Fiscal Year:	FY 2017	**Task Last Updated:**	FY 01/31/2017
PI Name:	Blattnig, Steve Ph.D.		
Project Title:	Space Radiation Risk Assessment Project		
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) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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PI Organization Type:	NASA CENTER	**Phone:**	757-864-1421
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City:	Hampton	**State:**	VA
Zip Code:	23681-2199	**Congressional District:**	2
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	Directed Research
Start Date:	02/01/2014	**End Date:**	12/31/2017
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:	Simonsen, Lisa	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 12/31/2017 per S. Monk/L. Simonsen/LaRC (Ed., 1/18/16)		
Key Personnel Changes/Previous PI:	January 2017: Carol Mullenax is new project manager.		
COI Name (Institution):	Kim, Myung-Hee Ph.D. (Wyle Laboratories, Inc.) Peterson, Leif Ph.D. (Houston Methodist Hospital Research Institute) Pluth , Janice Ph.D. (Lawrence Berkeley National Laboratory) Plante, Ianik M.D., Ph.D. (Wyle Laboratories, Inc.) Ponomarev, Artem L. Ph.D. (Wyle Laboratories, Inc.)		
Grant/Contract No.:	Internal Project		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The Risk Assessment Project at Langley Research Center is responsible for the integration of results from NASA space radiobiology research into computational models used for astronaut radiation risk assessments. The purpose of the Project is threefold: (1) evaluate the extent to which ongoing research leads to reduction in the uncertainty of risk assessments and provide, as a metric of program progress, the number of days in space during which the radiation exposure of astronauts remains below NASA limits within a 95% confidence interval ("safe days in space"); (2) perform mission planning studies to predict the number of safe days for any mission; (3) provide recommendations for research directions most likely to reduce risk or improve the accuracy of risk predictions. The four categories of risks from radiation in space are defined by the NASA Bioastronautics Roadmap (BR). They are:1) Carcinogenesis, 2) Acute and late effects to the Central Nervous System (CNS), 3) Degenerative Tissue Effects such as heart disease and cataracts, and 4) Acute Radiation risks. The number of safe days currently predicted for an astronaut's career is less than required by mission planning, due to the large uncertainties in risk prediction. In particular, a projection uncertainty below + or - 50% is the goal for the 1000-day Mars mission because the high level of risk will require high precision risk evaluations. The current approach used to project risk is based on epidemiology data and on phenomenological models used to derive risk prediction from them. This approach cannot lead to improvements in the accuracy of risk prediction beyond a factor of approximately 2. New approaches using molecular biology and genetics are the only viable ones for achieving the level of accuracy required by space exploration and a robust program to obtain the required data is supported by the Space Radiation Program. However, how to incorporate these data into risk prediction and assessment models is not well understood. This Project Plan describes the approaches that will be used to develop models of risk assessment based on mechanistic space radiobiology research funded by the Space Radiation Program, leading to incremental uncertainty reduction based on new experimental data, and to the development of application software to be used in the NASA operational radiation protection program. To accomplish these goals, we will establish new molecular based models of risk. The molecular pathways that are the hallmarks of genomic instability and cancer, and the perturbation of these pathways by radiation will be described using systems biology approaches and Monte-Carlo simulation. We will develop descriptive models of such pathways utilizing track structure models of biomolecular damage, and deterministic and stochastic kinetic models of dominant molecular pathways causative of BR radiation risks. These simulations will make maximum use of results from mechanistic space radiobiology, and will replace traditional hazard functions and their inherent uncertainties due to reliance on epidemiological or phenomenological approaches.
Rationale for HRP Directed Research:	This research is directed because it contains highly constrained research.
Research Impact/Earth Benefits:	Radiobiology research provides many important qualitative descriptions of biological effects of radiation on biomolecules, cells, and tissues. The Space Radiation Risk Assessment Project provides an important link that integrates qualitative experimental observations into detailed quantitative biophysical models of radiations risks. This research benefits all humans that will be exposed to ionizing radiation and supports the development of disease models in general. Models of cancer, heart disease, acute, and other risks developed by the Space Radiation Risk Assessment Project provide NASA with the ability to project risks and develop cost-effective mitigation approaches for future exploration missions.
Task Progress:	We built on findings from our previous study by defining additional relevant endpoints to improve our mechanistic understanding. We examined phosphorylation of fourteen key nodes in two different stress activated signaling pathways. Namely, the receptor tyrosine kinase signaling pathway, and the TNF alpha signaling pathway. We identified four key nodes in these pathways whose phosphorylation levels increase with age after high dose exposure to high LET (linear energy transfer) radiation. These results provide clues to the involvement of proteins and their related mechanisms in the age specific generation of cancer biomarkers noted in previous studies. In addition, we have also identified unique phospho-signatures that may underscore strain specific differences in susceptibility. In a second endeavor, to further understand the radiation and age dependent differences noted, we examined miRNA expression profiles in various age groups after high LET exposure. Overall, we have identified unique mechanistic signatures that underscore effects of age and individual susceptibility. These data together with our results on surrogate cancer risk markers will be crucial to reducing uncertainties pertaining to the effect of age and radiation quality in modeling cancer risk from heavy ion exposures. Overall, a healthier working population will have a lower all-cause morbidity (mortality) rate, ultimately shifting events to occur later in life. The healthy worker effect, also known as the healthy hired effect and healthy survivor effect, is a bias that causes morbidity or mortality to be lower among workers when compared with the general population, because unhealthy individuals are screened from or leave the workplace. In order to scope out the potential magnitude of the healthy worker effect, new estimates of survivor function for the astronauts were used to calculate an age-specific hazard function. The hazard function was employed during lifetime risk projections to generate baseline lifetime risks (BLR) and excess radiation-induced lifetime risks (ELR) of cancer mortality and incidence. A method of determining organ doses at different locations within a vehicle directly from dosimetry data from multiple locations was developed including initial testing with the Orion design. This will be a part of a tool being developed to monitor solar particle event exposures and potential acute radiation responses during missions. To this end, acute response modeling for the hematopoietic system was also improved to provide more clinically relevant information. In order to scope out the potential of such effects, initial calculations on the temporal profiles or organ dose rates for historical SPE (solar particle events) were performed. Work continued on the development and verification and validation of BDSTRACKS, which calculates chromosome aberrations using either the full Monte Carlo track structure simulation code RITRACKS or a simplified parametric track structure model. The code was modified to perform simulations for mixed fields in support of the galactic cosmic radiation (GCR) simulation effort. Also, photon transport was added to the Monte Carlo track structure model in order to better enable RBE (relative biological effectiveness) calculations. A significant effort was also made to streamline and test the code including comparisons of RITRACKS to TEPC (tissue equivalent proportional counter) data. We used cellular computer automata to investigate the relative cancer contribution of immediate damage to cell at the moment of exposure against the effect of long-term systemic changes such as chronic inflammation following exposure. Our computer model was able to recapitulate spontaneous breast cancer incidence as well as the cancer incidence in the

	A-bomb survival cohort. The model was then tested to predict cancer incidence in the same artificial cohort exposed to space radiation that we refined our DNA damage cluster model, which can explain RBE greater than one for high LET without the need of introducing DNA damage complexity as a mechanism. Instead, we propose a formalism where the combination of nuclear repair domains with very high local doses along ion tracks is sufficient to explain and predict cell death for any LET. We are finalizing the production of both survival curves and mutation frequencies for the 252 LET and dose conditions, so we can generate appropriate RBEs.
Bibliography Type:	Description: (Last Updated: 06/30/2023)
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