Dr. Mark C. Chappell, PhD, FAHA, is the recipient of the 2022 Arthur C. Corcoran Memorial Lecture Award sponsored by the Council on Hypertension. This honorary lecture, presented annually at the AHA Hypertension Scientific Sessions by a distinguished honoree from the field of hypertension, was established in 1977 in honor of Arthur Curtis Corcoran. Dr. Corcoran’s major achievement was his early application of clearance methods in both hypertensive patients and animals.

Dr. Chappell’s lecture “Evolving Concepts of the Renin-Angiotensin System: From Hypertension to COVID-19” is based on 30 years of research involving the role of the renin-angiotensin system (RAS) in fetal programming events, salt sensitivity, sex differences in hypertension and the role of the estrogen receptor GPER, as well as the influence of the intracellular RAS in the nucleus and mitochondria of the kidney.

Dr. Chappell presented the Arthur C. Corcoran Memorial Lecture on Thursday, September 8th in San Diego, CA at the Hilton San Diego Bayfront. He received an engraved plaque at the Annual Council on Hypertension Awards Banquet presented to him by his former fellow, Dr. Sarah Lindsey. Please join us in congratulating Dr. Chappell on receiving this prestigious award!
Dr. Ellie Rahbar is actively recruiting MD, DVM, or PhD postdoctoral fellows who are interested in the field of hemorrhagic shock and cardiovascular physiology. Individuals interested should email Dr. Rahbar (erahbar@wakehealth.edu) a copy of their CV and 2 references.

2022 Summer Research Programs to Increase Diversity in Biomedical Science Careers:

The Cardiovascular Sciences Center and Sticht Center for Healthy Aging and Alzheimer’s Prevention hosted two summer research programs: the Excellence in Cardiovascular Sciences (EICS) program directed by Drs. David Soto Pantoja and Debra Diz, which has been ongoing for 30 years, and a new program, Enhancing UNderGraduate Education and Research in AGing to Eliminate Health Disparities (ENGAGED – joint program with WSSU and WFU), directed by Drs. Tina Brinkley and Debra Diz, with additional Program Directors Drs. Gwathmey, Keith (WSSU) and Miller (WFU) in its third year. The EICS and ENGAGED undergraduate students were selected from across the country and they participated in research topics related to aging and cardiovascular disease, as well as health disparities. Current events topics ranged from COVID-19 to racism/social inequity and injustice and the impact of these on minority health. Guest speakers were from Howard University, Winston-Salem State University, Wake Forest University, Johnson C. Smith and the Center for Disease Control, as well as Wake Forest University School of Medicine. Panels of current and former graduate school and diversity-focused training program participants provided career insights in several professional development sessions. Students participated in sessions on data collection relevant to cardiovascular sciences and aging-related research, including blood pressure and gait speed, in addition to various basic science demonstrations. Joint sessions and social activities with summer trainees in programs sponsored by NSF (Biomedical Engineering), WFIRM and Precision Medicine created peer networking opportunities for the 120+ student participants. The EICS and ENGAGED summer session concluded with poster presentations of the research projects developed with their mentors over the course of the summer program. We thank the students and the faculty, many of whom are members of the Cardiovascular Sciences Center, who served as mentors, guest lecturers and journal club faculty, for contributing to the program’s success.

continued on page 3
The following 24 trainees and mentors participated in the programs for 2022:

