## **CFAES Center and Program Annual Review**



Title of Center:	Center for Advanced Functional Foods Research and Entrepreneurship			
Current Director:	Yael Vodovotz, PhD			
	Associate Director: Steven Clinton, MD, PhD			
Date of last meeting:	December 5, 2019			
Date of last Review:	N/A			

#### **Mission Statement**

The CAFFRE mission is to serve as a catalyst for research and development of novel functional foods and components that will enhance health.

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### Summary of Goals and Objectives

#### **Center History and Goals**

The surge in corporate interest for the development of foods, ingredients, and crops with unique qualities delivering health benefits spurred experienced and recognized OSU collaborators to develop the Center for Advanced Functional Foods Research and Entrepreneurship (CAFFRE). CAFFRE is a multidisciplinary program focused on enhancing the collaboration of investigators in the <u>specific area of functional foods</u>. Functional foods are defined as food products that can have a positive impact on health beyond just meeting basic nutritional needs and are utilized to enhance health and quality of life of all people.

Consumers are becoming more interested in maintaining health and quality of life, especially as life expectancy steadily increases<sup>1</sup>. According to Mintel, a trend that is driving food and drink purchases is "wellbeing"<sup>2</sup>. Consumers are seeking physical and mental wellness, which has influenced food and drink purchasing habits<sup>2</sup>. This has been especially true during the COVID-19 pandemic. Consumers are looking for more functional foods and drinks<sup>2</sup>. In fact, a 2021 Mintel report showed that "Overall nutritional

value" is an important food feature in 45% of the consumers surveyed<sup>3</sup>.

The market for CAFFRE member expertise includes not only consumers, but farmers, small businesses, and food companies. Ohio's agricultural community can capitalize on expanding markets for functional food products created for health-oriented consumers. A variety of prominent crops in Ohio such as soybeans, tomatoes, berries, pumpkins, cruciferous vegetable, and various grains are among the crops that contain biologically active components with promising physiological implications for disease prevention and control. Agricultural practices aimed toward value added crops as ingredients in functional food products provide an opportunity for economic development of small and medium sized farmers to produce and market fruits, vegetables, and grains with enhanced health benefit to consumers. These farmers can benefit from CAFFRE member assistance in producing crops with optimal bioactive levels. In addition, the State of Ohio has more than 800 food processing companies. Again, many of



Figure 1: High-protein soy pretzels developed by CAFFRE participants in collaboration with the Ohio Soybean Council.

these companies do not have the expertise, equipment, and facilities to evaluate novel functional foods, yet would benefit from collaborating with the CAFFRE members to complete specific aspects of product development and marketing.

There is no known organization that provides all the services of CAFFRE; many similar organizations exist, but each is missing at least one important aspect of CAFFRE's program, such as horticulture and plant science research, a strong link to commercialization and industry, or the association and near proximity of a hospital and world renown cancer center for clinical trials. With six colleges (Food, Agricultural, and Environmental Sciences; Medicine; Education and Human Ecology; Biological Sciences; Public Health; and Pharmacy) currently involved, the CAFFRE team is able to conduct research encompassing the entire spectrum in the process and development of functional foods, ingredients, or crops targeted to protect health or enhance quality of life. CAFFRE works to connect investigators from each of these colleges and promote collaboration.



Crops to the Clinic to the Consumer

Figure 2: Newly designed graphic showcasing the CAFFRE tagline "Crops to the clinic to the consumer". The mission of the center is to serve as a catalyst for research and development of novel functional foods and components that will enhance health and quality of life for people of all ages. Our vision is to be a leading force in directing well-researched functional foods to market in Ohio and beyond, and a primary source of functional foods and bioactive information for scientists, healthcare professionals, food industry representatives, and consumers.

"From Crops to the Clinic to the Consumer" is the paradigm that was created to define this expertise into a research center positioned to interact with academic institutions, industry, government agencies, trade associations and boards, and policy agencies and centers to enhance the availability of functional foods that promote health.

#### Objectives

# *Objective 1:* To enhance collaboration among investigators of diverse disciplines such as agriculture, nutrition, medicine, policy, and public health.

Semi-monthly meetings are organized to bring together investigators and educate members through research project presentations and seminars. The discussions emitting from these gatherings spur ideas for new or improved functional food projects, grants or new uses of current products.

# *Objective 2: To develop unique nutritionally enhanced functional food products for disease prevention and control.*

In the Department of Horticulture and Crop Science, Ohio plant varieties with enhanced levels of important phytonutrients have been developed. Research that aims to promote crop growth for quality and defined levels of bioactive compounds is conducted. Utilizing specific crops and animal products, we develop functional foods with the most desirable sensory and nutritional characteristics with potential for marketing. This is especially important as it is well known that taste and texture are the most important drivers of food purchasing. Formulated products are analyzed using both physical and analytical chemical techniques, evaluated in the sensory laboratory, and studied during processing and preservation in the Food Industry Center pilot plant. In addition, these capabilities facilitate scale-up of manufacturing processes for later marketing and commercialization of novel products in collaborations with industry and business partners. For example, the tomato juice containing soy that was developed by the Initiative for Future Agriculture and Food Systems group provided a successful program for functional foods research that has been used as a guideline for our future studies.

# Objective 3: To conduct research to study efficacy and safety of newly developed functional foods through laboratory protocols, mechanistic-based research, pre-clinical models, and human translational research.

New analytical techniques have been developed to assist in the identification and quantification of a complex array of phytochemicals. These new methods are applicable not only to foods but for biological tissues and biopsy samples to aid animal and clinical studies. These studies allow a food company to establish an FDA-approved health claim. We have utilized an *in vitro* digestion model system to measure digestibility of food compounds and couple this assay with human intestinal absorptive cells to systematically investigate uptake from individual food products and meals.

Toxicity, pharmacokinetic, and bioavailability human clinical studies are performed. Clinical trials are also used to investigate biomarkers of disease prevention in specific population groups.

