

2020 School of Medicine Research Round-up

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

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Department of Allied Health Sciences

Dana McCarty, PT, DPT received a KL2 award from the NCCIH to develop a structured, therapist-led program that uses weekly educational sessions to train parents to deliver motor interventions and massage to their extremely preterm infants during hospitalization. The Therapist Education and Massage for Parent-Infant Outcomes program (TEMPO) has demonstrated high levels of feasibility and parent acceptability, as well as potential effectiveness. All parents approached have consented to participate, and all remained enrolled for the duration of hospitalization. At discharge, 100% of parents “agreed” or “completely agreed” that TEMPO was feasible and acceptable, and post-discharge, 100% reported doing massage at least 2-3 times weekly. Furthermore, 90% of parents demonstrated reduced salivary cortisol post-massage administration, indicating a potential neurobiological mechanism for how this intervention alleviates parental stress. Given these promising results, McCarty plans to further define appropriate dosage, frequency, and refinement of the TEMPO intervention in a future pragmatic trial. [Further information can be found here.](#)



Infant massage benefits infants and parents. Preliminary evidence from McCarty's study shows that parent salivary cortisol, a biomarker for stress, is reduced after messaging their infant.

Katarina Haley, PhD, CCC-SLP, and **Adam Jacks, PhD, CCC-SLP**, of the [Center for Aphasia and Related Disorders](#), received an R01 from the NIDCD to study speech production disorders following a stroke. Such disorders include aphasia, apraxia of speech, and dysarthria. Objective methods to diagnose these conditions are required since current diagnostic methods are poorly defined and depend heavily on subjective impression. The project will define boundaries between normal and impaired speech production across key dimensions and metrics and identify a psychometrically sound and clinically feasible test for estimating severity and characterizing multidimensional speech profiles. Having standardized and robust methods for assessing speech impairments after left hemisphere stroke will improve transparency, consistency, and accuracy of clinical management. The study population will include 900 patients with left-hemisphere stroke recruited from UNC Health and Atrium Health.

Department of Anesthesiology

Faculty in the Department of Anesthesiology are not only providing the very best care, but also creating new knowledge through the conduct of research studies and clinical trials. For example, **Kathleen Smith, MD, FASA**, and **Lacey Straube, MD**, members of the Obstetric Anesthesia Division, recently ran a clinical trial that addressed the use of nitrous oxide for cephalic version, a procedure used to turn a fetus into a head-down position before labor begins to allow for a vaginal birth. The team found that while there has been growing popularity in the use of nitrous oxide for this procedure, it provided no analgesic benefit and increased number of version attempts. More about this study can be found in the article published in *Journal of Clinical Anesthesia* [linked here](#).



The Department of Anesthesiology is also home to the Institute for Trauma Recovery. The Institute conducts many large-scale studies and trials of trauma survivors and seeks to understand the pathogenesis and prevention of chronic pain, posttraumatic stress, and other adverse neuropsychiatric sequelae of trauma and traumatic stress. One investigator in the institute, **Matthew Mauck, MD PhD**, recently completed several observational studies ([which can be found in the journal Pain](#)) and a pilot clinical trial demonstrating that low Vitamin D levels result in worse pain outcomes after trauma. Furthermore, this study suggested that Vitamin D administration is a promising intervention to improve pain outcomes and reduce racial differences in pain outcomes after major thermal burn injury.



Department of Biochemistry and Biophysics

Researchers Reveal Safeguarding of a Key DNA Sensor in the Innate Immune System: A team led by **Qi Zhang, PhD**, Associate Professor of Biochemistry and Biophysics and **Robert McGinty, MD, PhD**, Assistant Professor of Chemical Biology and Medicinal Chemistry at the UNC Eshelman School of Pharmacy (ESOP) used cryo-electron microscopy to produce a high-resolution structure of protein cGAS bound to the nucleosome inside cells. They show how cGAS specifically attacks foreign or damaged DNA, but not healthy DNA. This research is [published in Science](#) and includes other UNC co-authors including **Joshua Boyer, PhD**, postdoctoral fellow in the Zhang lab; **Cathy Spangler**, graduate student in the McGinty lab; **Joshua Strauss, PhD**, Assistant Professor of Biochemistry and Biophysics and Director of the CryoEM Core Facility at UNC, **Andrew Cesmat** former ESOP lab technician, and **Pengda Liu, PhD**, Assistant Professor in the Department of Biochemistry and Biophysics. McGinty, Liu, and Zhang are also members of the Lineberger Comprehensive Cancer Center.

Neher Lab Publishes CryoEM Structure in PNAS: Researchers in the lab of **Saskia Neher, PhD**, Associate Professor of Biochemistry and Biophysics, used cryo-electron microscopy to identify a novel helical structure of the protein lipoprotein lipase (LPL), the enzyme that breaks down lipids from our blood. Spearheaded by **Kathryn Gunn, PhD** a postdoctoral fellow in the lab, the work showed that the LPL can exist in a unique helical state that is inactive. **Benjamin Roberts**, a graduate student in Neher's lab, used super resolution microscopy to show that LPL creates filament-like structures inside of storage vesicles in fat cells. The helical form of LPL is likely what gives rise to the filamentous structures, indicating helical LPL is the inactivate form used to store LPL before it is released into the capillaries to breakdown fat. Understanding LPL storage and trafficking is important for preventing heart disease and treating complications of diabetes. [PNAS paper linked here.](#)

Department of Biomedical Engineering



Biomedical Engineering's **Dayton Laboratory** collaboration with affiliated startup company SonoVol, co-founded by Professor and Interim Chair **Paul Dayton, PhD** and BME alumni **Ryan Gessner, PhD**, is distributing exciting new life science research tools that operate within the in vivo imaging technology market in both the U.S. and internationally. Located in RTP, SonoVol has been a major employer of local graduates, now employing 11 UNC, NC State, and Duke undergraduate and graduate alumni, and with several active collaborations with UNC and Duke faculty. SonoVol's products provide an easy-to-use scanning technology allowing researchers across a broad range of disease applications (e.g. cancer, cardiovascular, liver disease, etc.) to spend more of their time focusing on their science and less time operating their imaging equipment. Their high-throughput and high-resolution imaging systems make it easy for non-imaging experts to accurately collect and analyze large amounts of data in a short amount of time. [News story linked here.](#)



