

# 2021 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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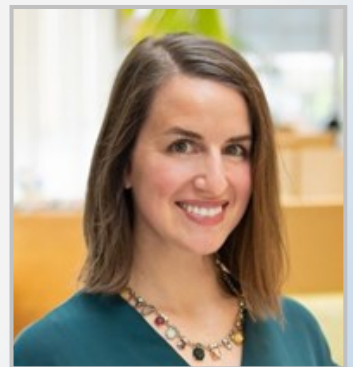
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## Department of Allied Health Sciences

**Khalilah Johnson, PhD**, assistant professor in the Division of Occupational Science and Occupational Therapy in the Department of Allied Health Sciences (DAHS) received a Robert Wood Johnson Foundation Health Equity Scholars for Action Award. This \$250,000 grant will support her project, *Disrupting the Cycle of Inaccessible Healthcare and Community Supports for Minoritized People with Intellectual and Developmental Disabilities*. The Robert Wood Johnson Foundation supports research to identify and address the root causes of health inequities in the United States that are strongly linked to structural and systemic racism and other forms of oppression. Health Equity Scholars for Action is a career development program aimed to support academic advancement of researchers from historically underrepresented backgrounds who conduct health equity research.



**Jessica Cassidy, PT, DPT, PhD**, assistant professor in the Division of Physical Therapy, DAHS, is the Principal Investigator of an NIH/NICHHD R00 award that involves the development of neuroimaging-based biomarkers to enhance the prediction of post-stroke motor recovery. In her project, *Brain Network Connectivity Measures in Early Stroke Rehabilitation*, Dr. Cassidy and her team collect an array of structural and functional neuroimaging measurements from individuals hospitalized in the inpatient rehabilitation unit at UNC Medical Center. Her preliminary work has shown that bedside-acquired measures of electroencephalography-based connectivity involving the stroke-affected primary motor cortex significantly predict motor recovery from hospital admission to discharge. She has also shown that changes in these functional connections parallel motor recovery over the first three months following stroke. Dr. Cassidy's follow-up work will investigate how individual factors such as mood, attention, and self-efficacy influence functional connectivity and her predictive models.



## Department of Anesthesiology

Anesthesiology Department faculty member, **Nicole Short, PhD** along with her mentor **Sam McLean, MD, MPH** were awarded a grant from the Mayday Fund to support an RCT testing an intervention to reduce the development posttraumatic stress and chronic pain after sexual assault. Dr. Short developed a smartphone-based cognitive behavioral intervention (“RISE”) designed to mitigate posttraumatic stress among women sexual assault survivors presenting for emergency care. Her study will test the efficacy of this intervention compared to a relaxation control in reducing posttraumatic stress, and, in turn, the development of chronic pain. Chronic pain is a common yet often overlooked sequela of sexual assault that currently has no cure or established preventative treatment. The RISE Study launched in July, 2021 will recruit 60 participants over three years, who will be followed one year post-assault. Results of this trial will inform emergency care practices and future research on how to best reduce negative health outcomes post-assault.

## Department of Biochemistry and Biophysics

Teams, co-led by **Greg Wang, PhD** and **Douglas Phanstiel, PhD** have uncovered a new biochemical mechanism that activates specific genes, leading to the development of cancers. They showed that oncogenic transcription factor proteins undergo a process called liquid-liquid phase separation, similar

to that seen when oil is mixed with water. Consequently, phase-separated transcription factors bind cognate target genes much more strongly, generating a unique pattern called super-enhancers, and impact on the three-dimensional structure of the genome by creating structures called chromatin loops. Taken together, the complex interplay of biology, physics, genomics and genetics inside a cell is now better understood due to this latest research finding. [This work was published in Nature](#). The first author is **Jeong Hyun (John) Ahn, PhD**. Other authors include **Eric S. Davis, Timothy A. Daugird**, and lab members of **Wes Legant, PhD, Douglas Phanstiel, PhD** and **Greg Wang, PhD**.

Every year, millions of people are infected with dengue virus resulting in dengue fever or dengue hemorrhagic fever. Despite decades of research, complete vaccine control has remained elusive. A collaborative team involving members of **Brian Kuhlman's laboratory** in the Department of Biochemistry and Biophysics and **Aravinda de Silva's laboratory** from the Department of Microbiology and Immunology have used protein engineering to stabilize the major surface protein from dengue virus, the E protein, so that it will associate with itself in a way that closely resembles its shape on the surface of the virus. The team demonstrated in animal studies that the stabilized E protein elicits high levels of antibodies that neutralize the virus, demonstrating the feasibility of using protein design to produce vaccines for dengue virus. The work was spearheaded by graduate student **Stephan Kudlacek** from the Department of Biochemistry and Biophysics and was recently published in [Science Advances](#).



