University of Washington Clinical Nutrition Research Unit
Start Date: 1985
Status: Ongoing
Funding Agency: NIDDK
Website: depts.washington.edu/uwcnru/

Organization and Goals

The overall theme of the research being supported by the CNRU at the University of Washington relates to the role of nutrition in the etiology, management, and prevention of chronic disease states. The 3 major areas of research focus are body weight regulation and obesity, diabetes, and lipids and atherosclerosis. Other areas of interest are aging, cancer, and women's health. The 80 Affiliate Investigators, who are broadly dispersed throughout a multitude of schools, departments, and divisions at the University of Washington, receive their research funding from a wide variety of sources. Because of the number and variety of investigators, nutrition research at the University of Washington uses multiple means to address problems relating to these chronic disease states, including state-of-the-art basic molecular and cellular biological techniques, clinical investigation, animal experimentation, and epidemiological and intervention trials. These various approaches are used in a complementary fashion to provide a broad-based and in-depth approach to the role of nutrition in chronic diseases. The CNRU has facilitated interaction and collaboration among investigators using these different experimental disciplines to address questions of mutual interest. There currently are 80 Affiliate Investigators that constitute the Research Base of the CNRU.

Core Laboratories

Administrative and Enrichment Core: Alan Chait, M.D., CNRU Director; Michael W. Schwartz, M.D., CNRU Associate Director; Edward W. Lipkin, M.D., Ph.D., Associate Director, Enrichment Component

External Advisor Group Members

Wilfred Y. Fujimoto, M.D., Professor Emeritus of Medicine, University of Washington

Daniel Porte, M.D., Professor of Medicine, University of California at San Diego, San Diego, CA

Ronald M. Krauss, M.D., Director of Atherosclerosis Research, Children's Hospital Oakland Research Institute, Adjunct Professor of Nutritional Sciences, University of California at Berkeley

Nutrition Laboratory Core: Mark Wener, M.D., Director; Hossein Sadrzadeh, Ph.D., Associate Director

Clinical Research and Data Management Core: Robert H. Knopp, M.D., Director; Edward W. Lipkin, M.D., Ph.D., Associate Director

Body Composition and Energy Expenditure Core: Michael W. Schwartz, M.D., Director; Greg Morton, Ph.D., Associate Director

Nutrient-Gene Core: Renee C. LeBoeuf, Ph.D., Director; Elizabeth Kirk, Ph.D., Associate Director

Pilot and Feasibility Studies

Population Genetics and Molecular Evolution of the Human Calcium Transporters TRPV5 and TRPV6. Joshua Akey, Ph.D., Assistant Professor in the Department of Genome Sciences, is performing studies to characterize the population genetics and molecular evolution of TRPV5 and TRPV6, two genes that mediate the rate-limiting step of dietary calcium absorption. To date, he has detected striking signatures of positive selection in samples from non-African populations. However, samples from an African population show evidence of balancing selection, which leads to higher degrees of polymorphisms relative to standard neutral models. He has also shown that human primates have accelerated rates of nonsynonymous amino acid substitutions, relative to non-human primates, consistent with positive selection in humans.

Dietary Iron and Gene Expression. Elizabeth Kirk, Ph.D., Assistant Professor in the Department of Pathobiology and a current CNRU New Investigator Awardee, is performing studies to identify iron responsive genes in cells of the artery wall that might influence atherogenesis. She is performing *in vivo* studies in mice fed iron deficient, iron-replete, or high iron diets to identify actual genes. She also is performing *in vitro* studies on macrophages and vascular smooth muscle cells to determine cell specificity of iron responsive gene expression. Surprisingly, both iron overload and deficiency reduced atherosclerosis in apo E deficient mice relative to iron replete animals. The most striking finding to date in her gene expression studies is the observation that MMP9, a matrix metalloprotease, is iron responsive.

Leptin and the Hypothalamic Control of Glucose Metabolism. Gregory Morton, Ph.D., Research Assistant Professor in the Department of Medicine, Division of Metabolism, Endocrinology and Nutrition, is performing studies to identify the key intracellular signaling mechanisms(s) through which leptin mediates its effect on glucose metabolism. Use of an adenoviral vector to express the long form of leptin receptor in the area of the arcuate nucleus in Koletsky rats, which are deficient in leptin receptors, markedly improved insulin sensitivity. He has gone on to demonstrate that this effect is mediated, at least in part, via PI-3 kinase.

