

University of North Carolina at Chapel Hill
Nutrition Obesity Research Center
Start Date: 1999
Status: Ongoing
Source of NIH Support: NIDDK
Website: <http://www.sph.unc.edu/norc/>

Organization and Goals

The focus of the University of North Carolina's Nutrition Obesity Research Center (UNC-CH NORC) is Trans-Disciplinary Nutrition Research: From Molecules to Public Health. Since the inception of our Center in 1999, we have adapted and translated expertise in community/population-based and clinical studies to facilitate the cross-disciplinary transfer of ideas and information to the laboratory and vice versa for the deployment of cutting-edge nutritional sciences and obesity-related research.

The specific aims of the UNC-CH NORC are as follows:

1. To provide core resources and leadership that enhance and extend an existing outstanding and well-funded research base in conducting basic science, epidemiologic, and intervention (including classical clinical and community-based) research in nutrition and obesity
 - a. Provide cost-effective infrastructure support for conducting such research
 - b. Provide expertise that facilitates access for nutrition and obesity researchers to cutting-edge methods and equipment at the UNC, and that assists with the analysis of the data derived
 - c. Promote interdisciplinary integration of research among members of the UNC-CH NORC
2. To enhance the impact and presence of nutrition and obesity research at the UNC
 - a. Assist promising young M.D.s and Ph.D.s in becoming independent nutrition/obesity investigators
 - b. Attract investigators from disciplines outside of nutrition for collaborations that include a nutrition/obesity focus
 - c. Establish collaborative arrangements with other research Centers and encourage these Centers to support nutrition and obesity research
3. To enhance nutrition education for health professionals and nutrition scientists and to strengthen nutrition training programs at the UNC
4. To translate findings from nutrition and obesity research so the public can use this information to improve their health.

The UNC-CH NORC has assembled a diverse group of 130 investigators from 36 departments and five schools on campus in the deployment of novel nutrition and obesity methodologies in

human research. The research supported by our investigators is organized around our Center's six research focus areas:

- The Causes and Prevention of Obesity
- Metabolic Responses and Requirements for Nutrients
- Pregnancy, Child Growth and Development
- Nutritional Interventions and Nutrition Behaviors
- Nutrition and Chronic Diseases in Populations
- Clinical Nutrition

Core Laboratories

- **The Administrative Core** is responsible for the overall management of the UNC-CH NORC. This includes organizing the Internal Executive Committee and the External Advisory Board and managing the **Biostatistics, Enrichment, and Pilot & Feasibility Programs**.

Steven Zeisel, M.D., Ph.D., Director

Rosalind Coleman, M.D., Associate Director and Director of the Pilot & Feasibility Program

Joseph Galanko, Ph.D., Biostatistician

Michelle Collins, MPA, Administrator

In addition to the Administrative Core, the UNC-CH NORC also supports **four research Cores**:

- **The Diet, Physical Activity, and Body Composition in Human Populations Core** offers assistance with assessing parameters in epidemiological studies, including diet assessment tools, conversion of food intake to individual nutrients consumed, human body composition analysis, physical activity assessment, and assistance with interpretation of nutrition epidemiological data.

Anna Maria Siega-Riz, Ph.D., R.D., Core Director

Dianne Ward, Ed.D., Co-Director, Physical Activity Assessment

Kathryn Cole, Ph.D., Co-Director, Human Body Composition

Margaret Mangan, M.S., Core Coordinator

- **The Nutrition Communication for Health Applications and Interventions Core** offers assistance in designing and implementing nutrition interventions, including website and graphics development, survey instruments, and assistance with interpretation of data from nutrition intervention studies.

Marci Campbell, Ph.D., M.P.H., R.D., Core Director

Carol Carr, MA, Administrative Director

- **The Nutritional Biochemistry and Molecular Biology Core** offers assistance in designing and implementing biochemical nutrition studies and provides nutrition-relevant molecular and biochemical assays and assistance with interpretation of data from such studies.

Melinda Beck, Ph.D., Core Director
Qing Si, M.S., Core Coordinator

- The **Animal Metabolism Phenotyping Sub-Core** provides access to advanced, state-of-the-art phenotyping of traits related to metabolism and energy balance in mouse models of nutrition and disease.

Daniel Pomp, Ph.D., Sub-Core Director
Kunjie Hua, M.D., Sub-Core Coordinator

Internal Executive Committee and External Advisory Board

- The **Internal Executive Committee** (consisting of the Director, Associate Director, Core Directors, and two representatives of the NORC Research Base) is responsible for maintaining the quality and objectivity of policies that govern the UNC-CH NORC. The representatives from the NORC research base who serve on the Internal Executive Committee are:
 - Deborah Tate, Ph.D., Assistant Professor, Department of Health Behavior and Health Education
 - Linda Adair, Ph.D., Professor, Department of Nutrition
- Our External Advisory Board (EAB) is comprised of world-renowned scientists who have an understanding of population-based, clinical, and basic biomedical research in nutrition and obesity. The EAB provides strategic and operations guidance to our Center. The members of our EAB are:
 - James O. Hill, Ph.D., Professor, Department of Pediatrics and Medicine, University of Colorado at Denver; Director, University of Colorado at Denver NORC
 - Marian L. Neuhouser, Ph.D., Associate Member, Division of Public Health Sciences, Fred Hutchinson Cancer Research Center
 - Ken Resnicow, Ph.D., Professor, Department of Health Behavior & Health Education, University of Michigan
 - Judith Storch, Ph.D., R.D., Professor, Department of Nutritional Sciences, Rutgers University
 - W. Allan Walker, M.D., Professor, Department of Nutrition and Pediatrics, Harvard Medical School; Director, Harvard NORC; Director, Division of Nutrition, Harvard Medical School

Pilot and Feasibility Studies

The UNC-CH NORC Pilot and Feasibility Program provides research support to investigators during their critical transition years as new faculty members. We also provide limited support to established investigators whose expertise and research lie outside the area of nutrition and/or obesity. Listed below are the project abstracts for the 2009 and 2010 awardees.

2010 Awardees

The Role of Macrophage Activation and Glucose Transport in Obesity

PI: Liza Makowski, Ph.D., Assistant Professor, Department of Nutrition
Funding period: 4/1/2010–3/31/2011
Eligibility: New Investigator
NORC theme: Causes and Prevention of Obesity
Core facilities used: Administrative, Nutritional Biochemistry, & Molecular Biology

According to the World Health Organization, more than 1 billion people worldwide are overweight or obese. Immune cells were recently shown to be vital in the formation of obesity and insulin resistance. The goal of this research is to study how certain immune cells, specifically macrophages, under states of metabolic stress can promote the progression of obesity. Specifically, this project will investigate the complex links between fuel metabolism and inflammation.

Nutrition Intervention by α -lipoic Acid, a New Therapeutic Strategy for Treatment of Hypothermia During Sepsis

PI: Xianwen Yi, M.D., Ph.D., Research Assistant Professor, Department of Pathology and Laboratory Medicine
Funding period: 4/1/2010–3/31/2011
Eligibility: New Investigator
NORC theme: Clinical Nutrition
Core facilities used: Administrative, Nutritional Biochemistry & Molecular Biology, Animal Metabolism Phenotyping

Sepsis remains a serious problem with a high morbidity and mortality rate. Sepsis causes an excessive host inflammatory response characterized by massive increases in reactive oxygen species (ROS) and nitric oxide. Body temperature changes, either fever (greater than 38°C) or reduction in body temperature (lower than 36°C), are key diagnostic criteria in all definitions of sepsis. The mechanism of the fall in body temperature remains unclear and, thus, no effective therapy is available. This proposed project will provide important information on nutrition intervention by α -lipoic acid as a potential therapeutic agent for the drop in body temperature during sepsis.

2009 Awardees

The Influence of FADS2 rs174575 on Recognition Memory Abilities of 6-Month-Old Breastfed Infants

PI: Carol Cheatham, Ph.D., Assistant Professor, Department of Psychology
Funding period: 10/01/2009–9/30/2010
Eligibility: New Investigator
NORC theme: Pregnancy, Child Growth and Development
Core facilities used: Administrative, Nutritional Biochemistry & Molecular Biology

A single nucleotide polymorphism (snp) of the FADS2 gene, rs 174575, has been related to lower IQ in a retrospective study of breastfed children and lower levels of fatty acids in breast

milk. This study will examine levels of fatty acids in breast milk as they relate to a mother's genotype. Infants will be genotyped and invited to a second session if they are homozygous for this snp. Homozygous major and minor allele groups will be assessed in an event-related potential oddball paradigm for differences in recognition memory. This study will also test the genetic moderation of developing cognitive abilities concurrent with breastfeeding using high-density electrophysiology techniques.

Epigenetics of the Nutrient-Carcinogen Interactions: Role of Folate in Transplacental Carcinogenesis Associated with Exposure to Arsenic

PI: Zuzana Drobná, Ph.D., Research Assistant Professor, Department of Nutrition

Funding period: 10/01/2009–9/30/2010

Eligibility: New Investigator

NORC theme: Metabolic Responses and Requirements for Nutrients

Core facilities used: Administrative, Nutritional Biochemistry & Molecular Biology

Chronic environmental exposures to inorganic arsenic (mainly through drinking water) have been associated with several cancers including skin, liver, lung, and bladder. However, the exact mechanisms underlying the carcinogenic effects of inorganic arsenic (iAs) remain unclear. Epigenetic changes induced by nutrition and environmental exposure during critical periods of development can play a crucial role. The goal of this study is to examine the potential of diets with modified levels in folate (precursor of methyl groups) and how they might reverse or prevent epigenetic changes in the livers of mouse fetuses caused by prenatal exposure to iAs.

Publications:

- Drobná Z, Walton FS, Harmon AW, Thomas DJ, Stýblo M. Interspecies differences in metabolism of arsenic by cultured primary hepatocytes. *Toxicol Appl Pharmacol*. 2010 May 15;245(1):47–56. Epub 2010 Feb 4. PMID: 20138079; PMCID: PMC2862857.
- Drobná Z, Walton FS, Paul DS, Xing W, Thomas DJ, Stýblo M. Metabolism of arsenic in human liver: the role of membrane transporters. *Arch Toxicol*. 2010 Jan;84(1):3–16. Epub 2009 Dec 18. Review. PMID: 20020104.
- Drobná Z, Naranmandura H, Kubachka KM, Edwards BC, Herbin-Davis K, Stýblo M, Le XC, Creed JT, Maeda N, Hughes MF, Thomas DJ. Disruption of the arsenic (+3 oxidation state) methyltransferase gene in the mouse alters the phenotype for methylation of arsenic and affects distribution and retention of orally administered arsenate. *Chem Res Toxicol*. 2009 Oct;22(10):1713–20. PMID: 19691357; PMCID: PMC2763928.

Grant Pending:

- NIH (R01 Series) PI: Drobná. Carcinogen-nutrient interactions in transplacental arsenic carcinogenesis. This proposed study will examine nutrient interactions and arsenic carcinogenesis. Proposed project period: 12/1/2010–11/30/2015.

Effects of Dietary Non-Cholesterol Sterols on Pancreatic β -cell Function

PI: Eric Klett, M.D., Instructor, School of Medicine
Funding period: 4/1/2009–12/31/2010
Eligibility: New Investigator
NORC theme: Metabolic Responses and Requirements for Nutrients
Core facilities used: Administrative, Nutritional Biochemistry & Molecular Biology

Type 2 diabetes mellitus (T2DM) is a growing public health problem. Fat and cholesterol in many diets can contribute to the development of this disease. The cells that produce insulin can become poisoned by too much fat and cholesterol. The amount of cholesterol in the body is regulated, in part, by the amount of cholesterol that is consumed in the diet. Complex mechanisms exist to control the amount of cholesterol that enters the body. Some people have abnormalities in these mechanisms that can allow too much cholesterol and other related sterol molecules to enter the body. This study seeks to understand how dietary cholesterol and other related sterol molecules contribute to the poisoning of insulin-releasing cells and the development of T2DM.

Publications:

- Nagle, CA, Klett EL, Coleman RA. Hepatic triacylglycerol accumulation and insulin resistance. *J Lipid Res.* 2009; 50 Suppl:S74–9. PMID: 18997164; PMCID: PMC2674743.
- Li LO, Klett EL, Coleman RA. Acyl-CoA synthesis, lipid metabolism and lipotoxicity. *Biochem, Biophys. Acta* 2010; 1801:246–251. PMID: 19818872.

Grant Pending:

- NIH (K08 Series). PI: Klett. Role of Acyl-CoA synthetases in mouse pancreatic β -cell function. This proposed research will examine acyl-CoA synthetases in mouse pancreatic β -cell function. Proposed project period: 12/1/2010–11/30/2015.

