

2023 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 Departments.

Table of Contents

Department of Anesthesiology	Page 2
Department of Biochemistry and Biophysics	Page 2
Department of Biomedical Engineering	Page 2
Department of Cell Biology and Physiology	Page 3
Department of Dermatology	Page 3
Department of Emergency Medicine	Page 4
Department of Family Medicine	Page 4
Department of Genetics	Page 5
Department of Health Sciences	Page 6
Department of Medicine	Page 6
Department of Microbiology and Immunology	Page 7
Department of Neurology	Page 8
Department of Neurosurgery	Page 9
Department of Nutrition	Page 9
Department of Obstetrics and Gynecology	Page 10
Department of Ophthalmology	Page 10
Department of Orthopaedics	Page 11
Department of Otolaryngology-Head & Neck Surgery	Page 12
Department of Pathology and Laboratory Medicine	Page 12
Department of Pediatrics	Page 13
Department of Pharmacology	Page 13
Department of Physical Medicine and Rehabilitation	Page 14
Department of Psychiatry	Page 14
Department of Radiology	Page 15
Department of Social Medicine	Page 15
Department of Surgery	Page 15
Department of Urology	Page 16

Department of Anesthesiology

The Department of Anesthesiology has a long commitment to advance the care of patients living in chronic pain through research. **Matt Mauck, MD, PhD**, has been serving, alongside investigators from the Department of Biostatistics and the UNC Collaborative Studies Coordinating Center, as the Principal Investigator for the Biomarkers for Evaluating Spine Treatments (BEST) Trial, which successfully completed recruitment in December of 2023. This trial is one of the largest precision medicine studies performed in the chronic low back pain population and aims to develop a precision medicine algorithm that uses biomarkers to individualize treatment selection. This trial is funded by the NIH HEAL Initiative and is a part of a collaborative Back Pain Consortium formed by the NIAMS (National Institute of Arthritis and Musculoskeletal and Skin Diseases). The trial has been recently featured in the *Wall Street Journal* ([Treating-Lower-Back-Pain-Nonsurgically-Could-Be-the-Key-WSJ.pdf \(unhealthcare.org\)](#)).

Department of Biochemistry and Biophysics

Science is a team sport. **Dale Ramsden, PhD**, and **Gaorav Gupta, MD, PhD** have had a long-standing research collaboration, [and together have pieced together the DNA repair pathway implicated in hereditary breast, ovarian, and prostate cancers](#). They have published over nine papers together during their 10-year research collaboration. Insights learned from this research has helped rationalize clinical trials to improve cancer outcomes. Their research program on this important DNA repair pathway got its start thanks to a Lineberger Developmental Award, and it has grown exponentially over the years into both an R01 and DOD breast cancer breakthrough award. They now lead a nationwide team, funded by an NCI \$8.8M [Program Project](#).

UNC has become a leading center for RNA research, with laboratories studying the form, function, and clinical applications of RNA at virtually all biological scales. We have many leaders in the newly formed [RNA Discovery Center](#) which include co-directors **Bill Marzluff, PhD**, and **Qi Zhang, PhD** and researchers **Dan Dominguez, PhD**, **Silvia Ramos, MD, PhD**, **Josh Boyer, PhD**, and **Ron Swanstrom, PhD**. The center provides a focal point for RNA research that supports graduate student and postdoctoral training, academic and industrial collaborations, and large-scale funding initiatives in RNA biology. In 2023, the Center received its first R01 grant! Boyer, Swanstrom, and Zhang received the inaugural RDC Collaborative Team Science Fellowship for the Project entitled “Developing Crosslinking and Anchoring Technologies for Cryo-EM Characterization of RNA Structures.” James Emerson, a graduate student in Conlon lab, received the inaugural Marzluff Graduate Fellowship for “Sex-differential miRNA Expression Mediates Sex Differences in Cardiac Calcium Handling and Disease.” [Link to all awardees.](#)

Department of Biomedical Engineering

A partnership between the Department of Surgery (**Kevin Chen, MD**), Joint Department of Biomedical Engineering (**Shawn Gomez, EngScD**), and Lineberger Comprehensive Cancer Center (**Kristalyn Gallagher, DO**) created an Artificial intelligence (AI) model that can predict whether or not cancerous tissue has been fully removed during breast cancer surgery. In current practice the tumor is resected taking a small amount of surrounding healthy tissue in an attempt to remove all cancer. The specimen is mammographically photographed, reviewed by surgical team, then sent to pathology for confirmation. Confirmation can take a week. To improve results the AI model was “taught” what positive and negative margins look like by using hundreds of specimen mammogram images, matched with the final specimen reports from pathologists as well as demographic data. The model’s

assessment of pathologic margins was as accurate as, if not better than, typical human interpretation. Findings were published in *Annals of Surgical Oncology*.

Researchers in the Department of Microbiology and Immunology (**Sarah Rowe-Conlon, PhD**) and Joint Department of Biomedical Engineering (**Virginie Papadopoulou, PhD**; **Paul Dayton, PhD**) developed improved drug delivery into chronic wound infections. Chronic wounds can be challenging to treat because of life-threatening methicillin-resistant *S. aureus* (MRSA) infections. Part of drug resistance comes from bacterial biofilm so thick neither immune cells nor antibiotics penetrate. Researchers developed a method combining palmitoleic acid, gentamicin, and ultrasound to improve drug delivery in chronic wounds infected with *S. aureus*. Phase change contrast agent (PCCA) liquid was applied topically to the wound then an ultrasound transducer created and oscillated microscopic gas-filled microbubbles in this liquid. The oscillation mechanically disrupted the biofilm increasing fluid flow. Ultimately the disruption and increased drug permeation killed the bacterial biofilm. This method reduced MRSA infection 94% in diabetic mice, and completely sterilized wounds in several subjects. Results were published in *Cell Chemical Biology*.

Department of Cell Biology and Physiology

Cells respond to environmental cues that affect cell shape and polarity, including in some cases inducing migration toward or away from these signals. The mechanisms that control how cells sense and respond to polarization signals are active areas of investigation in the Department. Research from the lab of **Richard Cheney, PhD** published in [*Biophysical Journal*](#) examined cell surface excess (CSE), the substantial reservoir of plasma membrane stored on the cell surface as blebs, microvilli, filipodia, and folds. They demonstrate the role of microtubules in CSE stability and mobilization that control cell shape in 3D environments. **Patrick Brennwald, PhD**, uncovered a novel mechanism regulating the exocyst, a multi-subunit tethering complex that establishes spatial specificity by localizing secretory vesicles to the proper place on the plasma membrane. Published in the [*Journal of Cell Biology*](#), the Brennwald lab's data supports a model of complex, non-binary modes of exocyst activation by multiple signaling pathways that may fine-tune cell polarity.