Animal studies using various rodent species, knock-out mice and rodent cancer transplants targeted for specific diseases are tested with formulated functional foods when appropriate. We also characterize the interactions of bioactive components on cellular and molecular processes associated with disease progression.



*Figure 3: The process of developing, analyzing, and commercializing functional foods. Adapted from a figure designed by Jennifer Ahn-Jarvis.* 

# *Objective 4: To disseminate scientifically sound information on health promoting functional foods and components to scientists, healthcare professionals, food industry representatives, and consumers.*

CAFFRE researchers continue to publish their findings in high impact peer-reviewed scientific journals and regularly present at top tear scientific conferences. Additionally, CAFFRE helped organized the multidisciplinary graduate-level coarse, *Phytochemicals in Human Health: Crops to the Clinic*, offered for the first time in autumn 2015 and repeated every two years. CAFFRE supports the Russell Klein symposia and helps send students to the John Milner Nutrition Research Practicum.

# *Objective 5: To collaborate with strategic food industry and business partners to identify viable opportunities to market functional foods and components with demonstrated health promoting properties.*

CAFFRE works with industry and government partners to develop and commercialize functional food products. CAFFRE has collaborated with 26 companies and commodity groups including Abbot Nutrition, Mead Johnson, nestle, Ohio Soybean Council, Haas Avocado Board, and Proctor & Gamble.

### Metrics: Advancement of Goals and Achievements

#### **Goal: Enhance Collaboration**

The first goal of CAFFRE is to promote collaboration among investigators of diverse disciplines in order to achieve our mission of enhancing human health with functional foods. The center includes members from 10 colleges across campus including, the College of Food, Agricultural, and Environmental Sciences, College of Medicine, College of Education and Human Ecology, College of Health and Rehabilitation Sciences, College of Pharmacy, College of Public Health, College of Dentistry, College of Nursing, College of Public Affairs, and the College of Veterinary Medicine. A list of CAFFRE members and their affiliations is shown in Appendix I. In 2021, many new projects were established through the networking and collaboration of CAFFRE members. Some of these projects are described below.



#### Trypsin Inhibitors in Lorikeet Feed

The expertise of CAFFRE members does not go unnoticed across the university. Suggestions from CAFFRE members to their peers has led to interesting and impactful projects. Dr. Vodovotz has long worked with soy and analyzed its components including the antinutrients, trypsin inhibitors. A collaboration was formed between Dr. Vanessa Hale in the College of Veterinary Medicine and Dr. Yael Vodovotz to measure trypsin inhibitors in lorikeet feed. The goal was to investigate a potential link between lorikeet enteritis and trypsin inhibitor in the diet. Trypsin inhibitor assays were carried out on several varieties of commercial lorikeet feed.

#### Blueberry confections

A new collaboration was formed in 2021 from networking of CAFFRE members. Dr. Bruno from Department of Human Sciences and Dr. Vonder Haar from Department of Neuroscience along with Dr.

Yael Vodovotz are designing a rat study to measure the cognitive and gut microbiome effects of blueberry and galacto-oligosaccharides (GOS) in the diet.

#### Coffee Grounds

James Warner, the Program Director for Nutrition Services, reached out to CAFFRE to find a use for spent coffee grounds from the Wexner Medical Center. This contact led to several projects using



coffee ground oil in bioplastics. While the end product was not a food, it would not exist without the CAFFRE reputation and network.

#### **Goal: Develop Functional Foods**

Functional food development is driven by several types of research including epidemiological, *in-vitro*, animal, and exploratory metabolomic studies. These studies generate hypotheses related to the foods and bioactive compounds that may enhance human health. Across the university, research is being conducted on a wide array of food-relevant bioactive compounds, leading to collaborations to develop functional foods containing these compounds. CAFFRE researchers work together to turn fundamental research into products that are viable in the clinic and/or commercially. Foods can have multiple bioactives with diverse mechanisms of action and can be, because of that, more effective in bringing about a health outcome. Multiple bioactives at modest doses with non-overlapping toxicity provide a margin of safety in clinical trials. Some example studies are described below.

#### **Omega-3s in Functional Foods**

Much research has been done in the area of omega-3 fatty acids such as EPA and DHA and fish oil by researchers in the department of Human Sciences and College of Medicine. An idea to create a functional food using these fatty acids was proposed by Dr. Clinton in the College of Medicine. Dr. Vodovotz and her graduate student, Abigail Sommer worked to create this food. A functional plant-based beverage was developed utilizing EPA and DHA from non-fish sources. Collaborators on the project include Dr. Martha Belury in the Department of Human Sciences and Dr. Osvaldo Campanella in Food Science and Technology. The combination of expertise from these faculty has helped create a successful product that will be used in sensory and clinical studies in 2022 and 2023. The deliverable from this project will be a plant-based milk beverage made from sustainable ingredients that is commercially viable.

#### Grapefruit Confections

Dr. Yael Vodovotz with collaborators in the Hebrew University in Israel, have developed a grapefruit confection as a functional food delivery vehicle of the flavonoid naringenin. Dr. Ken Riedl, a senior researcher, and Technical Director of Nutrient & Phytochemical Analytics Shared Resource (NPASR) helped to characterize the phytochemical profile. Naringenin is bitter in flavor, leading to poor acceptability by animals in preliminary studies and some consumers. Enzymatic treatments, encapsulation techniques, and careful ingredient sourcing were employed to maximize the amount of bioavailable naringenin contained in confections while minimizing the presence of furocoumarins, compounds which cannot be consumed with certain pharmaceuticals. Physicochemical and sensory analyses were also utilized to optimize product desirability and shelf life. This product has been utilized in studies in Dr. Belury's lab as well, looking at the impact of naringenin on cancer cachexia.

#### Horticulture and Crop Sciences

Functional foods research can also involve manipulating crops to produce more or less of certain components. This type of research can be used to increase bioactive content of foods. Dr. Cooperstone has been working on breeding of apples and tomatoes with the goal of understanding and modifying certain bioactives.