The Role of Protein Quality Control in Mechanisms of Glucose Homeostasis

PI: Cam Patterson, M.D., Ernest Craige Distinguished Professor,
Department of Medicine
Funding period: 10/01/2009–9/30/2010
Eligibility: Established Investigator
NORC theme: Metabolic Responses and Requirements for Nutrients
Core facilities used: Administrative, Nutritional Biochemistry & Molecular Biology

The body's ability to monitor and regulate blood glucose levels is essential for health and development. Given the importance of blood glucose homeostasis, it not surprising that the body has implemented numerous ways to accomplish this regulation. Effective insulin production and controlled insulin sensitivity are essential and rely on the coordinated activities of an interactive organ network within the body. The breakdown or deregulation of any component of this system can result in failure of blood glucose control and diabetes. The pancreas and proper pancreatic function is paramount in achieving viable blood glucose levels. It stands to reason that any disease or process that interferes with the pancreas can be a contributing factor in the development of diabetes. The aim of this study is to provide new insights into chronic

mechanisms of glucose homeostasis, and potentially to provide novel targets for the prevention or intervention of diabetes mellitus in humans.

Publication:

- Willis MS, Townley-Tilson WH, Kang EY, Homeister JW, Patterson C. Sent to destroy: the ubiquitin proteasome system regulates cell signaling and protein quality control in cardiovascular development and disease. *Circ Res.* 2010 Feb 19;106(3):463–78. Review. PMID: 20167943; PMCID: PMC2826711.

Dopamine Release in an Animal Model of Binge Eating

PI: Donita Robinson, Ph.D., Assistant Professor, Department of Psychiatry/Assistant Professor, Bowles Center for Alcohol Studies; Wendy Foulds Mathes, Ph.D., Research Assistant Professor, Department of Genetics

Funding period: 10/01/2009–9/30/2010

Eligibility: Established Investigator (DR)
New Investigator (WFM)

NORC theme: Nutrition and Chronic Diseases in Populations

Core facilities used: Administrative, Animal Metabolism Phenotyping, Nutritional Biochemistry & Molecular Biology

Binge eating (BE) is a maladaptive behavior that is characterized by episodes of rapid and excessive food consumption in a relatively short period of time, not necessarily driven by hunger or metabolic need. Overweight and obesity, together with the associated physical and psychological health concerns, commonly occur with BE. BE behaviors in both humans and animals have been associated with alterations in the brain chemical dopamine and involves a strong component of conditioning (or learning). While dopamine is an important brain signal in other disorders that involve compulsions, such as drug addiction and gambling, its role in BE is less understood. This study will examine the role that phasic dopamine release plays in the initiation and maintenance of BE behavior, representing a neuroadaptive process that is conditioned by environmental and physiologic cues.

Publication:

- Mathes WF, Nehrenberg DL, Gordon R, Hua K, Garland T Jr, Pomp D. Dopaminergic dysregulation in mice selectively bred for excessive exercise or obesity. *Behav Brain Res.* 2010 Jul 11;210(2):155–63. Epub 2010 Feb 13. PMID: 20156488.

Grant Pending:

- Klarman Family Foundation. PI: Foulds Mathes; Co-Investigator: Robinson. Dopamine release in an animal model of binge eating. This proposed study will examine dopamine release in an animal model of binge eating. Proposed project period: 7/1/2010–6/30/2012.

Obesity and Microglial Activation: Potential for Synergism in Neurodegenerative Diseases

PI: Patricia Sheridan, Ph.D., Research Assistant Professor, Department of Nutrition
Funding period: 4/1/2009–3/31/2011
Eligibility: New Investigator
NORC theme: Metabolic Responses and Requirements for Nutrients
Core facilities used: Administrative, Nutritional Biochemistry & Molecular Biology

The factors that result in the development of neurodegenerative diseases like Alzheimer's disease (AD) are not well understood. It is suggested that smoking, lack of exercise, and eating a diet high in fat may increase an individual's risk for developing AD. Obesity may also be another factor associated with the risk of developing the disease. As our population ages and becomes increasingly obese, the effects of diet on age-related neurological conditions are a significant public health concern. This study will examine how high-fat diets and obesity result in alterations in the brain that are associated with AD. To determine effects on inflammation, this study will also examine neurons, which are responsible for brain functioning including memory, and microglia, which protect neurons.

Maternal Genotype and Pregnancy Adiposity Study

PI: Alison Stuebe, M.D., M.S.C., Assistant Professor, Department of Obstetrics & Gynecology
Funding period: 4/1/2009–12/31/2010
Eligibility: New Investigator
NORC theme: Pregnancy, Child Growth and Development
Core facilities used: Administrative; Diet, Physical Activity, & Body Composition

During pregnancy, changes in a woman's metabolism can predict and affect her long-term health as well as affect the health of her child. In the span of 40 weeks, pregnant women gain an average of 30 pounds and dramatically change the way their bodies respond to glucose and insulin. Women who gain too much weight are more likely to be obese later in life, and their children are more likely to be overweight as well. These patterns likely reflect a combination of health behaviors and genetic differences in a woman's risk for gaining weight. Scientists have recently identified multiple differences in genes that affect the risk for obesity and type 2 diabetes. This study investigates how these genetic factors influence changes in a woman's body weight during pregnancy and examine how genes, combined with diet and exercise, influence weight gain.

Publications:

- Stuebe A, Ecker J, Bates DW, Zera C, Bentley-Lewis R, Seely E. Barriers to follow-up for women with a history of gestational diabetes. *Am J Perinatol*. 2010 Apr 12. PMID: 20387186.
- Stuebe A, McElrath TF, Thadhani R, Ecker JL. Second trimester insulin resistance, early pregnancy body mass index and gestational weight gain. *Matern Child Health J*. 2010;14(2):254–60. PMID: 19194791.

- Stuebe AM, Oken E, Gillman MW. Associations of diet and physical activity during pregnancy with risk for excessive gestational weight gain. *Am J Obstet Gynecol*. 2009 Jul;201(1):58.e1–8. Epub 2009 May 21. PMID: 19467640; PMCID: PMC2706304.

Funding Derived From Previous Pilot and Feasibility Studies

Listed below are research grants received in 2009 and 2010 by former awardees.

Midkine Expression and Colorectal Adenomas

Temitope Keku, Ph.D., Associate Professor, Department of Medicine

This P&F project compared subjects with and without colorectal adenomas to 1) determine the association between plasma midkine levels, messenger RNA (mRNA), and protein expression; 2) evaluate the relationship between midkine protein expression and apoptosis; and 3) assess the relationship between plasma levels and tissue expression levels of midkine, plasma retinoic acid, beta-carotene, and dietary factors.

P&F funding period: 9/30/2004–3/31/2007

Grants Received:

- NIH/NCI (R01CA136887) Co-PIs: Keku and Sandler. Intestinal microbiota, diet, and risk of colorectal adenomas. The major goals of this study are to (1) characterize the mucosal adherent bacteria and (2) to determine the association between mucosal adherent bacteria, adenomas, and diet. Project period: 5/1/2009–4/30/2014.
- NIH/NCI (R01CA044684) PI: Sandler. Inflammation, obesity, and the risk of colorectal adenomas. The goal of this American Recovery and Reinvestment Act (ARRA) supplement is to improve the understanding of the role of obesity and inflammation in the development of colorectal neoplasia and to predict mechanistic links between inflammation and adenoma risk. Project period: 9/30/2009–9/29/2011. (Role: Investigator).

Metabolism of Dietary N-Glycolylneuraminic Acid

Eric Park, Ph.D., Research Associate Professor, Department of Nutrition

This P&F project examined whether or not the changes in the candidate genes can increase the accumulation of N-glycolylneuraminic acid on the surface of human cells by observing the differences in sialic acid metabolism and gene expression between human intestinal (CaCO-2) and liver (HepG2) cell lines.

P&F funding period: 7/1/2006–6/15/2008

Grant Received:

- NIH/NCI (R21CA127836) PI: Park. Dietary modulation of sialic acid modifications. This study examines the sialic acid-binding property of the asialoglycoprotein receptor (ASGPR) and its link to dietary components and the inflammation process. Project period: 1/1/2009–12/31/2010.

Maternal Feeding Responsiveness During Infancy and Toddlerhood

Eric Hodges, Assistant Professor, Department of Nursing

This P&F project explored the relationship between maternal feeding responsiveness and the development and maintenance of obesity during infancy and toddlerhood.

P&F funding period: 4/1/2008–3/31/2010

Grant Received:

- Robert Wood Johnson Foundation. PI: Hodges. Maternal feeding responsiveness and risk of obesity from infancy through early childhood. This study explores the relationship between maternal feeding responsiveness and the risk of obesity from infancy through early childhood. Project period: 9/1/2009–8/31/2012.

Scientific Research Advances/Accomplishments

The UNC-CH NORC has had several significant scientific research advances and accomplishments during the past year. All of the research listed below was conducted by our Center's investigators and was supported and/or enhanced by our research Cores.

Diet, Physical Activity, and Body Composition Core

Body Mass Index Distributions in Australia, China, the United Kingdom, and the United States. To explore the global shift in body mass index (BMI), Dr. Barry Popkin (Professor, Department of Nutrition) examined BMI data for men, women, and children in Australia, China, the United Kingdom, and the United States. Results show that much larger increases were found among women in mean BMI at the 95th percentile in Australia (+5.7 BMI units) and the United Kingdom (+3.7 BMI units) than in the United States (+2.7 BMI units) in one-half the time. Among children, younger Chinese children experienced the largest increase. The mean BMI at the 95th percentile for 6-year-old Chinese children is 24.8 (a 5.0 increase), which is 2.6 BMI units more than the BMI at the 95th percentile for children in the United States. This evidence suggests that BMIs for U.S. children at the 95th percentile are below those in China and Australian, and U.K. women are rapidly approaching BMIs found in US women. This study was funded by the National Cancer Institute (PI: Barry Popkin–R01CA121152). The Diet, Physical Activity, and Body Composition Core provided consultation on dietary behavior and dietary assessment for this study.

- Popkin BM. Recent dynamics suggest selected countries catching up to US obesity. *Am J Clin Nutr.* 2010 Jan;91(1):284S–288S. Epub 2009 Nov 11. PMID: 19906804; PMCID: PMC2793114.

Examining the Relationship between Infant Weight and Delayed Motor Development.

Using participants from the Infant Care, Feeding, and Risk of Obesity project (a prospective, longitudinal study of low-income African American mother-infant dyads), Drs. Linda Adair and Margaret Bentley (Professors, Department of Nutrition) explored the relationship between infant weight, high subcutaneous fat, and motor development. Results show that motor delay was 1.80 times as likely in overweight infants compared with non-overweight infants and 2.32 times as likely in infants with high subcutaneous fat compared with infants with lower subcutaneous fat.

High subcutaneous fat was also associated with a delay in subsequent motor development. The Diet, Physical Activity, and Body Composition Core provided quality control assessment for this study.

- Slining M, Adair LS, Goldman BD, Borja JB, Bentley M. Infant overweight is associated with delayed motor development. *J Pediatr*. 2010 Mar 12. PMID: 20227724.

Food Price and Diet and Health Outcomes. Using participants from the CARDIA study, Drs. Penny Gordon-Larsen (Associate Professor, Department of Nutrition) and Barry Popkin (Professor, Department of Nutrition) explored the association between food price, dietary intake, overall energy intake, weight, and homeostatic model assessment insulin resistance (HOMA-IR) scores to determine whether food price has an impact on diet and health outcomes. Results show that a 10% increase in the price of soda or pizza was associated with a -7.12% or -11.5% change in energy from these foods, respectively. A \$1.00 increase in soda price was also associated with lower daily energy intake (-124 kcal), lower weight (-1.05 kg), and lower HOMA-IR scores (0.42); similar trends were also observed for pizza. A \$1.00 increase in the price of both soda and pizza was associated with greater changes in total energy intake (-181.49 kcal), body weight (-1.65 kg), and HOMA-IR scores (-0.45). This suggests that policies aimed at altering the price of soda or away-from-home pizza may be an effective mechanism to steer U.S. adults toward a more healthful diet and help reduce long-term weight gain or insulin levels over time. The Diet, Physical Activity, and Body Composition Core provided dietary assessments for this study.

- Duffey KJ, Gordon-Larsen P, Shikany JM, Guilkey D, Jacobs DR Jr, Popkin BM. Food price and diet and health outcomes: 20 years of the CARDIA Study. *Arch Intern Med*. 2010 Mar 8; 170(5):420–6. Erratum in: *Arch Intern Med*. 2010 Jun 28;170(12):1089. PMID: 20212177.

Vitamin Supplementation in Early Pregnancy and Risk of Miscarriage. Drs. Andrew Olshan (Professor, Department of Epidemiology), Amy Herring (Associate Professor, Department of Biostatistics), and Anna Maria Siega-Riz (Professor, Departments of Epidemiology and Nutrition) evaluated the relationship between self-reported use of prenatal vitamins in early pregnancy and the risk of miscarriage. Using data from 4,752 U.S. women enrolled in the Right from the Start program, results show that of the approximately 95% of participants who reported use of vitamins during early pregnancy, a total of 524 women had miscarriages. This evidence suggests that any use of vitamins during pregnancy is associated with decreased odds of miscarriage in comparison to no vitamin exposure. The Diet, Physical Activity, and Body Composition Core provided dietary assessment for this study.

- Hasan R, Olshan AF, Herring AH, Savitz DA, Siega-Riz AM, Hartmann KE. Self-reported vitamin supplementation in early pregnancy and risk of miscarriage. *Am J Epidemiol*. 2009 Jun 1;169(11):1312–8. Epub 2009 Apr 16. PMID: 19372214; PMCID: PMC2727248.