### ENGAGED

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Mentor/Program</th>
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</thead>
<tbody>
<tr>
<td>Taniya Ballard</td>
<td>Winston-Salem State University</td>
<td>Andrew South-Pediatrics Nephrology; CVSC</td>
</tr>
<tr>
<td>Nataley Der</td>
<td>University of Maryland, Baltimore County</td>
<td>Leah Solberg-Woods-Internal Medicine-Molecular Medicine; CVSC</td>
</tr>
<tr>
<td>Summayah El Azzioui</td>
<td>Emory University</td>
<td>Ken Kishida-Physiology &amp; Pharmacology;</td>
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<tr>
<td>Beatrice Gar</td>
<td>North Carolina A &amp; T University</td>
<td>Andrew South-Pediatrics Nephrology; CVSC</td>
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<tr>
<td>Ivy Greene</td>
<td>Wake Forest University</td>
<td>Kimberly Montez-Pediatrics</td>
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<tr>
<td>Christian Johnson</td>
<td>Virginia Commonwealth University</td>
<td>Kathryn Callahan-Internal Medicine-Gerontology &amp; Geriatric Medicine</td>
</tr>
<tr>
<td>Justin Lam</td>
<td>Carnegie Mellon University</td>
<td>Ashley Weaver-Biomedical Engineering; Critical Illness, Injury and Recovery Research Center</td>
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<tr>
<td>Luke Morton</td>
<td>Wake Forest University</td>
<td>Shannon Macauley- Internal Medicine-Gerontology &amp; Geriatric Medicine; CVSC</td>
</tr>
<tr>
<td>Ely Sanchez</td>
<td>University of Puerto Rico at Ponce</td>
<td>Justin Moore-Implementation Science; Office of Global Health/Comprehensive Cancer Center/Maya Angelou Center for Health Equity/Office of Women in Medicine &amp; Science</td>
</tr>
<tr>
<td>Adaiah Stevens</td>
<td>Wake Forest University</td>
<td>Tony Reeves-Internal Medicine-Molecular Medicine</td>
</tr>
<tr>
<td>Juleika Torres</td>
<td>University of Puerto Rico Mayaguez</td>
<td>Rachel Zimmer-Internal Medicine-Gerontology &amp; Geriatric Medicine</td>
</tr>
<tr>
<td>Arshum Mirzaeifard</td>
<td>University of North Carolina at Chapel Hill</td>
<td>David Soto-Pantoja-Surgery Hypertension/Comprehensive Cancer Center, CVSC</td>
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### EICS

<table>
<thead>
<tr>
<th>Name</th>
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<th>Mentor/Program</th>
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<tbody>
<tr>
<td>Marco Benavides</td>
<td>Tecnológico de Monterrey</td>
<td>Nicole Levi- Surgery Plastic Reconstructive</td>
</tr>
<tr>
<td>Makala Crawford</td>
<td>Winston Salem State University</td>
<td>Daniel Kim-Shapiro-Physics</td>
</tr>
<tr>
<td>Ellie Cyrus</td>
<td>Winston Salem State University</td>
<td>Katherine Cook-Surgery Hypertension/Comprehensive Cancer Center/CVSC</td>
</tr>
<tr>
<td>Romeo Espinosa-Ponce</td>
<td>Greensboro College</td>
<td>David Soto-Pantoja-Surgery Hypertension/Comprehensive Cancer Center, CVSC</td>
</tr>
<tr>
<td>Breuna (Bre) Lane</td>
<td>Radford University</td>
<td>Leslie Poole-Biochemistry</td>
</tr>
<tr>
<td>Daryna Lapomarede</td>
<td>Wake Forest University</td>
<td>Giselle Melendez- Internal Medicine-Cardiovascular Medicine</td>
</tr>
<tr>
<td>Nicole Morales</td>
<td>University of Puerto Rico-Cayey</td>
<td>Christina Hugenschmidt- Internal Medicine-Gerontology &amp; Geriatric Medicine Gerontology &amp; Geriatric Medicine; J. Paul Sticht Center for Health Aging &amp; Alzheimer’s Prevention/Claude Pepper Older Americans Independence Center, CVSC</td>
</tr>
<tr>
<td>Olivia Smith</td>
<td>North Carolina State University</td>
<td>Bumsoo Ahn- Internal Medicine- Gerontology &amp; Geriatric Medicine; CVSC</td>
</tr>
<tr>
<td>Yesenia Sosa</td>
<td>University of Texas at San Antonio</td>
<td>Gagan Deep- Internal Medicine- Cancer Biology</td>
</tr>
<tr>
<td>Brianna Thompson</td>
<td>University of North Carolina at Chapel Hill</td>
<td>Dhanendra Tomar- Internal Medicine-Cardiovascular Medicine/Cardiology; CVSC</td>
</tr>
<tr>
<td>Alexandra (Allie) Williams</td>
<td>Wake Forest University</td>
<td>Sarah Adjei-Fremah- Biology-Genetics &amp; Microbiology (WSSU)</td>
</tr>
</tbody>
</table>
Dr. Xuewei Zhu presented at the 2022 Gordon Research Conference-Immunometabolism in Health and Disease. The title of her talk was “Pyruvate dehydrogenase kinase supports macrophage NLRP3 inflammasome activation during acute inflammation”.

