

University of Alabama at Birmingham
Nutrition Obesity Research Center
Start Date: 2000
Status: Ongoing
Source of NIH Support: NIDDK
Website: <http://www.norc.uab.edu/>

Organization and Goals

Brief Description of the Major Activities of the Center

The University of Alabama at Birmingham (UAB) Nutrition Obesity Research Center (NORC) was inaugurated through National Institutes of Health (NIH) funding in 2000 and supported by UAB's formal system of University-Wide Interdisciplinary Research Centers. The NORC fosters multidisciplinary, collaborative approaches to basic, clinical and translational nutrition research, with emphasis on obesity. In 1996, UAB established an intramurally funded University-Wide Obesity-Nutrition Research Center, which, with NIH funding, evolved into the present NORC. Since first funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the research base has steadily increased and is roughly double what it was at the Center's inception.

Since our NORC's inauguration in 2000, we have diligently built our strength in obesity research. Our investigator membership has increased from 60 to over 100 members. At our inception, our research base included 11 R01s. At last formal count, it included over 40, with over 91% of our regular members (a subset of total members) as Principal Investigators (PIs) of at least one federally funded nutrition or obesity-related research grant. In addition to those research grants and others mentioned below, Dr. Mona Fouad, a member of our NORC, has received a P60 grant for a comprehensive minority and health disparities research center with well over \$1 million in annual direct costs, which includes as one of its primary specific aims to "advance our understanding of the complex interactions between biological, social, and clinical factors that cause health disparities in cancer screening and diabetes/obesity." This obviously enriches the research and training environment in obesity for our members. UAB also serves as the data coordinating center for the large U.S. Department of Agriculture-funded "Delta Obesity Prevention Research Unit" and plays the lead role in survey development. This research program works to identify potential factors that promote or hinder adherence to sound nutritional behavior among children in the southern United States, again further enriching our environment as a hotbed for research and training in obesity. Finally, the State of Alabama has just awarded (in May of 2010) a grant to UAB's NORC, with Dr. Allison as the PI, to begin an endeavor referred to as the Alabama Obesity Initiative (AOI). The AOI will involve coordinating efforts among investigators at virtually every academic institution and several nonprofit organizations and companies who have ongoing research and training activities in obesity. The AOI will aim to promote further research and training activities and acquisition of grant funding. This further shows the institutional and State support for our mission.

While at our inception we had no training grants specifically for obesity research, we now have an NIH-funded postdoctoral obesity training grant with four slots, support summer medical

student training (five slots) with a supplement to that grant, and have a 'pilot' obesity predoctoral training program funded by industry. Building on the strength of that pilot program, in the first half of calendar year 2010, we submitted three applications to NIH for predoctoral training in obesity research.

Our publication output has increased by every standard against which we have measured it (see chart below). During our prior funding cycle, we raised over \$3 million in philanthropic support for nutrition and obesity research. Additionally, during this interval, UAB contributed an average of \$442,000 annually to the NORC. All this has made our NORC fertile soil for emerging independent scholars in interdisciplinary obesity research. Our NORC fosters a multidisciplinary approach emphasizing understanding of obesity from the molecular through the macro-environmental. The NORC's specific aims are the following:

- **Research.** Foster multidisciplinary research focused on the biological, behavioral, and environmental bases for nutrition/obesity-related disorders. This occurs by promoting integrated and multidisciplinary research efforts in nutrition/obesity from the perspective of disciplines such as genetics, molecular biology, psychology/sociology, physiology, endocrinology and diabetes, economics, health policy, physics, pathology, epidemiology, statistics, exercise physiology/muscle metabolism, surgery, pediatric and adult medicine, and others.
- **Training.** Continue to offer a strong nutrition training environment to improve the education of medical students, house staff, practicing physicians, graduate and postgraduate trainees, allied health professionals, and research scientists. This occurs through an expanded Nutrition/Obesity Seminar Series, a dynamic Enrichment Program, and our training grants.
- **Translational Services.** Enhance patient care and public health through translation of research findings into applicable information for practitioners and the public.
- **Scientific Output.** One way of quantifying research output is through publications. We have tabulated our publication output from 1990 to 2009, as listed in PubMed and Web of Science, and we found that the total number of obesity publications coming from UAB has increased dramatically over the years. Yet, it could be argued that this is merely a function of general growth at UAB (i.e., more publications from UAB overall). To address this issue, we have also examined the proportion of all UAB publications which are obesity-focused. It is clear that since the NORC's inception, the proportion of UAB publications that are obesity-focused has increased by a factor of roughly 3.0.

Things have recently become better still. In 2008, a new NIDDK Diabetes Research and Training Center (DRTC) was established at UAB (P60 DK079626), with Dr. Garvey (an associate director on this proposed program) as PI, to serve this expanding research base and associated scientific and professional training efforts. The DRTC has established new core facilities, technologies, pilot award mechanisms, and enrichment activities that further enhance the environment for our obesity trainees.

In the past 12 months, UAB's NORC has directly helped recruit multiple new and established obesity and nutrition investigators, including, quite recently, Dr. Wendy Demark-Wahnefried.