### **Department of Biomedical Engineering**

Biomedical Engineering assistant professor **Rahima Benhabbour, PhD** received a Young Investigator Award from the Controlled Release Society for her group's work developing and commercializing innovative drug delivery devices, in particular an ultra-long-acting In-Situ Forming Implant drug delivery system for the prevention of HIV and unplanned pregnancy. [A recent article in NBC news](#) on the future of injectable HIV-prevention drugs shares the link to Benhabbour's publication *Biodegradable polymeric solid implants for ultra-long-acting delivery of single or multiple antiretroviral drugs*, and reports on "the early development at the University of North Carolina of a removable and biodegradable implant that delivered antiretroviral drugs in mice for up to 180 days." Dr. Benhabbour considers the supportive, innovative environment at Carolina an essential component of her success, especially the direct access to clinicians. "You really have to have that connection," she said. "If I don't know what their hurdles are, how can I design the right technology?"

Breaking up DNA is a necessary step to prepare samples for next-generation genomic sequencing but yielding the very short uniform segments required has proved difficult. **Paul Dayton, PhD** collaborated with **Samantha Pattenden, PhD** from the Eshelman School of Pharmacy to design acoustic nanodroplet "snippers" capable of shearing DNA into short, uniform segments of predictable length when exposed to sound waves. [This technology generated two patents and launched the start-up Triangle Biotechnology](#). Today, the company's main product is a nanodroplet reagent for biological samples capable of simultaneously shredding 96 DNA samples in 10 minutes. Their biggest competitor takes two hours to process the equivalent. Chief Technology Officer and Dayton group graduate, Sunny Kasoji, PhD, reports the technology's additional advantages of low cost and high consistency, as well as other applications such as breaking up tissues and bacteria, and extracting chromatin. Triangle Biotechnology products are now used at UNC's High Throughput Sequencing

Facility and peer institutions.

### ***Department of Cell Biology and Physiology***

Peripheral nerve injury induces a pro-inflammatory response in the spinal cord and can cause chronic neuropathic pain. Spinal microglia have traditionally been implicated in this pro-inflammatory response and pain hypersensitivity, though treatments targeting pro-inflammatory mechanisms, particularly in microglia, were ineffective in patients with neuropathic pain. **Mark Zylka, PhD** Kenan Distinguished Professor of Cell Biology and Physiology in the UNC Neuroscience Center, hypothesized that a more comprehensive understanding of which spinal cell types respond, or fail to respond, may reveal new regulators of pain hypersensitivity and new therapeutic targets. In their paper, [published in \*Neuron\*](#), the Zylka Lab discovered that a class of MRC1+ spinal macrophages up-regulated CD163 to actively limit neuroinflammation and pathological pain. Furthermore, they show that these spinal macrophages can be therapeutically coaxed to promote long-lasting recovery of neuropathic pain.

Mucoepidermoid carcinoma (MEC) is the most common salivary gland malignancy and is highly lethal due to recurrent and metastatic tumors. A team led by **Antonio Amelio, PhD** assistant professor in the Departments of Cell Biology and Physiology and Oral-Craniofacial Health Sciences, uncovered an unexpected mechanistic link between the fusion oncogene C1/M2 and peroxisome proliferator-activated receptor gamma coactivator-1 alpha alternative splice variant (PGC-1 $\alpha$ 4) that impacts the growth, survival, and oncogenic transformation of salivary gland precursors in mucoepidermoid carcinoma (MEC). Their work, [published in \*Cell Reports\*](#), revealed that this novel signaling axis is clinically exploited using small molecular agonists, opening up a new therapeutic vulnerability in MEC. First-of-their-kind datasets generated in this study (drug-screen and tumor RNA-seq) will be continually mined for years to generate novel hypotheses and fuel discoveries in salivary MEC.

### ***Department of Dermatology***

Cutaneous melanoma can metastasize early, but similarly staged patients have variable outcomes. A study led by **Kathleen Conway, PhD**, associate professor, and **Nancy Thomas, MD, PhD**, professor and Chair of Dermatology, published in *The Journal of Investigative Dermatology* identified a melanoma subtype exhibiting extreme CpG island DNA hypermethylation, tumor infiltrating lymphocyte deficiency, and a poor prognosis. Studies are ongoing to confirm these findings in the InterMEL study.

Another research focus is hidradenitis suppurativa (HS), an inflammatory condition characterized by recurrent abscesses and scarring affecting body folds such as the underarms and groin. Studies led by **Christopher Sayed, MD**, associate professor, published in the *Journal of Investigative Dermatology* and *JAMA Dermatology* highlighted the use golimumab and biosimilar infliximab for treating HS. Further, Dr. Sayed and collaborators **Karen Mohlke, PhD**, and **Yun Li, PhD**, report in the *British Journal of Dermatology* a 20-fold familial risk in HS using pedigrees from 280 patients.

### ***Department of Emergency Medicine***

The Department of Emergency Medicine (EM)'s Carolina Center for Health Informatics (CCHI) launched a new Web application for NC DETECT (statewide surveillance system maintained by CCHI) and added data from NC HealthConnex and additional urgent care centers to COVID-19 surveillance, a key indicator for the [NC COVID-19 dashboard](#). Additionally, CCHI launched the [Transportation Safety and Public Health Data dashboard](#) that combines health data and motor vehicle

crash reports in one place to provide data, stories, and suggestions for community response and prevention efforts.