Primary cilia are microtubule-based antennae-like organelles present in cerebral cortical neurons and glial cells that may function in non-traditional synaptic signaling mechanisms to shape or refine neuronal circuits in response to local environmental signals. To understand these signals and their impact on cortical circuit dynamics, **Eva Anton, PhD**, Professor of Cell Biology and Physiology, and his team mapped the distinct ultrastructural features of neuronal and astroglial primary cilia and their interactions in every layer of the human cerebral cortex using serial-section electron microscopy. In this work, published in [*Neuron*](#), Anton found cell-type and layer-specific variations in structure, contactome, and connectome of primary cilia that create local modulatory signaling ensembles that enable unique access to the surrounding neural circuitry. Disruptions in the primary cilia connectome may contribute to circuit dysfunction in ciliopathies and other human brain disorders.

Department of Dermatology

The Department of Dermatology continues to lead in the investigation of skin autoimmunity and inflammation. **Zhi Liu, PhD**, and **Ning Li, PhD**, have developed several murine models of bullous pemphigoid to elucidate the immunopathogenesis of the disease, including the identification of innate immune players critical in the disease process such as IgG and IgE autoantibodies, eosinophils, mast cells, and neutrophils. This work involves understanding cell-cell adhesion in the skin, especially the desmosomal proteins, which play a role in skin blistering diseases, including pemphigus vulgaris and

pemphigus foliaceus. Their expertise in the field has led to the development of novel animal models of atopic dermatitis (AD) to investigate the role of itch and itch-related mediators in AD and identify potential therapeutic targets for new treatment for this common and perplexing skin condition. This work has had both NIH and industry support.

The Department of Dermatology continues its translational research mission with the Clinical Trials Unit (CTU), which has been involved in breakthrough research for multiple pharmaceutical treatments for skin diseases. Led by **Aida Lugo-Somolinos, MD**, and **Donna Culton, MD, PhD**, the team of investigators, project managers, and study coordinators is highly qualified, dedicated to serving a diverse population and proficient in bilingual language skills. Current clinical trials include studying the efficacy of baricitinib for oral lichen planus, ritlecitinib for vitiligo, ruxolitinib in lichen sclerosis, and deucravacitinib in alopecia areata, among others. The dermatology CTU is a highly productive program with impactful results that guide treatment for a variety of skin conditions.

Department of Emergency Medicine

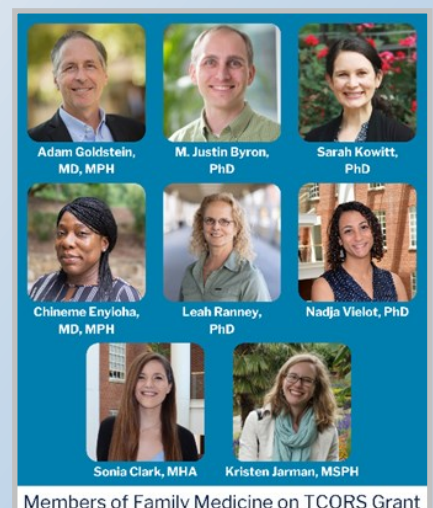
The Department of Emergency Medicine (EM)'s **Mehul Patel, PhD**, was awarded an R01 grant from the National Institute on Minority Health and Health Disparities (NIMHD) to address disparities in acute stroke care for rural populations. His project will model and compare the effectiveness of emergency medical services' (EMS) current system design and triage strategies across rural settings to inform optimal stroke systems of care. To understand provider perspectives, Patel first conducted interviews with rural EMS providers to discuss what does and does not work well within current stroke systems. Patel also investigates stroke time delay in North Carolina, utilizing UNC Health stroke data. Exploratory analysis of such data is ongoing to understand descriptive characteristics, patient experiences, and time delay.

Additionally, **Michelle Meyer, PhD, MPH**, launched a CDC-funded study (UNC Injury Prevention Research Center; PI: Marshall) called the pain intervention via video optimization trial (PIVOT). PIVOT is a randomized controlled trial comparing an interactive educational video on pain management to usual care for preventing the transition from acute to chronic musculoskeletal pain among adults in emergency department and urgent care settings. Many patients seeking care for acute musculoskeletal pain transition to chronic pain, increasing their risk for long-term opioid use. Our goal is to test and implement a scalable intervention to improve pain outcomes and reduce the conversion to long-term opioid use. Our primary outcome is change in self-reported pain scores through 3 months. We anticipate enrolling 200 patients at UNC emergency departments and orthopedic urgent care clinics.

Department of Family Medicine

Tobacco Center for Regulatory Science (TCORS)

The UNC-CH Tobacco Center for Regulatory Science (TCORS) has been granted \$18.6 million by the National Institutes of Health (NIH) and the US Food and Drug Administration (FDA) to advance research on tobacco product regulations. Spearheaded by **Kurt Ribisi, PhD**, Chair of the Department of Health Behavior at the UNC Gillings School of Global Public Health, TCORS boasts invaluable contributions from several Department of Family Medicine faculty members, including project leaders **Adam Goldstein, MD, MPH**,



director of the UNC Tobacco Intervention Programs; **Justin Byron, PhD**, assistant professor and adjunct assistant professor in the Department of Health Behavior; and **Sarah Kowitz, PhD**, assistant professor and member of the Lineberger Comprehensive Cancer Center. Their leadership in projects underscores the importance of addressing tobacco use disparities, particularly among priority populations. These interdisciplinary efforts align with TCORS' mission to inform FDA regulations, ultimately mitigating the adverse impact of tobacco products on public health.

Behavioral Health Workforce Research Center (UNC-BHWRC)

Brianna Lombardi, PhD, MSW, assistant professor of Family Medicine, and colleagues were awarded a \$4.5 million five-year HRSA grant to form the UNC Behavioral Health Workforce Research Center (BHWRC). Lombardi is the PI and director of the BHWRC, which will function as a sister center to the Carolina Health Workforce Research Center, directed by UNC Family Medicine's, **Erin Fraher, PhD, MPP**. Fraher and Family Medicine's **Donald Pathman, MD, MPH**, are also investigators for this initiative,



which is funded through the UNC Cecil G. Sheps Center for Health Services Research and UNC School of Social Work. The BHWRC is dedicated to addressing behavioral health workforce challenges and promoting equity. Producing timely, policy-relevant projects and contributing to the improvement of behavioral health treatment, access, and quality nationwide, the BHWRC stands as a vital force in shaping the future of behavioral health research and policy.

Department of Genetics



Identifying and retaining world class talent is critical for the success of the UNC research mission. The Department of Genetics has a long history of recruiting faculty with fixed-term contracts at UNC into tenure-track positions. Examples among our more seasoned faculty include **Beverly Koller, PhD**, a world-renowned expert in targeted modification of the mouse genome to create unparalleled mouse models of human disease. Lately, Koller has focused on the generation of revolutionary models by humanizing key mouse genes,



addressing a key limitation of mouse models. A second example is **Mark Heise, PhD**, a virologist with an outstanding track record of impactful publication and success in securing external funding. Recently, Mark has been co-leading the Rapidly Emerging Antiviral Drug Development Initiative (READDI) program, a strategic effort at UNC focused on preparing for the next pandemic.

