

# UNC SYSTEM

at the North Carolina Research Campus







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The North Carolina Research Campus

### **RESEARCH HIGHLIGHTS:**

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Appalachian State University North Carolina A&T State University North Carolina Central University North Carolina State University University of North Carolina at Chapel Hill University of North Carolina at Greensboro

Welcome



# Welcome to the North Carolina Research Campus

Welcome to the North Carolina Research Campus.

The seven research centers of the UNC System located at the NC Research Campus (NCRC) are once again proud to present this annual report highlighting research that is "empowering human health through nutrition."

This is an exciting time at the NCRC as Kannapolis transforms around us. With the renovation of the entire downtown area and the emergence of a new baseball stadium, the forward momentum in our community is energizing.

The trajectory of the improvements in our community is reflected in the accomplishments on our campus. In this year's report, you will read about exciting discoveries, many of which were made possible through collaborations bringing together researchers from different universities based at the NCRC. These partnerships bring to fruition the original vision for the campus, harnessing the power of collaboration among North Carolina's premier educational institutions.

In this report, you will also read about examples of translational research. One is a spin-out, personalized nutrition company based on discoveries in the Zeisel lab. Another example is the opening of the NC Food Innovation Lab, which will provide additional opportunities for our scientists to move discoveries from the lab into the marketplace.

Working together, we continue to evolve and grow as a community and as a campus. Thank you for joining us in our relentless pursuit of better human health.

**Cory R. Brouwer, PhD** Executive Director of Research, North Carolina Research Campus

Cory R. Brouwer, PhD



\* Cumulative since 2008

### Annual Report | Fiscal Year 2018-19

# Education and Outreach

### Community Events:

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- NCRC Catalyst Symposium and Poster Competition
- UNC-Chapel Hill Seminar Series
- Faculty Speaker Series
- NCRC Gene-EG Seminars
- UNC-Chapel Hill Appetite for Life Series
- UNC-Chapel Hill with Johnson and Wales University Demo and Nutrition Talks
- NC State Seminar Series
- NC State & UNC-Chapel Hill Summer Tours

# EVENTS 1,500 PARTICIPANTS

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### **STEM Events:**

- NC State Scientist for a Day Program with Kannapolis City Schools
- N.C. A&T Portable Garden Projections
- NCCU and Northwest Cabarrus High School Academy of Sciences & Biotech
- N.C. A&T and George Washington Carver Elementary School Mentoring & Tutor Program
- Cabarrus County Career Connections Day
- NC State & UNC Charlotte P2EP Summer Intern Program
- North Carolina Science Festival







The North Carolina Research Campus, now in its second decade, has become the core of regional research and education for its seven UNC System partner universities:

- Appalachian State University
- North Carolina A&T State University
- North Carolina Central University
- North Carolina State University
- University of North Carolina at Chapel Hill
- University of North Carolina at Charlotte
- University of North Carolina at Greensboro

The physical growth of the campus now encompasses all of Kannapolis, which is, itself, undergoing a complete transformation. Its \$300 million Downtown Revitalization Project is well underway, with infrastructure replacement nearing completion and streetscapes scheduled for a fall 2019 opening.

#### TRANSLATIONAL RESEARCH

Moving discoveries made during basic research out of the lab and applying it to people's lives is called translational research. Our researchers at the North Carolina Research Campus are making a difference in people's lives through their research. Many discoveries they have made in their labs have been directly translated into ways to improve human health through better nutrition and disease prevention.

Prevention is at the center of the new company, SNP Therapeutics, founded by Steven Zeisel, MD, PhD, Director of UNC-Chapel Hill's Nutrition Research Institute.



Zeisel is a world-renowned expert in the field of nutrition and brain development. With his business partner, Jon Kleu, CEO, he has devised a method to merge the latest advances in genomic testing with personalized nutritional formulations in order to treat individualized medical conditions. The company, opening in summer of 2019, works directly with physicians to prescribe scientifically based medical food solutions.

