

Fiscal Year:	FY 2019	Task Last Updated: FY 03/20/2019	
PI Name:	Turner, Russell T Ph.D.		
Project Title:	Housing Temperature: An Important Variable for Simulated Spaceflight Studies Using Mice		
Division Name:	Space Biology		
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Program/Discipline-- Element/Subdiscipline:			
Joint Agency Name:		TechPort:	No
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Human Research Program Risks:	None		
Space Biology Element:	(1) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Musculoskeletal Biology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
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Comments:			
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COI Name (Institution):	Branscum, Adam Ph.D. (Oregon State University) Iwaniec, Urszula Ph.D. (Oregon State University) Wong, Carmen Ph.D. (Oregon State University)		
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	<p>Spaceflight, by altering the differentiation program of hematopoietic and mesenchymal stem cells residing within bone marrow, results in bone loss, increased bone marrow adiposity, anemia, and impaired immune function. These closely associated disturbances may compromise the success of long-term missions. Thus, there exists an urgent need to identify the underlying mechanisms and implement effective countermeasures. Mice are currently the preferred animal model for evaluating adaptive responses to microgravity experienced during spaceflight and simulated spaceflight (e.g., hindlimb unloading). Mice have important advantages over other animal models for spaceflight studies, including small size and ease of genetic manipulation. Although mice and humans share many common characteristics, fundamental species differences in thermoregulation may contraindicate the mouse, as currently applied, as a model for human spaceflight.</p> <p>Humans are homeotherms and when exposed to a cold environment defend their core body temperature, whereas mice are obligatory daily heterotherms and experience cyclic changes in core temperature when subjected to cold stress (i.e., temperature below thermoneutral). Mice are typically housed at or near room temperature (~22°C), which is well below the thermoneutral zone for the species (~32°C). Therefore, mice must expend energy to maintain core body temperature. Cold stress induced by sub-thermoneutral housing increases sympathetic outflow to peripheral tissues, including brown adipose tissue, and has profound effects on metabolism. We have recently shown that cold stress induced by room temperature housing results in rapid cancellous bone loss in mice. Based on this finding, we hypothesize that activation of adaptive thermogenesis in mice housed at room temperature introduces unrecognized and uncontrolled confounding variables into mouse studies. Strategies used by weight-bearing mice to minimize heat loss during room temperature housing (e.g., huddling or postural adjustments) are less effective during spaceflight and simulated spaceflight. This results in increased dependence on adaptive thermogenesis, likely exaggerating the negative physiological effects of skeletal unloading on bone and immune cells. Additionally, the thermogenic mechanisms mediating cold stress-induced changes in metabolism in mice are unlikely to be directly translatable to astronauts and could therefore confound interpretation of experimental results as applicable to humans.</p> <p>This proposal will explore the individual and combined effects of mild cold stress induced by room temperature housing and hindlimb unloading (HLU) on the skeleton in C57BL/6 (B6) mice, a strain commonly used in spaceflight and HLU studies. To accomplish our goal, we propose 2 Specific Aims:</p> <p>Specific Aim 1: Determine the contribution of increased adaptive thermogenesis to bone loss during HLU in mice housed at room temperature.</p> <p>We will accomplish this aim by comparing HLU-induced bone loss in mice housed at room temperature (22°C) with mice housed at thermoneutral (32°C).</p> <p>Specific Aim 2: Determine the lowest sub-thermoneutral housing temperature able to prevent adaptive thermogenesis-associated bone loss.</p> <p>We will accomplish this aim by performing temperature response studies (20-32°C) to evaluate induction of adaptive thermogenesis. Once we identify the lowest sub-thermoneutral housing temperature that does not induce adaptive thermogenesis, we will perform a long-term study to verify that minimal premature bone loss occurs and that magnitude of HLU-induced bone loss does not differ from mice housed at thermoneutral.</p> <p>Successful completion of the proposed research will provide guidance to investigators for insuring housing conditions minimize the confounding effects of species-specific differences in thermoregulation on experimental outcomes with the ultimate goal of optimizing the mouse to model human responses to spaceflight.</p>
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2019.
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