



**USDA/ARS Children's Nutrition Research Center
at Baylor College of Medicine**

Studying Nutrition Today for the Health of Future Generations

2002 Faculty Research Summaries

Steven 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 by 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 regulation of interorgan transport of metabolic fuels; specifically, substrate and hormonal regulation of glucose, lipid, and protein/amino acid fuels. This work has taken two principal directions. The first entails the regulation of endogenous fuel availability for metabolic functions when a subject is ill and incapable of ingesting sufficient food. The second involves the assessment of the metabolic fates of ingested, exogenous fuels under various classical nutritional circumstances. In each instance, he has developed and employed a wide variety of stable isotope tracer kinetic methods to quantify substrate flux, metabolism, precursor-product relationships, and irreversible oxidation to excreted end products. The physiological information obtained also has been used to further assess aberrations in interorgan fuel transport consequent to a variety of pathological conditions.

Douglas G. Burrin, Ph.D.

Dr. Burrin's major research goal is to elucidate the critical cellular and hormonal signals that mediate the stimulatory effects of enteral nutrition on the growth and function of the neonatal intestine. Current studies are aimed at establishing the physiological and clinical significance of GLP-2 and enteral nutrition, and how they impact intestinal nutrient metabolism in his neonatal pig model. He is using isotope tracers coupled with arteriovenous organ balance and blood flow measurements in neonatal pigs to quantify the intestinal absorption and metabolism of macronutrients provided either enterally or parenterally. Using these approaches, he is examining amino acid and oxidative substrate metabolism in piglets fed parenterally, and evaluating whether this is altered by GLP-2 treatment. He will test whether the trophic effects of GLP-2 treatment during total parenteral nutrition translate into enhanced gut function. Additionally, he is investigating the underlying mechanisms of enteral nutrition and GLP-2 action at the tissue and cellular level. These studies are aimed at determining how these nutritional and hormonal factors modulate the rates of cellular protein turnover, proliferation and programmed cell death of mucosal epithelial cells. Dr. Burrin plans to identify how these factors affect the expression and activity of key signaling intermediates in these cellular pathways.

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.

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 focuses on establishing 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. Dr. Conneely's studies indicate that LF is not required for intestinal iron uptake, but plays a critical role in preventing against excessive iron absorption in mice. Dr. Conneely has generated a mouse deficient in LF to establish the essential physiological functions of this iron-binding protein. As described above, she has uncovered a critical temporally restricted function of LF in the prevention against excessive iron uptake 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 also will 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 of action of the transcription factor GCNF in regulating embryonic gene expression, and the influence of the maternal diet on its activity. To achieve this objective, 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 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 four main areas: the role of insulin and amino acids in the regulation of protein synthesis in the neonate; the role of insulin and amino acids 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; and the role of insulin and nutrient intake in the anabolic response to growth hormone.

Debby K. Demory-Luce, Ph.D.

Two focal points of interest of Dr. Debby 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.

The 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 counters, which monitor ⁴⁰K, a naturally occurring isotope in the human. Dr. Ellis has developed 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 regulation of muscle growth rate during early postnatal life and its impact on muscle function in adulthood comprise the focus of Dr. Fiorotto's research. The major objective of the work is to identify how the developmental stage of the 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 [growth hormone-releasing hormone (GHRH), growth hormone, and insulin-like growth factors.] In addition to overall growth and body composition effects, the responses that are being examined include the

rate of muscle protein turnover, the expression of muscle-specific protein genes and transcription factors, satellite cell replication and accretion. To carry out these studies, Dr. Fiorotto uses a variety of animal models, including 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, to drive the long-term expression of the hormone.

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 parents' role 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. A new project will assess 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.