Dr. Demark-Wahnefried, Professor and Webb Endowed Chair of Nutrition Sciences, is a nutrition scientist with training in biochemistry, genetics, and behavioral science. She was recently recruited (spring 2010) from M. D. Anderson Cancer Center, where she was a Full Professor in the Division of Cancer Prevention and Population Sciences; earlier in her career, she was at Duke University Medical Center. For the past two decades, her research career has ranged from basic science studies focused on determining mechanisms of action of food-related components on neoplastic progression, to clinical research that involves nutrition-related concerns of cancer patients, as well as determining effective lifestyle interventions that improve the overall health of cancer survivors and their families. Her laboratory has conducted some of the largest studies exploring metabolic and body composition changes in response to cancer treatment. An area of research in which Dr. Demark-Wahnefried has experienced particular success is the delivery of home-based lifestyle interventions among cancer survivors, an area in which she has led and continues to lead a number of NIH-funded trials aimed at improving the diet and exercise behavior of cancer survivors. She was named a Komen Professor of Survivorship for her work in this arena.

Currently, our NORC leadership oversees an NIDDK-funded T32 postdoctoral training grant for obesity research, an industry sponsored predoctoral obesity training grant, an NIH-funded R25 Cancer Prevention and Control Training Program emphasizing nutrition, an endowed professorship and endowed chair in nutrition sciences, an NIH-funded U54 Center for Nutrient-Gene Interaction, and an annual series of NIH-funded nutrition- and obesity-related short courses and conferences.

Core Laboratories

Individual Cores

- **Administrative Core:** David B. Allison, Ph.D., Director; W. Timothy Garvey, M.D., Associate Director; Ada Hudson, Chief Administrative Officer
- **Metabolism Core:** Barbara Gower, Ph.D., Director
- **Genetics Core:** W. Timothy Garvey, M.D., Director; José Fernández, Ph.D., Associate Director
- **Small Animal Phenotyping Core:** Tim R. Nagy, Ph.D., Director; Robert Kesterson, Ph.D., Associate Director
- **Biostatistics Core:** Renee Desmond, Ph.D., Director

Listing of External Advisory Groups Utilized

This year, we utilized a special external advisory group specifically because our NORC leadership decided to expand our research and research training in developmental aspects of obesity (the so-called womb to tomb approach). In preparation for designing a new training program in our NORC that would focus on doctoral (Ph.D.) training in developmental aspects of obesity, we applied for and received extramural grant funding from Abbott Nutritionals, specifically to host a 1-day workshop on developmental aspects of obesity at UAB. This workshop served to promote scientific exchange, networking, and education among our existing trainees and also our faculty. An outstanding group of internationally recognized investigators from the realms of basic molecular biology, physiology, and the social sciences offered its views

and research on developmental aspects of obesity. After the public sessions for this workshop were over, the invited speakers convened in a private session to serve as an advisory panel to us. They provided many useful suggestions. A proposal has now been submitted to and is pending review at the *Eunice Kennedy Shriver* National Institute of Child Health and Development at NIH. The Ad Hoc External Advisory Committee Members are listed below.

- **Mark Nijland, Ph.D.**, Assistant Professor, University of Texas–San Antonio, School of Medicine
- **Janos Zempleni, Ph.D.**, Professor of Molecular Nutrition, University of Nebraska–Lincoln, Department of Nutrition and Health Sciences
- **Barbara Corkey, Ph.D.**, Professor of Medicine and Biochemistry, Boston University School of Medicine
- **Caroline Davis, Ph.D.**, Professor, York University, School of Kinesiology and Health Science
- **Pathik Wadhwa, M.D., Ph.D.**, Director, University of California–Irvine, Behavioral Perinatology Research Program

Pilot and Feasibility Studies

Listing of Current Pilot and Feasibility Studies

Our pilot and feasibility (P/F) grant program has been successful in helping young investigators make the transition from beginning scientists to independently funded investigators. Here, we list our P/F grants for the past two years, beginning with P/F projects awarded in June 2008.

Role of TRB3 in Macrophage Foam Cell Formation and Adipose Tissue Infiltration. Xuxia Wu, Ph.D. The major goal of our study is to determine the function of Tribbles homologue 3 (TRB3), which acts as a dominant-negative regulator of several protein kinases, especially Akt, in foam cell formation and macrophage infiltration, which is increased significantly in obesity. The first aim will test whether TRB3 overexpression promotes the differentiation of THP-1 human monocytes into macrophage foam cells. The second aim will measure cholesterol and triglyceride levels in macrophages with overexpression of TRB3. The third aim will measure TRB3 protein expression together with macrophage infiltration in obese human adipose tissue.

Temporal Regulation of Muscle Mass and Regeneration via Conditional Expression of a Dominant Negative Myostatin (GDF-8) Transgene. Robert Kesterson, Ph.D. This proposal is creating a genetic mouse model to express a dominant negative myostatin transgene with temporal control via the cre/lox system. This model will allow the induction of increased muscle mass in an adult animal at differing times during its lifespan to determine if muscle mass alone will improve glucose homeostasis and other physiological measures. Several (7) independent lines of mice harboring the transgene have been created, three of which have been successfully bred to ubiquitously active cre mice to activate the transgene and are currently being evaluated for myostatin expression.

CRP-Mediated Maintenance of Homeostasis. Alexander Szalai, Ph.D. C-reactive protein (CRP) is a blood protein, synthesized and secreted mainly by hepatocytes, whose expression is

regulated at the level of transcription. We have engineered a novel mouse strain that cannot express the CRP gene. We propose that continuous expression of low levels of blood CRP is essential for maintenance of normal glucose metabolism and proper regulation of skeletal and somatic growth. We will pursue two aims: (1) to characterize the growth phenotype of moCRPko and (2) to characterize the diabetic phenotype of moCRPko.

