) and patient outcomes and perceptions following surgery for HS (**Christopher Sayed, MD** and **Jonathan Miles, MD, MPH**).

## **Department of Emergency Medicine**

The Department of Emergency Medicine (EM) welcomed two new research faculty. **Ming Ding, MSc, ScD** is a cardiovascular epidemiologist integrating lifestyle behaviors, -omics, and epidemiological method development, which is supported by a R21 grant. **Amy Ising, PhD**, focuses on leveraging syndromic surveillance to inform stakeholders, researchers, and the public. She is the Associate Director of EM's Carolina Center for Health Informatics and is fully grant-supported by NC DPH/CDC.

For research, **Martin Casey, MD, MPH**, received Society for Academic Emergency Medicine Foundation funding to understand patterns of potentially harmful albuterol utilization in patients with heart failure. EM Clinical Trials participated in a multisite trial to estimate the sensitivity and specificity of the Abbott BinaxNOW® COVID-19/Flu/A&B Combo Card test against the reference method in patients suspected of COVID-19 and/or influenza A or B. UNC EM has been designated a site for the NIH SIREN MAGNETIC hub and looks forward to participating in pragmatic trials.

## Department of Family Medicine

Two Family Medicine faculty recently received NIH Career Development awards. **Chineme Enyioha, MD, MPH**, was awarded a K23 grant from NIDA for research to create a mobile cessation system targeted at African American smokers. **Sarah Kowitt, PhD, MPH**, was awarded a five-year K01 grant from NCI and FDA to research how to communicate the harms of multiple tobacco product use among youth.

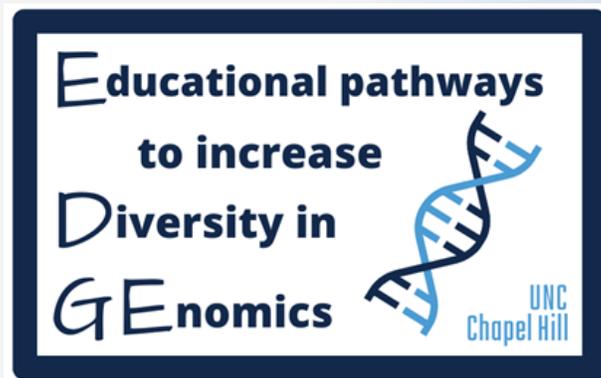


Family Medicine's **Donald Pathman, MD, MPH**, and **Jeffrey Sonis, MD, MPH**, published a paper reporting that moral distress was common among more than 2,000 primary care, dental, and behavioral clinicians who worked with low-income patients in safety net clinics during the pandemic's first nine months. Nearly 72% reported mild or intense levels of moral distress due to their inability to provide optimal care, but even more morally distressing to clinicians was witnessing inequities and other injustices for their patients and communities, and the

suffering of other clinical staff. [Link to publication.](#)

## Department of Genetics

Funded by NHGRI, the [UNC Educational Pathways to Increase Diversity in GENomics \(EDGE\)](#) is an innovative two-year summer program that provides training in laboratory research skills, genomic medicine, career education, and mentoring to undergraduate students from underrepresented and disadvantaged backgrounds who are interested in careers in genomics. This grant was awarded to co-PIs **Folami Ideraabdullah, PhD**, and **Jonathan Berg, MD, PhD** in 2022 and is a collaborative effort with the [UNC Program for Precision Medicine in Health Care \(PPMH\)](#). More than 45 Department of Genetics faculty have committed to participate in the program. The first cohort of 21 students from 10 colleges/universities matriculated in summer of 2022, and spent three weeks attending lectures, participating in career panels, and interacting with 25 faculty instructors and mentors. The second summer session will include eight weeks of independent research, additional mentoring, and professional development. Recruitment is underway for the 2023-2024 cohort.



## Department of Health Sciences

**Blaise Morrison, PhD, CRC, LPC**, received an award from the Patient-Centered Outcomes Institute (PCORI) to fund *Project BENEFIT: Building Effective Networks to Engage Families in Improving Transition*. The project aims to partner with underserved Intellectual and/or Developmental Disability (IDD) stakeholders from Black, Indigenous, and People of Color (BIPOC) communities to develop research products that improve capacity for IDD healthcare transition research. The short-term goals include developing (1) an IDD Healthcare Transition Research Roadmap, (2) an IDD-accessible online training on Patient-Centered Outcomes Research (PCOR) and Comparative Effectiveness Research (CER) in the area of healthcare transition, (3) a partnership framework and recommendations for future researchers to partner with diverse IDD stakeholders, and (4) a network of IDD stakeholders invested in being research partners in future healthcare transition research. The long-term goals are to increase IDD stakeholder engagement in research, improve IDD healthcare transition research and practices, and reduce health disparities for families from BIPOC and IDD communities.