Current evidence supports the idea that insulin-gene family members are necessary for all aspects of mammary gland development and lactation. Despite this, the mechanisms by which these peptides regulate mammary gland function are poorly understood. Research within Dr. Hadsell's laboratory focuses on three main goals. The first is to understand the specific mechanisms through which the receptors for insulin (IR) or IGF-I (IGF-IR) influence mammary gland development and/or lactation. The second is to understand the mechanisms through which nutrient availability influences mammary gland development and/or lactation. The last is to understand how these factors interact

at the transcriptional level to allow normal mammary gland development and lactation. The combined use of transgenic and knockout mice, tissue grafting strategies, and in-vitro cell culture models to modify IR or IGF-IR activity has provided insights into the mechanism through which apoptosis is regulated within the mammary gland. These strategies have also led to a focus on putative insulin-responsive transcription factors as a means to define insulin-dependent milk protein gene expression.

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

Dr. Haney's current long-term 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 the amount, activity and subcellular targeting of GLUT1, the only glucose transporter isoform identified in the mammary gland, in established and primary mammary epithelial cell lines, as well as 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, hormonally and developmentally regulated, 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. This work should ultimately help to understand and influence lactational performance in women, thereby promoting successful breastfeeding.

Morey W. Haymond, M.D.

Dr. Haymond's research focus is to delineate, and ultimately manipulate, the hormone and substrate factors that regulate the absorption, assimilation, mobilization and disposal of carbohydrates in infants and children. The delicate balance of nutrient availability to meet the energy and growth needs of children is frequently disturbed as a result of chronic disease, infection, trauma and/or organ failure. In addition, the increasing incidence of both type I and type II diabetes provides unique opportunities to study the effects of insulin, insulin resistance and obesity on macronutrient assimilation in children. Specific studies utilize a variety of stable isotope tracer techniques to estimate insulin sensitivity, absorption of carbohydrates, proteolysis, protein synthesis, gluconeogenesis, carbohydrate disposal, and protein and fat metabolism. Studies currently under way 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, the precursors for lactose production by the mammary gland as well as the factor(s) which regulate it, and the regulation of galactose and fructose metabolism and the effects of co-ingestion of glucose.

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 K. Hirschi, Ph.D.

Dr. Karen Hirschi's primary research interest 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 (endothelial and smooth muscle) 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 functionally integrated into existing vascular networks, are of particular interest. Insights gained from such cell and developmental 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 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 and chronic infections. He also studies glutathione metabolism and its relationship to oxidant damage of lipids and proteins in conditions of increased oxidant 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 primary research interest is to determine if, and how, an early nutritional event may have long-term effects on quality of growth, metabolic functions and development. His work has focused on the most common nutritional problems during early life: 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. His 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. A planned project will assess how and when in early life, optimization of protein intake will maximize catch-up growth and neurological development of very-low-birth-weight infants. Each project employs a wide variety of tools of in vivo investigation (e.g., indirect calorimetry, body composition assessment, stable isotope methodologies) as well as in vitro methods such as DNA microarray analysis. 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, M.S.

Ronald McNeel studies the pathways and nutritional controls of differentiation in preadipocytes as they relate to the pathological condition of obesity. Obesity research studies center on a key transcription factor that is the key regulator for adipocyte differentiation and proliferation, peroxisome proliferator-activated receptor γ (PPAR γ 2). These research studies are not limited to the effects of PPAR γ 2, but are inclusive of other transcription factors that regulate PPAR γ 2 and thereby influence adipocyte differentiation. Of key importance is the contribution of nutritional factors as they relate to differential regulation of preadipocyte differentiation through these transcription factor pathways that include PPAR γ 2. 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. Beta-adrenergic receptors are among the major regulators of adipocyte metabolism. Dietary components may alter the pattern of adipocyte growth and differentiation. 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. Using stable isotope techniques, she has found that lean body mass of adult women is preserved during lactation because of the downregulation of rates of whole body protein turnover, synthesis and degradation, 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. Using stable isotope techniques and whole-room calorimetry, 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.

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 gatekeeping 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 goblet cells instead of enterocytes. The mechanism of regulation of both isoforms is under study in a mouse intestinal cell line producing maltase-glucoamylase in wild-type and null MGA mice on different starch diets.

Theresa A. Nicklas, Dr. P.H.

