Fiscal Year:	FY 2021	**Task Last Updated:**	FY 06/10/2021
PI Name:	Cornforth, Michael Ph.D.		
Project Title:	Molecular Characterization of Transmissible Chromosome Aberrations Produced By Ions of Intermediate and High Atomic Number		
Division Name:	Human Research		
Program/Discipline:			
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:	(1) **Cancer**:Risk of Radiation Carcinogenesis		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	77555-5302	**Congressional District:**	14
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2013-14 HERO NNJ13ZSA002N-RADIATION
Start Date:	03/11/2015	**End Date:**	03/10/2021
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**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:**	NASA JSC
Contact Monitor:	Zawaski, Janice	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: Extended to 3/10/2021 per NSSC information (Ed., 6/9/21) NOTE: Extended to 1/10/2021 per NSSC information (Ed., 1/21/2020) NOTE: Extended to 3/10/2020 per NSSC information (Ed., 3/12/19)		
Key Personnel Changes/Previous PI:	January 2016: No changes.		
COI Name (Institution):	Loucas, Bradford Ph.D. (University of Texas Medical Branch, Galveston)		
Grant/Contract No.:	NNX15AG74G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	During deep space exploration, personnel will be exposed to charged particles of intermediate and high atomic number, often collectively referred to as densely ionizing radiations. For a given dose these are almost certainly more likely to cause cancer than the sparsely ionizing types of radiation typically encountered on Earth, such as x- and gamma rays. Since it is not possible to determine directly the carcinogenic potential of such radiations, it becomes necessary to rely on surrogate experimental systems to provide this information. For a number of reasons, the formation of nonlethal (transmissible) chromosome aberrations, mainly reciprocal translocations and inversions, is considered by many to represent the best surrogate endpoint. And yet, only recently have we begun to really understand the molecular processes governing their formation, including possible differences that probably exist in the way that aberrations produced by sparsely- versus densely-ionizing radiations are formed. We propose using advanced molecular methods, including genome sequencing, to characterize structural changes to the DNA of human cells that accompany the formation of transmissible chromosome aberrations caused by exposure to various types of radiation likely to be encountered in deep space.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Radiation-induced reciprocal chromosome translocations and inversions are particularly important in that regard as they relate to crewed space activities. In addition to causing cancer, their appearance also accompanies ongoing genome instability processes associated with their progression. The fact that these particular chromosome aberrations are transmissible (non-lethal) also makes them ideal candidate biomarkers of accumulated radiation exposure. We argue that molecular analysis of breakpoint junctions formed as the result of translocations and inversions is vital to understanding the process of exchange aberration formation, since it is here where underlying repair/misrepair pathways leave their “molecular fingerprints.” Regarding relevance to NASA’s concerns, the study of chromosome aberrations stands to tell us much about mechanisms underlying the cancer process itself. The relationship between particle energy/track structure and radiogenic changes to the genome represents an important first step in understanding 1) basic dose-response relationships at low fluences and 2) fundamental carcinogenic processes that may ultimately form the basis for subsequent mitigation strategies.
Task Progress:	Humans activities associated with deep space flight are exposed to a variety of radiation types not found on Earth. These include ions of heavy elements stripped of their electrons. These HZE (high energy) particles damage the DNA of cells to produce chromosome aberrations, most of which involve broken pieces of one chromosome rejoining with similar broken pieces from a different chromosome. These rearrangements can cause mutations and cancer. To understand more about the processes causing these types of chromosome aberrations, it becomes necessary to study, at the molecular level, changes in the DNA that occur precisely at the junctions where the two broken chromosomes rejoin with one another. The basis for this study involved a comparison between the type of damage caused by HZE radiations compared to that produced following exposure to more common terrestrial radiations, like gamma rays. The type of chromosome damage under investigation involves illegitimate rejoining of genetic material from one chromosome to another in the form of chromosome translocations. We investigated the DNA sequences surrounding the new junctions produced when such translocations are formed. For gamma rays we found that the junctions could be characterized by the resection of 1-6 basepairs of DNA, containing short stretches of sequence homology between the pieces of chromosomes being rejoined, and that the initial breaks in the chromosomes frequently occurred in repetitive DNA, as opposed DNA coding for genes. Ed. note July 2021: Project continues as Directed Research project, "Molecular Characterization of Transmissible Chromosome Aberrations Produced by Ions of Intermediate and High Atomic Number: grant 80NSSC21K0679," with the same PI, Dr. Michael Cornforth. See that project for subsequent reporting.
Bibliography Type:	Description: (Last Updated: 06/11/2025)
Articles in Peer-reviewed Journals	Cornforth MN, Bedford JS, Bailey SM. "Destabilizing effects of ionizing radiation on chromosomes: Sizing up the damage." Cytogenet Genome Res. 2021;161(6-7):1-24. Review. Published online first September 06, 2021. https://doi.org/10.1159/000516523 ; PMID: 34488218 , Sep-2021