Here are five fixed-term faculty who have competed for and secured tenure-track positions at UNC (in chronological order). **Bradford Powell, MD, PhD**, has a clinical program in adult and pediatric cancer genetics, is the key genetics educator of UNC medical students and essential member of the PPMH. **Katie Hoadley, PhD**, is an expert in cancer genomics who has been named a Clarivate Highly-Cited Researcher five years in a row. **Jesse Raab, PhD**, leveraged his computational expertise to secure DOD funding and start an innovative program on epigenetics and liver cancer in collaboration with Hoadley. **Laura Raffield, PhD**, has become a key member of national consortia such as TOPMeD and the Jackson Heart Study. **Jeremy Wang, PhD**, secured a tenure-track position in DPLM as an associate professor starting in 2024. He will continue to design computational tools to

understand human diseases. We are proud to have helped retained such a talented pool of scientists.



Department of Health Sciences



Louise Thoma, PT, DPT, PhD has led and contributed to several efforts this year to examine the integration of physical therapy and exercise into routine rheumatology care for adults with rheumatoid arthritis. She was part of the working group that published the first American College of Rheumatology Guideline for Exercise, Rehabilitation, Diet, and Additional Integrative Interventions for Rheumatoid Arthritis in the Spring and led an editorial that contextualized the guideline with respect to the role of physical therapy. She also published a study examining the association of rehabilitation dose with clinical outcomes among adults with rheumatoid arthritis in a large patient registry.

These efforts contribute to the training activities of her K23 Career Development Award from NIAMS, which seeks to develop and pilot test a scalable model (PREVAIL) for integrating rehabilitation into routine care to preserve function and delay disability in adults with rheumatoid arthritis.

Clare Harrop, PhD, is PI on multiple grants focused on sex differences and co-occurring conditions in autism across the lifespan. Her R01 (NICHD) charts developmental trajectories in autistic children, ages 4 to 8, by assigned sex using multiple quantitative and qualitative methods, with a key focus on the development of gender identity. An Eagles Autism Foundation award studies challenging eating behaviors in this same sample. A new multi-PI R21 (NIMH) aims to determine how social connections associate with suicidal thoughts and behaviors in older autistic adults, with an over-recruitment of autistic females. Harrop's work is highly collaborative, both intramurally (Depts. DHS, Psychiatry, UNC Frank Porter Graham Child Development Institute) and extramurally (Children's Hospital of Philadelphia, Children's National Hospital, Kansas University Medical Center). Her overarching goal is to characterize the experiences of autistic females to improve identification and supports for this under-studied group.



Department of Medicine

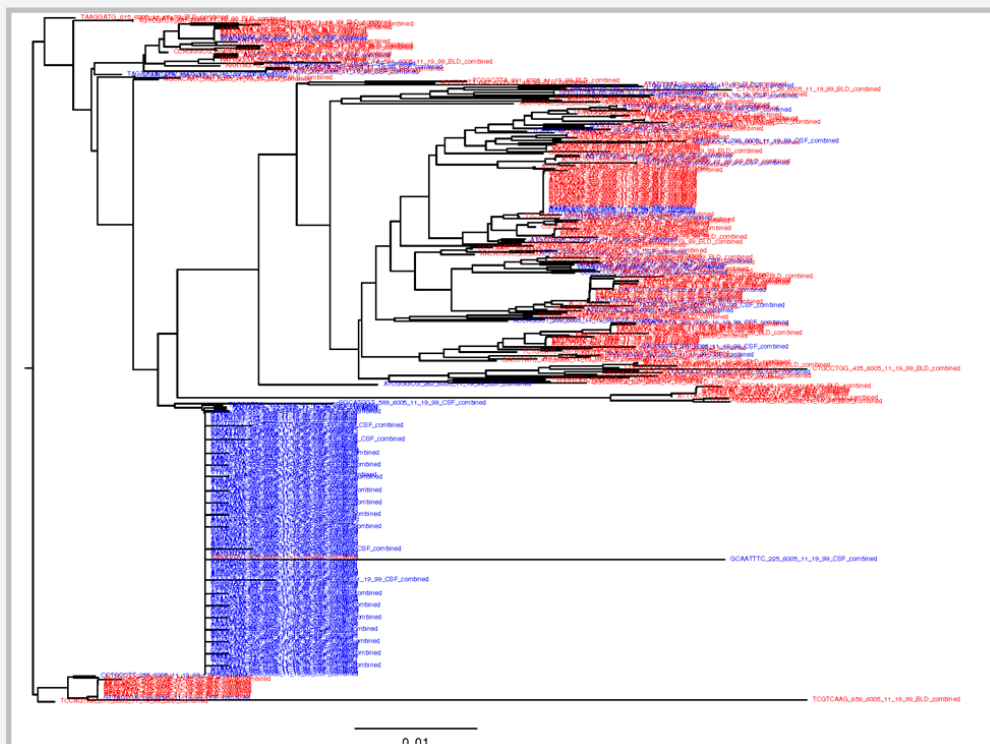
Anti-Neutrophilic Cytoplasmic Autoantibody vasculitis (ANCA) is an immunologic disease that causes systemic symptoms due to inflammation and damage to small blood vessels. Antibodies targeting white blood cell proteinase 3 (PR3) or myeloperoxidase proteins are the most common causes of this serious disease. Publishing [in JCI Insight in February 2023](#), **Dhruti Chen, MD**, and her

colleagues identified a polymorphism in proteinase-3 associated with increased leukocyte expression of this autoantigen. Proteinase 3 levels were low in healthy controls, despite carrying the variant, but in patients, leukocyte expression of this protein was significantly higher, and was associated with increased risk of relapse after treatment.

Ethan Basch, MD, MSc, and his colleagues have devised ways to allow cancer patients to self-report their symptoms through the electronic health record as published in [JAMA in late 2022](#). More than 1100 patients being treated for metastatic cancer from 52 oncology practices tested self-reporting weekly. Severe or worsening symptoms triggered response from their care teams. At 3 months, compared to the control (non-reporting) group, physical function, symptom control and quality of life measures were significantly improved. This paradigm has promise for realizing the goal of patient-centered medical care.

