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News from the NORC Director



Eric Ravussin, PhD
Boyd Professor
Associate Executive Director of
Clinical Science
Pennington Biomedical

Over the past 17 years, the Pennington / Louisiana NORC has conducted research covering the biological and environmental determinants of the energy balance equation in rodents and humans as well as the relationship between obesity and cardio-metabolic health. Our vision still emphasizes the general theme of **“nutrition and metabolic health through the lifespan”** with focus on mechanisms, prevention, and treatment modalities at each step of the lifespan. Our collective research base is related to the metabolic impact of nutrition on health and diseases.

Now in its 4th 5-year cycle, our NORC is serving investigators working in nutrition and obesity research not only at Pennington Biomedical but for the past 7 years, at other Louisiana academic institutions. Since its inception, our NORC has provided services to many of our 133 members and our 20-30 trainees using our three scientific cores: Human Phenotyping; Molecular Mechanisms; and Animal Model and Phenotyping. Furthermore, our NORC has funded 72 Pilot &

Feasibility grants selected from 196 full applications and 259 letters of intent. The Executive Committee of our NORC is proud of these achievements and committed to serving its members for many more years pending funding from NIDDK.

Since the time Dr. Donna Ryan and I wrote the first successful application in 2005, many investigators have been fortunate to benefit from our NORC core services. Entering the third year of our 4th cycle, it is now time to renew the leadership of our Center Grant. After 20 years as Principal Investigator, it is time for me to progressively pass the baton (rouge of course) to a younger leadership. After advertising nationally for a new Principal Investigator, we quickly realized that we do not need to go far to find outstanding talents in nutrition and obesity science and have decided to groom our own leader. Very quickly, we agreed that Dr. Leanne Redman would be an ideal leader for this prestigious Center. Therefore, from May 1st, 2023, and for at least a year, Leanne will become our new NORC Associate Director before assuming the role of Director later in 2024. Dr. Katzmarzyk becomes the Director of our Enrichment and Outreach component and to replace Dr. Redman in the Human Phenotyping core, Dr. Ursula White will join the executive committee as the Associate Director of the core. Welcome Ursula!

Other NORC Highlights:

Our NORC was awarded a Supplement in 2020 to hold the 2nd Trans-NORC Training Course. Due to COVID it was postponed but held on April 26-28, 2022, and entitled “Nutrition and Obesity Research Methods Course” focusing on human investigation. Each of the 11 other NORCs in the US sent 2 early-stage faculty and/or senior postdoctoral fellow to attend.

2022 NORC P&F applications. Applications were due on August 12, 2022, and three awards were issued:

- **Fatima Rivas** – “Synthesis of prenylated coumaric derived natural products as anti-diabetic agents.
- **Avinash Kumar** – “Investigating the Role of Particulate Matter Containing Environmentally Persistent Free Radicals in the Pathogenesis of Type 2 Diabetes”
- **Carrie Elks** – “Functions of ‘Creeping Fat’ in Crohn’s Disease”

2023 NORC P&F round. Applications were due on April 15, 2023, and awards will be announced in early May.

Awards For Pilot & Feasibility Studies

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.

Synthesis Of Prenylated Coumaric Derived Natural Products as Anti-Diabetic Agents.



Fatima Rivas, PhD
Assistant Professor
LSU Baton Rouge

Close to 42% of the adult American population experience obesity-related metabolic syndrome (MetS)--a group of health conditions, including insulin resistance, glucose intolerance, dyslipidemia, and Type 2 Diabetes Mellitus (T2DM). A high mortality rate among the T2DM patient population has become a global burden, indicating an urgent need for the discovery and development of new therapeutic agents. The identification of the potent benefits of Artemisia Scoparia Extracts (EAS) against T2DM by Dr. Jackie Stephens at Pennington Biomedical, enables the establishment of our drug discovery platform based on this prenylated molecular scaffold against T2DM.

