Fiscal Year:	FY 2016	Task Last Updated:	FY 10/12/2015
PI Name:	Bloomfield, Susan A. Ph.D.		
Project Title:	Sclerostin's Role in Regulating Bone Fo	rmation during Long-term Simu	ulated Microgravity and Subsequent Recovery
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline Element/Subdiscipline:	HUMAN RESEARCHBiomedical cou	intermeasures	
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	(1) HHC :Human Health Countermeasur	res	
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:	sbloom@tamu.edu	Fax:	FY 979-862-1692
PI Organization Type:	UNIVERSITY	Phone:	979-845-2871
Organization Name:	Texas A&M University		
PI Address 1:	Department of Health & Kinesiology		
PI Address 2:	400 Harvey Mitchell Pkwy, Suite 300		
PI Web Page:			
City:	College Station	State:	TX
Zip Code:	77843-4375	Congressional District:	17
Comments:			
Project Type:	Ground	Solicitation / Funding Source:	2013 HERO NNJ13ZSA002N-Crew Health (FLAGSHIP & NSBRI)
Start Date:	10/06/2014	End Date:	08/31/2017
No. of Post Docs:	0	No. of PhD Degrees:	0
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:	2	Monitoring Center:	NASA JSC
Contact Monitor:	Norsk, Peter	Contact Phone:	
Contact Email:	Peter.norsk@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: Extended to 8/31/2017 per NSS NOTE: Extended to 10/05/2016 per NSS	C information (Ed., 1/24/17) SC information (Ed., 10/28/15)	
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	NNX15AB05G		
Performance Goal No.:			
Performance Goal Text:			

Rationale for HRP Directed Research: Phase III clinical trials testing the efficacy of selerostin antibody (ScI-AB) are in progress, focusing on the value of this agent in reversing aging-related bone loss and osteoporosis. It will be very useful to have data on a physiologically relevant mammaliam model (skeletally matter rats) yielding information on the efficacy of ScI-AB for bone loss due to prolonged dissue. This applies to individuals subjected to prolonge the rest (complicated orthopedic injuries, frail clienty with sever subjects) to individuals subjected to prolonge the rest (complicated orthopedic injuries, frail clienty with sever subjects) or to conditions like spinal cord injury or even stroke (If significant muscle paralysis) is involved). Additionally, this study will provide a sex comparison, so we will have preliminary clues as to whether wore might respond similarly as do men to this potent anabolic treatment. The first major accomplishment was the acquisition, installation and training with an upgraded OsteoMeasure image analysis system in the Bloomfield Bone Biology Laboratory, completed by November 15, 2014. The improved resolution of the digital camera and a digitizing screen that allows training right on the screen itself has resulted in improved speed on analyses of histomorhymentry and of immunostaring sections. Both of these methods are central to the purpose of this project. We received our first binjment of bones from the parent protocol at UC-Davis in carly April of 2015 (n - 43) from young adult male rats, including samples from animals scrifted after 7, 14, 28, and 90 days of hindlinb unloading, as well as after 28 days of weight-bearing recovery. Our revised protocol at UC-Davis in carly April of 2015 (n - 43) from young adult male rats, including recovery or using transcore young cloted proposed work we would perform on the tibiab provides useful i	Task Description:	The tissue sharing opportunity outlined in Appendix A, Item B ("Ccrebral Spinal Fluid Production/Absorption") offers an exciting chance to study the evolution of changes over 90 days of hindlimb suspension (HLS) in a rodent model. Few laboratories have the capability or expertise to carry out HLS for such a long period; the impact of this experiment will be multiplied many-fold with piggyback projects making strategic use of other tissues harvested from these animals. This proposal focuses on tracking the evolution of changes in a protein important to bone integrity called sclerostin over the course of 90 days of unloading and then during the 90-day recovery phase. Importantly, we will also track alterations in the key physiological function sclerostin regulates in bone: osteoblast activity resulting in the formation of new bone. Sclerostin is produced by osteocytes, the bone cells embedded in bone matrix and the key sensors of loading/unloading; it works to inhibit the Wnt-Beta catenin signaling pathway in osteoblasts, which normally stimulates bone formation activity. Most studies to date document an increase in osteocyte's sclerostin expression with unloading, which provides the mechanism for the suppressed bone formation seen with HLS on Earth and, presumably, with microgravity exposure. A recent study examining the impact of a novel therapeutic agent (sclerostin antibody) on mice flown on STS-135 yielded very positive findings, suggesting that manipulating sclerostin expression could be an important therapeutic tool to augment the usual exercise countermeasures employed by astronauts. Hence it becomes critical, before any such systemic therapy is considered, to understand clearly the relationship between sclerostin expression and the functionally important outcome (bone formation activity) in multiple bone sites. Because there is evidence that Sost, the gene encoding the protein sclerostin, is expressed differently in mid-shaft vs metaphyseal bone, we will assess sclerostin expression and histomorphomet
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Ribliography Lype: Description: (Last Undated: ()5/28/2021)	Task Progress:	The first major accomplishment was the acquisition, installation and training with an upgraded OsteoMeasure image analysis system in the Bloomfield Bone Biology Laboratory, completed by November 15, 2014. The improved resolution of the digital camera and a digitizing screen that allows tracing right on the screen itself has resulted in improved speed on analyses of histomorphometry and of immunostaining sections. Both of these methods are central to the purpose of this project. We received our first shipment of bones from the parent protocol at UC-Davis in early April of 2015 (n ~ 43) from young adult male rats, including samples from animals sacrificed after 7, 14, 28, and 90 days of hindlimb unloading, as well as after 28 days of weight-bearing recovery. Our revised protocol submitted in August, 2014, after negotiations with Dr. Peter Norsk and the parent protocol Principal Investigator (PI) (C Fuller), described proposed work we would perform on the tibial bone samples targeted to our laboratory for analysis. Our first task was to run ex vivo pQCT scans to quantitate bone structural changes on both the metaphysis, a site very sensitive to disuse, and the mid-shaft bone. Outcomes here include volumetric bone mineral density (vBMD), bone mineral content, and cross-sectional geometry (e.g., bone area, cortical thickness, marrow area). Once these were complete, the proximal half of one tibia was prepared histologically for embedding in hard plastic in order for us to perform standard static histomorphometry on the proximal tibial metaphysis. Quantitating the extent of surfaces covered by newly formed bone matrix (osteoid) and by osteoclasts (bone resorbing cells) provides useful information on the balance between bone forming and bone resorbing activity. [Because the parent protocol PI was reticent to add more procedures to an already complicated protocol, there was no injection of fluorochrome labels in these rats during the experiments at UC-Davis, which disallows determination of bone formatin rate.]

Task Book Report