#### **Goal: Interdisciplinary and Translational Research**

CAFFRE researchers provide expertise at every step of functional food development and analysis, from concept ideation and food processing to clinical studies. These connections have led to unique and comprehensive research projects. Clinical studies are utilized to test the efficacy of functional food products in impacting health and preventing/treating disease. In 2021, CAFFRE investigators reported 29 clinical trials. 18 of these trials utilized functional foods as the primary intervention (Appendix II). Many of these studies were ongoing in 2021, with 8 studies "Recruiting", and 12 "Active, not recruiting". Some examples of interdisciplinary and translational functional food studies are described below.

#### Soy Studies

Dr. Steven Clinton's group has worked in the area of soy and cancer for 20 years. Initially, a soy powder was utilized in the studies that was dissolved in a beverage of choice. The product, however, was unpalatable. This led to the development of soy bread by Dr. Yael Vodovotz. Several iterations have existed. One contained almond to help improve isoflavone bioavailability. Currently, a trial is ongoing using soy and wheat bread in a prostate cancer cohort. The soy bread is utilized alongside hormone therapy to improve prostate cancer outcomes. The collaboration of Drs. Clinton and Vodovotz have led to several years of research on soy functional foods. These foods have much higher acceptability and because of this, higher compliance in the clinical studies.

#### Soy Pretzels and Exercise Recovery

Until now, collaborations between the Exercise Science and Food Science faculty have been lacking, despite the desire for food products to enhance exercise recovery and performance. A collaboration spawned from CAFFRE that included Dr. William Kraemer from exercise science and Dr. Yael Vodovotz in Food Science and Technology. In this project, the effect of high-protein soft pretzels on exercise recovery was compared to conventional wheat pretzels. Soy pretzels were found to resolve inflammation faster than wheat pretzels, possibly due to their protein and phytochemical contents. Without CAFFRE, the substantial support from Dr. Kraemer would have been missing.

#### Black Raspberry Studies

Research on black raspberries has been ongoing for several years. Multiple functional food matrices have been developed by CAFFRE faculty including black raspberry confections and nectar. In 2021, Dr. Kristen Roberts published fundamental research on black raspberry metabolism. An NIH-NCI U01 funded study led by Drs. Weghorst, Schwartz, Kumar, and Clinton is being completed. The study focuses on the interface between food, gender, smoking, and the microbiome in human oral carcinogenesis. Around 120 participants were recruited and randomized to receive black raspberry nectar or placebo. The impact of smoking was also evaluated.

Additionally, a black raspberry intervention is being utilized to modify gut microbiome and improve the response to immune checkpoint inhibitors in lung cancer patients. This study is being conducted by several CAFFRE members and colleagues including Dr. Elizabeth Grainger, Dr. Yael Vodovotz, Dr. Tong Chen, Dr. Steven Clinton, and Dr. Daniel Spakowicz. Emerging data demonstrates that responses to immune checkpoint inhibitor (ICI) therapy may depend on host microbiome. A placebo-controlled, randomized, cross-over trial examined the impact of 2x 80 mL black raspberry (BRB) nectar drink boxes per day for 4 weeks. There were 96 participants recruited and classified as being at high risk of

developing lung cancer. Pre- and post-dietary intervention gut microbiome, blood, and urine samples were collected. Stool from participants in the BEWELL study were gavaged into C57BL/6J mice to create human microbiome avatar models. Mouse colon cancer cells (mc38) were injected subcutaneously and then treated with anti-PD1 Ab (5mg/kg mouse; clone RMP1-14) or isotype control (clone 2A3). Preliminary experiments using avatar mice with post-BRB human microbiomes showed smaller tumors relative to control mice receiving stool from that same individual pre-BRB dietary intervention (t-test, p-value = 0.05). These results suggest that black raspberry nectar may modify the human gut microbiome in a way that promotes an improved response to immunotherapy.

#### Healthy Cookies

Center member Dr. Belury is recruiting for a clinical trial (NCT04677920) looking at the impact of healthy cookies with linoleic acid on mitochondrial biology. Linoleic acid has many health benefits including altering body composition and energy metabolism, possibly through its impact on cardiolipin and mitochondria. The research is an intervention and feasibility pilot trial designed to determine if short-term consumption of healthy cookies made with linoleic acid rich oil can influence mitochondrial biology in white blood cells and muscle. The hypothesis is that consuming 1 healthy cookie rich in linoleic acid each day for two weeks will improve mitochondrial biology in white blood cells and muscle.

#### Green Tea Confections

While green tea has been shown to have a variety of health benefits, they are limited in westernized countries since its consumption is lower than that of Asian countries. Starch based confections were developed by CAFFRE researchers as a snack food vehicle for green tea bioactive compounds. One study currently ongoing is investigating the impact of green tea confections on the gastrointestinal tract of obese individuals. Green tea confections are expected to provide an improved gut barrier and alleviate inflammation.

#### **Goal: Disseminate scientific information**

It is important not only to perform functional food research, but also to share findings. The CAFFRE website is used to showcase functional food research. In 2021, it was updated to include the new logos and up-to-date biographies of center members. CAFFRE researchers along with their students and post-docs presented at scientific meetings throughout the year. Some of the most attended meetings were The Institute of Food Technologists Annual Meeting, The American Society of Nutrition Annual Meeting, and the International Congress of Biochemical Engineering. CAFFRE members published extensively this year, with over 250 distinct publications. More detail is described in the section "Metrics: Transfer of Knowledge".

#### Goal: Collaborate with community

Once a product is successful in trials, it is important to scale up production. CAFFRE has worked with companies locally and nationally to produce functional food products.

Black raspberry confections developed by CAFFRE researchers are being produced by Chocolate Creations located in Ohio.

