Task Book Report Generated on: 04/25/2024

P. Name:   Risca, Viviana Ph.D.   Epigenetic State Modelation of Radiation-Induced DNA Damage: Namoscale Modeling and Validation of Radiation-Induced DNA Damage: Namoscale Modeling and Validation of Radiation Name:   Program/Discipline:   P	Fiscal Year:	FY 2021	Task Last Updated:	FY 04/16/2021
Project Title:			o p	
Division Name:   Human Research   Program/Discipline:   Program/Discipline:   Program/Discipline:   Program/Discipline:   Program/Discipline:   Program/Discipline:   Program/Discipline:   Program Elements:   Program Elements				
Program/Discipline:           Element/Suddiscipline:         TechPort:         Yes           Joint Agency Name:         TechPort:         Yes           Human Research Program Elements:         (1) SR.Space Radiation           Human Research Program Ribse:         (1) Caneer-Risk of Radiation Carcinogenesis           Space Biology Cross-Element:         None           Space Biology Cross-Element:         None           Space Biology Special Category:         None           PI Email:         vireadirackefeller.edu         Fax: FY           Pl Organization Type:         UNIVERSITY         Phone:         516-728-3406           Organization Name:         The Rockefeller University         Phone:         516-728-3406           Pl Address 1:         Laboratory of Genome Architecture and Dynamics         14-728-3406         Project Type:         State:         NY           Pl Address 2:         1230 York Ave, Rox 176         Yu. State:         NY         Project Type:         New York         State:         NY           Comments:         State:         NY         14-24-24-24-24-24-24-24-24-24-24-24-24-24	3			
Program/Discipline-  Element/Subdiscipline-  Element/Subdiscipline-  Subdiscipline-  Subdisc	Division Name:	Human Research		
Flement/Shobfiscipline:   TechPort   Yes   Yes   Minama Research Program Elements   (1) SR-Space Radiation   (1) Cancer-Risk of Radiation Carcinogenesis   (1) SR-Space Radiation Carcinogenesis   (1) SR-Sp	Program/Discipline:			
Human Research Program Elements: (1) SR: Space Radiation Human Research Program Risks: (1) Cancer: Risk of Radiation Carcinogenesis Space Biology Cross-Element Space Biology Cross-Element Space Biology Special Category: None PI Email: risea@rockefeller.edu Fax: FY PI Organization Type: UNIVERSITY Phone: 516-728-3406 Organization Name: The Rockefeller University PI Address 1: Laboratory of Genome Architecture and Dynamics PI Address 2: 1230 York Ave, Box 176 PI Web Page: City: New York State: NY Zip Code: 10065-6307 Congressional District: 12 Comments: Project Type: GROUND Solicitation / Founding OMNIBUS 2: Human Health Countermeasures, Surface Behavioral Perpendix OMNIBUS 2: Human Health Countermeasures, Surface Behavioral Perpendix Comments:  Start Date: 0401/2021 End Date: 3031/2022 No. of Post Docs: No. of Master' Degrees: No. of Post Docs: No. of Master' Degrees: No. of Master's Candidates: No. of Master's Ca				
Human Research Program Rislss: (I) Cancer:Risk of Radiation Carcinogenesis  Space Biology Element: None  Space Biology Cross-Element Discipline: None  Space Biology Special Category: None  PI Email: vrisca@rockefeller.edm Fax: FY  PI Organization Type: UNIVERSITY Phone: 516-728-3406  Organization Type: UNIVERSITY Phone: 516-728-3406  Organization Name: The Rockefeller University  PI Address 1: Laboratory of Genome Architecture and Dynamics  PI Address 2: 1230 York Ave, Box 176  PI Web Page:  City: New York State: NY  Zip Code: 10065-6307 Congressional District: 12  Comments:  Project Type: GROUND Solicitation / Funding OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Radiation-Appendix Commibus2-Appendix Districts  Start Date: 04/01/2021 End Date: 03/31/2022  No. of Post Dues: No. of Phat Degrees: No. of Post Dues: No. of Master' Degrees: No. of Post Dues: No. of Master' Degrees: No. of Master's Candidates: No. of Master' Degrees: No. of Bachelor's Candidates: Monitoring Center: No. of Master' Degrees: No. of Bachelor's Candidates: Monitoring Center: No. of Master' Degrees: No. of Bachelor's Candidates: Mone Research Selection of Contact Ponne: 281-244-0596 (e)/832-221-4576 (m)  Eligart, Robin Contact Famal: Selonac legarit@nass.gov  Flight Program:  Flight Assignment: Key Personnel Changes/Previous PI: COI Name (Institution): Plante, lank Ph.D. (NASA Johnson Space Center) Jecvarajan, Antony Ph.D. (NASA Johnson Space Center) Jecvarajan, Antony Ph.D. (NASA Johnson Space Center)	Joint Agency Name:		TechPort:	Yes