Dr. Michael Shapiro was invited to speak at two international conferences over the summer. He presented “Current guidelines for the use of CAC in preventive cardiology” at the 17th Annual Scientific Meeting of the Society of Cardiovascular Computed Tomography in Las Vegas, NV in July. He presented “Relationship of Inflammation and Dyslipidemia” at the American Society of Preventive Cardiology in Louisville, KY in July.

Dr. Michael Shapiro was invited to give Cardiology Grand Rounds at the University of Chicago. The title of his presentation was “Pushing the Envelope with PCSK9 – 20 years of progress”.

Dr. Christopher Schaich was invited to speak at The George Washington University Biostatistics Center on September 1, 2022. His presentation was titled “The Impact of Heart Failure with Preserved Ejection Fraction on Neurocognitive Function and Brain Health.”

Dr. Yashashwi Pokharel and team had three abstracts at national conferences as follows:

- Acharya S, Senner J, Lee J, Berlin M, Maul A, Hanford H, Pokharel Y. Addressing Gaps in Cholesterol Management in Primary Cardiovascular Prevention in a Resident Run Internal Medicine Clinic: A Mixed Method Approach. This abstract was presented at 2022 AHA Quality of Care and Outcomes Research Conference. Congratulations to Dr. Acharya, Dr. Pokharel’s mentee, for receiving the QCOR 2022 Early Career Investigator Travel Stipend Award to present this work!

- Jao G, Pu M, Pokharel Y. Constrictive pericarditis associated with COVID-19 infection. This abstract was presented at the 2022 American Society of Echocardiography.

- Caldarera T, Penmesta M, Seals A, Ip E, Virani S, Shapiro M, Pokharel Y. Clinicians’ Self-Reported Efficacy in Cardiovascular Prevention Practice in the Southeastern United States. This abstract was presented at the 2022 American Society of Preventive Cardiology.

Dr. Mark Chappell co-chaired the Session “Mechanisms of Sex Disparities in COVID-19 Outcomes for the NIH workshop “Sex/Gender-Specific COVID-19 outcomes and management relevant for heart, lung, blood and sleep disorders” June 16-17, 2022. He also gave a talk for this session “Signaling in SARS-CoV-2 entry, regulation and effects” on June 16.

Dr. Mark Chappell and team had three abstract presentations for the Council on Hypertension:

- Chappell M, Yamaleyeva L. Differential Expression of ACE2, Neprilysin and ACE in Extracellular Vesicles Isolated from Human Urine.

- Chappell M. Delta And Omicron Variants Of SARS-Cov-2 Do Not Stimulate ACE2 Conversion Of Ang II To Ang-(1-7).

- Mackert J, Wilson A, Cruz-Diaz N, Melo AC, Chappell MC, Soto-Pantoja D. Targeting The Thrombospondin-CD47 Axis Attenuates Blood Pressure And Renal Injury In Female Hypertensive (mRen2)27 Rats.