Examination of 9-*cis*-retinoids as Chemotherapeutics in Breast Cancer. Jisun Paik, Ph.D., Research Associate in the Department of Pathobiology, is evaluating whether 9-*cis*-retinoids other than 9-*cis*-retinoic acid could be possible chemotherapeutic agents for breast cancer. She has found that the combination of *cis*-retinol dehydrogenase and 9-*cis*-retinol can suppress the growth of breast cancer cells without producing detectable levels of 9-*cis*-retinoic acid. She has now identified the metabolite responsible for this growth inhibition as 13, 14-dihydroretinol.

Funding Derived from Previous Pilot and Feasibility Studies

Glycoxidation and Lipoxidation of Proteins in Diabetes. Xiaoyan Fu, Ph.D. Funding: NIH RO1HL075381.

Leptin-regulated Brain Pathways in Feeding and Obesity. J. Ernest Blevins, Ph.D. Funding: Department of Veterans Affairs, VA Merit Review Research Award.

The Effect of Hypertonic Resuscitation for Blunt Trauma. Eileen Bulger, M.D. Funding: NIH R01HL073233.

Drugs of Abuse in Dopamine-Deficient Mice. Michelle Brot, Ph.D. Funding: NIH/NIDA R03.

The Reinforcing Effects of Alcohol: Is Dopamine Required? Michelle Brot, Ph.D. Funding: University of Washington Alcohol and Drug Abuse Institute.

Regulation of Proteoglycan and Hyaluronan Synthesis in Human Monocyte-Derived Macrophages by Factors Associated with Diabetes. Mary Y. Chang, Ph.D. Funding: Atorvastatin Research Award, American Heart Association Scientist Development Grant.

Nutritional Regulation of Proteoglycan Synthesis. Mary Y. Chang, Ph.D. Funding: NIH/NIDDK P01DK002456, Pathobiology of Macrovascular Disease in Diabetes (supplement to promote re-entry into biomedical research careers).

Meal Initiation and Energy Homeostasis: Role of Ghrelin. David E. Cummings, M.D. Funding: NIH/NIDDK R01DK061516 (Presidential early career award).

Measurement of Molecular Determinants of Body-Weight Regulation in the Brain Using Magnetic Resonance Spectroscopy. David E. Cummings, M.D. Funding: Dana Foundation.

GLP-1 in Normal and Abnormal Glucose Tolerance. David D'Alessio, M.D. Funding: NIH/NIDDK R01.

The Role of Glucagon-Like Peptide 1 (GLP 1) in Glucose Homeostasis. David D'Alessio, M.D. Funding: NIH/NCRR.

Secretion, Metabolism and Action of Glucagon-like Peptide 1 and Related Peptides in Healthy and Diabetic Humans. David D'Alessio, M.D. Funding: American Diabetes Association Research Award.

Genetic Epidemiology of Coronary Heart Disease in Diabetes. Karen Edwards, Ph.D. Funding: ADA Research Award.

Vitamin C Gene Expression and Iron Absorption. Elizabeth Kirk, Ph.D. Funding: NIH/NIDDK R21DK071079, pending.

Behavioral Physiology of Body Weight Regulation. Dianne Figlewicz Lattemann, Ph.D. Funding: NIH/NIDDK 5R01DK040963.

CNS Mechanisms of Acute Hypoglycemia-Associated Autonomic Failure. Dianne Figlewicz Lattemann, Ph.D. Funding: VA Merit Review Program.

CNS Stress Pathways and the Development of HAAF. Dianne Figlewicz Lattemann, Ph.D. Funding: NIH/NIDDK R21DK062446.

Effect of Serum Amyloid A (SAA) on the Binding of HDL to Extracellular Proteoglycans. Katherine Lewis, Ph.D. Funding: Atorvastatin Research Award.

Surgery and IV Nutrition Modulate Macrophage Function. W. Scott Helton, M.D. Funding: NIH/NIGMS R29 FIRST Award.

Cortisol, Central Obesity and Insulin Resistance. Jonathan Q. Purnell, M.D. Funding: 1R03DK061996

Sex Steroid, HPA Regulation, and Fat Patterning. Jonathan Q. Purnell, M.D. Funding: NIH/NIDDK 5K23DK002689.

