



**FY 2017 Research Plan Narrative
National Processed Raspberry Council
For the period October 1, 2016 – September 30, 2017**

Nutrition Research

Awareness of the importance of a healthy diet is at an all time high, sparking changes in consumer purchasing decisions, which in turn stimulates the food industry to make pivotal shifts. Food manufacturers are reformulating and developing new products; restaurants are simplifying their menus; and retailers are positioning their dietitians at the front and center for shopper education. And at the core of this paradigm shift is a critical need for more credible science that helps explain the human health impact of foods.

The *2015 Dietary Guidelines for Americans*, released in early 2016, highlighted the importance of consuming a “healthy eating pattern,” which includes “fruits, especially whole fruits.” It is understood and accepted that whole fruits are “healthy.” And through the significant amount of research conducted over the past 20 years, the public is beginning to understand the bioactive components found in fruits and their mechanisms of action in the human body.

The goal of the Council’s nutrition research program is to establish a link between red raspberry consumption and human health. This research not only provides important scientific insights, but it also delivers information of interest to many of the Council’s target audiences— food manufacturers, foodservice decision makers, health professionals, and consumers.

To guide the Council’s research strategy, a biannual Raspberry Research Roundtable convenes leading berry researchers and Council marketing team members to review the current body of red raspberry nutrition research; discuss current research and consumer trends; and identify priorities for the Council’s research efforts. In October 2016, this Roundtable reinforced the Council’s focus on metabolic syndrome, diabetes, and cardiovascular function and also identified the following additional priorities for consideration:

- **Raspberry Powder:** Development of a standardized raspberry powder for research purposes
- **Fiber:** Deepen our understanding of raspberry’s fiber subtypes
- **Cognitive Function:** Focus on early memory complaint and pediatric cognition

- **Gut Microbiome:** Continue to elucidate the interaction between the gut environment and bioactive compounds

The Roundtable will again convene in 2017 to review these priority areas against new red raspberry research and trends.

Post-Harvest Research

The Council has recognized post-harvest research could drive increased demand by delivering value added new products, product innovation, or enhanced microbial control utilizing cutting edge technology. The Council will consider proposals in these areas.

FY 2017 Research Budget: Total recommended: \$641,939.

The FY 2017 research budget has three components:

1. Program management and services expenses. These annual administrative expense items are necessary to support research projects and related activities.
2. FY2017 Ongoing Multi-Year and New Research Projects. A Request for Proposal (RFP) was sent to scientists who have presented and/or attended the Berry Health Benefits Symposium. The proposed budget includes funds for new projects that result from the RFP and subsequent year expenses of previously approved multi-year projects.
3. FY 2016 Research Projects. This budget represents the balance remaining on FY 2016 funded research expenses which have yet to be invoiced pending receipt of final reports.

Program Management and Services: Total recommended: \$88,519. Included is a portion of the Executive Director's time and expenses to complete activities that support funded research and contractor oversight, administrative services including legal review of contracts, and Council travel to attend and participate in Council and committee meetings to discuss nutrition and post-harvest research. A Science Advisor assists the Executive Director and the Research Committee as it reviews and assesses the merits of current and potential future research projects, and to review marketing communications for scientific accuracy, and is funded from this budget category.

FY 2017 Nutrition Research Projects (Ongoing Projects and New Project Funding):

Total recommended: \$427,330.

- a. **Ana Rodrigues-Mateos: Impact of raspberry Polyphenol Consumption on Vascular Function in Healthy Individuals: \$12,010.** A randomized, controlled crossover study will be conducted in order to investigate the effects of raspberry polyphenols in vascular function in healthy individuals. The findings emanating from the present proposal will contribute to understand the potential cardiovascular health benefits of raspberry polyphenols and provide necessary scientific data for future dietary recommendations. Funding is to complete this one-year project.
- b. **Barbara Shukitt-Hale: The Effects of Raspberries on the Interaction Between Inflammation, Psychomotor, and Cognitive Behavior: \$15,687.** This study will

explore the interaction between baseline motor performance and daily raspberry intake required to achieve improvement in motor function. Three hypotheses will be tested: 1) consumption of raspberry will improve and/or preserve motor function; 2) daily consumption of raspberry will preserve the motor function among good motor performers; 3) the degree of improvement in motor performance observed will correspond to a reduction in inflammation biomarkers. Funding I to complete this one-year study.