Role of Secreted VAP MSP Domains in Insulin/FOXO Signaling and Fat Metabolism.

Michael Miller, Ph.D.. Obesity is a metabolic disorder associated with increased incidence of diabetes, hypertension, coronary heart disease, stroke, cancer, and infertility. Obese individuals often present with abnormalities in glucose and lipid metabolism, insulin signaling, skeletal muscle mitochondrial function, and blood hormone levels. A major obstacle in obesity research is defining the molecular circuitry that controls body growth and metabolism. We are using the nematode *Caenorhabditis elegans* to investigate vesicle-associated membrane protein-associated protein (VAP) proteins, which contain an amino-terminal MSP (major sperm protein) domain and a transmembrane domain. The MSP domain is named for its similarity to *C. elegans* MSP, a sperm-derived hormone that stimulates fertilization. The human genome encodes two VAP homologs, called VAPA and VAPB. Recently, we showed that VAP MSP domains are cleaved and secreted ligands for Eph receptors (EphRs), which also bind to membrane-associated ephrin ligands. The human VAPB MSP domain is secreted into the blood, but the biological role is not understood. In worms, a neuroendocrine signaling mechanism involving the insulin pathway and Forkhead Box Class O (FOXO) transcription factor regulates fat synthesis and storage. Worm VAP mutants have severe fat accumulation defects that are dependent on FOXO. Based on our preliminary data, we hypothesize that secreted VAP MSP domains bind to EphRs to inhibit FOXO transcriptional activity, resulting in increased fat metabolism.

Nitrite-Based Therapy for Targeting Dormant *Mycobacterium Tuberculosis*. Andries Steyn, Ph.D. Approximately one third of the world's population is latently infected with *Mycobacterium tuberculosis* (Mtb), and this, together with the emergence of multiple drug resistant (MDR), extensive drug resistant (XDR), and super XDR (S-XDR) Mtb strains, has created an alarming situation. A fundamentally important question in the TB field is how Mtb, which is contained within hypoxic granulomas in the human lungs, is able to persist in human tissues for months to decades without replicating, to then abruptly resume growth and activate disease. Dr. Steyn has recently fully dissected the biochemical and biophysical mechanism of how NO, CO, and O₂ are being sensed by Mtb. In a multidisciplinary study (published back-to-back in two PNAS papers in 2007), he has established a solid foundation for the mechanism of how Mtb senses protective host signaling molecules as “dormancy signals” to enter a drug resistant, persistent state. Importantly, in this proposal, a nitrite-based therapy mechanism will be addressed that may lead to the effective killing of dormant Mtb based on (1) acid reduction (disproportionation) of NO₂- to NO and (2) the fact that hemoglobin (Hb) can function as a nitrite reductase in tissue under physiological and pathological hypoxia to generate NO. This simple, nitrate-based therapeutic approach (via supplementation of green leaf vegetables or other sources of NaNO₂) of latent TB patients will have major public health and socioeconomic health implications.

Critical Periods of Exercise in Childhood. Olivia Affuso, Ph.D. (formerly Olivia Thomas). Early childhood (~3–6 years of age) is an important window for determining body composition trajectory and may be a critical period for the development of tissue partitioning patterns that influence obesity risk. As adiposity accelerates during this critical period, deposition/preservation

of fat stores may be sustained at the 'expense' of other tissues (i.e., energy homeostasis may be inherently biased toward fat gain). The type and amount of tissue mass accrued in early childhood has implications for metabolic profile and future obesity risk. An understanding of body tissue partitioning, particularly during periods of rapid growth and development (e.g., early childhood), is essential in efforts to address pediatric obesity. The interplay between fat and bone deposition can be considered a physiologic trait that enables the body to choose to shuttle 'energy' towards accrual among tissue types. Plausibly, the phenotype underlying obesity risk may be determined by the differentiation of cell type (adipocyte, osteocyte, etc.) during early childhood. Two aims will be pursued: (1) to examine the effects of physical activity on body composition via DXA and (2) to examine the effects of physical activity on adipose tissue distribution via MRI.

The Relationship of Dietary Polyunsaturated Fatty Acids (Omega 6 and Omega 3) to Inflammation in Zebrafish (*Danio rerio*). Mickie Powell, Ph.D. The zebrafish will serve as a model organism to understand the contribution of changes in the dietary poly-unsaturated fatty acid (PUFA) omega-6 (ω -6) to omega-3 (ω -3) ratio to changes in body growth, changes in body fat deposition/distribution, and promotion of systemic inflammation. Western diets have seen a dramatic shift to increased consumption of PUFA ω -6 and an associated decrease in the consumption of PUFA ω -3. This shift corresponds to an increase in chronic inflammation and associated chronic diseases in the human population. To investigate the biological mechanisms underlying this correlation, zebrafish will be maintained on diets containing 3 different ratios of ω -6: ω -3 PUFA for 11 months, starting at 1 month of age. The ratios used are 1:1, 5:1, and 20:1, representing an ancestral Paleolithic diet, a contemporary Mediterranean diet, and a contemporary Western diet, respectively.

