GOOD NEWS!
Wake Forest School of Medicine Cardiovascular Science Center
Winter 2021

NEW YEAR, NEW STUDY

Stroke division chief and professor of Neurology, Dr. Cheryl Bushnell, who is the PI of the Phased Large Award for Comparative Effectiveness Research (PLACER), was recently selected to receive a $29.9 million, six-and-a-half year award from Patient-Centered Outcomes Research Institute (PCORI). The other 4 funded applications were from Massachusetts General Hospital, Brigham and Women’s Hospital, University of Michigan, and Kaiser Foundation. The study will compare two ways to control high blood pressure in the first six months after a stroke. The first way is to teach the patient to use a Bluetooth-enabled blood pressure cuff at home and to provide clinical care remotely. The second way is to measure the patient’s blood pressure frequently at a clinic and provide clinical care in person. The team plans to enroll 3,200 people in the study. People who consent to be in the study will be assigned at random to one of two groups. Both groups will receive intensive blood pressure management for six months so there is a benefit to being in each group. Patients in one group will receive care via telehealth (Intensive Tailored Telehealth Management, or ITTM) while the other group will receive care in-person (Intensive Clinic Management, or ICM). This study is an extension of a previous research collaboration between WFSM and the UNC Gillings School of Global Public Health on post-acute stroke care – COMprehensive Post-Acute Stroke Services Study, or COMPASS.
AHA Scientific Sessions were held virtually November 13-15, 2021. Sanger Heart and Vascular/Wake Forest School of Medicine presented 35 total abstracts/posters this year. **Drs. Cheping Cheng** and **Heng-Jie Cheng’s** lab accounted for 9 of those abstracts. Dr. Heng-Jie Cheng was the first author on three of those presentations as follows:

- **Heng-Jie Cheng**, Zhe Chen, Peng Zhou, Jing Cao, Xiaqiang Sun, David M Herrington, David Zhao, Dalane W Kitzman, Che Ping Cheng. *Upregulation of Cardiac SERCA 2a is a Key Molecular Mechanism of the Protective Effect on Myocardial Aging in Beta3-Adrenergic Receptor Deficiency Mice.*
- **Heng-Jie Cheng**, Jing Cao, Xiaqiang Sun, Yixi Liu, Dalane W Kitzman, David Zhao, Donald McClain, Che Ping Cheng. *Molecular Mechanism of Chronic Beta3-Adrenergic Receptor Antagonist Caused Regression of Diabetic Cardiomyopathy in a Murine Model with Type 2 Diabetes.*
- **Heng-Jie Cheng**, Xiaoqiang Sun, Jing Cao, Zhe Chen, Yixi Liu, David M Herrington, David Zhao, Donald McClain, Dalane W Kitzman, Che Ping Cheng. *Chronic Beta3-Adrenergic Receptor Antagonist Therapy Rescues Diabetic Cardiomyopathy Through Ca2+/Calmodulin-Dependent Protein Kinase II Inhibition in a Type II Diabetes Murine Model.*

Dr. Che Ping Cheng was first author on the below two presentations:

- **Che Ping Cheng**, Xiaowei Zhang, Tiankai Li, Zhi Zhang, Xiaqiang Sun, Jing Cao, David M Herrington, David Zhao, Heng-Jie Cheng. *Effects of Acute Doses of Cocaine on Arterial Left Ventricular Coupling and Mechanical Efficiency in Conscious, Chronically Instrumented Dogs.*
- **Che Ping Cheng**, Zhe Chen, Jing Cao, Xiaqiang Sun, Peng Zhou, David Zhao, David M Herrington, Dalane W Kitzman, Heng-Jie Cheng. *Gender Differences and Aging on Beta-Adrenergic Receptor Subtypes Expression and Function in Murine Left Ventricular Myocytes.*

**Dr. Michael Shapiro** was invited to give Cardiology Grand Rounds at the University of Minnesota on December 8, 2021. The title of his talk was, “Pushing the PCSK9 Envelope – From Small Molecules to Science Fiction”.

