Pennington Biomedical Nutrition Obesity

**Research Center** 

# Pennington/Louisiana

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#### News from the NORC Director



#### Leanne Redman, PhD

Associate Executive Director for Scientific Education

Pennington Biomedical

This is my inaugural newsletter as the 3<sup>rd</sup> Director of the Pennington/Louisiana NORC. Last May, I was honored to formally be handed the baton by Donna Ryan and Eric Ravussin who led the Center over the past 22 years. For more than two decades, the Pennington/Louisiana NORC has supported "**nutrition and metabolic health research through the lifespan**" with a focus on mechanisms, prevention, and treatment modalities at each step of the translational continuum. I look forward to continuing lead our Centers' efforts in growing nutrition and obesity research in the deep south.

We are busy gearing up to renew our Center for its 5<sup>th</sup> cycle. Our NORC is proud to serve investigators working in nutrition and obesity research not only at Pennington Biomedical but across Louisiana. We have over 200 members now including 35 trainee members across several Louisiana Institutions including LSU Health Sciences Center in New Orleans, Tulane University and Tulane Primate Center, LSU A&M, Xavier University,



Pictured from left to right: Leanne Redman, Eric Ravussin, and Donna Ryan.

Pennington Biomedical and now LSU Health Sciences Center in Shreveport.

Members of our NORC consortium can access many services and programs including those provided by the Human Phenotyping Core; Bioinformatics and Molecular Mechanisms Core; and Animal Model and Phenotyping Core, our Enrichment program, the Pilot and Feasibility Studies program and our data and biospecimen repository (https://my.pbrc.edu/NORC).

Our NORC has funded 79 Pilot & Feasibility grants totaling more than \$2.5M. As hoped, more than 65% of our P&F award recipients have successfully competed for subsequent funding, including 34 NIH awards and during the 4th NORC grant cycle, 7 P&F recipients have achieved R01, K01, R21, R03 and mentored COBRE award funding.

#### Congratulations to the winners of the 2024-25 NORC P&F applications:

- Stephanie Compton "Feasibility and accuracy of D3-creatine in cancer cachexia compared with dual energy x-ray absorptiometry"
- Vance Albaugh "In Vivo Identification of Intestinal Nutrient Sensitive Brain Regions in Human Health and Obesity"

- Elizabeth Zunica "The role of hepatic uncoupling protein 2 in metabolic dysfunctionassociated hepatocellular carcinoma"
- Clovis Palmer "Controlling Diabetes by Modulating Immune Cell Metabolism"

#### Other notable accomplishments include:

- In January we hosted the inaugural 5-day "Nutrition and Obesity Research Methods Course" on our campus. Funded by NIH in September following our 3-day pilot, we welcomed 3 graduate students, 18 postdoctoral fellows, 3 Assistant Professors, and 1 Resident Physician for a total of 25 participants. Universities represented by our NORC include Pennington Biomedical, Tulane and LSU Health - New Orleans. Participants from other NORCs came from Columbia. Harvard Medical School and its associated hospitals, University of Alabama at Birmingham, and University of Michigan. Attendees trained on various methodologies including indirect calorimetry, body composition, cardiorespiratory fitness and carbohydrate metabolism. Thank you to our NORC members Drs. Martin, White, Flanagan, Johannsen, Newton, Staiano, Stephens, Mey, Heymsfield, Ravussin, Lowe, Caldwell, Drews, Carmichael, and Rood, for providing the instruction during the course. Stay tuned for the application deadlines for our next course. This annual course is supported by an NIDDK R25 funded through August of 2029. Stay tuned for the announcement of our next course!
- The 25<sup>th</sup> annual Irene W. Pennington Wellness Day for Women was held on International Women's Day on March 8, 2025. Once again we saw over 400 women from the Baton Rouge community on our campus for preventative health screenings, vaccines and to interact with exhibitors and hear nutrition lectures. Thank you to our NORC members Drs. Champagne, Cabre, Rebello, Dubin and Gilbert for participating in a panel 'What you've always wanted to know about diets but have been afraid to ask!'

**Finally, I'd like to formally announce our new partnership with LSUHSC in Shreveport.** We are excited to welcome Dr. Oren Rom to the Internal Advisory Board alongside Dr. Lu Qi of Tulane and also Dr. Patricia Molina of LSUHSC in New Orleans. The entire NORC Leadership will gather for an inaugural Louisiana/Pennington NORC Partner Meeting where we will share updates and establish a plan for enriching engagement and outreach for our members across Louisiana.

The NORC Executive Committee is proud of these achievements and committed to serving its members and continuing to support the growth of nutrition and obesity research in Louisiana for many more years pending funding from NIDDK.