The NC Food Innovation Lab (NCFIL) is nearing completion, with its grand opening scheduled for fall of 2019. The 15,000-square-foot facility, housed in the NCRC Core Lab building, will be the only one of its kind in the country, with a plant-based food focus and cGMP certification. Developed through a partnership between NC State University, the NC Department of Agriculture and Consumer Services, the NC Department of Commerce, and the Economic Development Partnership of NC, the NCFIL is designed to bring together local food entrepreneurs, researchers and industry partners, helping to translate collaborative ideas into new, commercially viable consumer products.



Steve Zeisel, MD, PhD, Founder, SNP Therapeutics, Director and Kenan Distinguished University Professor in Nutrition and Pediatrics



Bill Aimutis, PhD, Director, NC Food Innovation Lab

## **Appalachian State University**

#### Human Performance Lab

The mission of the Human Performance Laboratory (HPL) is to investigate unique nutritional products as countermeasures to exerciseand obesity-induced immune dysfunction, inflammation, illness, and oxidative stress.



David Nieman, DrPH, FACSM, Director and Professor of Health and Exercise Science

#### **KEY FINDINGS**

The HPL, in a collaborative study with NC State, showed that both a brisk walk and an intense run increases the movement of molecules from gut to blood after eating fruit and tea flavonoids. Intestinal bacteria process these fruit and tea flavonoids, creating "gut-derived phenolics" that then circulate through the body at higher levels after exercise. These small molecules exert healthful effects, such as reducing inflammation and oxidative stress. The benefit is short-lived, however, and requires increased fruit and tea intake along with near-daily exercise.

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In a collaborative study with UNC Charlotte and Dole Foods, the HPL developed a targeted metabolomics panel of 26 metabolites that can be used to gauge the level of exercise and recovery, future exercise and sports nutrition studies. Data from several large studies were combined to identify the 26 metabolites that represent hundreds of metabolites that increase to high levels in the body after marathon running and similar exercise. Additional analysis using this panel showed that consuming carbohydrates, such as those found in bananas, could aid in recovery.

In a collaborative study with investigators from Germany, the HPL developed a targeted proteomics panel that can be used to detect overreaching and overtraining in athletes and warfighters. When individuals exercise intensely without appropriate recovery, the immune system does not function normally, resulting in chronic fatigue, poor performance, increased illness, and heightened anxiety and stress. As the body tries to recover from the excessive physical and mental stress, proteins are secreted that can be measured from a single drop of blood. The targeted protein panel that was developed in this study can be used to help athletes avoid the long-term consequences of pushing too hard in training.

## North Carolina A&T State University

### Center for Excellence in Post-Harvest Technologies

The Center focuses on discovering better ways to preserve or process fruits and vegetables to prevent disease, enhance health, and increase value of North Carolina agriculture by finding better ways to retain freshness, preserve healthpromoting compounds and nutrients, and make food safer for consumption.



Leonard Williams, PhD, MBA, Director, Lead Scientist for Food Safety and Microbiology and Professor of Food Sciences

#### **KEY FINDINGS**

Severe peanut allergies affect approximately 1% of the US population. Because there is no cure, allergic individuals must go to great lengths to avoid exposure. Substantial research, therefore, is targeted at identifying ways to reduce these individuals' allergic response. Our group has found that specific combinations of peanut flour and peanut skin-derived polyphenols can significantly reduce the inflammatory response in an animal model, suggesting a potential desensitization strategy for peanut allergy sufferers. Publication: Bansode RR, Plundrich NJ, Randolph PD, Lila MA, Williams LL (2018). Peanut flour aggregation with polyphenolic extracts derived from peanut skin inhibits IgE binding capacity and attenuates RBL-2H3 cells degranulation via MAPK signaling pathway. Food Chem. 263:307-314.

