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

Studying Nutrition Today for the Health of Future Generations

Faculty Research Summaries

Steven A. Abrams, M.D.

Dr. Abrams' research projects are designed to use stable isotopes to evaluate mineral metabolism in infants and children. True dietary calcium absorption and bone formation and turnover are determined using orally and intravenously administered stable isotopes of calcium. Studies in children with mineral deficiencies are designed to determine the etiology of the mineral deficiency and the possible response to therapy. Studies are under way to evaluate the absorption of calcium and iron from milk, formula and dietary supplements in children age 4-12 months. Studies are being conducted to determine the iron needs of children with rheumatoid arthritis.

Cheryl B. Anderson, Ph.D.

Dr. Anderson's research is aimed at the promotion of regular physical activity by understanding its determinants, including self-identity as a motivational factor in health behavior, and the development of psychometrically valid and reliable measurement instruments of attitudes and behaviors. Her work focuses on the description and measurement of athletic identity and its relation to physical activity in adolescents, children, and parents, as well as the factors that contribute to identity formation, stability, and change.

Tom Baranowski, Ph.D. and Janice Baranowski, M.P.H.

The research of Dr. Tom and Janice Baranowski focuses on theory-based programs aimed at determining how to help children eat more fruit, 100% juice and vegetables. Their many community-based, nutrition education research projects have included "GIMME 5," a school-based class curriculum intervention; "5 A Day Boy Scout Achievement Badge;" "Squire's Quest!," a school-based, interactive, multimedia, nutrition education game; and "Bringing It Home," a school-based program designed toward influencing the parents of 4th-grade children. All the individuals targeted by these programs showed some change in dietary behavior. The researchers also demonstrated that an interactive, multimedia program for dietary assessment among 4th-grade children worked almost as well as a dietitian-conducted, 24-hour dietary recall. the Baranowskis are currently actively involved in the Houston-area "Fun, Food and Fitness Program," part of the national Girls' Health Enrichment Multi-site Study aimed at the prevention of obesity in 8-year-old African-American girls.

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 hasdeveloped 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 objective is to elucidate the cellular and hormonal signals that mediate the stimulatory effects of enteral nutrition on the growth and function of the neonatal intestine. Recent studies have established the quantity and quality of enteral nutrients necessary for maintaining normal intestinal growth and function. He has found that the neonatal intestine utilizes a substantial proportion of the dietary nutrients to maintain normal growth. He also has found that the secretion of the gut-derived peptide, glucagon-like peptide 2 (GLP-2), is closely correlated with enteral nutrient intake, and that infusion of GLP-2 produces intestinal trophic effects when given to neonatal pigs. In contrast, treatment with dexamethasone has a potent catabolic effect on the neonatal intestine. Future studies will investigate the physiological significance of GLP-2, and how it affects intestinal protein and amino acid metabolism in neonatal pigs. He will examine whether the catabolic effects of dexamethasone compromise intestinal absorptive function, and how the provision of either minimal enteral nutrition or GLP-2 ameliorates the actions of dexamethasone. To understand how these nutritional and hormonal factors modulate intestinal growth, he will quantify the rates of cellular protein turnover, proliferation and programmed cell death. How these factors affect the expression and activity of key intermediates in these cellular pathways will be identified.

Nancy F. Butte, Ph.D.

The energy requirements of reproductive women and their infants are the focus of Dr. Butte's research. Her major interests are the functional consequences of variations in energy balance on pregnancy outcome, lactation performance, and infant growth and development. To further these evaluations, methodologies have been developed to measure energy expenditure and body composition in the populations of interest, including room respiration calorimeters and the doubly labeled water method for the measurement of free-living energy expenditure. Factors that predispose women to postpartum weight retention and later development of obesity are under investigation. Also, genetic and environmental factors that predispose infants and children to the development of obesity are being explored.

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.

The objective of Dr. Conneely's research is to establish the role of nuclear receptors in vertebrate development. Nuclear receptors comprise a large family of structurally related transcription factors regulating the expression of genes that control a variety of developmental and physiological responses to diverse stimuli.

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 thisobjective, 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, using unique delivery channels. Current projects include implementing and evaluating an environmental behavior-change program involving middle-school cafeteria a la carte/snack bars; developing and implementing a school-based program aimed at the prevention of type 2 diabetes among youth; and conducting a feasibility study of 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; the role of hormones, cytokines, and nutrients in the regulation of muscle protein synthesis during sepsis; and the role of insulin and nutrient intake in the anabolic response to growth hormone.

Debby Demory-Luce, Ph.D.

Dr. Debby Demory-Luce is interested in 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 ^{40}K, 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.

Dr. Fiorotto is interested in the effects of chronic alterations in nutrient intake on the growth and development of skeletal muscle. Currently, she is attempting to show that the nature of skeletal muscle response is dependent on the developmental stage at which the organism is subjected to a nutritional insult. She is also attempting to identify the underlying factors responsible for the age-related change in the sensitivity of skeletal muscle to nutritional perturbations. Dr. Fiorotto also will evaluate the consequences of changes in sensitivity on the numerous functional roles of skeletal muscle in the body.

Jennifer Orlet Fisher, Ph.D.

Dr. Fisher's goal is to understand behavioral and environmental factors that modify food intake regulation and growth patterns during early childhood. To this end, her research focuses on children's early eating experiences and learning about eating within the family. In particular, Dr. Fisher's work evaluates children's eating patterns as a function of parents' choices regarding the types of foods that constitute the family diet, parents' models of eating behavior, and parents' child-feeding practices. Her current projects investigate the extent to which eating in the absence of hunger constitutes a behavioral phenotype of overweight Hispanic children, the extent to which it is related to characteristics of the family eating environment, and the extent to which this type of eating behavior reflects a shared eating style among family members.

