Fiscal Year:	FY 2010	**Task Last Updated:**	FY 10/29/2010
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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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. New Gaps added per HRR 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.
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 have 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. Biodosimetry measurements reflect the combined affects 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 individuals health risk from radiation exposure. Our major findings include: • Mutation induction in certain types of coding and non-coding microsatellite repeats is dose dependent in most tissues • Microsatellite markers sensitive to radiation-induced mutations are found almost exclusively within highly repetitive SINE and LINE elements in human and mouse genomes and recombination repair between these elements may contribute to mutagenesis • Microsatellite mutation induction is influenced by radiation quality, dose rate, LET, time and tissue type • The relative biological effectiveness for induction of microsatellite mutations of 1 GeV/n iron ions was less than that of gamma rays. The RBE of 1 GeV/n protons was <2 • Split dose, dual ions experiments indicate a potential adaptive response to sequential exposures of iron ions followed by protons, but not vice versa • There was evidence of delayed onset genomic instability in some tissue types (e.g., buccal cells) following exposure to 1 GeV/n iron ions and a high incidence of liver tumors within 2 years of exposure • Fractionated exposure to iron ions was additive (24 hours between doses) • Mismatch repair deficient mice exhibit a much higher level of spontaneous mutations, but only show radiation-induced mutations in colon
Bibliography Type:	Description: (Last Updated: 04/16/2019)
Articles in Peer-reviewed Journals	Haines J, Bacher J, Coster M, Huiskamp R, Meijne E, Mancuso M, Pazzaglia S, Bouffler S. "Microsatellite instability in radiation-induced murine tumours; influence of tumour type and radiation quality." International Journal of Radiation Biology 2010 Jul;86(7):555-68. PMID: 20545567 , Jul-2010
Articles in Peer-reviewed Journals	Halberg RB, Waggoner J, Rasmussen K, White A, Clipson L, Prunuske AJ, Bacher JW, Sullivan R, Washington MK, Pitot HC, Petrini JH, Albertson DG, Dove WF. "Long-lived Min mice develop advanced intestinal cancers through a genetically conservative pathway." Cancer Research 2009 Jul 15;69(14):5768-75.PMID: 19584276 , Jul-2009