Nutritional Biochemistry and Molecular Biology

Adherence to Walking or Stretching and the Risk of Preeclampsia in Sedentary Pregnant Women. Dr. Seon Ae Yeo (Associate Professor, School of Nursing) conducted a randomized trial with 124 sedentary pregnant women to compare the effects of walking exercise to stretching exercise on adherence and on the preeclampsia risk factors of heart rate, blood pressure, and

weight gain. Results show that walkers exercised less than stretchers, both overall and as pregnancy advanced. Additionally, heart rate and blood pressure were lower among stretchers than walkers, but weight gain did not differ between the groups. Adherence to exercise also decreased as the weeks of gestation increased. The top adherers maintained levels of adherence, and the bottom adherers decreased levels of adherence. Adherence patterns were influenced by the type of exercise performed throughout the study period. Dr. Yeo recently submitted an R21 application to the NIH based on the data from this study. The Nutritional Biochemistry and Molecular Biology Core provided oxidative stress measurements of the serum in the study participants.

- Yeo S, Cisewski J, Lock EF, Marron JS. Exploratory analysis of exercise adherence patterns with sedentary pregnant women. *Nurs Res*. 2010 Jul–Aug; 59(4):280–7. PMID: 20585224.
- Yeo S. Adherence to walking or stretching, and risk of preeclampsia in sedentary pregnant women. *Res Nurs Health*. 2009 Aug;32(4):379–90. PMID: 19415672; PMCID: PMC2895148.

Metabolomic Profiling, Liver Dysfunction, and Dietary Choline. Drs. Kerry-Ann Da Costa (Research Assistant Professor, Department of Nutrition), Leslie Fischer (Research Assistant Professor, Department of Nutrition), and Steven Zeisel (Professor, Departments of Nutrition and Pediatrics) examined whether metabolomic profiling of plasma can predict if humans will develop liver dysfunction when deprived of dietary choline. Using a sample size of 61 participants, 53 participants were fed a diet containing 550 mg choline/70 kg/day for 10 days and then fed less than 50 mg choline/70 kg/day for up to 42 days. Participants who developed organ dysfunction on this diet were repleted with a choline-adequate diet for at least 3 days. Results show that metabolomic profiling and targeted biochemical analyses were highly correlated for the analytes assessed by both procedures. Additionally, relative concentration changes of other small molecules were detected by the non-targeted metabolomic analysis after choline depletion. This evidence suggests that metabolomic profiling in humans can detect metabolic abnormalities in apparently healthy humans who will develop fatty liver when fed a low choline diet. This study (Human Requirements for the Nutrient Choline) is funded by the National Institute of Diabetes and Digestive and Kidney Diseases (PI: Steven Zeisel–R01DK055865). The Nutritional Biochemistry and Molecular Biology Core provided metabolomic and choline analyses for this study.

- Sha W, da Costa KA, Fischer LM, Milburn MV, Lawton KA, Berger A, Jia W, Zeisel SH. Metabolomic profiling can predict which humans will develop liver dysfunction when deprived of dietary choline. *FASEB J*. 2010 Apr 6. PMID: 20371621.

Diet-Induced Obesity and the T-Cell Memory Response to Influenza Virus Infection. In this study by Drs. Patricia Sheridan (Research Assistant Professor, Department of Nutrition) and Melinda Beck (Professor, Department of Nutrition), they found that in male, diet-induced obese C57BL/6 mice, a secondary H1N1 influenza challenge following a primary influenza A virus subtype H3N2 (H3N2) infection led to a 25% mortality rate (with no loss of lean controls), a 25% increase in lung pathology, failure to regain weight, and 10-fold to 100-fold higher lung viral titers. Results also suggest that mRNA expression for IFN- γ was 60% less in lungs of obese mice, along with one-third the number of influenza-specific CD8(+) T cells producing IFN- γ postsecondary infection versus lean controls. Memory CD8(+) T cells from obese mice had a

50% reduction in IFN- γ production when stimulated with influenza-pulsed dendritic cells from lean mice. Thus, the function of influenza-specific memory T cells is significantly reduced and ineffective in lungs of obese mice. The reality of a worldwide obesity epidemic combined with yearly influenza outbreaks and the current pandemic makes it imperative to understand how influenza virus infection behaves differently in an obese host. Impairment of memory responses has significant implications for vaccine efficacy in an obese population. This study (Role of Influenza Infection in a Vaccinated Obese Population) is funded by the National Institute of Allergy and Infectious Diseases (PI: Melinda Beck–R01AI078090). The Nutritional Biochemistry and Molecular Biology Core performed the immunoassays for antibody detection.

- Karlsson EA, Sheridan PA, Beck MA. Diet-induced obesity impairs the T-cell memory response to influenza virus infection. *J Immunol.* 2010 Mar 15;184(6):3127–33. Epub 2010 Feb 19. PMID: 20173021.

Hepatic Steatosis and Insulin Resistance. In this study, Dr. Rosalind Coleman (Professor, Department of Nutrition) and her research team examined whether ob/ob mice lacking glycerol-3-phosphate acyltransferase-1 (Gpat1) would have reduced hepatic steatosis and improved insulin sensitivity. Results show that, compared with ob/ob mice, the lack of Gpat1 in ob/ob mice reduced hepatic triacylglycerol (TAG) and diacylglycerol (DAG) content 59% and 74%, respectively, but increased acyl-CoA levels. Despite the reduction in hepatic lipids, fasting glucose and insulin concentrations did not improve, and insulin tolerance remained impaired. In both ob/ob and ob/ob-Gpat1(-/-) mice, insulin resistance was accompanied by elevated hepatic protein kinase C-epsilon activation and blunted insulin-stimulated Akt activation. These results suggest that decreasing hepatic steatosis alone does not improve insulin resistance, and that factors other than increased hepatic DAG and TAG contribute to hepatic insulin resistance in this genetically obese model. It also shows that the SREBP1-mediated induction of hepatic steatosis in ob/ob mice requires Gpat1. The Nutritional Biochemistry and Molecular Biology Core provided qRT-PCR analysis for this research study.

- Wendel AA, Li LO, Li Y, Cline GW, Shulman GI, Coleman RA. Glycerol-3-phosphate acyltransferase 1 deficiency in ob/ob mice diminishes hepatic steatosis but does not protect against insulin resistance or obesity. *Diabetes.* 2010 Jun;59(6):1321–9. Epub 2010 Mar 3. PMID: 20200319; PMCID: PMC2874692.

Animal Metabolism Phenotyping Sub-Core

Dopaminergic Dysregulation in Mice Selectively Bred for Excessive Exercise or Obesity. Dysregulation of the dopamine system has been linked to various aberrant behaviors, including addiction, compulsive exercise, and hyperphagia leading to obesity. The goal of this study by current P&F awardee Dr. Wendy Foulds Mathes (Research Assistant Professor, Department of Genetics) and her research team is to determine how dopamine contributes to the expression of opposing phenotypes, excessive exercise, and obesity. They hypothesized that similar alterations in dopamine and dopamine-related gene expression might underlie obesity and excessive exercise, as competing traits for central reward pathways. They also hypothesized that selective breeding for high levels of exercise or obesity might have influenced genetic variation controlling these pathways, manifesting as opposing complex traits. High performance liquid chromatography analysis showed significantly greater neurotransmitter concentrations in dorsal

striatum and nucleus accumbens of high rates of wheel running mice compared to M16 (mice with increased body mass and body fat) and ICR (a mouse strain from the Institute of Cancer Research). Additionally, microarray analysis showed significant gene expression differences between HR and M16 mice compared to ICR mice in both brain areas, with changes revealed throughout the dopamine pathway including D1 and D2 receptors, associated G-proteins (e.g., Golf), and adenylate cyclase (e.g., Adcy5). This evidence suggests that similar modifications within the dopamine system might contribute to the expression of opposite phenotypes in mice, demonstrating that alterations within central reward pathways can contribute to both obesity and excessive exercise. The Animal Metabolism Phenotyping Sub-Core provided magnetic resonance imaging (MRI), food intake, and calorimetry services for the mice in this study.

- Mathes WF, Nehrenberg DL, Gordon R, Hua K, Garland T Jr, Pomp D. Dopaminergic dysregulation in mice selectively bred for excessive exercise or obesity. *Behav Brain Res*. 2010 Jul 11;210(2):155–63. Epub 2010 Feb 13. PMID: 20156488.

Genetic Reduction of Lipoic Acid Synthase Expression in Apolipoprotein E-Deficient Mice.

Dr. Nobuyo Maeda (Professor, Department of Pathology & Laboratory Medicine) and her research team recently evaluated the effects of a genetic reduction of Lias gene expression on atherosclerosis development in mice. Results show that lesions at the aortic sinus in Lias (+/-) ApoE (-/-) males were significantly larger (1.5 times more) than those in Lias (+/+) ApoE (-/-) littermate males. The lesion size was inversely correlated with an increased erythrocyte reduced glutathione/oxidized glutathione (GSH/GSSH) ratio, a systemic index of body redox balance. Lias (+/-) ApoE (-/-) males also had significantly increased plasma cholesterol and reduced pyruvate dehydrogenase complex activity in the liver. Significant reductions in the expression of genes for antioxidant enzymes, including superoxide dismutase 1 (SOD1) and SOD2, were observed in aortas of Lias (+/-) ApoE (-/-) males. Female Lias (+/-) ApoE (-/-) also exhibited changes in these parameters, parallel to those observed in males. However, the Lias gene effects for the majority of these factors, including atherosclerotic lesion size, were not significant in females. This study (Dyslipidemia, Lipoic Acid, and Diabetic Vascular Complications in Humanized Mice) is funded by the National Heart, Lung, and Blood Institute (PI: Nobuyo Maeda-U01-HL087946). The Animal Metabolism Phenotyping Sub-Core provided MRI and calorimetry services for the mice in this study.

- Yi X, Xu L, Kim K, Kim HS, Maeda N. Genetic reduction of lipoic acid synthase expression modestly increases atherosclerosis in male, but not in female, apolipoprotein E-deficient mice. *Atherosclerosis* 2010 Mar 10. PMID: 20347443.

Role of Jhdm2a in Regulating Metabolic Gene Expression and Obesity Resistance. Recent studies indicate that the methylation state of histones can be dynamically regulated by histone methyltransferases and demethylases. The H3K9-specific demethylase Jhdm2a (also known as Jmjd1a and Kdm3a) plays an important role in nuclear hormone receptor-mediated gene activation and male germ cell development. By disrupting the Jhdm2a gene in mice, Dr. Yi Zhang (Professor, Department of Biochemistry and Biophysics) and his research team demonstrated that Jhdm2a is critically important in regulating the expression of metabolic genes. The loss of Jhdm2a function results in obesity and hyperlipidemia in mice. This evidence suggests that the loss of Jhdm2a function disrupts beta-adrenergic-stimulated glycerol release and oxygen consumption in brown fat, and decreases fat oxidation and glycerol release in

skeletal muscles. Results also show that Jhdm2a expression is induced by beta-adrenergic stimulation, and that Jhdm2a directly regulates peroxisome proliferator-activated receptor alpha (PPAR-alpha) and Ucp1 (uncoupling protein homologue gene) expression. It was also proven that beta-adrenergic activation-induced binding of Jhdm2a to the PPAR responsive element (PPRE) of the Ucp1 gene not only decreases levels of H3K9me2 (dimethylation of lysine 9 of histone H3) at the PPRE, but also facilitates the recruitment of PPAR-gamma and RXR-alpha and their co-activators Pgc1alpha (also known as PGC-1a), CBP/p300 (Crebbp: peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1alpha), cAMP response element-binding protein (CREBBP), and steroid receptor coactivator-1 (SRC1) to the PPRE. The Animal Metabolism Phenotyping Sub-Core provided calorimetry services for the mice in this study.

- Tateishi K, Okada Y, Kallin EM, Zhang Y. Role of Jhdm2a in regulating metabolic gene expression and obesity resistance. *Nature* 2009 Apr 9;458(7239):757–61. Epub 2009 Feb 4. PMID: 19194461.

Multi-Tissue Coexpression Networks Reveal Unexpected Subnetworks Associated with Obesity. To provide an inter-tissue view of obesity with respect to molecular states that are associated with physiological states, Dr. Daniel Pomp (Professor, Departments of Genetics, Cell and Molecular Physiology, and Nutrition) and his research team developed a framework for constructing tissue-to-tissue co-expression networks between genes in the hypothalamus, liver, or adipose tissue. These networks have a scale-free architecture and are strikingly independent of gene-gene co-expression networks that are constructed from more standard analyses of single tissues. This is the first systematic effort to study inter-tissue relationships and highlights genes in the hypothalamus that act as information relays in the control of peripheral tissues in obese mice. Results show that the subnetworks identified as specific to tissue-to-tissue interactions were enriched in genes that have obesity-relevant biological functions such as circadian rhythm, energy balance, stress response, or immune response. Additionally, tissue-to-tissue networks enable the identification of disease-specific genes that respond to changes induced by different tissues and they also provide unique details regarding candidate genes for obesity that are identified in genome-wide association studies. Identifying such genes from single tissue analyses would be difficult or impossible. The Animal Metabolism Phenotyping Sub-Core provided study design, MRI, and dual-energy X-ray absorptiometry services for the mice used in this study.

