Fiscal Year:	FY 2015	**Task Last Updated:**	FY 07/07/2015
PI Name:	de Lemos, James Andrew M.D.		
Project Title:	Improving Cardiovascular Risk Prediction		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Cardiovascular Alterations Team		
Joint Agency Name:		**TechPort:**	Yes
Human Research Program Elements:	(1) **ExMC**:Exploration Medical Capabilities		
Human Research Program Risks:	(1) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes (2) **Medical Conditions**:Risk of Adverse Health Outcomes and Decrements in Performance Due to Medical Conditions that occur in Mission, as well as Long Term Health Outcomes Due to Mission Exposures		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	75390	**Congressional District:**	30
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2013 HERO NNJ13ZSA002N-Crew Health (FLAGSHIP & NSBRI)
Start Date:	06/01/2014	**End Date:**	05/31/2017
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No. of PhD Candidates:	0	**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):	Levine, Benjamin (The University of Texas Southwestern Medical Center at Dallas) Khera, Amit (The University of Texas Southwestern Medical Center at Dallas) Hundley, William (Wake Forest University Health Sciences) Wang, Thomas M.D. (Vanderbilt University) Ballantyne, Christie M.D. (Baylor College of Medicine) Berry, Jarett (The University of Texas Southwestern Medical Center at Dallas)		
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Task Description:	The most likely cause of a non-traumatic life- or mission-threatening medical event in astronauts would be from acute cardiovascular disease (CVD). Current risk prediction models utilize only traditional atherosclerosis risk factors and focus narrowly on coronary heart disease events rather than global cardiovascular risk, ignoring outcomes such as heart failure or atrial fibrillation that could also be potentially mission-threatening. Numerous studies have evaluated novel risk markers in an attempt to improve CVD risk prediction, with several promising imaging and blood-based biomarkers identified. Most of these studies have investigated the incremental predictive value of a single biomarker added to a traditional risk factor model, with a few reporting combinations of biomarkers. Moreover, few studies have evaluated strategies for risk prediction that cross testing modalities. Such a multi-modality approach has the potential to markedly improve CVD risk prediction among potential and existing astronauts, and would have direct relevance to the general population. Our primary objective is to develop a consortium of biomarker and aerospace medicine leaders, with expertise in multiple different testing modalities, and with access to robust existing databases, to identify and validate novel strategies to enhance global CVD risk prediction over two time windows: 1) 10-20 years, representing the full career of the astronaut and 2) 2-5 years, representing the planning and operational phase of a manned mission to Mars. The Biomarker Consortium will provide real time advice to NASA on the design of existing screening programs, the status of new biomarkers, and the interpretation of test results. The team of collaborative investigators will pool data from multiple existing cohort studies to develop two distinct multi-modality risk prediction tools, one based on 10-year global CVD risk and one based on 3-year CVD risk. These models will sequentially evaluate novel testing modalities on top of standard risk factors, including coronary calcium (a measure of the extent of coronary atherosclerosis), multiple blood based protein biomarkers that reflect inflammation, cardiac injury and cardiac stress, as well as imaging-based assessments of cardiac function. Finally, we will work directly with NASA researchers in the Human Research Program to explore the feasibility of transforming the Longitudinal Study of Astronaut Health into a prospective state-of-the-art cohort study of the astronaut corps. We will utilize the expertise of the Biomarker Consortium to design a novel program for study of the effects of training and spaceflight on astronaut health. Significant progress has been made towards each of the four aims. The Biomarker Consortium had several teleconferences followed by a face to face meeting at National Space Biomedical Research Institute (NSBRI) Consolidated Research Facility (CRF) on October 8, 2014 to initiate the collaboration needed to operationalize the scientific aims of the grant. The consortium has also contributed, as was designed, to advising NASA leadership regarding cardiovascular safety in space. Members of the Advisory Subcommittee, for example, have contributed towards development of a detailed, step-by-step protocol for the management of myocardial infarction (heart attack) in space. The primary scientific aims of the grant require pooling of data from large cohort studies. Each of these studies has a unique regulatory structure, scientific proposal system, and approval process. The goals of the first year of funding were to obtain the necessary approvals and data transfer agreements to being the data pooling process. We have obtained approval for data transfer