#### **Pilot & Feasibility Awards**

The objective of the NORC P&F program is to encourage young investigators by providing research support to test innovative hypotheses involving nutritional programming-related research and other pilot studies related to the function of NORC. Below are the most recent P&F winners.

## Feasibility and accuracy of D<sub>3</sub>-creatine in cancer cachexia compared with dual energy x-ray absorptiometry



#### Stephanie Compton, PhD

Postdoctoral Researcher in Cancer Metabolism

#### Pennigton Biomedical

Cancer cachexia is a progressive whole-body wasting syndrome that occurs in 50% of patients with non-small cell lung cancer (NSCLC) and reduces patients' overall survival. While cachexia is clinically diagnosed by weight loss, it is primarily characterized by loss of skeletal muscle with or without loss of adipose tissue. If identified in at risk or early stages, cachexia progression may be preventable. However, the availability of instruments such as dual energy x-ray absorptiometry (DXA) for assessment of muscle mass in clinical settings is low. Isotopically labeled creatine (creatine-(methyl- $D_3$ ), or  $D_3$ -creatine) may be a non-invasive method for assessing skeletal muscle in this vulnerable population. D<sub>3</sub>-creatine has been validated against DXA and magnetic resonance imaging (MRI) and used in older adults and populations with sarcopenia and cancer. The D<sub>3</sub>-creatine method relies on several assumptions, including consistent concentrations of skeletal muscle creatine through weight stability. In patients with cachexia, who may have significant changes in weight along with increases in ascites and fat mass, these assumptions may be violated.

Determining the utility of  $D_3$ -creatine in patients with cachexia would inform both research use and clinical practice. However, the accuracy and feasibility of this measure in a population with cachexia is unknown.

This NORC P&F study will determine 1) the feasibility of establishing methodology for  $D_3$ creatine analysis and 2) determine the accuracy of  $D_3$ -creatine for measuring skeletal muscle compared to total and appendicular lean mass measured from DXA in participants with NSCLC who have experienced weight loss or weight stability. The findings from this study will establish a new methodology and inform research and clinical use of  $D_3$ -creatine to investigate changes in skeletal muscle in patients with cancer cachexia.

#### In Vivo Identification of Human Brain Regions Sensitive to Intestinal Glucose



Vance L. Albaugh, MD, PhD

Assistant Professor of Metabolic Surgery

Pennington Biomedical

Nutrient presence within the intestinal tract (i.e. the gut) is sensed by the brain through two fundamental mechanisms. These mechanisms include nutrient-stimulated hormonal signaling in which the presence of nutrients (e.g. glucose, fatty acids, amino acids) in the gut causes intestinal cells to produce hormones that are secreted into the blood. These hormones circulate in the blood and eventually reach the brain where they can exert their effects on hunger and satiety. Hormone mechanisms lead to slow onset of effects in response to nutrients. The second nutrient sensing mechanism is much faster and is mediated by direct neural connections between the gut and intestine. These pathways are akin to "electrical wiring" connecting the brain and the intestine and can communicate rapidly between organs. Preclinical studies in mice have shown that even a near infinitesimal amount of glucose or other nutrient can be sensed within the brain within a matter of a few hundred milliseconds. This sensing is much too rapid for slow endocrine responses and is likely mediated by these direct neural pathways.

Over the last several years our understanding of these gut-brain neural signaling pathways in

mice has grown exponentially, but we still know little about these pathways in humans. Thus, the goal of this NORC pilot and feasibility grant is to combine the clinical techniques of nutrient infusion and functional brain imaging (e.g. functional magnetic resonance imaging) to identify regions of the human brain that are sensitive to various macronutrients. The current project focuses on glucose sensing and identification of glucose sensitive brain regions in the absence of any changes in blood glucose, insulin, or GLP-1. While mouse studies are limited to examining a single brain region at a time, the real strength of combining these imaging techniques in humans is that individuals can be studied in a repeated manner, in response to various nutrients, while capturing changes in activity of the entire brain. This project will establish methods and provide pilot data on nutrient sensing in humans that will allow for mechanistic gut-brain signaling studies and investigation of various nutrient sensing pathways and their clinical significance with respect to obesity and diabetes.

## The role of hepatic uncoupling protein 2 in metabolic dysfunction-associated hepatocellular carcinoma



#### Elizabeth Zunica, PhD

Postdoctoral Researcher in Integrated Physiology and Molecular Medicine

**Pennington Biomedical** 

Hepatocellular carcinoma (HCC) is the most common form of liver cancer, which is the 5th most prevalent and 3rd most deadly cancer globally. Metabolic dysfunction-associated steatotic liver disease (MASLD) is independently associated with ~2-fold increased risk and is the fastest growing cause of HCC. However, the mechanisms whereby MASLD predisposes to HCC remains unclear.