Additionally, researchers have worked specifically with members of the community to improve outcomes in underserved communities. Dr. Colleen Spees is working on a project related to obesity and cancer prevention which targets low-resource and underserved youth and caregivers in central Ohio. This project was funded for 5 years by the USDA NIFA. Additional funding has been obtained from the Academy of Nutrition and Dietetics. The intervention involves education of participants. Many CAFFRE members were recruited to present research.

#### Challenges

Due to the COVID-19 pandemic, CAFFRE leadership decided to postpone in-person seminars during 2020 and 2021. Focus was placed on funding grants and fostering interdisciplinary research collaboration. However, in 2022, we have restarted the seminar program, with plans to host group meeting and seminars every two months.

# Metrics: Transfer of Knowledge

#### **Grant Awards**

Several grants were awarded to center faculty in 2021 to that related to functional food research. Some examples are shown below.

- **Steven Clinton**, Devin Peterson, Vicki Wysocki, Matthew Sullivan, **Martha Belury**, Jiangjiang Zhu. A New Paradigm in Foods for Health at Ohio State: Multi-Omics Integration In the Era of Precision Nutrition. *President's Research Excellence (PRE) Catalyst Grant Program*.
- Vanessa Hale, William McGraw, Tessa Cannon, and **Yael Vodovotz**. Relationship between diet, microbiome and SIV in wild and captive sooty mangabeys. *President's Research Excellence (PRE)* Accelerator Grant Program.
- **Rafael Jimenez-Flores.** Effect of lipids in digested MFGM ingredient on membrane composition of highly differentiated Caco-2 human intestinal cells. *Reckitt Benckiser (formerly Mead Johnson).*
- Yael Vodovotz. Development and optimization of EPA and DHA fortified soymilk emulsions. *Ohio Soybean Counil.* (Pending).
- Daniel Spakowicz, Yael Vodovotz, Steven Clinton, David Carbone. Increasing response to immunotherapy through diet-based alterations of the microbiome: a mouse validation study. *OSU Division of Medical Oncology Research Award.*

#### **Training Grants**

#### USDA National Needs Fellowship Grant - Metabolomics Across the Food System

The USDA Food and Agricultural Sciences National Needs Fellowship Grants program provides a stipend and fee waiver for graduate students. A USDA NNF proposal, *Metabolomics across the food system: an integrated graduate training program* was submitted by CAFFRE member Jessica Cooperstone along with Devin Peterson, Rachel Kopec and Emmanuel Chatzakis. The grant will fund three students pursuing advanced degrees, with each PI serving as a faculty advisor and mentor.

#### USDA National Needs Fellowship Grant - Trans-omics-assisted plant breeding for food quality

Jessica Cooperstone and colleagues were awarded another USDA NNF grant to supports three doctoral students with a focus on trans-omic solutions and applications in the improvement of crops and food quality.

#### **Publications**

CAFFRE faculty published over 250 peer-reviewed articles during 2021. Of these, 24 were related to the area of functional foods. A list of these publications is presented in Appendix II. Group members often published in collaboration with each other. 28 of the publications were authored by more than one CAFFRE member. While it is common for faculty to publish with their departmental peers, many of the publications included authors across departments and colleges. These collaborations are supported by CAFFRE networking opportunities.

#### **Intellectual Property**

Functional food research often leads to intellectual properties. Five patents were filed by CAFFRE members in 2021. One example was filed by Dr. Rafael Jimenez-Flores for "Methods and compositions related to a stable blend of casein and plant proteins with improved physical and flavor characteristics."

Additionally, invention disclosures on functional food products were filed with the university in 2021, including those for high-protein soy pretzels, omega-3 plant milk beverages, and the MyFoodChoice App.

#### Presentations

CAFFRE members presented at several local, national and international conferences.

Dr. Rafael Jimenez-Flores along with post-doctoral scholars, Drs. Joana Ortega and Israel Garcia Cano spoke at the 2021 International Congress of Biochemical Engineering on the topic of dairy products and health and their research on milk fat membrane composition and structure for its isolation and application in foods.

Dr. Jessica Cooperstone helped host the 2021 Metabolomics Association of North America (MANA) annual meeting.

Abstracts were submitted and presented at several conferences including the following.

- OSU Comprehensive Cancer Center Annual Meeting
- World Lung Conference
- American Association of Zoo Veterinarians and European Association of Zoo and Wildlife Veterinarians joint conference
- Klein Research Symposium
- College of Food, Agricultural, and Environmental Sciences Research Forum
- Hayes Graduate Research Forum
- Food Structure and Functionality
- Institute of Food Technologists Annual Meeting
- International Conference on Environmental Systems
- American Society of Nutrition Annual Meeting

#### Courses

Dr. Cooperstone taught the course Phytochemicals in Human Health: Crops to the Clinic. This course features guest lecturers presenting on every aspect of phytochemical research. Students learn about horticulture, food science, and clinical translation as they related to phytochemicals. The class was taught in the Fall of 2021. Dr. Yael Vodovotz gave a lecture on functional foods, showcasing their development, analysis, and use in clinical studies.

#### Website

#### https://u.osu.edu/caffre/

CAFFRE has a comprehensive website targeted for potential industry partners and members. The website is positioned to share resources with those interested in the area of functional foods. Recent

publications are posted and indexed by topic and discipline. There is a listing of CAFFRE members and a biography of each one, showcasing their research capabilities. In 2021, the CAFFRE website received 29% more pageviews than in 2020, showing increasing interest in the center and area of functional foods.

#### **Faculty Member Accomplishments**

CAFFRE faculty were awarded for their achievements in research, outreach, and teaching. Below is a short listing of some of these accomplishments.