This NORC P&F study will support the total synthesis of one the main components of EAS and establish its pharmacological (maximum tolerable dose and pharmacokinetic and pharmacodynamic

properties) potential in murine models. By developing efficient synthetic strategies towards these prenylated compounds, we will access sufficient compound quantities for in vivo murine studies and generate a focused-compound library to better understand these compounds' mode of action. The resultant data will enable the design of preclinical efficacy studies regarding dosage and in vivo tolerability of these compounds.

Investigating The Role of Particulate Matter Containing Environmentally Persistent Free Radicals In The Pathogenesis Of Type 2 Diabetes



Avinash Kumar, PhD
Postdoctoral Researcher
LSU Baton Rouge and Pennington Biomedical

Despite growing recognition of the problem, the diabetes epidemic continues in the U.S., and diabetes rates are increasing around the world. Obesity and diabetes are major causes of morbidity and mortality in the United States and major risk factors includes family history, age, excess nutrition, and physical inactivity. In addition to that several epidemiological studies suggest that air pollution is linked to an increased prevalence of diabetes. One of the major constituents contributing to air pollution is Combustion Derived Particulate Matter (CDPM). CDPM often contains a newly realized class of contaminants known as Environmentally Persistent Free Radicals (EPFRs). Once inhaled, EPFRs have tremendous potential to produce oxidative stress and can lower energy expenditure and damages skeleton muscle mitochondrial function. However, there is a significant knowledge gap regarding EPFRs exposure and its impact on human health, especially in the pathogenesis of diabetes.

The objective of this NORC pilot grant is to address how EPFRs exposure modifies cellular mechanisms that are integral in maintaining glucose homeostasis and link these to observations made in humans in vivo. To execute the study, we will use a novel murine model of EPFRs exposure and determine changes in whole-body glucose homeostasis and energy metabolism due to CDPM containing EPFRs exposure. The proposed

research will, for the first time, directly assess the role of EPFRs exposure in glucose homeostasis and the development of a diabetic state. Such a study will be important for shaping public health policy regarding EPFRs exposure and its role in predisposition to the development of metabolic diseases.

Functions Of “Creeping Fat” In Crohn’s Disease



Carrie Elks, PhD
Assistant Professor
Pennington Biomedical

Crohn’s Disease (CD) is a chronic inflammatory bowel disease that can affect any part of the gastrointestinal tract. CD was historically associated with weight loss, malnutrition, and decreased body mass index (BMI). In Baton Rouge and the surrounding areas, CD now occurs with similar frequencies in people with obesity and those of normal weight, with similar trends occurring across the United States. People with obesity are more likely to experience CD complications including the formation of intestinal strictures (sites of abnormal narrowing), decreased time to surgical intervention, ulcerations, and longer post-surgical recovery.

A unique feature of CD is the presence of “Creeping Fat” (CrF) – fat tissue that wraps around the CD-affected intestine. This CrF is not observed in any other disease state, and its role in CD is not understood. Current dogma describes CrF as an extension of Mesenteric Adipose Tissue (MAT), though several differences suggest that CrF may serve a distinct function.

Our hypothesis is that CrF adipocytes, via direct contact with the CD-affected gut, acquire characteristics that distinguish them from MAT adipocytes, both transcriptionally and functionally. We posit that CrF is a heterogeneous tissue and that CrF adipocyte gene expression and function depend upon a spatial gradient dictated by proximity to the gut. Hence, we expect that adipocytes nearest the inflamed gut are molecularly the most distinct from MAT adipocytes; and the further a CrF adipocyte is from the gut wall, the less molecularly distinguishable it becomes from MAT. Successful testing of our hypothesis requires

methodologies that allow us to analyze the spatial gradient of CrF, to distinguish between adipocytes with different proximity to the CD-affected gut. This NORC Pilot and Feasibility award will allow us to establish a methods workflow for the spatial analysis CrF from normal weight CD patients and CD patients with obesity. This represents a major step toward understanding CrF function – by obtaining the molecular profiles of adipocytes at varying proximity to the gut, we can then design future studies to determine what gut factors may be involved in CrF function.

