

## CFAES Center and Program Annual Review



# C · A · F · F · R · E

From **Crops** to the **Clinic** to the **Consumer**

**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:** October 11, 2022

**Number of Active Members:** 115

**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.*

**Contents**

Impact ..... 3

Active Grants and Contracts ..... 7

Publications..... 8

Student and Post Doc Accomplishments ..... 8

Intellectual Property ..... 9

Outreach Efforts..... 9

Challenges, Limitations and Bottlenecks ..... 9

Budget ..... 10

Goals for 2023..... 11

## Impact

### **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.

CAFFRE has also funded several seed grants for interdisciplinary research. Some of these are detailed below. 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 2023.

### ***Impact of Diet (Chow vs Semipurified) on Immune Responses and Microbiome during Oral Carcinogenesis***

Co-PIs: Dr. Steve Oghumu, Dr. Darrion Mitchell, Dr. Steve Clinton

Project budget - \$25,000

**Overview:** The goal of this research was to determine the impact of diet on oral cancer development in immunocompetent and immune-deficient mice. Oral cancer is common and deadly. It comprises about 85% of head and neck cancers, which is the 6th most commonly occurring cancer worldwide. Despite advances in oral cancer treatment, survival rates have not improved beyond 51% over the past 3 decades. Understanding how diet affects immune responses to oral cancer development is crucial to the design of complementary approaches to the prevention and treatment of oral cancer. This research was a key step in the development of optimal rodent models of oral carcinogenesis. For decades investigators utilized “laboratory chow” for mice in research settings, yet these diets are prepared from components found in the market to meet minimal defined standards, but contain a large array of different plant materials, grains, legumes, grasses, and other components based upon what is available in the market at the best cost. Thus, laboratory chow is variable in geographic locations and over seasons and time. It is an uncontrolled variable that can impact carcinogenesis. In comparisons, nutritional scientists typically use a semi purified diet, devoid of natural plant materials and phytochemicals, but consistent and reproducible. This research tested the hypothesis that a natural chow diet (such as in regular chow) favorably impacts host immunity to oral cancer in immunocompetent and in STAT1/STAT4 deficient mice, compared to semi-purified diet (such as in AIN-93G).

**Impact:** Based on the secondary objectives of the award, the following papers and grants (ongoing and pending) have resulted.

#### *Publications (Published):*

Nedungadi D, **Ryan N**, Anderson K, Lamenza FF, Jordanides PP, Swingler MJ, Rakotondraibe L, Riedl KM, Iwenofu H, **Oghumu S**. Modulation of the oral glucocorticoid system during black raspberry mediated oral cancer chemoprevention. *Carcinogenesis*. 2021 Dec 9;bgab118. doi: 10.1093/carcin/bgab118. Online ahead of print. PMID: 34888650. PMCID: PMC8832455 (**Published**) (**IF: 4.944**)

*Publications (Pending):*

Ryan NM, Lamenza FF, Upadhaya P, Pracha H, Springer A, Swingler M, Siddiqui A, **Oghumu S**, Black Raspberry Extract inhibits Regulatory T Cell activity in a Murine Model of Head and Neck Squamous Cell Carcinoma Chemoprevention. (2022). Submitted to *Frontiers in Immunology*.

*Grants (Funded):*

Period of funding:	09/01/2021 – 08/31/2022
Title of grant:	Defining the role of the oral glucocorticoid system in oral carcinogenesis and its modulation for improved treatment outcomes.
Source and amount of funding:	U.S. National Institutes of Health (\$561,415.00 Total)
Amount allocated to candidate:	\$561,415.00
Grant/Contract:	National, competitive, peer reviewed, Research Grant High Priority, Short-Term Project Award (R56DE030093)

*Grants (pending):*

Date of submission:	02/05/2022
Title of project:	Defining the role of the oral glucocorticoid system in oral carcinogenesis and its modulation for improved treatment outcomes.
Funding agency:	National Institutes of Health (NIH/NIDCR) R01 Research Grant Proposal