Biomedical Engineering was heavily involved in finding solutions to pandemic issues from face masks, to vaccines and ventilators. Associate Professor **Devin Hubbard, PhD** led a team to convert surgical masks into high protection face masks for frontline healthcare providers. Their technology, a patented frame that reduces gaps in masks, is now the basis of a startup company [Aerem Innovations, Inc.](#) that has received over \$150K of funding. Associate Professor **David Zaharoff, PhD** is developing a COVID -19 vaccine using the principles of cancer immunotherapy. His team applies techniques they developed to increase direct immune response to generate a vaccine against

coronavirus. Assistant Professor **Bill Polacheck, PhD** used teaching to address COVID-19 and led discussions regarding flow, mass transport, and drug delivery that generated questions about their relationship to coronavirus infection. Students prepared design papers creatively solving coronavirus problems such as modifying ventilators so one machine can serve two patients with different lung capacities. [Read more here.](#)

Department of Cell Biology and Physiology

Cell Biology and Physiology Neuroscientists Employ Cas9 Gene Therapy to Permanently Unsilence Target Gene as Treatment for Angelman syndrome: Angelman syndrome (AS) is a severe neurodevelopmental disorder caused by a mutation or deletion of the maternally inherited UBE3A allele. In neurons, the paternal UBE3A allele is silenced by a long non-coding RNA called UBE3A-ATS. **Mark Zylka, PhD**, Kenan Distinguished Professor of Cell Biology and Physiology in the UNC Neuroscience Center, used CRISPR–Cas9 to permanently reduce the expression of Ube3a-ATS non-coding RNAs and unsilence paternal UBE3A. This paper, [published in Nature](#), examined expression of UBE3A at the genetic and protein level using a mouse model of AS and primary human neurons. This groundbreaking work from Zylka and colleagues demonstrated how reactivation of this silenced gene permanently rescued anatomical and behavioral phenotypes in AS model mice, a discovery that greatly impacts future therapies for AS and other neurodevelopmental disorders.

Cell Biology and Physiology Researchers Examine the Process of Collateral Vessel Formation in the Heart: Collaterals are arteriole-to-arteriole connections present in most tissues, with critical importance in the brain and heart. Collaterals serve as bypass vessels and the extent of this vascular network is impacted by both genetic and environmental factors. The lab of **Jim Faber, PhD**, Professor of Cell Biology and Physiology and the McAllister Heart Institute, examined the effect that sustained reduction in systemic oxygen (hypoxia) has on collateral formation and function. The work, [published in the Journal of Molecular and Cellular Cardiology](#), identified protein and mechanistic bases for collateral formation in the heart in response to hypoxia. Their data demonstrate that hypoxia alone can induce collaterogenesis in the heart and depends on upregulated expression of Rabep2, Vegfa and Vegfr2 and cell migration. These findings by the Faber group have broad implications for various cardiovascular diseases.

Department of Dermatology

Cutaneous angiosarcoma is a rare, highly aggressive skin tumor. Surgery, radiation and chemotherapy are largely ineffective. A study led by **Paul Googe, MD**, Professor of Dermatology, found that angiosarcomas frequently express programmed death ligand-1 (PD-L1) and have tumor-infiltrating lymphocytes. PD-L1 expressed on cancer cells, when binding to programmed death-1 (PD-1) expressed on immune cells, protect tumor cells from being destroyed by the immune system. Drugs targeting the PD-1-PD-L1 pathway (also called checkpoint inhibitors) have been successful in treating lung and other cancers. The study's findings [published in the American Journal of Dermatopathology](#) suggested that checkpoint inhibitor-based immunotherapy may be beneficial for angiosarcoma. This work has led to a phase II trial, spearheaded by **Juneko Grilley-Olson MD**, Associate Professor of Medicine, and run through the NCI Alliance cooperative group network, to determine how patients respond to immunotherapy combined with conventional chemotherapy and what genetic and other abnormalities are associated with angiosarcoma.

Department of Emergency Medicine

The Department of Emergency Medicine (EM)'s Carolina Center for Health Informatics (CCHI) worked closely with the North Carolina (NC) Department of Health and Human Services (DHHS) to establish and improve COVID-19 public health surveillance for NC. Through NC DETECT (NC's statewide surveillance system developed and maintained by CCHI in collaboration with the NC Division of Public Health), NC DHHS, local health departments, and participating hospitals have access to

surveillance reports for COVID-19 and [additional conditions](#) based on data from emergency departments, urgent care centers, and EMS to track health impacts of the pandemic. COVID-like illness based on NC DETECT emergency department data is a key indicator on the [NC DHHS COVID-19 dashboard](#). Additionally, CCHI received NC DHHS funding to enhance COVID-19 surveillance using NC DETECT by adding data from NC HealthConnex and additional urgent care centers.

The EM Clinical Trials team is participating in a multi-site study to estimate the sensitivity and specificity of the Abbott BinaxNOW® COVID-19 Antigen test against the reference method in patients suspected of COVID-19 infection using nasal swab specimens tested directly. Expanded testing capacity is critical for surveilling and mitigating the pandemic. This rapid test can be used as a first line of defense to identify people who are currently infected and who should isolate themselves to prevent the spread of the disease. Additionally, EM launched an NIH/NIA-funded, three-arm, randomized clinical trial comparing an educational video, video plus nurse telecare, or usual care on pain symptoms for adults 50+ presenting to UNC EDs and OrthoNow with musculoskeletal pain. While recruitment and enrollment were initially conducted in-person, study activities transitioned to fully remote operations due to COVID-19 in early March 2020. Over 100 patients are enrolled in the study, and recruitment will continue through 2021.