**Jessica Steinbrenner, PhD**, received an award from the Institute of Education Sciences to continue her work focused on school-based intervention programs for students on the autism spectrum. This newest grant funds Project EXPRESS which examines the efficacy of two group-based programs for middle school students on the autism spectrum: PEERS® which targets peer relationships and social skills and Unstuck and On Target which targets executive functioning skills. The goal is to compare these programs to services-as-usual (SAU) as part of a unique dual efficacy randomized controlled trial. Much of her work involves providing training and coaching to educators in public school settings to support them in implementing programs and practices to address the core needs of autistic students with the hope of improving immediate and long-term outcomes. Project EXPRESS is a multisite project involving UNC-CH and San Diego State University.

## Department of Medicine

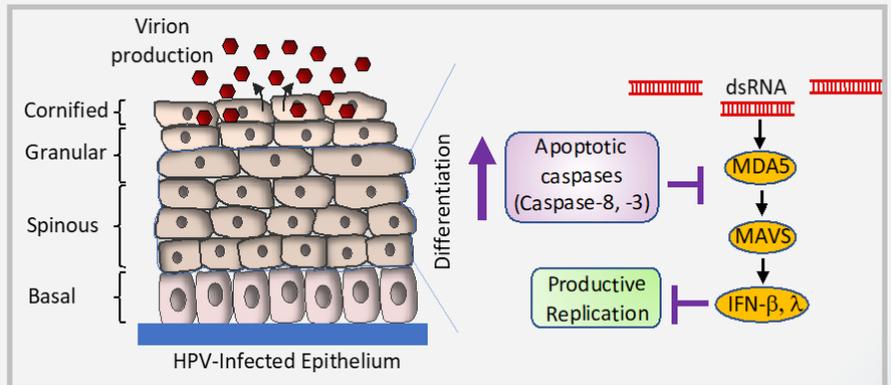
The Department of Medicine would like to highlight two impressive contributions to clinical science this year. **John Buse, MD, PhD**, from the Endocrinology and Diabetes Division continues to have a leading role in changing management of diabetes which include four *New England Journal of Medicine* papers, and an influential management paper published in *Diabetes Care* ([PMID: 36148880](#).) For the *NEJM* Dr Buse, joined by seven colleagues from UNC clinical trials, investigated use of a bionic pancreas to deliver insulin in patients with Type 1 diabetes ([PMID: 36170500](#)). In this trial, subjects had only to put in their body weight and specify when they were eating meals; thereafter the bionic pancreas made decisions as to insulin delivery. This delivery method was associated with a greater reduction in glycated hemoglobin level than standard care insulin delivery. Such devices are even now replacing standard of care insulin delivery systems, which is very exciting for the diabetes world.

**Mina Hosseinipour, MD, MPH**, from the Division of Infectious Disease, was senior author on a clinical trial aimed at preventing HIV-1 in women, who are disproportionately affected by HIV, published in *Lancet* ([PMID: 35378077](#)). This randomized, double blind superiority trial involved sexually active women from 7 countries in sub-Saharan Africa. More than 3000 women were assigned to receive injectable cabotegravir or an oral tenofovir-based standard treatment. For women at risk, an injection of cabotegravir every 8 weeks overcame some social barriers associated with daily dosing, which contributed to its superiority over the daily dosing of standard treatment:

cabotegravir decreased HIV infection risk by 88%. This trial supported FDA approval of cabotegravir for HIV prevention which has now been endorsed by the World Health Organization.

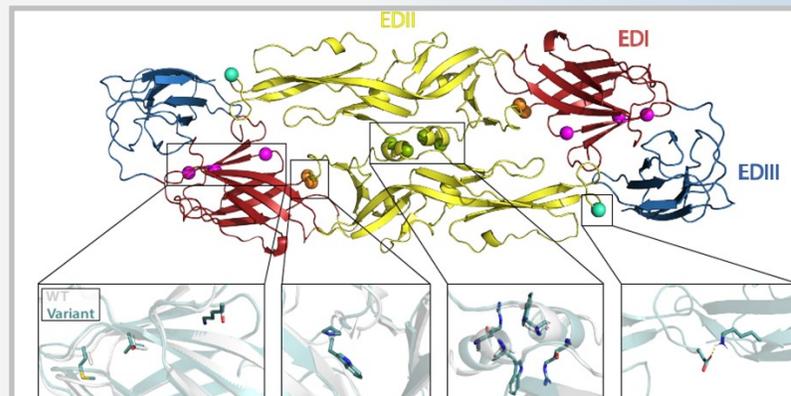
## Department of Microbiology and Immunology