- Dobrin R, Zhu J, Molony C, Argman C, Parrish ML, Carlson S, Allan MF, Pomp D, Schadt EE. Multi-tissue coexpression networks reveal unexpected subnetworks associated with disease. *Genome Biol.* 2009;10(5):R55. Epub 2009 May 22. PMID: 19463160; PMCID: PMC2718521.

Nutrition Communication for Health Applications and Interventions (CHAI) Core

Podcasting Weight-Loss Intervention. Drs. Marci Campbell (Professor, Department of Nutrition), Deborah Tate (Assistant Professor, Department of Health Behavior and Health Education), and Kimberly Truesdale (Research Assistant Professor, Department of Nutrition) explored the use of podcasting (audio files for a portable music player or computer) to promote weight loss. The study involved a 12-week randomized controlled trial of 78 overweight men and women (BMI of 25 to 40) in the Raleigh-Durham, North Carolina, area. Participants in a

control group listened to 24 episodes of a currently available weight-loss podcast, while another group listened to an enhanced podcast, designed using behavior change theories. The enhanced podcast used aspects of social cognitive theory, including that behavior change is based upon an individual's expectancy (how much they would value an end result) and expectation (whether they believe they will succeed or fail). The recordings included exercise and nutrition information, a soap opera that discussed weight loss, and an audio journal of another person trying to lose weight but whose progress was a week or two ahead of the participant's. As participants worked on setting calorie goals, decreasing fat intake and increasing exercise, the audio diarist was also able to set goals, adjust to setbacks, and succeed behaviorally. Results show the study participants who used the enhanced podcast experienced a significantly greater decrease in both weight and BMI than the control group. The enhanced group lost 6.4 pounds in 12 weeks, compared to 0.7 pounds in the control group, and dropped one point in BMI compared to a 0.1-point drop in the control group. The CHAI Core provided database development/management and administrative support for this project.

- Turner-McGrievy GM, Campbell MK, Tate DF, Truesdale KP, Bowling JM, Crosby L. Pounds Off Digitally study: a randomized podcasting weight-loss intervention. *Am J Prev Med.* 2009 Oct;37(4):263–9. PMID: 19765496.

Use of Text-Messaging in the Treatment of Bulimia Nervosa. Dr. Cynthia M. Bulik (Professor, Departments of Psychiatry and Nutrition) and her research team explored whether text messaging could be used as a self-monitoring tool within the context of cognitive-behavioral therapy. Results show that 87% of participants adhered to self-monitoring and reported good acceptability. The number of binge-eating and purging episodes as well as symptoms of depression, eating disorder, and night eating decreased significantly from baseline to both post-treatment and follow-up. Given the frequent use of mobile phones and text-messaging globally, this evidence suggests their use may enhance self-monitoring and treatment for bulimia nervosa, leading to improved attendance, adherence, engagement in treatment, and remission from the disorder. This study (Optimizing Technology in the Treatment of Bulimia Nervosa) is funded by the National Institute of Mental Health (PI: Cynthia Bulik-R01MH080065). The CHAI Core provided computer programming, database development, web development, and administrative support for this study.

- Shapiro JR, Bauer S, Andrews E, Pisetsky E, Bulik-Sullivan B, Hamer RM, Bulik CM. Mobile therapy: use of text messaging in the treatment of bulimia nervosa. *Int J Eat Disord.* 2009 Aug 28. PMID: 19718672.

Weight Loss Intervention for Low-Income Women. Low-income women in the United States have the highest rates of obesity, yet they are seldom included in weight loss interventions. To address this research gap, Drs. Carmen Samuel-Hodge (Research Assistant Professor, Department of Nutrition), Alice Ammerman (Professor, Department of Nutrition), and Thomas C. Keyserling (Associate Professor, Department of Medicine) combined components of two evidence-based weight loss interventions to create a 16-week intervention for low-income women. Of the 143 participants, 72 were randomized to the Weight Wise Program (WWP) and 71 to the Control Group (CG). Data from the five-month follow-up show WWP participants had a weight change of -3.7 kg compared to 0.7 kg in the CG. The difference between groups for change in body fat of 1.7% was also significant. For systolic blood pressure (SBP), change in the

WWP was -6.5 mm Hg compared to -0.4 mm Hg among controls; for diastolic BP (DBP), changes were -4.1 mm Hg for WWP compared to -1.3 mm Hg for controls. High-density lipoprotein cholesterol increased 0.8 mg/dl in the WWP and decreased 1.1 mg/dl in the CG. Of the 72 WWP participants, 64%, 47%, and 19% lost at least 3%, 5%, and 7% of their initial body weight, respectively. This evidence suggests that participation in the WWP is associated with statistically significant and clinically important short-term weight loss. This study (Intensive Behavioral Weight Management in Public Health Settings) was funded by the Centers for Disease Control and Prevention (PI: Carmen Samuel-Hodge–R18DP001144). The CHAI Core provided database development and management support for this study.

- Samuel-Hodge CD, Johnston LF, Gizlice Z, Garcia BA, Lindsley SC, Bramble KP, Hardy TE, Ammerman AS, Poindexter PA, Will JC, Keyserling TC. Randomized trial of a behavioral weight loss intervention for low-income women: the Weight Wise Program. *Obesity (Silver Spring)* 2009 Oct;17(10):1891–9. Epub 2009 Apr 30. PMID: 19407810.

Responses to Global Coronary Heart Disease. Drs. Stacey Sheridan (Assistant Professor, Department of Medicine) and Michael P. Pignone (Associate Professor, Department of Medicine) explored how individuals respond to global coronary heart disease (CHD) risk and how they use treatment information to make decisions to initiate and maintain risk-reducing strategies. The researchers conducted four focus groups of individuals at risk for CHD (n=29). Results show that participants generally regarded the concept of global CHD risk as useful and motivating, although many had questions about its precision and comprehensiveness. The participants identified several additional influential factors in decision making (e.g., achievable risk, the quickness and self-evidence of results) and generally preferred lifestyle changes (including diet and exercise) to medications (although most would accept medications under certain circumstances). They also noted the importance of participating in decision making. Overall, this evidence underscores the motivating potential of global CHD risk and the importance of patient participation in decision making. This study (An Intervention to Improve Decision-Making and Adherence to Heart Disease Prevention) was funded by the American Heart Association (PI: Stacey Sheridan–0530164N). The CHAI Core provided database development/management, usability testing, web development, technical consulting, and administrative support for this study.

- Sheridan SL, Behrend L, Vu MB, Meier A, Griffith JM, Pignone MP. Individuals' responses to global CHD risk: a focus group study. *Patient Educ Couns.* 2009 Aug; 76(2):233–9. Epub 2009 Mar 14. PMID: 19286342; PMCID: PMC2713789.

Specific Accomplishments

Our investigators have made several significant research advances and accomplishments in various key areas of public health. Listed below are some examples of these advances and accomplishments during the past year.

Women's Health

The Risks of Not Breastfeeding for Mothers and Infants. Current P&F awardee Dr. Alison Stuebe (Assistant Professor, Department of Obstetrics and Gynecology) is currently investigating

how breastfeeding impacts diabetes, heart disease, stress, and metabolism. She found that women who breastfed for 2 years or more had a 23% lower risk of heart attack. Results also showed that nursing mothers had a 15% lower risk per year of breastfeeding, and women who breastfed a single child for 1 year had a lower risk than women who breastfed two children for shorter periods totaling 1 year. Additionally, there was clear evidence that women who breastfeed have a different response to stress than those who bottle-feed. Oxytocin—a hormone that reduces fear and increases trust—is believed to be a key factor since it is released during breastfeeding.

- Stuebe A. The risks of not breastfeeding for mothers and infants. *Rev Obstet Gynecol.* 2009 Fall;2(4):222–31. PMID: 20111658; PMCID:PMC2812877.

Dietary Intakes of Choline and Betaine and Breast Cancer Risk and Mortality. Drs. Marilie Gammon (Professor, Department of Epidemiology) and Steven Zeisel (Professor, Department of Nutrition and Pediatrics) investigated the association between dietary intakes of choline and betaine and breast cancer risk and mortality in the population-based Long Island Breast Cancer study. Among the 1,508 case-group women, 308 (20.2%) deaths occurred, of which 164 (53.2%) deaths were from breast cancer. Results show that higher intakes of betaine, phosphocholine, and free choline were associated with reduced all-cause as well as breast cancer-specific mortality in a dose-dependent fashion. The researchers also explored associations of polymorphisms of three key choline- and betaine-metabolizing genes and breast cancer mortality. Results show that the betaine-homocysteine methyltransferase gene (BHMT) rs3733890 polymorphism was associated with reduced breast cancer-specific mortality. This study supports the important roles of choline and betaine in breast carcinogenesis by suggesting that high intake of these nutrients may be a promising strategy to prevent the development of breast cancer and to reduce its mortality. This study (Dietary Methyl Content, Epigenetics, and Etiology of Breast Cancer) is funded by the National Cancer Institute (PI: Marilie Gammon–R01CA109753). The Nutritional Biochemistry and Molecular Biology Core provided betaine and choline analysis for this study.

- Xu X, Gammon MD, Zeisel SH, Bradshaw PT, Wetmur JG, Teitelbaum SL, Neugut AI, Santella RM, Chen J. High intakes of choline and betaine reduce breast cancer mortality in a population-based study. *FASEB J.* 2009 Nov;23(11):4022–8. Epub 2009 Jul 27. PMID: 19635752; PMCID: PMC2775010.

Severe Obesity, Gestational Weight Gain, and Adverse Birth Outcomes. In this study, Dr. Anna Maria Siega-Riz (Professor, Departments of Epidemiology and Nutrition) explored the association between gestational weight gain and small-for-gestational-age (SGA) births, large-for-gestational-age (LGA) births, spontaneous preterm births (sPTBs), and medically indicated preterm births (iPTBs) among obese women who were stratified by severity of obesity. Results show a prevalence of excessive gestational weight gain declined, and weight loss increased, as obesity became more severe. Generally, weight loss was associated with an elevated risk of SGA, iPTB, and sPTB, and a high weight gain tended to increase the risk of LGA and iPTB. Weight gains associated with probabilities of SGA and LGA of 10% or less and a minimal risk of iPTB and sPTB were as follows: 9.1–13.5 kg (obesity class 1), 5.0–9 kg (obesity class 2), 2.2 to less than 5.0 kg (obesity class 3 white women), and less than 2.2 kg (obesity class 3 black women). This data suggests that the range of gestational weight gain to balance risks of SGA, LGA, sPTB, and iPTB may vary by severity of obesity.

- Bodnar LM, Siega-Riz AM, Simhan HN, Himes KP, Abrams B. Severe obesity, gestational weight gain, and adverse birth outcomes. *Am J Clin Nutr.* 2010 Mar 31. PMID: 20357043.

Sexual Functioning in Women with Eating Disorders. Dr. Cynthia M. Bulik (Professor, Departments of Psychiatry and Nutrition) and her research team examined the physical intimacy, libido, sexual anxiety, partner status, and sexual relationships of 242 women from the International Price Foundation Genetic Studies to determine whether there is a relationship between sexual dysfunction and eating disorders. Results show that women with restricting and purging anorexia nervosa had a higher prevalence of loss of libido than women with bulimia nervosa and eating disorder not otherwise specified (75%, 74.6%, 39%, and 45.4%, respectively). Absence of sexual relationships was associated with lower minimum lifetime BMI and earlier age of onset; loss of libido with lower lifetime BMI, higher interoceptive awareness, and trait anxiety; and sexual anxiety with lower lifetime BMI, higher harm avoidance, and ineffectiveness. Sexual dysfunction in eating disorders was found to be higher than sexual dysfunction in the normative sample.

- Pinheiro AP, Raney TJ, Thornton LM, Fichter MM, Berrettini WH, Goldman D, Halmi KA, Kaplan AS, Strober M, Treasure J, Woodside DB, Kaye WH, Bulik CM. Sexual functioning in women with eating disorders. *Int J Eat Disord.* 2010 Mar;43(2):123–9. PMID: 19260036; PMCID: PMC2820601.

Minority Health

Racial Differences in Kidney Function among Individuals with Obesity and Metabolic Syndrome. Using participants from the National Kidney Foundation’s Kidney Early Evaluation Program (KEEP), Dr. Philip Klemmer (Professor, Department of Medicine) was part of a research team that examined whether there was a difference between African Americans and Caucasians with obesity and metabolic syndrome regarding albuminuria, estimated glomerular filtration rate (eGFR), anemia, and bone/mineral metabolism derangements in chronic kidney disease (CKD). Of 37,107 obese participants, 48% were African American and 52% were Caucasian. Results show that Caucasians were more likely to have metabolic syndrome components (hypertension, 87.1% versus 84.8%; dyslipidemia, 81.6% versus 66.7%; diabetes, 42.7% versus 34.9%) and more profoundly decreased eGFR than African Americans (CKD stages 3–5 prevalence, 23.6% versus 13.0%). However, African Americans were more likely to have abnormal urinary albumin excretion (microalbuminuria, 12.5% versus 10.2%; macroalbuminuria, 1.3% versus 1.2%; and CKD stages 1–2 (10.3% versus 7.1%). For participants with CKD stages 3–5, anemia prevalence was 32.4% in African Americans and 14.1% in whites; corresponding values for secondary hyperparathyroidism were 66.2% and 46.6%, respectively. This evidence suggests that obesity and metabolic syndrome may both play an important role in explaining differences in long-term kidney and cardiovascular outcomes.

