Fiscal Year:	FY 2019	**Task Last Updated:**	FY 11/22/2019
PI Name:	Ade, Carl Ph.D.		
Project Title:	Omics and Biochemical Markers of Cardiovascular and Bone Health: Relationship with Bedrest and Standard Physiological Measures		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
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) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes (3) **Muscle**:Risk of Impaired Performance Due to Reduced Muscle Size, Strength and Endurance (4) **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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Zip Code:	66506	**Congressional District:**	1
Comments:	NOTE: formerly at the University of Oklahoma until fall 2016		
Project Type:	Ground	**Solicitation / Funding Source:**	2014-15 HERO NNJ14ZSA001N-MIXEDTOPICS. Appendix E: Behavioral Health & Human Health Countermeasures Topics
Start Date:	08/24/2016	**End Date:**	08/23/2019
No. of Post Docs:	0	**No. of PhD Degrees:**	1
No. of PhD Candidates:	0	**No. of Master' Degrees:**	4
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	4
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Norsk, Peter	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: Extended to 8/23/2019 per NSSC information (Ed. 5/21/19)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Bemben, Debra Ph.D. (University of Oklahoma, Norman)		
Grant/Contract No.:	NNX16AR26G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The long-range goal of our research effort is to identify and characterize the omics and biochemical mechanisms that underlie the changes in cardiovascular and musculoskeletal function following prolonged space flight. It is well established that microgravity elicits central and peripheral decrements within the cardiovascular system. Traditional cardiovascular measurements have demonstrated significant decreases in left ventricular volume and mass within only a few weeks of exposure. Similarly, human and animal models suggest that microgravity exposure significantly alters vasomotor reactivity to various physiologic stressors. However, despite the recognition that cardiovascular function is decreased with prolonged microgravity exposure, the mechanistic underpinnings of these changes are not completely understood. In addition to changes within the cardiovascular system, significant decreases in bone health occur with prolonged microgravity. These changes are mediated, in part, due to general deconditioning and muscular/mechanical unloading that occurs with microgravity. As such, the average monthly rate of loss in areal bone mineral density can reach 1.0-1.5% when measured over a 14 month period. Given the significant and time-dependent changes in cardiovascular function and bone health associated with microgravity exposure, a continued evaluation of these systems is required, particularly within the genomic and biochemical sciences. Using genomic techniques and biochemical markers combined with traditional physiologic parameters provides the opportunity to investigate the mechanisms by which the body responds to the microgravity environment coupled with the identification of new 'space flight biomarkers' for early detection of any decrements in cardiovascular and bone health. In the present plan we propose to test the working hypotheses that 30 day six-degree head-down bed rest at an ambient 0.5% CO2, to simulate International Space Station (ISS) Flight will 1) decrease ventricular mass, volume, and function and that a marker of myocardial injury will be increased (c-miRNA-208) and a marker associated with myocardial mass will be decreased (c-miRNA-1), 2) decrease c-miRNAs associated with anti-angiogenesis, anti-inflammation, and anti-proliferation functions (c-miRNA-126, c-miRNA-146a, c-miRNA-20a, and c-miRNA-133a) and that these will also serve as markers of the expected decrease in aerobic exercise capacity, 3) will induce bone turnover and resorption, as indicated by increases in serum concentrations of Sclerostin and TRAP5b, 4), will upregulate c-miRNA (c-miRNA-21, c-miRNA-100, and c-miRNA-125b) involved in the regulation of bone turnover, and 5) serum concentrations of Sclerostin, TRAP5b, and c-miRNA will be significantly related to dual-energy X-ray absorptiometry (DXA) derived measurements of bone mineral density. To test these hypotheses we will obtain blood, plasma, and serum samples from an already planned 30 day six-degree head-down bed rest platform that will be conducted at the :envihab bed rest facility located at the Institute for Aerospace Medicine in Cologne Germany per the NASA research announcement. The findings from this investigation will establish new biomarkers that can be used to evaluate astronaut health while simultaneously providing novel insight into the cellular and genetic regulation of the myriad responses that accompany the physiological manifestation of space flight deconditioning.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This study will identify which circulating microRNA are differentially expressed following prolonged bedrest. This will allow us to identify which microRNA can be used as biomarkers of cardiovascular and bone health, which has important implications for both long-duration space flight and Earth-based medical practice. Using this information we can design and implement procedures focused on early detection of changes in cardiovascular and bone health, which will be used to implement guided therapeutic interventions that specifically target the physiological processes most effected. Lastly, in terms of Earth benefits, this research will provide a better understanding of the underlying physiological mechanisms associated with changes in cardiovascular and bone health.
Task Progress:	Our work found significant alterations in cardiovascular-health related c-miRs following 30 days sedentary HDBR (head down bed rest). Importantly, several of these c-miRs were significantly correlated with changes in stroke volume, cardiac output, and maximal aerobic exercise capacity. We speculate that miR may play an epigenetic effect on modulating the cardiovascular responses associated with prolonged microgravity exposure. Future work will need to confirm these results in a larger bed rest cohort and in the true space flight environment. In addition, Serum levels of miRNAs associated with bone and muscle function (miR-21, -100, -125b, -126) were analyzed using qPCR. Sclerostin and TRAP5b concentrations were assayed using commercial ELISA kits. TRAP 5b ($p=0.001$) and sclerostin ($p=0.05$) significantly increased post bed rest. MiR-21 was significantly upregulated ($p = 0.019$) from pre to post bed rest. MiR-125b showed a trend ($p = 0.11$) for upregulation with 10 participants showing increased expression and 1 showing decreased expression post bed rest.
Bibliography Type:	Description: (Last Updated: 03/12/2021)
Articles in Peer-reviewed Journals	Ade CJ, Bemben DA. "Differential microRNA expression following head-down tilt bed rest: Implications for cardiovascular responses to microgravity." Physiol Rep. 2019 May;7(9):e14061. https://doi.org/10.14814/phy2.14061 ; PubMed PMID: 31087541; PubMed Central PMCID: PMC6513770 , May-2019
Articles in Peer-reviewed Journals	Bemben DA, Baker BS, Buchanan SR, Ade CJ. "Circulating MiR-21 expression is upregulated after 30 days of head-down tilt bed rest." Osteoporos Int. Published: 11 January 2021. https://doi.org/10.1007/s00198-020-05805-2 ; PMID: 33432460 , Jan-2021