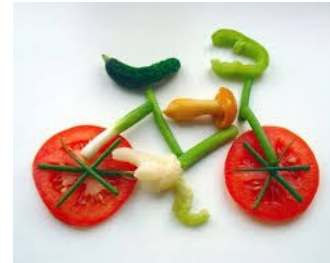


UAMS College of Medicine Series
Showcase of Medical Discoveries:
A focus on **NUTRITION**



Wednesday, November 12, 2014
4:30—6:00 p.m.

*A Wine & Cheese Reception Featuring
UAMS Investigators Discussing their
Research and Discoveries.*

Winthrop P. Rockefeller Cancer Institute
10th Floor Rotunda

Poster #1

Feasibility and Acceptability of Tailored Dietary Sodium Intervention and Its Effects on Sodium Reduction, Symptoms, and Quality of Life in Patients with Heart Failure



Seongkum Heo, PhD, RN, Jean McSweeney, PhD, RN, Elaine T. Prewitt, DrPh, Jeannette Y. Lee, PhD, Debra K. Moser, DNSc, RN, and Allison Shaw-Devine, MD, Audrey Fier, RN

Background: Patients with heart failure (HF) have poor dietary sodium adherence, and this is an important factor in worsening of HF symptoms, which, in turn, is associated with poor health-related quality of life (HRQOL).

Purpose: To examine the feasibility and acceptability of a tailored dietary intervention combined with technology (MyFitnessPal) and psychosocial support, and to examine intervention effects on dietary sodium adherence and factors affecting it, symptoms, and HRQOL.

Methods: A 6 session tailored dietary intervention based on sodium intake (MyFitnessPal) and on factors affecting dietary adherence (knowledge, skills, experience, confidence, perceived benefits and barriers, social support, and depressive symptoms) was delivered to 11 patients with HF (mean age 53 years). Repeated t-tests were used to analyze the data.

Results: The 11 patients completed 131 of 132 intervention sessions. The mean satisfaction scores for all sessions ranged from 98% to 100%. Sodium intake (24-hour urine) was reduced (3.9 to 2.6 g per day, $p = .034$), and HF symptoms (46.5 to 26.7, $p = .001$) and QOL (68.0 to 40.0, $p = .001$) were improved at 3-month follow-up. Factors affecting dietary adherence, including skills ($p < .001$), experience ($p < .001$), confidence ($p = .001$), perceived benefits and barriers ($p = .027$), social support ($p = .033$), and depressive symptoms ($p = .004$) were improved.

Conclusion: A tailored dietary intervention combined with technology and psychosocial support was feasible and acceptable and showed promising results in reducing dietary sodium intake and improving factors affecting dietary sodium intake, physical symptoms and HRQOL.

Poster #14

Early Diet Impact on Gastrointestinal Tract and Immune Function



Laxmi Yeruva, Nicole Spencer, Anne Bowlin, Martin Ronis, Thomas Badger and Roger Rank

The goal of our work is to understand whether breast-fed children have an advantage with respect to the development of immune function in the intestine, as well as programming of growth and body composition. It has been suggested that breast-fed infants have advanced immune system development compared to formula-fed infants, and the gut microbial environment may play a role. These bacteria can have a profound influence on intestinal function and intestinal immune response, and it has been shown that dietary factors in breast-milk and formulas can differentially alter the composition of the microbial environment in the gut. However, does the microbiota alone shape gut development and subsequent immune function in infants and do breast-fed children have better immune responses to infections? In order to understand and address these questions, ACNC scientists have developed a piglet model of infant formula feeding. Preliminary data demonstrate that gastrointestinal tract development and gut-associated lymphoid tissue is highly developed in breast milk fed piglets in comparison to formula-fed piglets. However, the long-term health consequences and the mechanisms by which these occur have not yet established. Our goal is to utilize piglet model to determine the effects of early diet on gastrointestinal development and function and to determine the role of gut microbiota in immune function at the local and systemic level. **Impact:** Determining the specific mechanisms by which breast milk influences the gut and immune system will aid efforts to improve commercial infant formula, by adding components that are unique to breast milk as well as to modify microbiota through probiotics to help boost the immune system in infants.

