PENNINGTON / LOUISIANNA
NUTRITION OBESITY RESEARCH CENTER

SEPTEMBER 2018

PENNINGTON BIOMEDICAL RESEARCH CENTER LSU

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MEET PENNINGTON BIOMEDICAL'S NEW EXECUTIVE DIRECTOR

John Kirwan, PhD
Executive Director
Pennington Biomedical Research Center

The Pennington/Louisiana NORC would like to extend a welcome to John Kirwan, PhD, who started as the New Executive Director of PBRC in January.

Before taking on this position, Kirwan served as the Director of the Metabolic Translational Research Center and Professor of molecular medicine at the Cleveland Clinic in Cleveland, Ohio. Kirwan was also a Professor of physiology and of nutrition at Case Western Reserve University School of Medicine in Cleveland. His professional expertise includes almost 30 years of research, teaching and service in the obesity and diabetes fields.

"I am enthusiastic to join the team with President Alexander and all of the wonderful people at Pennington Biomedical," Kirwan said. "As the pandemic of chronic disease and obesity garner more attention internationally, Pennington Biomedical is well-positioned to be a leader in clinical research on those issues, as well as discovering new treatments, and providing outreach to support healthier lifestyles."

Kirwan received his clinical physiology training at Washington University School of Medicine in St. Louis, Missouri; his Ph.D. in human bioenergetics at Ball State University, Muncie, Indiana; his master's degree in exercise biochemistry from the University of Massachusetts, Amherst, Massachusetts; and his bachelor's degree (Honors) from the University of Limerick, Ireland.

Kirwan leads an internationally acclaimed biomedical research program focused on diabetes, obesity, nutrition and exercise. He is currently PI or Co-Investigator on nine NIH grants, and to date he has generated more than $35 million in research funding, most which has come from the U.S. National Institutes of Health, and the food, pharmaceutical, and medical device industries. He has published more than 200 scientific papers related to diabetes and metabolism in prestigious peer-reviewed journals including the New England Journal of Medicine, JAMA, Diabetes and Diabetes Care. Among his most important research contributions is the discovery that for a significant number of patients, diabetes can be put into long-term remission by surgically altering the physiology of the intestine and stomach.

NEWS FROM THE NORC DIRECTOR

Eric Ravussin, PhD
Boyd Professor
AED of Clinical Science
Pennington Biomedical Research Center

I am very pleased to announce that the Pennington/Louisiana NORC has been awarded a supplemental grant from NIDDK to boost our collaborative research efforts across the eleven existing NORCs in the country. More specifically this grant will allow three major undertakings:

- ***Trans-NORC VISITING SCHOLAR PROGRAM***, which will support junior faculty to enhance their skillset in nutrition/obesity research by visiting laboratories of other NORCS.
- ***Trans-NORC PILOT & FEASIBILITY GRANT APPLICATION*** with the primary goal of encouraging and facilitating new, innovative and collaborative research around the NIDDK NORC overall program.
- ***Trans-NORC TRAINING COURSE IN NUTRITION AND OBESITY RESEARCH METHODS*****,** which will be held in mid-2019 at Pennington Biomedical Research Center. Each of the eleven NORCs will select a participant for whom all travel expenses will be covered. Other participants will have to cover their travel expenses.

NEWS ON ENRICHMENT & TRAINING

In May, our NIDDK T32 postdoctoral training grant entitled “Training in Obesity Research” was re-submitted for a third renewal cycle. The objective of this training program is to prepare postdoctoral fellows to become productive research scientists capable of establishing independent scientific careers in academia, governmental agencies, and in the private sector. These junior scientists will further the efforts of the NIH to understand obesity and attenuate its impact on public health. During their 2-3 years of training, the postdocs will be exposed to the model of team science and will receive instruction in scientific writing, grant writing, methods to assure rigor and reproducibility of research, and the use of big data and bioinformatics. The program will take advantage of the cutting-edge technologies and the wide range of research efforts related to obesity available at Pennington Biomedical. All program faculty are NORC members. These include Drs. Phil Brantley and Leanne Redman who will serve as program directors and 27 other faculty who will serve as primary or secondary mentors. Five postdoctoral training slots were requested and will be available in July 2019 pending renewal. Currently, we have no vacancies for new postdocs on the existing grant.