The EM Clinical Trials team is participating 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 infection by a healthcare provider. Expanded testing capacity is critical for surveilling and mitigating the pandemic and may help differentiate between COVID-19 and influenza infection.

### **Department of Family Medicine**

Two Family Medicine faculty members received NIH Grants for first-of-its-kind research. **Leah Ranney, PhD**, Director for the [Tobacco Prevention and Evaluation Program \(TPEP\)](#), and team received a \$1.2 million NIH R01 award for research to improve warnings for little cigars and cigarillos among youth, especially Black/African American youth. **Brad Wright, PhD**, and team received a [\\$427,625 NINDS R21 grant](#) to use Medicare claims and EHR data to further the understanding of those greatest at risk of developing Guillain-Barre Syndrome, those most likely to face barriers in access to diagnosis and treatment, and those most likely to experience worse outcomes.



[Sylvia Becker-Dreps, MD, MPH, and Nadja Vielot, PhD](#), were UNC site Co-PIs for the national [Prevent COVID U](#) research study, sponsored by [NIAID](#). The study focused on 18-26-year-old university students to learn if the Moderna COVID-19 vaccine protects individuals from infection and prevents transmission of SARS-CoV-2, the virus that causes COVID-19.

### **Department of Genetics**

The Department of Genetics recently made a strategic decision to target large, team-science awards. As a result, in 2021, the Clinical Genome Resource Consortium (ClinGen) team at UNC, led by **Jonathan Berg, MD, PhD** was renewed and awarded a five-year U24 grant from NHGRI to scale biocuration and expert evaluation of genes and variants. **Hyejung Won, PhD, Karen Mohlke, PhD** and **Michael Love, PhD** were awarded a five-year UM1 grant from NHGRI titled “Systematic in vivo characterization of disease-associated regulatory variants”. **Patrick Sullivan, MD** was awarded an R01 from NIMH as part of the ongoing Psychiatric Genomics Consortium titled “Advancing discovery and impact” focused on multiple psychiatric disorders.

Additional team science award recipients include **Yun Li, PhD**, who received a five-year U01 grant from NHGRI to improve utility of polygenic risk scores (PRS) in diverse populations, one of six awards in a new PRS consortium. **Karen Mohlke, PhD** was awarded a five-year UM1 grant from in NIDDK in mid-2020 titled “*Bridging the gap between type 2 diabetes GWAS and therapeutic targets*”. **Mark Heise, PhD** has received significant funding from the Rapidly Emerging Antiviral Drug Discovery Initiative (READDI) program for his project “*JAK inhibitors as SARS-CoV-2 therapeutics*”. To assist with large grants (U, P, and R mechanisms), the department hired an Assistant Director of Research, **Sarah Schoenrock, PhD** who also serves as a project manager for several of these awards.

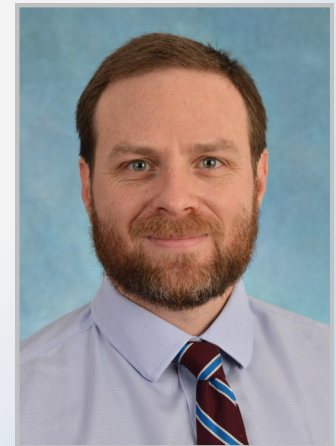
## Department of Medicine

As we all desperately await a way to treat COVID-19, beyond prevention, the following publication has metrics that are incredible (following February publication, by December 2021 it had been accessed >107K times with a >1700 Altmetric). Using **Victor Garcia, PhD**'s humanized mouse model, **Angela Wahl, PhD** led the work in the [Nature publication, "SARS-CoV-2 infection is effectively treated and prevented by EIDD-2801"](#).



The study used immunodeficient mice implanted with human lung tissue to show that the antiviral agent EIDD-2801 efficiently inhibited SARS-CoV-2 replication in the lung post infection, as was also effective as pre-exposure prophylactic treatment. Kudos to the team! For a more nuanced experience, readers are referred to Dr. Garcia's marvelous DOM Grand Rounds available on line: ["The COVID-19 Pandemic: A View From the Bench."](#)

A second highly significant paper is from our Division of General Internal Medicine. Led by **Seth Berkowitz, MD, MPH**, ["Supplemental Nutrition Assistance Program Participation and Health Care Use in Older Adults : A Cohort Study"](#) published in *Annals of Internal Medicine* concerns a specific, and growing group in the US, seniors who are not only using Medicare, but also Medicaid, a program which serves low income families. These seniors, who have high rates of health care use, also have issues with nutrition. While they are eligible for nutrition assistance from SNAP (Supplemental Nutrition Assistance Program), they frequently don't participate in programs. Dr. Berkowitz's group examined data from these federal programs to estimate how gaining food assistance affected use of medical resources: they found that participation in SNAP was associated with ~25% fewer inpatient admissions and lower health care costs (~\$2400). This data should convince us that small outlays in nutrition assistance can substantially improve the health of senior Americans.