Poster #13

Physical Activity and Energy Metabolism Unit

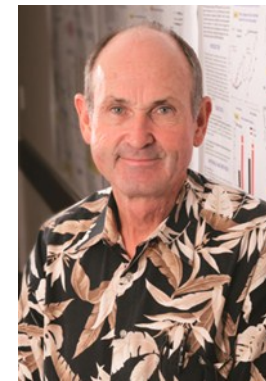


Elisabet Børshem, Leybi L. Ramirez, Eva C. Diaz, Nicholas M. Hurren, Eugenia Carvalho, Matthew Cotter, Aline Andres, Kartik Shankar, Thomas Badger and Sean Adams

The goal of the Physical Activity and Energy Metabolism (PAEM) Unit is to determine the effects of physical activity and/or nutrition on normal growth and development in children, specifically as it pertains to energy and substrate metabolism and to prevention of obesity. It is recognized that suboptimal nutrition and sedentary behavior are essential in the development of obesity, and that improvement of these factors are vital for the reversal of obesity and its corresponding disturbances in metabolism. The structure of this improvement is however debated. Can exercise alone, without changes in body weight, improve obesity-related metabolic disturbances? Would improvements in maternal physical activity lead to beneficial effects on the baby and healthier outcomes in the child? The PAEM Unit includes a physical activity facility for controlled studies of exercise training, plus a human performance lab for testing of fitness and determination of energy and fuel metabolism. The Unit assists investigators in performance of exercise and metabolic studies including use of stable isotope tracer techniques to determine substrate flux rates, and high resolution respirometry (Oroboros) to measure function of mitochondria, the “powerhouse” of the cell. Some ongoing/new studies include prenatal physical activity intervention; fat oxidation and energy expenditure in babies from lean vs. obese mothers; substrate oxidation in lean vs. obese children during rest and exercise; and protein nutrition, liver lipids and whole body protein metabolism in children.

Poster #2

ACNC History, Mission, Vision and Accomplishments



Sean H. Adams and Thomas M. Badger

The Arkansas Children’s Nutrition Center (ACNC) is one of six human nutrition research centers funded by the USDA Agricultural Research Service, and only the second to focus on childhood development and health. The Center is celebrating its 20th year, and is a growing and vibrant place focusing on improving child health and optimizing function throughout development. The faculty and scientific staff are dedicated to discovering the fundamental biology of childhood brain and metabolic processes, bone development, and the mechanisms by which diet and physical activity (both maternal and child) impact these networks. Much of the focus at the ACNC is to determine how maternal health and physical activity during pregnancy--as well as the influence of formula vs. breastfeeding--impact obesity, cognitive, and metabolic health outcomes in the baby and as children get older.

To tackle these questions, ACNC scientists employ strategies and tools that are truly “molecule-to-whole body” in nature, including the monitoring of naturally-occurring bacteria in the gut (gut microbiome), thousands of small-molecule metabolites present in the blood and tissues that track metabolic health status (metabolomics), bone 3D-architecture and markers of bone health, brain networks, anatomy and neuronal “wiring” associated with cognitive development and behaviors, and unique modifications of DNA and expression of thousands of genes in placenta and cells. In the end, our mission is to perform research that will have a positive impact on the health of children and families in Arkansas and beyond, by translating basic science into actionable intervention strategies during the prepartum, pregnancy, and postpartum periods.