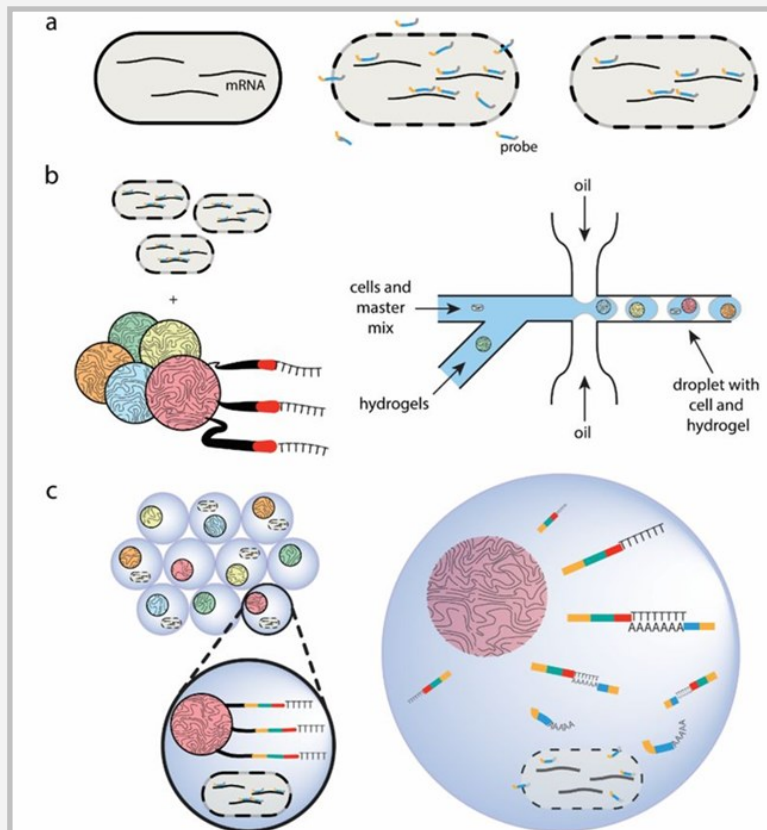
Department of Microbiology and Immunology

HIV-1 persists in all people on antiretroviral therapy (ART). If ART is stopped, HIV-1 quickly rebounds, replicating to high levels throughout the body. Understanding the types of cells and tissues that produce rebound virus may reveal the cells that must be eliminated to cure people of HIV-1. This year, **Ron Swanstrom, PhD, Sarah Joseph, PhD**, and colleagues published a study in *Nature Microbiology* describing the first detailed phylogenetic and phenotypic analysis of rebound HIV-1 populations in cerebrospinal fluid (CSF) and blood soon after ART is stopped. Using blood and CSF samples from eleven people, this study observed that the HIV-1 populations that rebound in the CSF and blood were adapted to replication in CD4+ T cells but that the viral populations between the blood and CSF could differ. This study raises the possibility that infected CD4+ T cells within the CNS could be an independent source of rebound virus distinct from the cells in the blood.



Phylogenetic analyses of HIV-1 partial *env* genes revealed that soon after stopping antiretroviral therapy (ART), clonal HIV-1 lineage commonly emerge in cerebrospinal fluid (blue) that are poorly represented in blood (red) and are adapted to replication in CD4+ T cells (sequences from one representative participant shown). This is consistent with HIV-infected CD4+ T cells persisting in the CNS during ART and contributing to viral rebound when ART is stopped.

Many bacterial pathogens rely on toxin expression for infection. This expression is often controlled by environmental cues. However, the complex infection environment raises questions about whether all cells respond uniformly to these cues. New research from the **Rosenthal group** in the department of Microbiology and Immunology found that in a culture of *Clostridium perfringens* only a subset of cells produces toxin. This finding is consistent with long-standing observations that many people carry pathogenic bacteria asymptotically. The study, published in Nature Microbiology, further found that *C. perfringens* cells that do not produce toxin utilize different nutrients than toxin producing cells. With this knowledge it is possible to add selected nutrients that reduce both the number of cells that are in the virulent state and the level of toxin that each virulent cell produces. These discoveries offer insights into bacterial heterogeneity and a new way to understand and control bacterial virulence.



ProBac-seq: a probe-based microfluidic method for measuring bacterial single cell transcriptomes. a, Cells fixed, permeabilized, and probes hybridized. b, Single cells encapsulated by droplets. c, Contents of each droplet amplified for sequencing.

Department of Neurology

Irena Basuroski, MD led the UNC MS center to Comprehensive Care recognition. **Monica Diaz, MD** received an Alzheimer's Association research grant to study frailty and dementia in Eastern Uganda. **Gwenn Garden, MD, PhD** helped [understand microglia in AD](#). **James Howard Jr, MD** and **Manisha Chopra, MBBS** led a groundbreaking rCART trial and their [5th FDA approved drug for treating myasthenia gravis](#). **Senyene Hunter, MD, PhD**, received an NINDS Child Neurologist K12 award. **David Hwang, MD** received the Neurocritical Care Foundation INCLINE award and a Duke-UNC NIH U24 Center grant for stroke research. **Rick Meeker, PhD** and **Monica Diaz, MD** received an NIA award for an HIV neuroprotection trial. **Soma Sengupta, MD, PhD** [advanced glioblastoma treatment](#), initiated the Imvax trial for glioblastoma, and received the American Brain Tumor Association discovery grant. **Miriam Sklerov, MD** received an NIH K23 award to study brain stimulation in apathy and received the James Woods Junior Faculty Award.

Todd Cohen, PhD [developed a new mouse model of frontotemporal dementia](#) that is more physiologically relevant to human disease. **Gwenn Garden, MD, PhD** [identified miR-155 as a novel](#)

[modulator of microglia A \$\beta\$ internalization and synaptic pruning for AD pathology](#). **Sung-Ho Lee, DVM, PhD** received an NSF grant to develop MRI-compatible electrodes for deep brain stimulation and recording. **Ian Shih, PhD** examined the neuromodulatory effects of the anterior insular cortex on the brain default mode network, revealed neural dynamics between the default mode and salience network switching, [contributed to a multi-center rodent fMRI study](#), received two NIH R01 and three R21 awards, and completed the installation of a new 9.4T MRI system supported by an NIH high-end instrumentation award. **Weiting Zhang, MD, PhD** received an NINDS R21 award to study functional connectivity in the striatum.

Department of Neurosurgery

In 2023, **Dominique Higgins, MD, PhD**, received two prestigious awards. Higgins was named recipient of the NIH/NINDS K12 Neurosurgeon Research Career Development Program award to fund his research focused on the ferroptosis cell death pathway in recurrent glioma. Higgins was also named recipient of the Robert A. Winn Diversity in Clinical Trials Career Development Award. February 2023, Vibhor Krishna, MD, was first author on a New England Journal of Medicine publication demonstrating that focused ultrasound treatment improved dyskinesia and motor impairment in patients with Parkinson's disease: "Trial of Globus Pallidus Focused Ultrasound Ablation in Parkinson's Disease." As of November 2023, **Soma Sengupta, MD, PhD, MBA, FRCP, FANA, FAAN** (study site PI), Dominique Higgins, and **Carlos David, MD**, are enrolling patients as part of a multicenter clinical trial for newly diagnosed glioblastoma (GBM) patients. The phase 2b clinical study administers a combination immunotherapy developed by biotech company, Imvax.