Yismeilin Feliz-Mosquea, mentored by Drs. Katherine Cook and David Soto-Pantoja, will give an oral presentation at the Society for the Advancement of Chicanos/Hispanics and Native Americans in Science (SACNAS) National Diversity in STEM (NDiSTEM) Conference, October 27-29, 2022, in San Juan, Puerto Rico. The title of her presentations is “Targeting inositol-requiring enzyme-1 (IRE1) affects triple-negative breast cancer chemotherapy sensitivity and prevents chemotherapy-related cardiotoxicity.”
During the months of May - August, CVSC members were awarded several new grants. Below we highlight some of these awards.

**FUNDING**

Dr. TanYa Gwathmey received a Duke Endowment grant titled “The Triad Pastors Network – Congregational Health Ambassadors Program to Improve Cardiovascular Health.” The major goal of this project is to reduce cardiovascular health disparities within African American communities through an academic partnership with Faith Leaders and houses of worship in the Piedmont Triad region of North Carolina.

Dr. Xuewei Zhu received a pilot grant titled “Pyruvate dehydrogenase kinase is a critical metabolic switch controlling microglia NLRP3 inflammasome and mitochondrial health in AD” from the Alzheimer’s Disease Research Center with co-investigators Drs. Tao Ma and Shannon Macauley.

Dr. Oguz Akbilgic, as an MPI (with MPIs Kwon and Azarbarzin), has received a fundable score (7 percentile) with pending NOA on an R21 titled "Deep learning of awake and sleep electrocardiography to identify atrial fibrillation risk in sleep apnea."

Dr. Oguz Akbilgic as a Co-I (PI Makowski, Site PI Cook) has received an R24 Administrative Supplement Award for R24Da055306 "Wake Forest IMPOWR Dissemination Education and Coordination Center (IDEA-CC)."

Dr. Yashashwi Pokharel is the Site PI for a NIH Subaward from Tulane University Medical Center titled the IMPACTS-MIND “Effectiveness of Implementing an Intensive Blood Pressure Reduction Intervention on Cognitive Decline in Low-income and Minority Hypertensive Patients.” The IMPACTS-MIND (Implementation of Multifaceted PATient-Centered Treatment Strategies for Intensive Blood Pressure Control to Minimize Cognitive Decline) study is a cluster-randomized hybrid implementation-effectiveness trial to test the effectiveness of a multifaceted strategy for intensive blood pressure treatment to slow cognitive decline. The study is being conducted in real-world primary care settings serving racial minority and low-income hypertension patients.

Dr. Ellie Rahbar, in collaboration with Drs. Tim Williams, Jim Jordan, Lucas Neff, and Alberto Figueroa at the University of Michigan, has received two federally funded grants (NIH and DOD-over $5.4 million for the next 4-5 years) to support the development and validation of a new multi-scale 3D-0D closed-loop computational model for hemorrhagic shock, which will be used to optimize the design and implementation of endovascular hemorrhage control devices such as REBOA. These projects aim to develop a novel computational fluid dynamic (CFD) model that can accurately simulate transitional blood flow during phases of active bleeding, aortic occlusion, and resuscitation. In addition, the CFD models will provide new insights into the acute cardiovascular physiologic response to blood loss by integrating both hemodynamic and biologic responses, including oxygen transport, vascular autoregulation, and key biomarkers of acute inflammation.

A team led by Dr. Dalane Kitzman has received three NIH grant awards in just the past year, totaling $35 million. Dr. Kitzman’s team includes collaborators from Wake Forest Cardiovascular Medicine, Geriatrics and Gerontology, Public Health Sciences, Wake Forest University Reynolda Department of Exercise and Sports Science, and Sanger Heart and Vascular Institute. The successes from these collaborations were recently highlighted by Eugene Woods at an Academic Forum. The largest, most recent NIH award is a 5-year trial called Physical Rehabilitation for Older Patients with Acute HFpEF (REHAB-HFpEF). The application was funded on first submission and involves 20 sites, 46 investigators plus staff, 880 patients, and a budget of $30 million. This phase 3 trial is based on the promising results of the phase 2 REHAB-HF trial which was reported last July in NEJM. The REHAB-HFpEF trial will determine whether a novel physical rehabilitation intervention will improve the primary outcome of combined all-cause rehospitalizations and mortality in patients hospitalized for heart failure with preserved ejection fraction (HFpEF), which is

Continued on page 6
FUNDING continued

nearly unique to older persons, particularly women and Black persons, and for which there are few treatment options.