Mitochondria are an evolutionarily conserved organelle that mediate cell survival by conferring energetic plasticity and adaptive potential. Mitochondria occupy 15-20% of hepatocyte volume and play an important role in mitigating cellular damage related to energy burden resulting from MASLD. Uncoupling protein 2 (UCP2) is an inner mitochondrial membrane antiporter that couples metabolite transport to proton efflux. As a result, UCP2 activation triggers uncoupling of substrate

oxidation from ATP synthesis by lowering the mitochondrial membrane potential ( $\Delta\Psi$ m). To this end, obesity increases hepatocyte UCP2 expression and loss of function mouse models exhibit increased susceptibility to MASLD. These findings collectively support the notion that UCP2 restricts the onset and progression of MASLD-related HCC.

For this NORC P&F, I will investigate the role of hepatic mitochondrial uncoupling in the onset and progression of MASLD-related HCC. I will utilize a hepatocyte-specific UCP2-deficient mouse model to study putative mechanisms related to carcinogenic potential. These observations will be translationally supported by evaluating hepatic UCP2 expression and mitochondrial function in donors across the MASLD continuum and in hepatic tumors of donors with MASLD-related HCC.

### Controlling Diabetes by Modulating Immune Cell Metabolism.



#### **Dr Clovis Palmer, PhD**

Assistant Professor of Microbiology and Immunology

Tulane University, National Primate Research Center

According to the Centers for Disease Control and Prevention (CDC), currently over 37 million Americans are diagnosed with Type 2 diabetes (T2D). This includes about 500,791 adults in Louisiana (LA), representing 14.2% of the LA population.

The economic burden of diabetes in LA is staggering costing the state a whopping \$5.7 billion per year (American diabetes association).

Inflammation is an important source of T2D and may be triggered by excessive intake of high fructose diet such as sugary drinks. Like all living cells in the body, immune cells require glucose to survive and function. However, recent studies including ours found that immune cells can drive inflammation if they are unable to utilize nutrients like glucose efficiently.

The objective of this NORC pilot study is to administer a sugary drink in the form of cool aid to non-human primates (NHPs) in order to understand how high fructose diet affects the way immune cells break down glucose into energy pockets called ATP. We are also testing a new diabetes treatment technique to reduce metabolically abnormal and inflammatory immune cells in tissues using antibodies that can bind to a certain protein on the surface of these cells. Our research hopes to exploit new metabolic processes in immune cells to ultimately cure or develop long-acting T2D treatment.

#### **Enrichment Updates**

#### T32 Trainees

Pennington Biomedical's NIDDK-supported T32 on Training in Obesity Research began its 21<sup>st</sup> consecutive year of funding in 2024.

In the past year, two trainees successfully graduated from the program. **Emily Woolf** secured an F32 grant on "Examining dietary and metabolomics patterns on cardiometabolic outcome variability in response to calorie restriction". **Alexandra Niclou** graduated from the program and is continuing her postdoctoral training at USARIEM. During Grant year 21, the program recruited and appointed one new trainee who is highlighted below.



**M. Catherine Prater** received her Ph.D. in Nutritional Science from The University of Georgia. Dr. Prater began training in the T32 program in July 2024 and will pursue research with mentors Ursula White and Leanne Redman.

#### **Visiting Scientist Seminars**

Each year, the Pennington/Louisiana NORC sponsors speakers who are prominent scientists from national and international universities as well as governmental and industrial labs. These seminars are available to all NORC members. Listed below are those invited for 2024.

Date:	Speaker:	Title / Topic:
Feb 22	John Graham Thomas, PhD Brown Alpert Medical School	Engineering Health: Harnessing Digital Tools and Innovative Methods in Behavioral Obesity Treatment Research
Mar 7	Doug Mashek, PhD University of Minnesota Medical School	Lipid droplets: a cellular hub for integrating nutrition, cell signaling, and disease etiology
Mar 28	Christopher Buettner, MD, PhD Rutgers Medical School	What Causes Insulin Obesity (if it is not impaired insulin signaling)?
Apr 11	John Speakman, MD University of Aberdeen	Models of Body Weight Regulation in Animals and Humans
May 9	Matt Kaeberlein , PhD University of Washington Medicine	The Dog Aging Project: An Open Science Study of Aging in Companion Dogs
Aug 29	Jill Kanaley, PhD University of Missouri	Does Exercise Timing Matter?
Sep 12	Dympna Gallagher, EdD Columbia University Medical Center	Weight Change and Composition – Implications for Understanding Resting Metabolic Rate and Energy Balance
Nov 14	Andrew Bremer, M.D., PhD. National Institute of Health	Nutrition Science at NIH
Dec 12	James O. Hill, PhD University of Alabama at Birmingham	Weight Loss Maintenance: Has Its Time Finally Come?