- c. **Amanda Carey: Effects of Red Raspberry Supplementation on High Fat Diet-Associated Alterations in Behavior, Inflammation, and Brain Plasticity: \$8,972.** This project proposes to determine if dietary supplementation with red raspberry (*rubus idaeus*) can allay the cognitive dysfunction associated with consumption of a High Fat Diet. Funding is to complete this one-year study.
- d. **Shanil Juma: Effect of Red Raspberry Juice on Range of Motion, Pain Symptoms, and Cartilage/Inflammatory Markers in Individuals with Symptomatic Knee Osteo-Arthritis: \$14,891.** Although there is a lack of agreement regarding the definition of Osteo-Arthritis (OA), it is generally viewed as a degenerative disorder involving cartilage degradation in aging. In addition to age, a number of other factors have been suggested as risk factors for the development of OA including: genetics, obesity, joint hypermobility, and trauma. An alarming number of both men and women are afflicted with this disorder, particularly knee OA. Given the limitations and side effects of established osteoarthritis medications, there is increased interest in complementary and alternative treatments. One such area that shows promise includes the exploration of bioactive components found in berries such as red raspberries. Raspberries are a rich in polyphenolic compounds including anthocyanins and proanthocyanidins. These phenolic compounds have been shown to be potent inhibitor of the inflammatory process. Funding will complete this one-year project.
- e. **Min Du: Browning of White Fat to Prevent Obesity and Metabolic Syndrome: Role of Raspberry Polyphenols: \$14,908.** The hypothesis of this project is that polyphenols and dietary fibers associated with raspberry ingestion increase circulatory polyphenols, which activate AMP-activated protein kinase (AMPK) and promote browning of white fat, eliciting strong hypoglycemic, hypolipidemic, and anti-obesity effects. The project will pursue two specific objectives: 1) Examine the impact of dietary raspberry on the browning of white fat, and 2) Explore the role of AMPK in mediating the beneficial effects of dietary raspberry. A whole fruit approach will be pursued so that data obtained will be directly applicable to the raspberry industry. Funding is to complete year two of a two-year study.
- f. **Giuliana Noratto: Protective Effects of Raspberries Against Diabetes Through Modulation of Gut Microbiota: \$54,027.** Noratto's proposal calls for approximately \$25,000/year of matching funds, doubling resources available for this multi-year project. Recommended funds are for year three of a proposed three-year study. The objective of this project is to assess the health benefits of raspberry consumption as it pertains to diabetes, diabetes-induced metabolic disorders, inflammation, and cardiovascular risk factors. The moderation of Metabolic Syndrome through dietary change by improving

gut microbiotic health could have a significant impact on overall health by lowering multiple risk factors.