from the Dallas Heart Study, MESA, and Atherosclerosis Risk in Communities Study (ARIC), and have submitted the necessary documents for the Framingham Heart Study. This meets our timelines and positions us well for data transfer early in the second year of funding, which is right on schedule. We have also been working on harmonizing data definitions and data fields between the cohort databases, to facilitate pooling and analysis. Several notable areas of progress have occurred with regard to exploratory Aim 4, which will explore the feasibility of transforming the Longitudinal Study of Astronaut Health (LSAH) into a prospective state-of-the-art cohort study of the astronaut corps. First, Greg Hundley, MD, has been named the coordinator of this Aim. Second, LSAH leadership has expressed interest in moving forward with collaboration towards this Aim. Finally, a meeting is planned in Dallas on May 19, 2015 to further explore collaboration within the LSAH.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The outcome of this research program will have widespread benefits and Earth based applications. Identifying optimal combinations of biomarkers to improve cardiovascular risk assessment is one of the holy grails of preventive cardiology, as the majority of CV events continue to occur in individuals NOT previously considered high risk. Because the absolute number of low risk individuals is so large, it is impractical to treat every person with aggressive medical therapy, not just for cost and compliance issues, but because of the possibility of side effects of even the safest medicines. Therefore refinement of the algorithms to reclassify patients into higher risk categories is essential for optimization of medical management and reduction of morbidity and mortality from cardiovascular disease. As only one example, the Astro-CHARM tool developed by Drs. Khera, Locke, and Levine is likely to be used widely in routine clinical medicine. Optimizing such scores to include modern biological assessments (biomarkers and advanced imaging) will make such risk assessment and personalized therapy even more effective.
Task Progress:	Steering Committee, NASA Advisory subcommittee, & Research Subcommittee met at kick off meeting on 7/31/2014 and regularly thereafter during Year1 of project. The NASA Advisory subcommittee has met formally and multiple times ad hoc to discuss a protocol for the management of acute coronary syndrome (heart attack) in space. Members of the committee provided expert advice regarding testing and treatment if a heart attack were to occur during a manned space mission. The first Research Subcommittee planning session was held on 9/4/2014 to review Specific Aims, discuss components of each database, create a strategy for obtaining the data, identify which databases should be obtained first, and assign point persons for each database. A subsequent subcommittee meeting was held on 4/23/2015 to discuss progress made in database request approval aquisition and to plan next steps. Our goal for the first year of funding was to complete the necessary planning, coordination, and infrastructure development to obtain the data for pooling for scientific Aims 2 and 3. So far, we have received approval to obtain MESA and ARIC data. UTSW (University of Texas Southwestern) has approved database agreements for both MESA and ARIC. Framingham database request has been submitted and is pending approval. The next meeting will occur in July, 2015. Our first Face-to-Face Biomarker project meeting was held on 10/8/2014 in Houston at NSBRI Consolidated Research Facility (CRF). Multiple speakers presented followed by comments from specially selected round table experts. Over lunch the meeting split into sub-committee sessions for the NASA Advisory and Research Sub-committee to strategize project startup. Another face-to-face meeting will be held in October of 2015. This meeting will occur annually and include work in progress presentations regarding progress towards Aims 2 and 3, discussion of priorities for NASA and the consortium, planning of new research initiatives, and review of new developments in the biomarker, imaging, and genetics fields. UT Southwestern Medical Center Institutional Review Board approved the project on 10/30/2014.

	Next Steps: 1. LSAH meeting in Dallas in May 19, 2015 to meet and leverage the expertise of the biomarker consortium and the collaborative relationships with the Human Research Program at NASA to plan the transformation of the LSAH into a high-yield cohort study to comprehensively study the effects of training and spaceflight on astronaut health. 2. Data transfer from the cohort studies will begin for aims 2 and 3 and data will be pooled across the multiple cohort studies, including Dallas Heart Study, Framingham Heart Study, ARIC, and MESA. 3. Data definition harmonization is in progress and will be completed when the data pooling has been completed. 4. The statistical analysis plan is being developed and will be shared with collaborators and consultants prior to statistical analyses being performed. 5. A second face to face meeting will be held in October 2015.
Bibliography Type:	Description: (Last Updated: 09/05/2020)