Joint Mathematical and Biological Investigation of Glucose Tolerance. Xujing Wang, Ph.D. The long-term goal is to develop a mathematical model of glucose tolerance that can efficiently dissect the relative contribution to a disease process from the functional or anatomical loss of β -cells, insulin resistance, and the interplay between them, and hence accurately assess disease risks. Some mathematical and laboratory studies are already underway. In this pilot we plan to utilize several large, human glucose tolerance test data sets, totaling over 2,500 subjects, to develop and test a new mathematical model of whole body glucose-insulin dynamics, with an emphasis on improving the description of insulin dynamics that is presently available.

Diet and Husbandry Optimized for Growth and Reproduction in Zebrafish (*Danio rerio*) as a Predictor of Reduced Health and Longevity. Daniel Smith, Ph.D. Understanding the nutritional and genetic basis of disease and aging requires well established research protocols and organisms. Although the zebrafish (ZF - *Danio rerio*) has been used extensively in a number of scientific disciplines, its utility as a model of nutrition research has been limited, partly due to the lack of standardized, defined dietary and husbandry conditions. This project will have two aims: (1) dietary protein source and amount, in addition to specific amino composition, have significant effects on growth and reproduction in ZF, and (2) reduced water temperature (T_w) will retard growth, egg production, and food intake. This project will be preparatory for systematic studies of nutrition in ZF.

Differential Gene Expression of Ribosomal Proteins and Its Implication to Obesity. Degui Zhi, Ph.D. The overall goal of this project is to investigate differential ribosomal protein (RP)

transcription by using the now-emerging technology of RNA-Seq. About 80 ribosomal proteins are encoded in a mammalian genome, and one copy of each kind is required to build a ribosome. Cells keep a balanced yet elastic expression level of all RPs to maintain normal protein syntheses and to respond to nutritional shifts. Unsurprisingly, a number of RP genes have been implicated in cell size regulation, which is linked to obesity. However, the analysis of RP transcription is complicated by the presence of a large number (over 2,000) of processed pseudogenes of RP genes littered throughout the human genome. These pseudogenes are commonly thought to be non-functional due to the lack of promoters and the presence of disrupting mutations. Interestingly, some RP pseudogenes were found to be transcribed or evolutionarily conserved and might be functional through bioinformatics analyses. Two aims will be pursued: (1) to analyze the existing large collection of RNA-Seq data for the identification and quantification of transcripts of RP genes and their pseudogenes and (2) to quantify the expression levels of RP genes in adipose tissues of normal and obese mice.

Funding Derived From Previous Pilot and Feasibility Studies

Past Pilot and Feasibility Studies that Have Lead to Success in Obtaining Other Research Funding

Here, we highlight just four past P/F awardees from the relatively recent past who have gone on to receive extramural funding to continue their research. This is an illustrative and not exhaustive list of recent P/F awardees who have gone on to secure additional funding.

Monica L. Baskin, Ph.D. Dr. Baskin received a NORC P/F grant entitled “A Family-Based Intervention for African American Children at Risk for Overweight and Obesity.” She has since gone on to receive multiple related grants, as listed in the table below.

Dates of Funding	Agency	Grant #	Title of Award
9/25/09–4/30/12	National Institutes of Health	R01MD003997-01	Sociocultural influences on dietary intake among black women in the Deep South
1/1/09–12/31/10	Robert Wood Johnson Foundation	65659	If you build it, will they come? Interactive effects of social/cultural factors and the built environment on physical activity among African-American Youth
9/1/08–4/30/09	University of Pennsylvania/ Robert Wood Johnson Foundation	N/A	Community action to increase demand for healthy food in African American communities

Dates of Funding	Agency	Grant #	Title of Award
1/1/06–6/31/07	JP Morgan Private Bank	N/A	Impact of fruit and vegetable cost on obesity in children and parents
10/1/05–4/30/07	UAB Minority Health and Research Center	N/A	Childhood obesity intervention at Chris McNair Health Department
6/1/05–11/30/06	MetLife Foundation/ Association of Schools of Public Health	M3624-01/01	UAB/Washington Middle School Partnership for Good Health

Nefertiti Durant, M.D. In Dr. Durant’s NORC pilot grant “Efficacy of Moderate Intensity Exercise in Promotion of Weight Loss and Prevention of Weight Gain in Young African American Women,” overweight and obese African American young women attending UAB were recruited into a randomized trial to either (1) complete four 3-mile, supervised, moderate-intensity group walks per week for 12 weeks (monitoring done via research assistants, accelerometers, and heart rate monitors worn by participants) or (2) receive materials encouraging walking and describing the benefits of walking. All participants were instructed to maintain their diets as they were at entry. This study did not produce a significant difference in amount of weight loss between study groups. However, the pilot data were key in obtaining subsequent related extramural funding, including (1) CDC funding (Subcontract UAB MHRC REACH US Project), PI: Nefertiti Durant, 9/30/07–9/29/08; (2) The Coronary Artery Risk Disease in Young Adults (CARDIA) Year 25 Study Young Investigator Award, funded by the National Heart, Lung, and Blood Institute, 9/30/07–9/29/08; (3) A Robert Wood Johnson Faculty Scholars Program Award, PI: Nefertiti Durant, 7/09–8/12; and (4) The American Heart Association Scientific Development Grant, FIT HARRT (Fitness with Technology - Heart Risk Factor Reduction Tool): Decreasing Cardiovascular Risk Factors in Young Overweight African American Women Through a Technology Based Fitness Intervention, PI: Nefertiti Durant, 9/09–8/12.