NEW 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.

Validity and Reliability of the Activity Preference Assessment: A Shape Up Kids Ancillary

Nicole Fearnbach PhD
NIDDK T32 Fellow
Pennington Biomedical Research Center

The Activity Preference Assessment (APA) is a novel, computerized behavioral task based on the psychometric properties and task design of the Leeds Food Preference Questionnaire (LFPQ), which is a widely used and well-validated measure of liking and wanting for different types of food. The LFPQ has been shown to correlate with objectively measured food intake, self-reported eating behaviors, and markers of obesity. We have applied this framework to assess similar cognitive constructs around physical and sedentary activity preferences. We know that high levels of sedentary behavior are associated with adverse health outcomes, but the cognitive

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determinants of these habits are not well understood.

The APA task consists of two parts. First, each participant is asked to rate how much they like to do and want to do a variety of common physical and sedentary activities using sliding scales. Then they see pairs of activities in a "would you rather" type of game. In order to assess decision-making, subjects are asked to select as quickly as possible the activity they most want to do out of each pair of activity images. From the choices made, we will use an equation to calculate bias scores based on "wins" (which choice was selected) and reaction times. Positive scores will represent a bias towards engaging in or choosing sedentary activities and negative scores will represent a bias towards physical activities. Those with higher bias scores may be more at risk for health complications related to greater amounts of time spent in sedentary activities. The purpose of this study is to determine whether scores from the APA are associated with children's objectively measured activity behaviors, as well as markers of physical fitness, obesity, and cardiometabolic health.

Identification of molecular modulators of stress and feeding in the lateral hypothalamus

Emily Qualls-Creekmore PhD
Assistant Professor
Former NIDDK T32 Fellow
Pennington Biomedical Research Center

Stress has a significant impact on metabolic health through a variety of biological mechanisms, including strong influences on feeding behavior. A region in the brain known as the lateral hypothalamus (LHA) is a well-established regulator of feeding behaviors, but is less known for its role in stress-related behaviors. The LHA is a large area that produces many different signaling molecules (neurotransmitters and neuropeptides) and has an expansive neural circuit that permits influence on many other brain regions. Therefore, the mechanisms regulating the LHA's influence on feeding and stress are not well understood. Recent research from our lab demonstrated that synthetic activation of LHA neurons that express the neuropeptide galanin results in increases in motivated feeding, while also robustly decreasing stress and anxiety-like behavior. Additionally, we found that neurons in the LHA increase their activity in response to stressful stimuli. Although our data demonstrate an important role of galanin-expressing LHA neurons in motivated feeding and stress behavior, it is unclear whether galanin itself mediates these effects or if some other neuropeptide/neurotransmitter is the critical functional mediator. This Pennington Nutrition Obesity Research Center (NORC) pilot and feasibility project will use gene expression profiling to investigate the molecular profile of LHA neurons that are activated by stress, and will also sequence LHA galanin neurons specifically to identify other signaling molecules which may contribute to feeding and stress behaviors. Considering that obesity and feeding disorders often present with comorbidities of psychological stress and emotional disorders, such as anxiety, the identification of molecular messengers which modulate both feeding and stress-related behavior will present a strong target for the development of pharmacological intervention in these disorders.

Mesenteric Lymphatic Vessel Leak and Metabolic Dysregulation

Liz Simon, PhD
Assistant Professor
Louisiana State Univ. Health Sciences Center

Flavia Souza-Smith, PhD
Assistant Professor
Louisiana State Univ. Health Sciences Center