Green saw palmetto (Serenoa repens) is widely used as a medicinal herb and shows particular potential as a treatment of benign prostatic hyperplasia. S. repens grows in the wild in the Southeast US and is thus potentially at risk for habitat loss. While the silver saw palmetto variety tolerates a wider growth climate and is easier to cultivate, its medicinal properties are largely unknown. Our group has shown, through a combination of 3D imaging and metabolomics, that the silver saw palmetto berries and green saw palmetto berries have similar lipid and smallmolecule metabolite profiles. Thus, the **silver saw palmetto** could potentially serve in place of the green saw palmetto as a sustainable medicinal herb. Publication: Jaiswal Y, Weber D, Yerke A, Xue Y, Lehman D, Williams T, Xiao T, Haddad D, Williams L (2019). A substitute variety for agronomically and medicinally important Serenoa repens (saw palmetto). Sci Rep. 9(1):4709.

Genistein is a phytoestrogen commonly found in soy that has shown promise as an anti-cancer agent. We have shown that **dietary genistein can also act to counter some cellular stressors resulting from a high-fat diet.** 

# North Carolina Central University

#### Nutrition Research Program

Our research groups in NCCU/Kannapolis have established unique expertise in zebrafish and mouse models to study hematopoietic disease and cancer biology. Our unique research program facilitates collaborations with researchers from different universities on the NCRC as well as among different university campuses of the UNC System.



Deepak Kumar, PhD, Director of the Julius L. Chambers Biomedical and Biotechnology Research Institute, which includes the NCCU Nutrition Research Program

#### **KEY FINDINGS**

In collaboration with N.C. A&T, our research team discovered that a component of ginger, 10-gingerol, can rescue a genetic blood defect in the model organism zebrafish. Publication: Ferri-Lagneau KF, Haider J, Sang S, Leung T. Rescue of hematopoietic stem/progenitor cells formation in plcg1 zebrafish mutant. Sci Rep. 2019 Jan 21;9(1):244.

Collaborating with researchers at UNC-Chapel Hill's main campus, we are in the process of developing a humanized zebrafish model that can support human bone marrow and peripheral blood cells for drug screening. Publication: *Ma Z, Parris AB, Howard EW, Shi Y, Yang S, Jiang Y, Kong L, Yang X, Caloric restriction inhibits mammary tumorigenesis in MMTV-ErbB2 transgenic mice through the suppression of ER and ErbB2 pathways and inhibition of epithelial cell stemness in premalignant mammary tissues. Carcinogenesis. 2018 Oct 8;39(10):1264-1273.* 

Continuing research on RTK signaling, we found that FGFR overexpression renders breast cancer resistant to Palbociclib, a novel class of drugs targeting CDK4/6 Publication: Lee H, Saini N, Howard EW, Parris AB, Ma Z, Zhao Q, Zhao M, Liu B, Edgerton SM, Thor AD, Yang X. Ganetespib targets multiple levels of the receptor tyrosine kinase signaling cascade and preferentially inhibits ErbB2-overexpressing breast cancer cells. Sci Rep (2018) 8(1), 6829.

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In collaboration with UNC-Chapel Hill and NCCU investigators, and by using a data set from The Cancer Genome Atlas, a public repository of cancer genomic data, and NanoString technology, we have identified a number of key cellular markers that are associated with breast cancer in African American patients.

# North Carolina State University

### Plants for Human Health Institute

The NC State Plants for Human Health Institute uses a transdisciplinary approach to drive its research efforts toward the discovery and translation of the links between plant compounds, disease prevention, and health maintenance. NC State Extension provides a bridge to the community through K-12 STEM education and healthcare-focused outreach.



Mary Ann Lila, PhD, Director and David H. Murdock Distinguished Professor

### **KEY FINDINGS**

One of the most evident features of the inflammatory response is the generation of a pro-oxidative environment, which begins locally, close to the site of tissue damage or infection, but eventually can become a chronic challenge for the organism. Giuseppe Valacchi, PhD, developed a new term in physiopathology: OxInflammation. The term describes a permanent pro-oxidative feature present in a not-yet-clinically-detectable inflammatory process, leading, in the long run, to systemic damage. OxInflammation is useful as a biomarker of inflammation although an inflammatory status is not clinically evident. Publication: Valacchi G, Virgili F, Cervellati C, Pecorelli A. OxInflammation: From Subclinical Condition to Pathological Biomarker. Frontiers in Physiology. 2018 Jul 9;9:858.