Space Biology Element:         None           Space Biology Cross-Element Discipline:         None           Space Biology Special Category:         None           PI Email:         Vrisea@rockefeller.edu         Fax:         FV           PI Organization Type:         UNIVERSITY         Phone:         516-728-3406           Organization Name:         The Rockefeller University         Phone:         516-728-3406           PI Address I:         Laboratory of Genome Architecture and Dynamics         Project Type:         Laboratory of Genome Architecture and Dynamics           PI Address 2:         Lajon York Ave, Box 176         State:         NY           PI Web Page:         State:         NY           City:         New York         State:         NY           Zip Code:         10065-6307         Congressional District:         12           Comments:         2019-2020 HERO 80JSC019N0001-HHCBPSR, OMNIBUS2: Human Realth Countermeasures, Behavioral Performance, and Space Radiation-Appendix C Omnibus2-Appendix D           Start Date:         04-01/2021         End Date:         03/31/2022           No. of PhD Candidates:         No. of Master's Degrees:         No. of Master's Candidates:         No. of Master's Degrees:           No. of Master's Candidates:         No. of Bachelor's Candidates:         Monitoring	<b>Human Research Program Elements:</b>	(1) SR:Space Radiation		
Space Biology Cross-Element Discipline:  Space Biology Special Category:  None  PI Email:  PI Organization Type:  UNIVERSITY  Phone:  S16-728-3406  Organization Name:  The Rockefeller edu  PI Address 1:  Laboratory of Genome Architecture and Dynamics  PI Address 2:  1230 York Ave, Box 176  PI Web Page:  City:  New York  New York  State:  NY  Zip Code:  10065-6307  Congressional District:  Comments:  Froject Type:  GROUND  GROUND  Solicitation / Funding Solicitation / Solicitation / Funding Solicitation / Funding Solicitation / Solicita	Human Research Program Risks:	(1) Cancer: Risk of Radiation Carcinogen	nesis	
Discipline:   None   None   Space Biology Special Category:   UNIVERSITY   Phone:   516-728-3406	Space Biology Element:	None		
PI Email:		None		
Pl Organization Type: UNIVERSITY Phone: 516-728-3406 Organization Name: The Rockefeller University PI Address 1: Laboratory of Genome Architecture and Dynamics PI Address 2: 1230 York Ave, Box 176 PI Web Page: City: New York State: NY Zip Code: 10065-6307 Congressional District: 12 Comments:  Project Type: GROUND Solicitation / Funding OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance and Space Relation-Appendix D OMNIBUS2: Human Health Countermeasures, Behavioral Performance Relation-Appendix D OMNIBUS2: Human Health C	Space Biology Special Category:	None		
Organization Name: The Rockefeller University P1 Address 1: Laboratory of Genome Architecture and Dynamics P1 Address 2: 1230 York Ave, Box 176 P1 Web Page: City: New York State: NY Zip Code: 10065-6307 Congressional District: 12 Comments:  Project Type: GROUND Solicitation / Funding OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Radiation-Appendix C; Omnibus2-Appendix D Start Date: 04/01/2021 End Date: 03/31/2022 No. of Post Docs: No. of PhD Candidates: No. of Master' Degrees: No. of Master's Candidates: No. of Master' Degrees: No. of Bachelor's Condidates: No. of Master' Degrees: No. of Bachelor's Candidates: Monitoring Center: NASA JSC Contact Monitor: Elgart, Robin Contact Phone: 281-244-0596 (o)/832-221-4576 (m) Contact Email: shona.eleant@masa.gov F1light Program: F1light Assignment: Key Personnel Changes/Previous P1: COI Name (Institution): Plante, lanik, Ph.D. (NASA Johnson Space Center) Jecvarajan, Antony Ph.D. (NASA Johnson Space Center) Grant/Contract No.: 80NSSC21K0565 Performance Goal No.:	PI Email:	vrisca@rockefeller.edu	Fax:	FY