- Bombback AS, Kshirsagar AV, Whaley-Connell AT, Chen SC, Li S, Klemmer PJ, McCullough PA, Bakris GL. Racial differences in kidney function among individuals with obesity and metabolic syndrome: results from the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis.* 2010 Mar;55(3 Suppl 2):S4–S14. PMID: 20172446.

Obesity in Transition to Adulthood: Predictions across Race, Ethnicity, Immigrant Generation, and Sex. Using participants from the National Longitudinal Study of Adolescent Health, Dr. Krista Perreira (Associate Professor, Department of Public Policy) examined racial, ethnic, and immigrant disparities in BMI change over time for adolescents (defined as ages 11 years to 19 years) transitioning into young adulthood (defined as ages 20 years to 28 years). Results show significant differences in both the level and change in BMI across age by sex, race/ethnicity, and immigrant generation. Females who are second- and third-generation immigrants and Hispanic and African American participants experienced more rapidly increasing BMIs from adolescence into young adulthood. Increases in BMI are relatively lower for males, first-generation immigrants, and white and Asian individuals. This evidence suggests that disparities in BMI and the prevalence of overweight and obesity widen with age as adolescents leave home and begin independent lives as young adults in their 20s.

- Harris KM, Perreira KM, Lee D. Obesity in the transition to adulthood: predictions across race/ethnicity, immigrant generation, and sex. *Arch Pediatr Adolesc Med.* 2009 Nov;163(11):1022–8. PMID: 19884593; PMCID: PMC2788784.

Body Mass Index and Hypertension of East and Southeast Asians. In this research study, Drs. Ka He (Associate Professor, Departments of Nutrition and Epidemiology) and Barry Popkin (Professor, Department of Nutrition) examined the association of BMI with hypertension in Chinese, Indonesian, and Vietnamese adults. Participants included 7,562 Chinese, 18,502 Indonesian, and 77,758 Vietnamese 18 years to 65 years old. Results show that despite a low mean BMI, the prevalence of hypertension in Chinese, Indonesian, and Vietnamese men was 22.9%, 24.8%, and 14.4%, respectively, and in women was 16.6%, 26.9%, and 11.7%, respectively. At all BMI levels, the sex-specific prevalence of hypertension was higher in Indonesian adults than in Chinese and Vietnamese adults at almost all BMI levels. The overall and stratified analyses suggested optimal BMI cutoffs of 23–24, 21–22.5, and 20.5–21 for Chinese, Indonesian, and Vietnamese adults, respectively. These cutoffs were approximately 0.5 to 1.0 units higher in women than in men and in the older (41 to 65 years old) than in the younger (18 to 40 years old) participants. This evidence suggests that country-specific or even country-, sex-, and age-specific BMI cutoffs might be needed to identify persons at high risk of cardiovascular diseases.

- Nguyen TT, Adair LS, Suchindran CM, He K, Popkin BM. The association between body mass index and hypertension is different between East and Southeast Asians. *Am J Clin Nutr.* 2009 Jun;89(6):1905–12. Epub 2009 Apr 15. PMCID: PMC2714374. PMID: 19369374.

AIDS

Regulation of CCR5 Expression in Human Placenta: Mother-to-Child Transmission of HIV in Malawi. Dr. Kari North (Associate Professor, Department of Epidemiology) and her research team evaluated the associations between infant chemokine co-receptor 5 gene (CCR5) polymorphisms, measures of maternal infection, and placental expression of CCR5 among mother-infant pairs in Blantyre, Malawi. Through linear regression, they observed that CCR5-2554T and -2132T were significantly associated with reduced placental expression of CCR5. An incremental increase in CCR5 expression was observed for incremental increases in expression of two heparan sulfate genes involved in viral infection, HS3ST3A1 and HS3ST3B1. Among

HIV-infected mothers, an incremental increase in maternal HIV viral load was also associated with higher CCR5 expression. Higher CCR5 expression was observed for mothers with malaria but was not statistically significant. These results provide *in vivo* evidence for genetic and environmental factors involved in the regulation of CCR5 expression in the placenta. This evidence suggests that the measurement of placental expression of CCR5 alone is not an adequate indicator of the risk of mother-to-child transmission of HIV.

- Joubert BR, Franceschini N, Mwapasa V, North KE, Meshnick SR. Regulation of CCR5 expression in human placenta: insights from a study of mother-to-child transmission of HIV in Malawi. *PLoS One* 2010 Feb 15;5(2):e9212. PMID: 20169157; PMCID: PMC2821402.

Unmet Therapeutic Needs in the New Era of Combination Antiretroviral Therapy for HIV-

1. Dr. Joseph Eron (Associate Professor, Department of Medicine) along with several other investigators explored the relationship between combination antiretroviral therapy (cART) and unmet therapeutic needs in patients living with HIV. Results show neurocognitive impairment is an important source of ongoing morbidity in HIV-infected individuals taking cART. HIV itself has been implicated in this process, but comorbidities including vitamin B12 deficiency are potential confounders. Thus, supplementation of vitamin B12 is important in preventing early-onset cognitive changes in patients. HIV also affects the immune system senescence and bone turnover. HIV infection is associated with decreased bone mineral density, osteopenia, and osteoporosis. Results show that Efavirenz (a drug associated with severe vitamin D deficiency) induces cytochrome P450 enzymes and may accelerate the metabolism of active vitamin D to inactive metabolites. Optimally, antiretroviral therapy should aim to interrupt and reverse bone disorders in these patients.

- Taiwo B, Hicks C, Eron J. Unmet therapeutic needs in the new era of combination antiretroviral therapy for HIV-1. *J Antimicrob Chemother.* 2010 Mar 25. PMID: 20348088.

Inflammatory Bowel Disease

Polyunsaturated Fatty Acids and Distal Large Bowel Cancer Risk in Caucasians and African Americans. Dr. Joseph Galanko (Research Assistant Professor, Department of Medicine) and Robert Sandler (Professor, Departments of Medicine and Epidemiology) examined the association between intakes of different long-chain omega-3 polyunsaturated fatty acids (PUFAs) and distal large bowel cancer in a population-based case-control study of 1,503 Caucasians (716 cases; 787 controls) and 369 African Americans (213 cases; 156 controls) in North Carolina. Results show that increased consumption of long-chain omega-3 PUFAs was associated with reduced risk of distal large bowel cancer in Caucasians. Intake of individual eicosapentaenoic acids and docosahexaenoic acids was inversely related to distal large bowel cancer risk, whereas the ratio of omega-6 to long-chain omega-3 PUFAs was associated with increased risk of distal large bowel cancer in Caucasians but not among African Americans. This evidence suggests that long-chain omega-3 PUFAs have beneficial effects in colorectal carcinogenesis. However, whether or not there is a possible benefit of long-chain omega-3 PUFAs varies by race and warrants further evaluation.

- Kim S, Sandler DP, Galanko J, Martin C, Sandler RS. Intake of polyunsaturated fatty acids and distal large bowel cancer risk in whites and African Americans. *Am J Epidemiol*. 2010 May 1;171(9):969–79. Epub 2010 Apr 14. PMID: 20392864; PMCID: PMC2877478.

Isotretinoin Use and the Risk of Inflammatory Bowel Disease. In this study, Drs. Michael Kappelman (Assistant Professor, Department of Pediatrics) and Robert Sandler (Professor, Departments of Medicine and Epidemiology) explored the relationship between the use of isotretinoin (a medication for the treatment of severe acne and a Vitamin A analog) and inflammatory bowel disease (IBD). The investigators conducted a case-control study using administrative claims data obtained from individuals captured within the PharMetrics Patient-Centric Database (Intercontinental Marketing Services Health in Watertown, Massachusetts), January 1, 2000, to December 21, 2005. The study population consisted of 8,189 cases (3,664 Crohn's disease (CD), 4,428 ulcerative colitis (UC), and 97 IBD unspecified) and 21,832 controls. A total of 60 subjects (24 cases and 36 controls) were exposed to isotretinoin for a 24-month period. Results show that UC was strongly associated with previous isotretinoin exposure. However, there was no apparent association between isotretinoin and CD. Increasing the dose of isotretinoin was also associated with elevated risk of UC (per 20 mg increase in dose). Compared with non-users, the risk of UC was highest in those exposed to isotretinoin for more than 2 months. This also shows that UC, not CD, is associated with previous isotretinoin exposure; higher dosage seems to augment this risk. This evidence suggests that while the absolute risk of developing UC after taking isotretinoin is likely quite small, clinicians prescribing isotretinoin as well as prospective patients should be aware of this possible association.

- Crockett SD, Porter CQ, Martin CF, Sandler RS, Kappelman MD. Isotretinoin use and the risk of inflammatory bowel disease: a case-control study. *Am J Gastroenterol*. 2010 Mar 30. [Epub ahead of print] PMID: 20354506.

Obesity

New Loci Associated with Body Mass Index Highlight a Neuronal Influence on Weight Regulation. Common variants at only two loci, FTO and MC4R, have been associated with BMI in humans. To identify additional loci, Dr. Karen Mohlke (Associate Professor, Department of Genetics) and several other investigators conducted a meta-analysis of 15 genome-wide association studies for BMI (n greater than 32,000) and followed up top signals in 14 additional cohorts (n greater than 59,000). Results confirmed FTO and MC4R and identified six additional loci: TMEM18, KCTD15, GNPDA2, SH2B1, MTCH2, and NEGR1 (where a 45-kb deletion polymorphism is a candidate causal variant). Several of the likely causal genes are highly expressed or known to act in the central nervous system (CNS), emphasizing, as in rare monogenic forms of obesity, the role of the CNS in predisposition to obesity.

- Mohlke KL et al. Six new loci associated with body mass index highlight a neuronal influence on body weight regulation. *Nat Genet*. 2009 Jan;41(1):25–34. Epub 2008 Dec 14. PMID: 19079261; PMCID: PMC2695662.

Ontogeny and Nutritional Control of Adipogenesis in Zebrafish. Former P&F awardee Dr. John Rawls (Assistant Professor, Departments of Cell & Molecular Physiology and Microbiology & Immunology) and his research team examined whether optical transparency of

the developing zebrafish (combined with the amenability of the zebrafish to genetic and chemical screens) can provide new opportunities to investigate the mechanisms underlying adipocyte biology. Results show that neutral lipid droplets first accumulate in visceral adipocytes during larval stages and increase in number and distribution as zebrafish grow. The researchers showed that the cellular anatomy of zebrafish adipocytes is similar to mammalian white adipocytes, and identify PPAR-alpha and fatty acid binding 11a (fabp11a; homolog of mammalian FABP4) as markers of the zebrafish adipocyte lineage. By monitoring adipocyte development prior to neutral lipid deposition, results show that the first visceral preadipocytes appear in association with the pancreas shortly after initiation of exogenous nutrition. Zebrafish reared in the absence of food fail to form visceral preadipocytes, indicating that exogenous nutrition is required for adipocyte development. These results reveal homologies between zebrafish and mammalian adipocytes and establish the zebrafish as a new model for adipocyte research. This study was funded by the National Institute of Diabetes and Digestive and Kidney Diseases (PI: John Rawls–R01DK081426). This study was the cover story for the August 2009 edition of the *Journal of Lipid Research*.

- Flynn EJ, Trent CM, Rawls JF. Ontogeny and nutritional control of adipogenesis in zebrafish (*Danio rerio*). *J Lipid Res*. 2009 Aug;50(8):1641–52. Epub 2009 Apr 14. PMID: 19366995; PMCID: PMC2724053.

NRXN3 is a Novel Locus for Waist Circumference. Dr. Kari North (Associate Professor, Department of Epidemiology) was a member of a research team that examined common variants influencing central abdominal fat. The researchers conducted a two-stage genome-wide association analysis for waist circumference (WC). In stage 1, 31,373 individuals of Caucasian descent from eight cohort studies confirmed the role of fat mass and obesity (FTO) gene and the MC4R gene and identified one novel locus associated with WC in the neurexin 3 gene [NRXN3 (rs10146997, $p = 6.4 \times 10^{-7}$)]. The association with NRXN3 was confirmed in stage 2 by combining stage 1 results with those from 38,641 participants in the Genetic Investigation of Anthropometric Traits consortium for combined analysis ($n=70,014$). Results show the mean waist circumference increase per copy of the G allele was 0.0498 z-score units (0.65 cm). This SNP was also associated with BMI and the risk of obesity. Because the NRXN3 gene has been previously associated with reward behavior, it further explains the evidence that common forms of obesity may be a CNS-mediated disorder.