The following CVSC Pilot Projects were funded:

**Dr. Stacey Wolfe - Neurosurgery**

“Hypertension worsens secondary brain injury after ICH by Piezo1 mechanoreceptor-induced IL-12 release from monocyte/macrophages” Key Personnel – Drs. Debra Diz (Surgery-Hypertension), Resto Asmis (Internal Medicine) and Zhidan Xiang (Neurosurgery).

The proposal/study will characterize the cellular mechanisms involved in intracerebral stroke (ICH).

**Dr. Katherine L. Cook - Surgery-Hypertension**

“Targeting inositol-requiring enzyme-1 (IRE1) to prevent chemotherapy-related cardiotoxicity in triple negative breast cancer. Key Personnel – Dr. Katherine Cook (Surgery-Hypertension).

The proposal/study will characterize the cellular mechanisms involved in intracerebral stroke (ICH).

**Dr. Andrew South - Pediatrics**


This proposal/project/study will characterize the circulating and urinary components of the renin-angiotensin system (RAS), klotho and uric acid to determine their association with mother-child determinants in the origin of cardiovascular disease (CVD) such as hypertension; specifically, associations of maternal cardiovascular health and offspring early-life weight gain, as well as offspring blood pressure and target organ damage.

The study assesses the role of IRE-1 in Adriamycin/Cyclophosphamide (AD/CYP)-induced cardiac damage in mice fed a Western diet with a tumor burden.

**PUBLICATIONS**

Between the months of May-August, Cardiovascular Sciences Center members published **114** manuscripts. Of these, **8** were CVSC first author publications. Below we highlight several of those.


*This article was selected by the editors as the “Best Clinical Science Paper” of the year for the Journal Hypertension.*
**AWARDS AND ACCOMPLISHMENTS**

Dr. Dermot Phelan served as Co-Chair for the recently published American Society of Echocardiography Practice Guidelines for the imaging evaluation of patients with hypertrophic cardiomyopathy. The document entitled “Recommendations for Multimodality Cardiovascular Imaging of Patients with Hypertrophic Cardiomyopathy: An Update from the American Society of Echocardiography, in Collaboration with the American Society of Nuclear Cardiology, the Society for Cardiovascular Magnetic Resonance, and the Society of Cardiovascular Computed Tomography” was published in the Journal of the American Society of Echocardiography (JASE) in June. Dr. Phelan is Co-Director of the Sanger Heart & Vascular Institute’s Hypertrophic Cardiomyopathy Association (HCMA) Center of Excellence.

Dr. Christopher Schaich received the award for Best Poster – Vascular Cognitive Disorders presented at the Alzheimer’s Association International Conference (AAIC) 2022 for presenting the following abstract: Schaich CL, Mujtaba M, Hugenschmidt CE, Jung Y, Bertoni AG, Shah SJ, Chen H, Kitzman DW, Hughes TM. Heart Failure Associations with Cerebral Structure: A Combined Analysis from the Multi-Ethnic Study of Atherosclerosis and SECRET-II Trial of Heart Failure with Preserved Ejection Fraction.

Dr. Chia-Chi Chuang Key was selected as the recipient of the 2022 Daryl and Marguerite Errett Discovery Award which provides support for one outstanding post-doctoral fellow or early career faculty member to conduct cutting-edge research in biomedicine and launch promising projects that nurture the careers of gifted young investigators who will have an impact on pioneering developments that advance human health.