Dr. Shapiro was also invited to give an oral presentation at AHA Scientific Sessions. The title of that presentation was, “Efficacy and Safety of Bempedoic Acid in Patients with Metabolic Syndrome”. In addition, he also had 3 other abstracts accepted for presentation at Sessions as follows:

- Karwatowska-Prokopczuk E, Tardif JC, Gaudet D, Ballantyne CM, Shapiro MD, Moriarty PM, Baum SJ, St. Amour E, Alexander VJ, Xia S, Otvos JD, Witztum JL, Tsimikas S. *Effect of APOCIII-LRx on Lipoprotein Size and Particle Numbers Measured by NMR in Patients with Hypertriglyceridemia: Results of the AKCEA-APOCIII-LRx Trial.*
- Chevli PA, Islam T, Pokharel Y, Rodriguez F, Virani SS, Blaha MJ, Betoni AG, Budoff M, Otvos JD, Shapiro MD. *Association Between Remnant Cholesterol, High-Sensitivity C-reactive Protein, and Risk of Atherosclerotic Cardiovascular Disease Events in the Multi-ethnic Study of Atherosclerosis (MESA).*

**Drs. Carolyn Park** and **Yashashwi Pokharel** had their abstract accepted at to the Society for Cardiovascular Magnetic Resonance (SCMR) conference as a poster presentation. The title of the abstract is, “Fibrosing Mediastinitis: A Rare Case Associated with Immune Checkpoint Inhibitor Use in a Melanoma Patient.” The conference is scheduled for February 2022.
Dr. Anita Kelkar had two abstracts accepted to the International Society of Heart & Lung Transplant Conference scheduled to be held in April 2022. The titles of these abstracts are, “Clinical Utility of Patient Reported Outcome Instruments in the Management of Pulmonary Hypertension” (senior author) and “Clinical Decision Support to Identify Care Gaps and Improve Efficiency of Health Maintenance Documentation for Heart Transplant Recipients”.

Dr. Olivia Gilbert was invited to give a lecture at the ACC’s North Carolina and South Carolina Chapter Meeting held in September 2021. Her lecture was titled, “Advances in Hypertrophic Cardiomyopathy: Current Standards & Frontiers.” She also served on a panel discussion at the same meeting, titled, “Choosing the Right Practice for You” during the Fellows-In-Training session.

In recognition of World Heart Day on September 29, 2021, Dr. Olivia Gilbert was invited by Philips for a discussion on cardiovascular disease. She was joined by two other leading cardiologists, Drs. Jennifer Franke (Philips Medical Officer) and Magnus Jensen (Amager og Hvidovre Hospital, Copenhagen, Denmark). The discussion highlighted the resurgence of cardiovascular disease, what needs to happen to reverse the trend, the role of technology in tackling the challenges, and how to build a cardiac care system that improves the quality of care and experience for both patients and professionals. Read the interview here.

Dr. Saraschandra Vallabhajosyula was invited to speak at Internal Medicine Grand Rounds, Texas Tech University Health Science Center in December. The title of his talk was, “Cardiogenic Shock in 2021: Opportunities and Challenges.” In the same month, he also presented at SOA 21, Intensive Care Society in London UK. The title of that presentation was, “Critical Care Training in the United States: Past Present, and Future.” In addition to these two presentations in 2021, Dr. Vallabhajosyula also participated as a session moderator for the ACC-Indonesian Society of Interventional Cardiology in a session on Support Strategies in Cardiogenic Shock and moderated an ACC session on Interventional, Early Career, & FIT Monthly Cath Case Discussions.

Dr. Oguz Akbilgic has an abstract accepted for presentation at The Alzheimer’s & Parkinson’s Disease Conference in Barcelona, Spain in March 2022. The title of his abstract is, “Deep Learning on ECGs to Identify Parkinson’s Disease at Prodromal Stage.”

Drs. Andrew South, Patricia Gallagher, Liliya Yamaleyeva, Mark Chappell and Debra Diz presented invited talks virtually at the XIII International Symposium on Vasoactive Peptides, October 15th -18th, Brazil. The presentations are as follows:

- Dr. Andrew South “Angiotensin-(1-7) in Pediatric Hypertension: New Mechanistic Insights” https://vasoactivepeptides.org/andrew-south/
- Dr. Liliya Yamaleyeva “Apelin Receptor System and Cardiovascular Health in Preeclampsia” https://vasoactivepeptides.org/liliya-yamaleyeva/
- Dr. Mark Chappell “Characterization of the RAS enzymes ACE, ACE2 and Neprilysin in Human Exosomes” https://vasoactivepeptides.org/mark-chappell-2/
- Dr. Debra Diz “Sex-dependent brain signaling changes accompany dysregulation of blood pressure in sheep with fetal-programmed brain RAS alterations and neuro-inflammation” https://vasoactivepeptides.org/debra-diz/