Previous studies showed that sublethal apoptotic caspase activity is required for productive replication of cancer-associated human papillomaviruses (HPV). Caspase cleavage of the E1 viral helicase is necessary for efficient viral genome amplification upon differentiation; however, whether caspase activity promotes viral replication through



other mechanisms has not been explored. [A recent study by Cary Moody, PhD's group](#) demonstrated that HPV31 and HPV16 commandeer apoptotic caspases to suppress an interferon (IFN) response upon differentiation. Caspase inhibition results in the secretion of Type I IFN-β and Type III IFN-λ that induces the expression of IFN stimulated genes and blocks viral replication in neighboring cells through the MDA5-MAVS pathway, identifying a role for double-strand RNA (dsRNA) in activating the cell intrinsic innate immune response in HPV infected cells. These observations demonstrate a mechanism by which HPVs reprogram the cellular environment through caspase activation, hijacking proteins to prevent excessive IFN production and support viral replication in differentiating cells.

With support from the NIH and DoD, **Aravinda de Silva, PhD, Shaomin Tian, PhD, and Brian Kuhlman, PhD**, have been collaborating to develop 2<sup>nd</sup> generation dengue protein subunit vaccines. Using computational tools developed for protein engineering, the team previously discovered a set of mutations that stabilized the native structure of recombinantly produced envelope protein from dengue type 2. Mice immunized with the stabilized proteins developed high levels of neutralizing antibodies that targeted native epitopes on the infectious virus. Most recently, the group discovered that mutations that worked for serotype 2 also led to the stabilization of the envelope proteins from the other three dengue serotypes and the more distantly related Zika virus. Therefore, lessons learned from these studies may be broadly applicable to the development of subunit vaccines for other pathogenic flaviviruses. Based on these results, the investigators have also established a partnership with Moderna Vaccines to design and test mRNA vaccines against dengue and Zika viruses.



A conserved set of mutations for stabilizing soluble envelope protein dimers from dengue and Zika viruses to advance the development of subunit vaccines. [T. Phan et al. Journal of Biol Chem.](#)

## Department of Neurology

Faculty in the Department of Neurology have made numerous advances in clinical research. The Neuroscience Clinical Trials Unit (**NCTU**) supported 51 faculty, fellows, and residents and managed a total of 94 industry, NIH, and investigator-initiated trials. **James Howard, MD** and **Manisha Chopra, MBBS** examined several FDA approved drugs to treat myasthenia gravis, creating additional treatment options that meet individual patient's needs ([Vu et al., NEJM Evidence](#), [Guglieri et al., JAMA](#), [press release](#)). **Varina Boerwinkle, MD** published a landmark article highlighting the use of fMRI to discern seizure onset and propagation zone ([Boerwinkle et al., NeuroImage: Clinical](#)). **Senyene Hunter, MD, PhD** was named Simmons Scholar and American Epilepsy Society Sergievsky Scholar for her exceptional research in improving understanding of genetic epilepsies through the inclusion of ancestrally diverse and medically underrepresented individuals and related aspects of health equity. Dr. Hunter and the Epilepsy Neurogenetics Initiative team are part of the [Epi25 Collaborative](#) for Large-Scale Whole Genome Sequencing in Epilepsy, which will address the phenotypic spectrum associated with specific forms of epilepsy.



In the area of basic science, the laboratory of **Todd Cohen, PhD** helped understand Alzheimer's disease pathogenesis through identifying novel mechanisms that control the formation ([Journal of Biological Chemistry](#)) and disposal ([Acta Neuropathologica Communications](#)) of pathological tau. **Rick Meeker, PhD**, in collaboration with **Leslie Morrow, PhD**, revealed that inflammatory activity can be controlled by naturally occurring neurosteroids and opened a new avenue to suppress neurodegenerative activity ([Frontiers in Immunology](#)). **Ian Shih, PhD**'s team addressed how large-

scale brain network dynamics is altered by selective activation of the locus coeruleus – a small brain nucleus in the brainstem that releases norepinephrine ([Science Advances](#), [press release](#)). The Shih lab also developed an improved fiber-based optical technique for accurately measuring brain activity changes ([Cell Reports Methods](#), [press release](#)) and received the 2022 NeuroImage Paper of the Year award – an honor given to the best paper submitted to the journal over the past year – for their study examining dopaminergic activity and tissue oxygen transients during fMRI ([NeuroImage](#), [press release](#)).



