Good News. Wake Forest School of Medicine Cardiovascular Sciences Center

First Quarter 2020

CVSC Faculty Contribute to National Guidelines and Scientific Statements about ACEis and ARBs in COVID-19 Infections



Dr. South

The enzyme Angiotensin Converting Enzyme 2 (ACE2), which degrades the pro-hypertensive hormone Angiotensin II to form the counter regulatory peptide Ang-(1-7), is also the co-receptor for SARS-COV-1 and the new coronavirus SARS-COV-2. Recognition of ACE2 as a factor in COVID-19 has increased interest in publications on regulation and function of ACE2 by CVSC faculty in Hypertension and Vascular Research (HVR). Interest in recent publications on the Renin-Angiotensin System (RAS) in children and young adults by **Dr**. **Andrew South, MD, MS**, Assistant Professor, Department of Pediatrics, CVSC and HVR with perinatal research col-

leagues (**Drs. Washburn, Chappell, Shaltout, Diz, Jensen**) led to Dr. South's role as an expert contributor on the NephJC website and the NephJC COVID-19 and ACE2 in Cardiovascular, Lung and Kidney working group (<u>https://cjasn.asnjournals.org/content/</u> <u>early/2020/03/27/CJN.03530320</u>), among

other society guideline publications. A first author Perspective for American Journal of Physiology: Heart and Circulation co-authored by **Drs. Diz and Chappell** (<u>https://journals.physiology.org/doi/ abs/10.1152/ajpheart.00217.2020</u>) addresses the need for information related to the regulation of ACE2 and continued use of the antihypertensive ACE inhibitors and AT1 receptor blockers during COVID-19. **Drs. Gwathmey and Brosnihan** [Bioanalytical Core Laboratory (BAC)] and **Dr. Chappell** are part of internal and external collaborations for expertise on measurements of the RAS.



Dr. Chappell

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Wake Forest School of Medicine

Grant Awards by CVSC Faculty July-December 2019

During the time period of December 15, 2019, -March 25, 2020, there were **28** new grants awarded to CVSC faculty members. **22** different CVSC faculty from many areas of the institution were either a PI or Co-I on these projects. The total dollars awarded were **\$10,284,248!** Below we highlight a few of the top awardees.



Justin Moore, PhD R21- "A Coordinated Parent/Child Dyad Weight Loss Intervention: Dyad Plus" Key Personnel: Jamy Ard, MD \$201,094



Kiran Solingapuram Sai, PhD R01- "Evaluating Microtubule Binding As a Potential Imaging Biomarker for Alzheimer's Disease" Key Personnel: Suzanne Craft, PhD \$499,595



Genesio Karere, PhD was the recipient of a basic/translational pilot award from CTSI/co-funded by the CVSC. The title of his project is, "MicroRNA-gene Networks Underlying Early Coronary Atherosclerosis."



Lindsay Reynolds, PhD, received CTSI Pilot funding for: A Feasibility Study Incorporating DNA Methylation-Predicted Aging with a Dietary Intervention to Improve Cardiometabolic Health co-funded by the Cardiovascular Sciences Center.



David Soto-Pantoja, PhD American Cancer Society- "Targeting CD47 Prevents Cancer Therapy Adverse Effects" Key Personnel: Giselle Melendez, MD \$782,000



Chad Miller, MD

National Foundation of Emergency Medicine Training Grant- "NFoEM Scholar/ Mentor Program" \$30,000



Tina Brinkley, PhD, and collaborators: Mechanisms Underlying Cerebrovascular Dysfunction in Obesity and Weight Loss was funded by the CVSC for 1 year at \$30,000.



Stacey Wolfe, MD, and collaborators: "The Effect of Cardiometabolic Disease on the Neuroinflammatory Response after Intracerebral hemorrhage in the hypertensive Ren-2 transgenic rat" was funded by CVSC for 1 year at \$30,000.



Timothy Williams, MD received two grant awards from the Department of the Army. The two projects were titled, "Portable Device for Rapid Vascular Access in Trauma and Hemorrhage Control" and the other is, "Evaluation of

Partial Flow Strategies in Hemorrhage and Traumatic Brain Injury with Endovascular Variable Aortic Control." One of the awards is with Wake as the prime, for \$1 million. The other is with Wake as a sub-awardee, for \$400K.

Accomplishments and Awards



Yoshi Otaki, MD, PhD, was accepted to the American Association of Thoracic Surgery and will be inducted during a ceremony in New York on April 25th.

Dr. Otaki

Congratulations to Lauren West-Livingston (Vascular Surgery) on receiving her PhD (mentors are Gabriela Velazquez-Ramirez, MD, and Randolph Geary, MD)

Brett Frye, MD, was appointed to the Gerontology T32 and was accepted into the CTSI K&R Writers Series led by **Debra Diz, PhD, and Barbara Nicklas, PhD**.