Pl Address 1:	PI Organization Type:	UNIVERSITY	Phone:	516-728-3406
PI Address 2: 1230 York Ave, Box 176  PI Web Page:  City: New York State: NY  Zip Code: 10065-6307 Congressional District: 12  Comments:  Project Type: GROUND Solicitation / Funding OMNEINES2: Human Health Countermeasures, Behavioral Performance, and Space Radiation-Appendix C; Omnibus2-Appendix D  Start Date: 04/01/2021 End Date: 03/31/2022  No. of Post Does: 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  Contact Monitor: Elgart, Robin Contact Phone: 281-244-0596 (o)/832-221-4576 (m)  Contact Email: shona.elgart@nasa.gov  Flight Program: Flight Assignment: Key Personnel Changes/Previous PI:  COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center) Jecvarajan, Antony Ph.D. (NASA Johnson Space Center) Grant/Contract No.: 80NSSC21K0565  Performance Goal No.:	Organization Name:	The Rockefeller University		
Pl Web Page:   City: New York State: NY	PI Address 1:	Laboratory of Genome Architecture and Dynamics		
City: New York State: NY  Zip Code: 10065-6307 Congressional District: 12  Comments:  Project Type: GROUND Solicitation / Funding Source: Behavioral Performance, and Space Performance Source: No. of PhD Degrees: No. of Post Docs: No. of PhD Degrees: No. of PhD Candidates: No. of Master' Degrees: No. of Master's Candidates: No. of Master' Degrees: No. of Bachelor's Degrees: No. of Bachelor's Candidates: Monitoring Center: NASA JSC  Contact Monitor: Elgart, Robin Contact Phone: 281-244-0596 (o)/832-221-4576 (m)  Contact Email: shona.elgart@nasa.gov  Flight Program: Flight Assignment: Key Personnel Changes/Previous PI:  COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center) Jeevarajan, Antony Ph.D. (NASA Johnson Space Center) Grant/Contract No.: 80NSSC21K0565  Performance Goal No.:	PI Address 2:	1230 York Ave, Box 176		
Zip Code: 10065-6307 Congressional District: 12  Comments:  Project Type: GROUND Solicitation / Funding Source: Behavioral Performance, and Space Radiation-Appendix C; Omnibus2-Appendix D  Start Date: 04/01/2021 End Date: 03/31/2022  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  Contact Monitor: Elgart, Robin Contact Phone: 281-244-0596 (o)/832-221-4576 (m)  Contact Email: shona eleart@nasa.gov  Flight Program: Flight Assignment: Key Personnel Changes/Previous PI:  COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center)	PI Web Page:			
Comments:    Project Type: GROUND   Solicitation / Funding Source: Behavioral Performance, and Space Radiation-Appendix C; Omnibus2-Appendix D	City:	New York	State:	NY
Project Type:  GROUND  Solicitation / Funding Source:  Solicitation / Funding Source:  Solicitation / Funding Source:  MNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space Radiation-Appendix C; Omnibus2-Appendix D  Start Date:  04/01/2021  End Date: 03/31/2022  No. of Post Docs:  No. of PhD Candidates:  No. of Master' Degrees:  No. of Master's Candidates:  No. of Master's Candidates:  No. of Bachelor's Degrees:  No. of Bachelor's Candidates:  No. of Master' Degrees:  No. of Bachelor's Candidates:  No.	Zip Code:	10065-6307	<b>Congressional District:</b>	12
Project Type:  GROUND  Solicitation / Funding Source:	Comments:			
No. of Post Docs: No. of PhD Degrees: No. of PhD Candidates: No. of Master's Candidates: No. of Master's Candidates: No. of Bachelor's Degrees: No. of Bachelor's Candidates: Monitoring Center: NASA JSC Contact Monitor: Elgart, Robin Contact Phone: 281-244-0596 (o)/832-221-4576 (m) Contact Email: shona.elgart@nasa.gov Flight Program: Flight Assignment: Key Personnel Changes/Previous PI: COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center) Jeevarajan, Antony Ph.D. (NASA Johnson Space Center) Grant/Contract No.: 80NSSC21K0565 Performance Goal No.:	Project Type:	GROUND		OMNIBUS2: Human Health Countermeasures, Behavioral Performance, and Space