The research conducted by Dr. Nicklas focuses on epidemiological and intervention aspects of chronic disease prevention and health promotion. Specifically, how do eating behaviors and other lifestyles influence the development of chronic disease risk factors early in life? Also, what are the behavioral factors influencing the development of adverse lifestyles early in life? Areas of interest include environmental factors influencing the development of eating patterns early in childhood; how these eating patterns relate to the onset of obesity, cardiovascular disease, cancer and type 2 diabetes; and effective intervention strategies for changing and maintaining healthful behavior

changes, particularly in children and adolescents. 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-American and Hispanic-American preschool children attending Head Start; and a behavior-based family intervention designed to increase fruit, fruit juice, and vegetable consumption by preschool children.

Jeffrey M. Rosen, Ph.D.

The research objectives of Dr. Rosen's laboratory are to elucidate the mechanisms regulating the normal development of the mammary gland, including the hormonal control of milk protein expression, and to determine how these regulatory mechanisms have deviated in breast cancer. Critical periods of development in the mouse mammary gland include the ductal proliferation and branching that occur during sexual maturity, lobuloalveolar proliferation that occurs during pregnancy, terminal differentiation that results in lactation, and involution characterized by increased apoptosis and extensive tissue remodeling. Studies of the role of systemic hormones (e.g., prolactin, glucocorticoids, estrogens and progestins) and local growth factors, including members of the Wnt and Fgf families, on each of these processes are under way. The roles of specific transcription factors and their dominant-negative isoforms, including members of the C/EBP, Stat and NF I families, also are being examined using transgenic and knockout mouse models. Gene arrays and subtractive hybridization techniques are employed to identify downstream targets of these transcription factors. Postnatal mammary gland development is being studied in knockout mice displaying late embryonic or neonatal mortality by transplantation of mammary epithelium into the cleared mammary gland fat pad of syngeneic recipients. In addition, methods that permit the analysis of both gain and loss of specific gene function selectively in the mammary gland have been developed. Finally, transgenic and knockout mouse models are being used to elucidate 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.

Richard J. Schanler, M.D.

Dr. Schanler's research focuses on clinical aspects of feeding premature infants human milk. Current investigations address the potential protection from infection and necrotizing enterocolitis afforded by human milk, the effect of stress on lactation performance, and the growth and body composition of premature infants during the first few years after hospital discharge.

Robert J. Schwartz, Ph.D.

Dr. Robert Schwartz conducts research focused on defining the molecular basis underlying the establishment and maintenance of skeletal, cardiac and smooth muscle differentiation. He has devoted considerable attention to Nkx2-5, a transcription factor instrumental in the patterning of the embryonic heart. Dr. Schwartz notes that 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 of the heart appear to originate from separate lineages, which develop according to their positions along the anteroposterior axis of the embryo. Recent studies conducted by Dr. Schwartz have revealed cis-regulatory elements that direct cardiac transcription specifically in the left or right ventricular chambers and atria, and even within subdomains within the chambers. Whether this regional specificity of transcription is important for the physiologic and functional differences of the chambers of the adult heart, and how these transcriptional territories are established and maintained, are issues of intense interest to Dr. Schwartz.

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 which 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 study is being done in collaboration with Dr. C. Langston, Department of Pathology, Baylor College of Medicine, and Dr. B. Bejjani, Department of Human Genetics, Baylor College of Medicine. 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, and has initiated 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 40 K 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. C. Wayne Smith, who is the head of the Leukocyte Biology Section of the Pediatrics Department as well as a CNRC researcher, has a multifaceted research focus involving

the roles of neutrophils in host resistance to infection and tissue injury under conditions of inappropriate inflammation. Dr. Smith is actively involved in a number of projects with other researchers. He works with Dr. Michele Mariscalco in a project on neonatal neutrophil function; with Dr. Mark Entman of Baylor's Department of Medicine on neutrophil-mediated injury to myocardium; with Dr. Christie Ballantyne on the phenotypes of mice with CD18 subunit deficiency; with Dr. Jim Smolen on the influence of stress on leukocyte functions; and with Dr. Alan Burns on the molecular and cellular mechanisms of neutrophil transendothelial migration. Dr. Smith also is collaborating with Dr. Hartmut Jaeschke of the University of Arkansas on neutrophil-mediated liver damage. Further, Dr. Smith is working with CNRC researcher Dr. Harry Mersmann on the potential role of leukocytes in the development of obesity.

