



Studying Nutrition Today for the Health of Future Generations

2003 Faculty Research Summaries

Steven A. Abrams, M.D.

Dr. Abrams' research focuses on the mineral nutritional needs of infants, children and adolescents. His first major area of interest is in calcium and bone mineral requirements of children. The goal of this work is to evaluate methods for optimizing bone mass in childhood, using stable isotopes to measure calcium absorption and bone kinetics. His second area of interest is in identifying the optimal forms and amount of iron and zinc to provide to small children, especially those who live in developing countries. In these countries, iron deficiency anemia and zinc deficiency are extremely common and strategies must be developed for fortifying food sources and providing complementary foods with adequate amounts of bioavailable minerals. His team frequently travels to other countries to assess these issues and assist in developing research programs using iron and zinc stable isotopes.

Cheryl B. Anderson, Ph.D.

Dr. Anderson's research is aimed at promoting regular physical activity through understanding its determinants, including self-identity as a motivational factor in health behavior. A primary focus is the description and measurement of athletic identity and its relation to physical activity in children, adolescents, and parents, as well as factors that contribute to identity formation, stability, and change. Another focus of her research is the development of psychometrically valid and reliable measurement instruments of attitudes and behaviors, as well as the statistical evaluation of existing measurement instruments that are used in behavioral research.

Janice Baranowski, M.P.H., R.D., L.D.

Ms. Baranowski is interested in dietary and physical activity health promotion, and obesity and chronic disease prevention among children and their families. She designs, implements and evaluates programs to help children and their families change dietary and physical activity behaviors. Ms. Baranowski currently is co-principal investigator on an obesity prevention project among African-American girls, a diet and physical activity badge program for Boy Scouts, and an investigation of influences on availability of fruit, juice and vegetables in the home.

Tom Baranowski, Ph.D.

Dr. Baranowski is interested in obesity and chronic disease prevention among children and their families. Toward this end, he develops and tests new measures of diet and physical activity; assesses correlates of diet and physical activity; and designs, implements and evaluates programs to help children and their families change dietary and physical activity behaviors. He currently is principal investigator on an obesity prevention project among African-American girls, a diet and physical activity badge program for Boy Scouts, a diabetes prevention trial among middle-school students, and an investigation of influences on availability of fruit, juice and vegetables in the home.

Dennis M. Bier, M.D.

Dr. Bier's primary research interest is the integrated regulation of interorgan transport of metabolic fuels; specifically, substrate and hormonal regulation of the macronutrient fuels, glucose, fatty acids, ketones, and proteins/amino acids. This work has contributed broadly to the endocrine, nutritional and physiological regulation of endogenous fuel availability for biochemical and nutritional functions in otherwise healthy infants born very prematurely, normal newborn infants born at term, growing children, maturing adolescents, and healthy young and elderly adults. Further, his laboratory has helped both

define and refine assessment of the altered metabolic fates of ingested, exogenous fuels under various pathophysiological circumstances that detrimentally change nutritional homeostasis, for example the metabolic fuel derangements accompanying diabetes and renal failure. In these endeavors, his laboratory has developed and employed a wide variety of stable isotope tracer kinetic methods that have now become the standards in the field for quantifying substrate flux, metabolism, precursor-product relationships, and irreversible oxidation to exhaled or excreted end products.

Douglas G. Burrin, Ph.D.

Dr. Burrin's major research goal is to elucidate the critical cellular and hormonal signals mediating the stimulatory effects of enteral nutrition on the growth and function of the neonatal intestine. Current studies examine the physiological and clinical significance of GLP-2 and enteral nutrition, and how they impact intestinal nutrient metabolism in his neonatal pig model. Isotope tracers coupled with arteriovenous organ balance and blood flow measurements are used to quantify the intestinal absorption and metabolism of macronutrients provided either enterally or parenterally, and to examine whether GLP-2 treatment alters amino acid and oxidative substrate metabolism in piglets fed parenterally. Whether the trophic effects of GLP-2 treatment during total parenteral nutrition translate into enhanced gut function and the underlying mechanisms of enteral nutrition and GLP-2 action at the tissue and cellular level are also studied to determine how they modulate mucosal epithelial cell protein turnover, proliferation and programmed cell death rates.

Nancy F. Butte, Ph.D.