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The incidence of diet-induced obesity and metabolic syndrome increases with menopause and poses a significant risk factor for cardiovascular disease. Besides presenting a significant increase in weight gain in the early post-menopausal years, there is a shift in fat distribution with greater proportion of visceral adipose accumulation compared to lower-body adipose accumulation. Moreover, consumption of a Western diet (high fat diet) increases the odds for development of metabolic syndrome in menopausal women. A crosstalk between lymphatic vessels and adipose tissue with metabolic disease is recognized, with leaky lymphatic vessels resulting in lymphatic dysfunction and obesity, particularly visceral obesity. Understanding the mechanisms that lead to obesity and metabolic dysregulation post-menopause is imperative. Our studies will unravel the mechanisms of mesenteric lymphatic vessel leakage into perilymphatic adipose tissue (PLAT) due to gonadal hormone loss and high fat diet using a rodent model. Based on our preliminary data, we propose to explore the epigenetic mechanisms (in particular, miRNA-mediated alterations) that impair lymphatic tight junction protein, and the subsequent systemic and mesenteric PLAT-specific metabolic changes. Our proposal is innovative and holds the potential to understand diet manipulation and gonadal hormone loss-induced mesenteric lymphatic vessel dyshomeostasis and the related metabolic consequences.

NEWS FROM THE MOLECULAR MECHANISMS CORE

The mission of the NORC Molecular Mechanism Core is to serve as bridge between the Animal Phenotyping Core and the Human Phenotyping Core. The two components of the Molecular Mechanism Core- Genomics and Bioimaging- together provide the technologies to conduct investigations on the molecular, cellular, and histological level.

Lots of Power in a Little Box

The Chromium platform by 10xGenomics is not much bigger than a shoebox, but the small size packs a lot of scientific punch. Housing microfluidics hardware, the Chromium box provides the technology to perform RNA sequencing of single cells. Single-cell RNA sequencing technology represents the next step in the evolution of measuring gene expression, as it permits assessment of RNA repertoires from individual single cells in complex cell populations. Classical methods such as bulk RNA-Seq - which we established at the Pennington COBRE Genomics Core several years ago - are quite powerful to reveal transcriptome information at significant depth, but generally average such information across all cell types in a given sample. However, normal healthy tissues typically consist of more than one cell type, and it is not uncommon in disease that cells of the immune system infiltrate affected tissues. Cell populations in culture also are not always homogenous, particularly in situations that involve induction of cell differentiation. Single-cell sequencing is a powerful method to reveal the diversity of gene expression in a cell-specific fashion, and therefore permits new insights into molecular processes that govern the interaction of cells in a given tissue. The Genomics Core has recently obtained a Chromium instrument and is currently in the process of establishing the single-cell RNA sequencing technology for investigators at Pennington Biomedical.

NEWS FROM THE CELLULAR BIOLOGY & BIOIMAGING CORE (CBBC)

The Cellular Biology and Bioimaging Core is one component of the NORC Molecular Mechanisms Core. The mission of this CBBC is to provide access to state-of-the-art imaging, analytical, and histological equipment, as

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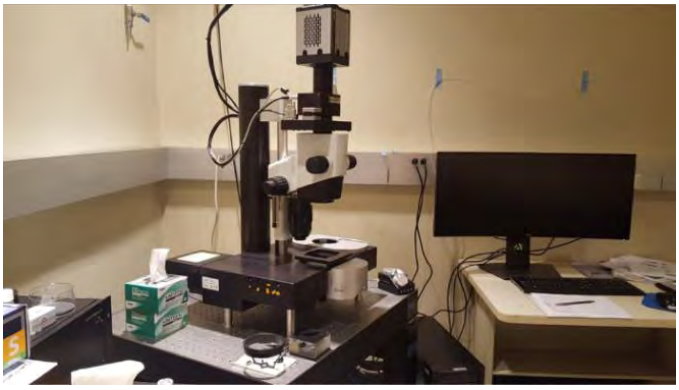
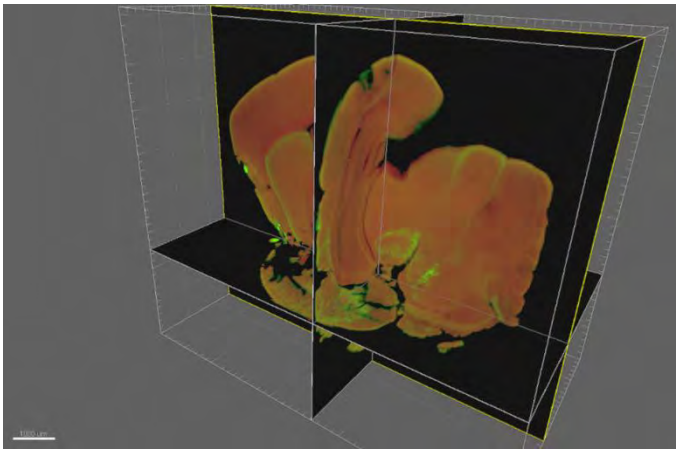
well as technical expertise and assistance to researchers at PBRC, LSU's main campus, and outside the LSU system.