Enrichment Core Updates

Update on T32 Trainees

Pennington Biomedical’s NIDDK supported T32 on Training in Obesity Research began its 20th consecutive year of funding in 2023. In the past year, two trainees successfully graduated from the program. **Melissa Linden** was promoted to a Faculty Position at the University of Massachusetts, Boston. **Chloe Lozano** secured a USDA ARFQ grant and is continuing her postdoctoral training at the University of Hawaii at Manoa. During grant year 19, the program recruited and appointed two trainees whose bios are below.



Alex Niclou received her Ph.D. in Anthropology from Notre Dame. Dr. Niclou began training on the T32 in January 2023 and will pursue research with mentors Leanne Redman, Ph.D. and Eric Ravussin, Ph.D.



Hannah Cabre received her Ph.D. in Human Movement Sciences, from the University of North Carolina, Chapel Hill. Dr. Cabre will begin her T32 training in May 2024 and will pursue research with mentor Leanne Redman, PhD, and Eric Ravussin, Ph.D.

NORC Day 2023

NORC Day was held on January 30, 2023, at the University Medical Center in New Orleans, LA. There were 45 attendees from Pennington Biomedical, LSU Health Sciences Center, and Tulane. Thus, this event offered a conduit for

scientific exchange between members of the NORC community. This half day event featured a welcome from Eric Ravussin, NORC Director, and presentations from each Core Director. Highlights of the success of the Pilot and Feasibility program were presented with four P&F presenters including past successful recipients (Drs. Cristal Hill & Maria Sanchez-Pino) a presenter close to completing her P&F grant (Dr. Rebecca Solch-Ottaiano) and one current P&F holder (Dr. Wagner Dantas).

Welcome to New NORC Faculty



Robert (Bob) A. Kesterson, PhD

*Professor of Genetics
Pennington Biomedical
Research Center*

Dr. Kesterson is Professor of Cancer Precision Medicine and Director of the Genetically Engineered Models (GEMs) core facility at Pennington Biomedical Research Center (effective August 1, 2022). Dr. Kesterson brings >30 years of experience in rodent genetics and animal model generation in the field of obesity and diabetes having trained with Roger Cone at the Vollum Institute until establishing his

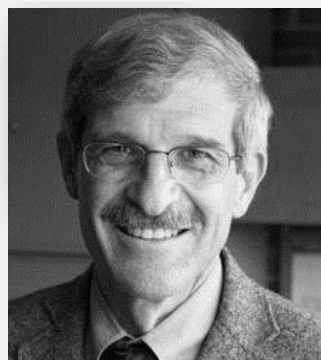
own lab at Vanderbilt in 1997, and then moving to the University of Alabama at Birmingham to lead the Transgenic & Genetically Engineered Models (TGEMs) facility for 18 years. He has broad expertise in creating and phenotyping animal models of disease. His laboratory is currently examining molecular mechanisms associated with Neurofibromatosis Type 1 (NF1), a tumor suppressor gene associated with many types of cancer. He is funded to develop gene therapy approaches using numerous “humanized” mouse and rat models as well as cell lines (ES and iPSCs) harboring NF1 mutations found in patients. Dr. Kesterson is also Director of the UAB U54 Center for Precision Animal Modeling Disease Modeling Unit, one of three NIH sponsored national centers creating novel animal models for rare diseases. Dr. Kesterson plans to further expand the PBRC NORC Animal Models sub core to 1) maintain critical animal models to support research into nutrition, obesity, and metabolic health, and 2) provide CRISPR-mediated gene targeting services to create next generation mice and rat models that harbor patient-specific mutations associated with obesity and diabetes linked to increased cancer risk. NORC investigators are encouraged to contact Dr. Kesterson to nominate genetic variants and desired animal models to be developed by the core.

NORC External Advisory Board

The Pennington / Louisiana NORC 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 of the center.



Rudolph L. Leibel, M.D.
Professor of Medicine
Columbia University



William Kraus, M.D.
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Philipp Scherer, Ph.D.
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