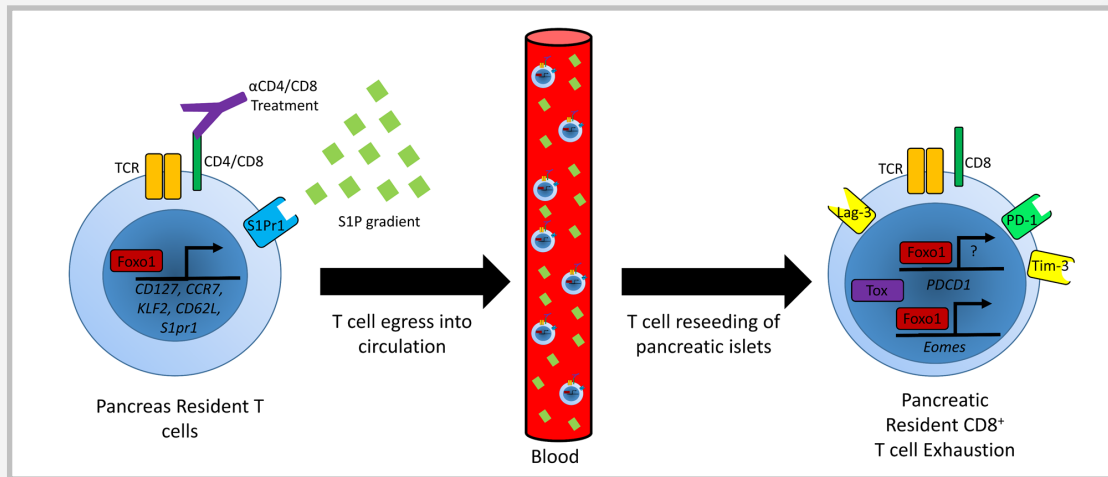
## Department of Microbiology and Immunology



Viral epidemics and pandemics continue to emerge with ever-increasing frequency. Even as we face the ongoing COVID-19 pandemic, we know that the next virus could emerge at any time to cause widespread viral disease. Yet, we currently lack antiviral drugs for most viruses with epidemic or pandemic potential. To address this pressing unmet need, M&I faculty members **Nat Moorman, PhD**, **Mark Heise, PhD** and **Ralph Baric, PhD** co-founded READDI (the Rapidly Emerging Drug Development Initiative), which is a global, non-profit public-private partnership whose mission is to develop antiviral drugs effective against entire families of viruses that cause widespread viral

outbreaks *before* the next pandemic begins. In partnership with the Eshelman Institute for Innovation, this year READDI has raised over \$23 million dollars to support its goal of developing five broad spectrum antiviral drugs through Phase I testing over the next five years. [You can learn more about READDI here.](#)

**The Roland Tisch group** has previously reported that a short-course of non-depleting antibodies specific for the CD4 and CD8a co-receptor molecules expressed by T cells, rapidly reverses diabetes in NOD mice, a model of type 1 diabetes (T1D). Diabetes remission is indefinite despite antibody clearance. Their recent study [published in JCI Insight](#) demonstrates that antibody binding transcriptionally “reprograms” the autoreactive effector T cells ( $T_{eff}$ ) that destroy the insulin producing beta cells in the pancreatic islets. Antibody-binding to CD4 or CD8 upregulates the Foxo1 transcription pathway, which: 1) drives egress of pancreatic  $T_{eff}$ , but also 2) induces immune exhaustion that blocks the pathogenicity of  $T_{eff}$  that reseed the pancreas after antibody clearance. Analogous results in a humanized mouse model support the translational potential of the approach. These observations identify the Foxo1 pathway as a novel target to tolerize tissue resident autoreactive T cells. The results are not only applicable to T1D, but also to other autoimmune diseases.



## Department of Neurology

Tuberous sclerosis (TSC) is a genetic disorder that causes seizures, autism and tumor predisposition. **Jamie Capal, MD** is advancing TSC research at UNC as a Principal Investigator and Neurodevelopmental lead on a new R01-funded project, “*Sirolimus TSC Epilepsy Prevention Study (STEPS)*”. This phase IIb, randomized, double-blind, placebo-controlled multicenter clinical trial (TSC-STEPS) will use sirolimus, an mTOR inhibitor, to reduce seizures in infants with TSC, starting in early 2022.

HIV-associated neurocognitive disorder (HAND) affects up to 50% of older people with HIV and remains a clinical challenge. **Monica Diaz, MD, MS** was awarded a Clinical Research Training Scholarship Award from the American Association for Neurology for her study “*Neurofilament light as a marker of synaptic loss in cognitively impaired older people with HIV*”. With co-mentors **Rick Meeker, PhD** (UNC, Neurology) and **David Murdoch, MD, MPH** (Duke, Internal Medicine) she will develop new diagnostic methods for early detection of HIV-related cognitive decline.