- g. **Jack Losso: Molecular Mechanisms Underlying the Protective Effects of Red Raspberries Against Insulin Resistance: \$20,795.** This clinical project will establish the effects of whole red raspberry consumption on insulin sensitivity and inflammation, and provide data on how Type 2 diabetes patients respond to red raspberry intervention. The in vitro portion of the project will determine the molecular mechanisms of cellular protection. Recommended funding is for year three of a proposed three-year study.
- h. **Min Du: Browning of White Fat to Prevent Obesity and Metabolic Syndrome: Role of Raspberry Polyphenols: \$60,745.** The hypothesis of this project is that polyphenols and dietary fibers associated with raspberry ingestion increase circulatory polyphenols, which activate AMP-activated protein kinase (AMPK) and promote browning of white fat, eliciting strong hypoglycemic, hypolipidemic, and anti-obesity effects. The project will pursue two specific objectives: 1) Examine the impact of dietary raspberry on the browning of white fat, and 2) Explore the role of AMPK in mediating the beneficial effects of dietary raspberry. A whole fruit approach will be pursued so that data obtained will be directly applicable to the raspberry industry. Funding is for year two of a two-year study.
- i. **Dorothy Klimis-Zacas: Role of Red Raspberries (*Rubus idaeus*) on Inflammation and Endothelial Dysfunction as Related to the Metabolic Syndrome: \$50,000.** Subclinical inflammation and vascular dysfunction are two of the major hallmarks of Metabolic Syndrome that eventually lead to increased incidence of CVD and Type 2 Diabetes. This proposal will address the possible anti-inflammatory role of Red Raspberries (*Rubus idaeus*) as well as their potential in attenuating vascular dysfunction in an animal model. Funding is for year one of a two-year study.
- j. **Frederico Rey: Gut microbial metabolism of red raspberry phenolics: a critical step for health effects: \$29,534.** The main goal of the project is to evaluate gut-microbial metabolism of phenolic compounds present in red raspberries, with a major focus on anthocyanins, as a function of health status in humans, and to test whether interpersonal differences in microbiota-dependent phenolic metabolism modify the beneficial effects associated with the consumption of red raspberries. There is a large degree of interpersonal variability in these microbial transformations, which remain poorly characterized. Results from this study will be used to identify probiotics that may be given together with raspberries to enhance their effects against cardiovascular disease (and potentially other diseases). Funds are for year one of a two-year project.
- k. **Chris Gill: The impact of raspberries on dis-regulation of cerebral microvasculature-mediated cognitive decline: \$26,861.** Disruption and deregulation of the microvascular architecture is a common pathogenic mechanism in the progression of numerous chronic diseases including cardiovascular disease cancer and Alzheimer's disease (AD). A direct relationship can be readily observed between microvascular pathology and cognitive decline. Berries have positive effects on aspects of cognition that cannot be fully explained by effects on either neurogenesis or inflammation. This project will determine whether a diet rich in raspberries can improve

cerebral microvascular architecture and murine cognition. Funds will be used for the first year of a two-year project.

- i. Neil Shay: The Healthful Effects of Raspberries Polyphenols, Fiber, and Other Raspberry Components: \$60,000.** This project will examine the role of raspberry food products, raspberry phytochemicals, and raspberry fiber in terms of their ability to reduce the development of a set of related metabolic disease conditions including obesity, elevated blood lipids, diabetes, fatty liver disease, hypertension, chronic inflammation, and osteoporosis. The objective is to evaluate the beneficial effect of processed raspberry products and to identify the relative contributions of raspberry polyphenols and fiber to the healthful effects associated with the consumption of raspberries. This project builds off a successful study previously funded by the NPRC which demonstrated that the addition of a raspberry puree concentrate (RPC) or raspberry juice concentrate (RJC) to a High Fat (HF) diet reduced the development of obesity due to consumption of the HF diet alone. That prior project will be extended by examining the effect of a variety of polyphenol- and fiber-containing fractions in year one followed by an examination of other fractions containing various levels of raspberry phytochemicals and fiber in years two and three. An animal trial will be completed each year followed by post-mortem analysis of metabolic factors. This project is intended to support and strengthen existing health messages. After a successful 2-year project funded by the NPRC (2015-2016), the present proposal will further clarify the healthful components of raspberry and expand the knowledge on raspberry fiber. Funds will be used for the first year of a three-year project.
- m. Britt Burton-Freeman: Red Raspberries and Insulin Action in Humans: \$58,900.** Preliminary results from an ongoing red raspberry trial suggest a decrease in the amount of insulin required to manage (and in some cases even reduce) post meal glucose concentrations in people with insulin resistance in an acute meal setting. The effects are preliminary but reveal activity associated with improved insulin sensitivity and less pancreatic β -cell burden, both critical in maintaining glycemic health and reducing risk of Type 2 Diabetes Mellitus. Additionally, as limited information is available about the type and properties of red raspberry dietary fibers (of which red raspberries are an excellent dietary source), fermentable fibers have been shown to improve insulin action in other studies, particularly as it relates to “second meal” effects. The proposal looks to extend and expand the current / ongoing study: 1) to increase sample size and power of analysis in both the insulin resistant and healthy reference group on acute endpoints of insulin and glucose and secondary endpoints as appropriate; 2) to increase the sample size of the acute breathe hydrogen sub-study; and 3) to extend the findings of the acute study with the aim of testing chronic effects of red raspberry on insulin sensitivity and exploring the relationship between shifts in the gut microbiome composition with concomitant assessment of the urolithin metabolite pool as potential mechanisms of for the observed clinical effects. Budgeted funds will be used for year one of a two-year project.