Poster #3

Maternal Programming of Offspring Metabolism: A Translational Approach to Prevent Childhood Obesity



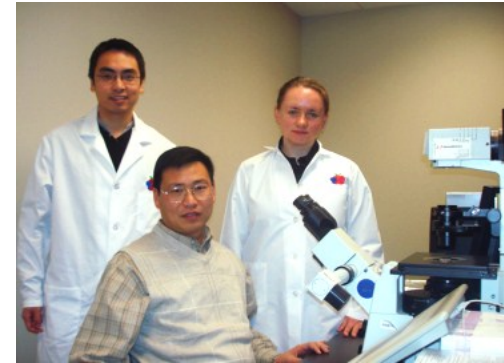
Keshari Thakali, Meghan Ruebel, Forrest Lindsey, Thomas Badger, Elisabet Børshheim, Aline Andres and Kartik Shankar

The risk of obesity in adulthood is unambiguously influenced by experiences in utero. Of note, maternal diet and obesity are now recognized as important determinants of obesity risk in later life. This is particularly significant since, over 60% of pregnancies currently are in women who are either overweight or obese at conception. Our group, using a translational approach, focuses on identifying the mechanisms whereby maternal obesity influences the offspring. Studies are aimed at uncovering changes during key windows of development such as pre-conception, in utero and infancy. Using a controlled model of pre-conception obesity, our studies clearly show that offspring born from obese dams show changes in metabolism, energy expenditure and differentiation of fat cells, associated with epigenetic alterations (chemical modifications that “decorate DNA” and can regulate gene expression without changing the genetic code). Likewise, studies using the placenta from both animals and human subjects are allowing us to understand how maternal obesity influences the baby during gestational development. Changes in offspring gene expression have been identified as early as the blastocyst stage. Whether these changes are present before conception in the oocyte is under investigation. Analogous questions are being addressed in a large clinical study to identify risk factors in humans that lead to the programming of metabolism in the offspring.

Impact: Ultimately, results will be used to develop strategies to decrease the effect of maternal obesity on the offspring metabolism, thereby attempting to reduce the incidence of childhood obesity. We are currently testing whether physical activity or probiotic supplementation could help offset the negative effects of maternal obesity on the offspring.

Poster #12

The Role of Dietary Factors in Skeletal Development



Jin-Ran Chen, Oxana P. Lazarenko, Aline Andres, Martin J.J. Ronis and Thomas M. Badger

Diet plays a major role in skeletal development, affects fracture risk in children and influences optimal peak bone mass, a risk factor for the development of degenerative bone disorders such as osteoporosis. Epidemiological studies suggest that fruit and vegetable consumption increases bone size and mass in children, and some foods, including soy beans and blueberries, significantly promote skeletal development/growth during early development. However, the bioactive components in foods and their molecular mechanisms remain unknown. In addition, recent studies suggest reduced bone quality, cortical bone strength and increased fracture risk in obese or overweight children. However, it is unknown what specific diet components can improve bone health and thwart the negative impact of obesity on bone. We have designed a set of translational studies to determine if the bone anabolic effects of blueberries involve signaling effects of food-derived phenolic acids [hippuric acid (HA) and 3-(3-hydroxyphenyl) propionic acid (PPA)] via a specific cell receptor system (GPR-109A-p38- β -catenin pathway) in bone-forming osteoblasts. We have also tested if HA-rich fruits and vegetables or soy protein isolate stimulate bone growth in rodent obesity models or bone cells in culture. Positive effects of soy protein isolate were discovered to be due to its ability to prevent obesity-associated osteoblastic cell senescence. In children, we will use peripheral quantitative computerized tomography (pQCT) and blood markers to study bone health and quality in lean versus obese pre-pubertal children. Dietary interventions using blueberries will determine if we can ameliorate obesity-induced skeletal impairment.

Impact: Our studies provide evidence that treatment and prevention of bone degeneration may be possible through consumption of bone-promoting phytochemicals. These studies will provide valuable information for evidence-based nutrition recommendations and health management of children.

Poster #11

Effects of Obesity on Development of Oxidative Stress and DNA Damages in Liver of the Obese Zucker Rat



Reza Hakkak, Soheila Korourian, Teresa Evans, Oleksanda Pavliv and Stepan Melnyk

The obesity epidemic is continuing in the United States for two decades. Obesity leads to significant change in redox balance, targeting both systemic and targeted organs/tissues. Previously, we reported obesity promotes DMBA-induced mammary tumor development using the obese Zucker rat model.

