Integrating Tradition and Technology for Fermented Foods for Maternal Nutrition

A Grand Challenge

THE OPPORTUNITY

Embracing the tradition of microbial fermentation to transform locally available foods into naturally vitamin-fortified, toxin-free, flavorful, and shelf-stable products could empower local communities to mitigate the impact of COVID-19 on supply chain/food security and improve the health and nutrition of mothers and children in the most vulnerable settings. Historical advances in food processing have largely employed strategies that involve supplementation with micronutrients and additives to improve nutritional content and stability, but these approaches require highly centralized supply chains.[1] In addition, chemical additives for preservation, flavor and texture purposes may have unintended consequences of contributing to compromised gut health and increased prevalence of metabolic disease (hypertension, diabetes, obesity).[2]

Fermentation is an ancient practice through which locally-sourced food substrates can be transformed naturally by environmentally occurring microbes. These processes are thought to be intricately intertwined with human biology, and it is hypothesized that our primate ancestors adapted to natural fermentation processes millions of years ago.[3] While many fermented foods (e.g., yogurt, cheese, coffee and alcohol) remain popular, certain types of fermentation are a dwindling art in many settings, representing a loss of cultural heritage and a natural way to improve the qualities of foods across several distinct axes[4]:

- Improve macro- and micro-nutrient quality and bioavailability (e.g., B vitamins)[5]
- Remove anti-nutrients (mycotoxins; phytates, which decrease iron availability)[6]
- Transform taste, flavor and texture[7]
- Improve the preservation and stability of foods by excluding pathogens (through lowering pH, bacteriocin production, removing simple sugars)[8]

Historical approaches of macronutrient supplementation and micronutrient fortification have been the basis for transformative global health nutrition interventions, ultimately saving millions of lives each year.[9] These approaches have also focused on pediatric populations, although recent work suggests that solutions targeting maternal nutrition may be even more impactful on pediatric health and have the important benefit of also improving maternal health.[10] Given limited access of nutritional interventions by the populations in greatest need[11] and formulations that are not optimized for gut and metabolic health,[12] malnutrition remains one of the most significant global health problems facing society today.

COVID-19, with disruption of supply chains and a predilection for individuals with metabolic diseases, has served to increase the urgency for identifying locally-sourceable health-promoting maternal nutrition solutions that treat undernutrition without increasing the risk of obesity, diabetes, and hypertension. Ironically, it may be that these new solutions already exist in the form of ancient traditions reevaluated and revalued through a next-generation and evidence-based lens.

THE CHALLENGE

Beyond many of the well-known examples of microbial fermentation, the vast majority of fermentation processes around the world remain uncharacterized and their potential human health benefits are unknown. These ancient practices may hold the key to impactful and locally targeted nutritional interventions that combine tradition and science to tackle malnutrition. Rigorous scientific evaluation has been limited and characterization to understand potential benefits could be pursued to validate and underscore the importance of preserving this cultural heritage.

What we are looking for

This call seeks to fund pilot studies that investigate the biological effect of traditional locally fermented foods on key microbiome, gut, and health biomarkers in local populations. The goal is to provide investigators in Sub-Saharan Africa and South Asia with the resources to build local capacity to investigate fermented foods as novel maternal nutrition interventions. In particular, sequencing technology – a transformative tool that has enabled in-depth investigation of microbial communities – will be provided to all investigators to democratize the ability to investigate foods and health effects, and build local capacity. Ultimately, the goal is to empower local communities to develop geography and culture specific interventions powered by fermentation, in country.

