**IAFNS Gut Microbiome Committee**

**Request for Pre-Proposals**

**February 2023**

**Investigation of the Relationship Between Live Dietary Microbe Intake and Health Outcomes**

The Institute for the Advancement of Food and Nutrition Sciences (IAFNS) is a non-profit, 501(c)(3) scientific organization that pools funding from industry collaborators and advances science through the in-kind and financial contributions from public and private sector participants.

The IAFNS Gut Microbiome Committee advances the science required to substantiate dietary modulation of the gut microbiome in ways that are conducive to health.

IAFNS adheres to rigorous procedures to maintain scientific integrity in all work we support. These requirements are described further in the attached TOP Guidelines and 9 Guiding Principles for Scientific Integrity addendums.

Pre-proposals meeting the following criteria may be invited to submit a full proposal (which would include detailed research plans that reflects the work to be completed, a budget, and timeline).

1. Team composed of persons with demonstrated expertise in food and nutrient intake analysis (such as with NHANES/WWEIA/FNDDS), and strong relevant publication record.

2. Rigorous and transparent research approach addressing the research objective.

3. Rough cost estimate and realistic timeframe.

**Background**

Evidence from human microbiome research, randomized controlled trials testing interventions containing probiotics on preventive and therapeutic endpoints, and associative studies linking fermented food consumption with improved health, all point to the value of the consumption of live microbes for supporting human health ([Marco et al. 2020](https://pubmed.ncbi.nlm.nih.gov/33269394/)). Various international organizations are interested in moving the concept of a dietary recommendation for live microbes forward. Although several researchers have independently hypothesized that consuming live microbes may be beneficial to health, understanding this relationship and developing a recommended intake range requires a systematic approach, including evaluation of existing evidence, addressing evidence gaps, and aligning the information with a framework of data needs required to support a recommendation.

One way to examine hypotheses that live dietary microbes impact health outcomes is through interrogation of existing datasets that include dietary information and health outcome metrics collected from study participants. As a first step to advancing this approach, ISAPP proposed a method for classifying foods in What We Eat in America (WWEIA) that could be used to estimate dietary intake of live microbes ([Marco et al. 2022](https://pubmed.ncbi.nlm.nih.gov/35583208/)). This system was recently applied by Han and Wang ([2022](https://www.mdpi.com/2072-6643/14/22/4908)) to examine live dietary microbe intake and associations with cardiovascular disease outcomes using NHANES. These authors identified a significant association between live dietary microbe intake and the prevalence of stroke and heart attack. Hill et al. (paper under review), similarly leveraged the WWEIA categorization scheme and NHANES survey data focused on a different set of health-related biomarkers.

The IAFNS Gut Microbiome Committee is interested in further evaluating live dietary microbe-health relationships by leveraging additional existing databases in secondary data analysis. This committee is seeking pre-proposals focused on (separately) 1) KNHANES specifically because of the potentially greater quantity and/or more frequent intake of foods containing live microbes, or 2) prospective longitudinal datasets to understand intake over time and health relationships. This document requests separate pre-proposals for analysis of each dataset.

*References:*

Han and Wang. 2022. Association of Dietary Live Microbe Intake with Cardiovascular Disease in US Adults: A Cross-Sectional Study of NHANES 2007–2018. Nutrients. 14(22), 4908; <https://doi.org/10.3390/nu14224908>

Marco et al. 2022. A Classification System for Defining and Estimating Dietary Intake of Live Microbes in US Adults and Children. J Nutr. 152(7):1729-1736. doi: 10.1093/jn/nxac074

Marco et al. 2020. Should There Be a Recommended Daily Intake of Microbes? J Nutr. 150(12):3061-3067. doi: 10.1093/jn/nxaa323

Hill et al. 2023. Positive health outcomes associated with live microbe intake from foods, including fermented foods, assessed using NHANES database. J Nutr. S0022-3166(23)12622-8.

 doi: 10.1016/j.tjnut.2023.02.019

**Specific Proposal Requirements**

Proposals must be directed at understanding associations between live dietary microbe intake and health outcomes using existing datasets. Particular attention will be paid to the approaches used for the following steps:

1. Quantifying intake of live microbes,
2. Categorization of intake by population subgroups of interest,
3. The statistical evaluation of associations between live microbe intake and health outcomes/biomarkers.