- Dr. Rafael Jimenez-Flores was named the 2021 OARDC Innovator of the Year.
- Dr. Monica Giusti was named the 2021 CFAES Distinguished Professor.
- Dr. Ken Lee was awarded the 2021 North American Colleges and Teachers of Agriculture Educator Award.
- Dr. Chris Simons was part of a team using hard candy to help detect probable cases of COVID-19.
- Dr. Chris Simons received the Rodney F. Plimpton Teaching Award at the 2021 CFAES Celebration of Students.
- Dr. Yael Vodovotz received the Spirit of the Land Grant award at the 2021 CFAES Celebration of Students.
- CFAES gave several CAFFRE faculty 2021-2022 Faculty and Staff Awards. Dr. Rafael Jimenez-Flores won the 2021-2022 Innovator of the Year Award. Dr. Monica Giusti won the Distinguished Graduate Mentor Award.
- Dr. Martha Belury was elected Vice President (and Incoming President) of the American Society for Nutrition.

#### Student and Post-doctoral Scholar Accomplishments

Those advised by CAFFRE faculty also received a host of awards throughout 2021.

- Danielle Voss, advised by Dr. Monica Giusti, won 2<sup>nd</sup> place at the 2021 CFAES Annual Research Conference.
- Abigail Krentz, advised by Dr. Rafael Jimenez-Flores, Sydney Grouge, advised by Dr. Monica Giusti, and Danielle Voss, advised by Dr. Monica Giusti, places 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup>, respectively, in the Hayes Graduate Research Forum oral presentation competition.
- Abigail Sommer, advised by Dr. Yael Vodovotz, won first place for her poster the Hayes Research Forum. The poster described optimization of eicosapentaenoic acid production by *Yarrowia lipolytica*. Erica Grush, advised by Dr. Monica Giusti, also received an honorable mention for her poster.
- Brittany Miles, advised by Dr. Chris Simons was awarded a 2021 North American Colleges and Teachers of Agriculture award.
- Gonzalo Miyagusuku-Crazado, advised by Dr. Monica Giusti, received the Graduate Student Research Award from the Food Science and Technology department for having at least 4 publications during his PhD program.
- Abigail Krentz, advised by Dr. Rafael Jimenez-Flores, won 1<sup>st</sup> in the 2021 National Dairy Council Graduate Student Poster Contest in Dairy Foods Research.

• Erica Grush, advised by Dr. Monica Giusti, won a 2021 Council for Agricultural Science and Technology Communication Scholarship.

# Metrics: Current Support

#### OARDC

CAFFRE was initially funded through the AgBiosciences Innovation Grant (ABIG) program in 2005 with the mission to foster the development of novel food products for health. Since that time, CAFFRE has historically received annual funding from OARDC to support staff and programmatic efforts. From 2005-2017, CAFFRE received approximately \$100,000 per year. The total investment was \$1.45 million and was used to cover the operating expenses of the center, including a program manager and a percentage of the director and associate director's salaries and benefits. More than 25% of the OARDC support is returned to faculty in the form of seed grants. However, this funding ended in 2019.

#### **Fueling the Cure**



The Cooperatives for Fueling the Cure Endowment Fund was established April 6, 2012. The annual distribution from this fund supports cancer research focuses on identifying dietary and nutritional components for cancer treatment and prevention including supplies, equipment, personnel, lab space, fellowship awards, cost of travel, educational conferences, other training opportunities, and activities required for high quality research. Fifty percent of the annual distribution is allocated to the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (the James) and Comprehensive Cancer

Center. The remaining fifty percent is allocated to CAFFRE to support seed grants. In 2021, \$212,917.45 was awarded from Fueling the Cure. The distribution to CAFFRE each year is around \$25,000-\$35,000.

#### Seed Grants

Funding from Fueling the Cure goes directly into seed grants for faculty members. Since 2009, CAFFRE has awarded \$682,890 for 75 grants. The Molecular Carcinogenesis and Chemoprevention program often provides matching funds for CAFFRE for seed grants. These matching funds have totaled \$417,950 since 2009, supporting 73 of the 75 grants. Many of these grants involved multiple CAFFRE investigators across disciplines. In 2021, two grants were submitted and awarded to CAFFRE members.

#### Development of a Brainy Phytochemical Confection for Cognitive Health

Richard Bruno (Human Nutrition), Yael Vodovotz (Food Science and Technology), Joanna Hodges (Human Nutrition)

Low-energy confection snacks are a promising strategy to safely, conveniently, and effectively deliver dietary phytochemicals that can support healthy aging. Vitamin E, phospholipids, and anthocyanins are suggested to alleviate age-associated losses in cognitive health. Although observational studies and preclinical studies support this premise, controlled trials in humans that can establish causality are lacking, in part, by the absence of a convenient food vehicle to incorporate these phytochemicals into

the diet at appropriate levels for rigorous hypothesis testing. The Bruno and Vodovotz teams will expand their collaboration by formulating a novel snack food confection that can support cognitive health. The hypothesis, consistent with on our track-record of formulating confection with acceptable sensory attributes, is that a low-energy confection enriched with appropriate levels of dietary constituents important for brain health (vitamin E, phospholipids, anthocyanins) can be successfully formulated towards a long-term goal of assessing its efficacy on cognitive health. Project outcomes, including a fully developed snack food product, will therefore position us ideally for future competitive awards aimed at establishing efficacy of this novel confection to alleviate cognitive decline in relevant human cohorts.

# Attenuation of Cancer Cachexia by Flavonoids: Identifying the Neuromuscular and Neuroimmunologic Effects of Naringenin

#### Martha Belury (Human Nutrition)

Cancer cachexia is characterized by the loss of skeletal muscle that results in functional impairment, dysregulated macronutrient metabolism and reduced quality of life. Naringenin is a flavonoid that is protective against loss of muscle strength and the onset of insulin resistance and hyper-inflammation. In addition, qualitative observation indicated that despite weight loss, mice with cancer cachexia but fed a diet with naringenin were physical active and showed no signs of moribund. We seek to identify the neuromuscular effects of naringenin in mice with cachexia.

#### Budget

The CAFFRE budget for 2020 to 2022 is shown in Appendix III. Funding for director and manger salaries are supported by the CAFFRE operating funds. Seed grants are awarded from Fueling the Cure fund distributions.

# **Future Goals**

In 2022, CAFFRE directors will work to continue to meet our center goals.