#### **Outreach Updates**

#### Men's Health Summit

Nearly 300 men of all ages and from all over the state came to Pennington Biomedical for the 2024 Men's Health Summit on Saturday, September 14. The health and wellness event, themed "Empowering Men to Live Healthier Lives," featured 788 free health screenings and 189 vaccinations. These included blood glucose screens, EKGs, blood pressure, BMI, colorectal cancer kits and other cancer screens. The event also included interactions with 23 local health and wellness exhibitors, fitness and self-defense demonstrations and short educational sessions on Foundational Health for Men, Nutrition Essentials for Men. and Overcoming Depression. From this event, there were more than 60 who signed up to participate in clinical trials put on by NORC members.

#### Scientific Symposia

Pennington Biomedical's Symposia attracts world-renowned scientists to Baton Rouge, LA and gives them the opportunity to interact and synthesize knowledge on the chosen topic.

In April 2024, the topic focused on "Precision Prevention, Diagnostics and Treatment of Obesity: Pipedream or Reality?". Co-chairs were Corby Martin, Ph.D., Pennington Biomedical and Caroline Apovian, M.D., Harvard University.



2024 Spring Symposium Participants

In December 2024, we held a symposium cochaired by Tiffany Stewart, PhD, Pennington Biomedical and Guillaume Spielmann, PhD, Louisiana State University. This symposium covered the topic of "Optimization of Health, Performance, & Resilience: Courtside, Warside, & Spaceside".

The Spring 2025 symposium was co-chaired by Amanda Staiano PhD, Peter Katzmarzyk, PhD from Pennington Biomedical, and Paul Estabrooks PhD, from the University of Utah. This symposium focused on "Disseminating and Implementing the Science of Child Obesity Treatment and Prevention".



Above: 2025 Spring Symposium Participants



Left: Co-Chair, Peter Katzmarzyk speaks to visitors about the Greaux Healthy Initiative.

**Right:** Co-Chair, Amanda Staiano talks about Evidence-based Interventions from Clinical Practice Guidelines



#### **NORC External Advisory Board Meeting**

On Feburary16-17 2025, we welcomed our External Advisory Board Members to Baton Rouge, LA for a full day of presentations about the progress of the center and discussions on planning for the renewal application in June 2025. We would like to express our gratitude and acknowledge the contributions of our external advisory board members. Their advice and feedback are invaluable to the operations and strategic planning.



#### Save the Date

The following are Enrichment Core events for 2025 partially sponsored by our NORC.

## Pennington Biomedical Bray Obesity Symposium

The Pennington Biomedical Bray Obesity Symposium is now fully available online, with 180 participants already registered! This on-demand symposium offers 30 AMA PRA Category 1 Credits and is designated by the American Board of Obesity Medicine (ABOM) as a Group One Primary Medicine Obesity CME partner.

Topics include obesity genetics, pediatric obesity, lifestyle intervention, pharmacotherapy, and metabolic surgery. Accreditation is provided by Tulane University Health Sciences Center.

For more information or to subscribe, please visit the <u>website</u>.

#### **Spring Visiting Scientist Seminars**

- April 10, Geltrude Mingrone, MD, PhD, Professor of Medicine, Catholic University
- April 16, Tim Church, MD, PhD, Chief Medical Officer, Wondr Health
- May 1, Bret Goodpaster, PhD, Scientific Director, Translational Research Institute, AventHealth

#### December 5-7, 2025 - Scientific Symposium

The Fall 2025 symposium will focus on "Brain-Body Communication and Metabolic Diseases" and will be co-chaired by Drs. Heike Muenzberg and Brad Lowell of Pennington Biomedical and Harvard University, respectively.

### Obesity Medicine Fellowship at Pennington Biomedical

Pennington Biomedical Research Center, in collaboration with LSU Health New Orleans School of Medicine, is offering a one-year Obesity Medicine Fellowship. Training will take place at the Metamor Institute in Baton Rouge, primarily providing comprehensive training in obesity medicine and care for patients undergoing metabolic surgery. Open to graduates of ACGMEapproved residencies in internal medicine, family medicine, and endocrinology, the fellowship features specialty training under renowned experts from LSU Health and Pennington Biomedical. Leadership at Metamor Institute includes Pennington Biomedical faculty, with support from Our Lady of the Lake Regional Medical Center. Learn more at our website.