Yismeilin Feliz-Mosquea, a graduate student mentored by Drs. Katherine Cook and David Soto-Pantoja, presented a selected talk for the session: Cardiovascular Biology & ECM Remodeling, on Wednesday, September 15 at 11:30am at the 2021 American Society for Matrix Biology (ASMB) Meeting. Her talk was titled “Inositol-requiring enzyme-1 (IRE1) signaling impacts triple-negative breast cancer chemotherapy sensitivity preventing chemotherapy-related cardiotoxicity”.

Steven M. Bronson, DVM, a post-doctoral fellow mentored by Dr. David Soto-Pantoja, presented a selected talk at the 2021 American Society for Matrix Biology (ASMB) Meeting. His 15-minute talk was titled “Blockade of CD47/Thrombospondin-1 signaling modulates cellular energetics as a protective mechanism from chemotherapy-induced cardiac injury.”

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The following abstracts were presented by EICS/ENGAGED students who also received registration waivers for the Annual Biomedical Research Conference for Minority Students (ABRMMS) meeting November 10-13, 2021

**EICS Students**

- **Don Asafu-Adjaye** (Emory University); Dr. Mark Chappell- Mentor “Optimal Conditions for Assessment of the SARS-COV-2 Binding Protein ACE2 in Human Serum”
- **Alex Bart** (Lafayette College); Dr. Allison Caban-Holt- Mentor “Is Cigarette Smoking Good for Problem Solving”
- **Dana Carreno** (Johns Hopkins University); Dr. Joanne Sandberg- Mentor “Diabetes Inheritance and Causation: Lay Beliefs among Latina immigrants with Limited Education”
- **Evelyn Farkas** (Georgia State University) Dr. Ken Kishida- Mentor “Adaptive Choice Behavior and Subjective Feelings are Predictive of Clinical Outcomes in Depression”
- **Erian Watkins** (Washington University in St. Louis); Dr. David Soto-Pantoja- Mentor “Role of RIE1 Signaling in Chemotherapy-related Cardiac Toxicity”

**ENGAGED Students**

- **Elili Brown** (Occidental College); Drs. Christopher Schaich and Nildris Cruz-Diaz – Mentors “Visit-to-visit Glucose Variability and its Association with Dementia-related Neuroimaging Markers: Preliminary Analyses from the Multi-Ethnic Study of Atherosclerosis (MESA)” and “Young Hypertensive Male and Female Rats Have Increased Carotid Arterial Stiffness”
- **Drew Nwokeafor-Laz** (Wake Forest University); Dr. Bethany Kerr-Mentor “Effect of SCF and DCC-2618 Treatment on Prostate Cancer Bone Homing”
- **Moriah Wells** (Winston Salem State University); Dr. Ashley Sanderlin-Mentor “Sleep Oxygen Saturation Association with Mood and Behavior in MCI”
AWARDS AND ACCOMPLISHMENTS

In October, Dr. Dalane Kitzman received the 2021 Michael L. Pollock Established Investigator Award from the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) in recognition of his outstanding work in the field of cardiac rehabilitation. This award is presented to an individual who has made significant advances in the field of cardiac rehabilitation through his/her research and scholarly contributions and has earned national prominence in his/her field through contributions in contemporary research and/or education.

Dr. Dalane Kitzman and Mr. Ben Nelson were selected for a Top Research Site Award for their outstanding performance in the REHAB-HF clinical trial. This award is given on behalf of Dr. Christopher O’Connor, HFSA Research Committee Chair and HF-Collaboratory PI. In addition to an invitation with complementary registration to the Heart Failure Society of America Scientific Sessions where they were be recognized for the award, Dr. Kitzman and Mr. Nelson were also been invited to join the HFSA Research Network, which is comprised of clinical investigators and coordinators within the HFSA.