#### **Enhance collaboration**

In order to promote collaboration, CAFFRE will continue to provide interdisciplinary grants in the area of functional foods. Through continuing meetings and seminars, we will help foster collaboration between investigators.

#### **Develop functional foods**

In January of 2022, CAFFRE hosted its first meeting since 2019. The goal of this meeting was to provide updates on current projects and provide a forum for discussion on functional foods. This acted to spur new ideas and discussions surrounding future products. A future goal is to continue these conversations about new products, utilizing the knowledge and expertise of center members.

#### Interdisciplinary and translational research

A goal of providing seed grants to investigators is to pave the way for larger Federal grants, primarily from NIH and USDA. Many projects have resulted in these large grants, a trend that we wish to continue in 2022.

#### **Disseminate scientific information**

In 2022, CAFFRE will disseminate scientific information by providing a seminar series for students, postdocs, and trainees. The series will focus on functional food clinical trials, with an emphasis on study design. CAFFRE faculty members will present in the short course and share their experiences with these trials. The series will be open to other interested parties across campus.

Additionally, regular CAFFRE seminars will continue every two months where members will present on current research and discuss future projects.

#### **Collaborate with community**

We will continue to keep the website up to date in 2022, allowing industry professionals and community members to keep up with CAFFRE.

We will work with local businesses with interest in the functional food space. One local business (SOW Plated) has already been working with CAFFRE.

# Appendix I

#### List of CAFFRE Members

College	Name	Department		
Dentistry	Purnima Kumar	Periodontology		
Education and Human	Martha Belury	Human Sciences		
Ecology	Joshua Bomser	Human Sciences		
	Richard Bruno	Human Sciences		
	Julie Chitchumronnchokchai	Human Sciences		
	Earl Harrison	Human Sciences		
	Sanja Ilic	Human Sciences		
	Jeff Volek	Human Sciences		
	Ouliana Zioyzenkova	Human Sciences		
Food, Agricultural, and	Josh Blakeslee	Horticulture and Crop Sciences		
Environmental Science	Jessica Cooperstone	Food Science and Technology		
	David Francis	Horticulture and Crop Sciences		
	Gary Gao	Horticulture and Crop Sciences		
	Monica Giusti	Food Science and Technology		
	Rafael Jimenez-Flores	Food Science and Technology		
	Matthew Kleinhenz	Horticulture and Crop Sciences		
	Ken Lee	Food Science and Technology		
	Ken Riedl	Food Science and Technology		
	Joseph Scheerens	Horticulture and Crop Sciences		
	Christopher Simons	Food Science and Technology		
	Yael Vodovotz	Food Science and Technology		
Health and Rehabilitation	Nicholas Funderburg	Medical Laboratory Science		
Sciences	Colleen Spees	Medical Dietetics		
	Chris Taylor	Medical Dietetics		
John Glenn School of Public Affairs	Neil Hooker	Food Policy		
Medicine	Miachael Bailey	Pediatrics		
	Theodore Brasky	Internal Medicine		
	Tong Chen	Internal Medicine		
	Steven Clinton	Internal Medicine		
	Zobeida Cruz-Monserrate	Internal Medicine		
	Elizabeth Grainger			
	Hisham Hussan	Internal Medicine		
	Maryam Lustberg	Internal Medicine		
	Thomas Mace			
	Ewy Mathe	Biomedical Informatics		
	Darrion Mitchell	Radiation Oncology		

	Amir Mortazavi	Internal Medicine		
	Tatiana Oberyszyn	Molecular Virology, Immunology and		
		Medical Genetics		
	Kristen Roberts	Internal Medicine		
	Fred Tabung	Internal Medicine		
	Kathleen Tober	Pathology		
Nursing	Sonia Duffy	Nursing		
Pharmacy	Robert Curley	Pharmacy		
Public Health	Thomas Knobloch	Environmental Health Sciences		
	Steve Oghumu	Environmental Health Sciences		
	Susan Olivo-Marston	Epidemiology		
	Chris Weghorst	Environmental Health Sciences		
Veterinary Medicine	Nong Inpanbutr	Veterinary Biosciences		

