Fiscal Year:	FY 2013	**Task Last Updated:**	FY 11/08/2013
PI Name:	Paddon-Jones, Douglas Ph.D.		
Project Title:	An Integrated Low-Volume Nutritional Countermeasure to Maintain Muscle Mass and Function During Space Exploration		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Musculoskeletal Alterations Team		
Joint Agency Name:		**TechPort:**	Yes
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Aerobic**:Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (2) **Muscle**:Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Galveston	**State:**	TX
Zip Code:	77555-1124	**Congressional District:**	14
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2008 Crew Health NNJ08ZSA002N
Start Date:	07/01/2009	**End Date:**	06/30/2013
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Urban, Randall (The University of Texas Medical Branch) Protas, Elizabeth (The University of Texas Medical Branch) Rasmussen, Blake (The University of Texas Medical Branch) Sheffield-Moore, Melinda (The University of Texas Medical Branch)		
Grant/Contract No.:	NCC 9-58-MA02001		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Our long-term goal is to identify, prevent, and remedy defects in the metabolic pathway that contribute to the loss of muscle mass and function during exposure to microgravity. Demographic data indicate that the average age of shuttle crew members has increased from 40.7 yrs in 1995 to 46.7 yrs in 2007 with an increasing number of astronauts over 50 yrs of age. We contend that the loss of muscle mass and function during spaceflight is facilitated by an age-associated, progressive impairment in the ability to mount an anabolic response to standard mixed nutrient meals. We propose that enriching daily meals with a low-volume leucine supplement will reduce the deleterious effects of microgravity on skeletal muscle and facilitate recovery during rehabilitation. We employed our established 14 day bed rest protocol to model the skeletal muscle unloading that occurs during microgravity. We also examined recovery of muscle mass and functional capacity during a 7 day rehabilitation period. We studied 2 groups: CON (Bedrest/Recovery + Placebo), LEU (Bedrest/Recovery + Leucine). We assessed: a) markers of translation initiation, b) muscle protein synthesis, c) muscle mass and body composition, and d) strength and aerobic capacity. We tested the following hypotheses: 1. Bedrest will blunt the anabolic response to a mixed nutrient meal, facilitating a loss of muscle mass and functional capacity that is only partially restored during rehabilitation. 2. Enriching daily meals with leucine will promote protein synthesis and maintain the anabolic response to mixed nutrient meal ingestion. This will preserve lean muscle mass and function during bedrest and facilitate the recovery of functional and metabolic capacity during rehabilitation. This project builds on our recent series of bed rest studies and seeks to provide a refined and practical countermeasure that is supported by comprehensive mechanistic evidence. Primary findings were: 1) leucine attenuated the loss of whole body lean mass during the first 7 d of bed rest compared to control subjects (LEU: -0.6±0.2 kg vs. CON: -1.1±0.2 kg, $p<0.05$) and reduced or prevented decrements in knee extensor strength (LEU: -8±3% vs. CON: -15±3%, $p<0.05$), ankle extensor strength (LEU: -13±5% vs. CON: -20±5%, $p<0.05$), and knee extensor endurance (LEU: -2±4% vs. CON: -14±3%, $p<0.05$) during 14 d bed rest; 2) LEU maintained both post-absorptive and post-prandial MPS during bed rest; in contrast, bed rest decreased post-absorptive MPS (pre-bed rest: 0.061% • h-1 vs. post-bed rest: 0.043% • h-1, $p<0.05$); 3) insulin area under the curve during an oral glucose tolerance test was unchanged in LEU after bed rest (21±8%) but elevated in CON (52±23%, $p<0.05$) and whole body insulin sensitivity in LEU was significantly increased above pre-bed rest values after 7 d rehabilitation (17±10% vs. CON: -9±9%, $p<0.05$). Leucine is an inexpensive, low volume supplement that can be easily incorporated into the daily meals of middle-aged adults to maintain muscle protein synthesis and protect muscle mass, strength, and insulin sensitivity during periods of physical inactivity characteristic of hospitalized acute illness and spaceflight.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our long-term goal is to identify, prevent, and remedy defects in the metabolic pathway that contribute to the loss of muscle mass and function during exposure to microgravity. Protein catabolism and muscle loss occurs in many circumstances. The regulatory mechanisms controlling protein turnover are particularly sensitive to a reduction in the neuromuscular stimulus that occurs during physical inactivity or exposure to microgravity and it is clear that muscle loss is greatly exaggerated with increasing age. Demographic data indicate that the average age of shuttle crew members has increased from 40.7 yrs in 1995 to 46.7 yrs in 2007 with an increasing number of astronauts over 50 yrs of age. We contend that the loss of muscle mass and function during spaceflight is facilitated by an age-associated, progressive impairment in the ability to mount an anabolic response to standard mixed nutrient meals. Protein supplementation is routinely employed to combat inactivity and age-related muscle loss. However, aggressive supplementation regimens are often impractical or ineffective due to issues including increased satiety, poor palatability, cost, and compliance. Enriching daily meals with a low-volume leucine supplement reduced some of the deleterious effects of inactivity on skeletal muscle. This supplement has the potential to also benefit individuals whose ability to perform physical activity is compromised (e.g., hospitalized patients, frail elders).
