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

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?
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>
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<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>
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<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>
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<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>
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<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>
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<tr>
<td>Reduced anxiety</td>
<td>Rao et al. (2009)</td>
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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

2/11/2015
Stability of Commercially Available Probiotic

Nonfat Dry Milk as a Delivery Vehicle
### Storage Temperature

**PBS**

- **$T_0$**
- **22°**
- **4°**
- **-80°**

**Milk**

- **$T_0$**
- **22°**
- **4°**
- **-80°**

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<thead>
<tr>
<th>Survival (CFU)</th>
<th>Eight Months of Storage</th>
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<tbody>
<tr>
<td>1.00E+10</td>
<td></td>
</tr>
<tr>
<td>1.00E+09</td>
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<tr>
<td>1.00E+08</td>
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<tr>
<td>1.00E+07</td>
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<tr>
<td>1.00E+06</td>
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HOW: Respond to Microgravity

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

LSMMG Orientation

Control Orientation

orbit path of cell
solid body rotation of the media
Microgravity Response

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

Illumina MiSeq
Acknowledgments

- Sarah Castro, Ph.D.
- Mark Ott, Ph.D.
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- Microbiology Laboratory
Questions
Probiotic Mechanisms

Probiotic bacteria

Naïve T-cell

AG and co-stimulatory molecules

IL-6

IL-10

TNF-α

IL-12

Dendritic cell (DC)

M cell

Modulate responses

IFN-γ

IL-2

IL-12

IL-4

IL-10

T_{H2}

T_{Reg}

T_{H1}

homeostasis