Dr. Yashashwi Pokharel was selected as a WFUSOM CTSI Translational Research Academy Scholar.

Dr. Elizabeth Stirling won the Gordon A. Melson Outstanding Doctoral Student Award.

**AUSTIN’S DATA, TIPS & TOOLS**

**Variable Selection using LASSO Regression**

A common problem in many statistical association analyses is the identification of informative independent variables in a dataset with moderate or highly correlated data. This issue can be compounded in datasets with a high number of features (hundreds of features). Examples of this include RNAseq data or micro-array data.

One method for variable selection is LASSO regression. LASSO regression is similar to the typical regression techniques like linear and logistic regression in that it produces beta (or coefficient) estimates for each independent variable’s effect on the outcome. What makes LASSO distinct is that it incorporates a regularization parameter. This parameter forces independent variables that are correlated with other independent variables, but not associated with the outcome, to have coefficient estimates equal to zero. Variables with a non-zero coefficient can be considered as import variables and can be used subsequent analysis/modeling. It should be noted that is best suited for data with continuous variables; however, it can handle categorical data as well.

The LASSO regression algorithm is implemented in common statistical programming languages like R (the “glmnet” package) and SAS (“PROC GLMSELECT”). This technique is also implemented in JMP.

If you have any questions about these resources (or others not mentioned) don’t hesitate to contact me!

Austin Seals, MSA
601-383-2073
aseals@wakehealth.edu
Dr. Cheryl Bushnell and team developed the Center for Transformative Stroke Care which is supported by the Opportunity Fund. The mission of the Center for Transformative Stroke Care is to expand and synergize translational stroke research to transform stroke care across the continuum with the aLHS approach. The Center programs will specifically address health equity and diversity across the lifespan. The Center for Stroke Transformative Care Director will recruit a Director and Associate Director with international reputations in stroke clinical research, specifically in population health, epidemiology, and/or health services research.

Under the leadership of Dr. Mike Miller, an Opportunity Fund award has been designated to recruit leadership to establish a new Center for Remote Patient and Participant Monitoring (CRPPM). The CRPPM will be developed to promote innovative development and effective, efficient, and equitable use of remote and digital engagement technologies. The Center will recruit a Director and Associate Director with goals of: growing extramural funding, and evaluating and harnessing existing expertise to provide a centralized entity with expertise spanning the AH/WFUSM Enterprise; generating high levels of collaboration across new and existing institutional centers; cataloging existing technology and infrastructure (e.g., dissemination channels) available to researchers; and developing new technology applicable to piloting and implementation of new research discoveries into clinical care.

Those involved in developing the CRPPM concept include the following individuals:

Biomedical Engineering – Joel Stitzel, PhD
Biostatistics and Data Science
    Walter Ambrosius, PhD
    Scott Rushing
Cancer Biology – Umit Topaloglu, PhD
Cardiology
    Oguz Akbilgic, PhD
    David Herrington, MD, PhD
    Elsayed Soliman, MD, MS
CTSI Informatics Program
    Brian Ostasiewski
General Internal Medicine
    Metin Gurcan, PhD
    David Miller, MD, MS
Gerontology and Geriatric Medicine
    Timothy Hughes, PhD
    Jeff Williamson, MD, MHS
Information and Analytics Services
    Will Showalter, MPA, MURP
Neurology – Cheryl Bushnell, MD
Pediatrics – Eric Kirkendall, MBI, MD
Psychiatry and Behavioral Medicine
    Ruth Benca, MD, PhD
Public Health Sciences
    Michael E. Miller, PhD
    Lynne Wagenknecht, DrPH
Social Sciences and Health Policy
    Kathleen Hayden, PhD

WFU Health & Exercise Science
    Jason Fanning, PhD

CHARLOTTE REGION:
Sanger Heart & Vascular Institute
    William Downey, MD
Virtual Care
    Guy Glorioso, MBA, MHA
    Molly McColl, MBA
    Joshua Brown, PhD