The PREVENTABLE trial investigator team was selected to receive a WFSOM Research Award for New Team Science in November 2021. Faculty members who are involved with PREVENTABLE include: Drs. Walter Ambrosius (MPI), Jeffery Williamson (MPI), Michael Bancks, Kathryn Callahan, Denise Houston, Dalane Kitzman, Barbara Nicklas, Nicholas Pajewski, Steve Rapp, David Reboussin, Gary Rosenthal, Bonnie Sachs, and Jamie Speiser. The award was presented to the team November 17, 2021 at the WFSOM Research Awards Day Ceremony. Funded by the National Institute on Aging, the PREVENTABLE trial is the largest (30,000 patients) and most expensive trial ever funded by the NIA. The purpose of the trial is to determine whether atorvastatin improves geriatric and cardiovascular outcomes in persons 75 years and older.

Dr. Saraschandra Vallabhajosyula was recognized by the Cardiovascular Research Technologies (CRT) as a Yong Leader. CRT provides a forum for exemplary education for interventional cardiologists, general cardiologists, cardiothoracic and vascular surgeons, catheterization laboratory managers, nurses and technologists, scientists and those with an interest in cardiovascular medicine.

Dr. Olivia Gilbert was appointed to the planning committee for the ACC’S Faculty Quality Summit and participated in a moderated session titled, “The New Normal: Innovative Approaches to Managing and Measuring Your Accreditation and Registry Workforce.” The Quality Summit was held virtually in September 2021. In addition, Dr. Gilbert has also been nominated by the American College of Cardiology to be considered as a writing committee member for the 2023 HRS/EHRA/APHRS/LAHRS Expert Consensus Statement on Practical Management of the remote Device Clinic. Dr. Gilbert has also been invited to serve on the ACC’S Clinical Policy Approval Committee for a 3-year term. That committee is comprised of 40 College leaders with the charge of reviewing and approving clinical policy documents on behalf of the College.

WFSOM/Atrium Health held the 2021 Research Awards Day ceremony on November 17, 2021. Several CVSC members were among the awardees:

- **Dr. Giselle Melendez**: Early Career Investigator in Clinical/Population Science
- **Dr. Kylie Kavanagh**: Mid-Career Investigator in Basic/Translational Science
- **Dr. Allyn Howlett** and **Dr. Timothy Howard**: Established Investigator in Basic/Translational Science
- **Dr. Katherine Cook**: Early Career Investigator in Basic/Translational Science

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Dr. Elijah Beaty was named to the Board of Editors for Circulation: Arrhythmia and Electrophysiology. In this new role, Dr. Beaty will work with Dr. Paul Wang, Editor in Chief, to review EP specific articles submitted to the journal for publication.

Yismeilin Feliz-Mosquea, mentored by Drs. Katherine Cook and David Soto-Pantoja, received the Silver Award in the basic science student category at the 2021 Surgical Sciences Residents’ and Fellows’ Research Day.

IBM Watson Health recognizes Atrium Health Pineville as a winner of the 2022 Top 50 Cardiovascular Hospitals award, part of the Watson Health 100 Top Hospitals national benchmark series.

Sanger Heart and Vascular TAVR program has been granted a 3-star rating by the STS/ACC TVT public reporting ranking — its highest designation. This is granted to only the top 10% of TAVR programs in the US. SHVI is now one of only a small number of programs in the US to receive both the highest STS/ACC TVT Star Rating (3/3) and the highest USNWR ranking (5/5).

TAVR program at Atrium Health Cabarrus completed its 100th TAVR case. In addition to rapid growth under Dr. Terence Hill and Dr. Christopher Cici’s leadership, the team also achieved 0% 30-day mortality rate; 0% 1-year mortality rate and stroke rates; and 0% 30-day mod/severe AI in their first 53 patients at the 1-year mark.

AUSTIN’S DATA, TIPS & TOOLS

Creating a Propensity Score Matched Cohort

Match cohort analysis is often used when investigators want to compare the effects of a treatment against a control while taking into account the effect of confounders in observational studies. These are variables that might be associated with both the treatment variable and the outcome of interest. In a matched analysis a member of the treatment group is matched with a control member with similar characteristics.

There are two main steps to creating a propensity score matched cohort. The first includes creating a logistic regression model to estimate propensity (probability) of being in the treatment group. In the second step, each treatment member is matched to a control member based on propensity score. There are several methods that can be used here but the most common is nearest neighbor matching. Most implementations will use 1:1 matching schema, but 1: many, where a treatment member is matched to multiple control members, can also be done. However, any multivariate modeling done after 1: many matching will need to be weighted. Propensity score matching is implemented in most statistical software. In R, it can be found in MatchIt package and in SAS it can be done with PSMatch procedure. If you have any questions about how this approach can be applied to your data please don’t hesitate to contact me!