## Department of Neurosurgery

Faculty in the Department of Neurosurgery are embarking on ground-breaking research. **Vibhor Krishna, MD**, received an R01 from the NIH to fund his focused ultrasound ablation research that will benefit patients with movement disorders, specifically those patients with essential tremor. **Yasmeen Rauf, MD**, will lead a groundbreaking CAR-T clinical trial for patients with glioblastoma beginning next year at the UNC Medical Center. **Dominique Higgins, MD, PhD**, will work with Dr. Rauf in this clinical trial. **Dawn Kernagis, PhD**, and **Brian Sindelar, MD**, are part of a research team that received NeuroSpark pilot funding for their research on serum biomarkers in severe traumatic brain injury. **Eldad Hadar, MD**, **Dominique Higgins, MD, PhD**, and **Vibhor Krishna, MD**, received a UNC SOM DEI Mini Grant to establish the Black Lives Matter Neurosurgery Neuroscience Summer Opportunity.

## **Department of Nutrition**

Department of Nutrition professors **Barry Popkin, PhD, Shu Wen Ng, PhD, and Lindsey Smith Taillie, PhD**, teamed up with researchers from around the globe to investigate the impact of government policies on the consumption of ultra-processed food (UPF) in Mexico, Chile, Brazil, and South Africa. The study, "[Towards unified and impactful policies to reduce ultra-processed food consumption and promote healthier eating](#)" was published earlier this year in *Lancet Diabetes & Endocrinology*, and demonstrated the efficacy of combining policy initiatives to successfully reduce the amount of UPF purchased. There is still much to learn about the impact of government policies on the consumption of UPF, but this article provides research-backed groundwork for future studies.

**Kyle Burger, PhD MPH, RD** along with graduate students **Jennifer Sadler** and **Grace Shearrer** recently concluded an investigation into when in the progression of type 2 diabetes (T2D) brain function alterations become apparent independent of BMI. After studying 44 pre-diabetic participants, they concluded that participants with prediabetes had stronger connectivity between brain networks associated with sensory and attention to stimuli suggesting that cognitive insulin resistance begins in patients with T2D earlier than previously recognized and this effect is present despite current body mass. More information about this study can be found in [Nutrition Neuroscience's](#) February 2022 issue.

## **Department of Obstetrics and Gynecology**

In 2022, OB/GYN faculty successfully competed for grants to help reduce health disparities in North Carolina. **Alison Stuebe, MD** received an award from the American Heart Association to improve perinatal and reproductive health services through improved interprofessional education and collaboration. The UNC Horizons team, led by **Hendree Jones, PhD**, was funded by the North Carolina Department of Health and Human Services to expand access to evidence-based treatment options for women with substance use disorder leaving prisons across the entire state. **Kate Menard, MD, MPH** and a multidisciplinary team of UNC researchers will work to improve access to hypertension services in pregnancy and postpartum via innovative outpatient- and community-based strategies. Finally, the Carolina Endometrial Cancer Study, co-led by **Victoria Bae-Jump, MD, PhD** (alongside **Andrew Olshan, PhD** and **Hazel Nicols, PhD**), will enroll over 1500 women—including at least 500 Black women—to understand how tumor biology and social determinants of health influence treatment outcomes.

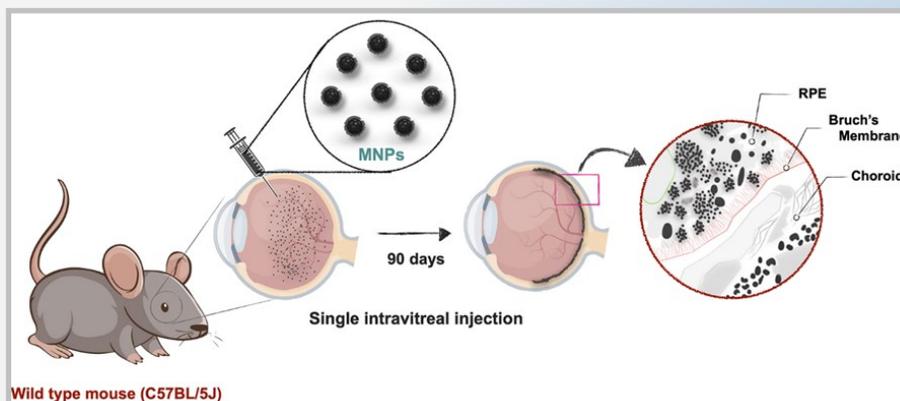
The Department of Obstetrics and Gynecology is committed to developing a pathway for research careers for our faculty. The successes of our early-stage investigators represent an important accomplishment over the past year. **Andrea Knittel, MD, PhD** was awarded a Doris Duke Clinical Scientist Award to implement and evaluate treatment services for perinatal substance use disorders during incarceration. **Chemtai Mungo, MD, MPH** received funds from the Victoria's Secret Global Fund for Women's Cancers to evaluate topical treatments for cervical precancer in Kenya and Malawi. **Christine Chu, MD, MSCI** is investigating strategies to optimize urinary tract infection prevention, with a focus on the urinary, gut, and vaginal microbiomes. This work is supported by the American Urogynecology Society and the PFD Research Foundation. Finally, **Bridget Spelke, MD** was funded by the Fogarty International Center to evaluate the use of multiparameter wearable sensors to detect complications in the postpartum period.

