Assessment of Individualizing *lactobacillus plantarum* Supplementation with Precision Health to Preserve Muscle Health in Astronauts During Long Duration Spaceflight

Joseph Blumer[1]; Lauren Schrader MPH, MS[2]; Carol Mullenax PhD, PE, PMP[3]; Corey Theriot PhD[4]

[1]University of Pikeville-Kentucky College of Osteopathic Medicine; [2]Universities Space Research Association;
[3]NASA Johnson Space Center; [4]University of Texas Medical Branch

Background

Muscle atrophy is an unfortunate reality seen after spending time in microgravity. Decreases in muscle strength, size, and endurance can negatively impact mission productivity and increase the risk of injury in astronauts. In preparing for long-duration spaceflight aboard future orbiting stations and interplanetary vessels, supplementation with *lactobacillus plantarum* has been suggested as a possible countermeasure for crew members. Early clinical trials have shown the probiotic to improve muscle strength, endurance, and associated biomarkers, even without significant physical exercise by influencing the gut-muscle-axis. While current onboard exercise protocols have significantly helped limit degradation (as seen below), individualized implementation of this supplement could not only add another layer of protection but also protect against inadequate exercise equipment on future missions due to payload constraints.

Examples of Spaceflight-Induced Muscle Atrophy

Mission	Duration	Exercise	Result
Skylab 2	28 days	Cycle	-25% Quad Strength
Skylab 4	84 days	Cycle + **MKI + MKII + Treadmill**	-7% to 10% Quad Strength
ISS	~180 days	Cycle + Treadmill + **iRED**	-19.5% Knee Flexor Strength
ISS	~180 days	Cycle + Treadmill + **ARED**	-11.1% Knee Flexor Strength
Mars	~180 days (one way)	Potentially minimal in transit	

*Data obtained from Ploutz-Snyder and colleagues

Methods and Objectives

- Literature review of muscle data from previous space missions and NASA databases, as well as published trials with this strain (4)
- Synthesis of results to identify overall benefits from supplementation
- Development of operational considerations and gaps to be answered to make progress towards serious clinical evaluation
- Identifying possible areas of interest for Precision Health, which would enable individual protocol adjustment to maximize benefit