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CAREER CORNER

Wake Forest School of Medicine summer programs provide increased opportunities for underrepresented students to diversify the pipeline of future students by offering a range of STEM research experiences. Programs funded by Wake Forest School of Medicine, philanthropy and grants from NSF, NHLBI and NIA and led by faculty in the Cardiovascular Sciences Center, Center for Precision Medicine, Wake Forest Institute for Regenerative Medicine, Informatics, Biomedical Engineering, the Hypertension and Vascular Research Center and the Sticht Center for Healthy Aging and Alzheimer’s Prevention. Undergraduate and high school students in the Biomedical Engineering (BME), Excellence in Cardiovascular Sciences (EICS), and Enhancing Undergraduate Education and Research in Aging to Eliminate Health Disparities (ENGAGED) summer programs participate in research projects that study aging, cardiovascular disease, trauma, informatics and health disparities. To learn more about the summer programs offered at WFSOM, visit their information page here:
https://school.wakehealth.edu/Features/Education/DiversifyingPipeline
Below we highlight several of those.


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**ANNOUNCEMENTS**

A $5.2M grant has been awarded by the National Institute of Aging to **Drs. Shively, Craft**, and **Whitlow** (MPIs) for the Development of an Innovative Vervet (Chlorocebus aethiops sabaeus) Model of Early Alzheimer’s-like Neuropathology and Symptomatology (R24AG073199). This project will further establish a novel and promising model of late-onset sporadic Alzheimer’s disease – the most common type – in vervet monkeys. Development of this novel animal model will yield insights into the causes and early neuropathology of Alzheimer’s disease, and identify promising targets for early intervention that could alter the course of this devastating disease.

We will determine age-related changes in cognitive and physical function, cerebrospinal fluid and imaging biomarkers; identify targets for early intervention by characterizing modifiable risk factors for late-onset sporadic AD; and assess the predictive validity of these risk factors for neuropathology in 30 vervets from our Vervet Research Colony (from 10 to 30 years old) which comprise the Aging Vervet Cohort. This award will support the Aging Vervet Cohort until natural death at which time the brain will be collected and characterized for early Alzheimer’s disease (AD)-like neuropathology. Premortem risk factors to be regularly assessed include psychosocial stress, sleep, gait speed, physical activity, autonomic function, adiposity, blood pressure, and glucose metabolism.

CVD risk factors are also prominent risk factors for Alzheimer’s disease. Ancillary studies are very welcome! Contact Dr. Shively for further information.

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The Cardiovascular Sciences Center (CVSC) is seeking proposals for projects in need of support to promote new areas or technologies for cardiovascular research (basic, clinical, population), as well as to foster collaborative efforts or new collaborations, particularly across the Atrium Health System. The goal of the pilot project is to allow investigators to pursue novel and innovative ideas that will improve the likelihood of obtaining extramural funding. The funding is also meant to allow investigators to perform critical experiments, access core facilities or improve analyses that address specific critiques raised by reviewers for extramural funding.

Wake Forest Contributes to National COVID-19 Collaborative Research

Four Wake Forest NHLBI-funded cohort studies are participating in the “Collaborative Cohort of Cohorts for COVID-19 Research” (aka, C4R) to learn about COVID-19 health effects. These studies include ARIC, MESA, SARP, and SPIROMICS. This national study includes more than 50,000 participants and will help us learn why some people get infected and become very ill, while others do not. This study will evaluate people with and without prior COVID infections.

These four cohort studies are also involved in a collaboration called “Researching COVID to Enhance Recovery” (RECOVER). This study will focus primarily on people with prior infections to learn why some people recover quickly, while others have prolonged symptoms such as heart problems, brain fog, shortness of breath, depression, or sleep problems. Results from these studies will help doctors learn more about how to treat infected people and how to prevent COVID infections.

If you would like to review the Center’s information, including mission, goals, and current membership, please refer to the following link: https://school.wakehealth.edu/Departments/Internal-Medicine/Cardiovascular-Medicine/Cardiovascular-Sciences-Center