Proposals should specifically address the following core elements, but investigators are welcome to propose creative strategies and designs to accomplish the core goals of this call and account for local cultural traditions. In addition, it is expected that study design will be refined after award through a collaborative forum invovling other awardees and the foundation:

- Identification of a local (geographic/cultural) fermented food for study
    - Many foods may not be colloquially considered to be fermented, but any process that incorporates biotransformation by microbes is acceptable
    - Living microbes were actively employed as a part of the fermentation process and final product consumed retains live organisms
    - Fermentation may be driven by known organisms, e.g. bacterial *Lactobacillus* sp., fungal *Aspergillus* sp., or less studied food-borne organisms
    - Must be plant-based (e.g., grains, pulses or staple crop). Plant-based fermented foods are a requirement due to lower cost of goods for scalability compared to animal-based foods
    - Food with a cultural precedent in maternal nutrition are of high interest
    - The food being investigated must be produced in compliance under all relevant local food manufacturing regulations and modern food safety practices

- Pilot study design for longitudinal intervention study for understanding the effect of the fermented food in a naïve (no, or limited, fermented food consumption) population
    - The target population should be women of reproductive age, and a naive population not currently consuming or with limited consumption of the target fermented food to better understanding the biological effects of the food itself. Different subpopulations (urban vs. rural, various cultural groups, different sub-geographies within a country, etc.) with lower consumption of the target fermented food could be specifically targeted. If populations traditionally consuming fermented foods are considered, it would be important to undertake a baseline to understand the additive effect after consumption of “target foods”.

    - Longitudinal intervention studies are recommended, with small cohort sizes (20-30 participants) and sustained exposure to the fermented food (e.g., at least daily >5 days) but ultimately the study design should be motivated by the end goal of characterizing the effects of the food on maternal nutrition through host (blood and fecal) and gut microbiome biomarkers.
    - A template dietary questionnaire will be provided and can be customized to local foods and traditions
    - Existing infrastructure that may improve ability to execute on the proposed study can and should be highlighted

- Biological sample biobanking and characterization before and after food intervention
    - Fermented foods themselves (metagenomic analysis of fungal [ITS] and bacterial [16S] constituents), potentially across distinct batches and preparation methods
    - Serial fecal samples from participants (metagenomic analysis; lipocalin-2, myeloperoxidase, and calprotectin of particular interest)
    - Serial serum/blood samples from participants (Iron studies, B-vitamin analysis; lipocalin-2, IL-6 and CRP are of particular interest given the association of inflammation biomarkers with maternal nutrition and birth outcomes) [13]
    - Other characterization approaches of food (including effects of fermentation on the nutritional profile) or biological samples using conventional or existing techniques
    - Proposals should specifically address existing laboratory infrastructure and capacity for integrating next generation sequencing into existing laboratory workflows (e.g. nucleic acid extraction, PCR, etc.)

As a part of this Grand Challenges award, sequencing platforms (funded with up to USD $40K for sequencing technology out of this USD $200K award) and training will be provided to investigators to enable local sequence-based characterization of the fermented foods and microbiome effects. The output of this study will be pilot data evaluating the biological effect of traditional fermented foods on gut, microbiome and health axes in local populations. Any additional points on the sustainability of the intervention and the empowerment of local champions to continue the work, integrating with state and national level Maternal, Infant and Young Child Nutrition (MIYCN) programs would also be welcome.

What we will not consider funding

- Investigators and institutions not located in Sub-Saharan Africa or South Asia
- Investigators not studying local foods (specific to the culture or geography)
- Investigators not investigating local populations
- Proposals that do not contain a human interventional study targeted towards women of reproductive age. No studies on child populations will be funded.
- Proposals not addressing all the stated study design criteria above
- Proposals that do not demonstrate a capacity to perform the research proposed; investigators should describe capacity for human studies, sample collection, processing and storage, including but not limited to:
    - Relevant approvals from local authorities/institutions/Government on the research methodology and sharing of data among collaborators, eventually for global access
    - Data analysis and adherence to relevant local laws/ policies pertaining to data sharing, hosting and data protection.
    - Secure handling of personally identifiable information data and research results

- Institutional Review Boards or equivalent human study regulation strategy
- Sample collection capacity/protocols and capacity for sample storage
- Ability to perform human biological sample characterization as proposed

References

[1] https://www.fao.org/3/a-i3953e.pdf
[2] https://www.nature.com/articles/nature14232/
[3] https://www.pnas.org/content/112/2/458
[4] https://www.sciencedirect.com/science/article/pii/S0958166919300990
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