## Department of Ophthalmology

Corneal transplantation (CT) to treat genetic and acquired corneal blindness is the most common form of tissue transplantation worldwide. Unfortunately, over 20% of these surgeries are termed high risk and have a rejection rate of over 70% within 3 years. Steroid and non-steroid immunosuppression are employed to prevent CT rejection, but fail to improve the clinical outcome while also having adverse effects. **Matthew Hirsch, PhD**'s lab has developed an Adeno-Associated Virus (AAV) gene therapy approach to address this deficit that employs an optimized immune suppression molecule that naturally protects healthy corneas. This approach prevented 100% of high risk CT rejections in a large animal model. This drug was not directly applied to the patient so it remained restricted to the donor tissue with no adverse events observed throughout these experiments. The Hirsch lab is working with a biotech company, the NIH, and the FDA to translate this work to millions of patients globally that require CT.



Melanin is found in most organisms and tissues, such as skin and the retinal pigment epithelium (RPE) in eyes where it acts as a photoprotector, a free radical scavenger, and a heavy metal/chemical binding reservoir. In contrast to skin melanin, melanin in the RPE does not regenerate. An age-related decline occurs in reduction of either quantity or quality of melanin in adult RPE. Conversely, lipofuscin (A2E), a major component of a toxic product, is found in age-related macular degeneration (AMD) patients and is actively deposited on melanin granules throughout life. This phenomenon correlates with the progression of lipid peroxidation and protein oxidation of cellular components in AMD pathology. The **Zongchao Han, MD, PhD** lab has developed melanin-like nanoparticles for the treatment of AMD that can effectively replace the natural melanin in the RPE and act as a natural free radical scavenger and photoprotector to combat photic stress and oxidizing conditions to treat AMD.



## **Department of Orthopaedics**

Research growth in the Department of Orthopaedics in 2022 has involved faculty collaborators across UNC and NCState, residents, fellows and medical students. **Andrew Chen, MD, MPH** has joined a DOD funded trauma surgery research consortium (METRC) as site PI and was selected for the NCTraCS Clinical Trialist training program. **Stuart Mitchel, MD**, has been named site PI for 2 NIH funded clinical trials for fracture care in children and **David Berkoff, MD**, is site PI for two NIH funded trials studying innovative approaches to treating patients with knee osteoarthritis. **Daniel Bracey, MD, PhD**, in collaboration with **Richard Loeser, MD**, of the Thurston Arthritis Research Center are initiating a large-scale biorepository to study patients with total knee arthroplasty. Our clinical research coordinator team has grown considerably to serve our increase in orthopaedic clinical trials. We are in the process of hiring additional research faculty to lead our orthopaedic basic and translational research program.

## **Department of Otolaryngology**

Noise-induced hearing loss (NIHL) affects 6-24% of adults in the US and can lead to tinnitus and contribute to dementia. These consequences of hearing loss depend on changes in the brain, including the electrical excitability of cells, synapses, and network connectivity. **Paul Manis, PhD's** lab has developed methods for high-resolution analysis of excitability and synaptic connections. The recent identification of a mouse line that tags the inner ear neurons most sensitive to noise damage and aging allows the lab to study the effects of NIHL on the specific central neurons and pathways served by those noise-sensitive neurons. The lab is also mapping the precise connections of the early parts of the auditory pathway (with the Spirou lab at the University of South Florida) and delineating non-traditional brain circuits that deliver sound information faster to the auditory cortex than the main pathways (with the **Kato** lab in UNC Psychiatry). [This work is described in a paper on bioRxiv.](#)

Unilateral hearing loss can cause significant impairments, and children may be even more negatively affected than adults as they are still learning language, frequently in noisy classrooms, in which an inability to hear with both ears can be even more detrimental. Conventional treatment options fail to re-establish binaural hearing, but a cochlear implant could. **Kevin D. Brown, MD, PhD, Margaret T. Dillon, AuD, PhD**, and **Lisa R. Park, AuD**, evaluated the impact of cochlear implantation in children with unilateral hearing loss, and found that providing a cochlear implant to children with unilateral hearing loss improves sound source localization, speech perception in noise (regardless of the orientation of noise relative to speech), and subjective hearing abilities. This study was published as a Triological Thesis by Kevin D. Brown and was awarded the highest prize for clinical research in otolaryngology, The Harris P. Mosher Award in 2021.