Genetic and environmental causes of childhood obesity are the current focus of Dr. Butte's research. A genomic scan for loci associated with the development of obesity is being performed in 1,600 Hispanic individuals from 300 nuclear families. Extensive phenotyping of the children includes measurements of body composition, food intake, eating behavior, energy partitioning during growth, energy expenditure, physical fitness and activity, and serum hormones and metabolites. Extensive research on the food intake, energy expenditure and body composition of infants and children preceded this work on childhood obesity. Other major interests include the functional consequences of variations in energy balance on pregnancy outcome, postpartum weight retention, lactation performance, and infant growth and development.

Joan Carter Clark, R.D., M.B.A.

Ms. Clark's focus is the dissemination of information about the research activities of the USDA/ARS Children's Nutrition Research Center through print and electronic materials describing the center's mission, organization, and research efforts. She is editor of the CNRC's award-winning consumer-oriented newsletter, *Nutrition & Your Child*, and webmaster for the center's web site, www.kidsnutrition.org, as well as for related faculty and research project web sites. She also serves as the center's liaison to the public, the media, and Baylor College of Medicine communications personnel.

David M. Cohen, Ph.D.

Dr. Cohen's research concerns the regulated coordination of metabolic fluxes that is fundamental to health and sustained by adequate nutrition. Study of the quantitative relationships among metabolic flux rates depends on accurate measurement of those rates, preferably in vivo. To this end, he has investigated mathematical aspects of modeling rates of metabolic pathways, subsequent to the administration of isotope-labeled precursors. An important focus of Dr. Cohen's work is the measurement of cerebral metabolism in vivo, using nuclear magnetic resonance spectroscopy. Currently, he is developing a new method for estimation of the rate of cerebral glucose metabolism, with a substantial improvement in time resolution. In the long term, he hopes to learn more about the role of diet in support of brain metabolism and function.

Orla M. Conneely, Ph.D.

Dr. Conneely's research concerns the role of the iron-binding protein, lactoferrin (LF), in the regulation of homeostasis, growth and development of the gastrointestinal tract and in protection against bacterial infection and inflammation. Lactoferrin is a multifunctional protein found at very high levels in milk and in the body secretions that interface with the external environment. The second most abundant protein in human breast milk, LF is inactivated in infant formulae. Studies in LF-deficient mice generated by Dr. Conneely indicate that LF is not required for intestinal iron uptake, but plays a critical role in preventing excessive iron absorption during the neonatal period of development. She plans to continue her studies

on the neonatal iron sequestration role of LF, and to examine its role in prevention against bacterial infections. She will also examine the consequences of LF ablation on intestinal inflammation, using mouse models of Crohn's disease and ulcerative colitis.

Austin J. Cooney, Ph.D.

Dr. Cooney's research goal is to understand the mechanism by which the transcription factor GCNF regulates embryonic gene expression, and the influence of the maternal diet on its activity. His research focuses on identifying GCNF-responsive target genes expressed during embryogenesis and studying the GCNF mode of regulation of these genes. To date, he has been able to identify Oct4 as a GCNF-responsive gene that is silenced in somatic cells after gastrulation by GCNF. Using a yeast two-hybrid screen, he has identified DNA methyl transferases as interacting partners of GCNF. Methylation of DNA around genes has been implicated in the silencing of genes, so this would be the first example of regulated and targeted DNA methylation by specific recruitment of a DNA methyltransferase. His laboratory is using knockout mouse models and the multipotent embryonic carcinoma cell P19 to study GCNF's regulation of Oct4 expression via DNA methylation.

Karen Weber Cullen, Dr. P.H.

Dr. Cullen's research focuses on the prevention of diet-related chronic diseases through the development, implementation, and evaluation of nutrition behavior change programs for children and adolescents. Of particular interest are programs aimed at increasing children's fruit and vegetable consumption utilizing unique delivery channels. Current projects include implementing and evaluating an environmental behavior change program for middle-school cafeteria a la carte/snack bars that includes social marketing within the cafeteria environment, developing and implementing a school-based program for the prevention of Type 2 diabetes among youth, and conducting a feasibility study on an Internet-based dietary behavior change program aimed at families.

Teresa A. Davis, Ph.D.

Dr. Davis' research goal is to identify the mechanisms by which hormones and nutrients interact to regulate the high rate of skeletal muscle protein deposition in the neonate. To achieve this objective, her research focuses on five main areas: the role of insulin, amino acids, and glucose in the regulation of protein synthesis in the neonate; the role of insulin, amino acids, and glucose in the regulation of the insulin signaling pathway which leads to translation initiation in the neonate; the role of hormones, cytokines, and nutrients in the regulation of muscle protein synthesis during sepsis in the neonate; the role of development in the regulation of the protein synthetic response to a chronic high protein diet; and the role of insulin and nutrient intake in the anabolic response to growth hormone.

