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 enhance overall nutritional intake from the nominal shelf-food, 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.

Enhanced Diet Will: Expected Benefits:

- Increase Fruit and Vegetable Consumption
  - Improved nutritional status/bone health
  - Reduced inflammation/Immunomodulation
  - Improved microbiota diversity
  - Increased short chain fatty acid (SCFA) production

- Increase fish/omega-3 consumption
  - Improved nutritional status/bone health

- Increase lycopene consumption
  - Improved nutritional status/bone health
  - Decreased oxidative damage

- Provide 1000-1200 mg Ca/day
  - Improved nutritional status/bone health

- Reduce sodium intake
  - Improved nutritional status/bone health

<table>
<thead>
<tr>
<th>Standard Diet</th>
<th>Enhanced Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>48</td>
</tr>
<tr>
<td>2-3</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>921</td>
<td>1177</td>
</tr>
<tr>
<td>2955</td>
<td>2655</td>
</tr>
</tbody>
</table>

Spaceflight Food System: Potential Countermeasure for Physiological Changes

- **CURRENT ISS SPACEFLIGHT DIET**
  - 200 options in 8 Standard Menu Categories
  - Freezer-Orient
  - Low-Moisture
  - Refrigerated Thermostabilized or Inertiated
  - Powdered Beverages

- **Immune dysregulation, 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 compounds (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 and to design targeted more-efficient dietary interventions.**

- **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.

- **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 activated 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.

**Acknowledgments**

Members of the Space Food Systems Laboratory, Nutritional Biochemistry Laboratory, Immune Laboratory, and Flight Analogs Personnel at JSC, and associated laboratories at JFC for assistance with procedures and HERA mission setup.