## Appendix II

#### **Selected Publications**

- 1. Martha A. Belury, Susan Raatz, and Zach Conrad. Modeled substitution of traditional oils with high oleic acid oils decreases essential fatty acid intake in children. *The American Journal of Clinical Nutrition*. 2021. https://doi.org/10.1093/ajcn/nqab407
- M. Bittoni, A. Bibi, N. Williams, M. Mendelson, E. Grainger, Y. Vodovotz, K. Riedl, S. Clinton, D. Carbone, and D. Spakowicz. Report on a Phytochemical-rich Dietary Intervention Trial to Prevent Lung Cancer: Implementation in a High-Risk Lung Screening Clinic. *Journal of Thoracic Oncology*. 2021; 16(3). <u>https://doi.org/10.1016/j.jtho.2021.01.812</u>
- Rachel Cole, Austin Angelotti, Genevieve Sparagna, Ai Ni and Martha Belury. Consumption of Cookies Made With a Linoleic Acid-Rich Oil Alters Cardiolipin Species in the Peripheral Blood Mononuclear Cells of Healthy Adults. *Current Developments in Nutrition.* 2021; 5(2). <u>https://doi.org/10.1093/cdn/nzab041\_005</u>
- Israel Garcia-Cano, Po-Wei Yeh, Diana Rocha-Mendoza, and Rafael Jimenez-Flores. Supercritical CO2 treatment reduces the antigenicity of buttermilk β-lactoglobulin and its inflammatory response in Caco-2 cells. *JDS Communications*. 2021; 2(1). <u>https://doi.org/10.3168/jdsc.2020-0028</u>
- Emily B. Hill, Ashley J. Kennedy, Kristen M. Roberts, Ken M. Riedl, Elizabeth M. Grainger, and Steven K. Clinton. Considerations for Use of the Phenol-Explorer Database to Estimate Dietary (Poly)phenol Intake. *Journal of the Academy of Nutrition and Dietetics*. 2021; 121(5). https://doi.org/10.1016/j.jand.2021.02.010
- Joanna Hodges, Geoffrey Sasaki, and Richard Bruno. Epigallocatechin Is Eliminated Faster From Plasma Than Epigallocatechin Gallate: Mathematical Modeling of Green Tea Catechin Metabolism in Healthy Adults. *Current Developments in Nutrition.* 2021; 5(2). <u>https://doi.org/10.1093/cdn/nzab037\_033</u>
- Erica Kosmerl, Israel Garcia-Cano, Diana Rocha-Mendoza, and Rafael Jimenez-Flores. Characterization of milk and soy phospholipid liposomes and inflammation in 3T3-L1 adipocytes. JDS Communications. 2021; 2(5). <u>https://doi.org/10.3168/jdsc.2020-0054</u>
- 8. Erica Kosmerl, Diana Rocha-Mendoza, Joana Ortega-Anaya, **Rafael Jimenez-Flores**, and Israel Garcia-Cano. Improving human health with milk fat globule membrane, lactic acid bacteria, and bifidobacteria. *Microorganisms*. 2021; 9(2). <u>https://doi.org/10.3390/microorganisms9020341</u>
- 9. Abigail Krentz, Israel Garcia-Cano, Joana Ortega-Anaya and **Rafael Jimenez-Flores**. Use of casein micelles to improve the solubility of hydrophobic pea proteins in aqueous solutions via low-temperature homogenization. 2021; 105(1). <u>https://doi.org/10.3168/jds.2021-20902</u>
- Brett Loman, Emily Hill, Michael Bailey, Jiangjiang Zhu, Amrik Singh Khalsa, Kelly Kelleher, and Colleen Spees. A High-Fiber Diet Intervention Improves Diet Quality and Is Related to Blood Pressure and Bacteriome Composition in Caregiver-Child Dyads. *Current Developments in Nutrition.* 2021; 5(2). <u>https://doi.org/10.1093/cdn/nzab054\_023</u>
- 11. Stephen Martinez, **Christopher A. Taylor**, and **Neal H. Hooker**. Measuring the Potential Impact of New and Reformulated Bread and Breakfast Cereal Products on Nutrient Intakes. *USDA Contractor and Cooperator Report*. <u>https://doi.org/10.22004/ag.econ.312956</u>
- 12. Alba C. Mayta-Apaza, Israel Garcia-Cano, Konrad Dabrowski, and **Rafael Jimenez-Flores**. Bacterial Diversity Analysis and Evaluation Proteins Hydrolysis during the Acid Whey and Fish

Waste Fermentation. *Microorganisms*. 2021; 9(1). https://doi.org/10.3390/microorganisms9010100

- Gonzalo Miyagusuku-Cruzado, Rafael Jimenez-Flores, and M. Monica Giusti. Whey protein addition and its increased light absorption and tinctorial strength of model solutions colored with anthocyanins. *Journal of Dairy Science*. 2021; 104(6). <u>https://doi.org/10.3168/jds.2020-19690</u>
- Divya Nedungadi, Nathan Ryan, Kelvin Anderson, Felipe F Lamenza, Pete P Jordanides, Michael J Swingler, Liva Rakotondraibe, Kenneth M Riedl, Hans Iwenofu, and Steve Oghumu. Modulation of the oral glucocorticoid system during black raspberry mediated oral cancer chemoprevention. *Carcinogenesis*. 2021. <u>https://doi.org/10.1093/carcin/bgab118</u>
- 15. Caleb J. Orchard, Jessica L. Cooperstone, Elisabet Gas-Pascual, Marcela C. Andrade, Gabriel Abud, Steven J. Schwartz, and David M. Francis. Identification and assessment of alleles in the promoter of the Cyc-B gene that modulate levels of β-carotene in ripe tomato fruit. *The Plant Genome*. 14(1). <u>https://doi.org/10.1002/tpg2.20085</u>
- 16. Joana Ortega-Anaya, Alice Marciniak, and Rafael Jimenez-Flores. Milk fat globule membrane phospholipids modify adhesion of Lactobacillus to mucus-producing Caco-2/Goblet cells by altering the cell envelope. *Food Research International.* 2021; 146. https://doi.org/10.1016/j.foodres.2021.110471
- 17. Shuai Ren and **M. Monica Giusti**. Monitoring the Interaction between Thermally Induced Whey Protein and Anthocyanin by Fluorescence Quenching Spectroscopy. *foods.* 2021; 10(2). <u>https://doi.org/10.3390/foods10020310</u>
- Shuai Ren and M. Monica Giusti. The effect of whey protein concentration and preheating temperature on the color and stability of purple corn, grape and black carrot anthocyanins in the presence of ascorbic acid. *Food Research International*. 2021; 144. https://doi.org/10.1016/j.foodres.2021.110350
- 19. Shuai Ren, **Rafael Jimenez-Flores**, and **Maria Monica Giusti**. The interactions between anthocyanin and whey protein: A review. *Comprehensive Reviews in Food Science and Food Safety*. 2021; 20(6). <u>https://doi.org/10.1111/1541-4337.12854</u>
- Diana Rocha-Mendoza, Erica Kosmerl, Abigail Krentz, Lin Zhang, Shivani Badiger, Gonzalo Miyagusuku-Cruzado, Alba Mayta-Apaza, Monica Giusti, Rafael Jimenez-Flores, and Israel Garcia-Cano. Invited review: Acid whey trends and health benefits. *Journal of Dairy Science*. 2021; 104(2). <u>https://doi.org/10.3168/jds.2020-19038</u>
- Stelios D. Sarantis, Necla Mine Eren, Barbara Kowalcyk, Rafael Jimenez-Flores, and Valente B. Alvarez. Thermodynamic interactions of micellar casein and oat β-glucan in a model food system. *Food Hydrocolloids*. 2021; 115. <u>https://doi.org/10.1016/j.foodhyd.2020.106559</u>
- 22. Ni Shi, Xiaoxin Chen, and **Tong Chen**. Anthocyanins in Colorectal Cancer Prevention Review. *antioxidants*. 2021; 10(10). <u>https://doi.org/10.3390/antiox10101600</u>
- Lorena Silva Pinho, Marluci Palazzolli da Silva, Marcelo Thomazini, Jessica L. Cooperstone, Osvaldo H. Campanella, Christianne Elisabete da Costa Rodrigues, and Carmen Silvia Favaro-Trindade. Guaraná (Paullinia cupana) by-product as a source of bioactive compounds and as a natural antioxidant for food applications. *Journal of Food Processing and Preservation*. 2021; 45(10). https://doi.org/10.1111/jfpp.15854
- 24. Deena B. Snoke, Yuko Nishikawa, Rachel M. Cole, Ai Ni, and Austin Angelotti, **Yael Vodovotz**, and **Martha Belury**. Dietary Naringenin Preserves Insulin Sensitivity and Grip Strength and