The Department of Neurosurgery has also had several exciting additions, expanding both patient care and research capabilities: **Atil Kargi, MD**, joined the UNC Pituitary Center team as a Professor and Co-director of the Pituitary Center in the Department of Neurosurgery. **Soma Sengupta, MD, PhD, MBA, FRCP, FANA, FAAN**, joined UNC Health's Departments of Neurology and Neurosurgery. **Daniel Pomeranz Krummel, PhD**, joined UNC Health's Department of Neurosurgery as a research faculty member studying malignant brain tumors. **Mark Attiah, MD, MS, MBE, MPH** joined UNC Health's Department of Neurosurgery as an Assistant Professor of Neurosurgery and Director of Peripheral Nerve Surgery.

Department of Nutrition

Research from tobacco, alcohol, and sugar-sweetened beverages finds that policies such as warning labels and taxes reduce purchases of these products. However, little is known about whether these policies would similarly reduce purchases of red meat, an important contributor to noncommunicable disease risk and environmental damage. Lindsey Taillie, PhD, and colleagues [published in PLOS Medicine](#) a study that evaluated the effects of health and environmental warning labels and taxes on red meat purchases using a randomized controlled trial in a realistic online supermarket. Warning labels, taxes, and a combination of warning labels and taxes all led to modest but statistically significant reductions in red meat purchases compared to control. The condition that included both warning labels and taxes had the largest impact on red meat purchases and reduced calories and saturated fat purchased. Implementing warning labels and taxes could reduce red meat purchases in the US, ultimately providing health benefits.

Many medical conditions need prescribed nutritional treatments. Often, they work well for some patients, but less so in many others. It is the ambition of precision nutrition to apply evidence-supported algorithms for predicting which patients are most likely to benefit from a specific dietary

treatment of a particular medical condition, such as obesity, hypertension, or excessive liver fat. In a study led by **Martin Kohlmeier, MD, PhD**, a list of evidence-based nutrigenetic algorithms was collated based on replicated studies. With the resulting one-page look-up table, physicians get specific phrases to guide typically responsive patients to nutritional treatment success. For example, carriers of the common APOA2 rs5082 CC genotype are much more likely to lose excess body fat when they keep their saturated fat intake low. With the look-up table, the efficacy of familiar nutrition interventions can be greatly boosted when particular treatments are reserved for likely responders and alternative treatment opportunities considered for likely non-responders.

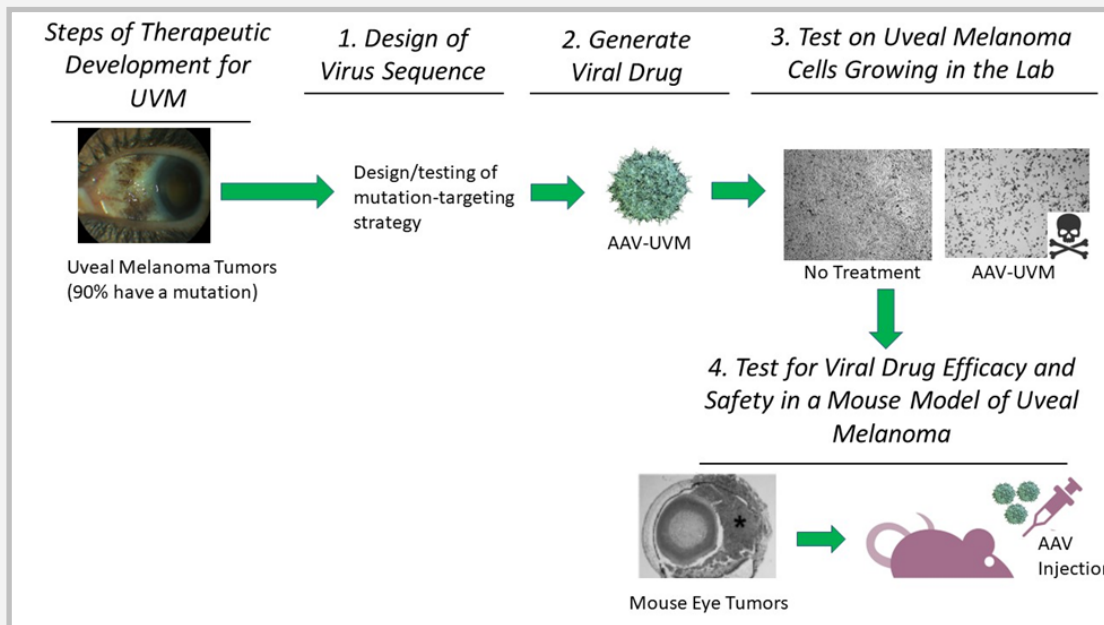
Department of Obstetrics and Gynecology

In 2023, UNC was successfully renewed as a clinical center for the Maternal Fetal Medicine Units (MFMU) Network, the preeminent perinatal clinical trials consortium funded by NICHD. Building on a 25-year track record, this award ensures that UNC remains actively engaged in the consortium's portfolio of high-impact clinical trials. This has included discovery of magnesium for cerebral palsy prevention in imminent preterm births, treatment of mild gestational diabetes, use of steroids in late preterm birth, and risk-reducing labor induction in the 39th week of pregnancy. Each of these studies has changed obstetric practice around the world. Our latest trial in which over 11,000 women were enrolled explored the use of tranexamic acid to prevent bleeding after childbirth. Our new award expands the unit's footprint to include facilities at UNC and WakeMed, and is led by **John Thorp, MD, Kelly Clark, RN, Molly Leatherland, MSN, NP, Sally Timlin, RN, and Tracy Manuck, MD**.