## **Department of Pathology and Laboratory Medicine**

**Li Qian, PhD** (associate professor), **Ben Keepers** (MD/PhD student), and **Haofei Wang, PhD** (postdoctoral fellow) led an important study of cell fate published in [Cell Stem Cell \(PMID: 36206732\)](#). Direct reprogramming is the molecular mechanism of converting one somatic cell type to another without a transition through an intermediate pluripotent state. Direct reprogramming is of particular interest in the cardiology field as a way of potentially restoring cardiac myocytes that are lost to ischemic damage. They discovered that the neuron-specific transcription factor, *Asc1*, can also activate the cardiac myocyte transcriptional program by partnering with the transcription factor *Mef2c* to repress neuronal and fibroblast cell identity. *Asc1* is not expressed in the heart at any developmental stage. Thus, their paper is landmark in that it questions the dogma that transcription

factors are uniquely tied to specific cellular identities.

## ***Department of Pediatrics***

Investigators in the Pediatric Hematology-Oncology division furthered a history of stellar team science work to deliver new therapeutics and support to children and young adults with cancer. **Kate Westmoreland, MD**, and collaborators at UNC Project-Malawi advanced cancer care for children globally (PMID: [35731580](#), [35175832](#), [35045815](#)) via observational and implementation studies to improve outcomes. **Andrew Smitheman, MD, MSc**, led several quality-of-life studies investigating health disparities in young adult cancer survivors as well as reproductive outcomes following fertility preservation in adolescent women survivors (PMID: [36316813](#), [35319782](#), [35169982](#)). **Thomas Alexander, MD, MPH**, and colleagues investigated techniques to accelerate transcriptional profiling in leukemia to quickly categorize and diagnose acute disease subtypes, particularly in low-resource settings (PMID: [35442720](#)). **Barbara Savoldo, MD, PhD**, and her team continued groundbreaking work enhancing immune responses to adoptive CAR-T cell therapy, with encouraging implications for other solid tumors presenting with metastases in the brain (PMID: [35443752](#)).

Ongoing research efforts in the Pediatric Critical Care division have contributed to several large scale, multidisciplinary, multicenter studies investigating therapeutics, disease outcomes and vaccination responses in children with COVID-19 and multi-inflammatory syndrome (MIS-C). Led by site investigators **Stephanie Schwartz, MD**, and **Tracie Walker, MD**, and supported by clinical research staff in the Pediatric Clinical Research Unit (Peds CRU) of the Children's Research Institute, these collaborations led to high-profile publications including characterizations of neurological complications following acute COVID-19 infection (PMID: [35066369](#)) and risk factors for long term sequelae following discharge (PMID: [35765138](#)). Other notable work from our PICU team includes a study investigating the effectiveness of maternal vaccination against hospitalization in infants with COVID-19 (PMID: [35731908](#)) as well as clinical trials investigating the effectiveness of vaccines against hospitalization and ICU-stays in children infected with delta and omicron variants of COVID-19 (PMID: [35021004](#), [35353976](#)).

## ***Department of Pharmacology***

The January/February 2022 issue of Carolina Alumni Review featured two separate profiles of UNC Pharmacology faculty. One describes **Jude Samulski, PhD**'s decades-long effort to develop viral vectors for human gene therapy. His inventions are being used in nearly all gene therapy trials, of which there are thousands now underway. The other profile was about **Bryan Roth, MD, PhD**'s efforts to develop variants of psychedelic drugs, targeting the serotonin 2A receptor, for the treatment of neurological disorders. Roth's research has led to the development of a new drug candidate, one having the long-lasting antidepressant effects of LSD, but without the psychedelic side-effects. His recent findings were profiled in several national news outlets including NPR and the *New York Times*.

## ***Department of Physical Medicine and Rehabilitation***

The Department of Physical Medicine and Rehabilitation has had several research funding successes. The **NIH NCCIH T32** grant that provides training for postdoctoral and pre-doctoral research fellowships in Complementary and Integrative Healthcare was recently renewed for its fourth consecutive 5-year cycle. The Department recently celebrated its first **NIH K01** award, "Scaling

-up Integrative Pain Management in Federally Qualified Health Centers,” to develop strategies to integrate Integrative Medical Group Visits into community health centers. The Department’s **NIH NIMHD R01** award, “Stress Management Intervention Leveraging Electronic Health Records for racial and ethnic populations during the COVID-19 pandemic (SMILE),” will investigate the utility of digital mindfulness-based interventions and examine associations between COVID-19 related stress and mental health outcomes, resilience and HRV. The Department is also home to the **NC Collaboratory Long COVID study**: a collaboration with the Division of Infectious Diseases and the Gillings School of Global Public Health that will provide a year-long longitudinal study of long COVID in North Carolinians.