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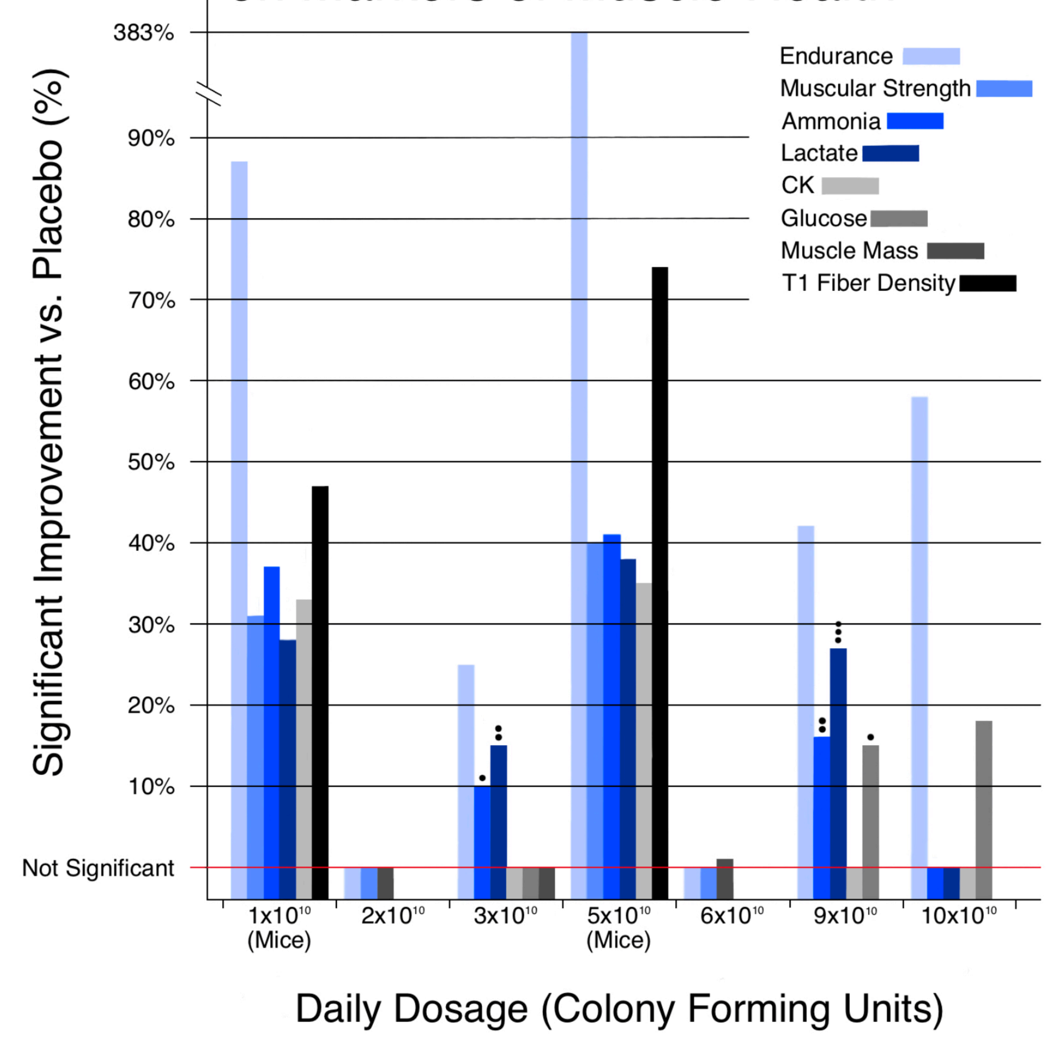
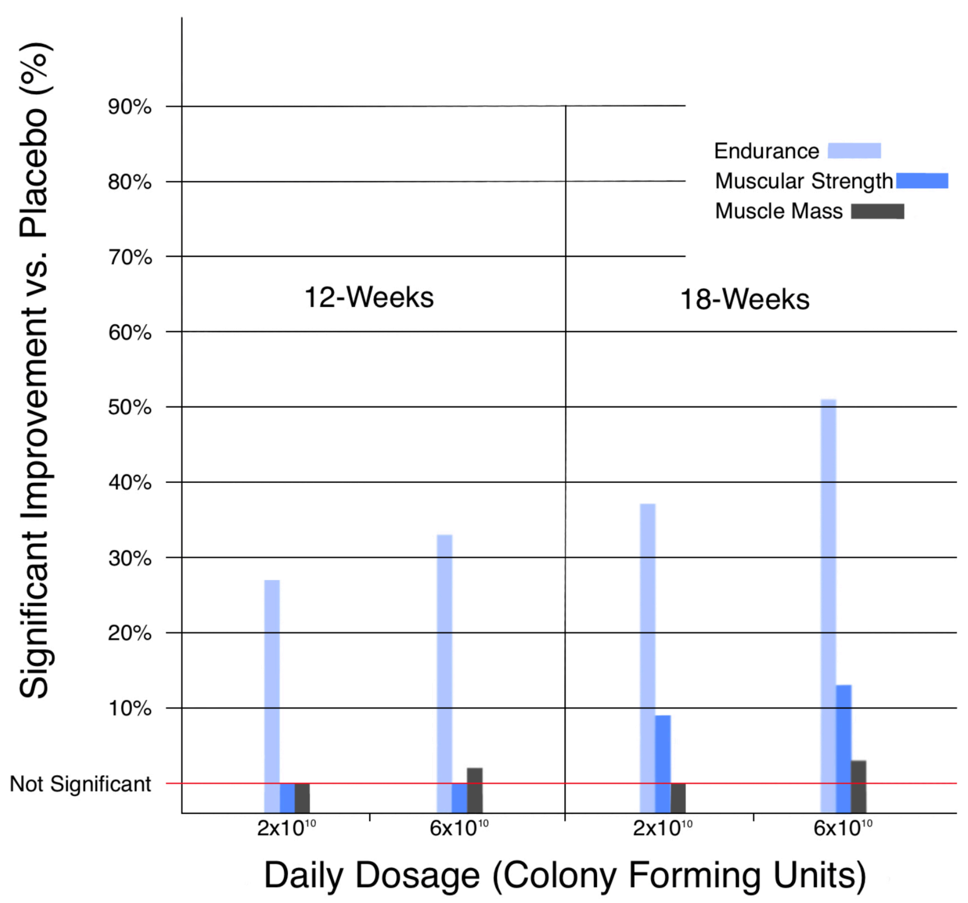
Effect of 6-Week Supplementation on Markers of Muscle Health