Debby Demory-Luce, Ph.D.

Two focal points of interest of Dr. Demory-Luce are the eating habits of preschool children and pediatric nutrition education for primary care providers. A current research area involves the examination of how preschool children's eating habits are affected by environmental factors and their parents' personal characteristics, such as weight and health-related beliefs.

Kenneth J. Ellis, Ph.D.

A primary goal of Dr. Ellis' research is to establish reference standards for body elemental composition in infancy, childhood and adolescence. This research focuses on the development and application of nuclear-based techniques for in vivo studies of human body composition. This approach provides knowledge of changes in growth and body composition that reflect the body's cumulative response to basic physiologic and metabolic processes. Detection of these changes often requires unique instrumentation like the CNRC's whole body counter, which monitors ⁴⁰K, a naturally occurring isotope in the human. Dr. Ellis has continued to develop in vivo neutron activation techniques for clinical research and postmortem examinations, and he has extended the use of dual-energy X-ray absorptiometry to the examination of infants and children.

Marta Fiorotto, Ph.D.

The focus of Dr. Fiorotto's research is the regulation of muscle growth rate during early postnatal life and its impact on muscle function in adulthood. The major objective is to identify how the developmental stage of muscle tissue influences both the short- and the long-term response of the muscle to two of the primary regulators of muscle growth: nutrient availability and endocrine factors (GHRH, growth hormone, and

insulin-like growth factors). In addition to overall growth and body composition effects, Dr. Fiorotto is also examining the rate of muscle protein turnover, the expression of muscle-specific protein genes and transcription factors, satellite cell replication and accretion. For these studies, she uses animal models, such as transgenic mice with altered muscle growth and growth factor expression, as well as gene-transfer techniques in which an exogenous gene for GHRH is administered postnatally, or prenatally to the mother.

Jennifer Orlet Fisher, Ph.D.

Dr. Fisher's research investigates the development of food preferences and the controls of food intake during infancy and early childhood. The broad goal of her research program is to understand how early eating environments modify young children's eating behavior and health outcomes. Of particular interest is the role of parents in selecting foods of the family diet, in serving as models of eating behavior, and in making child-feeding decisions that affect child food preferences, selection, and intake patterns. Currently studies are being conducted to understand the influence of maternal feeding practices on the development of food intake regulation and growth during infancy. Another line of research evaluates the role of maternal feeding practices and family eating styles in problematic food intake regulation and overweight among Hispanic children. Finally, experimental research is being conducted to determine the effects of large portions on daily intake in young children and their mothers.

Ian J. Griffin, M. B., Ch. B.

Dr. Griffin's work focuses on understanding the mechanisms by which humans regulate zinc metabolism, particularly the metabolic adaptations to low zinc intakes, and the importance of marginal zinc status in human disease (e.g., Crohn's disease.) His research uses stable nonradioactive isotopes and mathematical modeling techniques to describe zinc metabolism in health and disease.

Michael A. Grusak, Ph.D.

Dr. Grusak's laboratory is involved in both plant physiology and human nutrition research. His plant physiology research is focused on the mechanisms and regulation of nutrient transport in plants. His long-term goals are to characterize the dynamics of nutrient flow within plants in order to determine the biophysical/molecular signals that regulate source-to-sink nutrient partitioning, and ultimately to use this information to enhance the nutritional quality of plant foods for human consumption. With regard to his human nutrition research, his laboratory group has developed hydroponic growth facilities and various protocols to intrinsically label plant foods with stable isotopes of important nutrients; these are then used to assess nutrient bioavailability and metabolism in humans.

Darryl L. Hadsell, Ph.D.

Insulin-like growth factors (IGFs) are necessary for mammary gland development and lactation. Despite this, the mechanisms by which these peptides regulate mammary gland function are poorly understood. The focus of Dr. Hadsell's research is to understand the specific signaling mechanisms through which the IGF-I receptor (IGF-IR) regulates mammary gland development and lactation. Transgenic and/or gene targeting strategies are used to modify the activity of key IGF-IR signaling pathway intermediates within the mammary gland. These strategies have demonstrated: 1) that IGF-IR regulates early mammary ductal development through the ability to regulate cell cycle progression within specialized structures called terminal endbuds; 2) that IGF-I also acts during lactation to maintain mammary cell survival; 3) that specific intracellular scaffolding proteins, termed insulin receptor substrates (IRS), are important to both the cell survival actions and to other potential actions of IGF-I on the regulation of milk volume and composition during early lactation.

Peter M. Haney, M.D., Ph.D.