Department of Family Medicine



Justin Byron, PhD was awarded a \$892,455 K01 grant from NCI and FDA to [design communication messages](#) for dual users of cigarettes and e-cigarettes. Of the 11 million adult e-cigarette users in the US, more than 50% still use conventional cigarettes and these dual users are at high risk of lung cancer, cardiovascular disease, and other negative health outcomes. The five-year project uses Zoom interviews, eye tracking experiments, and a smartphone messaging randomized controlled trial to design and test mass media campaign messages to educate dual users about their health risks and support dual users in quitting cigarettes and eventually e-cigarettes.



The Department of Family Medicine had two significant publications in the *Journal of the American Medical Association (JAMA)*. **Adam Goldstein, MD, MPH** and **Kimberly Shoenbill, MD, PhD** authored [an editorial in JAMA](#) that moves the research field on tobacco use treatment in cancer forward by calling for more funding and better reimbursement for smoking cessation counseling for cancer patients, which has been associated with improved

quality of life, fewer complications, and longer survival. **Phil Sloane, MD, MPH** and colleagues published a [first-of-its-kind study](#) in JAMA evaluating the effectiveness of their *Mouth Care Without a Battle* training program. After one year, nursing homes that implemented the program saw a 31% reduction of pneumonia cases compared to nursing homes that did not use the program.



Department of Genetics

The Department of Genetics played a key role in the SARS-CoV-2 response. The laboratory of **Mark Heise, PhD**, received three SARS-CoV-2 supplements to his NIAID U19 grant “Systems Immunogenetics of Biodefense and Emerging Pathogens in the Collaborative Cross” along with a new R01 “Genetic Analysis of COVID-19 Susceptibility and Resistance Determinants in the Collaborative Cross”. Heise is also participating in the Rapidly Emerging Antiviral Drug Development Initiative (READDI) to discover and develop drugs for clinical trial testing in anticipation of future viral pandemics. A team lead by **Terry Magnuson, PhD**, that also included **Bev Koller, PhD**, and **Mark Heise, PhD**, received an administrative supplement to develop, archive, distribute and test three

SARS-CoV-2 mouse models through the U42 MMRRRC. The UNC Chapel Hill Superfund Research Program (**Rebecca Fry, PhD**, PI and **Fernando Pardo Manuel de Villena, PhD**, P2 lead) was also awarded an administrative supplement to test the effect of arsenic exposure in a SARS-CoV2 infection model.

Multiple Assistant Professors in the Department received distinguished awards in 2020. Some include **Folami Ideraabdullah, PhD**, who was named to the list of “100 Inspiring Black Scientists in America” by Cell Press and **Laura Raffield, PhD**, who was named an NHLBI “BioData Catalyst Fellow”. **Katie Hoadley, PhD**, was honored by the Breast Cancer Research Foundation with the Marion R. Wright Award for Scientific Excellence. **Hyejung Won, PhD**, had her work on a new computational tool (H-MAGMA) featured on the cover of Nature Neuroscience in April 2020. The Chan Zuckerberg Initiative recognized **Michael Love, PhD, (Essential Source Software for Science)** and **Kasia Kedziora, PhD, (Imaging Scientist)** with prestigious awards. We also welcome the new assistant professor hires in the department included **Adriana Beltran, PhD, Kimberly Foss, MS, CGC, Zahra Girnary, MS, CGC, Matthew Halvorsen, PhD, Jesse Raab, PhD, Laura Raffield, PhD, Christoph Rau, PhD, Alexander Rubinsteyn, PhD, Sarah Schoenrock, PhD, and Courtney Thaxton, PhD.**

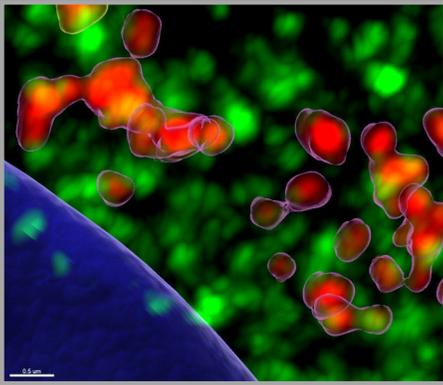
Department of Medicine

The Department of Medicine (DOM) has been involved in high profile COVID-19 work that underscores the collaborative spirit of UNC, and demonstrates UNC’s vast contribution to the rapidly advancing knowledge regarding this pandemic. Spurred by foundational knowledge in the **Baric lab**, Medicine’s **ID and Pulmonary Divisions** have contributed to two critical papers in this sphere (among others). [The first, appearing this spring in Cell](#) detailed SARS-CoV-2 replication in the respiratory tract. The second was published in November in *Science*, co-authored by DOM physicians **Alena Markmann, MS, MD, PhD** (now supported by the School of Medicine Physician Scientist Training Program), **Luther Bartelt, MD, David Margolis, MD, and Richard Boucher, MD.** [The Science paper](#) showed that a globally prevalent SARS-CoV-2 variant that overtook the ancestral strain is more easily transmitted; it is not certain yet if patients infected with the D614G variant have increased disease severity. Fortunately, the current vaccine approaches should be effective against this new strain.

DOM researchers continue to make progress in our pre-COVID research portfolio. **Evan Dellon, MD, MPH** from our GI Division helped to lead a multicenter double blind Phase 2 clinical trial on patients with eosinophilic gastritis/duodenitis, a rare but increasingly recognized disease. The group’s publication in the [New England Journal of Medicine in October](#) entitled “[Anti-Siglec-8 Antibody for Eosinophilic Gastritis and Duodenitis](#)”, describes their trialed an antibody treatment (lirentelimab) that targets sialic acid-binding immunoglobulin-like lectin 8 (Siglec-8). The Siglec-8 receptor is selectively expressed on the eosinophils and mast cells that are involved in disease pathogenesis and cause severe symptoms of abdominal pain, nausea and vomiting. By inhibiting this receptor, lirentelimab decreased gastrointestinal eosinophilia by nearly 90% compared to no change with placebo, and decreased symptom severity by more than 50%, nearly double than placebo. This new treatment appears to be safe, and is now in wider investigative trials.