Homocysteine, Inflammation, and Atherogenesis. Michael E. Rosenfeld, Ph.D. Funding: NIH/NHLBI 5R01HL058954.

C. Pneumoniae and Atherosclerotic Plaque Destabilization. Michael E. Rosenfeld, Ph.D. Funding: NIH/NHLBI 5R01HL066115.

Integration of Long- and Short-term Control of Feeding. Michael W. Schwartz, M.D. Funding: NIH/NIDDK R01.

Neuroendocrine Regulation of Energy Balance. Michael W. Schwartz, M.D. Funding: NIH/NIDDK R01DK052989.

Hypothalamic Peptides, Food Intake, and Diabetes. Michael W. Schwartz, M.D. Funding: NIH/NINDS R01NS032273.

Hypothalamic Control of Food Intake and Body Weight. Michael W. Schwartz, M.D. Funding: NIH/NIDDK P01DK068384.

Regulatory Responses to Positive Energy Balance. Randy Seeley, Ph.D. Funding: NIH/NIDDK R01DK054080.

CNS Mediation of Visceral Illness. Randy Seeley, Ph.D. Funding: NIH/NIDDK R01.

CNS GLP-1: Multiple Roles in Ingestion and Adiposity. Randy Seeley, Ph.D. Funding: NIH/NIDDK R01DK054890.

Loss in HMECs: A Model of Breast Cancer Prevention. Victoria Seewaldt, M.D. Funding: NIH/NCI 1R01CA098441.

Extracellular Matrix Mediated Apoptosis in p53 (-) HMECs. Victoria Seewaldt, M.D. Funding: NIH/NCI 5R01CA088799.

Retinoic Acid Receptor Beta and Breast Cancer. Karen Swisshelm, Ph.D. Funding: NIH/NCI 5R01CA082455.

Glucosamine, Proteoglycans and Atherosclerosis. Lisa Tannock, M.D. Funding: NIH/NCCAM 5R21AT000555.

Lipoprotein Retention in Diabetic Complications. Lisa Tannock, M.D. Funding: American Diabetes Association Junior Faculty Award.

Metabolic Consequences of Antiretroviral Therapy. D. Scott Weigle, M.D. Funding: NIH/NIDDK R01DK055460.

Studies of Regional Fat Distribution and Energy Balance. D. Scott Weigle, M.D. Funding: NIH/NIDDK K24.

Melanocortins, Energy Balance and Cancer Anorexia. Brent Wisse, M.D. Funding: NIH/NIDDK K08DK061384.

Treatment of Cancer Anorexia with a Selective Melanocortin 4 Receptor Antagonist. Brent Wisse, M.D. Funding: American Institute of Cancer Research Investigator Initiated Grant.

The Body Weight Regulations of Older Adults. Michi Yukawa, M.D. Funding: NIH/NIA K23.

Scientific Advancements/Accomplishments

The unique feature of the University of Washington CNRU is the extent and wide-ranging scope of nutrition-related research being conducted in a diversity of disciplines at this large research-based university. Studies range from in-depth basic research, nutritional studies using laboratory animals, metabolic ward and outpatient clinical investigation to epidemiological and intervention studies. The overall goal of these studies is to provide a broad based and better understanding of the physiology and pathophysiology of fuel utilization and clinical disorders that are related to nutrition, both causally and therapeutically. Several major areas are under investigation at the University of Washington, particularly nutritional aspects of body weight regulation and obesity, diabetes, and lipids and atherosclerosis. Examples of the scope of research in some of these 3 areas are as follows:

An area of intense research interest at the University of Washington is body weight regulation, obesity, and their relationship to the development of type 2 diabetes. This award of research is very timely and topical, due to the "epidemic" of obesity being experienced in this country and in several other industrialized nations. Two areas of current intense interest are the regulation of appetite and of fat mass. Several groups of investigators are evaluating key events in energy homeostasis, appetite regulation, and regulation of fat mass. These studies are being performed in both human subjects and experimental animals. More recently there has been an increased thrust in understanding molecular mechanisms of several of the hormones, enzymes, and satiety factors involved in body weight and appetite regulation. Other investigators have been studying the relationship of obesity to the risk of type 2 diabetes and insulin resistance and have shown the importance of body fat distribution in this relationship. Studies are underway to further identify the mechanisms that may be responsible for this relationship. A deeper understanding of these processes is likely to lead to more rational approaches to the prevention and management of obesity than exist at present.