Dr. Haney's research goal is to understand the molecular cell biology of lactation. Current work focuses on glucose transport in the lactating mammary gland. Dr. Haney is studying the regulation of GLUT1, the only glucose transporter isoform identified in the mammary gland and in established and primary mammary epithelial cell lines in humans and rodents. He has shown that GLUT1, normally a plasma membrane protein, is diverted to the intracellular site of lactose synthesis in lactating mammary epithelial cells, suggesting that these cells have a unique and nutritionally important mechanism to alter GLUT1 targeting. Efforts are under way to elucidate this mechanism by identifying structural determinants of intracellular GLUT1 targeting in mammary epithelial cells. Video confocal microscopy demonstrates that intracellular GLUT1 targeting is highly dynamic and can be altered with certain drugs. Dr. Haney is also examining how GLUT1 gene expression and subcellular targeting regulate the synthesis of lactose.

Morey W. Haymond, M.D.

Dr. Haymond's research focus is to delineate and ultimately manipulate hormone and substrate factors regulating absorption, assimilation, mobilization, and disposal of carbohydrates in infants and children. Nutrient availability to meet the energy and growth needs of children is frequently disturbed by chronic disease, infection, trauma and/or organ failure. The increase in type 1 and type 2 diabetes provides opportunities to study the effects of insulin, insulin resistance, and obesity on macronutrient assimilation in children. Specific studies utilize stable isotopic tracer techniques to estimate insulin sensitivity, absorption of carbohydrates, proteolysis, protein synthesis, gluconeogenesis, carbohydrate disposal, and protein and fat metabolism. Current studies explore the impact of diet composition (fat and carbohydrate) on glucose homeostasis and macronutrient accretion in normal and obese children, the impact of lactation on glucose homeostasis, precursors for and regulation of lactose production by the mammary gland, and the regulation of galactose and fructose metabolism.

William C. Heird, M.D.

Dr. Heird's studies focus on the nutrient needs of low-birth-weight infants and other infants and children with special needs, including the specific amino acid needs of those who depend upon parenterally delivered nutrients, as well as ways of meeting these needs. An additional interest concerns the metabolism of essential fatty acids during infancy and childhood and the role of long-chain polyunsaturated fatty acids in infant development.

Karen Hirschi, Ph.D.

Dr. Karen Hirschi's goal is to understand, at the cellular and molecular level, the events leading to blood vessel formation. She is interested in elucidating regulators of vascular cell recruitment, proliferation and differentiation needed for blood vessel assembly and maintenance. One aim is to define mechanisms by which soluble effectors, such as retinoids and TGF-beta, and cell-cell junctional components such as gap junctions, modulate vascular cell phenotype and cell cycle progression. Another focus is to investigate the potential of adult stem cells to contribute to neovascularization in response to tissue injury and growth. The mechanisms by which adult stem cells are recruited, induced to differentiate into vascular cells, and are functionally integrated into existing vascular networks, are of particular interest. Insights gained from such studies are applied to the optimization of clinically relevant treatments, including autologous vascular cell and gene therapy, assembly of blood vessels grafts, and vascularization of engineered tissues.

Kendal D. Hirschi, Ph.D.

Plants cannot run from environmental stresses; they must adapt. Dr. Kendal Hirschi is studying the mechanisms by which plants sequester nutrients and toxic metals into the plant vacuole to cope with environmental challenges. At the molecular level, his goal is to understand the structure, biological function, and regulation of transporter proteins that control trafficking into and out of the plant vacuole. Another major goal is to learn how to manipulate the expression and function of these transporters to increase the nutritional content of crop plants, improve plant productivity, and cleanse polluted soils. He views these objectives as integral components of the Green Revolution, the global agricultural movement whose aim is to end world hunger by developing innovative ways of increasing grain yields, particularly via the use of genetically improved food plant varieties.

Judy A. Hopkinson, Ph.D.

Dr. Hopkinson's research goal is to define physiological and behavioral factors associated with optimal breastfeeding practices. To achieve this goal, her research focuses on the following areas: the impact of lactation on maternal and infant physiology, with special emphasis on bone metabolism; the identification of cultural factors that limit breastfeeding duration and/or exclusivity; the characterization and etiology of breast and nipple discomfort encountered by breastfeeding women; and the evaluation of intervention strategies and counseling techniques designed to increase optimal breastfeeding behaviors.

Farook Jahoor, Ph.D.

Dr. Jahoor's research focuses on the metabolic alterations of specific nutrient transport and acute-phase proteins, amino acids, carbohydrate and lipids in response to different pathologies, including undernutrition, diabetes mellitus, sickle cell disease and chronic infections. He also studies glutathione metabolism and its relationship to oxidant damage of lipids and proteins in conditions of oxidative stress.