Department of Microbiology and Immunology

Human rhinoviruses comprise a large group of common respiratory tract pathogens associated with asthma, pneumonia, and exacerbations of chronic lung disease. There are no antiviral therapies or vaccines available to prevent these infections. The **Stan Lemon Laboratory** studies these viruses and made the surprising discovery that a large proportion of rhinoviruses require ‘STING’ (stimulator of interferon genes), a human protein that helps cells sense infection and enhance immune responses to DNA viruses, in order to infect and replicate within cells from the respiratory tract. Because rhinoviruses have RNA genomes, they are not sensed by the STING pathway making rhinoviruses unique; their ability to infect cells actually requires STING – the typical virus-host immunity



relationship turned upside-down! **Karen Swanson, PhD** and **Kevin McKnight, PhD** in the Lemon laboratory were the lead investigators of this study. **Maryna Kapustina, PhD** in Cell Biology and Physiology and **Shihyun You's group** at GSK were essential collaborators. [PNAS publication linked here](#).

This is an Airyscan super-resolution image of the cytoplasm of a rhinovirus-infected cell. The red fluorescence represents rhinovirus RNA, which is near STING protein (green). The blue at the lower left is the nucleus of the cell.

Photo credit: Maryna Kapustina, Department of Cell Biology and Physiology

The leading cause of death in Cystic Fibrosis (CF) patients is respiratory failure from chronic pulmonary infection. While *Pseudomonas aeruginosa* typically initiates life-long infection in the lungs of very young CF patients, *Burkholderia cepacia* complex (Bcc) bacteria infect only teenage and adult CF patients and causes more severe disease that can be fatal. Both *P. aeruginosa* and Bcc use type VI secretion systems (T6SS) to compete with neighboring bacteria. The **Cotter Laboratory** in collaboration with the **Wolfgang Laboratory** and the **Rasko and Ernst Laboratories** at the University of Maryland, showed that many *P. aeruginosa* strains from teenage and adult CF patients contain T6SS-abrogating genomic mutations that render them susceptible to being outcompeted by Bcc. These results indicate that some mutations that arise in *P. aeruginosa* make its human host susceptible to Bcc superinfection, suggesting that the T6SS functionality of resident *P. aeruginosa* may predict susceptibility of CF patients to more dangerous Bcc infections. [Cell Host Microbe paper linked here](#).



Department of Neurology

The Department of Neurology has had two research breakthroughs related to significant neurological impairments. **James F. Howard Jr., MD**, was the principal investigator of the phase 3 trial for the experimental drug efgartigimod, developed by Argenx. The company plans to seek U.S. approval of the drug by the end of year in response to data showing rapid and robust responses in people with generalized myasthenia gravis (read more in the [news article linked here](#)). **Todd Cohen, PhD**, along with other UNC and University of Pennsylvania researchers published "An HDAC6-dependent surveillance mechanism suppresses tau-mediated neurodegeneration and cognitive decline" in [Nature Communications](#) (November, 2020). This study suggests that therapeutic approaches to increase or activate HDAC6 in the brain could be helpful for patients with Alzheimer's and related types of dementia.

The Center for Animal MRI (CAMRI) at the Biomedical Research Imaging Center (BRIC), led by **Ian Shih, PhD**, Associate Professor in the Department of Neurology, received two National Institutes of Health grants totaling \$2.6 million for a new MRI instrument and to upgrade an existing MRI system. Shih will use the first grant to purchase a new 9.4T MRI scanner, and the second will allow for much needed updates to the existing Bruker 9.4T MRI system. Together, the new instrument and updated older machine will allow UNC researchers to conduct more advanced imaging experiments relevant to not only Neurology but biomedical research across UNC's campus. More information about these purchases [can be found here](#).

Department of Neurosurgery

Randaline Barnett, PhD, and **Carolyn Quinsey, MD** made a presentation at the National Pediatric Neurosurgery Section Meeting in December 2020 entitled 'Implementation Of Telemedicine In Pediatric Neurosurgical Practice During The COVID-19 Pandemic: Does Virtual Care Perpetuate

Health Care Disparities?’ Barnett was awarded the American Academy of Pediatrics Section on Neurosurgery Award for her work. This presentation was well received not only for its relevance to the virtual care all of medicine has experienced, but also because it recognized the importance of identifying and addressing disparities in neurosurgical care by the specialty as a whole.

Department of Nutrition

Lindsey Smith Taillie, PhD, was lead author on [a *PLOS Medicine* publication on](#) the first study to evaluate the impact of mandatory warning labels on sugary drinks to prevent obesity and non-communicable disease. The labels reduced sugary drink purchases by nearly 25%, a much larger impact than previous standalone sugary drink policies like soda taxes. The article received attention in the lay media including a [New York Times article that was tweeted by Obama and 3,500 others and liked 18,500 times](#). In October 2020, the article was used by health advocates to implement a similar policy in Mexico, and in Colombia’s house of representatives to pass a similar labeling law, now under debate in the Senate. Warning labeling systems like Chile’s are now being implemented in five Latin American countries (Chile, Peru, Uruguay, Brazil, and Mexico) and Israel, with at least another six countries actively considering this policy in Latin America, Asia, and Africa.

Mirek Styblo, PhD (Nutrition) and **Beverly Koller, PhD** (Genetics) created a novel mouse strain described in their August 2020 [Environmental Health Perspective article](#). This mouse strain contains the human gene encoding arsenic methyltransferase, a key enzyme in the metabolism of arsenic (*AS3MT*). The humanized mice metabolize arsenic less efficiently than existing mouse strains and the distribution of arsenic and its metabolites in tissues resemble that in humans. This humanized mouse strain has human-like metabolism of arsenic and will allow studies of arsenic associated diseases at environmentally relevant levels of exposure. The mice will be used in the UNC Superfund Research program, including in a transdisciplinary project examining the role of arsenic exposure and susceptibility to SARS-CoV-2 infection and severity of COVID-19 disease. Several leading laboratories in the US and Europe have already requested access to these mice, providing further evidence of the significant impact of this work on the field of environmental toxicology of arsenic.