This study's objective was to investigate the effects of obesity on oxidative stress development and oxidative DNA damage in the rat liver. Female lean and obese Zucker rats (n=8/group) at 5 weeks of age were fed AIN-93-G diet for 8 weeks. Liver sample metabolites were measured using HPLC-electrochemical detection or LC-MS. We found lean rats have significantly (P<0.05) higher levels of reduced free Glutathione (GSH), significantly (P<0.04) lower levels of oxidized Glutathione (GSSG) and 20% lower (P<0.03) GSH/GSSG oxidative ratio compared to the obese group. Also, an indicator of oxidative DNA damage, 8-hydroxy-Guanosine (8-OH-G), was 25% (P<0.03) higher in obese rats compared to the lean group and there was a significant (P<0.03) spike in 5-hydroxymethyl-Cytosine (5-hmC) in obese rats. Supported by ABI to RH.

Poster #4

Metabolomic Influences in Maternal and Neonatal Programming



Maria Elena Diaz-Rubio, Horacio Gomez-Acevedo, Lindsay Pack, Shanggong Yu, Sudeepa Bhattacharyya, Kelly E. Mercer and Nianbai Fang

Metabolomics is the analysis of unique chemical signatures of the thousands of small molecules (metabolites) that are in our bodies, some of which are involved in regulating biological processes. Some metabolites can serve as fuel sources while others are involved in structural activities, signaling, gene transcription or other cell processes. Metabolomics is a robust tool that provides an instant readout encompassing physiological changes in cells, tissues or ultimately an individual. At Arkansas Children's Nutrition Center, we apply these newly-emerging analytical techniques to unravel the complex metabolic profiles and molecular mechanisms underlying maternal and neonatal programming, metabolic health, and childhood disease risk. In particular, we are interested in understanding the interplay between bacterial and mammalian metabolism, since naturally-occurring gut bacteria are responsive to diet and host health and can impact specific metabolic pathways linked to whole-body function.

Impact: As nutrition plays a key role in the interaction between bacteria and their host, we strive to identify metabolic profiles driven by obesity (maternal and postnatal), metabolic health status, and the influence of diet. This will provide an important foundation to determine how diet modification can prevent adverse outcomes, and optimize health and function in infant and childhood development.

Poster #5

Effects of high isoflavone soy diet vs casein or arginine-supplemented casein diet on liver steatosis



Reza Hakkak, Starrett William, Tang, Xinyu, and Soheila Korourian

Non-alcoholic fatty liver disease (NAFLD), the major cause of abnormal liver function, is often associated with obesity. Arginine (Arg) plays a role in reducing body fat, but there is limited data as to the role that Arg may play in soy protein's ability to protect from fatty liver. The objective of this study was to find the role of native Arg in soy to protect from fatty liver in male obese Zucker rats (N=49; 6 weeks old). Rats had *ad libitum* access to water and were randomly assigned to one of 3 diets for 8 or 16 weeks: Casein (CAS) diet as control (0.6% Arg) or a casein diet supplemented to contain 1.3% Arg (ARG) or a soy protein isolate diet with high isoflavones (SPI) (1.3% Arg). SPI and ARG rats gained more weight ($P<0.05$) than CAS rats after 16 weeks only. The SPI rats had lower liver steatosis after 8 and 16 weeks ($P<0.05$ and $P<0.001$, respectively) compared to CAS & ARG rats. SPI rats had lower serum alanine amino transferase (ALT) & aminotransferase (AST) levels ($P<0.05$) compared to CAS after 16 weeks and AST was lower ($P<0.05$) compared to ARG rats. After 16 weeks the SPI rats had lower ($P<0.05$) serum ALT and AST levels than SPI rats at 8 weeks. Supported by ABI to RH.

Summary: Results suggest that a longer period of SPI feeding results in lower liver steatosis and serum ALT and AST levels while an ARG diet had no effect on steatosis or ALT and AST levels. The protective effect of soy protein to reduce fatty liver does not appear to be due to its arginine content.