Olivia Affuso, Ph.D. Dr. Olivia Affuso, the most recent recipient of the NORC’s Named New Investigator Award and a P/F recipient, is currently funded through several NIH-sponsored grants. Specifically, she is co-investigator on the Design Issues in Obesity Study (R01DK07882; PI: Dr. David B. Allison), junior investigator on the CARDIA Study (N01HC48047; PI: Dr. Beth Lewis), and PI of a subcontract to the Cuban Health Study (R01DK074687; PI: Dr. Jose Szapocznik). In addition, Dr. Affuso is funded by the UAB School of Public Health’s Back of the Envelope Award for her project entitled “Photobody” and has submitted an R01 application as PI to follow up on this research.

Bradley Yoder, Ph.D. Dr. Yoder offers a wonderful illustration of how we use our P/F grants program, our core laboratories, and indeed our entire NORC to not only serve our established obesity and nutrition researchers but also proactively inspire new research projects in areas of

burgeoning importance to the field. For example, our Action Committee, Enrichment Program, P/F Program, and Small Animal Phenotyping Core (SAPC) all joined efforts to promote new research in the study of obesity in invertebrate models. In 2003, NIDDK released an RFA for Genetic Studies of Obesity-Related Traits in Model Organisms (RFA DK-03-018) for proposals to “identify and characterize genes influencing obesity-related phenotypes in fruit flies (*Drosophila melanogaster*), soil nematodes (*Caenorhabditis elegans*), and zebrafish (*Danio rerio*).” Our Action Committee had already recognized the importance of this approach and had begun steps to promote its development at UAB. Next, the Enrichment Program invited four speakers who were working with such models to visit our NORC, speak in our seminar series, and consult with interested members. Meanwhile, our P/F Program provided support to several investigators using such models, including Dr. Yoder. Dr. Nagy of the SAPC worked to help sort out methods that could measure body fat in not only rodents but also small invertebrates. The ability to measure obesity-related traits in such small invertebrates was applied to work in nematodes by Dr. Yoder, in the Department of Cell Biology, whose main research focus is the role of primary cilia tissue physiology and how defects in this organelle can lead to developmental abnormalities. He found that inducible ciliary dysfunctions lead to obesity in mice and was helped by Drs. Nagy and Kesterson in the SAPC to extend this work to nematodes. Dr. Yoder then received an R01 (R01DK075996) for this work entitled “Ciliary Dysfunction and Pathogenesis of Obesity.”

Scientific Advances/Accomplishments

Selected Publications Highlighting the Role of the Center in Advancing Knowledge

Our NORC members published at least 40 obesity-focused papers in 2009 and more on other nutrition topics or that were related to but less tightly focused on obesity. Here, we list just a few from 2009–2010 that we believe are especially interesting, creative, or important.

1. Allison, D. B. & Mattes, R. D. (2009). Nutritively-sweetened beverage consumption and obesity: the need for solid evidence on a fluid issue. *Journal of the American Medical Association*, Jan 21;301(3):318–20. PMC2864605
2. Alvarez, J.A., Bush, N.C., Choquette, S.S., Hunter, G.R., Darnell, B.E., Oster, R.A., & Gower, B.A. (2010). Vitamin D intake is associated with insulin sensitivity in African American, but not European American, women. *Nutr Metab (Lond)*, Apr 14;7:28. PMC2868016
3. Colman, R. J., Anderson, R. M., Johnson, S. C., Kastman, E. K., Kosmatka, K. J., Beasley, T. M., Allison, D. B., Cruzen, C. Simmons, H. A., Kemnitz, J. W., & Weindruch, R. (2009). Caloric restriction delays disease onset and mortality in rhesus monkeys. *Science*, 325:201–204. PMC2812811
4. Cope, M. B. & Allison, D. B. (2010). White hat bias: examples of its presence in obesity research and a call for renewed commitment to faithfulness in research reporting. *International Journal of Obesity*, 34(1):84–8; discussion 83. PMC2815336

5. Cope, M. B., Li, X., Jumbo-Lucioni, P., DiCostanzo, C. A., Jamison, W. G., Kesterson, R. A., Allison, D. B., & Nagy, T. R. (2009). Risperidone alters food intake, core body temperature, and locomotor activity in mice. *Physiology & Behavior*, 96(3):457–63. PMC2692091
6. Elobeid, M., Padilla, M., McVie, T., Thomas, O., Brock, D., Musser, B., Lu, K., Coffey, C., Desmond, R., St-Onge, M-P, Gadde, K., Heymsfield, S., & Allison, D. (2009). Missing data in randomized clinical trials for weight loss: scope of the problem, state of the field, and performance of statistical methods. *PLoS One*, Aug 13;4(8):e6624. PMC2720539
7. Jumbo-Lucioni, P., Ayroles, J.F., Chambers, M.M., Jordan, K.W., Leips, J., Mackay, T.F., & De Luca, M. (2010). Systems genetics analysis of body weight and energy metabolism traits in *Drosophila melanogaster*. *BMC Genomics*, May 11;11:297. PMC2880307
8. Liu, Y., Ordovas, J. M., Gao, G., Province, M., Straka, R. J., Tsai, M. Y., Lai, C., Zhang, K., Borecki, I., Hixon, J. E., Allison, D. B., & Arnett, D. K. (2009). Pharmacogenetic association of the APOA1/C3/A4/A5 gene cluster and lipid responses to fenofibrate - the genetics of lipid lowering drugs and diet network (GOLDN) study. *Pharmacogenetics and Genomics*, 19(2):161–169. PMC2733171
9. Smith, D., Johnson, M., & Nagy, T. (2009). Precision and accuracy of bioimpedance spectroscopy for determination of *in vivo* body composition in rats. *Int J Body Compos Res*, Jan 1;7(1):21–26. PMC2722071
10. Zhu, S., Kim, J., Ma, X., Shih, A., Laud, P. W., Pintar, F., Shen, W., Heymsfield, S. B., & Allison, D. B. (2010). BMI and risk of serious upper body injury following motor vehicle crashes: concordance of real-world and computer-simulated observations. *PLoS Medicine*, Mar 30;7(3):e1000250. PMC2846859.