Completion of projects funded in FY 2016: Total recommended: \$86,090.

- a. **Meijin Zhu: Dietary Gut Microbiota: \$13,605.** Recommended funds are to complete the second year of a two-year study. Matching grant funds of \$120,598 over the two-years proposed more than doubled funds available to support this project. The project will study the impact of whole fruit rather than an extract. Gut Microbiota and biological metabolites, rather than consumed compounds, are rapidly becoming recognized as the key to bioactivity. Creating a large body of science on biomechanisms will be critical to establishing any future health claim for raspberries. Recommended funds are for year two of a two-year study.
- b. **Neil Shay: Defining the Metabolic Benefits of Raspberries and Raspberry Compounds: \$18,750.** Shay's project is designed to examine the ability of raspberries and specific raspberry compounds to influence a series of metabolic conditions of interest to the raspberry industry including diabetes, chronic inflammation, obesity, and cardiovascular health. Recommended funds are to complete the second year of a two-year study.
- c. **Giulianna Noratto: Protective Effects of Raspberries Against Diabetes Through Modulation of Gut Microbiota: \$10,482.** Noratto's proposal calls for approximately \$25,000/year of matching funds, doubling resources available for this multi-year project. Recommended funds are to complete year two of a proposed three-year study. The objective of this project is to assess the health benefits of raspberry consumption as it pertains to diabetes, diabetes-induced metabolic disorders, inflammation, and cardiovascular risk factors. The moderation of Metabolic Syndrome through dietary change by improving gut microbiotic health could have a significant impact on overall health by lowering multiple risk factors.
- d. **Jack Losso: Molecular Mechanisms Underlying the Protective Effects of Red Raspberries Against Insulin Resistance: \$9,232.** This clinical project will establish the effects of whole red raspberry consumption on insulin sensitivity and inflammation, and provide data on how Type 2 diabetes patients respond to red raspberry intervention. The in vitro portion of the project will determine the molecular mechanisms of cellular protection. Recommended funding is to complete year two of a proposed three-year study.
- e. **Britt Burton-Freeman: Red Raspberries and Insulin Action: \$19,564.** Burton-Burton-Freeman's clinical study will examine the relationship between red raspberries and oxidative inflammatory stress, and the relationship of these responses to insulin action and red raspberry consumption to reduce diabetes risk factors. Recommended funding is to complete year two of a proposed two-year study.
- f. **Ara Kirakoysan: Cardioprotective Benefits of Red Raspberries: \$14,457.** Kirakoysan's proposal draws its hypothesis from Crozier's work on biomechanisms. Taking a holistic view of health, it addresses the moderation of metabolic syndrome to lessen the public health burden of heart disease by reducing cardiovascular risk factors of elevated cholesterol and insulin resistance. Recommended funding is to complete year two of a two-year study.

Research Support: \$40,000

- a. **USDA Nutrition Research Manuscript: \$15,000.** To be written under separate contract by the Council's Science Advisor, this manuscript will be used to publish to results of the nutrient content analysis being completed in FY 2016 under contract with USDA/ARS. Publication in this format will raise visibility of new and accurate data for all forms of processed raspberries.
- b. **Freeze Dried Raspberry Powder and Processed Raspberry Samples: \$25,000.** Investigators and product developers have requested either freeze dried raspberry powder or processed raspberries in various forms to support funded studies. Funds from this budget will be used to acquire, package, and ship product to be used during studies funded by the Council.