Poster #10

Dietary Influences on Psychological, Physiological and Neurocognitive Development and Function in Children



R. Terry Pivik, Aline Andres, Xiawei Ou, Patrick H. Casey, Mario A. Cleves, and Thomas M. Badger

Research being conducted at the Arkansas Children's Nutrition Center (ACNC) is addressing the influence of dietary factors on behavioral and cognitive development and function in healthy infants and children. This is done through longitudinal and cross-sectional studies integrating measures of brain structure and function (EEG, fMRI) with standardized measures of psychological and behavioral development. Our longitudinal study tracking infant diet-related development of 600 participants from 3 months to 6 years Beginnings is creating a normative database, which can be used to address questions regarding the influence of early diet on a broad spectrum of CNS processes and behaviors as children pass through critical developmental stages.

Impact: These studies evaluate, for the first time, whether there are differences in neuroanatomical, behavioral, or cognitive outcomes comparing children primarily breastfed or formula-fed. Other cross-sectional studies are designed to provide guidance for Nutrition Assistance Program policy regarding dietary recommendations that will enable children to optimize learning and performance while in school. These studies will also contribute to the identification of neurocognitive correlates, consequences, and risk factors for childhood obesity that will assist in the development of effective prevention strategies.

Poster #9

**Relationship between Childhood Food Allergies
and Family Quality of Life**



A. Colvin, T. Crook, L. Christie, D. Gonzales, J. Phelps, L. Maddox, R. Hakkak

Family quality of life (QOL) may be negatively impacted in households with food allergic children. The Food Allergy Impact Scale (FAIS) was administered to 39 parents of food allergic children to assess QOL. A negative correlation was found between mean FAIS scores and age, $r(39) = -.380$, $p = .017$. Higher FAIS scores equate to lower QOL indicating lower QOL in families with younger children. Positive correlations between the following variables and number of food allergies were observed: (1) "eating out", $r(39) = 0.326$, $p = 0.043$ (2) "free time", $r(39) = 0.479$, $p = 0.002$, (3) "spouse's employment", $r(39) = 0.336$, $p = 0.045$, (4) "finances", $r(39) = 0.538$, $p = 0.001$, (5) "special foods", $r(36) = 0.558$, $p < 0.001$, and (6) "other expenses", $r(38) = 0.532$, $p = 0.001$. This indicates that families of children with multiple food allergies eat out less, have less free time, are more likely to live on one income and have additional expenses related.

These data suggest food allergies negatively impact QOL in several areas. Further study is needed to explore the financial impact of food allergies and to identify resources for this population.

Poster #6

**A Substantial Proportion of Pregnant Women are Marginally
Biotin Deficient Early and Late in Pregnancy**



Katelin Estes, Anna Bogusiewicz, Horace J. Spencer, David Kasper, Jeffery H. Moran, Zachary Stowe, and Donald M. Mock

Background. Marginal biotin deficiency is a putative human teratogen, and evidence is emerging that marginal biotin deficiency may be common in pregnancy.

Objective. To assess biotin status in two groups of pregnant women: 1) a community population of 53 women and 2) a "clinic population" of 74 women with a psychiatric diagnosis.

Methods. Urinary excretion of 3-hydroxyisovaleric acid (3HIA) and 3HIA carnitine (3HIAc), indicators of biotin status, and three ratios of the acylcarnitines arising from reactions involving three biotin-dependent carboxylases were quantitated by LC-MS/MS.

Results. Compared to 26 non-pregnant controls, 3HIA was increased in both the clinic population ($p=0.0003$) and in the community population ($p=0.080$). Moreover, in the clinic population, 3HIA increased from prepartum to intrapartum, increased over the trimesters, and decreased from intrapartum to postpartum ($p < 0.0001$ for each). However, urinary excretion of 3HIAc was not increased in either population, suggesting that these pregnant women might be functionally carnitine deficient. Consistent with marginal biotin deficiency, acetylcarnitine to malonylcarnitine ratio was increased in both populations, and propionylcarnitine to methylmalonylcarnitine ratio was increased in the community population.

