Fiscal Year:	FY 2007	**Task Last Updated:**	FY 11/13/2007
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 Teams		
Program/Discipline--Element/Subdiscipline:	NSBRI Teams--Bone Loss 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		
PI Email:	Mitchell.Schaffler@mssm.edu	**Fax:**	FY 212-426-7750
PI Organization Type:	UNIVERSITY	**Phone:**	212-241-1625
Organization Name:	Mount Sinai School of Medicine		
PI Address 1:	One Gustave L. Levy Place		
PI Address 2:	Box 1188		
PI Web Page:			
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:	1	**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):	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 examine 1) the efficacy of antiresorptive therapy in slowing the bone loss that occurs with loss of mechanical loading, and 2) the use of the bone anabolic agent, PTH, to accelerate bone recovery. Since we are working with pharmacological agents that are already approved for clinical use, 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 immobilization.
Task Progress:	In vivo studies (Immobilization with and without bisphosphonate, followed by restored weight bearing with and without anabolic PTH treatment, total duration 18 month durations) have been completed. MicroCT analysis of all cortical bone samples has been completed, and reveal that bishosphonate antiresorptives may adversely affect bone recover from disuse Analyses of metaphyseal cancellous bone are ongoing, as are bone histomorphometry and biomechanical studies for all sites.
Bibliography Type:	Description: (Last Updated: 08/21/2020)
Articles in Peer-reviewed Journals	Li CY, Jepsen KJ, Majeska RJ, Zhang J, Ni R, Gelb BD, Schaffler MB. "Mice lacking cathepsin K maintain bone remodeling but develop bone fragility despite high bone mass." J Bone Miner Res. 2006 Jun;21(6):865-75. PMID: 16753017 , Jun-2006