Human Nutrition (NP 107)
2020 Annual Report

The Human Nutrition National Program (NP 107) addresses high-priority problems of national importance as outlined in ARS Research Goal 1.1 of the ARS Strategic Plan for FY 2018-2020: Define the Role of Food and its Components in Optimizing Health throughout the Life Cycle for all Americans. Our research also addresses USDA Strategic Goal 7, Provide all Americans access to a safe, nutritious and secure food supply and USDA Science Blueprint Program Theme 3, Food and Nutrition Translation.

The vision of the program is that well-nourished Americans make health-promoting diet choices based on scientific evidence. To accomplish these goals, the Human Nutrition Program of ARS conducts basic and applied research resulting in discoveries at the molecular, cellular, individual, and population levels on nutrient requirements, metabolism and health, and intake of foods and nutrients in the U.S.

There are five research components in the Human Nutrition Action Plan for 2019-2024:

- Linking Agricultural Practices and Beneficial Health Outcomes
- Monitoring Food Composition and Nutrient Intake of the Nation
- Scientific Basis for Dietary Guidance
- Prevention of Obesity and Obesity-Related Diseases
- Life Stage Nutrition and Metabolism

Selected accomplishments completed during fiscal year 2020 and expected to have high impact in the field are listed below. Links to publicly available documentation are provided after each result.

Dietary carbohydrate intake contributes to reduced stress. Mental stress is linked to risk of chronic diseases. In an eight-week randomized controlled trial that compared effects of a healthy Dietary Guidelines for Americans (DGA)-based diet compared against the less healthy typical American diet, ARS scientists in Davis, California, found that increasing dietary carbohydrate as part of the DGA diet reduced concentrations of a key stress response hormone, cortisol, and dampened stress-induced cortisol reactions. These novel findings provide new evidence suggesting that, in the context of a healthy diet, carbohydrate consumption may provide some protection from stress-related disease risk. Furthermore, this apparent stress and cortisol dampening effect could reduce stress-related eating and improve the ability to sustain a healthier diet based on the DGA. (Project No. 2023-51530-022-00D, NP107, C3, PS3A)

Publication: Soltani H, Keim NL, Laugero KD. Increasing Dietary Carbohydrate as Part of a Healthy Whole Food Diet Intervention Dampens Eight Week Changes in Salivary Cortisol and Cortisol Responsiveness. Nutrients. 2019;11:2563.

Obesity dampens immune responses in young women to level of elderly. Both obesity and aging are associated with muted immune and inflammatory responses. There is limited knowledge, however, on differences in the immune system between young and older adults with obesity. ARS-supported scientists in Boston, Massachusetts conducted a study to compare circulating indicators of immunity in young and older women with obesity. Twenty-three young (23-43 years) and 21 older (60-83 years) women with obesity participated. Older women with obesity had significantly fewer circulating immune cells of four specific types compared to young women. However, with few exceptions, there was no significant difference in inflammation markers or stimulated lymphocyte proliferation and cytokine production by peripheral blood mononuclear cells between young and older participants. These findings contrast with those previously reported in young and old subjects with healthy weight and call for further investigation into the impact of obesity on premature aging of the immune system. (Project No. 8050-51000-100-00D, NP107, C3, PS3B)

Publication: Dao MC, Saltzman E, Page M, Reece J, Mojtahed T, Wu D, Meydani SN. Lack of Differences in Inflammation and T Cell-Mediated Function between Young and Older Women with Obesity. Nutrients. 2020;12:237.

Intestinal permeability is affected by gender and genetics in children. A certain amount of absorption by the intestine is essential for life but excess permeability is associated with adverse health consequences. ARS supported researchers in Houston, Texas, studied large numbers of children who were normal, had irritable bowel syndrome (IBS), or functional abdominal pain (FAP), along with their siblings and parents. Several partially absorbable sugar derivatives were administered orally, and amounts recovered in urine over a day measured intestinal permeability. As expected, children with IBS had increased intestinal permeability but this was not found in those with FAP. Boys had significantly weaker intestinal barrier than girls and both the siblings and parents of children with higher permeability showed the same pattern of results. Because recent studies show that bacteria in the intestine contribute to liver disease and perhaps obesity, the stronger the gut barrier, the less likely those microorganisms and their potentially harmful products can enter the bloodstream. These data may help explain why boys are more susceptible than girls to liver disease. (Project No. 3092-51000-062-00D, NP107, C4, PS4A)

Publications: Shulman RJ, Devaraj S, Heitkemper M. Gut permeability is affected by sex and increased in children with irritable bowel syndrome but not in functional abdominal pain. Neurogastroenterol Motil. 2020;32:e13765.