Conclusions. This study provides novel evidence that marginal biotin deficiency develops in pregnancy and, further, that the degree of the deficiency increases during pregnancy.

Poster #7

Structured Food Experiences: A Preliminary Evaluation of the WISE Curriculum



Taren Swindle, Ph.D. and Leanne Whiteside-Mansell, Ed.D.

WISE is a classroom curriculum designed to provide children with hands-on exposure to eight target foods. In 2013-2014, WISE was implemented in 10 classrooms across three HS agencies. Primary caregivers (N=62) completed pre- and post-test interviews on intake of the target food outside of HS hours, willingness of children to try new foods, and parent nutrition practices.

Children's average intake of target foods increased significantly for 4 of 7 foods based on t-test mean comparisons. Hierarchical regression analyses were conducted predicting the DVs at post-test controlling for pre-test levels of the outcomes and child willingness to try new foods at pre-test (for nutrition outcomes). The set of predictors accounted for a significant portion of variance in all outcomes with program exposure having impact beyond baseline measures for all outcomes. That is, program exposure was predictive of gains in intake of target foods, decrease of junk food, and improvement of parenting practices.

Data suggest that targeted food experiences with a parent outreach component can impact young children's diets. Program exposure, as reported by the parents, significantly predicted across outcomes of interest beyond baseline levels in the desired direction. The WISE curriculum holds promise to improve dietary intake for children and their families.

Poster #8

Metformin and Soy Bioactives Limit the Frequency of the CD133⁺CD44⁺ Epithelial Sub-population in Human Colon Cancer Cells



Maria Theresa E. Montales, Adam R. Brown, Rosalia C.M. Simmen, and Frank A. Simmen, Ph.D.

Colon cancer is the third leading cause of cancer-related deaths worldwide. Obesity and diabetes, due in part to high-caloric diet and sedentary lifestyles, underlie increased colon cancer risk. Epidemiological studies suggest that the biguanide Metformin (Met), commonly used as a first-line treatment for Type 2 diabetes, may exhibit anti-cancer activity by reducing blood glucose and hence insulin levels that fuel growth of cancer cells and by activating the AMPK pathway that regulates their metabolic state. While Met has been evaluated for its ability to inhibit the malignant potential of colon cancer cells, studies addressing the effects of dietary factors with health benefits and their combined effects with Met have not been reported. Herein we performed *in vitro* studies to evaluate whether Met and the soy bioactive components genistein (GEN) and Lunasin (LUN) alone and in combination inhibit the tumor potential of the metastatic human colon cancer line HCT116. The abundance of the CD133⁺CD44⁺ epithelial sub-population of HCT116 cells, that form non-adherent colonies (termed colonospheres) under anchorage-independent conditions, is an *in vitro* measure of tumor formation. Met (5 µg/ml) decreased cell viability, induced cell apoptosis, decreased the frequency of sphere formation, promoted tumor suppressor PTEN expression and inhibited pro-tumorigenic FASN transcript levels in HCT116 cells. Similar to Met, GEN (2µM) and the soy peptide LUN (2 µM) reduced cell viability (GEN>LUN>Met), inhibited colonosphere formation, and enhanced PTEN mRNA expression. The effects of Met on colonosphere formation were enhanced by GEN but not by LUN; co-addition of all three reduced colonosphere numbers. To evaluate if Met limits colonosphere formation partly through KLF9, Met-treated cells were evaluated for KLF9 mRNA expression, and siKLF9-targeted HCT116 cells were assessed for proliferation. Met reduced KLF9 and FASN gene expression by 2h and 6h, respectively, suggesting a temporal relationship, and siKLF9 targeting decreased proliferation. Results suggest that Met, when used in conjunction with dietary bioactives, may limit the expansion of colon tumor-initiating cells. The intriguing possibility of mechanistic linkages among Met, KLF9 and FASN in colon tumorigenesis warrants further study.