**Additional considerations**

* The committee is considering two separate projects. Please submit a pre-proposal for KNHANES or a prospective cohort dataset. One group can submit two separate pre-proposals, if desired.
* The approach proposed in Marco et al. 2022 is an option for classification of foods. However, the committee is open to other approaches, which should be clearly described.
* There are no scope limits for biomarkers or health outcomes, although those relationships that can be supported by some existing evidence or that address existing hypotheses would be of interest.
* Although KNANES is cross-sectional, other work should focus on prospective cohort datasets. Examples include EPIC, Nurse’s Health Study, Framingham, and the Dutch Lifeline Cohort among others (note that these datasets have not been vetted for appropriateness for addressing the question). There are no geographical limits for the selected dataset(s).
* Live microbes tend to be present in foods that are already considered healthy (such as fresh fruits and vegetables, fermented dairy) – the committee is interested in possible ways of accounting for this confounding fact.

**Pre-Proposal Content**

1. **Background:** Briefly describe background relevant to the project and proposed approach to address the research objective.
2. **Research Approach:**
* Overall methodology
* Questions to be answered
* Primary outcomes (and secondary if warranted) clearly identified
* Research approach in broad terms, including the source of data, methods to be used, and how data will be analyzed and presented.
1. **Research Team:** Principal investigator(s), co-investigators, key team members, and collaborators that may be affiliated but not part of the grant, indicating all potential conflicts of interest.
2. **Investigator Credentials:** Describe the experiences that make you and your team a candidate for carrying out this project. In addition, the CV of the principal investigator(s) is required. Demonstrated success publishing in this topic area in a quality peer-reviewed journal is a minimum criterion.
3. **Estimated budget range and timelines:** Please provide proposed budget (a range is acceptable), noting that if overhead is necessary, IAFNS limits overhead to 10% of total project costs. IAFNS will cover publication costs separately so they do not need to be included in the budget. Timelines should include both apresentation of results to committee by webinar, a submit date for a final manuscript in a top tier peer-reviewed journal for publication, and a potential 1-hour public webinar to share the results with the IAFNS audience.

Successful pre-proposals will be in the range of $40-60K.

1. **References**

Pre-proposals are to be submitted to Marie Latulippe (mlatulippe@iafns.org) by midnight eastern time, **March 22, 2023**. Pre-proposals should be submitted using the template shown below in the addendums, which is provided in a separate document for your use.

**Addendum for RFPs**

**IAFNS’s Guiding Principles for Funding Food Science**

**and Nutrition Research**

Background:

The scientific process requires open, transparent examination and honest interpretation of data, regardless of a researcher’s affiliation or source of funding. The following Guiding Principles1 address the potential influence of funding source on scientific research. All projects supported by IAFNS must adhere to these principles.

Guiding Principles for Funding Food Science and Nutrition Research:

In the conduct of public/private research relations, all relevant parties shall:

1. Conduct or sponsor research that is factual, transparent, and designed objectively; according to accepted principles of scientific inquiry, the research design will investigate an appropriately phrased hypothesis and/or question, rather than favor a particular outcome;

2. Require control of the study design, the research itself, and the interpretation of findings to remain with scientific investigators;

3. Not offer or accept remuneration geared to the outcome of a research project;

4. Prior to the commencement of studies, ensure that there is a written agreement that the investigative team has an obligation to attempt to publish the findings within some specified timeframe and the freedom to choose the journal to which the work will be submitted;

5. Require, in publications and conference presentations, full written or oral disclosure, as appropriate of all relevant relationships (financial and non-financial competing interests);

6. Not participate in undisclosed authorship arrangements in publications or presentations;

7. Guarantee accessibility to all data and control of statistical analysis by investigators and appropriate auditors/peer reviewers; when possible, encourage the practice of open science, including depositing data and methodology on a public repository;

8. Require that academic researchers, when they work in contract research organizations or act as contract researchers, make clear statements of their affiliation; require that such researchers publish under the auspices of the contract research organization;

9. Require, in publications and conference presentations, disclosure of whether the funder advised on the study design, conduct of research and/or the development of the manuscript.