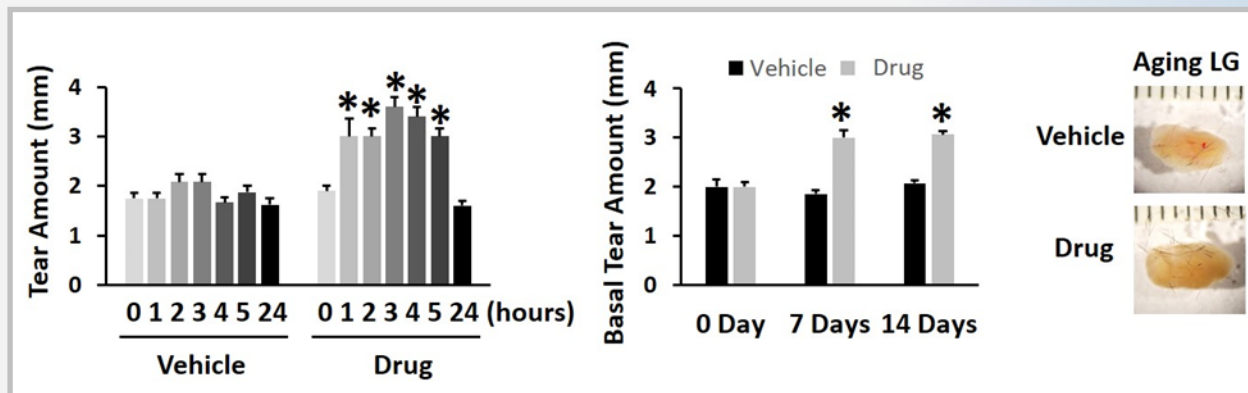
Several faculty members have received NIH SBIR awards to commercialize medical devices. **Erin Carey, MD**, is working on *SmartWand*, a therapy device for high tone pelvic floor disorder. With **Rahima Benhabbour, PhD**, she has invented a thin film for release of lidocaine for vulvodynia. **Kristin Tully, PhD** designed the *Couplet Care Bassinet*, a device that can be positioned over the bed for convenient newborn access. **Jeffrey Stringer, MD** and **Teeranan (Ben) Pokaprokarn, PhD** are developing app-based ultrasound tools for gestational characteristics using "blind sweeps" of handheld probes. **Margaret Kasaro, MD** is evaluating use of these devices in Zambia. Kasaro is also collaborating with Benhabbour and **Carol Golin, PhD** to explore user preferences for a vaginal ring capable of concomitantly delivering contraception and HIV pre-exposure prophylaxis. Finally, our faculty worked with FastTraCS to create the new FemTech Advisory Council that will ensure that clinical Ob-Gyns have a voice in the design and innovation for women's health.

Department of Ophthalmology

Uveal melanoma is the most common intraocular tumor occurring in adults, and up to 50% of patients will experience metastatic disease. Approximately 90% of uveal melanomas exhibit a single point mutation that affects disease progression. Due to these unique genetic features, **Jacquelyn Bower, PhD**, aims to use a gene therapy approach to eliminate the expression of the mutant genes which cause tumor cell growth, accumulation of additional mutations, and eventually metastasis. Because the uveal melanoma tumors are "addicted" to the mutant gene signaling, removal of the mutant gene products results in tumor cell death. The overall goal is to provide an additional treatment option for uveal melanoma patients that prevents progression to metastatic disease. A therapy interfering with the progression of uveal melanoma could continuously "seek and destroy" residual tumor cells that often escape other drug treatments; thus, if successful, almost all uveal melanoma patients at high risk for metastasis could benefit from this type of therapy.



Dry eye disease (DED) is due to the lack of functional tears. A new drug Tyrvaya was approved to stimulate natural tear secretion but with unbearable side effects or limited efficacy for a substantial portion of patients. **Hua Mei, PhD**, discovered a novel DED drug which stimulates natural tear secretion via a different mechanism. A single dose of eye drops stimulates an immediate tear secretion. A 1-week treatment leads to an increased basal tear secretion. The tear-stimulating effect of this drug makes it a good symptom-relieving drug, as an alternative of Tyrvaya. The data suggest that this novel drug may serve as an immediate symptom-relieving drug for sustained tear secretion, as well as a treatment drug to address the root of the disease. The Mei lab is collecting the preclinical data of this drug and trying to bring it to clinical trials.



Methods and compositions for regulating tear production and treating dry eye (U.S. Provisional Patent Application No. 63/509,929)

Department of Orthopaedics

Ming-Feng Hsueh, PhD and **Geoff Handsfield, PhD**, will both join the Department in early 2024. Hsueh is a basic scientist collaborating with TARC. Handsfield will also join the Department as a joint hire with BME. Like our current faculty, both scientists bring successful grant-funded research programs in musculoskeletal science. **Reid Draeger, MD**, received a grant to study the biomechanics of hand fracture treatment. **James Sanders, MD**, received funding to develop a computational spine model for idiopathic scoliosis in children. **Alex Creighton, MD**, engages with a large total shoulder

arthroplasty patient registry and **Trapper Lalli, MD**, received an industry grant to support research in ankle fusion surgery. Finally, in collaboration with Exercise and Sport Science and **Jeff Spang, MD**, our department was recently awarded R01 funding, led by **Joe Hart, PhD**, to identify risk factors for re-injury after knee ligament reconstruction. We are excited about our growing research programs and interdisciplinary collaborations from within and outside UNC.

Department of Otolaryngology-Head & Neck Surgery

The Rhinology Division in OHNS mentored medical students, trainees, and international fellows, demonstrating a continued commitment to education and research. This year, they facilitated valuable research experiences for two UNC medical students, two visiting medical students, two international research fellows, and numerous clinical trainees. **Taylor Stack**, a UNC Holderness Fellow, made significant contributions, authoring four first-author publications. Stack's work focused on elucidating the impact of Primary Ciliary Dyskinesia on sinonasal quality of life ([PMIDs 37203268](#) & [37937377](#)), shedding light on the complication profile of biological modulators for chronic rhinosinusitis ([PMID 37963438](#)), and characterizing racial and ethnic bias in letters of recommendation in Otolaryngology ([PMID 37040732](#)). **Sulgi Kim**, a UNC MS3, demonstrated exceptional dedication by authoring two first-author publications within the Rhinology group. Her research in Rhinology played a pivotal role in defining the pathogenesis of Primary Ciliary Dyskinesia-related sinus disease ([PMID 37997295](#)) and raising awareness about atypical sinonasal manifestations of vasculitis.

Researchers within the Cochlear Implant Clinical Research Labs and Division of Otology/Neurotology investigated the effectiveness of image-guided, personalized programming (mapping) of cochlear implant (CI) and electric-acoustic stimulation (EAS) devices. Imaging was used to determine the electrode array placement for each patient and individualize the mapping of frequency information. EAS patients with personalized maps (known as place-based maps) experienced better early speech recognition than patients with maps configured using current clinical procedures ([PMID 36800505](#)). Much of this work was supported by a Multi-PI NIH grant awarded to **Margaret Dillon, AuD, PhD** and **Kevin Brown, MD, PhD**. In a related study, **Evan Nix, MD**, and colleagues found a high incidence (~60%) of CI recipients with one or more electrodes within the functional acoustic hearing region, which can result in electric-on-acoustic interference and negatively impact speech recognition ([PMID 37758328](#)). Taken together, these data support the utility of using imaging to personalize the maps for CI and EAS users.