Department of Obstetrics and Gynecology

Victoria Bae-Jump, MD, PhD, established the UNC Program for Translational Research of Endometrial Cancer Disparities (UNC TREND), with co-Founders **Andy Olshan, PhD**, Department of Epidemiology, and **Tope Keku, PhD**, Department of Medicine. UNC TREND aims to bring together an interdisciplinary team of researchers who will address this alarming racial disparity. As part of UNC TREND and with the generous support from LCCC, the team opened the Carolina Endometrial Cancer Study (CECS) in September 2020. Other co-Investigators for this study include **Hazel Nichols, PhD**, Department of Epidemiology, **Russell Broaddus, MD, PhD** and **Jason Merker, MD, PhD**, both from the Department of Pathology and Laboratory Medicine. CECS is a population-based study across the entire state of NC that will use a comprehensive approach to integrate tumor biology with clinical, socioeconomic, and other factors that contribute to worse outcomes in Non-Hispanic Black women diagnosed with endometrial cancer. We anticipate enrollment of 1000 women within 3 years.

Racial disparities in preterm deliveries contribute to poor neonatal outcomes for Non-Hispanic Black women. Unfortunately, the disparities observed in preterm deliveries is even greater in women infected with HIV. 17-hydroxyprogesterone improves pregnancy outcomes in women at risk for preterm labor. However, the benefit of 17-hydroxyprogesterone in Non-Hispanic Black women with HIV infection is unclear. Working with long-standing partners in Zambia and Malawi, faculty in the **Division of Global Women’s Health** recently completed the randomized trial Improving Pregnancy Outcomes with Progesterone (IPOP) (R01HD087119), which randomized 800 HIV-infected women to 17-hydroxyprogesterone versus placebo to prevent preterm birth. The investigators hypothesized that weekly prenatal 17-hydroxyprogesterone will reduce the risk of HIV-related preterm

birth, and showed that access to this inexpensive intervention to prevent preterm birth among pregnant women with HIV could have substantial global public health impact.

Department of Ophthalmology

Glaucoma surgery is often a vision-saving procedure. However, there is a significant post-operative investment and burden on the patient following many of these surgeries. Patients must attend their post-operative visits in order to ensure they are healing well and not suffering from potentially dangerous complications. A study by **David Fleischman, MD, FACS** and colleagues found that patients are likely to miss post-operative visits the further they live from their eye center. Another important factor seems to be rurality, extrapolated by patient's home address distance to interstate access. Only 63% of patients living beyond 20 miles from interstate access made all of their post-operative visits by the 6-month post-operative mark. The results of the study suggest that glaucoma surgeons should consider their patient's distance from clinic or interstate access when deciding upon type of surgery to perform.

Mucopolysaccharidosis I (MPA I) is a monogenetic lysosomal storage disease in which patients lose vision due to corneal opacity. In pioneering work, **Matthew Hirsch, PhD** and colleagues used an adeno-associated virus (AAV) gene addition strategy inserted into the corneas of MPS I dogs, whose vision loss mimics MPS I human patients. A single administration of the gene therapeutic prevented the onset of corneal clouding and completely reversed pre-existing corneal opacity, thereby restoring vision. This gene therapy approach will be the first AAV vector clinical application to the anterior eye and provides optimism for extrapolation of the approach to vision loss in other lysosomal storage diseases and to the treatment of blindness caused by corneal diseases in general. Read more about Hirsch's research [in the article linked here](#).

Department of Orthopaedics

Brian Pietrosimone, PhD and **Jeff Spang, MD** received Arthritis Foundation funding to study biomechanical changes following Anterior Cruciate Ligament (ACL) injuries that influence post-traumatic osteoarthritis. Younger, physically active individuals who experience a knee injury are at greater risk of developing knee osteoarthritis early in life. Pietrosimone and Spang are leading an interdisciplinary research team (Exercise and Sport Science, Orthopaedics, Thurston Arthritis Research Center, Biomedical Engineering, and Radiology) to study how changes in joint movements following knee injuries during activities like walking, running, and jumping influence the subsequent development of osteoarthritis, and how altered muscle function, walking biomechanics, and physical activity impact early changes in knee cartilage during the first year following ACL injury and reconstruction. Following completion of the study, the team will be positioned to employ targeted treatments to correct harmful biomechanical and behavioral changes following knee injury to prevent osteoarthritis onset. More information is available [at this video linked here](#).

Department of Otolaryngology

Cochlear implants are neuroprosthetic devices that restore access to sound for patients with sensorineural hearing loss. They therefore represent one of the most far-reaching advancements in modern medical science. The cochlear implant consists of an array of metal contacts which is inserted into the inner ear, and the speech processor transforms sound from the environment into electrical stimulation. Good performers can use the phone and converse in quiet environments, but not everyone achieves this level of success. Our research has shown that individual differences in speech perception abilities with the implant are predicted by [cochlear health](#), measured as residual physiological responses to sound ([research led by **Douglas Fitzpatrick, PhD**](#)), and by [insertion depth](#) of the electrode array, a surgical factor ([led by **Brendan O'Connell, MD**](#)). In combination, these two variables can account for approximately 70% of



Photo release from patient received.

the variability in outcomes. This information will support innovation and development of rehabilitative strategies to improve outcomes for cochlear implant users.

As a result of the SARS-CoV-2 pandemic, mitigation of viral transmission between patients and healthcare providers has become a paramount concern. Aerosol-generating procedures like endoscopic endonasal surgery pose a potential exposure risk, particularly when they are performed in an outpatient clinic setting with limited environmental controls. We undertook a prospective study to measure particle size and concentration during diagnostic and debridement endoscopy. Diagnostic nasal endoscopy with a rigid scope was not associated with increased aerosolization over baseline, however the use of endonasal cold and suction instrumentation required for debridement was associated with significant increases in particle aerosolization. Results indicate that endonasal debridement may pose an increased risk for SARS-CoV-2 transmission, highlighting the need for personal protective equipment and patient screening for office-based endonasal procedures. This work led by senior author **Adam Zanation, MD, FACS**, appears as a recent paper in *Laryngoscope* entitled, "[Quantification of Aerosol Particle Concentrations During Endoscopic Sinonasal Surgery in the Operating Room](#)".

