Fiscal Year:	FY 2011	**Task Last Updated:**	FY 12/19/2011
PI Name:	Bacher, Jeff Ph.D.		
Project Title:	A Novel Biodosimetry Method		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
Joint Agency Name:	**TechPort:**		No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Madison	**State:**	WI
Zip Code:	53711-5399	**Congressional District:**	2
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2007 Space Radiation NNJ07ZSA001N
Start Date:	09/01/2007	**End Date:**	09/14/2011
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA JSC
Contact Monitor:	Cucinott1a, Francis	**Contact Phone:**	281-483-0968
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Flight Program:			
Flight Assignment:	NOTE: End date is now 9/14/2011, per NSSC information (Ed., 9/23/2011) NOTE: Received NCE through 8/31/2011, per C. Guidry/JSC (08/2010)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Bailey, Susan (Colorado State University) Halberg, Richard (University of Wisconsin)		
Grant/Contract No.:	NNX07AQ02G		
Performance Goal No.:			
Performance Goal Text:			
Task Description:	Exposure of astronauts to space radiation during extended space missions may cause serious health problems. Accurate methods for measuring the biological effects of radiation exposure are, therefore, critical for estimating an individual's health risks. Biodosimetry measurements reflect variation in radiation sensitivity and consequently result in highly individualized estimates of dose and risk. Our novel biodosimetry approach is based on the hypothesis that non-coding repetitive DNA sequences are sensitive to radiation-induced mutations and that these mutations are not harmful to a cell. Therefore, mutations in non-coding repetitive DNA sequences can accumulate and provide a stable molecular record of genetic damage that can be used to determine cumulative radiation exposure and health risk. In our previous NASA grant, we demonstrated the feasibility of using radiation-induced mutations in non-coding repetitive DNA sequences to estimate radiation dose. Our initial data indicate that radiation-induced mutations in non-coding repetitive DNA markers are stable over time and additive over multiple exposures. In this successor proposal, we plan to extend our previous work by developing optimized multiplex marker panels for human and mouse biodosimetry, validate our approach by comparing our assay to current gold standard cytological methods and then utilize the novel system to assess risks from space radiation and improve our understanding of how these risks are affected by variations in dose rate, dose fractionation and genome stability. The main contribution of the proposed research to manned space exploration is the validation of a novel biodosimetry method for estimating dose and risks from exposure to space radiation. Completion of this research should provide new insights into the effects of space radiation on DNA mutagenesis and establishes panels of human and mouse biomarkers with broad utility for future studies in radiation biology, toxicology and cancer research.		
Rationale for HRP Directed Research:			
Research Impact/Earth Benefits:	Mutational load profiling, through analysis of mutations in tandem DNA repeat sequences, is a simple, non-invasive and generalized approach for monitoring an individual's cumulative record of mutations that may be useful for determining health risks and effectiveness of countermeasures for astronauts or other individuals exposed to ionizing radiation or chemical mutagens. Biomarkers identified in this study are also sensitive to free radical DNA damage and therefore may be useful markers for detection of cancer and other degenerative diseases in which oxidative stress is involved. Completion of this research should provide new insights into the effects of space radiation on DNA mutagenesis and establishes panels of human and mouse biomarkers with broad utility for future studies in radiation biology, toxicology and cancer research. Biomarkers developed for this NASA project are currently being evaluated in clinical studies for use in the early detection of colon cancer.		

Task Progress:	This research has led to the discovery and development of novel biomarkers and methodologies for monitoring radiation-induced mutations in humans and in mouse models. We demonstrated that under some conditions and in certain tissues (e.g., blood) our biodosimetry method can be used to assess dose. However, we have found that the dose response was influenced by numerous factors, including; radiation quality, dose rate, LET, time and tissue type. The sensitivity of our assay to a broad range of factors was surprising, but suggests a much broader utility of this approach for estimating an individual's risk from radiation exposure. Biodosimetry measurements reflect the combined effects and interactions of all factors that influence mutation induction in an individual. Thus, biodosimetry is generally a rather poor estimator of actual dose, but can be an important estimator of an individual's health risk from radiation exposure. Our major findings include: (1) Some non-coding microsatellite repeats are sensitive to radiation-induced mutations in a dose dependent manner (in some tissues) and therefore, monitoring changes in mutational load may is a viable biodosimetry method, (2) Spontaneous mutations in microsatellite repeats accumulated linearly over time, indicating these mutations are stable, (3) Fractionated exposures to iron ions, protons and gamma rays given in 24 hour intervals were additive, (4) The relative biological effectiveness for induction of microsatellite mutations of 1 GeV/n iron ions was <1 and for 1 GeV/n protons <2, (5) Microsatellite mutation induction was influenced by dose, dose rate, radiation quality, dose fractionation, LET, time, tissue type and DNA repair status, (6) Microsatellite repeats containing long polyA runs typically occur within highly repetitive SINE and LINE elements and DNA damage induced recombination between these elements may contribute to the observed mutagenesis in polyA microsatellites, (7) Microsatellite repeats containing long polyA runs are predicted to contain sequences associated with matrix attachment regions and this may be related to the observed differences in tissue specific radio-sensitivity, (8) Radiation-induced microsatellite mutations appears to require a functional mismatch repair system in most tissues, suggesting error prone repair of radiation-induced lesions in repeat sequences, (9) Split dose, dual ion experiments indicate a potential in vivo adaptive response to mixed beams of HZE iron ions and protons. Knowledge gained from this research project will provide new insights into the effects of radiation on DNA mutagenesis and establishes novel biomarkers and methods with broad utility not only for the benefit of NASA, but also for future studies in radiation biology, toxicology, and cancer research. Biomarkers developed for this NASA project are currently being evaluated in clinical studies for use in the early detection of colon cancer.
Bibliography Type:	Description: (Last Updated: 04/16/2019)
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