## ***Department of Psychiatry***

For the first time, scientists led by **Jessica Girault, PhD**, assistant professor in the Department of Psychiatry, have found that brain differences in the visual brain systems of infants who later are diagnosed with autism (ASD) are associated with inherited genetic factors. The team’s work entitled “Infant Visual Brain Development and Inherited Genetic Liability in Autism” was published in [\*The American Journal of Psychiatry\*](#) and describes how the team looked at the association between proband ASD traits and sibling brain development at 6, 12, and 24 months in MRI phenotypes in a sample of 384 proband-sibling pairs. The team found that greater levels of proband ASD traits were associated with larger cerebral volume and reduced white matter integrity in visual system components in siblings who developed ASD.

Dissociation is a common, disabling phenomenon that involves profound detachment from the self or surroundings. In the largest prospective, longitudinal neurobiological study of dissociation to date, work by the AURORA team including **Sam McLean, MD, MPH**, Jeffrey Houpt Distinguished Investigator, suggests feeling detached from one’s surroundings may suggest a higher risk of later developing psychiatric symptoms, highlighting the importance of screening for feeling detached to identify patients who might benefit from preventive care. The team’s research entitled “Persistent Dissociation and Its Neural Correlates in Predicting Outcomes After Trauma Exposure” [and published in \*The American Journal of Psychiatry\*](#) emphasizes that the neural correlates of trauma-related dissociation may serve as potential targets for treatment engagement to prevent posttraumatic stress disorder.

## ***Department of Radiation Oncology***

Xerostomia, or dry mouth, is a common side effect of head and neck radiotherapy due to damage to the salivary glands. In order to address this issue, **David Fried, PhD, DABR** and a team of researchers in the UNC Department of Radiation Oncology are investigating a new approach to radiotherapy planning that aims to selectively spare the salivary duct regions that contain stem cells, which may be necessary for regenerating salivary function after injury. The team conducted a pilot clinical trial to determine the feasibility and safety of this approach. In a paper published in [\*Radiotherapy and Oncology\*](#), they reported on the results of the trial, including the feasibility and safety of the new approach and encouraging early results indicating a reduction in patient-reported xerostomia after head and neck radiotherapy, compared to a control group treated with standard radiotherapy.

The Division of Healthcare Engineering in the Department of Radiation Oncology aims to create a top-tier research and service program focused on patient safety, quality improvement, and well-being. Led by **Lukasz Mazur, PhD**, the team has developed simulation-based training for radiation oncology

treatment planning and delivery, as well as a systems analysis method for identifying and addressing quality and well-being issues in healthcare settings. In a recent publication in *Applied Ergonomics*, the team found that factors such as moral distress, high workload, and negative-patient behavior were major contributors to burnout. The team is now searching for interventions to address these issues.

## **Department of Radiology**

The Department of Radiology would like to highlight three studies that may provide better diagnostic methods for diseases. A study led by **Sarah Nyante, PhD** published [in \*Cancer Epidemiology, Biomarkers and Prevention\*](#) reports varying diagnostic mammography performance across racial/ethnic groups and signifies the importance of including racially and ethnically diverse populations to provide an accurate view for future diagnostic mammography performance studies. **William Stanford** in **Eran Dayan, PhD**'s laboratory and colleagues report in [the \*Proceedings of the National Academy of Sciences\*](#) that age-related differences in episodic memory in healthy middle- and old-aged adults were positively related to brain core resilience, which indicates a potential role for core resilience in protection against cognitive decline. [A study published in \*Nature Genetics\*](#) led by **Bingxing Zhao, PhD**, sheds light on our understanding of the genetic architecture of brain functional networks and their genetic links to brain-related complex traits and disorders.

Faculty within the Department of Radiology also conduct work illustrating the capabilities of PET and MRI technologies. A study led by **Wei Chen, PhD** and **Zibo Li, PhD**'s laboratory [published work in \*Nature Chemistry\*](#) that reports a novel approach to construct PET agents through convenient halide exchange using readily available precursors. Synthesizing FDOPA used to require complex multistep reactions; this new approach substantially simplifies the processes without compromising yields and quality. **Gang Li, PhD**'s laboratory published research in [the \*Proceedings of the National Academy of Sciences\*](#) that leverages greater than 1,000 infant MRI scans from perinatal and postnatal periods, and uncovers the developmentally distinct cortical parcels that correspond well to structurally or functionally meaningful regions.