Department of Pathology and Laboratory Medicine

Two associate professors in the Department of Pathology and Laboratory Medicine, **Li Qian, PhD**, and **Jiandong Liu, PhD**, each won prestigious Established Investigator Awards from the American Heart Institute ([news release linked here](#)). These awards support investigators whose careers are in a rapid growth phase, have unusual promise, and show established records of accomplishments. Qian studies how to transform damaged heart cells into viable muscle cells. By understanding the molecular basis of cardiomyocyte specification and maturation, they can apply the knowledge to improve efficiency and clinical applicability of cellular reprogramming in heart disease. Liu combines genetics with molecular and cell biology to study cardiac development and function, focusing on the molecular mechanisms that link mechanical forces and genetic factors to cardiac morphogenesis using zebrafish as a model system.

Associate Professor **Scott Williams, PhD** also studies the molecular mechanisms of stem cell biology, but in a different system – epithelial cells of the oral cavity. In a [Cell Stem Cell paper](#), Williams identified a previously uncharacterized stem cell population for the hard palate that responds to masticatory stresses and promotes wound healing. Cancers arising in the hard palate are uncommon, so knowledge of the molecular programs that regulate these stem cells may shed light on important mechanisms for resisting malignant transformation.

Department of Pediatrics

UNC Food Allergy Initiative (UNCFAI) Investigators have continued to advance our understanding of the development and treatment of food allergies. On behalf of the NIH-sponsored Consortium for Food Allergy Research (CoFAR), **Edwin Kim, MD, MS**, Director of the UNC FAI, reported 5-year follow-up data demonstrating successful and sustained introduction of dietary egg after completion of egg powder oral immunotherapy (OIT).¹ Next, Kim investigated common baked egg products as treatments, and reported on the novel CoFAR7 study comparing baked egg versus egg OIT.² The stronger treatment effect seen with egg OIT has suggested an unexpected potential role for egg OIT in baked egg tolerant patients. With regards to food allergy mechanisms, work by **Johanna Smeekens, PhD**, in conjunction with the laboratory of **Tim Moran, MD, PhD**, demonstrated an important role for environmental adjuvants and for the timing of these exposures in the development of peanut allergy pointing to possible environmental approaches to allergy prevention.³

Vaping and e-cigarettes have surged in popularity with today's youth but there are several unanswered questions regarding how "safe" these alternatives are to traditional tobacco products.^{1,2,3,4,5,6} The research group of **Ilona Jaspers, PhD**, is exploring this topic and published findings demonstrating that in addition to nicotine and flavoring chemicals, base components of e-liquids can induce their own adverse effects in respiratory cells⁷. Her group also demonstrated that antiviral host defense responses are altered in e-cigarette users, marked by enhanced inflammatory signatures and reduced virus-specific nasal mucosal antibody levels.⁸ Going beyond the lab, Jaspers and her colleagues have been highly active in voicing these and other concerns regarding vaping/e-cigarette use in both scientific and public forums. Developing K-12 classroom materials, informational podcasts, infographics for health care providers, and talking directly to teenagers are just some of the ways her group tries to educate about the potential health effects of vaping.

Department of Pharmacology

Jonathan Schisler, PhD, is an Assistant Professor in the Department of Pharmacology and Pathology and Laboratory Medicine who uses genomic-biologic data to look at risk relationships in cardiovascular disease and protein quality control mechanisms. Schisler and collaborators from NASA and research universities around the country recently [published an article in *Cell*](#) illustrating that mitochondrial dysfunction underlies many health issues experienced by astronauts, including loss of bone and muscle mass, as well as immune, heart and liver problems. Other NASA scientists have been making connections to space-related cardiovascular issues as well, and the UNC-NASA team hopes that their findings will lead to improved health of astronauts and also help space exploration programs in the future.

Jude Samulski, PhD, is a Professor in the Department of Pharmacology and a pioneer in Gene Therapy Research. In July of 2020, Samulski was featured in an NPR story that describes his decades-long effort to develop Gene Therapy as a cure for Duchenne muscular dystrophy (DMD), a severe type of muscular dystrophy characterized by progressive muscle weakness. Samulski has spent over 30 years addressing many obstacles to make gene therapy a reality, including the large size of the gene that is defective in DMD and designing a delivery virus that would reach the billions of muscle cells throughout the body. Despite these difficulties, Samulski created an effective gene therapy strategy for DMD, which has been given successfully to 8 boys with the disease, who are demonstrating improved strength and endurance. Based on these results, studies have progressed to Phase III clinical trials. [Read this outstanding NPR article here.](#)

Department of Physical Medicine and Rehabilitation

PM&R received funding as part of a \$7.3 million, multi-site clinical trial awarded by the NIH's National Center on Complementary and Integrative Health, entitled "**Optimizing Pain Treatment in Medical Settings Using Mindfulness (OPTIMUM)**". The study involves a pragmatic trial of group-based mindfulness training for patients with chronic low back pain, and is part of the massive, \$945 million trans-agency NIH HEAL (Helping to End Addiction Long term) initiative. Investigators are now launching a four-year implementation phase involving a total of 450 patients randomized to either 8 weeks of mindfulness-based stress reduction as part of a group medical visit, or to usual primary care alone. Funding was awarded to Boston University as the lead institution, with other institutions including the University of Pittsburgh, University of Massachusetts, and UNC-Chapel Hill. The UNC team consists of PM&R faculty **Susan Gaylord, PhD (PI)**, **Kim Faurot, PhD (co-PI)**, and Family Medicine faculty **Gaby Castro, MD (co-I)**.