McOmber M, Rafati D, Cain K, Devaraj S, Weidler EM, Heitkemper M, Shulman RJ. Increased Gut Permeability in First-degree Relatives of Children with Irritable Bowel Syndrome or Functional Abdominal Pain. Clin Gastroenterol Hepatol. 2020;18:375-384.e1

Non-inherited changes in DNA due to diet are associated with cardiovascular disease risk factors and all-cause mortality. Although genetics is known to play a role in heart disease and

expected lifespan, there are also changes to genetic material that are not inherited. Such changes include binding of methyl groups to DNA which changes the expression, or activity, of various genes. ARS supported scientists at both Boston, Massachusetts and Houston, Texas, took part in a consortium that analyzed blood samples from 5 population-based cohorts including 6662 European ancestry, 2702 African ancestry, and 360 Hispanic ancestry participants. Habitual diet quality was associated with differential methylation levels in sites on DNA of white blood cells, most of which were also associated with multiple health outcomes, in European ancestry individuals. These findings demonstrate that integrative genomic analysis of dietary information may reveal molecular targets for disease prevention and treatment that are amenable to improved dietary choices. (Projects Nos. 8050-51000-103-00D and 3092-51000-063-00D, NP107, C5, PS5B

Publication: Ma J, Rebholz CM, Braun KVE, et al. Whole Blood DNA Methylation Signatures of Diet Are Associated With Cardiovascular Disease Risk Factors and All-Cause Mortality. Circ Genom Precis Med. 2020;13:e002766.

Neonatal diet alters gut bacteria and metabolite signals in infants. Early nutrition can significantly affect intestine colonization by normal bacteria and modulate host health through a series of bacterial metabolites that interact with cells of the body. ARS supported scientists in Little Rock, Arkansas, analyzed fecal samples from a longitudinally followed cohort to describe the bacteria and their metabolites of infants over the course of their first year of life who were exclusively fed breastmilk or formula. Breast feeding resulted in increased abundance of bacteria that produce short chain fatty acids, metabolites that serve as signals in development of the gut and other organs. In addition, bacterial metabolites such as kynurenic acid – which helps optimize immune responses including inhibiting allergy – were higher in breastfed infants. These results provide new information about how breastfeeding promotes intestinal and immune health in infants and adds to the scientific basis for the U.S. Center for Disease Control & Prevention's recommendation to breastfeed infants. (Project No. 6026-51000-012-00D, NP107, C5, PS5A)

Publication: Brink LR, Mercer KE, Piccolo BD, et al. Neonatal diet alters fecal microbiota and metabolome profiles at different ages in infants fed breast milk or formula. Am J Clin Nutr. 2020;111:1190-1202.

Maternal diet and body fat alter placental DNA methylation. Epigenetic changes, or changes in gene expression rather than alterations of the genetic code itself, provide a possible explanation of how the *in utero* environment programs health throughout the life course. Epigenetic marks can include addition or removal of natural chemicals such as methyl groups on the DNA or the proteins (histones) around which DNA is wrapped. Researchers in Little Rock, Arkansas, compared DNA methylation in placentas from 150 women who were either normal weight or overweight/obese. Both maternal weight status and dietary saturated fat intake were associated with epigenetic changes in placental DNA and many of the modified genes related to fat synthesis, insulin signaling pathways, and DNA packaging. These data indicate that improved

diet and weight status can modify placental function and development of the fetus. (Project No. 6026-51000-012-00D, NP107, C5, PS5B)

Publication: Thakali KM, Zhong Y, Cleves M, Andres A, Shankar K. Associations between maternal body mass index and diet composition with placental DNA methylation at term. Placenta. 2020;93:74-82.