## **Department of Neurosurgery**

If sleep is disrupted, the glymphatic system is disrupted, leading to cognitive impairment like faulty motor coordination, attention deficits, slower processing speed, decreased decision-making capabilities, and hampered short-term memory. Inefficient clearance by this system has been shown to increase the risk of neurodegenerative disease later in life. These issues can have life-or-death consequences for service members in the military. The Department of Defense is funding a three-year, \$4.3-million, project with the goal of helping service members overcome acute sleep deprivation and chronic sleep restriction led by **Dawn Kernagis, PhD** in the Department of Neurosurgery. This project will focus on new ways to image the brain glymphatic system in humans while also investigating a novel approach for stimulating glymphatic function and clearance. Dr. Kernagis and the UNC team, will be collaborating with University of Washington School of Medicine, the Brain Electrophysiology Lab Oregon Health & Science University, and Montana State University.

## **Department of Nutrition**

**Elle Glenny, PhD** recently completed her PhD under the supervision of **Ian Carroll, PhD** with whom she investigated the consequences of severe calorie restriction on intestinal stem cell function and potential interactions of the gut microbiota. Among her multiple accomplishments, Dr. Glenny published an exciting study in [Gut Microbes](#)—a leading journal in the field.

**Anna Kahkoska, MD, PhD** and team used precision medicine statistical methods and a large, observational cohort of youth and young adults with type 1 diabetes to evaluate the health impacts of disparities in diabetes management. The study, “*The Impact of Racial and Ethnic Health Disparities in Diabetes Management on Clinical Outcomes: A Reinforcement Learning Analysis of Health Inequity Among Youth and Young Adults in the SEARCH for Diabetes in Youth Study*,” found that mathematically modeling an equalized distribution of diabetes self-management tools and technology accounted for part of (~33%) but not all disparities in glycemic control between youth and young adults of color and their non-Hispanic White counterparts. The study represents one of the first applications of reinforcement learning methods to untangle complex patterns of health inequity and to inform targeted interventions to equitably allocate use of diabetes technology and other resources for management. Doctoral student **Teeranan Pokaprakarn** is co-first author of the manuscript, which was published in [Diabetes Care](#).

## **Department of Obstetrics and Gynecology**

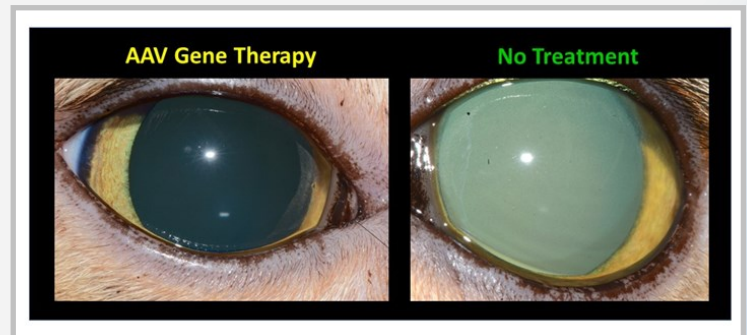
**Steven Young, MD, PhD**, was awarded a multicenter \$7 million NIH/NICHD center grant focused on developing the tools to improve diagnosis and treatment of endometriosis, a disease that affects 8% of reproductive aged women and a common cause for pain and infertility. This new center examines novel radiological approaches to diagnosis endometriosis as well as pre-clinical targeting of novel metabolic and immune pathways that modulate and treat endometriosis. **Jennifer Tang, MD, MSCR** and **Rachel Urrutia, MD, MSCR** were awarded a \$10 million PCORI grant to explore community-based solutions to disparities in maternal and fetal morbidity and mortality. **Leslie Clark, MD, Lauren Dockery, MD, Emma Rossi, MD, and Paola Gehrig, MD** collaborate on several phase I-II investigator initiated clinical trials designed to treat endometrial and ovarian cancer. These trials have clinical and translational endpoints such as pathways of synthetic lethality with PARP inhibition, neoadjuvant targeted systemic therapy for advanced endometrial cancer, and a Phase I CAR-T ovarian cancer trial.



## Department of Ophthalmology

Detection of glaucoma progression and determination of the rate of visual field (VF) change are key aspects of the long-term disease management. While these are routinely assessed, population-based-related glaucoma progression data remain patchy worldwide and inexistent on the African continent. In a seminal population-based study conducted in an urban setting in Ghana, Mwanza, colleagues found an astonishingly high incidence of glaucoma progression (9.7%/year) after an 8-year follow-up. The incidence was greater when progression occurred by VF alone than by optic disc alone or both modalities. The rate of VF mean deviation (MD) change in progressing eyes (-1.02 dB/year) was tenfold higher than that in non-progressing eyes. MD worsened significantly faster in eyes progressing by both VF and optic disc (-1.29 dB/year) and by VF alone (-1.21 dB/year) than by optic disc alone (-0.55 dB/year). [These findings published by Jean-Claude Mwanza, MD, PhD, MPH and colleagues in Journal of Glaucoma](#) may be valuable to clinicians and healthy policy makers in this setting.