No. of PhD Candidates:  No. of Master's Candidates:  No. of Master's Candidates:  No. of Bachelor's Degrees:  No. of Bachelor's Candidates:  Monitoring Center: NASA JSC  Contact Monitor:  Elgart, Robin  Contact Phone: 281-244-0596 (o)/832-221-4576 (m)  Contact Email:  shona.elgart@nasa.gov  Flight Program:  Flight Assignment:  Key Personnel Changes/Previous PI:  COI Name (Institution):  Plante, Ianik Ph.D. (NASA Johnson Space Center)  Jeevarajan, Antony Ph.D. (NASA Johnson Space Center)  Grant/Contract No.:  80NSSC21K0565  Performance Goal No.:	Start Date:	04/01/2021	End Date:	03/31/2022
No. of Master's Candidates:  No. of Bachelor's Degrees:  No. of Bachelor's Candidates:  Monitoring Center: NASA JSC  Contact Monitor: Elgart, Robin Contact Phone: 281-244-0596 (o)/832-221-4576 (m)  Contact Email: shona.elgart@nasa.gov  Flight Program:  Flight Assignment:  Key Personnel Changes/Previous PI:  COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center)  Grant/Contract No.: 80NSSC21K0565  Performance Goal No.:	No. of Post Docs:		No. of PhD Degrees:	
No. of Bachelor's Candidates:  No. of Bachelor's Candidates:  Monitoring Center: NASA JSC  Contact Monitor:  Elgart, Robin  Contact Phone: 281-244-0596 (o)/832-221-4576 (m)  Contact Email:  shona.elgart@nasa.gov  Flight Program:  Flight Assignment:  Key Personnel Changes/Previous PI:  COI Name (Institution):  Plante, Ianik Ph.D. (NASA Johnson Space Center)  Jeevarajan, Antony Ph.D. (NASA Johnson Space Center)  Grant/Contract No.:  80NSSC21K0565  Performance Goal No.:	No. of PhD Candidates:		No. of Master' Degrees:	
Contact Monitor: Elgart, Robin Contact Phone: 281-244-0596 (o)/832-221-4576 (m)  Contact Email: shona.elgart@nasa.gov  Flight Program:  Flight Assignment:  Key Personnel Changes/Previous PI:  COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center )  Jeevarajan, Antony Ph.D. (NASA Johnson Space Center )  Grant/Contract No.: 80NSSC21K0565  Performance Goal No.:	No. of Master's Candidates:			
Contact Email: shona.elgart@nasa.gov  Flight Program:  Flight Assignment:  Key Personnel Changes/Previous PI:  COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center)  Jeevarajan, Antony Ph.D. (NASA Johnson Space Center)  Grant/Contract No.: 80NSSC21K0565  Performance Goal No.:	No. of Bachelor's Candidates:		<b>Monitoring Center:</b>	NASA JSC
Flight Assignment:  Key Personnel Changes/Previous PI:  COI Name (Institution):  Plante, Ianik Ph.D. (NASA Johnson Space Center)  Jeevarajan, Antony Ph.D. (NASA Johnson Space Center)  Grant/Contract No.:  80NSSC21K0565  Performance Goal No.:	Contact Monitor:	Elgart, Robin	<b>Contact Phone:</b>	281-244-0596 (o)/832-221-4576 (m)
Flight Assignment:  Key Personnel Changes/Previous PI:  COI Name (Institution):  Plante, Ianik Ph.D. (NASA Johnson Space Center)  Jeevarajan, Antony Ph.D. (NASA Johnson Space Center)  Grant/Contract No.:  80NSSC21K0565  Performance Goal No.:	Contact Email:	shona.elgart@nasa.gov		
Key Personnel Changes/Previous PI:  COI Name (Institution): Plante, Ianik Ph.D. (NASA Johnson Space Center) Jeevarajan, Antony Ph.D. (NASA Johnson Space Center)  Grant/Contract No.: 80NSSC21K0565  Performance Goal No.:	Flight Program:			
COI Name (Institution):  Plante, Ianik Ph.D. (NASA Johnson Space Center ) Jeevarajan, Antony Ph.D. (NASA Johnson Space Center )  Grant/Contract No.:  80NSSC21K0565  Performance Goal No.:	Flight Assignment:			
Grant/Contract No.:  80NSSC21K0565  Performance Goal No.:	Key Personnel Changes/Previous PI:			
Performance Goal No.:	COI Name (Institution):			
	Grant/Contract No.:	80NSSC21K0565		
Performance Goal Text:	Performance Goal No.:			
	Performance Goal Text:			