Department of Pathology and Laboratory Medicine

Department of Pathology and Laboratory Medicine investigators in the Blood Research Center continued to make significant advances. Two of these were published in the high impact journal *Blood*. **Alisa Wolberg, PhD** ([Blood; PMID: 37883802](#)) detailed how plasma levels of transglutaminase factor (F)XIII, an essential hemostatic protein in circulation, are regulated. FXIII is composed of A (synthesized by hematopoietic cells) and B (synthesized by the liver) subunits. Using human patient data and a mouse model of FXIII-A deficiency, Wolberg demonstrated a unique reciprocal relationship between FXIII A and B subunits. **Matthew Flick, PhD**, along with postdoctoral fellow **Steve Hur, PhD**, ([Blood; PMID: 37832029](#)) studied fibrinogen, a protein that when elevated in circulation increases the risk of cardiovascular and venous thromboembolic diseases. Using a mouse model, they demonstrated that a nonpolymerizable variant of fibrinogen can inhibit thrombosis but has preserved hemostatic potential. These findings may ultimately have a profound impact on therapeutic approaches to patients at-risk for thromboembolic disease.

Department of Pediatrics

Investigators in General Pediatrics and Adolescent Medicine worked across several thematic areas during the past year. **Brittany Raffa, MD, Samantha Schilling, MD, MSHP, and Bianca Allison, MD, MPH** reported on impacts of the COVID-19 pandemic within US-based primary care (PMID: [37083660](#), [37815761](#)) while **Tisu Mvalo, MD**, reported poorer perinatal and neonatal outcomes linked to the pandemic in infants in Malawi (PMID: [37387545](#)). **Colin Orr, MD, MPH**, published work examining linkages between educational debt and choices around subspecialty training (PMID: [37791418](#)) and **Mike Steiner, MD, MPH**, examined the ongoing transition of pediatric care from general hospitals to children's hospitals which may be linked to improved care quality, but reduced total capacity and regional access (PMID: [37902774](#)). Last, **Neal deJong, MD, MPH** is undertaking a trial to improve healthcare communications between families and providers in chronic conditions ([R03TR004311](#)) and Schilling is leading a study involving a novel child-adult relationship enhancement intervention to prevent child maltreatment (PMID: [36823526](#)).

Division of Pediatric Genetics and Metabolism is especially proud and excited for the establishment of the **Joe Muenzer, MD, PhD**, [National MPS Research and Clinical Center](#) at UNC. The Center is currently involved in leading over 7 clinical trials for this rare condition, several of which are being spearheaded by **Elizabeth Jalazo, MD** (e.g. [NCT04573023](#)), who joined the Division early last year. **Michael Adams, MD**, has led a collaborative effort to improve diagnosis and treatment of patients with familial hypercholesterolemia. **Cynthia Powell, MD**, and **Arti Pandya, MD, MBA** are working with RTI ([Early Check Study](#)) and the State Newborn Screening services ([NC NBS program](#)) to improve newborn screening for rare conditions including inborn errors of metabolism. In recognition of the division's excellent patient care, research, and advocacy, which encompasses more than is relayed here, UNC-Children's was honored by being named as a [NORD Rare Disease Centers of Excellence](#).

Department of Pharmacology

In adult human brains, the hippocampus generates new neurons throughout life, thereby helping us to maintain memories and regulate emotions. **Juan Song, PhD**, demonstrated a new way to stimulate these new neurons and reverse some functional deficits associated with Alzheimer's disease in animals. Published in the journal *Cell Stem Cell*, Song and colleagues used leading-edge technologies known as optogenetics (which involves the use of light to alter the activity of brain cells expressing a light-sensitive protein) and chemogenetics (use of a synthetic neurotransmitter to alter the activity of brain cells expressing a synthetic neurotransmitter receptor). They discovered that a two-step procedure using light stimulation followed by chemogenetic stimulation of the supramammillary nucleus was effective in reversing the cognitive and affective deficits in mouse models of the disease. Ultimately, the hope is to use this new information to develop therapies to treat Alzheimer's and related dementia.

The proteins that do the work of the cell do not last forever. Proper functioning requires proper timing of protein production and degradation. When a protein is not degraded properly, it can drive cell growth leading to cancer and other diseases. Proteins destined for degradation usually carry a molecular tag known as ubiquitin. However the process of tagging proteins with ubiquitin has been difficult to study due to its rapid time course and complex nature. To tackle this challenge, UNC pharmacologists **Nick Brown, PhD, Mike Emanuele, PhD, and Klaus Hahn, PhD**, as well as their collaborators, used cryo-electron microscopy to visualize each step of the process, much like a stop

motion movie. The study, published in the journal *Nature Structural and Molecular Biology*, provides scientists with a much better understanding of mechanisms that regulate proteins essential for human health and diseases.

Department of Physical Medicine and Rehabilitation

2023 has seen substantial growth in innovative research in the department. New projects include investigations into the health of eSports competitors (**Katie Bartolo, MD**), symptom trajectories among children with concussion (**Pete Duquette, PhD, ABPP-CN** in collaboration with Duke), and self-compassion for parents/caregivers of children with physical disabilities (**Christine Lathren, MD, MSPH**). Other notable investigations include three studies in cancer populations led by **Sasha Knowlton, MD**: 1) assessing the impact of physical and occupational therapy for patients admitted for bone marrow transplant; 2) assessing the impact of physical therapy pre-cystectomy for patients with bladder cancer; and 3) assessing pre-treatment needs for patients with metastatic breast cancer. **William Filer, MD** is collaborating with the Department of Biomedical Engineering on neural control of a powered prosthetic ankle.

Another ongoing study (**OPTIMUM**) is testing a mindfulness intervention delivered via telehealth-based primary care for people with chronic low back pain - part of the **NIH's HEAL Initiative**. Leadership includes **Susan Gaylord, PhD**, and **Kim Faurot, PA, MPH, PhD**, **Jessica Barnhill, MD**, and **Isabel Roth, DrPH, MS**. The **SMILE study** led by Gaylord seeks to test synchronous group online mindfulness training compared with a mindfulness app and a waitlist control for Hispanics/Latinos and Blacks/African Americans with anxiety. **Project BrEAthE (Brothers, Reclaiming, Emotional, Awareness, Tranquility, Healing & Existence)** co-led by Gaylord, is developing a mindfulness intervention for young Black men at risk for substance use disorders. Gaylord, **Cheryl Giscombe, PhD, RN, PMHNP-BC, FAAN** in the School of Nursing, and Faurot collaborate on the **HARMONY study**, a clinical trial investigating a culturally tailored diet, exercise, and mindfulness intervention for African-American women with metabolic syndrome. Finally, the **Wheelchair CHAMPS study** is developing user-centered powered mobility device charging stations and infrastructure.