Lysosomal storage diseases (LSDs) are commonly associated with corneal clouding resulting in loss of vision. In previous publications, **Matthew Hirsch, PhD** and colleagues used a corneal adeno-associated virus (AAV) gene therapy strategy to prevent/reverse of MPS I vision loss. Team Hirsch has since expanded this approach to the treatment of MPS VI blindness. Within 2-3 weeks of a



single AAV vector intracorneal injection to MPS VI felines, pre-existing corneal cloudiness was reversed and clarity was maintained with no adverse events. Sequential dosing of the contralateral cornea weeks following later demonstrated similar efficacy suggesting that AAV corneal gene therapy is independent of pre-existing, or induced, capsid antibodies. With these validations of safety and efficacy of corneal gene therapy for MPS I, and now MPS VI, in preventing/reversing vision loss, the Hirsch lab is working on similar strategies to address the unmet need of correcting blindness in the remaining LSDs.

## Department of Orthopaedics

In 2021, Orthopaedics published numerous research reports. Many are part of our fruitful development of the Sports Medicine Institute which includes efforts across the School of Medicine, Exercise and Sports Science, Biomedical Engineering, and the Gillings School of Global Public Health. Capping these efforts, we are particularly proud of our successful search for a Vice Chair of Research, **Joe Hart, PhD**, who began in January 2022. Dr. Hart has an interest in the effects of gender, core instability and previous joint injury on quadriceps muscle function, balance and neuromuscular performance during activities. He brings two grants with him from his position at University of Virginia. The first focuses on determining the risk factors for second ACL injury by using a wearable sensor. The second grant is looking at hamstring injuries in football players to gain better understanding as to the cause, evaluation, treatment, and prevention of the injury.

## Department of Otolaryngology

Human papillomavirus-positive (HPV+) squamous cell carcinoma of the oropharynx (OPSCC) is the most prevalent HPV-associated malignancy in the United States. Favorable treatment outcomes have led to increased interest in treatment de-escalation to reduce treatment morbidity, as well as the

development of prognostic markers to identify low-risk patients. A multi-institutional study led by UNC researchers recently found that both intratumor genomic heterogeneity and high-burden copy number alterations are strongly associated with poor recurrence-free survival in patients with HPV+ OPSCC. Clinically, this means that copy number alteration burden and intratumoral heterogeneity represent promising avenues for risk stratification of patients with HPV+ OPSCC. Results are reported in a recent paper by **Travis Schrank, MD, PhD** and colleagues, "[Genomic heterogeneity and copy number variant burden are associated with poor recurrence-free survival and 11q loss in human papillomavirus-positive squamous cell carcinoma of the oropharynx](#)".

Traditional methods for collecting patient-reported outcome measurements (PROMs) by phone, email, or mail are limited by poor response rates, need for manual data entry, and lack of real-time data collection. To address these limitations, **Rupali Shah, MD** and her team in the UNC Voice center developed the Encore iOS app, a user-friendly smartphone application that collects validated survey responses and voice recordings. They recently tested this app on a group of patients undergoing vocal fold injection augmentation and type I medialization thyroplasty. Both patients and providers reported high levels of satisfaction with ease of enrollment and application functionality. Patients were highly motivated to participate, with initial response rates that are superior to traditional methods of PROM collection. These results demonstrate feasibility and efficiency of the Encore app for collecting PROM. Future directions include analysis of longitudinal voice and swallowing outcomes after treatment, comparison of different interventions, and cost analysis.

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

The Department has had significant publications in the area of blood research. **Alisa Wolberg, PhD** developed a novel mouse model of venous thromboembolism to evaluate the role of factor XIII in pulmonary embolism risk. [This work was published in the Journal of Thrombosis and Haemostasis](#). **Matt Flick, PhD** [published a PNAS paper](#) that identified a novel molecular mechanism for fibrinogen action. Fibrinogen is typically characterized as a blood clotting protein, but in this study Dr. Flick found another unique action – host antimicrobial defense against Staph aureus peritonitis.

**Matt Karafin, MD, MS** was the senior author for an [NIH consortium \(National Heart Lung and Blood Institute Recipient Epidemiology and Donor Evaluation\) paper](#). The overall goal of the consortium is to better define current transfusion practices in the United States. In this paper, the consortium examined 4766 pediatric oncology patients undergoing stem cell transplant. These types of patients frequently undergo some type of transfusion. This study suggests heterogeneity in transfusion practices in the pediatric oncology patients undergoing stem cell transplants. The data suggest that a percentage of transfusions may be administered at laboratory values higher than supported by the best available evidence.