- North KE et al. NRXN3 is a novel locus for waist circumference: a genome-wide association study from the CHARGE Consortium. *PLoS Genet*. 2009 Jun;5(6):e1000539. Epub 2009 Jun 26. PMID: 19557197; PMCID: PMC2695005.

Relationship Between Leptin and Measures of Fitness, Fatness, and Obesity Status in Youth. Dr. Robert McMurray (Professor, Department of Exercise & Sport Science) and his research team explored the relationship between peak aerobic fitness (peakVO₂) and plasma leptin. Using data from 25 normal (BMI lower than 85th percentile) and 25 overweight (BMI higher than 85th percentile) youth, 7 to 17 years old, results show that the overall analysis peakVO₂ was related to leptin when expressed in mL/kg/min ($R^2=0.516$), or as ml/kg(FFM)/min ($R^2=0.127$). The relationships between peak VO₂ and leptin were not significant when percent body fat was added to the models. In the subanalyses by weight groups, peak VO₂:leptin relationships were not evident for normal weight youth but remained for overweight youth. This

evidence suggests that the relationship between aerobic fitness and leptin in youth is dependent upon weight status.

- Hosick PA, McMurray RG, Cooper DM. The relationships between leptin and measures of fitness and fatness are dependent upon obesity status in youth. *Pediatr Exerc Sci*. 2010 May;22(2):195–204. PMID: 20567041.

Cross-Sectional Study of the Comorbidities in Obese Preschool Children in the United States. Using data from the National Health and Nutrition Examination Survey, Dr. Eliana Perrin (Assistant Professor, Department of Pediatrics) carried out a cross-sectional analysis of children 3 to 5 years old to examine the effect of weight status on 17 available measures of current child health potentially related to obesity. Except for very obese children, results show that weight status had minimal effect on most measures of health for preschool-aged children (n=2792). Parents of very obese children reported poorer general health and more activity limitations for their children. Additionally, very obese girls had more frequent and severe headaches, while overweight/obese boys had more asthma diagnoses. This evidence suggests that only severe obesity appears consistently related to immediate health problems in preschool-aged children. Parental perception that very obese children have worse health and more activity limitations may also lead to decreases in physical activity, which would perpetuate obesity.

- Cockrell Skinner A, Perrin EM, Steiner MJ. Healthy for now? A cross-sectional study of the comorbidities in obese preschool children in the United States. *Clin Pediatr (Phila)*. 2010 Jul;49(7):648–55. Epub 2010 Mar 22. PMID: 20308197.

Health Promotion or Disease Prevention

Prevention and Treatment of Cystic Fibrosis-Related Bone Disease in Children.

Malnutrition, physical inactivity, and vitamin D and vitamin K deficiencies are all factors that have been associated with poor bone health. In this study, former P&F awardee Dr. Robert Aris (Associate Professor, Department of Medicine) and his colleagues examined the strategies for optimizing bone health and explored preventive care measures that are necessary from childhood through adolescence to minimize the presence of cystic fibrosis-related bone disease in adult cystic fibrosis patients. Results show that lean body mass in bone health plays not only an important role in maintaining mechanical forces on bone, but it also reflects disease severity, in patients who are less physically active and more nutritionally compromised. To solve this issue, exercise in healthy prepubertal and early pubertal children is recommended. These weight-bearing activities can influence calcium accretion and maintenance of bone mass. Additionally, vitamin A and vitamin K supplementation is shown to improve biochemical markers leading to reduced bone resorption and improved bone formation in patients with cystic fibrosis.

- Sermet-Gaudelus I, Castanet M, Retsch-Bogart G, Aris RM. Update on cystic fibrosis-related bone disease: a special focus on children. *Paediatr Respir Rev*. 2009 Sep;10(3):134–42. Epub 2009 Jul 17. Review. PMID: 19651384.

Promotion of Walking for Transportation: A Report from the Walk to School Day Registry. In this study, Drs. Laura Linnan (Assistant Professor, Department of Health Behavior and Health Education) and Dianne Ward (Professor, Department of Nutrition) surveyed 493

Walk to School (WTS) program coordinators to determine whether the impact of this program is useful in promoting active transportation among youth. Results show that almost all respondents (98.2%) participated in a 1-day WTS event. Other common activities included promotional activities (72.7%), safety trainings (49.6%), walkability audits (48.5%), and designated safe walking routes (46.5%). As part of their WTS efforts, 24.4% of respondents made policy changes and 38.4% made changes to the physical environment. Logistic regression analyses also showed that policy changes, physical environment improvements, and number of activities were associated with the largest perceived increase in children walking to school. These findings help address the gap in knowledge about schools' participation in WTS programs, and suggest strategies to increase active transportation to school in the future.

- Vaughn AE, Ball SC, Linnan LA, Marchetti LM, Hall WL, Ward DS. Promotion of walking for transportation: a report from the Walk to School day registry. *J Phys Act Health* 2009 May;6(3):281–8. PMID: 19564655.

Implementation of a School-Based State Policy To Increase Physical Activity. In this publication, Dr. Alice Ammerman (Professor, Department of Nutrition) describes how school districts in the State of North Carolina are meeting the physical activity-related portion of this policy and explores the policy implementation successes and challenges. Using an online survey, respondents were asked to describe the implementation successes and challenges associated with including 30 minutes of physical activity in the school day. Results show that the physical activity requirement was most often met through recess, physical education, classroom energizers, and intramural sports. School districts reported numerous positive effects of the policy in elementary schools and middle schools. Benefits included increased student focus on studies, physical activity participation, awareness of healthy habits, alertness and enjoyment, and higher staff involvement. Implementation challenges to the policy included lack of time in the school day, teacher participation, and concerns about academics. This evidence suggests that the implementation of this policy produced many positive results for students and staff, and addressing implementation challenges common across school districts would strengthen the ongoing success of this policy.

- Evenson KR, Ballard K, Lee G, Ammerman A. Implementation of a school-based state policy to increase physical activity. *J Sch Health* 2009 May;79(5):231–8, quiz 244–6. PMID: 19341442.

Mechanism for Prevention of Alcohol-Induced Liver Injury by Dietary Methyl Donors. In this study, former P&F awardee Dr. Ivan Rusyn (Associate Professor, Department of Environmental Sciences and Engineering) and his research team explored whether the protective action of dietary methyl donors is mediated by an effect on the oxidative metabolism of alcohol in the liver. Male C57BL/6J mice were administered a control high-fat diet or a diet enriched in methyl donors with or without alcohol for 4 weeks using the enteral alcohol feeding model. Results show that attenuation of alcohol-induced liver injury (ALI) and an increase in reduced glutathione:oxidized glutathione ratio were achieved with dietary methyl donor supplementation. Methyl donors led to a 35% increase in blood alcohol elimination rate. While there was no effect on alcohol metabolism in the stomach, a profound effect on liver alcohol metabolism was observed. The catalase-dependent pathway of alcohol metabolism was induced, yet the increase in CYP2E1 activity by alcohol was blunted, which may mitigate production of oxidants.

Additional factors contributing to the protective effects of methyl donors in ALI were increased activity of low- and high-K(m) aldehyde dehydrogenases leading to lower hepatic acetaldehyde, maintenance of the efficient mitochondrial energy metabolism, and promotion of peroxisomal beta oxidation.

- Powell CL, Bradford BU, Craig CP, Tsuchiya M, Uehara T, O'Connell TM, Pogribny IP, Melnyk S, Koop DR, Bleyle L, Threadgill DW, Rusyn I. Mechanism for prevention of alcohol-induced liver injury by dietary methyl donors. *Toxicol Sci.* 2010 May;115(1):131–9. Epub 2010 Jan 29. PMID: 20118189; PMCID: PMC2855354.

Reduction in Health Care Costs

Cost-Effectiveness of a Behavioral Weight Loss Intervention for Low-Income Women. Drs. Carmen Samuel-Hodge (Research Assistant Professor, Department of Nutrition), Alice Ammerman (Professor, Department of Nutrition), and Thomas C. Keyserling (Associate Professor, Department of Medicine) assessed the cost-effectiveness of a 16-week weight loss intervention (WWP) for low-income, midlife women. Effectiveness measures included changes in weight, systolic and diastolic blood pressure, total cholesterol, and HDL cholesterol. They also calculated life-years gained from changes in weight, based on an excess years-life-lost algorithm. Results show that intervention participants had statistically significant decreases in weight (-4.4 kg) and in systolic blood pressure (-6.2 mm Hg) compared to controls. Total cost of conducting the WWP was \$17,403, and the cost per participant in the intervention group was \$242. The incremental cost per life year gained (discounted) from a decrease in obesity was \$1,862. This evidence suggests that the WWP may be a cost-effective approach to improving the health of low-income women.

- Gustafson A, Khavjou O, Stearns SC, Keyserling TC, Gizlice Z, Lindsley S, Bramble K, Garcia B, Johnston L, Will J, Poindexter P, Ammerman AS, Samuel-Hodge CD. Cost-effectiveness of a behavioral weight loss intervention for low-income women: the Weight Wise Program. *Prev Med.* 2009 Nov;49(5):390–5. Epub 2009 Sep 10. PubMed PMID: 19747937.

Cost-Effectiveness of Diabetes Self-Management Programs in Community Primary Care Settings. The purpose of this study is to examine the cost-effectiveness of diabetes self-management programs (includes meetings with a nutritionist to discuss nutrition and dietary information) in real-world community primary care settings. Based on clinical results and program costs from the Diabetes Initiative from the Robert Wood Johnson Foundation, Dr. Edwin Fisher (Professor, Department of Health Behavior and Health Education) and his fellow investigators used a Markov simulation model to estimate the long-term effects of self-management interventions. Results show that the intervention reduced lifetime treatment and complication costs by \$3,385; however, it was offset by the cost of implementing the intervention and maintaining its effects in subsequent years (\$15,031). Results also show that the incremental cost-effectiveness ratio is \$39,563/quality adjusted life years (QALYs), well below a common benchmark of \$50,000/QALY. This evidence suggests that self-management programs for type 2 diabetes are cost effective from a health systems perspective when the cost savings due to reductions in long-term complications are recognized. These findings may justify increased reimbursement for effective self-management programs in diverse settings.

- Brownson CA, Hoerger TJ, Fisher EB, Kilpatrick KE. Cost-effectiveness of diabetes self-management programs in community primary care settings. *Diabetes Educ.* 2009 Sep-Oct;35(5):761–9. Epub 2009 Jul 21. PMID: 19622716.

Educational Activities/Accomplishments

The NORC is committed to enhancing and increasing the visibility of nutritional sciences and obesity research on the UNC-CH campus and in the local community. Our enrichment program serves as a valuable way to educate people (on campus and elsewhere) about the work of our Center and our investigators. Listed below is a sampling of educational activities and accomplishments during 2009 and 2010.

Community Outreach and Education

Promoting Nutrition and Obesity Research Nationally and Internationally. During the past year, many NORC investigators were in the forefront of educating the public about nutrition- and obesity-related research on both the national and international levels. NORC Director, Dr. Steven Zeisel, and the new UNC Nutrition Research Institute were featured on *The Oprah Winfrey Show* (http://nri.unc.edu/Media/Oprah_NRI_medium.mpg) and on UNC Public Television (“Carolina People”). Dr. Barry Popkin wrote a popular press book on nutrition called “*The World is Fat: The Fads, Trends, Policies, and Products That Are Fattening the Human Race.*” In addition, many of our other investigators have been featured on national TV talk shows, newspapers, and magazine articles, including CNN, *The New York Times*, National Public Radio, *The Wall Street Journal*, ABC National Radio, Australian TV, and *USA Today*.

Appetite for Life Academy. Through our collaborative partnership with the UNC Nutrition Research Institute (NRI), the Appetite for Life Academy was created to give residents of the Kannapolis community (near Charlotte, NC) an opportunity to learn about the latest nutrition and obesity research from some of the most respected names in the field. Leading experts in nutrition and obesity present an array of topics ranging from the mysteries of metabolism to the emerging problem of global obesity. Participants have not only praised the lecture topics but have also praised the speakers. Event evaluations revealed that the series made a positive impact on participants and the wider community. Since its debut in 2008, the Appetite for Life Academy has been a resounding success, with attendance exceeding expectations and topping at more than 200 participants per session. Each speaker featured in the Appetite for Life Academy series is a NORC investigator. Below is a list of the featured speakers and their lecture topics.