Kenysha Clear from Dr. Katherine Cook's lab has been accepted into Wake Forest Graduate School.



Gabriela Velazquez-Ramirez, MD, was promoted to Associate Professor of Vascular and Endovascular Surgery as of July 1, 2020

Andrew Michael South, MD, became a member of the Mid-West Pediatric Nephrology Consortium and the Neonatal Kidney Collaborative.

Dr. Velazquez-Ramirez

uez- **David Soto-Pantoja, PhD**, has been invited to serve in the Florida Breast Cancer Foundation Study Section.

CV COE Faculty Publications from January—March 2020

Over the last three months, Wake Forest School of Medicine CV COE faculty published **84** manuscripts in peer-reviewed journals including PLoS One, JAMA Cardiology, Hypertension, JACC, and Circulation. Below are a few articles from the list. All of the publications can be found at https://www.ncbi.nlm.nih.gov/sites/ myncbi/1JSeQsdreOokM/collections/59382808/public/



Leanne Groban, MD. in collaboration with other CVSC colleagues including Cheping Cheng. MD, Dalane Kitzman, MD, and others, recently published their manuscript titled, "Female Heart Health: Is GPER the missing link?" in Front Endocrinology.

Dr. Groban



Dr. German

Charles German, MD, was first author on a manuscript published in the American Journal of Cardiology, titled, "Relations between Physical Activity, Subclinical Myocardial Injury, and Mortality Cardiovascular in the General Population."



Christopher Schaich, MS, PhD, et al. published a manuscript titled, "Amyloidosis of the Brain and Heart: Two Sides of the Same Coin?" in JA CC Heart Failure.

Dr. Schaich



Bharathi Upadhya, MD, and Dalane Kitzman, MD, published their manuscript titled, "Heart Failure with Preserved Ejection Fraction: New Approaches to Diagnosis and Management" in *Clinical Cardiology*.

Dr. Upadhya

David Soto-Pantoja, PhD, has been invited to talk on a panel at the Integrating Metabolism and Immunity Keystone Symposia in Colorado April 4-8, 2020. He was also invited to give a talk at the 6th Annual Immuno-Oncology Young Investigators' Forum (IOYIF) being held at The Houstonian Hotel, April 16-18, 2020. In addition to these invited presentations, Dr. Soto-Pantoja was also invited participate as a speaker at the National Institute of Environmental Health Sciences on April 15^{th.}

Dr. Soto-Pantoja

Jason Stopyra, MD, MS, had three HEART Pathway Implementation abstracts accepted for presentation at the Society for Academic Emergency Medicine meeting. These abstracts were titled, "HEART Pathways Implementation

safely Reduces Hospitalizations at 1-Year in Patients with Acute Chest Pain," "Age Differences in the Safety and Effectiveness HEART Pathway Accelerated Diagnostic Protocol," and "Sex/Race Differences in Safety and Effectiveness of a Chest Pain Accelerated Diagnostic Protocol at 1-Year."

Invited Presentations



Giselle Melendez, MD, was invited to give a talk titled, "Cardiac Fibrosis and Heart Failure with Chemotherapies" during the Cardio-oncology: Cancer, Chemotherapy and CVD Risk session at the North American Artery Meeting. Also of note, Tina Brinkley, PhD, is on this year's NAA program committee [Conference canceled due to COVID-19].

Dr. Melendez

Catherine Tegeler will present a poster presentation at the American Academy of Neurology annual meeting in Toronto Canada, April 25th to May 1st, titled, "A Pilot, Placebo-controlled Trial of Cereset Research-Standard Operating Procedures for Insomnia." Authors on the project are Catherine Tegeler, Lindsay Howard, Kenzie Brown, Dawn Kellar, Lee Gerdes, Charles Tegeler, MD, and Hossam Shaltout, PhD. [Conference canceled due to COVID-19].



Katherine Cook, PhD, was invited to be the 2020 Louise M. Nicosia Lecturer on Women's Cancer Research at the University Of South Florida Morsani College Of Medicine March 18th in Tampa, FL.

Dr. Cook

Debra Diz, PhD, was scheduled to speak at the American Journal of Physiology-Heart and Circulatory Physiology Editors Symposium at the EB Meeting in San Diego, CA on Monday, April 6th, 2020. The title of her presentation is "Fetal Programmed Angiotensin-(1-7) Deficiency and Sex Differences in Brainstem Signaling Pathways in Sheep." [Conference canceled due to COVID-19].

Diego's Data Tips and Tools



When dealing with a categorical response variable with more than two levels, there are two strong reasons for preferring models that take the ordering into account:

- 1) They are more straightforward, and therefore easier to interpret
- 2) Hypothesis tests are more powerful
- The disadvantage of ordered models is that they impose restrictions that may not be consistent with the
- data. So whenever you use an ordered model, it's important to test whether its restrictions are valid.