Department of Psychiatry

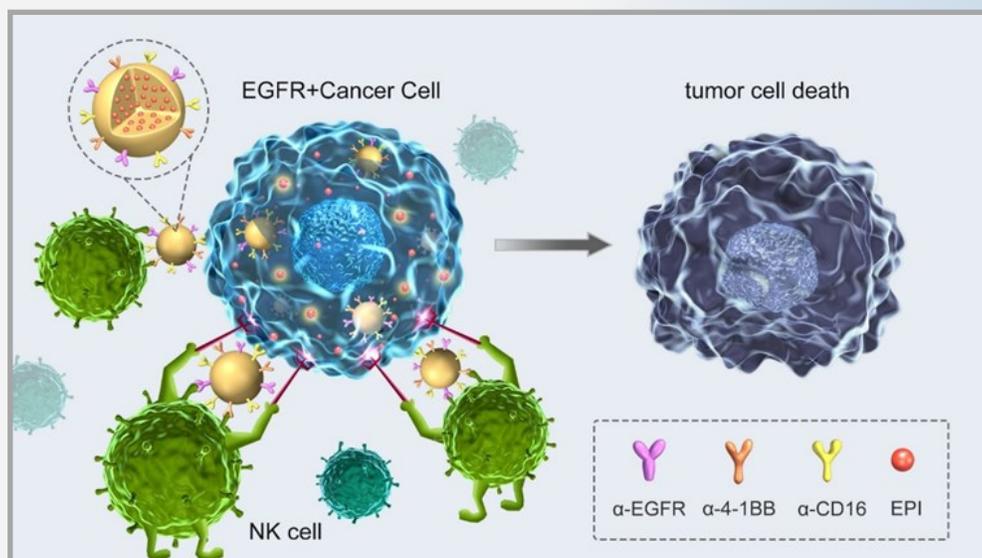
Karen Grewen, PhD, is a Professor of Psychiatry whose research focuses on the effects of prenatal drug exposures (PDE) on infant brain and behavioral development and on neurobiological correlates of mother-infant attachment formation. This includes using MRI and EEG to study infant

brain development, prenatal exposure effects on infant cognitive development and on the quality of infants' attention-eliciting signals during mother-infant interactions, as well as fMRI to study maternal brain activity which may be altered by perinatal drug use, and examination of maternal responses to infant contact. Grewen and colleagues [published an article in *Human Brain Mapping*](#) that demonstrated how prenatal exposures to different substances impact fetal/infant brain development of functional connectivity (FC) in different patterns using neonatal functional MRI. Connections that showed significant drug effects also demonstrated significant correlations with 3-month behavioral outcomes, and mediation analyses supported a mediation role of the detected brain FCs between PDE status and cognitive/language outcomes.

Zoe McElligott, PhD, is one of the 2020-2021 recipients of the prestigious UNC SOM Jefferson-Pilot Fellowships in Academic Medicine. She is a basic neuroscientist in both the Bowles Center for Alcohol Research and the Department of Psychiatry who focuses on the area of addiction, and is internationally known for her state-of-the art translational research on brain circuits and plasticity that govern drug abuse, anxiety, and alcohol usage. McElligott is also interested in understanding the neural circuitry underlying opioid-seeking behavior, information that is greatly needed to combat the opioid crisis. In January 2020, McElligott [published an article in *The Journal of Neuroscience*](#) that demonstrated that projects from neurotensin neurons in the central nucleus of the amygdala of male mice influences the expression of reward-related phenotypes and is a novel circuit promoting consumption of ethanol and sweet fluids. These findings illuminate the role of neurotensin neurons in alcohol use disorder.

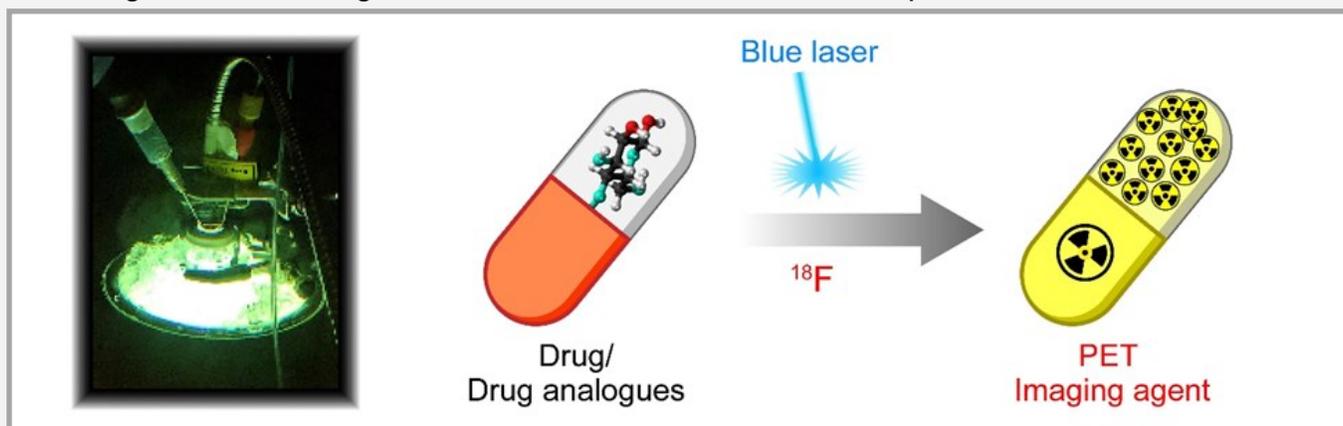
Department of Radiation Oncology

Engineering Multifunctional Nanoparticles to Improve Cancer Immunotherapy: Andrew Z. Wang, MD, is a UNC Lineberger member, Professor and Director of Clinical and Translational Research in the Department of Radiation Oncology. [In the journal *Science Advances*](#), his group reported the development of a new type of cancer immunotherapy treatment. Using nanotechnology, the researchers engineered nanoparticles that can engage both tumor cells and natural killer (NK) cells, a type of immune cell. These nanoparticles activate the NK cells and enable them to eradicate tumor cells, providing a unique strategy for cancer immunotherapy. Moreover, the nanoparticles can also deliver chemotherapeutics to tumor cells in a targeted manner, to further improve cancer treatment. This work has generated a patent application, which has been licensed by a UNC startup company (Archimmune Therapeutics). The researchers are working diligently to bring this novel treatment to clinical practice.