The Ferruzzi lab continues to work on the development of nutritionally enhanced porridges for nutrient deficient populations in West Africa.

The initial formulation work to develop an iron-rich porridge using a carotenoid-rich native plant has transitioned to consumer field research, where consumer acceptance (or resistance) of the product characteristics is being evaluated to help ensure successful adoption of the porridge and subsequent health improvement. Publication: *van der Merwe R, Kruger J, Ferruzzi MG, Duodu KG and Talyor JRN. Improving iron and zinc bioaccessibility through food-to-food fortification of pearl millet with tropical plant foodstuffs (moringa leaf powder, roselle calyces and baobab fruit pulp). Journal of Food Science and Technology. 2019 Apr 56(4):2244-2256.* 

The Kay lab has been working toward establishing the human metabolome of commonly consumed phytochemical-rich foods using an in-house mass spectrometry library. Foods evaluated include strawberry, blueberry, chocolate, banana, mango, tea, and a polyphenolrich supplement (containing quercetin, anthocyanins and flavan-3-ols). The common finding across these interventions is that the human metabolome is more reflective of the microbiome than our own human metabolic enzyme potential. These findings will ultimately aid in establishing the utility of phytochemical-rich foods in nutrition and disease prevention. Publication: *Williamson G, Kay CD, Crozier A: The bioavailability, transport, and bioactivity of dietary flavonoids: A review from a historical perspective. Comprehensive Reviews in Food Science and Food Safety. 2018 17(5):1054-1112.* 

# University of North Carolina at Chapel Hill

### Nutrition Research Institute

The Nutrition Research Institute is committed to conducting innovative basic and translational science studying precision nutrition, how individual differences in requirements and responses to diet affect our individual nutritional needs. We believe that our advances in nutrition science are leading to successes in preventing or mitigating the negative effects of chronic diseases and aging, and in improving human development, even prior to conception.



**Steven H. Zeisel, MD, PhD,** Director and Kenan Distinguished University Professor in Nutrition and Pediatrics

#### **KEY FINDINGS**

Blood pressure in 529 participants of the biracial (black and white) CARDIA study (Coronary Artery Risk Development in Young Adults) was associated with the person's microbiome in their gut. **People had lower blood pressure when they had a more diverse population of bacteria in their microbiome. Diet is an important modifier of your microbiome; eating well increases the diversity of bacteria.** The NRI studies how our nutritional needs are changed by differences in our microbiome. Publication: *Sun, S, Lulla, A, Sioda, M, Winglee, K, Wu, MC, Jacobs, DR, Jr., Shikany, JM, Lloyd-Jones, DM, Launer, LJ, Fodor, AA and Meyer, KA (2019). "Gut Microbiota Composition and Blood Pressure." Hypertension 73: 998-1006.* 

Obesity increases the risk of multiple gastrointestinal cancers and worsens disease outcomes. The effect of weight loss interventions - such as modifications of diet and/or physical activity or bariatric surgery - remains unclear. **This paper reviews the available** science to help develop effective, personalized diet and exercise interventions to reduce the burden of obesity on gastrointestinal cancer. The NRI studies why obesity makes people more likely to get certain types of cancer. Publication: *Ulrich, CM, Himbert, C, Holowatyj, AN and Hursting, SD (2018). "Energy balance and gastrointestinal cancer: risk, interventions, outcomes and mechanisms." Nat Rev Gastroenterol Hepatol 15: 683-698.* 

Low maternal intake of the essential nutrient choline results in abnormal development of the retina in the eye and disrupts normal vision. **These studies in a mouse model suggest that women should be sure that they eat foods containing choline during pregnancy.** In 2018 the American Academy of Pediatrics listed key nutrients that are needed during pregnancy to build a healthy baby, including protein, zinc, iron, choline, folate, iodine, longchain polyunsaturated fatty acids and vitamins A, D, B6, and B12. The NRI's investigators have been international leaders in the study of choline. Publication: *Trujillo-Gonzalez, I, Friday, W., Munson, C, Bachleda, A, Weiss, E, Alam, N Sha, W Zeisel, S, Surzenko, N. (2019) "Low availability of choline during pregnancy disrupts development of the retina and visual function in the offspring: evidence from a mouse model." FASEB Journal [In Press] 33: 9193-9209.* 