Task Book Report Generated on: 04/25/2024

## BACKGROUND

The risks of cellular dysfunction associated with exposure to space radiation, including transcriptional and epigenetic perturbations and genomic instability due to DNA breaks, have been studied in cell lines, with DNA repair foci and products as the main readouts. Such genetic and cell biological readouts show that high linear energy transfer (LET) charged nuclei, such as those found in galactic cosmic rays (GCR), cause persistent cellular changes in stress response and genomic integrity. These effects are different from the effects of low-linear energy transfer (LET) radiation such as X-rays and occur in the context of the genome-wide epigenetic landscape of each cell, which includes nucleosome positions, nucleosome modifications, and variant histone substitutions in those nucleosomes. Epigenetic states differ in chromatin fiber conformations, with transcriptionally active chromatin adopting more open, extended structures. These differences can affect DNA break patterns in response to ionizing radiation, potentially creating distinct DNA repair and signaling outcomes. The epigenetic state landscape of a cell depends on its differentiation state, cell type, and responses to external stimuli. Because it is not practical to experimentally investigate every cell type, a more generalizable approach is needed to predict how the cell's distinctive epigenetic landscape will interact with radiation to give rise to a certain pattern of DNA breaks and associated cellular response. A generalizable approach that takes local epigenetic map information into account can leverage the large and diverse epigenomic data sets available for a large number of human cell types. Previous investigations of chromatin structure's role in regulating DNA damage by radiation assumed that chromatin adopts stable, regular structures such as 30-nm fibers. Recently emerging consensus in the field suggests this single-structure view is inaccurate and the ensemble of conformational fluctuations of the fiber must be taken into

## HYPOTHESIS

**Task Description:** 

We hypothesize that the pattern and lethality of DNA breaks generated at a given genomic locus depend on the combination of (1) the incoming ionizing radiation, with differences between low LET photons and high LET GCRs, and (2) the epigenetic state of that locus, which is associated with a characteristic ensemble of chromatin fiber conformations.

## **DELIVERABLES**

We propose to develop a generalizable mechanistic approach to determining how DNA breaks are generated by ionizing radiation including GCRs and photons. We will integrate realistic chromatin fiber ensembles with Monte Carlo simulations of photons or GCR nuclei interacting with those fibers, and Green's function based calculation of radiochemistry kinetics after the particle delivers its energy. The chromatin fiber ensembles will be generated through a coarse-grained simulation based on a stretchable shearable worm-like chain model of linker DNA between nucleosomes that is constrained by pairwise DNA-DNA contact data. We will measure chromatin fiber contact distances, simulate sub-kilobase chromatin conformation ensembles consistent with those contact distances, and predict how these ensembles give rise to ensembles of DNA break patterns. These measurements and simulations will be carried out for multiple chromatin states across several cell types as well as for in vitro reconstituted chromatin fibers in order to build a general, cell type independent model of the relationship between epigenetic state and vulnerability to radiation induced DNA damage. The resulting software package will enable the simulation of user-programmable chromatin states, to produce chromatin state specific predictions of expected DNA fragmentation patterns for each type of heavy ion or photon of incoming radiation. These fragmentation patterns can then form the basis for future mechanistic studies of the cell's differential repair and signaling responses to varied break cluster types.

Rationale for HRP Directed Research:

**Research Impact/Earth Benefits:** 

Task Progress: New project for FY2021.

Bibliography Type: Description: (Last Updated: 03/15/2024)