**Adoption of the Center of Open Science’s**

**Transparency and Openness Promotion Guidelines by IAFNS**

Background: The Center for Open Science's [Transparency and Openness Promotion (TOP) Guidelines](https://www.cos.io/initiatives/top-guidelines) provide actionable steps for institutions to practice and promote transparent, reproducible, and rigorous research. IAFNS is a TOP Guidelines signatory. By becoming a signatory, IAFNS is supporting the principles expressed in the guidelines through their implementation by its funded researchers. The TOP Guidelines include eight modular standards for promoting transparent, reproducible and rigorous research, each with three levels of increasing stringency.

TOP Guidelines:

**1. Data Citation Standards (Level 3):** Cite shared data. Don’t publish until it is appropriately cited.

**2. Data Transparency (Level 2):** Data must be shared to the maximal extent allowed by ethical and legal constraints.

**3. Analytic Methods (Code) Transparency (Level 2):** Analytic methods (code) must be shared to the maximal extent allowed by ethical and legal constraints.

**4. Research Materials Transparency Level 2):** Materials must be shared to the maximal extent allowed by ethical and legal constraints.

**5. Design and Analysis Transparency (Level 2):** The researcher must use reporting guidelines when writing up publications. Equator-network website provides a huge choice of standards for research designs. <http://www.equator-network.org/> The researcher is asked to select one and register the standard you have selected.

**6. Study Preregistration (Level 2):** When the researcher preregisters his/her study in an independent, institutional registry (e.g., <http://osf.io/>, <https://www.crd.york.ac.uk/prospero/>, <http://clinicaltrials.gov/>), which is encouraged but not required, IAFNS will request a third party (e.g., Center for Open Science) verify that preregistration adheres to the specifications for preregistration before data collection.

**7. Analysis Plan Preregistration (Level 2):** When the researcher preregisters his/her study analysis plan in an independent, institutional registry (e.g., <http://osf.io/>, <https://www.crd.york.ac.uk/prospero/>, <http://clinicaltrials.gov/>), which is encouraged but not required, IAFNS will request a third party (e.g., Center for Open Science) verify for adherence to preregistered plan (deviations must be transparently reported) before data collection.

**8. Replication (Level 1):** IAFNS will occasionally put out a call for replication studies as part of our RFP process.

**Template IAFNS Pre-Proposal on**

 **Investigation of the Relationship Between Live Dietary Microbe Intake and Health Outcomes**

(2-page maximum, single space, 11 font minimum)

**Date:**

|  |  |
| --- | --- |
| **Lead Investigator, affiliated organization for the grant, email, phone** |  |
| **Overview of approach** (1-3 sentences) |  |

**Background** (1-3 sentences)

**Primary hypothesis**

* X

**Secondary hypotheses**

* X
* Y

**Research approach**

**Investigator credentials of PI, co-PI, co-investigators, and collaborators**

|  |  |  |
| --- | --- | --- |
| **Name** | **Affiliation** (Institution and department) | **Disclose potential conflicts of interest and all funding sources over $5,000 (2016+)** |
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**Attach PI/co-PI CV or NIH biosketch**

**Estimated budget and timeline**

Range with a clear estimated upper limit to costs inclusive of all direct and if necessary indirect costs (the latter of which are limited to 10%). Publication costs will be covered directly by IAFNS.

Estimated maximum time from agreement to submitted manuscript for publication.