The Integrated Impact of Diet On Human Immune Response, the Gut Microbiota, and Nutritional Status During Adaptation to a Spaceflight Analog

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ABSTRACT

Spaceflight impacts human physiology, including well documented immune system dysregulation. Diet, immune function, and the microbiome are interlinked, but diet is the only one of these factors that we have the ability to easily, and significantly, alter on Earth or during flight. As we understand dietary impacts on physiology more thoroughly, we may then improve the spaceflight diet to improve crew health and potentially reduce flight-associated physiological alterations. It is expected that increasing the consumption of fruits and vegetables and bioactive compounds (e.g., omega-3 fatty acids, lycopene, flavonoids) and therefore enhancing overall nutritional intake from the nominal shelf-stable, fully-processed space food system could serve as a countermeasure to improve human immunological profiles, the taxonomic profile of the gut microbiota, and nutritional status, especially where currently dysregulated during spaceflight. This interdisciplinary study will determine the effect of the current shelf-stable spaceflight diet compared to an “enhanced” shelf-stable spaceflight diet (25% more foods rich in omega-3 fatty acids, lycopene, flavonoids, fruits, and vegetables). The NASA Human Exploration Research Analog (HERA) 2017 missions, consisting of closed chamber confinement, realistic mission simulation, in a high-fidelity mock space vehicle, will serve as a platform to replicate mission stressors and the dysregulated physiology observed in astronauts. Bio sampling of crewmembers will occur at selected intervals, with complete dietary tracking. Outcome measures will include immune markers (e.g., peripheral leukocyte distribution, inflammatory cytokine profiles, T cell function), the taxonomic and metatranscriptomic profile of the gut microbiome, and nutritional status biomarkers and metabolites. Data collection will also include complete dietary tracking. Statistical evaluations will determine physiological and biochemical shifts in relation to nutrient intake and study phase. Beneficial improvements will provide evidence of the impact of diet on crew health and adaptation to this spaceflight analog, and will aid in the design and development of more-efficient targeted dietary interventions.

OBJECTIVE

Implement a ground-control study with HERA analog crew randomized between either the current nominal ISS food system or a spaceflight food system designed to improve dietary quality. Determine the effects of each diet on immune dysregulation, including leukocyte distribution, inflammatory cytokine profiles, T cell function, and other relevant immunological markers, the taxonomic and metatranscriptomic profile of the gut microbiome, and nutritional biomarkers and metabolites at selected intervals, and statistically evaluate to associate shifts across each measure and in relation to nutrient intake.

Spaceflight Food System: Potential Countermeasure for Physiological Changes

The food system is one of only a few daily environmental influences that is greatly modifiable for spaceflight and has the potential to promote health.

CURRENT ISS SPACEFLIGHT DIET

200 options in 8 Standard Menu Categories

1. Breakfast
2. Rehydratable Meats
3. Meat and Fish
4. Side Dishes
5. Vegetables and Soups
6. Fruits and Nuts
7. Desserts and Snacks
8. Beverages

Limited condiments
No food refrigeration

The food system is one of only a few daily environmental influences that is greatly modifiable for spaceflight and has the potential to promote health.

Immunodysregulation, changes in nutritional status, and changes in the gastrointestinal microbiota have occurred in spaceflight.

Diet and nutritional status is linked to the gastrointestinal microbiota and immune status on Earth.

Increasing consumption of fruits, vegetables, and other foods rich in bioactive components (e.g., omega-3 fatty acids, lycopene, flavonoids) and enhancing overall nutritional intake during spaceflight (or a ground-based analog of spaceflight) is expected to improve human immunological profiles, the taxonomic profile of the gut microbiota, and nutritional status biomarkers and will provide evidence to better inform the impact of diet on crew health and adaptation to spaceflight.

METHODS

Implement a study in the Human Exploration Research Analog (HERA) to Determine the impact of an ‘enhanced’ spaceflight diet compared to the current spaceflight diet on immune markers, nutritional status, and the gut microbiota.

The study will occur in 2017 in HERA Campaign 4.

Analog Attributes:
- Astronaut-like crews and work schedules
- Mimics stressful and isolated conditions
- Altered sleeping patterns
- Closed-system spaceflight
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Mission plan:
- 4 - 45 day missions
- 2 missions current ISS spaceflight diet
- 2 missions enhanced spaceflight diet
- 4 subjects per diet

The HERA missions will provide a ground-control for baseline physiological data that results from each diet.

EXPECTED OUTCOMES

This effort will provide pilot data and a ground-control for the impacts of the spaceflight diet on human adaptation to spaceflight. The enhanced diet is expected to:

- Improve nutritional biomarkers and metabolite concentrations (increases in omega-3 fatty acid, flavonoids, and SCFAs in blood, urine, and fecal samples, and decreases in oxidative damage)
- Improve general immune status and mitigate dysregulation, as demonstrated by improvements in T cell function, plasma and secreted cytokine profiles and inflammatory markers that may be associated with target nutrients in the diet.
- Improve overall taxonomic profile of the gut microbiota, such as increments in species diversity, which has been associated with improved gut homeostasis and human health.
- Indicate genes and pathways that participate in the functional response of the gut metagenome to changes in diet habit and environmental factors such as stress. It is expected that among affected genes and pathways will be those that participate in the processing of high-fiber, flavonoid-, lycopene- and omega 3-rich food and in the synthesis of SCFAs and butyrate in the case of samples derived from the enriched-diet cohort.
- Identify genes and pathways whose expression patterns might indicate potential risks to human health, such as downregulation of antibacterial genes or pathways that participate in the production of essential metabolites.

EXPECTED OUTCOMES

Determine the effect of each spaceflight diet on crew immune markers, nutritional status, and the microbiome throughout the mission.

BIological Samples and Analysis

Biological Samples will be obtained at 2 pre-mission timepoints and 3 in-mission timepoints (△) to determine the effect of each spaceflight diet on crew immune markers, nutritional status, and the microbiome throughout the mission.

<table>
<thead>
<tr>
<th>Biological Sample</th>
<th>Analysis</th>
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<tbody>
<tr>
<td></td>
<td>Nutrition: HPLC-MS, HPLC-ESI-MS, GC-MS - Vitamin and mineral status, flavonoids, omega-3 and -6, oxidative markers</td>
</tr>
<tr>
<td>Urine</td>
<td>Nutrition: HPLC-MS, HPLC-ESI-MS: Vitamin and mineral status, flavonoids, oxidative markers</td>
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<tr>
<td>Fecal</td>
<td>Microbiome: 16S Sequencing: Taxonomic Profiling</td>
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<td></td>
<td>Nutrition: HPLC/UV-VIS – butyrate, acetate, propionate</td>
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<tr>
<td>Saliva</td>
<td>Immune: Cytometric Bead Array – Salivary cytokine profiles</td>
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<tr>
<td>Diet Record</td>
<td>Daily: ISS FIT app</td>
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<tr>
<td>Body Weight</td>
<td>Daily</td>
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</tbody>
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Statistical associations will be evaluated across each measure and in relation to nutrient intake. The primary aim is to measure effect sizes and variability so we will have a better understanding of the magnitude of the effect of the enhanced diet, and the power to determine the effects in a spaceflight environment when the proposed diet transitions to spaceflight.

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