## **Department of Social Medicine**

**Gail Henderson, PhD**, coauthored a new book, [Bioethics Reenvisioned: A Path Toward Health Justice](#) (UNC Press, 2022). The book, coauthored with two former Social Medicine faculty members, Nancy King and Larry Churchill, argues it is time for bioethics to take full account of the problems of health disparities and structural injustice that are made newly urgent by the COVID-19 pandemic and the effects of climate change. Henderson and coauthors make the case for a more social understanding and application of justice, a deeper humility in assessing expertise in bioethics consulting, a broader and more relevant research agenda, and greater appreciation of the profound health implications of global warming.

RADx-UP is an NIH-funded consortium of community-academic partnerships studying strategies to reduce COVID-19 testing and vaccination disparities within communities most affected by the pandemic. The consortium represents the largest health equity research investment in NIH history. The Coordination and Data Collection Center (CDCC), co-led by **Giselle Corbie, MD, MSc**, is the project's leadership hub, supporting the NIH and over 130 research projects nationwide. Recent CDCC accomplishments include the enrollment of over 350,000 participants, administration of more than 400,000 COVID tests, and collection of over 300 common data elements across all consortium projects. Research findings and best practices in community-engaged research were shared in 54

posted resources - receiving more than 13,000 page views – and through the project’s scientific meetings and the 3<sup>rd</sup> Annual Equity Evidence Academy. UNC also leads the evaluation of the RADx-UP initiative, under the direction of **Gaurav Dave, MD, PhD, MPH**.

## ***Department of Surgery***

**Gita N. Mody, MD, MPH, FACS**, Director of Thoracic Surgical Oncology, Assistant Professor of Surgery, and a recipient of the [2022 Award for Carolina Care Excellence](#), received a five-year, \$1.01 million K23 award from the National Heart, Lung, And Blood Institute for *Improving Thoracic Surgical Care using electronic Patient-Reported Outcomes (ePROs)* that builds upon preliminary work in which she developed and demonstrated feasibility of [postoperative symptom monitoring with ePROs](#) among patients undergoing thoracic surgery at UNC. Dr. Mody’s research is focused on improving surgical care using patient-centered outcomes. **Jen Jen Yeh, MD** Oliver Smithies Investigator and Professor of Surgery and Pharmacology and members of the Pancreatic Cancer Center of Excellence were awarded a coveted Specialized Program of Research Excellence (SPORE) grant to develop new therapeutic approaches and establish do clinical trial paradigms for pancreatic cancer, as well as the PDAC Stromal Reprogramming Consortium U01, from the National Cancer Institute.

**Anthony Charles, MD, MPH**, the Oliver R. Rowe Distinguished Professor and **Jared Gallaher, MD, MPH**, Assistant Professor, published a review article for [JAMA on acute cholecystitis](#). Acute cholecystitis is a gallbladder condition typically due to gallstone obstruction of the cystic duct, which affects approximately 200,000 people in the United States annually. Their comprehensive literature review focused on the epidemiology, diagnosis, and management of acute cholecystitis, showing that early laparoscopic cholecystectomy is the first-line therapy for most patients.

## ***Department of Urology***

**Angela Smith, MD MS**, Director of Urologic Oncology and Vice Chair for Academic Affairs, is co-PI on the PCORI Large Pragmatic Study, CISTO (Comparison of Intravesical Therapy and Surgery as treatment Options for bladder cancer). This translational patient-centered outcomes research study builds on Dr. Smith’s innovative series of PCORI-supported Engagement Awards to bring the patient’s voice into the research process, in close partnership with the Bladder Cancer Advocacy Network. Dr. Smith’s contributions as a leader in patient-centered outcomes research have been recognized with multiple awards including, most recently, her selection as the 2022 recipient of the American Urological Association Gold Cystoscope Award, recognizing the urologist with the greatest contributions to the field in the first ten years of their career.

**Ray Tan, MD, MSHPM** assistant professor of Urology is leading a multidisciplinary team developing new risk communication tools for patients and physicians considering complex cancer surgery. In addition to his ongoing American Cancer Society Mentored Research Scholar Grant in this focus area, Dr. Tan is leading a multidisciplinary team, including researchers from the UNC School of Nursing (Lixin Song) and the UNC Hussman School of Journalism (Alison Lazard) whose work received funding from the US Department of Defense Kidney Cancer Research Program. **David Friedlander, MD MPH**, assistant professor of Urology, has received multiple awards from NC TraCS and the American Urological Association supporting his work defining opportunities to enhance patient-centered, high value care for patients with kidney stone disease. **Marc Bjurlin, DO**, Director of Clinical Trials, and colleagues at NYU received R01 funding from NCI to support the development of tailored screening for urinary system cancers in patients with chronic kidney disease.