This tutorial will focus on ordinal logistic regression (where there is an inherent ordering to the categories). For this tutorial, we'll use the cumulative logit model – aka the ordered logit or ordinal logit model – which is widely applicable and also happens to be the easiest to implement in SAS. Whenever PROC LOGISTIC encounters more than two categories on the dependent variable, it automatically estimates a cumulative logit model. So to run this model, you will write the same SAS code you would for binary logistic regression. You'll notice your output is very similar to a simple PROC LOGISTIC other than the appearance of the table Score Test for the Proportional Odds Assumption – it's sufficient to say that this statistic tests whether the ordinal restrictions are valid, and high p-values are desirable.

The default of the model is to predict the probability of being a lower category rather than a higher category. If you want the probability of being in the jth category or higher, or in other words, you want the model to predict the probability of being in a higher category, then use the DESCENDING option in the MODEL statement. The model defaults to predicting the probability of being in a lower category so each reported odds ratio can be interpreted as the effect of the variable on the odds of being in a lower rather than in a higher category. As a very rough rule of thumb, it's reasonable to estimate a cumulative logit model if there are at least 10 observations for each category on the dependent variable. As the number of categories on the dependent variable gets larger, ordinary linear regression becomes an attractive alternative, especially if the distribution of cases is not highly skewed.

You still need to check for problems of multicollinearity, the way you would typically do in any regression problem. Ordinal logistic regression is even easier in JMP - just make sure your variable type is correct before hitting Fit Model. I can expand upon this nonmathematical explanation with its derivation when you swing by my office!

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In the News

On November 8th, 2019, a baby was born in the Cardiac Cath Lab. The mother was under the care of **Michael Kutcher**, **MD** after she suffered a rare type of heart attack. On November 3rd, 2019, the expectant mother had a spontaneous coronary artery dissection and underwent emergency stenting on her left main coronary artery. During the procedure, she sustained cardiac arrest. Five days later, baby girl Nova was born via cesarean in the cath lab so that Dr. Kutcher and his team could perform advanced cardiac intervention in the event she went into cardiac arrest during the procedure. In the end, the patient gave birth to a healthy baby girl without cardiac events for either the mother or child. News reports on this exciting event were published in US News and the Winston-Salem Journal as well as a feature on Good Morning America.

Dr. Kutcher holding baby Nova with mother, Brittany

On December 13, 2019, the Cardiovascular Medicine Conference room located in Watlington Hall, was rededicated to Dr. C. Glenn Sawyer. Dr. Sawyer helped create the medical school's section on Cardiology and served as chair of the section from 1973 to 1981. As one of his many contributions to the school, Dr. Sawyer and his wife Betsy endowed the C. Glenn Sawyer Scholarship at the WFSM which provides significant financial support to medical students. During the rededication ceremony, **Dr. David Zhao** gave the introduction and welcome, while Dr. Sawyer's son, Mr. Christopher G. Sawyer gave remarks to honor his late father. A portrait of Dr. Sawyer now hangs in the conference room.



Dr. Zhao with Mr. Christopher G. Sawyer, son of Dr. C. Glenn Sawyer

Events

The Women Faculty Pinning Ceremony was held February 11th at the Babcock Auditorium. The ceremony honored the achievements of our women faculty leaders who were among the first full professors in the history of the institution. **Drs. Bridget Brosnihan (#5), Debra Diz (#14), Ann Tallant (#37), and Patricia Gallagher (#78)** were among those receiving pins, as well as many other female CVSC members.



Career Development Corner

2020 Summer Research Programs

Within the Cardiovascular Sciences Center, we now have 2 summer programs-the Excellence in Cardiovascular Sciences (EICS) summer research program which has been ongoing for many years and a new program, Enhancing UNderGraduate Education and Research in AGing to Eliminate Health Disparities (ENGAGED) program (Debra Diz and Tina Brinkley, Co-Directors), which will address the need to increase the diversity of biomedical scientists involved in aging research and the dearth of under-represented (UR) trainees in graduate programs in the biomedical sciences, particularly in aging-related fields. Our plan is to hold the programs together, from May 31st to July 31st. Twenty-four (24) undergraduate students will spend the summer in research laboratories (basic or clinical) on our campus, to learn about biomedical research. We had a number of outstanding applicants, from all over the continental US, and many students have already accepted our invitation to participate in the summer programs. Our NHLBI- and NIA-funded program pays for the stipend, travel and housing cost during the summer for each participant-the only costs to the faculty hosts are expenses related to the research project. If you are interested in hosting one of our students this summer, please contact Dr. Ann Tallant (atallant@wakehealth.edu), Dr. Debra Diz (ddiz@wakehealth.edu) or Dr. Tina Brinkley (tbrinkle@wakehealth.edu). The students, selected based on their academic records and their interest in biomedical research, work in the laboratory for 9 weeks and present a poster of their work at the end of the summer. It is very rewarding to watch these undergraduate students learn about biomedical research and subsequently follow their careers as biomedical scientists.