2010 Appetite for Life Academy Speakers:

- February 2. The Future of Health: Individualized Nutrition. Steven H. Zeisel, M.D., Ph.D.; Professor, Departments of Nutrition & Pediatrics
- February 9. Fish or Flax: Does Your Brain Need an Oil Change? Carol Cheatham, Ph.D.; Assistant Professor, Department of Psychology
- February 16. Polar Bear to Pop: The Changing Diet of the Inuit. Sangita Sharma, Ph.D.; Associate Professor, Department of Nutrition

2009 Appetite for Life Academy Speakers:

- February 3. The Hand that Rocks the Cradle: Infant and Toddler Feeding and Care for Healthy Growth. Margaret Bentley, Ph.D., Professor, Department of Nutrition
- February 10. Fat and Thin: How Metabolism Works. Rosalind Coleman, M.D., Professor, Departments of Nutrition and Pediatrics
- February 17. Can a Healthy Diet Help You Fight the Flu? The Role of Nutrition in the Response to Infectious Disease. Melinda Beck, Ph.D., Professor, Department of Nutrition
- February 21. The World is Fat: The Foods, Trends, Policies, and Products that are Fattening the Human Race. Barry Popkin, Ph.D., Professor, Department of Nutrition

Tai Chi. Tai Chi is the ancient art of gentle physical exercise and stretching that is often used for stress reduction. In Fall 2009 (in partnership with the UNC Department of Nutrition), the NORC assisted in the promotion of a weekly Tai Chi session for students, faculty, and staff on the UNC campus. Lisa Marcusson, a Tai Chi instructor for more than 20 years, led the weekly “Tai Chi in The Courtyard” program at the Gillings School of Global Public Health. For a nominal fee, this 9-week program introduced participants to the basic principles of Tai Chi and the Yang Short Form and was designed for both beginners and experts in the art. Due to the overwhelming response, the NORC is looking to assist the Department of Nutrition in expanding the program in Fall 2010 to reach more participants on campus.

USDA Food Composition and Nutrient Databases Workshop. In January 2010, the UNC-CH NORC, in partnership with the UNC Nutrition Research Institute in Kannapolis, sponsored a 2-day USDA Food Composition and Nutrient Databases workshop at the NC Research Campus in Kannapolis. This workshop was conducted by Mr. David B. Haytowitz from the U.S. Department of Agriculture. The workshop focused on the compilation, maintenance, and dissemination of authoritative food composition and nutrient databases. The workshop also included hands-on exercises (sampling, composition and querying for standard references) for the participants.

A Personal Conversation with Mr. David Murdock. In late February 2009, Mr. David H. Murdock, Chairman and Owner of Dole Food Company and creator of the North Carolina Research Campus (NCRC), came to the UNC-CH campus to speak with students, faculty, and staff about his long and highly successful career in the food industry and his passion for nutrition. Mr. Murdock spoke about his deep commitments to finding a cure for cancer, advancing nutrition, and life extension.

Nutrition Education for Health Professionals and Nutrition Scientists

Nutrition in Medicine. Members of our NORC, Drs. Martin Kohlmeier (Research Professor, Department of Nutrition) and Steven H. Zeisel (Professor, Department of Nutrition), created an outstanding web-based course in nutrition (Nutrition in Medicine) that has been used by more than 150 medical schools to teach 13,000 medical students since 2005; more than 5,500 medical students used the web version of this course in 2009. This course is widely recognized as one of the most successful resources for facilitating the teaching of nutrition to medical students (<http://www.nutritioninmedicine.org>). Each of the 10 programs that were developed present basic nutrition science within the framework of a student interaction with a simulated patient.

Rather than using a traditional teaching structure (i.e., lectures on vitamins, minerals, lipids, protein, etc.), each program presents a number of issues derived from the simulated patient's condition to teach the principles of nutrition and to illustrate the interaction between nutrition and health or disease. In addition to the biochemical bases of nutrition, the series of programs covers nutrition epidemiology, clinical nutrition, nutrition assessment, and nutritionally related preventive health care.

Nutrition Education for Practicing Physicians (NEPP). Under the guidance of NORC investigators Drs. Kohlmeier and Zeisel, a web-based, postgraduate curriculum was created to include a comprehensive set of learning modules covering critical nutrition-related knowledge and practice skills that are essential for physicians to effectively treat their patients or to counsel them on preventing chronic diseases such as cancer. Each module in this NCI-funded study covers a tightly focused nutrition topic, which allows physicians to improve their knowledge without investing a lot of time. The program emphasizes clinical skill building by translating the most current guidelines and clinical expertise into an instructionally sound and user-friendly format. In 2009, the research team produced the first 10 online modules. These 10- to 20-minute modules teach specific knowledge items and clinical skills for the prevention and treatment of cancer and other common diseases. Modules include nutrition assessment for cancer patients, assessment of waist circumference, refeeding syndrome, behavior change counseling, physical activity assessments and breastfeeding of healthy infants.

Community-Based Intervention Programs

Nutrition and Physical Activity Self-Assessment for Child Care (NAP SACC) (PI: Dianne Ward). NAP SACC is a statewide intervention program aimed at improving the eating and physical activity environments in North Carolina childcare centers. The program consultants train childcare providers on how to improve nutritional quality of food served, how to correct the amount and quality of physical activity, and on staff-child interactions. Ninety-six childcare centers (58 intervention, 38 control) across the State participated in this study, which included self-assessment, action planning, workshop delivery, and technical assistance to childcare providers. In Spring 2010, this program was identified as one of three programs by the White House Task Force on Childhood Obesity as an intervention to combat childhood obesity in early childhood. The task force is part of First Lady Michelle Obama's campaign to reduce childhood obesity.

WAY to Health (PI: Laura Linnan, U48 DP000059). Under the leadership of Dr. Laura Linnan, more than 1,200 overweight employees at 14 participating North Carolina colleges and universities were recruited for a study of workplace weight-loss programs. The "WAY to Health" project (WAY is an acronym for Worksite Activities for You) is an 18-month study funded by the NHLBI that focuses on weight loss and changes in the campus environment to support employee health. The project will test four worksite-based weight-loss programs. Group 1 received a web-based weight-loss program that offers dietary and physical activity resources and recommendations; behavioral strategies; problem-solving skills; weekly lesson plans; worksheets, recipes, and other printable documents; links to information libraries; and message boards where participants can talk to others in the program. Group 2 received cash payments for losing weight. Through this research, investigators hope to uncover cost-effective ways for employers to help employees lose weight and keep it off.

Student Scholars Programs

Transdisciplinary Training Program in Functional Foods, Bioactive Food Components, and Human Health (Co-PIs: Drs. Steven Zeisel and Jack Odle [North Carolina State University]). Through a \$1,000,000 grant from the U.S. Department of Agriculture's Agriculture & Food Research Initiative (USDA-AFRI), the Transdisciplinary Graduate Training Program was implemented to recruit exceptional graduate students from multiple disciplines who are interested in transdisciplinary, integrated research focusing on complex problems within the broad domain of functional foods, bioactive food components, and human health. This scholars program is a collaboration among eight North Carolina universities. Training will focus on such topics as exercise-induced changes in immune function (Appalachian State University); speeding the movement of new therapies from the research laboratory to patients (Duke University); research in post-harvest technologies and food science (NC A&T State University); advancing knowledge of human nutrition at the cellular and genetic level (NC Central University); utilizing emerging technologies for plant improvement and human health benefits (NC State University); understanding the role of diet and activity in brain development, cancer prevention, and prevention and treatment of obesity (UNC-CH); developing novel computational technologies to help solve important biological problems (UNC Charlotte); and understanding cellular and molecular mechanisms of action in bioactive food components (UNC Greensboro).

Nutrition Training Program (PI: June Stevens, Co-PI: Rosalind Coleman; T32 DK007686). The goal of the Nutrition Training Grant is to train predoctoral students in integrative nutrition research to become future leaders in the basic and applied aspects of the science of nutrition. Because the Department of Nutrition is uniquely located in both a School of Medicine and a School of Public Health, this training program focuses on both the public health and medical science foundations of nutrition research.

Reproductive, Perinatal, and Pediatric Epidemiology Training Program (PI: Anna Maria Siega-Riz; T32 HD052468). The overall goal of the Reproductive, Perinatal, and Pediatric Epidemiology (RPPE) training program is to provide students with a multidisciplinary perspective in epidemiologic concepts and methods, as well as an understanding of the biology of reproduction and childhood development and growth. The program involves aspects of epidemiology, nutrition, and maternal and child health, and is conducted under the guidance of experienced program faculty members from each of these three departments.

Interdisciplinary Obesity Center (IDOC) Predoctoral Training Grant in Maternal and Child Obesity (PI: Barry Popkin, T32 MH075854). This grant provides interdisciplinary training for doctoral students interested in pursuing research careers related to maternal and/or child obesity. While the focus is on obesity-related issues linked with mothers, children, and adolescents, the interdisciplinary nature of the program brings faculty members and doctoral students together from many departments.

The Cancer Health Disparities Training Program (PI: Marci Campbell, T32 CA128582). The overall goal of this program is to educate and train future investigators in cancer health disparities research. The program offers training to three postdoctoral fellows with a focus on health disparity issues across the cancer continuum, from etiology and primary prevention to survivorship. The program is inclusive of the major cancers (lung, breast, colorectal, prostate,

skin, and others) and cancer risk factors (e.g., diet, physical activity, obesity, tobacco, screening/early detection, and environmental exposures).

Research Symposium

Emerging Issues in Pediatric Nutrition. The UNC-CH NORC, in partnership with the Mead Johnson Center for Excellence in Children's Nutrition, hosted its biannual symposia in Fall 2009. The "Emerging Issues in Pediatric Nutrition" symposium was a 3-day event that brought together investigators from diverse research backgrounds to discuss issues regarding feeding and dietary intake of 0 to 6 year olds. The symposium included a series of presentations and integrated discussions that addressed questions about biological, behavioral, and environmental influences on parental food choices and children's food acceptance and preferences of foods and beverages.

Seminar Series

The UNC-CH NORC Seminar Series features lectures and discussions with leading investigators and experts in the fields of nutrition and obesity. Listed below are seminars from 2009 and 2010.

2010 Seminars

- June 25: Methodological Issues in Nutritional Epidemiology: Assessing Diet and Related Risk Factors in Obesity and Cancer. Michelle Mendez, Ph.D., Epidemiologist and Staff Scientist, Center for Research in Environmental Epidemiology;; Barcelona, Spain
- June 7: Researching the Prevalence and Characteristics of Fetal Alcohol Spectrum Disorders in South Africa, Italy, and the USA. Philip May, Ph.D., Professor, Departments of Sociology and Family & Community Medicine, Center on Alcoholism Substance Abuse & Addictions; University of New Mexico
- June 3: Familial Obesity Risk: Implications for Lifestyle Behaviors and Obesity Prevention. Myles Faith, Ph.D., Assistant Professor, Department of Psychology; University of Pennsylvania School of Medicine
- May 12: Lights! Camera! Action for Health: The Use of Entertainment Education in Health Promotion. Caree Jackson, Ph.D., Postdoctoral Fellow, School of Community Health and Policy; Morgan State University
- May 10: Engaging Families in Childhood Obesity Preventions: Fundamental Questions and Challenges. Kirsten Davison, Ph.D., Associate Professor, Department of Health Policy, Management, and Behavior; University of Albany
- April 19: Food to Fork: Celebrating Local Food. Alice Ammerman, Dr.P.H., Professor, Department of Nutrition; Director, UNC Center for Health Promotion and Disease Prevention; University of North Carolina at Chapel Hill
- April 6: Etiology and Survival of Non-Hodgkin Lymphoma. Xuesong Han, Doctoral Candidate, Department of Epidemiology; Yale University
- February 23: How Should We Eat? Examining Food Ethics. Alice Ammerman, Dr.P.H., Professor, Department of Nutrition; Director, UNC Center for Health Promotion and Disease Prevention; University of North Carolina at Chapel Hill
- February 23: SITAR: A Useful Instrument for Growth Curve Analysis. Tim Cole, Ph.D., Sc.D.; Professor, Department of Medical Statistics; Institute of Child Health

- February 22. Variability in the Development of Infant Memory: Nutritional and Genetic Sources. Carol Cheatham, Ph.D.; Assistant Professor, Department of Psychology; University of North Carolina at Chapel Hill
- January 28. The Cost of Food: an Unholy Alliance. Alice Ammerman, Dr.P.H., Professor, Department of Nutrition; Director, UNC Center for Health Promotion and Disease Prevention; University of North Carolina at Chapel Hill
- January 27. Images of Illness: The Influence of Causal Claims and Racial Associations on Public Opinion Toward Type 2 Diabetes. Sarah Gollust, Ph.D.; Robert Wood Johnson & Health and Society Scholar; University of Pennsylvania
- January 25. The Role of CGI-58 in Hepatic Macronutrient Metabolism: Insights from a Mouse Model of Chanarin-Dorfman Syndrome? J. Mark Brown, Ph.D., Instructor, Department of Pathology; Wake Forest University School of Medicine

2009 Seminars

- December 17. Advances in Obesity. Samuel Klein, M.D., William H. Danforth Professor of Medicine and Nutritional Science; Washington University School of Medicine
- December 17. Bariatric Surgery. Samuel Klein, M.D., William H. Danforth Professor of Medicine and Nutritional Science; Washington University School of Medicine
- December 17. Obesity and Non-Alcoholic Fatty Liver Disease. Samuel Klein, M.D., William H. Danforth Professor of Medicine and Nutritional Science; Washington University School of Medicine.
- December 14. Assessment of Supplemental Feeding with Ready-to-Use Food Among Underweight Children in Western Uganda. Scott Ickes, Ph.D., Postdoctoral Fellow, Department of Nutrition; University of North Carolina at Chapel Hill
- December 14. Determinants of Children's Food Preferences: Genetic and Behavioral Factors. Lucy Cooke, Research Associate, Behavioral Research Center; University College at London
- October 8. Disease Control and Prevention. Thomas R. Friedan, M.D., M.P.H., Director, U.S. Centers for Disease Control and Prevention (CDC)
- August 25. Research on Intergenerational Correlates of Obesity with an Eye Toward Intervention. Bernard Fuemmeler, Ph.D., M.P.H., Assistant Professor, Department of Community and Family Medicine; Duke University Health System
- May 28. Pounds Off Digitally (POD): An Examination of the Use of Podcasting To Promote Weight Loss. Brie Turner McGrievy, Ph.D., Postdoctoral Fellow, Department of Nutrition; University of North Carolina at Chapel Hill

NORC E-Newsletters, Brochures, and Website

The NORC e-newsletters, brochures, and website serve as three ways in which we remain connected to our Center members. E-newsletters are sent to members of our research base, to investigators in various health science departments, and to visiting scientists in the Department of Nutrition via the NORC list serve. In these e-newsletters, we highlight the work of our Cores, upcoming trainings and seminars, the accomplishments of our members, and any new services or equipment the Center has acquired. The brochures serve as a brief synopsis about who we are, what we do, and how our work serves the public. These brochures are sent out electronically to potential users of our services and also to current users to make them aware of the other services that our Center offers. The website is updated with information that helps other researchers find

the resources that they need at the NORC; this includes a request form for our Core services. Additionally, listed in the e-newsletters, brochures, and website is a friendly reminder to our investigators to remember to acknowledge the NORC grant in their publications. We also use the NORC list serve to send emails to our membership base encouraging them to cite the NORC grant when preparing publications.