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

Dr. Griffin's work is to understand 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 (i.e., 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.

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 long-term research goal is to understand the molecular cell biology of lactation. Human milk is recognized as the ideal source of nutrition for infants, but the mechanisms and regulation of milk secretion are poorly understood at the cellular and molecular level. Current work is focused 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. Efforts are under way to elucidate the mechanisms of altered glucose transporter targeting, including Golgi sequestration and polarization of plasma membrane distribution, that he has observed during lactation. He will examine how GLUT1 gene expression and subcellular targeting regulate the synthesis of lactose. Dr. Haney has observed a novel protein, structurally similar to GLUT1, that resides in the Golgi, and is expressed only during lactation. He is pursuing the purification of this protein, the cloning of its cDNA, and its possible role in regulating the targeting of GLUT1.

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 isotopic 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 as well as ways of meeting these needs, including the specific amino acid needs of those who depend upon parenterally delivered nutrients. An additional interest concerns the metabolism of essential fatty acids during infancy and childhood, including the role of long-chain polyunsaturated fatty acids in this population.

Karen Hirschi, Ph.D.

Dr. Hirschi' is interested in understanding how blood vessels are assembled; elucidating the regulators of cellular recruitment, proliferation and differentiation needed for vessel formation and maintenance; and exploring the role of such effectors in prevention and treatment of vascular pathologies. She is also interested in examining the potential of stem cells derived from adult tissues to give rise to vascular cells in vivo, and utilizing such cells to enhance or suppress normal and pathological neovascularization. These issues are being addressed using novel in vitro coculture systems, murine embryo culture, and transgenic mouse models

Kendal Hirschi, Ph.D.

Unable to flee when challenged by an environmental threat, plants must adapt by altering their physiology. Calcium ions play a central signaling role in the cascade of events that empower plant cells to initiate these responses. Dr. Kendal Hirschi has utilized mutants in budding yeast to isolate plant genes that regulate intracellular calcium levels. Future work in his lab will be directed toward molecular and genetic approaches to study calcium transport and signaling in the model plant *Arabidopsis thaliana.*

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 intermediary metabolism of macronutrient fuels. One area of primary interest is the altered metabolic response to the stress of infections, and its impact on nutritional requirements during early growth and development. Studies are being performed in both animals and humans to determine how stress alters protein (and specific amino acids), carbohydrate and lipid metabolism. Another area of research looks at how the production of antioxidants and proteins involved in the immune response is affected by conditions such as protein-energy malnutrition, HIV infection, aging and diabetes mellitus. Specific studies focus on the metabolism of glutathione, cysteine, acute-phase proteins and nitric oxide. Stress-induced changes in the partitioning of nitrogen for the synthesis of muscle proteins, acute-phase proteins and nutrient transport proteins are also being investigated. Dr. Jahoor is also involved in the development and use of different stable isotope tracer methodologies to investigate intermediary metabolism.

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. Dr Lapillonne's overall research goal 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.

how stress alters protein (and specific amino acids), carbohydrate and lipid metabolism. Another area of research looks at how the production of antioxidants and proteins involved in the immune response is affected by conditions such as protein-energy malnutrition, HIV infection, aging and diabetes mellitus. Specific studies focus on the metabolism of glutathione, cysteine, acute-phase proteins and nitric oxide. Stress-induced changes in the partitioning of nitrogen for the synthesis of muscle proteins, acute-phase proteins and nutrient transport proteins are also being investigated. Dr. Jahoor is also involved in the development and use of different stable isotope tracer methodologies to investigate intermediary metabolism.

Harry J. Mersmann, Ph.D.

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 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. 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.

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.

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. 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.

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 mice and children with deficient starch digestion. The mechanism of regulation is under study in a mouse intestinal cell line producing maltase-glucoamylase.

Theresa A. Nicklas, Dr. P.H.

Dr. Nicklas' research focuses on the 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: (1) environmental factors influencing the development of adverse eating patterns early in childhood; (2) how these eating patterns relate to the onset of obesity, cardiovascular disease, cancer and type 2 diabetes; and (3) effective intervention strategies for changing and maintaining healthful behavior changes, particularly in children and adolescents. A current area of research involves a detailed investigation of the relationship between eating patterns and obesity in children and young adults. Planned studies include an examination of family and caregiver influences on fruit, juice and vegetable consumption by preschool children from different ethnic groups, and a behavior-based intervention aimed at favorably influencing food preferences and consumption by African-American and Hispanic-American preschool children attending Head Start.

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. 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 thatthe 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.

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.

C. Wayne Smith, M.D.

Dr. 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. 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 L. 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.

Dr. Van den Veyer's research investigates the role 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 research focuses on the treatment and prevention of obesity and chronic diseases. He is currently the principal investigator of a Texas Department of Health-funded project to determine the prevalence and risk factors of childhood obesity in Texas. He is also the principal investigator of a phase 3 clinical trial funded by Pharmacia & Upjohn to test the safety and efficacy of a new drug for the treatment of type 2 diabetes mellitus. Further, Dr. Wong is the project director of a USDA-funded, multicenter study aimed at determining the safety, efficacy, and optimal dosage of soy isoflavones to prevent osteoporosis in postmenopausal women.

Issa F. Zakeri, Ph.D.

Dr. Zakeri's research has focused on the analysis, modeling and understanding of data consisting of multiple measurements on each observational unit and data that accrue over time. His current research interest is Nutrimetrics, which involves the application of statistical methods to problems in nutrition. The 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. The research program involves theoretical studies as well as computational methods in many branches of statistics, particularly analysis of high-dimensional and longitudinal data.