Women's Health (Selected Examples)

- By means of her newly funded NIH R01 (MD003997) “Sociocultural Influences on Dietary Intake Among Black Women in the Deep South,” Dr. Monica L. Baskin and colleagues are testing hypotheses that (1) there is a direct relationship between individual psychosocial factors and dietary intake, and (2) the relationship between socio-cultural factors and dietary intake is mediated by individual psychosocial factors. This study leverages the ongoing academic–community partnership of the UAB Deep South Network for Cancer Control and Prevention (DSN) that includes 22 counties in Alabama and Mississippi. Approximately 300 black women across the DSN will participate in concept mapping, a participatory and mixed methods design, to characterize the socio-cultural influences on dietary intake. An additional 350 black women will participate in a cross-sectional study to investigate the relationship between socio-cultural influences, individual factors, and dietary intake. Baskin and colleagues will then use cluster analysis to develop a typology of dietary intake influences among black women residing in the Deep South. Findings from this study have the potential to better explain the limited successes of black women achieving recommended dietary intake and, more importantly, better inform future interventions for black women at greatest risk for obesity and other chronic conditions.

- Dr. Paula Channandler-Laney has received an NIH-funded F32 grant titled “Effects of Maternal Obesity and Gestational Diabetes on Offspring Health.” Using this grant, she will recruit African American women for whom information is available regarding their glucose tolerance during pregnancy and seek permission to enroll their 5-to-8-year-old children in our study. Children will be grouped according to their mothers' weights (obese vs. normal weight) and gestational diabetes mellitus (GDM or non-GDM) status during pregnancy. During an inpatient clinical research center visit to ensure controlled food intake conditions, children's body compositions will be assessed by dual-energy x-ray absorptiometry (DXA); their blood lipid, cytokine, and satiety hormone profiles will be obtained; and their insulin sensitivity, secretion and clearance assessed via a mixed-meal tolerance test. In addition, children's physical activity will be measured via accelerometers, and their dietary intake via three 24-hour recalls, to determine whether any between-group differences in these variables contribute to differences in body composition and metabolic health. By gaining an understanding of the independent and interactive effects of maternal obesity and of GDM on pediatric health, we can better identify the population at greatest risk for chronic health problems before they develop, and we may be able to elucidate mechanisms to overcome the adverse effects of prenatal exposure to obesity and/or GDM.
- Through her NIH-funded NIH K99 award, Dr. Krista Casazza aims to develop diet interventions to address pediatric obesity that are specifically tailored to an individual's metabolic profile. Her specific interest is the interaction of diet quality with the changes in insulin secretion and action that occur during the pubertal transition. This entails a study involving a diet intervention in African American peripubertal girls.
- Through his NIH-funded R01, Dr. Gary Hunter is studying older women to evaluate the relative benefits of various exercise protocols on muscle size, bone density, strength, aerobic capacity, power, ease of physical activity (PA), amount of PA, and energy expenditure. Seventy-eight (> 60 years of age) African American and Caucasian women, matched for age, race, and BMI, are participating.
- Using her NIH-funded R01 award, Dr. Chandrika Piyathilake is evaluating the effect of folate on specific types of cells (normal, dysplastic, and invasive carcinoma cells) of the cervix of subjects who were diagnosed with these lesions before the dietary folate fortification started (1990–92) and in similar lesions of age, smoking status, and race matched subjects who were diagnosed after folate fortification (2000–2002).

Minority Health (Selected Examples)

- Dr. Ambika Ashraf (Pediatric Endocrinologist collaborator from Children Hospital), and Nutrition Sciences Ph.D. Candidate Jessica Alvarez are studying the role of vitamin D in insulin sensitivity in African Americans and Hispanic Americans. Findings to date indicate that greater dietary vitamin D is significantly associated with greater insulin sensitivity in African American women and that serum vitamin D is associated with a proxy index of insulin sensitivity in African American girls. Ongoing research is evaluating the association of serum vitamin D with both insulin sensitivity and cardiovascular function, using robust, state-of-the-art methodology.