Light Sheet Sensor Microscope

The Cell Biology and Bioimaging Core, in collaboration with Dr. Heike Muenzberg's SPARC NIH project and PBRC, has recently installed a light sheet microscope. The LaVision Biotek Ultramicroscope II is capable of imaging large (~1.5 x 1.5 x 0.6 cm) cleared tissue specimens that have been labeled with fluorescent antibodies.



The system is currently being used to image mouse adipose and other peripheral tissues processed following the iDisco protocol. Please contact Dr. David Burk (David.Burk@pbrc.edu) in the Cell Biology and Bioimaging Core if you want to learn more about this new piece of equipment.



NEWS FROM THE HUMAN PHENOTYPING CORE

The mission of the NORC Human Phenotyping Core is to provide investigators with the expertise and tools necessary to phenotype human participants across the lifespan. Importantly, the Human Phenotyping Core works closely with the Animal Phenotyping Core and the Molecular Mechanism Core to facilitate translational science.

The Human Phenotyping Core now provides a variety of cutting-edge biomedical imaging techniques to NORC investigators. Functional magnetic resonance imaging (fMRI) paradigms are now available to assess basic cognitive and motor functioning, responses to food stimuli, aversive stimuli (electric shock), risk-taking, and emotion processing. Body composition MRI is able to assess full-body and depot-specific fat and muscle stores, as well as the fat content of the liver. Liver fibrosis is measurable via Fibroscan and MR elastography. MR spectroscopy techniques to measure dynamic biochemical fluxes in the brain and skeletal muscle are also available. Current work in this core is developing techniques for body composition in infants, with a specific focus on brown adipose tissue.

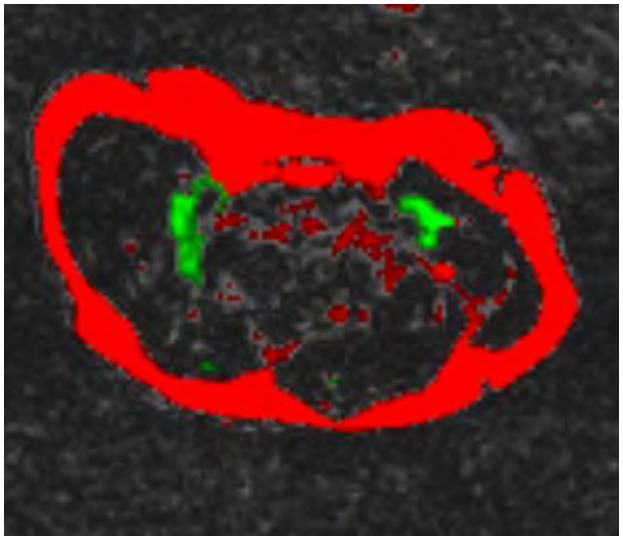
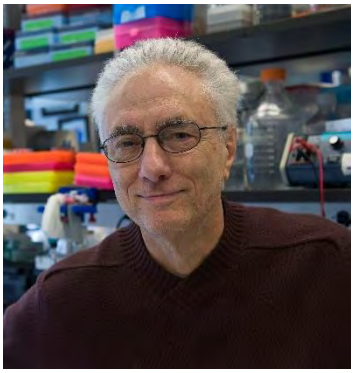


Image shows white adipose tissue (red) and brown adipose tissue (green) in the thorax of a baby.

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 operation and strategic planning of the center



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