***Production and Characterization of Eicosapentaenoic Acid by Yarrowia Lipolytica***

PI: Dr. Yael Vodovotz

**Project Budget - \$6,500**

**Overview:** In the 2015-2020 Dietary Guidelines for Americans, it was recommended to consume 8 oz of seafood per week, providing an average of 250 mg of the polyunsaturated fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). In addition to the cardiac benefits, there is also evidence that omega-3 polyunsaturated fatty acids EPA and DHA inhibit tumor growth in some cancers. A reduction in inflammatory markers has also been found in multiple studies. Sustainability challenges along with dietary restrictions and allergens of fish have led to the search for non-fish sources of long chain PUFAs including EPA and DHA. Currently some sustainable alternatives to fish oil do exist commercially. Algae is the main source of sustainable long chain PUFAs. However, the most common strains of algae used commercially produce almost solely DHA and little EPA. To combat the lack of EPA availability from non-fish sources, scientists at DuPont genetically engineered strains of *Yarrowia lipolytica* that can produce an oil that is over 50% EPA. In fish oil, the ratio of EPA to DHA ranges from 0.6 (cod liver oil) and 1.5 (menhaden oil) according to the USDA FoodData Central . Using the commercially available algal DHA and genetically engineered *Yarrowia lipolytica*-produced EPA, an oil

could be made that contains optimal levels of both PUFAs at custom ratios for desired clinical outcomes. The goals of this research were to recreate and optimize the production of EPA from high producing strains of *Yarrowia lipolytica* and analyze the fatty acid profiles of microbially produced EPA oil, commercially available algal oil, and fish oils using gas chromatography.

**Results:**

The optimal conditions for *Y.lipolytica* cell growth and oil accumulation were determined. Cells were able to produce approximately 25% of dry cell weight oil and 31% of total oil was EPA.

**Impact:**

This research will be utilized in further research studies that will utilize yeast-based EPA oil in plant milk beverages. Additionally, several publications are in the process of being prepared.

*Grant (Funded):*

Period of funding:	04/01/2020 – 12/31/2021
Title of grant:	Development of EPA- and DHA-fortified plant milks for use in clinical studies.
Source and amount of funding:	CFAES Internal Grants Program
Amount allocated to candidate:	\$4,000

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

Co PIs: Dr. Richard Bruno, Dr. Yael Vodovotz, and Dr. Joanna Hodges

**Project Budget: \$16,740**

**Overview:**

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***

PI: Dr. Martha Belury

**Project Budget: \$23,584**

**Overview:** 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 hyperinflammation. 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. The two aims of this study were to set temporal markers of neuromuscular and neuro-immunologic alterations in the C-26 cachexia model and to determine the neuromuscular and neuro-immunologic effects of naringenin on C-26 induced cachexia. These studies will lead to an R01 submission to identify the neuromuscular and neuro-immunologic mechanisms of naringenin to slow the trajectory of cancer cachexia.

## Active Grants and Contracts

### 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 2022, \$246,444 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 \$406,474 for 76 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. Many of these grants involved multiple CAFFRE investigators across disciplines. In 2022, one grant was distributed. We intent to accept more applications for additional grants.

#### *Attenuation of Cancer Cachexia by Flavonoids: Identifying the Neuromuscular and Neuroimmunologic Effects of Naringenin – Dr. Martha Belury*

Cancer cachexia is characterized by the loss of skeletal muscle that results in functional impairment, dysregulated metabolism and reduced quality of life. Naringenin is a flavonoid found in grapefruit that is protective against loss of muscle strength and the onset of insulin resistance and hyper-inflammation. In addition, previous studies have indicated that despite weight loss, mice with cancer cachexia fed a diet with naringenin were more physically active.

The aims of this study are to set markers of neuromuscular and neuroimmunologic alterations in a cachexia mouse model and determine the effects of naringenin in this model.

## Publications

CAFFRE faculty published over 180 peer-reviewed articles during 2022. Of these, 24 were related to functional foods. 21 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. A list of selected publications is presented in Appendix II.

## Student and Post Doc Accomplishments

Students and post-doctoral scholars presented at several local, national, and international conferences in 2022.

Abstracts were submitted and presented at conferences including the following.

- American Association for Cancer Research Annual Meeting
- American Diabetes Association Meeting
- American Society of Hematology Meeting
- American Society of Clinical Oncology Meeting
- The Society for Immunotherapy of Cancer Annual Meeting
- Institute of Food Technologists Annual Meeting
- Food Structure and Functionality Symposium
- American Dairy Science Association Annual Meeting
- American Oil Chemists Society Annual Meeting
- American Society of Nutrition Annual Meeting
- College of Food, Agricultural and Environmental Sciences Research Forum
- Hayes Graduate Research Forum
- Klein Research Forum
- Interdisciplinary Research Fall Forum
- Foods for Health Annual Meeting

Some other achievements by students and post-docs of CAFFRE faculty follow.

Daniel Do, a graduate student in Dr. Jessica Cooperstone's lab, won second place in the University 2022 Interdisciplinary Research Fall Forum for his poster "Pharmacokinetics of tomato steroidal alkaloids in healthy adults following consumption of two doses of tomato juice."