### ***Department of Pediatrics***

Neonatal-perinatal researchers **Genevieve Taylor, MD; Heather Campbell, MD; Wayne Price, MD; Rebecca Fry, PhD; and Michael O'Shea, MD, MPH** continue to investigate long-term outcomes for extremely preterm infants. This year Drs. Taylor, Price, Fry, and O'Shea found a hopeful message for parents at risk for delivery of an extremely preterm infant; infant neurodevelopmental impairment (NDI) only weakly predicts middle childhood NDI. One-third of surviving children classified as having profound NDI and nearly two-thirds of those classified as having moderate to severe NDI at 2 years, had none to mild NDI at 10 years (PMID: [33824183](#)). Drs. Campbell, Fry, and O'Shea also found that for children born extremely preterm, cranial ultrasound abnormalities, particularly those indicative

of white matter damage, are predictive of NDI at 10 years of age. The strongest associations were found with cerebral palsy (PMID: [34090894](#)). Through their research, parents and clinicians can know what to watch for and be prepared for proper treatment.

**Michael Kappelman, MD, MPH** (Pediatric Gastroenterology) researches the burden, risk factors, quality of care, and safety and effectiveness of treatments for IBD, publishing 48 articles in 2021. In highlighting a few, Dr. Kappelman and **Erica Brenner, MD** (Pediatric Gastroenterology) provided evidence for treating rheumatic diseases, IBD, and psoriasis using international COVID-19 registries, determining that treatment of TNF inhibitors to ameliorate immune-mediated inflammatory diseases were associated with lower risk of adverse COVID outcomes compared with other immunomodulatory treatments (PMID: [34661663](#)). Dr. Kappelman published further evidence that IBD patients mount detectable humoral immune response to mRNA vaccinations, supporting vaccinations regardless of immunosuppressive treatment (PMID: [34144046](#)). Drs. Kappelman and Brenner found that combination therapy and thiopurines may be associated with increased risk of severe COVID, but significant differences weren't observed when comparing biologicals (PMID: [33082265](#)). Dr. Kappelman and **Neal deJong, MD, MPH** (General Pediatrics) found that cross-team coordination among families and care teams is needed to improve overall care quality (PMID: [33798510](#)).

### ***Department of Pharmacology***

The labs of **Tim Elston, PhD** and **Klaus Hahn, PhD** received some nice press for their recent paper in *Cell*, describing a new “binder-tag” technique to pinpoint and track proteins that are in a desired conformation and to do so in real time inside living cells. They demonstrate the utility of the method by tracking the active version of the Src oncoprotein within the cell, and were able to show the dynamics of activation. Protein confirmation changes are essential to understanding both normal biology and disease, and because this is the first technique that allows this level of protein tracking, the team's work will likely have a large impact on many scientific fields. [This research was featured in Vital Signs in October 2021.](#)

The laboratory of **Tom Kash, PhD** published a paper in the journal *Neuron*, showing how neurons in two brain regions use dopamine to promote pain responses differently in male and female mice. Previous findings from the group showed that dopaminergic neurons were responsible for how opiates dampened pain. However, interestingly when looking at female mice, activation of the same pathway resulted in more movement in female mice, indicating that dopamine helps female focus attention elsewhere while in the presence of pain. [Read more about this important work here.](#)

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

The Department is highlighting three projects targeting health equity. With the UNC School of Nursing, UNC PM&R has launched the HARMONY study. HARMONY tests the effects of a culturally-tailored mindfulness self-management intervention on sustained improvements in healthy eating and exercise through improved mindful stress management, self-regulation, and self-efficacy in overweight African American women at risk for chronic cardiometabolic illness. Investigators continue research on Easing the Burden of Dementia Caregiving: A Telephone-delivered Mindfulness Intervention for Rural, African American Families. This project studies the effectiveness of telephone-delivered mindfulness intervention and the willingness of caregivers to use telephone and web-based technologies to enhance mindful family communication and reduce caregiving burden. UNC PM&R received a \$102k subaward for Project B.R.E.A.T.H.E. (Brothers, Reclaiming, Emotional, Awareness, Tranquility, Healing & Existence.) Project B.R.E.A.T.H.E. is a collaboration with the University of

Connecticut Health Center which focuses on disrupting racialized stress, trauma, and problematic substance use in young adult black men.

## ***Department of Psychiatry***

**Mary Kimmel, MD** a physician scientist in the UNC Center for Women's Mood Disorders published an article in [\*Translational Psychiatry\* entitled "Heart rate variability in late pregnancy: exploration of distinctive patterns in relation to maternal mental health"](#). Dr. Kimmel and her team demonstrate how photoplethysmography (PPG), a low cost, non-invasive, optical technique that can detect volumetric changes in blood, can be used to measure heart rate variability (HRV) in pregnant women in order to assess emotional regulation and identify individuals who are at risk for mood and anxiety disorder episodes during pregnancy and the postpartum period. Individuals with past or current anxiety disorders, greater trait anxiety, or greater exposure to childhood traumatic events had significantly different HRV findings from others. This work describes an easy-to-use tool that can be easily implemented in maternal care settings, even at home, providing better access to mental health care for women.