# **University of North Carolina at Charlotte**

# Bioinformatics Research and Services

Researchers from UNC Charlotte's Bioinformatics Services Division and the Department of Bioinformatics and Genomics work at the intersection of computer science and biology to develop the tools and resources necessary for analyzing large, complex datasets in order to answer critical biological questions.



**Reference Genomes:** Knowing the complete genome of the species you are studying is an essential first step in being able to determine which genes and mutations are controlling a particular trait or potentially causing a disease, but obtaining the full sequence is a computational challenge that requires the generation of hundreds of millions of smaller DNA sequences, which must be put back together in the correct order.

Robert Reid, PhD, is collaborating with several different research groups to help them assemble reference genomes for their study species; once completed, these new genomes will be made available to the public so that all researchers can take advantage of them. One of Dr. Reid's projects includes the assembly of the very large and complex oat genome, which will provide new insights into the nutritional quality of this staple crop.

Elizabeth Cooper, PhD, published a new reference genome for sweet sorghum (BMC Genomics 20:420), a widely grown cereal crop that is important for both food and fuel. Dr. Cooper is currently working with the DHMRI genomics lab to sequence 11 additional sorghum genomes in order to gain a better understanding of how breeding for different varieties has changed plants at the DNA sequence level.

**Databases:** As the sheer volume of publicly available data from different biological studies continues to rapidly increase, finding meaningful connections and insights from different studies and types of data can become more challenging. Well-organized databases and user-friendly programs that can search them are vital tools for today's scientists seeking to fully understand how nutrition can affect human health and diseases, which means considering the complex networks that link plants, their genes, and the nutrients they produce to our own genes and pathways.

• Jeremy Jay, PhD, Alexa Sanders, Robert Reid, PhD and Cory Brouwer, PhD, created and published a dataset which integrates the USDA nutrient composition database with both biological pathway information and published results from biomedical studies (BMC Research Notes 11:883).



**Cory Brouwer, PhD,** Director, Bioinformatics Services and Professor of Bioinformatics and Genomics

### University of North Carolina at Greensboro



**Zhanxiang Zhou, PhD,** Co-director and Professor of Nutrition, UNC Greensboro Center for Translational Biomedical Research



**Gibin Zhang, PhD,** Co-Director and Associate Professor of Chemistry, UNC Greensboro Center for Translational Biomedical Research

#### Center for Translational Biomedical Research

The UNC Greensboro Center for Translational Biomedical Research conducts basic and translational research in the area of liver diseases and diabetes. Our research is primarily focusing on the mechanisms and development of therapeutic approaches for treatment of alcohol-induced liver disease. We also focus on developing bioanalytical tools for systemic biological investigation of diabetes and early biomarkers of diabetic complications.

#### **KEY FINDINGS**



Discovered that intestinal immune dysfunction is a causal factor in alcohol-induced bacterial translocation and hepatic inflammation. This provides a new direction in treatment of alcoholic liver disease.



Developed a comprehensive method for analysis of inflammatory lipid mediators. This provides an innovative way to assess the effectiveness of functional food in sports medicine.

#### Publications:

Chen, G.Y., and Zhang, Q. (2019) Comprehensive analysis of oxylipins in human plasma using reversed-phase liquid chromatography-triple quadrupole mass spectrometry with heatmap-assisted selection of transitions, Analytical and Bioanalytical Chemistry 411, 367-385.

Nieman, D.C., Gillitt, N.D., Chen, G.Y., Zhang, Q., Sakaguchi, C. A., and Stephan, E.H. (2019) Carbohydrate intake attenuates post-exercise plasma levels of cytochrome P450-generated oxylipins, PloS one 14, e0213676.