Jennifer Janovick, a PhD student working under Dr. Emmanuel Hatzakis, was selected to receive funding for her proposal to the Alumni Grants for Graduate Research and Scholarship Competition.

A paper written by post-doc Joana Ortega-Anaya and Dr. Rafael Jimenez-Flores was recognized as among the 100 most highly cited papers published in the Journal of Dairy Science, "Symposium Review: The relevance of bovine milk phospholipids in human nutrition-Evidence of the effect on infant gut and brain development."



## Intellectual Property

Functional food research often leads to intellectual properties. 5 patents were awarded to CAFFRE members in 2022, with several more filed. One example was filed by Dr. Michael Bailey for “Prebiotic Formulations and Methods for Use”.

Additionally, invention disclosures on functional food products were filed with the university in 2022 including those for green tea confections and omega-3 fortified plant milk beverages.

## Outreach Efforts

In order to enhance collaboration between CAFFRE members and reach out to other potential members and collaborators, CAFFRE hosts groups meetings and seminars. Seminars are advertised within multiple departments in the University to encourage attendance of new members.

Seminars in 2022 included the following:

### **1/27/2022 | Updates from CAFFRE members in various disciplines**

Speakers: Dr. Steven Clinton, Dr. Beth Grainger, Dr. Jessica Cooperstone, Dr. Colleen Spees, Dr. Martha Belury

### **4/28/2022 | Fiber and Health**

Speakers: Dr. Osvaldo Campanella and Dr. Chris Zhu

### **10/11/2022 | Research Presentations**

Speakers: Dr. Richard Bruno and Dr. Steven Clinton

## Challenges, Limitations and Bottlenecks

CAFFRE has been well funded through Fueling the Cure since 2009. These funding is primarily used to fund see grants. Funding for general operation and salaries has been limited. Therefore, CAFFRE will need to adapt programming and seek new sponsorship to meet budget goals.

Since the COVID-19 pandemic began, attendance at in person and online meetings has lacked. There is reduced motivation to attend extra meetings. CAFFRE has combatted this by offering both in-person and Zoom options and providing lunch or heavy snacks at meetings.

## Budget

### Budget and Spending

	FY2022	FY2023*
<b>Beginning Fund Balance</b>		
Fueling the Cure Co-op (GF641441)	47,810.84	51,762.20
CAFFRE Operating Funds (GR111409)	69,680.33	17,342.56
<b>Total Beginning Balance</b>	<b>117,491.17</b>	<b>69,104.76</b>
<b>Income</b>		
CAFFRE Annual Fund Gift Account (GF313955)		
Fueling the Cure Co-op (GF641441)	35,395.12	42,199.63
CAFFRE Operating Funds (GR111409)		
<b>Total Income</b>	<b>35,395.12</b>	<b>42,199.63</b>
<b>Operating Expenses</b>		
Salaries		
<i>Program Manager</i>	17,159.25	12,334.97
<i>Director</i>	27,943.19	29,089.74
<i>Associate Director</i>	4,545.67	4,545.67
Miscellaneous		
<b>Total</b>	<b>49,648.11</b>	<b>45,970.38</b>
<b>Program Expenses</b>		
Seminars and programs	2,189.66	2,000.00
CAFFRE seed grants	31,443.76	30,000.00
Travel support	500.00	1,000.00
Conference sponsorships		
<b>Total</b>	<b>34,133.42</b>	<b>33,000.00</b>
<b>Total Expenses</b>		
<b>Total</b>	<b>83,781.53</b>	<b>78,970.38</b>
<b>End of Year Balance</b>	<b>69,104.76</b>	<b>32,334.01</b>
		*Projected

The main expenses incurred by CAFFRE are seed grants to CAFFRE members, programming supplies, and salaries of directors and administrative staff. Current income streams from the Fueling the Cure Coop.

## Goals for 2023

The goals for 2023 are to increase student engagement in CAFFRE. This will be achieved with at least monthly seminars targeted towards graduate students and other trainees. These seminars will be in the form of casual coffee hours hosted by an expert. The topics were sourced from interested students currently involved with CAFFRE and in the departments of food science and technology, horticulture and crop science, and the OSU nutrition program.

Seminars will include a 10-minute presentation by an expert in the area, followed by an open question and answer period. Questions will be prepared in advance by the program coordinator if needed. Coffee and light snacks will be provided.

A tentative seminar schedule is proposed below, with the first seminar planned for January 24.