National survey data and related databases for recent years are available. ARS has partnered with the Centers for Disease Control & Prevention on producing dietary data from the National Health and Nutrition Examination Survey, NHANES for many years. ARS Scientists in Beltsville, Maryland, released nationally representative survey data for 2017-2018 as part of What We Eat in America, NHANES. In addition, the 2017-2018 update of the Food and Nutrient Database for Dietary Studies was released. Tables providing national dietary intake estimates compared to nutrient requirements were also made public. Additionally, seven dietary data briefs were published providing information for nutrition policy and education on topics such as: intake of added sugars; vegetable, fruit, and dairy intake; late evening snacking; and, convenience stores as sources of foods and nutrients. Regular updates of nationally representative data are essential for dietary guidance from the Federal government, including the Dietary Guidelines for Americans published jointly by USDA and HHS. (Project No. 8040-53000-020-00D, NP107, C2, PS2B)

Website: Food Surveys Research Group

First ever expert advice to parents and caregivers on healthy eating behaviors in young children. Researchers know that how children eat may be as important as what they eat from the view of preventing childhood obesity. In addition, we know that the first five years of life are a critical period for helping children learn how to regulate their food intake to match their energy needs. ARS supported researchers in Houston, Texas, led a partnership with other scientific experts and the American Heart Association to release their first ever scientific statement giving advice on how to foster healthy eating behaviors in children under 5 years of age. This guidance will broadly reach parents and caregivers across the country providing strategies for healthy eating behaviors with the goal of reducing childhood obesity. (Project No. 3092-51000-063-00D, NP107, C4, PS4A)

Publication: Wood AC, Blissett JM, Brunstrom JM, et al. Caregiver Influences on Eating Behaviors in Young Children: A Scientific Statement From the American Heart Association. J Am Heart Assoc. 2020;9:e014520.

Fruit pigment metabolites cross the blood brain barrier. The blood brain barrier is a special feature of the circulatory system that protects the brain from many factors circulating in the blood. Because of that, there has been much speculation about whether potentially health-promoting dietary compounds can reach the brain and improve mental performance. ARS scientists in Beltsville, Maryland, collaborated with colleagues in several European universities to show for the first time that flavanols abundant in fruits, cocoa, and pulses, are metabolized

by the intestinal bacteria to a form that is absorbed and circulates in the blood that can be recovered from brain tissue. A series of in silico, in vitro blood vessel cells, and in vivo rat and pig models fed grapes or cocoa were used to clearly demonstrate the permeability of the blood brain barrier to a bacterial metabolite of a food component, but not the parent compound itself that has been associated with improved health and mental function, giving additional evidence for a gut-brain axis and potential health benefits from eating a variety of plant foods. (Project No. 8040-51530-058-00D, NP107, C3, PS3A)

Publication: Angelino D, Carregosa D, Domenech-Coca C, et al. 5-(Hydroxyphenyl)-γ-Valerolactone-Sulfate, a Key Microbial Metabolite of Flavan-3-ols, Is Able to Reach the Brain: Evidence from Different in Silico, In Vitro and In Vivo Experimental Models. Nutrients. 2019;11:2678.

High intake of plant pigments is associated with reduced risk of Alzheimer's disease.
Alzheimer's disease is the cause of 60-80% of dementia cases making it a major public health challenge for which there is no effective therapy. ARS supported researchers in Boston, Massachusetts, followed 2809 men and women over the age of 50 for an average of 20 years as part of the Framingham Heart Study. Specific fruits and vegetables rich in plant compounds known as flavonoids associated with significantly reduced risk of Alzheimer's dementia included blueberries, strawberries, and red wine with apples, pears, oranges, bananas, and tea also showing some beneficial associations. These results suggest that adding certain fruits to the diet may be linked to reduced risk of the most widespread type of senility and support the recommendation of the Dietary Guidelines for Americans to eat a variety of fruits and vegetables. (Project No. 8050-51530-014-00D, NP107, C3 and 5, PS3B and 5A)

Publication: Shishtar E, Rogers GT, Blumberg JB, Au R, Jacques PF. Long-term dietary flavonoid intake and risk of Alzheimer disease and related dementias in the Framingham Offspring Cohort. Am J Clin Nutr. 2020;112:343-353.