**Justin Riddle, PhD** a postdoctoral fellow in the lab of **Flavio Frohlich, PhD** in the Department's program on neuromodulation published in *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* results of a clinical trial addressing the treatment of depression and anhedonia: ["Reduction in Left Frontal Alpha Oscillations by Transcranial Alternating Current Stimulation in Major Depressive Disorder Is Context Dependent in a Randomized Clinical Trial"](#). The team used transcranial alternating current stimulation to reduce left frontal alpha oscillations (these oscillations are associated with decreased approach motivation) in patients with major depressive disorder. In an assessment of eighty-four participants, the team found that left frontal alpha oscillations were reduced after a single session of stimulation compared to healthy control patients. This critical study demonstrates that transcranial alternating current stimulation could be a future treatment for major depressive disorder.

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

In one of the first studies to ascertain the utilization of postmastectomy radiation for women with breast cancer in sub-Saharan Africa, **Shekinah Elmore, MD**, and colleagues found that in a national referral hospital cohort of women with breast cancer in Harare, Zimbabwe, only 33% of eligible women received postmastectomy radiation. Postmastectomy radiation has been shown in prior studies to improve survival, and further research is needed to increase its utilization and to estimate the survival benefit in this context. [This work was published in \*Breast Cancer Research and Treatment\*](#).

[In the journal \*Nucleic Acids Research\*](#), **Gaorav Gupta, MD, PhD**, and colleagues published a new method that enables comprehensive profiling of DNA repair in mammalian cells at a specific type of DNA damage called double strand breaks. Their work showed that gene mutations observed in cancer can alter the pattern of DNA repair, and that this may be predictive of how cells respond to different types of cancer therapy. Ongoing work will apply this new method to patient-derived cancer models, such as tumor organoids, to better understand the relationship between DNA repair and treatment response.

## **Department of Radiology**

**Tengfei Li, PhD** and colleagues applied a tract-specific functional principal component technique and performed a Genome-wide association analysis on dMRI scans from 43,802 subjects and identified 151 genomic regions associated with white matter microstructure. The British GWAS results were validated based on additional analysis in nine independent validation datasets. The genetic relationships between white matter and a wide variety of complex traits in association lookups, genetic correlation estimations, and gene-level analyses were evaluated. It was discovered that a number of loci co-localized with brain diseases, such as glioma and stroke; genetic correlations were observed between white matter microstructure and 57 complex traits and diseases. Bioinformatics analyses found tissue- and cell-specific functional enrichments and many enriched biological pathways. The results indicate that a better understanding of the etiopathogenesis and treatment of many brain disorders could be achieved from a more balanced perspective that includes both gray matter regions and white matter tracts. [Read the team's Science publication here.](#)

## **Department of Social Medicine**

**Mara Buchbinder, PhD**, professor and Vice Chair of Social Medicine, published a book with University of California Press, [Scripting Death: Stories of Assisted Dying in America](#). Medical aid in dying has expanded rapidly, yet very little is publicly known about how it is put into practice. *Scripting Death* chronicles two years of ethnographic research documenting the implementation of Vermont's 2013 "Patient Choice and Control at End of Life" Act. Buchbinder, who is also Core Faculty in the UNC Center for Bioethics, collects stories from patients, caregivers, health care providers, activists, and legislators to illustrate how it works, what motivates people to pursue it, and ultimately, why upholding the "right to die" is very different from ensuring access to this life-ending procedure.

**Jean Cadigan, PhD**, associate professor of Social Medicine, and **Eric Juengst, PhD**, professor of Social Medicine, have received a four-year, \$1.9 million R01 award from the National Human Genome Research Institute at NIH (Cadigan and Juengst are both Core Faculty in the UNC Center for Bioethics). Their project, *Incidental Enhancement: Addressing a Neglected Policy Issue in Human Genome Editing*, supports a mixed methods study by a team of 6 UNC faculty of the ethical and science policy challenges raised by the prospect of preventive applications of human gene editing in healthy humans. Qualitative interview data with scientists and other experts engaged in the development of governance for gene editing research will be used to explore these neglected challenges and develop case studies to anticipate policy issues before they arise in practice.

## **Department of Surgery**

**Katharine L. McGinagle, MD MPH**, associate professor of Surgery in collaboration with **Michael R. Kosorok, PhD**, Distinguished Professor of Biostatistics collaborated to perform a series of studies that were among the first applications of precision medicine to the treatment of patients with peripheral artery disease (PAD). The novel research design offered the methodologic advancements needed to identify optimal initial and subsequent treatments to maximize patient-centered outcomes over time. Improving upon existing risk calculators, Drs. McGinagle and Kosorok delineated survival-based stages of disease at the time patients present with severe PAD. Drs. McGinagle and Kosorok are continuing to characterize how the frequency and intensity of medical and surgical treatments, not just presenting patient characteristics, affect disease progression and outcomes.

## ***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 this year from the US Department of Defense Kidney Cancer Research Program](#). Dr. Tan and **Soohyun Hwang, MPH**, a PhD Candidate in the Department of Health Policy and Management, have been awarded a [pilot grant sponsored by Advancing Cancer Treatment \(ACT\)](#), focused on improving accrual to clinical trials for patients with prostate cancer.