Department of Radiology

Although ^{18}F has been one of the most widely used radioisotopes in positron emission tomography (PET) radiopharmaceuticals, it is challenging to install $^{18}\text{F}^-$ into electron-rich arenes through nucleophilic aromatic substitution ($\text{S}_{\text{N}}\text{Ar}$) due to kinetic barriers associated with C–F bond formation. In a collaborative work between **Zibo Li, PhD** Professor of Radiology and a member of the Biomedical Research Imaging Center and **David Nicewicz, PhD**, Professor of Chemistry, a polarity-reversed photoredox-catalyzed arene deoxyfluorination has been [developed and published by *Nature Catalysts*](#), which enables the fluorination of electron-rich arenes with $^{19}\text{F}^-$ and $^{18}\text{F}^-$ under mild conditions. This approach provides access to radiofluorinated compounds that can be difficult to synthesize through classical $\text{S}_{\text{N}}\text{Ar}$ strategies. This newly developed novel approach has precise control of fluorination position. The purification of final product also becomes easier thanks to the well separated retention between precursor and product. This approach holds great potential for synthesizing and discovering established and innovative PET radiopharmaceuticals.



Simple and Efficient Conversion of Drug/Drug Analogues to PET Agents Using Blue Light

Department of Social Medicine

Jill A. Fisher, PhD, Professor of Social Medicine, published [Adverse Events: Race, Inequality, and the Testing of New Pharmaceuticals](#). This research monograph focuses on Phase I clinical trials, which largely recruit healthy volunteers to test the safety and tolerability of investigational drugs. Drawing on two years of fieldwork in 6 U.S. clinics and 268 interviews with participants and staff, the book illustrates how decisions to take part in Phase I trials are often influenced by poverty and lack of employment opportunities. It shows that healthy participants are typically recruited from Black and Hispanic communities and that they are often serial participants who obtain a significant portion of their income from these trials. This book reveals how social inequality fundamentally shapes these drug trials, while also describing the important validity concerns inherent in this mode of testing new pharmaceuticals.

Tonia Poteat, PhD, MPH, PA-C, Assistant Professor of Social Medicine and core faculty in the [Center for Health Equity Research](#), and **Krista Perreira, PhD, MSPH**, Professor of Social Medicine, received a \$3.5 million grant from the National Heart, Lung, and Blood Institute to conduct a groundbreaking [study](#) of sexual orientation, gender identity, and cardiovascular disease risk among a cohort of over 9,000 Latinx adults enrolled in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). They will examine the role of stigma, discrimination and stress on cardiovascular health in a matched sub-cohort of sexual and gender minorities compared with cisgender heterosexual participants. Study findings will be used to build on identified Latinx cultural strengths to inform new interventions.

Department of Surgery

Clinicians traditionally associate ultrasound with grey fuzzy images. Quantitative ultrasound does not produce images but provides quantitative parameters that reflect tissue structure. Ultrasound waves transmitted into heterogeneous tissue like aerated lung results in ultrasound multiple scattering (USMS). Delivering ultrasound waves from a probe individually instead of simultaneously allows for interpretation of USMS. **Tom Egan, MD, MSc** in collaboration with **Marie Muller, PhD** at North Carolina State University used USMS to determine scattering mean free path (SMFP) and backscatter frequency shift (BFS) in animal models. SMFP reflects the density of air-filled lung alveoli. BFS determines the amount of additional water in lung tissue. They show that using this method, the *absence* of USMS can localize pulmonary nodules in large animal studies. These findings may provide a way to follow patients with pulmonary fibrosis, heart failure, and to locate pulmonary nodules for safer resection with quantitative ultrasound.

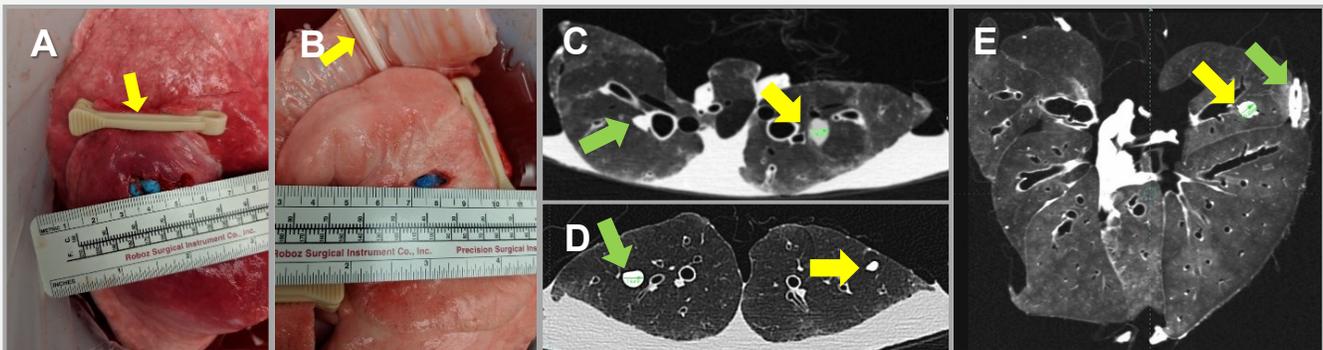


Figure: A. Plastic umbilical cord clip to prevent air leak where blue dental amalgam (DA) nodule was injected and dissected. B. Plastic umbilical cord clip to seal trachea for ex-vivo CT scan. C. Coronal CT section with DA nodule (green arrow) and Vaseline nodule (yellow arrow). D. Coronal CT section with DA nodule (green arrow) and smallest DA nodule (4.7 mm) localized with USMS. E. Sagittal CT section with DA nodule (yellow arrow) and plastic umbilical cord clip to prevent air leak (green arrow).

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 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.

The Department of Urology is proud of our highly-collaborative research endeavors. **Marc Bjurlin, DO, MSC, FACOS** Associate Professor of Urology, is leading a team of collaborators spanning UNC and multiple other centers examining potential carcinogenic metabolites associated with e-cigarettes and bladder cancer. **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. The department continues to see growth in clinical trials enrollment, and looks forward to welcoming **Kate Chan, MD, MPH** as an Associate Professor of Urology in the spring, bringing her NIH-funded research program in pediatric urology to Chapel Hill.