Craig L. Jensen, M.D.

Dr. Jensen's research is directed toward determining the optimal intakes of polyunsaturated fatty acids for term and preterm infants. The ability of infants to synthesize longer-chain n-3 and n-6 polyunsaturated fatty acids from their precursors, alpha-linolenic and linoleic acids, respectively, is being investigated using stable isotope techniques. The effects of different dietary intakes of essential fatty acids on biochemical and functional outcomes in both term and preterm infants are being assessed.

Heidi Karpen, M.D.

Dr. Karpen's research involves the study of Patched, a tumor suppressor gene responsible for Gorlin Syndrome. Patched is a member of the Sonic Hedgehog signaling pathway, critical for early embryonic patterning and development. Dr. Karpen is using mutations identified in Gorlin patients and sporadic basal cell carcinomas to define functional domains important for protein trafficking and function. The goal of this research is to better understand mechanisms of aberrant embryonic development and cancer formation so that targets for intervention may be identified.

Gerard Karsenty, M.D., Ph.D.

Dr. Karsenty's research focus is on the regulation of bone remodeling by hormones that also affect body weight and reproduction. To that end, Dr. Karsenty is using mutant mouse strains in which either specific hormones or their receptors are deleted. He currently is studying how leptin controls bone mass. He hopes to determine whether leptin acts through a different set of secondary messengers to regulate body weight and bone mass, using mouse models generated in the laboratory. He also is exploring the concept that antagonizing the leptin pathway may be a way to treat osteoporosis without affecting body weight. Lastly, he is studying other hormones that may regulate body weight and bone mass.

Alexandre Lapillonne, M.D., Ph.D.

Dr. Lapillonne's research interest is to determine whether, and how, early nutritional events affect long-term growth, metabolic function and development. His work has focused on the effect of intrauterine growth on body composition and postnatal growth, the effects of specific nutrients on gene transcription, and how alterations in gene transcription affect growth and body composition. Current research focuses specifically on the effect of n-3 polyunsaturated fatty acids on weight gain, body composition, fat oxidation, energy expenditure and transcription of genes controlling lipid oxidation and thermogenesis. He is also planning to assess how and when in early life, optimization of protein intake can maximize catch-up growth and neurological development of very-low-birth-weight infants. The overall goal of Dr. Lapillonne's research is to optimize the nutritional management of extremely low-birth-weight infants in order to overcome long-lasting effects on growth and development.

Carlos Lifschitz, M.D.

Dr. Lifschitz currently is conducting a multicenter study aimed at determining the effect of growth hormone on intestinal adaptation in children with short bowel syndrome. His future plans include the initiation of a Houston study that will focus on the relationship between food allergy and gastrointestinal dysfunction in children.

Ronald L. McNeel, Dr. P.H.

Dr. McNeel studies the pathways and nutritional controls of differentiation in preadipocytes and fat mass accretion as they relate to the pathological condition of obesity. Obesity research studies center on key transcription factors that are regulators of preadipocyte differentiation, metabolism, and proliferation, including, peroxisome proliferator-activated receptor delta (PPAR δ), gamma 2 (PPAR γ 2), and alpha (PPAR α). These research studies are not limited to the effects of these transcription factors only, but are inclusive of other transcription factors that influence preadipocyte differentiation and adipocyte metabolism. This research is focused on a more complete understanding of the molecular mechanisms involved in fat mass accretion, which are critical in the design of nutritional or pharmacological intervention strategies aimed at decreasing nutritional obesity. Another area of research investigates the association between multiple candidate gene variations and quantitative measures of body size and fat in populations. Analysis includes gene-gene and gene-environment interaction.

Harry J. Mersmann, Ph.D.

Adipocyte growth and differentiation are regulated by various hormones and growth factors and may be altered by dietary components. Dr. Mersmann's laboratory has studied the influence of the stage of

development and of dietary factors on adipocyte beta-adrenergic receptors. Currently, the focus of his efforts is on adipocyte development. Porcine adipocyte precursor cells may be isolated from adipose tissue and when grown in culture in vitro under the proper conditions, differentiate to adipocytes. He has used this system to evaluate factors regulating the differentiation process and the influence of dietary components of differentiation. In addition to mRNA for the beta-adrenergic receptors, mRNA for various transcription factors that regulate differentiation (e.g., C/EBP-alpha or PPAR-gamma) and mRNA for key proteins that characterize the adipocyte (e.g., lipoprotein lipase and aP2) are being measured. He is particularly interested in the role of individual fatty acids in the stimulation or inhibition of adipocyte differentiation.