Several investigators are examining aspects of lipid and lipoprotein metabolism that relate to nutrition and atherosclerosis. There is a major thrust nationwide to lower cholesterol levels by diet and/or drugs. The effect of these strategies has been an impressive reduction in the incidence of cardiovascular disease and in cardiovascular disease mortality rates. Several studies at the University of Washington are evaluating precise dietary requirements for cholesterol

lowering and their impact on atherosclerosis and atherosclerosis risk factors. Included among these is a large study of several different cholesterol-lowering diets aimed at providing the public with state-of-the-art recommendations based on strong scientific grounds, an important study that has directly evaluated the effect of cholesterol lowering on angiographically detected coronary artery lesions and the role of dietary cholesterol in the regulation of plasma lipoprotein levels. Other investigators are studying basic mechanisms by which lipids and lipoproteins affect many of the processes involved in atherogenesis, including inflammation. The effect of nutrients that can affect atherosclerosis by non-lipid mechanisms, e.g., homocysteine and antioxidants, also is being studied intensively.

There also is great interest at the University in aging, and many of the investigations are directly related to nutrition. Aging is highly relevant to an understanding of type 2 diabetes, atherosclerosis, obesity, and metabolic bone disease. All are more prevalent in the aging relative to the younger American population. Studies in this area cover the range of basic research, animal experiments, clinical investigation, population-based research, and intervention trials.

Another major thrust at the University of Washington involves studies of women's health. This includes studies related to nutrients and breast cancer; metabolic bone disease such as osteoporosis, to which women are particularly prone; and nutrition approaches to menopause since estrogens are now relatively contraindicated because of their adverse effects on cardiovascular disease. The effect of menopause on cardiovascular risk factors also is being studied.

It is noteworthy that much of the research carried out by CNRU Affiliate Investigators includes areas that have been targeted by the NIH or Congress to be of special importance. In addition to obesity, diabetes, and aging, other targeted areas include women's health, studies in minority populations, and AIDS.

Of the special facilities at the Center, the Laboratory Core has made available cost-effective state-of-the-art laboratory testing to which many investigators otherwise would not have had access. This has increased the scope and interest of several investigators' research projects. The recent scaling down of biochemical assays for measurement in rodents reflects the increased use by Affiliate Investigators of rodent models in their research. The facilities offered by the Clinical Research Core have also facilitated the performance, analysis, and completion of several studies. The availability through this Core of consultation and assistance in the design and analysis of clinical studies has been of major importance in improving the quality of studies. The Body Composition and Energy Expenditure Core has been used by over a dozen Affiliate Investigators to measure body composition and energy expenditure in small animals. The Nutrient-Gene Core provides support in the use of methods to identify genes important in nutrient biology and how these contribute to disease by the use of mouse models, an approach that is being used by an increasing number of CNRU Affiliate Investigators.

Thus, a wide array of studies of important and common diseases is supported by the CNRU at the University of Washington. Through the availability of its Core facilities, the CNRU is designed to facilitate, enhance, and integrate research efforts of multiple investigators widely dispersed throughout various Schools and Departments of the University of Washington. It brings together investigators with common interests from a diversity of backgrounds and aims to foster interdisciplinary collaborative research efforts and directions. In addition, the increased nutrition-related research activity and awareness that has resulted from the existence of the

CNRU at the University of Washington will undoubtedly result in improved nutrition education to medical students, physicians, and other healthcare professionals, and should result in improved delivery of clinical care. Many of the nutrition-related disorders that are under active investigation at the University of Washington are highly relevant to the future health and well-being of our country. An integrated attack on better understanding these disorders is likely to lead to advances in early detection, treatment and, hopefully, prevention of several of these disorders, for example, coronary atherosclerosis and diabetes.

Specific Accomplishments

Women's Health. The presence of small, dense LDL is an important cardiovascular risk factor in men and women. Women with the gene for small, dense LDL may not manifest this lipoprotein phenotype in the premenopausal state. The appearance of small, dense LDL may only occur postmenopausally, which may account for the increase in cardiovascular disease risk at this time. A large prospective study is underway to evaluate the effect of menopause and estrogen replacement on the expression of small, dense LDL in genetically susceptible individuals, and to evaluate the role of a polymorphism in the hepatic lipase promotor in the remodeling of lipoproteins in response to estrogens.