- Dr. Gary Hunter is conducting a study designed to determine the optimal frequency of combined aerobic and resistance exercise to improve health outcomes in African American women.
- Dr. Monica Baskin is using ethnographic and community action strategies to characterize the food marketing environment contributing to caloric overconsumption among African American children (ages 3 to 11 years). In addition, she is examining the role of social and cultural factors in dietary intake among African American women residing in the Deep South.
- Dr. W. Timothy Garvey is studying the impact of race on the metabolic syndrome trait cluster. In current studies, he is assessing the differential impact of intramyocellular lipid on insulin resistance in European- and African Americans, as well as racial differences in muscle oxidative stress and metabolomic analyses (acylcarnitines) from plasma and muscle tissue. These data point to racial differences in the pathogenesis of insulin resistance and the Metabolic Syndrome trait cluster.
- Drs. Garvey, Fernandez, and Hunter are studying the effect on the plasma metabolome following exercise in subjects with and without the UCP3 exon 6-splice donor polymorphism. This gene variant is only detected in individuals of African descent and confers increased risk of obesity in Gullah-speaking African Americans.
- Dr. Nefertiti Durant is studying the impact of self efficacy and social support of exercise in college-age African American women, comparing internet-based support tools to traditional group-based support.
- A prospective cohort study is examining 648 community-dwelling older adults to identify racial differences in potentially modifiable risk factors of immobility among black and white adults.
- Dr. Olivia Affuso is examining infrastructural needs indicated for the creation of a community-based collaboration to develop policy and environmental changes designed to impact health behaviors of African American girls attending an afterschool program.
- Dr. Jamy Ard is conducting studies in African American populations to address optimal dietary patterns for weight control and cardiometabolic disease risk and social and behavioral factors that affect adoption of healthy behaviors.
- Dr. José Fernández studies the effect of genetic and environmental variables on racial/ethnic differences in diabetes-related traits by modeling individual estimates of genetic admixture and environmental measures of energy intake, energy expenditure, and socioeconomic status on measures of fasting insulin, sensitivity to insulin, and initial phase of insulin secretion after exposure to glucose among African American and Hispanic persons.

AIDS

Members of our NORC, including Dr. Donna Arnett, have participated in a genome-wide association study of atherosclerosis in men with HIV.

Obesity (Selected Examples)

Obesity is the greatest area of emphasis for our NORC. Some of our activities and accomplishments have already been listed in the preamble to this report and in the publications list above. Additional examples follow.

- Drs. Jong, Allison, and others are collaborating on an R01 with investigators at Medical College of Wisconsin to use engineering simulations to study the effect of obesity on injuries in motor vehicle collisions. Several other UAB investigators are also studying connections among obesity, driving ability, and vehicle injuries and deaths. Two recent papers emerging on this topic are as follows:
 - Viamonte, S., Vance, D., Wadley, V., Roenker, D., & Ball, K. (2010). Driving-related cognitive performance in older adults with pharmacologically treated cardiovascular disease. *Clin Gerontol*, Apr 1;33(2):109–123. PMC2882795
 - Zhu, S. Kim, J., Ma, X, Shih, A., Laud, P. W., Pintar, F., Shen, W., Heymsfield, S. B., & Allison, D. B. (2010). BMI and risk of serious upper body injury following motor vehicle crashes: concordance of real-world and computer-simulated observations. *PLoS Medicine*, Mar 30;7(3):e1000250. PMC2846859
- Several NORC investigators, led by Dr. Maria De Luca have cleverly used drosophila (fruit flies) as a model to rapidly study genes and pathways involved in obesity. See: Jumbo-Lucioni, P., Ayroles, J.F., Chambers, M.M., Jordan, K.W., Leips, J., Mackay, T.F., & De Luca, M. (2010). Systems genetics analysis of body weight and energy metabolism traits in *Drosophila melanogaster*. *BMC Genomics*, May 11;11:297. PMC2880307
- Drs. David Allison and Douglas Childers offered a novel mathematical model that potentially explains the fact that the body mass index (BMI) associated with the lowest death rate seems to increase with age and the fact that there is a U-shaped relation between BMI and death rate. See: Childers, D.K. & Allison, D.B. (2010). The 'obesity paradox': a parsimonious explanation for relations among obesity, mortality rate and aging? *Int J Obes* (Lond), May 4. [Epub ahead of print]. PMID in process.
- Dr. Barbara Gower and colleagues have shown that the relationship of intramyocellular lipid (fat within the muscle cells) to insulin sensitivity appears to differ with ethnicity in healthy girls and women.
- With Dr. David Allison as PI, we have been informed that we will be receiving an R13 grant from NIH (combined funding from the National Institute of Mental Health and NIDDK) to host a 2-day national research conference on adipogenic and metabolic effects of antipsychotic drugs. This meeting will be held in Newark, NJ, within the next 12 months.

- Drs. Molly Bray and Martin Young, two newly recruited members of UAB's NORC published an intriguing paper that received much positive press attention and showed that the metabolic effects of a high-fat meal can depend on the time of day in which it is consumed.
- Dr. Bradley Yoder has an NIH R01 to study the effect of aberrant cilia functioning on obesity in experimental organisms.
- Dr. Jose Fernandez and colleagues are using the combination of genetic and psychosocial research methodology to understand the origins of racial disparities in obesity.
- Drs. Shikany, Ard, and Allison are conducting a randomized trial of a novel dietary weight-loss approach.
- Dr. Jamy Ard and colleagues have new R01 funding from NIH to study the effects of weight loss procedures on obese African Americans.
- Drs. Tiwari, Allison, and others are collaborating on an R01 with Drs. Rudy Leibel and Wendy Chung of Columbia University on studies of the genetic influences on obesity in general and antipsychotic-induced weight gain in particular.
- Drs. Nagy and Allison have just received a new R01 from the National Institute on Aging to conduct a mouse longevity study examining the effects of weight cycling on lifespan.
- Dr. Allison and colleagues have an R01 to study the effects of obesity on mortality rate in epidemiologic data.
- Drs. Thomas and Allison have an R01 to study design issues in obesity treatment trials via meta-analytic methods.
- Dr. Mickie Powell has just begun a new pilot study to investigate obesity phenotypes in zebrafish.
- Drs. Gower, Garvey, Hunter, Fernandez, and other NORC investigators have continued long-term prospective studies examining determinants of weight-regain patterns in post-obese European-American and African American women. These studies continue to yield valuable insights regarding the role of metabolic factors, muscle physiology, and exercise interventions in weight regain.