David D. Moore, Ph.D.

The receptors for retinoic acid, thyroid hormone, steroids, and other potent biological regulators belong to a nuclear hormone receptor superfamily. This family also includes a number of additional proteins called orphan receptors, which do not have known ligands. The conventional receptors regulate a variety of processes in developing and adult animals. The orphans are less well characterized, but it is thought that they also play important roles in diverse areas. The broad-ranging effects of these proteins are a consequence of their function as ligand-dependent, or in some cases, ligand-independent transcription factors. The main goal of Dr. Moore's laboratory is to understand the mechanisms of action of the members of this superfamily. Toward this aim, he has identified a number of proteins that interact with both conventional and orphan receptors, and he is characterizing their functions.

Kathleen J. Motil, M.D., Ph.D.

Dr. Motil's studies focus on estimating dietary protein and amino acid needs of lactating women and adolescents and elucidating the mechanisms that underlie increased nutrient needs for milk production. She has found that lean body mass of adult women is preserved during lactation, suggesting that nutrient conservation occurs because of the needs of milk production. In contrast, lean body mass of adolescents increases during lactation at the expense of a reduction in milk production. Dr. Motil's studies also focus on estimating the dietary protein and energy needs of girls with Rett syndrome and elucidating the mechanisms that underlie the universal finding of growth failure in this disorder. She has found that involuntary motor movements associated with Rett syndrome do not increase rates of energy expenditure, and that poor growth results from reduced dietary energy intakes associated with oropharyngeal and gastroesophageal dysfunction.

Paul Nakata, Ph.D.

Calcium in plants is sequestered as a complex with other substances such as oxalates, phytates, fiber, fatty acids, proteins and other anions. Some of these substances (oxalates and phytates) are considered antinutrients, and render the calcium in plant foods unavailable for nutritional absorption by the human. The purpose of Dr. Nakata's research program is to elucidate the mechanism regulating calcium partitioning and sequestration in plants. The acquired information will be applied toward the rational design of strategies to enhance calcium abundance and bioavailability in plant food products.

Buford L. Nichols, M.D.

Starch from grains and tubers provide the major source of calories in the human diet. The ultimate objective of the research being conducted by Dr. Buford Nichols is the determination of the mechanisms by which dietary starch interacts with the gene expressing maltase-glucoamylase. Maltase-glucoamylase is the gate-keeping enzyme that determines small intestinal starch digestion into glucose or, by default, colonic fermentation into short-chain fatty acids. The function and regulation of maltase-glucoamylase are under investigation in knockout (KO) mice and children with deficient starch digestion. The most recent discovery is the presence of a spliced secreted isoform, which participates in starch digestion in the lumen of the ileum of KO mice. This secreted isoform of the enzyme is produced in the Paneth cells instead of enterocytes. The mechanism of regulation of both isoforms is under study in wild type and null MGA mice on different diets.

Theresa A. Nicklas, Dr. P.H.

Dr. Nicklas's research focuses on nutritional epidemiology and intervention aspects of chronic disease prevention and health promotion: specifically, how eating behaviors and other lifestyles influence the development of chronic disease risk factors early in life and the behavioral factors influencing the development of adverse lifestyles in childhood. Current areas of research include a detailed investigation of the relationship among eating patterns, diet quality, and obesity in children and young adults; an

examination of environmental influences on fruit, juice, and vegetable consumption and body mass index of Head Start preschool children; and development of a valid and reliable computerized food preference measure for use with preschool children. Planned studies include a behavior-based intervention aimed at favorably influencing food preferences and consumption by African- and Hispanic-American preschool children attending Head Start, and a behavioral-based family intervention designed to increase fruit, fruit juice, and vegetable consumption by preschool children.

Jeffrey M. Rosen, Ph.D.

Dr. Rosen's research objectives are to elucidate the mechanisms regulating the normal development of the mammary gland and to determine how these regulatory mechanisms deviate in breast cancer. Studies of the role of systemic hormones and local growth factors on critical periods of development in the mouse mammary gland are under way. Transgenic and knockout mouse models are being used to examine the roles of specific transcription factors and their dominant-negative isoforms, postnatal mammary gland development, and the changes in normal signal transduction pathways that are involved in the progression from the normal mammary gland to preneoplasias, as well as the role of mutant p53 in genomic instability and the development of aneuploidy. In addition, methods that permit the analysis of both gain and loss of specific gene function selectively in the mammary gland have been developed.