Minority Health. The effect of race on lipoprotein-related risk factors, especially Lp(a), is under study in African Americans, who have high levels of this cardiovascular risk factor. Also under study is the distribution of body fat and its relationship to type 2 diabetes in Asian Americans (see Body Weight Regulation, Obesity, and Diabetes). In addition, older persons are being studied in reference to the role of diet and exercise on cardiovascular risk factors and for their ability to adequately compensate for caloric restriction.

AIDS. Individuals infected with HIV frequently lose weight and suffer nutritional deficiencies, which may affect immune function. Affiliate Investigators are determining the prevalence of nutrient deficiencies in HIV-seropositive persons and the association of deficiencies with dietary intake of nutrients and CD4 cell counts. Deficiencies for most nutrients were most common in subjects with the lowest CD4 cell counts. The investigators concluded that nutrient deficiencies are seen commonly in HIV-infected patients and that routine screening and treatment for selected nutrients should be considered in primary care clinics for HIV-infected patients. Studies also are ongoing concerning the pathogenesis of the lipodystrophic syndromes that are seen with retroviral therapy for HIV.

Obesity. Considerable basic research is occurring in the area of appetite and body weight regulation. Clinical studies include evaluation of the role of visceral obesity and associated risk factors in the pathogenesis of diabetes and atherosclerosis in Japanese Americans who have a particularly high risk for developing type 2 diabetes independent of the degree of obesity. A related study is targeted at preventing the onset of type 2 diabetes in susceptible individuals, with strategies including weight control and exercise. The CNRU Body Composition and Energy Expenditure Core serves the needs of the many investigators in these interrelated areas.

Studies concerning mechanisms underlying the hypothalamic regulation of appetite and body weight continue to provide new information. Hypothalamic neuropeptide systems containing neuropeptide Y (NPY), melanocortins, and corticotrophin releasing hormone (CRH) that are implicated in energy homeostasis were observed to be sensitive to leptin. During investigations of whether the effect of fasting to increase hypothalamic NPY and reduce proopiomelanocortin

(POMC) and CRH mRNA levels, a combination that stimulates food intake, was attributable to low leptin levels, it was found that intracerebroventricular (ICV) leptin infusion significantly lowered NPY, while raising POMC and CRH, gene expression. This finding establishes these hypothalamic neuropeptide systems as candidate mediators of CNS leptin action. In addition, leptin receptor mRNA is highly expressed in the same hypothalamic areas in rat brains that respond to leptin by changing neuropeptide mRNA levels, and leptin receptor mRNA is expressed on NPY and POMC neurons. Additional findings included the demonstration that the effect of leptin to reduce food intake is antagonized by glucocorticoids, suggesting that the effect of adrenal insufficiency to cause weight loss may result in part from enhanced sensitivity to leptin, with the reverse applying to the obesity syndrome associated with Cushing's Disease. Leptin receptor gene expression in the hypothalamus was shown to be regulated by leptin itself, providing a plausible explanation for the effect of genetic leptin deficiency in ob/ob mice to increase leptin sensitivity. Further insights into the mechanisms underlying genetic obesity in ob/ob mice include the demonstration of low levels of POMC mRNA in the hypothalamus, and that leptin administration reverses this defect. Since melanocortins reduce food intake, the effect of leptin deficiency to lower melanocortin production may contribute to the pathogenesis of obesity in these mice.

Recent studies focused on the role of ghrelin, a hormone that increases food intake in rodents and humans. It is produced primarily in the stomach, and its secretion was found to be markedly impaired after gastric bypass surgery, in part accounting for the dramatic weight loss that is seen in these patients. Abnormalities of its regulation also were shown to occur in the Prader-Willi syndrome, in which affected individuals have marked hyperphagia leading to gross obesity.

Health Promotion and/or Disease Prevention. A major emphasis of many of the studies being undertaken by CNRU Affiliate Investigators relates to the prevention of disease, particularly cardiovascular disease, diabetes, osteoporosis, and cancer. Several examples are listed above. Of particular note is the Diabetes Prevention Project (DPP) in which diet is an important component. Since prevention of disease is considerably less expensive than dealing with the dire consequences of these various disease states, this focus on preventive medicine is likely to reduce healthcare costs in the long term. The focus on prevention of disease by dietary means also is likely to be cost-effective relative to the use of expensive drugs and other strategies.