Task Progress:	Mechanical unloading, an inherent characteristic of spaceflight, results in a loss of muscle mass and muscle strength. These losses threaten the integrity of space missions and crew health upon return to Earth's gravity. Nutrition-based countermeasures represent one of the few viable intervention strategies available during long-duration spaceflight. We added leucine (0.06 g • kg lean mass • meal-1; LEU) to the regular meals served 3 • d-1 to middle-aged adults (45-60 y, representative of long-duration crew members) during 14 d of horizontal bed rest (BR) and 7 d of rehabilitation. Changes in muscle mass were assessed by dual-energy X-ray absorptiometry (DEXA); strength was evaluated with standard isokinetic dynamometry. Stable isotope tracer methodology was used to quantify muscle protein synthesis pre-BR, post-BR, and post-rehabilitation. Ongoing analysis of muscle samples for measures of protein metabolism and cell signaling continues to be batched. All subjects have tolerated the supplement (leucine or placebo) well, with no complaints. Primary findings were: 1) leucine attenuated the loss of whole body lean mass during the first 7 d of BR compared to control subjects (LEU: -0.6±0.2 kg vs. CON: -1.1±0.2 kg, $p<0.05$) and reduced or prevented decrements in knee extensor strength (LEU: -8±3% vs. CON: -15±3%, $p<0.05$), ankle extensor strength (LEU: -13±5% vs. CON: -20±5%, $p<0.05$), and knee extensor endurance (LEU: -2±4% vs. CON: -14±3%, $p<0.05$) during 14 d BR; 2) LEU maintained both post-absorptive and post-prandial MPS during BR; in contrast, BR decreased post-absorptive MPS (pre-BR: 0.061% • h-1 vs. post-BR: 0.043% • h-1, $p<0.05$); 3) insulin area under the curve during an oral glucose tolerance test was unchanged in LEU after BR (21±8%) but elevated in CON (52±23%, $p<0.05$) and whole body insulin sensitivity in LEU was significantly increased above pre-BR values after 7 d rehabilitation (17±10% vs. CON: -9±9%, $p<0.05$).
Bibliography Type:	Description: (Last Updated: 09/28/2016)
Articles in Peer-reviewed Journals	Casperson SL, Sheffield-Moore M, Hewlings SJ, Paddon-Jones D. "Leucine supplementation chronically improves muscle protein synthesis in older adults consuming the RDA for protein." Clinical Nutrition. 2012 Aug;31(4):512-9. Epub 2012 Feb 20. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3640444/ ; PubMed PMID: 22357161 , Aug-2012
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Awards	English K. "Charles F. Otis Endowed Award for Clinical Research, November 2011." Nov-2011
Awards	English K. "Environmental and Exercise Physiology's (EEP) Space Biomedical Research Institute Predoctoral Gravitational Physiology Award (APS), April 2012." Apr-2012
Awards	English K. "NASA/Texas Space Grant Consortium Graduate Fellowship, June 2012." Jun-2012