Department of Psychiatry

Elizabeth Andersen, PhD, an assistant professor of Psychiatry in the UNC Department of Psychiatry is studying the pathophysiological role of sex hormones in regulating frontal cognitive control, cortisol stress reactivity and interpersonal factors associated with depression in peripubertal girls. In March of 2023, Andersen and colleagues published a paper entitled "[Life Stress Influences the Relationship Between Sex Hormone Fluctuation and Affective Symptoms in Peripubertal Female Adolescents](#)" in *Development and Psychopathology*. They found that exposure to stressful life events proximal to the pubertal transition can expose directional effects of hormone change on affective symptoms. Specifically, greater affective symptoms were associated with increases in hormones in a high stress context and decreases in hormones in a low stress context. These findings provide support for a diathesis-stress model of adolescent psychopathology in which life stress modifies the brain's sensitivity to hormone fluctuation and precipitates vulnerability to depressive symptoms in the presence of normal peripubertal hormone fluctuation.

Bradley Gaynes MD, MPH, is a Professor and the Division Head of Global mental Health in the Department of Psychiatry. His latest report published in JAMA from the U.S. Preventive Services Task Force (USPSTF) recommends screening for depression in all adults without a diagnosed mental

health disorder or recognizable signs or symptoms of depression or suicide risk, including pregnant and postpartum people and adults age 65 years and older. You can read more in the report [“Depression and Suicide Risk Screening: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force.”](#)

Department of Radiology

The Department of Radiology celebrated its Annual Research Day on October 12th with trainee oral and poster presentations, and university speakers. A total of 53 abstracts were submitted, with over 25 posters presented by trainees. Sessions included university initiatives, the State of Radiology Research, Global Radiology and Comparative Medicine.

Our faculty continue to publish in high impact journals, including *Nature Communications*, *Nature Protocols*, *Cell and Science*, with work focused on AI for understanding early brain development, novel radiotracer synthesis approaches, and radiogenomics. Radiology is now ranked 19th in NIH funding (2022), 11th of public universities. **Joseph KT Lee, MD** received the Gold Medal from RSNA for his contributions to abdominal radiology. **Eran Dayan, PhD**, and **Yueh Lee, MD, PhD**, were inducted as Distinguished Investigators in the Academy of Radiology. **Nima Kokabi, MD** will lead the first human trial of Holmium-166 radioembolization in the US. **Louise Henderson, PhD**, will be the PI of a multi-institutional project aimed at reducing racial inequalities in lung cancer screening.

Department of Social Medicine

Addressing the ethical challenges of conducting research needed for safe and effective use of treatments during pregnancy has been a focus of **Anne Drapkin Lyerly, MD, MA**'s research for more than a decade. She is currently leading, alongside co-PI **Suzanne Day, PhD, MA**, the [PREPARE](#) (Promoting Equity for Pregnant Adolescents in Research) Project, an international effort funded by the National Institutes of Health, building on the [PHASES Project](#), which developed [ethics guidance](#) for HIV and co-infections research in pregnancy. She has partnered with [AVAC](#) and has advised the [FDA](#), the CDC, and the World Health Organization in their efforts to advance equitable, pregnancy-specific research.

Krista Ferreira, PhD, is MPI, along with Kathleen Mullan Harris in the Department of Sociology and Joseph Hotz and Naomi Duke at Duke University, of a new five-year, \$25.3 million National Institute of Aging (NIA) award. The award will address gaps in our understanding of potential risks for Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD). The new grant builds upon the Add Health Parent Study ([AHPS](#)), an ongoing study of social, behavioral, and biological factors influencing healthy aging and the development of AD/ADRD in a national sample of the baby boom generation. It will enable investigators to increase samples of Non-Hispanic Black and Hispanic parents in AHPS and link to longitudinal data on their children to make possible intergenerational research on racial/ethnic disparities in cognitive aging and ADRD risk.

Department of Surgery

Kristalyn Gallagher DO and **Kevin Chen MD** worked with **Shawn Gomez PhD** in the UNC/NCSU Joint Department of Biomedical Engineering to develop an artificial intelligence (AI) model to predict margin status during breast cancer surgery. Their work, published in the *Annals of Surgical Oncology*, will help revolutionize the use of AI in cancer surgery. **Phil Spanheimer MD** received a NCI K08 award to develop a novel ex-vivo treatment platform to identify heterogeneity in breast cancer tumors.

This model, published in *Clinical Cancer Research*, was used to identify cells resistant and responsive to tamoxifen in patients using single cell RNA sequencing in ER+/Her2- breast cancers.

Adesola Akinkuotu MD was awarded the American Surgical Association Foundation's Junior Faculty Career Development Award and the UNC Provost's Junior Faculty Development Award, supporting her research on the impact of maternal health literacy on outcomes of children with congenital anomalies. **Adam Akerman PhD**, **John Ikonomidis MD**, and **Chris Agala PhD** were awarded a NHLBI R01 with researchers at the University of Virginia School of Medicine to standardize a screening technique for aortic aneurysms. **Jen Jen Yeh MD** and colleagues in the Division of Oncology (Ashwin Somasundaram MD and Marjorie Charlot MD) were awarded the inaugural Lustgarten Foundation Lustgarten Equity, Accessibility, and Diversity (LEAD) Project grant for *PROmoting CLinicAl TrIal EngageMent for Pancreatic Cancer App Study* (PROCLAIM Study). This is a multi-center study, in collaboration with Ugwuji Maduekwe MD at the Medical College of Wisconsin, that will open January 2024.

Department of Urology

UNC Urology Shines in AUA Early-Career National Recognitions. The Department of Urology was proud to receive multiple recognitions from the American Urological Association (AUA) in 2023 for our trainees and early-career faculty. One highlight is the selections of second-year urology resident **Brooke Spratte, MD**, and urologic oncology fellow **Colton Walker, MD**, for the AUA's "Early Career Investigator's Workshop." Only about 30 invitations are extended annually and having two representing UNC in one year is exceptional. Additionally, assistant professor **David Friedlander, MD, MPH** was nominated to participate in the "AUA's Early-Career Investigator's Showcase" at the 2024 Annual Meeting. The showcase is the only session at the AUA Annual Meeting completely dedicated to highlighting the work of early-career investigators. Friedlander's selection is in recognition for his significant contributions to research in value-based care in nephrolithiasis – an area where he is quickly becoming a leader in the field.

UNC Urology Participates in Impactful Research. 2023 was another successful year for urologic research. **Marc Bjurlin, DO, MSc, FACOS**, and **David Friedlander, MD**, are set to serve as site PIs for Patient-Centered Outcomes Research Institute (PCORI)-funded studies with Cornell University and the University of Michigan, respectively. **Ray Tan, MD, MSHPM** and **Katherine Chan, MD, MPH**, both submitted R01-level proposals. Tan's proposal was to the DOD on testis cancer survivorship and Chan's proposal was to the NIH on shared decision-making in hypospadias care. Four other grant submissions featured urology faculty as site Principal Investigators. Finally, a joint grant-writing group including members of the Departments of Urology and Surgery was created this year by Chan and **Jessica Schumacher, PhD**. The goal of this group is to foster a culture of mentorship and collaboration emphasizing pilot grant mechanisms and career development initiatives. The group has successfully reviewed six proposals in just the last Quarter of 2023.