• = 2 time points average •• = 3 time points average ••• = 4 time points average
1x10 and 5x10 dosages were from the same study (**)
2x10 and 6x10 dosages were from the same study (**)
3x10 and 9x10 dosages were from the same study

Effect of 12- and 18-Week Supplementation on Markers of Muscle Health



Implementation considerations:

- Is there a ceiling to the dosage where results plateau?
- Are there unidentified adverse effects?
- How will individual variability of the gut microbiome affect needed dosage or outcome?
- Is the cost/benefit enough to justify taking up valuable payload space on a spacecraft?
- If not, is there a way to independently grow and process this supplement on the Moon or Mars?
- Could certain macronutrient-intake profiles prove to be more efficient with these SCFAs, improving results?

Discussion

Prior study results clearly indicate a measurable muscular benefit to supplementation with *l. plantarum*, with many of these improvements being dose-dependent. Specifically, these improvements are seen in muscular endurance, muscle mass, muscle strength, type 1 fiber density, lactate, glucose, CK, and ammonia.

Studies focused heavily on exercise endurance, with dramatic improvements in several data sets-hypothesized as due to the metabolic contributions from this probiotic. *Lactobacillus, a* lactate-producing bacteria, generates lactate as a substrate for surrounding bacteria to produce short chain fatty acids (SCFAs) such as butyrate, propionate, and acetate, especially in the human colon. In a microbial analysis of the microbiome, a 16S rRNA sequence identified the clostridial cluster XIVa, one of the most abundant groups of bacteria, as producing butyrate from lactate (2). These SCFAs enter the blood stream for efficient uptake by both the liver and muscle without additional transport proteins, plasma membrane translocase, or cytosolic fatty-acid binding proteins to enter the cell (3). Ultimately, SCFAs are broken down by beta oxidation inside mitochondria to form acetyl-CoA, which-enters the TCA (Krebs) cycle as a substrate to produce large amounts of electron carriers that subsequently aid in the electron transport chain to make large amounts of ATP, the ultimate energy molecule for muscle contraction. This identifies a direct pathway from the lactate from *l. bacillus* to ATP used by muscle tissue.

Conclusion/Future Recommendations

Precision Health focuses on the individual application of interventions and protocols for astronauts, offering unique opportunities to maximize the impact of health solutions.

A precision health framework offers opportunities to tailor L. plantarum supplements to individual crew members based on muscle loss, gut microbiome composition, dosage, and effectiveness, among other factors. Trial supplementation periods could be utilized as a first step to determine tolerability. The best time period would be at least 18-months prior to launch. A moderate dosage of 9×10^{10} CFU daily for a period of 16-20 weeks while tracking physical progress and subjective feedback from the astronaut would be a reasonable starting point. Dosage can be adjusted as needed for each individual, while closely monitor for adverse effects or intolerances.

Overall, this evidence shows that this supplement has significant potential in future utilization for attenuation of muscle loss during spaceflight. In order to move forward, flight surgeons must consider that any incremental improvements will prove invaluable with the significant constraints and limitations that are likely to impact future long duration spaceflight exploration.