

Fiscal Year:	FY 2016	Task Last Updated:	FY 03/04/2016
PI Name:	Costes, Sylvain Ph.D.		
Project Title:	Blood-based Multi-scale Model for Cancer Risk from GCR in Genetically Diverse Populations		
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:	94035-0001	Congressional District:	18
Comments:	NOTE: Previously at Lawrence Berkeley National Laboratory until December 2016.		
Project Type:	GROUND	Solicitation / Funding Source:	2014-15 HERO NNJ14ZSA001N-RADIATION. Appendix D: Ground-Based Studies in Space Radiobiology
Start Date:	02/04/2016	End Date:	02/03/2019
No. of Post Docs:		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:		Monitoring Center:	NASA JSC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	NNJ16HP24I		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	<p>Crews on future exploration missions to Mars and other destinations in our solar system will be exposed to acute low doses (< 100 mSv) and chronic low doses (< 0.1 mSv/min) of high-LET ionizing radiation from solar particle events (SPE) and galactic cosmic radiation (GCR). Predicting cancer risk associated with these radiation types is a mission-critical challenge for NASA radiation health scientists and mission planners. Epidemiological methods lack sensitivity and power to provide detailed risk estimates for cancer, mainly because the number of exposed individuals to date is relatively small, limited to several hundred individuals exposed to trapped radiation in low Earth orbit and fewer than two dozen Apollo astronauts exposed to GCR for several days at a time. Moreover, population-based studies do not take individual radiation sensitivity into account, are sensitive to the presence of other confounding environmental insults, and require long follow-up times.</p> <p>In collaboration with the radiation Biodosimetry Laboratory and the modeling group at NASA Johnson Space Center and with the International Computer Science Institute (ICSI) at UC Berkeley, our team will bring unique inter-disciplinary expertise to integrate the large array of cancer data generated over the past 25 years and archived by NASA under the various Human Research Program (HRP) funded projects. The main goal of this proposal is to identify factors influencing radiation-induced carcinogenesis and integrate them into a multi-scale model already started at the Berkeley Lab that encompasses DNA damage response and inter-cellular signaling to predict cancer risk for any types of HZE. Because experimental data are dispersed across many different cancer models, radiation qualities, and measurement types, this project will also generate a complete set of experimental data designed to fully inform and validate the model. In this project, the model will impose the types of measurements being made, with a strong emphasis on well-established blood biomarkers. In our approach we hypothesize that genetic factors strongly influence risk of cancer from space radiation and that biomarkers reflecting DNA damage and inflammatory processes in the blood are great tools to predict risk and monitor potential health effects post-flight. By using blood as a surrogate organ, the proposed work will allow extrapolation of cancer risk from mice to humans. A cohort of 6 different strains of mice (collaborative cross-mouse) with expected sensitivity to ionizing radiation will be monitored for biomarkers and cancer after exposure to 0.3 Gy of 1 GeV/amu Fe particle and compared to 1 Gy exposure of gamma ray control. Because we favor larger number of animals per radiation condition, we selected only one dose and the most carcinogenic particle to prove the principle of our approach while validating our model on a complete set of ex-vivo data and in-vivo longitudinal data. The collaborative cross-mouse model is an SFA resource that will make it possible for our team to examine the impact of genetic diversity in an animal model in a systematic and reproducible manner. In parallel, we propose to fully characterize the DNA damage response and cell death from ionizing radiation administered ex-vivo to 30 genetically different strains of mice and to 1000 human's blood donors, matching the age and gender distribution of the astronaut population. Taken together, an array of ex-vivo phenotypic features will be associated to genetic traits across mice and humans as a function of age and gender. At the end of this proposal, our team will provide NASA with a model to estimate individualized risk for an astronaut before a flight as well as estimating the risk during the flight. Information generated in this proposal will also be useful to generate guidelines and suggest the best biomarkers to monitor the healthy recovery of astronauts post-flight.</p>
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2016.
Bibliography Type:	Description: (Last Updated: 06/01/2023)