Attenuates Inflammation but Accelerates Weight Loss in a Mouse Model of Cancer Cachexia. *Molecular Nutrition & Food Research*. 2021; 65(22). <u>https://doi.org/10.1002/mnfr.202100268</u>

#### Selected Clinical Trials

- 1. Martha Belury. The Healthy Cookie Energy Study: Understanding How Healthy Cookies Affect Mitochondrial Biology. NCT04677920. *Recruiting.*
- 2. Martha Belury. Dietary Oils to Sustain Energy Study (DOSE). NCT04975763. Recruiting.
- 3. Martha Belury. The Healthy Cookie Study: Understanding How Healthy Cookies Affect Fat in the Blood. NCT02841618. *Active, not recruiting.*
- 4. Martha Belury. Weight, Energy, Lipids, and the Liver (WELL) Study. NCT05199948. *Not yet recruiting.*
- 5. Martha Belury. Dietary Oil to Improve Sleep Quality (SNACk). NCT04677946. *Not yet recruiting*.
- 6. Nicholas Funderburg. Soy Modulation of Immune Activation, LDL-Levels, and Lowering. NCT02818283. *Recruiting.*
- 7. Purima Kumar. Effect of Black Raspberry Phytochemicals on Oral Microbiome in Current Smokers and Non-smokers. NCT02439255. *Active, not recruiting.*
- 8. Richard Bruno. Alleviation Of Metabolic Endotoxemia In Adults With Metabolic Syndrome With Milk Fat Globule Membrane. NCT03860584. *Completed.*
- 9. Richard Bruno. Dietary Green Tea Confection For Resolving Gut Permeability-Induced Metabolic Endotoxemia In Obese Adults. NCT03413735. *Active, not recruiting.*
- 10. Richard Bruno. Achieving Nutritional Adequacy Of Vitamins E and K With An Egg/Plant-Based Food Pairing - Study 1. NCT04287816. *Recruiting*.
- 11. Richard Bruno. Achieving Nutritional Adequacy Of Vitamins E and K With An Egg/Plant-Based Food Pairing - Study 2. NCT04286321. *Recruiting.*
- 12. Steven Clinton. Soy bread diet in improving immune function in participants with prostate cancer. NCT03654638. *Recruiting.*
- 13. Steven Clinton. Absorption and Metabolism of Lyophilized Black Raspberry Food Products in Men With Prostate Cancer Undergoing Surgery. NCT01823562. *Active, not recruiting.*
- 14. Yael Vodovotz. Metabolism and Absorption of Anthocyanins From Extract and Whole Blueberry Powder Confections in Healthy Adults. NCT04329962. *Active, not recruiting.*
- 15. Yael Vodovotz. Soy Isoflavones in Treating Patients With Recurrent Prostate Cancer or Rising Prostate-Specific Antigen. NCT01682941. *Active, not recruiting.*
- 16. Yael Vodovotz. The Use of Functional Confections in Promoting Oral Health. NCT01514552. *Active, not recruiting.*
- 17. Yael Vodovotz. Functional Snack Foods With Safflower Oil and Soy in Postmenopausal Women Having Metabolic Syndrome. NCT02199054. *Active, not recruiting.*
- 18. Yael Vodovotz. Black Raspberry Confection in Preventing Oral Cancer in Healthy Volunteers. NCT01961869. *Active, not recruiting.*

# Appendix III

# **Budget and Spending**

	FY2020	FY2021	FY2022			
Beginning Fund Balance						
CAFFRE Annual Fund Gift Account (GF313955)	0.00	100.00	6.16			
Fueling the Cure Co-op (GF641441)	2,901.63	30,117.93	47,810.84			
CAFFRE Operating Funds (GR111409)	197,753.72	134,001.79	69,689.33			
Total Beginning Balance	200,655.35	164,219.72	117,506.33			
Income						
CAFFRE Annual Fund Gift Account (GF313955)	100.00	0.00	0.94			
Fueling the Cure Co-op (GF641441)	27,216.30	34,432.91	35,395.12			
CAFFRE Operating Funds (GR111409)	0.00	0.00	0.00			
Total Income	27,316.30	34,432.91	35,396.06			
Operating Expenses						
Salaries						
Program Manager	25,892.25	28,224.03	30,607.41			
Director	28,520.00	26,469.30	27,943.19			
Associate Director	4,464.00	4,471.77	4,545.65			
Miscellaneous	2.86	17.01				
Total	58,879.11	59,182.11	63,096.25			
Program Expenses						
Seminars and programs	4,872.82	5,233.19	1,000.00			
CAFFRE seed grants		16,740.00	50,000.00			
Travel support			500.00			
Conference sponsorships			1,000.00			
Total	4,872.82	21,973.19	52,500.00			
Total Expenses						
Total	63,751.93	64,490.00	115,596.25			
End of Year Balance	164,219.72	134,162.63	37,306.14			
			*Projected			