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, development of 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 broad area of interest is that of nutritional epidemiology and the role of nutrition in chronic diseases and public health problems. A focus area is research on methodologies to assess dietary intakes in populations. Currently, Dr. Stuff collaborates with the USDA/ARS Delta Nutrition Intervention Research Initiative. The initial purpose of this initiative is to measure the nutrition and health status of individuals and communities in the Lower Mississippi Delta region. Specifically, Dr. Stuff has helped in efforts to develop and validate dietary methodology in the Lower Delta, which now will be applied to assess dietary intakes in cross-sectional and longitudinal designs. Other interests include the impact of food insecurity on the nutritional requirements and health status of children; nutritional interventions for children in high-risk, low-income areas; and the application of research findings on mineral and caloric requirements of children to interpreting nationwide nutrition surveys and databases.

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

The focus of Dr. Sunehag's research is carbohydrate metabolism in infants and children. In particular, she is interested in the metabolism of very premature infants during their first days of life. The aim of her studies is to determine how these infants utilize their gluconeogenic pathway to produce glucose from parenterally administered lipid and amino acid solutions. The ultimate goal of these studies is to optimize the composition of neonatal parenteral nutrition solutions to prevent both hypo- and hyperglycemia, while providing a sufficient energy intake for normal growth. Her other major research interest is to determine the effects of dietary carbohydrate and fat intakes on parameters of glucose metabolism, particularly insulin sensitivity, in obese and nonobese children. The aim of these studies is to determine whether the macronutrient content of the diet affects the development of insulin resistance and, thus, the risk of type II diabetes, and whether obese children differ from nonobese with regard to metabolic adaptation to changes in dietary carbohydrate and fat content.

Ignatia B. Van den Veyver, M.D.

Rett syndrome is caused by mutations in a gene on the X chromosome named MECP2. This gene encodes methyl-CpG-binding protein 2, which is the molecular link between DNA methylation and suppression of transcription of genes with methylation at their promoters. Based on the discovery that this mechanism is at the basis of this devastating neurodevelopmental disorder, Dr. Van den Veyver hypothesizes that DNA methylation may play a role in the proper downregulation of certain genes during development. There is some evidence that DNA methylation can be influenced by methyl donor-enriched diets containing substances such as folic acid and betaine. Hence, she is investigating in cultured cells and in laboratory mice whether this treatment can alter DNA methylation and gene expression. This is not only important with regard to conditions such as Rett syndrome, but may also provide a better understanding of the role of such agents in other prenatal-onset disorders and birth defects, for example, in the mechanism by which folic acid may prevent neural tube defects.

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 that 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 the project director of a USDA-funded, multicenter, 2-year follow-up, randomized, double-blind, placebo-controlled study to determine the safety, efficacy, and optimal dosage of soy isoflavones to prevent osteoporosis in postmenopausal women. Dr. Wong also is the principal investigator of a project to determine the effects of soy isoflavones on nitric oxide production and blood pressure in postmenopausal women with high-normal blood pressure. This project has received a score of 156 from the National Institute of Aging. Dr. Wong serves as the director of the Gas-Isotope-Ratio Mass Spectrometry Core Laboratory, the chairman of the Space and Equipment Committee, and the chairman of the Equipment Maintenance/Repair Program at the USDA/ARS Children's Nutrition Research Center. He has been appointed by the Texas Board of Health to serve on the Texas Department of Health Osteoporosis Advisory Committee between January 1, 2001 and December 31, 2006.

Issa Zakeri, Ph.D.

Dr. Zakeri is interested in Nutimetrics, 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.