Accomplishments of the UNC-CH NORC Research Base

Our investigators are highly regarded in the nutrition and obesity research community, and many of them have received national and international recognition for their work. Below is a list of some of the awards received by our investigators in 2009 and 2010:

- Angela Kashuba: 2009 Leon I. Goldberg Young Investigator Award from the American Society for Clinical Pharmacology and Therapeutics
- Barry Popkin: 2010 Rank Prize in Nutrition from the British Nutrition Society
- Sangita Sharma: 2010 Silver Medal in Nutrition from the British Nutrition Society
- Steven Zeisel: 2009 Atwater Lectureship of the U.S. Department of Agriculture's Agricultural Research Service

Bringing New Investigators to Nutrition Research

We have seen an increase in the number of investigators conducting nutrition and obesity research for the first time due to the services offered by the UNC-CH NORC. Listed below are a few examples of projects conducted by these investigators in 2009 and 2010.

Nutrition and HIV. Dr. Lisa Hightow-Weidman (Clinical Assistant Professor, Department of Medicine) is an infectious disease specialist whose research background is in acute HIV infection and sexual network exploration. Dr. Hightow-Weidman worked with the CHAI Core to develop an innovative and highly interactive website for HIV risk reduction. This site includes avatars, creative graphics, and new approaches to engage a younger and harder-to-reach population. The CHAI Core has also conducted usability testing with several individuals who match the study population. This testing was done throughout the entire development of the site, leading to new directions and the assurance that the site was culturally sensitive and on target for communicating its message. The messaging includes the importance of nutrition and diet and its impact on maintaining good health.

Exploratory Analgesic Dietary Intervention for Chronic Daily Headache. Dr. John Douglas Mann's (Professor, Department of Neurology) research background is in acupuncture, hypnosis, and chronic pain interventions. Dr. Mann recently added a nutrition component to his research to explore the relationship between targeted dietary modifications and chronic daily headaches (CDH). This study, funded by the Mayday Fund, explores whether targeted dietary modification can reduce headache frequency and intensity, and improve quality-of-life in subjects with CDH. The Diet, Physical Activity, and Body Composition Core is providing 24-hour recalls and nutritional counseling for patients in this study. Additionally, the CHAI Core has developed the website for this study, which contains periodic online surveys and is linked to an online headache diary. An R01 application will be submitted in late 2011 based on the findings from this study.

Evaluation of Special Olympics Young Athletes Program. Dr. Susan Zeisel's (Adjunct Associate Professor, UNC Frank Porter Graham Child Development Institute) research background is in language development and school competence among African American students. Through the Young Athletes program (developed by Special Olympics and funded by the CDC), Dr. Zeisel added a physical activity component to her research that focuses on improving motor development in young children through the use of games and physical activities. The Diet, Physical Activity, and Body Composition Core trained Dr. Zeisel's staff on the use of Actigraph accelerometers. The Core also assisted her in analyzing physical activity levels among the children; this included instructions on best practice use of the equipment, protocol development, and support.

Oxidative Stress in the Progression of Experimentally Induced Osteoarthritis. Dr. Ronald Graff's (Research Assistant Professor, Department of Orthopedics) research background is in cartilage biology and osteoarthritis. He has recently added a nutrition component to his research to examine how oxidative stress can contribute to osteoarthritis and determine if antioxidant nutrients can mitigate the effect of the oxidative stress. Using an animal model of osteoarthritis, Dr. Graff found that increasing oxidative stress does lead to increasing pathology. Dr. Graff is now studying the effects of selenium and vitamin E in reducing pathology in this setting. The Nutritional Biochemistry and Molecular Biology Core is providing measurements of glutathione peroxidase (GPX), glutathione (GSH), and glutathione disulfide (GSSG) oxidative stress for this study. A publication based on the data from this study is currently in progress.

Amino Acids and Disease Models in *Drosophila Sechellia*. Dr. Corbin Jones' (Assistant Professor, Departments of Biology and Genetics) research background is in the susceptibility, etiology, and pathogenesis of multiple genetic diseases. Recently, Dr. Jones incorporated a nutrition component to his research that would explore the relationship between amino acids and disease models in *Drosophila sechellia*. He co-authored two publications based on the findings from this study. The Nutritional Biochemistry and Molecular Biology Core provided fatty acid analysis.

Examining the Relationship Between Drug Abuse and Exercise. Dr. Linda Dykstra's (Professor, Departments of Pharmacology and Psychology) research background is in drugs of abuse and other psychoactive compounds. Dr. Dykstra recently included an obesity component in her NIH-funded (T32 DA007244) Training on Research in Drug Abuse Program that will examine the relationship between drug abuse and exercise. The Animal Metabolism Phenotyping Sub-Core is working with Dr. Dykstra to provide voluntary running wheel services for the mice in this study. A publication based on the data from this study is expected in the near in the future.

Weight Gain Induced by Chronic Treatment with the Antipsychotic Drug Clozapine. Dr. Fernando Pardo Manuel de Villena's (Associate Professor, Department of Genetics) research background is in evolution, chromosome segregation, mouse genetics, and meiotic drive. He recently received a grant from the National Institute of Mental Health (P50MH090338) to identify high-probability etiological models (which can be realistically complex) and to prove the predictive capacity of these models by generating novel strains of mice bred to be at either very low or very high risk of a given phenotype. He has included a nutrition component to this grant that will explore the genetic basis of susceptibility of weight gain induced by chronic treatment

with the antipsychotic drug clozapine. The Animal Metabolism Phenotyping Sub-Core is currently providing MRI scans for the mice in this study.

Benefits and Interactions Resulting From the Existence of the NORC

Collaboration Among the Research Base. The UNC-CH NORC is designed to encourage collaborative, interdisciplinary research across many disciplines in public health. In fact, most of the research supported by the NORC is collaborative and creates a great environment for training students and supporting junior investigators. The NORC has assisted researchers from more than 36 departments and divisions on campus and has enhanced collaborations among our 130 investigators, with approximately 80% of our research base co-authoring publications or serving as co-investigators on research grants.

Funding for Nutrition and Obesity Research. In 2009 and 2010, more than \$45 million in direct funding for nutrition- and obesity-focused research was received by NORC investigators, of which \$2.3 million was ARRA funds.

Nutrition and Obesity Focused Publications. From 2009 to 2010, NORC investigators published more than 350 peer-reviewed nutrition- and obesity-focused publications. These publications have appeared in various prestigious journals such as *Cell Metabolism*, *PNAS*, *American Journal of Clinical Nutrition*, and the *American Journal of Epidemiology*.

Success of our Pilot & Feasibility Awardees. In 2009 and 2010, former Pilot & Feasibility program awardees received more than \$462,000 in direct funding for research based on data from their pilot projects.

Leaders in Collaborative Nutrition- and Obesity-Focused Research Studies. Our investigators serve as leaders for some of the largest collaborative NIH-funded nutrition and obesity-focused epidemiological studies. This includes the Long Island Breast Cancer Study (18,000 women), Atherosclerosis Risk in Communities (ARIC: 15,792 men and women), Trial of Activity in Adolescent Girls (TAAG: 8,728 women), WAY to Health Study (1,200 employees at 12 community colleges), the Hispanic Cohort Health Study (16,000 men and women), and the Carolina Head and Neck Cancer Study (CHANCE: 1,400 men and women).

Leveraging of Shared Resources

UNC Nutrition Research Institute. This year, the University increased its commitment to the NORC's partner facility, the UNC Nutrition Research Institute. This new commitment was slightly in excess of \$10 million/year and is expected to rise in 2011 to \$10.5 million/year, the full permanent appropriation for this Institute. The UNC NRI (<http://www.uncnri.com>) focuses on studying the underlying causes of metabolic variation using nutrigenomic, metabolomic, and other methodology. It is directed by Dr. Steven Zeisel, the principal investigator for the NORC, and he is charged with integrating the activities of the NRI with the activities of the NORC. Under Dr. Zeisel's direction, eight new tenure-track faculty slots for the NRI were included in the funding for 2010 (four were filled in early Spring 2010 and four searches are active as of July 2010), with 10 additional new tenure-track slots to be opened in the 2010–2011 fiscal year. This makes for a total of 18 new tenure-track faculty members and their research teams at the NRI.

These faculty members are housed in a 125,000 square foot state-of-the-art laboratory building with outstanding facilities for clinical/community nutrition and laboratory-based nutrition research.

A private donor created a 501(c)(3) foundation with a \$150 million endowment, and this foundation provides needed animal facilities and core instrumentation (NMRs, mass spectrometers, microscopy, gene expression and sequencing, etc). This new research institute is located on a new UNC campus approximately 2 hours from the main campus (in Kannapolis, which is near Charlotte, North Carolina).

The UNC NRI has purchased sophisticated teleconferencing equipment (Tandberg Edge 95) and installed portable units at the NRI and in several places on the Chapel Hill campus so investigators at both locations can remain connected. With these units we are able to conduct consultations between Core facilities and NORC investigators and it also makes it possible for investigators to attend seminars virtually at both campuses. Through our collaborative partnership, NORC members have access to all Core facilities located at the NRI.

The David H. Murdock Research Institute (DHMRI). The David H. Murdock Research Institute (www.dhmri.org) is a nonprofit research catalyst for major scientific discoveries in health and nutrition. The DHMRI is the first of its kind to provide advanced research technologies to academic, government, and industry scientists in their pursuit of improved human health through advancements in nutrition, pharmaceuticals, and agricultural products. Housed in the David H. Murdock Core Laboratory Building, the DHMRI covers more than 105,000 square feet of specialized laboratory space. The DHMRI is located in the building next to the NRI at the NC Research Campus in Kannapolis. The UNC-CH NORC has a collaborative agreement with the DHMRI for the use of their Core facilities for NORC members in Kannapolis and in Chapel Hill.

UNC Clinical and Translational Research Center. The NORC works collaboratively with the UNC Clinical and Translational Research Center (CTRC) to provide investigators with a broad range of clinical services for nutrition and obesity research studies. Funded by the North Carolina Translational and Clinical Sciences Institute (<http://traacs.unc.edu/>), the CTRC is a highly rated clinical center; most investigators on campus conducting clinical research use this Center for their studies. The Human Body Composition Facility is co-sponsored by both the NORC and the CTRC, and is fully equipped with state-of-the-art equipment for body composition, energy balance, and metabolic assessment in human populations.

UNC Gillings School of Global Public Health—Gillings Innovation Labs. UNC's Gillings Innovation Labs (GILs) brings together interdisciplinary research groups to focus concentrated efforts to solve major public health problems. Investigators receive grants upwards of more than \$150,000 per year for 1- to 2-year projects that are innovative, that have impact, and that accelerate solutions to public health problems across North Carolina and around the world.

- **Technology to Improve the Understanding of Arsenic.** Former P&F awardee, Dr. Miroslav Stýblo (Associate Professor, Department of Nutrition and Adjunct Associate Professor, Environmental Sciences & Engineering) and his research team have developed instrumentation and methodologies to examine individual differences in the metabolism of

inorganic arsenic and to explore individual susceptibility to adverse effects associated with chronic arsenic exposure. With the establishment of this new Core laboratory funded by the GILs, the NORC has entered into a collaborative agreement with Dr. Stýblo to offer Atomic Absorption Spectrometry services to NORC investigators. Atomic Absorption Spectrometry is a common technique used to determine the concentration of different metals and some metalloids in biological or environmental samples. With this new service, we are able to help NORC investigators determine the levels of arsenite, arsenate, and other organic forms of arsenic in solutions or matrices in an effort to improve risk assessment and treatment for diseases such as cancer, peripheral vascular diseases, cardiovascular diseases, hypertension, and diabetes mellitus.