Robert J. Schwartz, Ph.D.

Dr. Schwartz conducts research focused on defining the molecular basis underlying the establishment and maintenance of skeletal, cardiac and smooth muscle differentiation. Of special interest is Nkx2-5, a transcription factor instrumental in the patterning of the embryonic heart. The heart appears to develop as a modular organ, such that a distinct transcriptional regulatory program controls each anatomical region. Consistent with this notion, the heart tube can be divided into segments that form the atria, left ventricle, right ventricle, and ventricular outflow tract. Precursors of these regions appear to originate from separate lineages, which develop according to their positions along the anteroposterior axis of the embryo. Recent studies have revealed cis-regulatory elements that direct cardiac transcription specifically in the left or right ventricular chambers and atria, which could be important for the physiologic and functional differences of the chambers of the adult heart.

Partha Sen, Ph.D.

Dr. Partha Sen is the director of the Child Health Research Center (CHRC) Molecular Core Laboratory. The laboratory provides DNA sequencing and DNA synthesis services to the CHRC awardees and their mentors and Baylor faculty at large. Dr. Sen is also involved in research related to alveolar capillary dysplasia (ACD). This is a genetic disorder that causes misalignment of lung blood vessels, and is also characterized by a severe reduction of capillaries in the lungs of the patient. The relentless course of the disease culminates in the death of the neonate despite intensive therapy. The inheritance of the disease is presumed to be autosomal recessive. The primary goal of the research project is to identify the causative gene for this human disorder.

Robert J. Shulman, M.D.

Dr. Shulman is investigating the factors regulating the development of gastrointestinal function in the premature infant. He is interested particularly in carbohydrate digestion and absorption and the interaction of carbohydrates with other nutrients both as facilitators and potential inhibitors of digestion and absorption of other nutrients. The long-term goal is to understand and, thereby be able to treat, feeding intolerance in premature infants. These data also can be applied to treat infants with short bowel syndrome. Most recently, he has been broadening his research efforts, initiating studies to understand the factors that contribute to health care-seeking behaviors in children with recurrent abdominal pain.

Roman J. Shypailo, B.S.

The unprecedented growth of technology during the past decade has created challenges for researchers. Powerful computers and data acquisition equipment enable rapid accumulation of information that requires processing. The CNRC Body Composition Laboratory houses sophisticated instruments designed to measure the elemental composition of the human body using nuclear-based techniques. Each instrument is in a dynamic state of evolution. New measurement systems are being developed, including a multiparameter whole-body counter capable of isolating and measuring a signal coming from a specific site in the body, and a portable ⁴⁰K counter for use in a hospital setting. Coordinating these efforts and incorporating new technology are the primary focus of Mr. Shypailo's work.

C. Wayne Smith, M.D.

Dr. Smith's research involves the roles of neutrophils in host resistance to infection and tissue injury in conditions of inappropriate inflammation. He is currently collaborating on projects investigating neonatal neutrophil function, neutrophil mediated injury to myocardium, the phenotypes of mice with CD18 subunit deficiency, the influence of stress on leukocyte functions and neutrophil mediated liver damage, and the molecular and cellular mechanisms of neutrophil transendothelial migration. He mentors postdoctoral fellows investigating the development and use of gene array technology to define gene expression in neutrophils stimulated with IL-15; the expression of oncostatin M by neutrophils, the stimuli that lead to expression, and the potential effects of neutrophil OSM on endothelial cell functions; the mechanisms of obesity in mice that are deficient in ICAM-1; and the contribution of leukocytes to the regrowth of corneal epithelium. He also mentors a Ph.D. student working on the use of artificial extracellular matrix in tissue engineering.

E. O'Brian Smith, Ph.D.

Dr. E. O'Brian Smith provides statistical design, analysis, and teaching support to the USDA/ARS Children's Nutrition Research Center, the General Clinical Research Center, the Pediatrics Department, and Baylor College of Medicine investigators. This support includes teaching statistical methods, developing grant applications, the design of research protocols, statistical analysis, interpretation, and manuscript preparation. His support services range from basic consultation to extensive involvement in a project.

Janice E. Stuff, Ph.D.

Dr. Stuff's interest is nutritional epidemiology and the role of nutrition in chronic diseases and public health problems. One emphasis is to understand dietary carcinogen and chemopreventive exposure, the genetic susceptibility to dietary carcinogens, and their interaction as determinants for cancer. Dr. Stuff is developing and validating databases of N-nitroso compounds and isothiocyanate compounds in foods in order to investigate their role in the development and prevention of cancer. Another interest is to investigate the role of diet, body composition, and hormone levels in the development of risk factors for breast cancer. Dr. Stuff also collaborates with the USDA/ARS Delta NIRI (Nutrition Intervention Research Initiative), an initiative designed to measure the nutrition and health status of individuals and communities in the Lower Mississippi Delta region, and to develop interventions. This project also investigates the impact of food insecurity on the health, nutritional requirements and nutritional status of children.

