Fiscal Year:	FY 2008	**Task Last Updated:**	FY 10/08/2008
PI Name:	Schaffler, Mitchell B. Ph.D.		
Project Title:	Bone Recovery Potential After Bisphosphonate and PTH Treatment of Disuse Osteoporosis		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Musculoskeletal Alterations Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Bone Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (2) **Osteo**:Risk Of Early Onset Osteoporosis Due To Spaceflight		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	New York	**State:**	NY
Zip Code:	10029-6500	**Congressional District:**	14
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2003 Biomedical Research & Countermeasures 03-OBPR-04
Start Date:	06/01/2004	**End Date:**	05/31/2008
No. of Post Docs:	2	**No. of PhD Degrees:**	1
No. of PhD Candidates:	2	**No. of Master' Degrees:**	0
No. of Master's Candidates:	2	**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):	Jepsen, Karl (Mount Sinai School of Medicine) Majeska, Robert (Mount Sinai School of Medicine)		
Grant/Contract No.:	NCC 9-58-BL00406		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Bone loss in microgravity and the resulting bone fragility have been identified by NASA as key barriers to successful long-term space flight. Effective countermeasures must therefore prevent bone loss, but also to maintain the mechanical integrity of the tissue during prolonged space flight and allow rapid recovery of normal function. Disuse osteoporosis in humans and higher mammals results from elevated bone resorption. Thus, targeting osteoclasts with antiresorptive agents like bisphosphonate to prevent bone loss is a key strategy. While anti-resorptive drugs have been the cornerstones of osteoporosis therapy, anabolic agents, such as PTH, that stimulate bone formation represent an important new advance in the treatment of osteoporosis. We hypothesize that PTH may be especially valuable in reversing disuse if the deterioration of bone architecture can be slowed such that the anabolic agent has a better initial bone scaffold on which to work. The studies examine whether bone that remains after bisphosphonate-treatment during long-term immobilization can recover its architecture and mechanical function after restoration of mechanical usage (remobilization). We will then assess whether addition of anabolic PTH during immobilization will improve recovery of disuse bone. Recovery after long-term disuse with bisphosphonate treatment will be examined in an immobilization model. MicroCT imaging will be used to evaluate microstructure, biomechanical testing to assess function and histomorphometry to measure tissue physiological responses.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The current research applies directly to prevention and treatment of osteoporosis on Earth. In particular, these studies will examine 1) the efficacy of antiresorptive therapy in slowing the bone loss that occurs with decreased of mechanical loading, and 2) the role of the bone anabolic agent, PTH, in accelerating bone recovery and restoring bone strength. This research uses pharmacological agents that are already approved for clinical use; thus the findings from this research can be expected to see rapid implementation in bone loss situations occurring as a result of unloading, such as spinal cord injury and long-term immobilzation.
Task Progress:	Experiments and analyses are completed. Manuscripts in preparation.
Bibliography Type:	Description: (Last Updated: 08/21/2020)
Abstracts for Journals and Proceedings	Fritton JC, Li CY, Zhang X, Roth H, Tommasini SM, Laudier D, Mann R, Schaffler MB. "Bisphosphonate and PTH treatments adversely affect cortical bone adaptation to restored weight-bearing." 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008. Transactions Orthopaedic Research Society, 2008 Mar;54:970. , Mar-2008
Abstracts for Journals and Proceedings	Zhang X, Fritton JC, Li CY, Laudier DM, Mann R, Schaffler MB. "Remobilization recovers cancellous bone mass and risedronate improves microarchitecture after long-term disuse." 54th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA, March 2-5, 2008. Transactions Orthopaedic Research Society, 2008 Mar;54:342. , Mar-2008
Articles in Peer-reviewed Journals	Cardoso L, Schaffler MB. "Changes of elastic constants and anisotropy patterns in trabecular bone during disuse-induced bone loss assessed by poroelastic ultrasound." J Biomech Eng. 2015 Jan;137(1):0110081–9. https://doi.org/10.1115/1.4029179 ; PMID: 25412022; PMCID: PMC4290507 , Jan-2015