Date	Topic
1/24/23	Functional food product development considerations
2/7/23	Developing or choosing an appropriate control
2/21/23	Functional food physical and chemical analysis methods
3/7/23	Updates in cancer treatment
3/28/23	Sample size calculation
4/11/23	Nutrition clinical trial design best practices
4/25/23	Measuring nutrient intake and the diet

Additionally, we will continue to engage CAFFRE faculty mentors through member meetings and provide seed grants to help facilitate collaborative research projects.

## Appendix I: List of CAFFRE Members

College	Name	Department
Education and Human Ecology	Martha Belury	Human Sciences
	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 Environmental Science	Josh Blakeslee	Horticulture and Crop Sciences
	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
	Joseph Scheerens	Horticulture and Crop Sciences
	Christopher Simons	Food Science and Technology
	Yael Vodovotz	Food Science and Technology
Health and Rehabilitation Sciences	Nicholas Funderburg	Medical Laboratory Science
	Colleen Spees	Medical Dietetics
	Chris Taylor	Medical Dietetics
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
	Thomas Mace	
	Darrion Mitchell	Radiation Oncology
	Amir Mortazavi	Internal Medicine
	Tatiana Oberyszyn	Pathology
	Kristen Roberts	Internal Medicine
	Fred Tabung	Internal Medicine
	Kathleen Tober	Pathology
Nursing	Sonia Duffy	Nursing
Public Health	Thomas Knobloch	Environmental Health Sciences
	Steve Oghumu	Environmental Health Sciences
	Susan Olivo-Marston	Epidemiology
Veterinary Medicine	Nong Inpanbutr	Veterinary Biosciences

## Appendix II: Selected Publications

Shuai Ren, Luis Rodriguez-Saona, and **M. Monia Giusti**. Analyzing the Interaction between Anthocyanins and Native or Heat-Treated Whey Proteins Using Infrared Spectroscopy. *molecules*, 2022, 27(5).

Nathan M. Ryan, Felipe F. Lamenza, Puja Upadjaya, Husan Pracha, Anna Springer, Michael Swingler, Arham Siddiqui, and **Steve Oghumu**. Black raspberry extract inhibits regulatory T-cell activity in a murine model of head and neck squamous cell carcinoma chemoprevention. *Frontiers in Immunology*, 2022.

Geoffrey Sasaki, **Yael Vodovotz**, Zhongtang Yu, and **Richard S. Bruno**. Catechin Bioavailability Following Consumption of a Green Tea Extract Confection Is Reduced in Obese Persons without Affecting Gut Microbial-Derived Valerolactones. *Antioxidants*, 2022, 11(12).

Minu Thomas, Marissa DiBella, Christopher Blesso, Olga Malysheva, Marie Caudill, Maria Sholola, **Jessica Cooperstone**, and Maria Luz Fernandez. Comparison between Egg Intake versus Choline Supplementation on Gut Microbiota and Plasma Carotenoids in Subjects with Metabolic Syndrome. *Nutrients*, 2022, 14(6).

Láisa Gomes Dias, Adriele Hacke, Ernane dos Santos Souza, Seema Nath, Miriam Regina Canesin, Omar Vieira Vilella, Bruno Geloneze, Juliana Azevedo Lima Pallone, Cíntia Baú Betim Cazarin, **Joshua John Blakeslee**, Lilian Regina Barros Mariutti, and Neura Bragagnolo. Comparison of chemical and nutritional compositions between aromatic and non-aromatic rice from Brazil and effect of planting time on bioactive compounds. *Journal of Food Composition and Analysis*, 2022, 11.

Xiaowei Sun, Priyankar Dey, **Richard S. Bruno**, and **Jiangjiang Zhu**. EGCG and catechin relative to green tea extract differentially modulate the gut microbial metabolome and liver metabolome to prevent obesity in mice fed a high-fat diet. *The Journal of Nutritional Biochemistry*, 2022, 109.

Cong W, Tello E, **Simons CT**, Peterson DG. Identification of Non-Volatile Compounds That Impact Flavor Disliking of Whole Wheat Bread Made with Aged Flours. *Molecules*. 2022; 27(4).

Cole, R. M., Angelotti, A., Sparagna, G. C., Ni, A., & **Belury, M. A.** Linoleic Acid-Rich Oil Alters Circulating Cardiolipin Species and Fatty Acid Composition in Adults: A Randomized Controlled Trial. *Molecular Nutrition & Food Research*, 2022, 66(15).

Nedungadi, Divya, 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*, 2022, 43(1).

Sommer, Abigail A., and **Yael Vodovotz**. Soy enhanced soft pretzels designed for exercise recovery. *Journal of Functional Foods*, 2022, 94.