Agneta L. Sunehag, M.D., Ph.D.

Dr. Sunehag studies carbohydrate metabolism in infants and children. In particular, she is interested in how well very premature infants utilize the gluconeogenic pathway to produce glucose from parenterally administered lipid and amino acid solutions. This research is needed in order to develop neonatal parenteral nutrition solutions that prevent both hypo- and hyperglycemia while providing a sufficient energy intake for normal growth. Her other research projects are aimed at determining whether the macronutrient content of the diet affects the development of insulin resistance and, thus, the risk of type 2 diabetes in children, whether obese children differ from non-obese with regard to metabolic adaptation to changes in dietary carbohydrate and fat content, and whether exercise will improve glucose metabolism and insulin sensitivity in obese children. Dr Sunehag is also involved in studies of glucose metabolism in lactating women and in children with type 1 diabetes.

Deborah I. Thompson, Ph.D.

Dr. Thompson is interested in children's problem solving to overcome barriers to physical activity and in the design, development, and evaluation of electronic media programs. Dr. Thompson is studying the use of Dual Code Theory and how to best design interactive multi media programs to promote health behavior change, as well as the impact of monetary incentives on log-on rates to electronic media promoting diet and physical activity change. She also coordinates qualitative research for a large, multi-site study to prevent type 2 diabetes among middle school youth.

Qiang Tong, Ph.D.

The study of adipose tissue development may reveal clues about the molecular mechanisms of metabolic diseases, such as type 2 diabetes and cardiovascular disease. Dr. Tong has established the mammalian GATA transcription factors as molecular gatekeepers in the early stages of adipogenesis. He demonstrated that both GATA-2 and GATA-3 transcription factors are negative regulators of adipocyte differentiation. This effect is mediated through direct suppression of the promoters of adipogenic factors

PPAR γ and C/EBP α by GATA factors and protein-protein interactions between GATA and C/EBP α or C/EBP β . Currently he is investigating the regulation of GATA factors at the protein level, with the goal of characterizing the identity and dynamics of the GATA protein complexes during adipogenesis, and the role of GATA in the lineage determination of adipogenic progenitor cells. He also plans to identify new regulators of adipogenesis and to develop mouse models to study the roles of these genes in obesity.

Ignatia B. Van den Veyver, M.D.

The neurodevelopmental disorder Rett syndrome is caused by mutations in a gene on the X chromosome, *MECP2*. This gene encodes methyl-CpG-binding protein 2, thought to be a transcriptional repressor that binds to methylated CpGs in DNA. Based on this, we propose the more general hypothesis that DNA methylation is important for regulation of gene expression during development, especially of the brain. There is evidence that DNA methylation can be influenced by methyl-donor enriched diets, containing substances such as folic acid and betaine. We are investigating in animal and cell culture models whether this treatment can alter DNA methylation and gene expression in the brain. This is not only important for conditions such as Rett syndrome, but may also provide a better understanding for the role of such agents in other prenatally-onset disorders and birth defects, such as neural tube defects or for the fetal origin of adult-onset disorders.

William W. Wong, Ph.D.

Dr. Wong's main research interests include strategies to prevent childhood obesity and the use of dietary supplementation to prevent chronic diseases. Based on the data he collected in the Houston Independent School District to document the prevalence and risk factors of childhood obesity, a grant application designed to determine the appropriateness and effectiveness of an after-school physical activity program to prevent obesity among Hispanic children has been submitted to the National Institutes of Health. With respect to projects related to the use of dietary supplements to prevent chronic diseases, Dr. Wong is currently investigating the safety, efficacy, and optimal dosage of soy isoflavones to prevent osteoporosis in postmenopausal women and the effects of soy isoflavones on nitric oxide production and blood pressure in postmenopausal women with high-normal blood pressure.

Issa F. Zakeri, Ph.D.

Dr. Zakeri is interested in Nutrimetrics, the application of statistical methods to problems in nutrition. His goal is to advance, develop and apply more accurate and computationally flexible statistical techniques to analyze and better understand many complex problems in nutrition, particularly behavioral nutrition. His primary research interests in statistics are time series analysis, multivariate analysis, sequential analysis, and statistical pattern recognition.