Probiotics in the Space Food System: Delivery, Microgravity Effects, and the Potential Benefit to Crew Health

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Influences are Environment, stress, mood, and health:
- Microgravity
- Sleep shift
- Temperature
- Air Quality
- Light
- Exercise
- Antibiotics/Meds
- Pathogens

**FOOD**

**HUMAN GENETICS AND EPIGENETICS**

**MICROBIOME**
- 90% of cells in the human are microbe, impacted by external factors

**OPTIMUM HUMAN STATE**

**FOOD SYSTEM**
- Daily environmental influence that is greatly modifiable

**EFFECTS:** Cardiovascular, bone, muscle, behavioral health and performance, immune response, etc.
Probiotics

- **Why?**
  - Why probiotics?

- **How?**
  - How do we deliver probiotics in spaceflight?
  - How do probiotics respond to microgravity?

- **What?**
  - What is the human response to probiotics in microgravity?

[Image sources](http://www.livestrong.com/article/355913-list-of-fermented-milk-products/)
WHY: Probiotics?

HUMAN STATE IN SPACEFLIGHT

Stress, Anxiety, Depression
(Slack et al. 2009)

Elevated inflammatory cytokines
(Crucian et al. 2014)

Reduced immune cell function
(Crucian et al. 2008)

POSSIBLE OUTCOMES

Withdrawal, Conflict

Major Psychological Event

Illness

Performance Decrement

NEED FOR NONINVASIVE COUNTERMEASURES
Lactobacilli and health

1907
Elie Metchnikoff publishes *The Prolongation of Life: Optimistic Studies.*

1915
Leo Rettger proposes *L. acidophilus* as a suitable probiotic.

1930
Minoru Shirota isolates *L. casei*, develops and commercializes Yakult.

1950+
Techniques developed enabling genomic elucidation of probiotic mechanisms.

2010
Human gut microbiome catalogued.
Probiotics are “live microorganisms which when administered in adequate amounts confer a health benefit on the host” (WHO/FAO)

<table>
<thead>
<tr>
<th>Probiotic-Associated Benefit</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Protection against infection</td>
<td>Corr et al. (2007)</td>
</tr>
<tr>
<td>Lowered incidence of diarrhea</td>
<td>Leyer et al. (2009)</td>
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<tr>
<td>Lowered risk of antibiotic-associated diarrhea</td>
<td>Gao et al. (2010)</td>
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<tr>
<td>Lowered levels of cold and influenza-like symptoms</td>
<td>Leyer et al. (2009)</td>
</tr>
<tr>
<td>Inhibition of H. pylori</td>
<td>Fujimura et al. (2012)</td>
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<tr>
<td>Prevention of upper respiratory infection</td>
<td>Hao et al. (2011)</td>
</tr>
<tr>
<td>Return to pre-antibiotic baseline flora</td>
<td>Engelbrektson et al. (2009)</td>
</tr>
<tr>
<td>Epithelial barrier function</td>
<td>Mennigen and Bruewer (2009)</td>
</tr>
<tr>
<td>Increased humoral Immunity via secretion of IgA</td>
<td>Viljanen et al. (2005)</td>
</tr>
<tr>
<td>Competitive exclusion of pathogens</td>
<td>Lee et al. (2003)</td>
</tr>
<tr>
<td>Neuroactive compound production</td>
<td>Wall et al. (2014)</td>
</tr>
<tr>
<td>Reduced psychological distress</td>
<td>Messaoudi et al. (2011)</td>
</tr>
<tr>
<td>Reduced anxiety</td>
<td>Rao et al. (2009)</td>
</tr>
</tbody>
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Modified from O’Flaherty and Klaenhammer, 2010
Probiotic Mechanisms

Dinan and Cryan, 2013

Modified from Selle and Klaenhammer, 2013
HOW: deliver within Food System Constraints

Mars Expedition Scenario:
- 2.5 year mission
- Microgravity and reduced gravity
- No resupply
- Food may be prepositioned (5 year shelf life)
- Constrained mass and volume

Within this scenario, probiotics must:
- Survive
- Maintain probiotic attributes
- Provide similar benefits as those recorded on Earth
Probiotic Survival

CAPSULE VS FOOD

ROOM TEMPERATURE STORAGE VS COLD STORAGE

SURVIVAL THROUGH DIGESTIVE TRACT

pH 2, pepsin VS pH 8, pancreatic juice
Stability of Commercially Available Probiotic

Nonfat Dry Milk as a Delivery Vehicle

![Graph showing survival (CFU) over time (minutes) for different delivery vehicles: Capsule + PBS, Capsule + PBS > Intestinal, Capsule + PBS > Gastric, Capsule > Intestinal, Capsule > Gastric, La + Milk, La + Milk > Intestinal, La + Milk > Gastric.](image)

2/11/2015
Storage Temperature

Eight Months of Storage

PBS
- $T_0$
- 22°
- 4°
- -80°

Milk
- $T_0$
- 22°
- 4°
- -80°

Survival (CFU)

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HOW: Respond to Microgravity

Rotating-wall vessel (RWV)
Synthecon (Houston, TX)

LSMMG Orientation

Control Orientation

orbit path of cell
Microgravity Response

- Effect on survival in simulated GI conditions
- Effect on growth
- Effect on gene expression

Illumina MiSeq
Acknowledgments

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- Microbiology Laboratory
Questions
Probiotic Mechanisms

Probiotic bacteria

Naïve T-cell

AG and co-stimulatory molecules

TNF-α
IL-12
IL-10
IL-6

Dendritic cell (DC)

M cell

T_{H2}

T_{Reg}

T_{H1}

homeostasis

Modulate responses

IL-4
IL-10
IFN-γ
IL-2
IL-12