Health Promotion or Disease Prevention

Again, we have many activities ongoing in this realm. Here we highlight just one new and innovative one.

- Dr. Tamilane Blaudeau and colleagues established and have received extramural grant funding for a physical activity and education program that capitalizes on the new found interest in ballroom dancing. The program targeted inner-city African American children between the ages of 11 and 18 as a means of promoting health and reducing obesity by introducing ballroom dancing as an alternative form of physical activity. In conjunction with

the introduction of ballroom dancing, the program also included a nutrition and health education component. Dance 4 Health: As a Coca-Cola Company funded Active Healthy Living study, 60 children from the A. G. Gaston Boys & Girls Club participated in a 3-hours-per-day, 3-days-per-week, 6-week program that introduced ballroom dancing as an alternative form of physical activity. Approximately 2 hours were dedicated to dance, and the other hour was dedicated to lectures and teaching in diet, nutrition, food buying, preparation, health assessment, risky behaviors, attitudes towards physical activity, body image, body composition, anthropometrics, and physical fitness, all of which were assessed pre and post study. Evaluations of these assessments are currently underway.

Educational Activities/Accomplishments

- **Professional Development Workshops.** For our NORC members, we organized, funded, and hosted one professional development workshop in 2009 with four more in 2010. For details and videos, see: <http://www.norc.uab.edu/courses/professionaldevelopment>
 - 05/21/2009 Peer Review: Improving Your Effective Manuscript Review Writing
 - 08/27/2010 Tenure and Promotion
 - TBD Creativity (Managing Careers for Success)
 - 05/07/2010 Negotiating, Financial, and Ethical Considerations
 - 09/20/2010 Successful Grant Writing—from the Perspective of Funding Institutions
- On April 22, 2010, we hosted a 1-day conference on Developmental Origins in Obesity. This conference, funded in part by a grant from Abbott Nutrition, was open to the public and video proceedings were placed on our website for free viewing. For more details, see <http://www.norc.uab.edu/courses/conferences/conference2010>. The panel of five speakers included Mark Nijland (University of Texas), Barbara Corkey (Boston University), Caroline Davis (York University), Pathik Wadhwa (University of California at Irvine).
- Our NORC posts its seminars in video format on the web for free public viewing. See <http://www.norc.uab.edu/courses/seminars>.
- UAB provides intensive and comprehensive nutrition education for health professionals. Programs include required and elective educational opportunities for medical students throughout their 4 years of training, for nursing and dental students, for medical residents, and for M.D.s training to be Physician Nutrition Specialists. Members of the NORC in the Department of Nutrition Sciences provide all didactic teaching in nutrition for the Schools of Medicine and Dentistry. Both schools have converted to an organ-based modular system of education such that nutrition lectures are now provided at different points in time throughout the freshman and sophomore years for medical and dental students, instead of in one single block. The bulk of these lectures are provided in the introductory, gastrointestinal, endocrine, and cardiovascular modules. In 2009, NORC member Dr. Douglas Heimburger, who organized the nutrition curriculum in addition to serving as co-module director for the gastrointestinal module, was nominated for Best Module Co-Director, Best Module, and Best Lecturer in the *Gastrointestinal Module* for the 2009 UAB School of Medicine Argus

Awards by medical school Class of 2011. Physician members of the NORC incorporate nutrition principles in disease management of obesity, cardiometabolic disease treatment and prevention, osteoporosis, cancer treatment and prevention, and hospital nutrition support. In the context of these respective clinics and hospital services, our faculty provides medical education for students, residents, and fellows as Attending Physicians (i.e., a physician who practices within the UAB system as a member of hospital staff who may admit and treat patients and supervise or teach trainees). A relatively unique feature of our NORC at UAB is the training of physicians for certification as Physician Nutrition Specialists in the Department of Nutrition Sciences. This latter program is supported by funding from a Cancer Prevention and Control Training Grant (R25-CA047888) directed by NORC members Drs. Tim Nagy and Wendy Demark-Wahnefried, with Dr. Sarah Morgan serving as director of the clinical fellowship training component. In 2009, two outstanding fellows, Drs. Lisa Carlson and Jessica Barfield, trained as Physician Nutrition Specialists, and we have signed another outstanding fellow, Dr. Taraneh Soleymani, to begin her training in the summer of 2010.

- The EatRight Information Service provides nutrition information to both the public and health professionals through community programs and through a nationwide 1-800, toll-free line.
- NORC faculty members participate as part of the Alabama State Obesity Task Force, which is chaired by NORC member Dr. Bonnie Spear.
- National Conferences. Here at UAB, we have stepped up our efforts in recent years to provoke dialogue and interchange at the national level on key topics in nutrition and obesity. Our members have secured multiple NIH R13 (conference grants) for this purpose.
 - In addition to the conference listed above on Developmental Origins of Obesity, we are planning a meeting on Antipsychotic Induced Weight Gain. The conference is tentatively planned for the last quarter of 2010 or first quarter of 2011.