Education Activities/Accomplishments

Enrichment Program. This program consists of CNRU-sponsored research seminars, an annual CNRU retreat, and coordination of University-wide nutrition-related lectures. The objective of this program is to foster exchange of ideas and facilitate interdisciplinary individual exchange and research collaboration. A web page is available and includes a calendar of events and links to nutrition-related sites. CNRU Core Directors and Affiliate Investigators participate in the recently established "Nutrition for Physicians" core course required for second year medical students. Affiliates also are instrumental as instructors in various courses offered through the Interdisciplinary Graduate Program in Nutritional Sciences, including a Ph.D. program where they participate as research mentors. In addition, Affiliate Investigators participate in noon conferences for house staff at the University of Washington Medical Center and other University-affiliated hospitals in the area.

Awards. Major new support was acquired through the receipt of a large and prestigious award from the Murdock Charitable Trust Fund to support state-of-the-art equipment for a burgeoning

area of research by Affiliate Investigators. The Murdock Charitable Trust Fund provided approximately $400,000 to support the UW System-wide Resource for the Study of Obesity with Dr. Michael Schwartz, Director of the Body Composition and Energy Expenditure Core, as recipient. This resource provided substantial new equipment that has allowed enhancement and augmentation of the research functions of this Core, with particular emphasis on small animal research. This grant is being used to increase emphasis on small animal research aimed at understanding the role of obesity in chronic disease states. As a result of this award, additional space was made available at the Research & Training Building at Harborview Medical Center to accommodate this resource. A grant from the Seattle Foundation provided funding for the ultrasound equipment to be used for vascular research, as described in the Clinical Research and Data Management Core report.

Dr. Steven Kahn was awarded a clinical site for a multicenter NIH grant entitled "Look AHEAD (Action for Health in Diabetes)." Look AHEAD is a multicenter, randomized clinical trial designed to determine whether interventions designed to produce sustained weight loss in obese individuals with type 2 diabetes will improve overall health and how the benefits and risk of interventions designed to produce weight loss compare with the benefits and risk related to treatment of obesity-related comorbid conditions in the absence of weight loss interventions. This study is an extension of the DPP described earlier. Investigators at the University of Washington are playing major leadership roles on the committee structure of Look AHEAD. Both DPP and Look AHEAD, if successful, should help substantially reduce healthcare costs.

Examples of Basic Science and Clinical Interactions

Several interactions between basic science and clinical investigation have resulted from the presence of the CNRU. In particular, several groups of investigators are collaborating in studying many aspects of appetite and body weight regulation and obesity, with a particular focus on the metabolic syndrome. Also, there is a strong interface between basic science in atherosclerosis research and clinical studies focusing on the regulation of plasma lipids and lipoproteins and on atherosclerosis prevention, including the role of antioxidants.

In addition, there is a long history of considerable and extensive interaction between the CNRU and the GCRC at the University of Washington. The CNRU Director (Dr. Chait) was a previous Clinical Associate Physician of the GCRC and has had research projects on the GCRC for many years. The recently retired CNRU Associate Director (Dr. Fujimoto) previously was the Associate Director of our GCRC and Chair of its Scientific Advisory Committee. Many Affiliate Investigators of the CNRU also have GCRC protocols. Conversely, many GCRC users are also Affiliate Investigators of the CNRU and take active advantage of the CNRU Core facilities (e.g., Laboratory Core). The strong interfacing between our CNRU and GCRC is documented by many joint publications.

Our GCRC recently built a vector laboratory to be used for cell and gene therapy. The Nutrient-Gene Core of the CNRU currently is focusing on small animal models. Increased interaction between this CNRU Core and the GCRC vector laboratory will provide new opportunities for increasing the interface between basic and clinical science.

During the past few years, there has been increasing interaction with the University of Washington's Center for Ecogenetics and Environmental Health (CEEH) funded by the NIH.

This interaction benefits CNRU Affiliate Investigators by providing them access to CEEH Core, and benefits CEEH Investigators by providing them access to Nutritional Science and to CNRU Cores.

From its inception, the Pilot and Feasibility Program has continued to attract a large number of applications annually from individuals with diverse backgrounds from multiple Departments and Schools at the University of Washington. Many Pilot and Feasibility and New Investigator awardees over the years have gone on to receive peer reviewed funding, have continued careers in nutritional research, and several have taken on leadership roles at this University and elsewhere in the U.S.