Fiscal Year:	FY 2014	**Task Last Updated:**	FY 08/02/2013
PI Name:	Wang, Minli M.D.		
Project Title:	Mechanistic Study of the Risk of Low Doses of HZE Particles on Human Cell Pre-Malignant Transformation		
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:	(1) **Cancer**:Risk of Radiation Carcinogenesis		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	minli.wang@nasa.gov	**Fax:**	FY
PI Organization Type:	NON-PROFIT	**Phone:**	281-483-4986
Organization Name:	Universities Space Research Association		
PI Address 1:	3600 Bay Area Blvd		
PI Address 2:			
PI Web Page:			
City:	Houston	**State:**	TX
Zip Code:	77058-1113	**Congressional District:**	22
Comments:	USRA corporate address: 10211 WINCOPIN CIR 500, Columbia, MD 21044-3405.		
Project Type:	GROUND	**Solicitation / Funding Source:**	2012 Space Radiobiology NNJ12ZSA001N
Start Date:	10/01/2012	**End Date:**	11/30/2014
No. of Post Docs:	2	**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:	Simonsen, Lisa	**Contact Phone:**	
Contact Email:	lisa.c.simonsen@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: Extended to 11/30/14 per PI; original end date was 9/30/13 (Ed., 7/31/13)		
Key Personnel Changes/Previous PI:	ED. NOTE (December 2015): Per Space Radiation Element Manager L. Simonsen, PI Dr. Minli Wang moved from Universities Space Research Association in 2014; the study is now inactive.		
COI Name (Institution):	Wang, Ya (Emory University)		
Grant/Contract No.:	Internal Project		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Establishing the scientific basis of radiation cancer risk is a primary goal for the NASA Space Radiation Program. There are large uncertainties in approaches to extrapolate experimental or human epidemiology data from high to low doses, and from high LET to low LET radiation. In this proposed study, we will use the cell transformation (pre-malignance) assay, which occurs much earlier than carcinogenesis after radiation exposure, to elucidate mechanisms and to provide important quantitative data on radiation quality effects related to cancer risks from low doses of HZE particles. We proposed two aims to test our hypothesis that p63 plays an important role in HZE particle-induced human cell pre-malignant transformation. Aim1: Investigate how p63 promotes HZE particle-induced human epithelial cell transformation through the JAG1/Wnt4#Myc pathway. Aim2: Investigate how p63 promotes HZE particle-induced human epithelial cell transformation through the CD95#JNK#Jun pathway. The results from this proposal are expected to reveal the importance of p63 in HZE particle-induced human epithelial cell transformation. Since majority of human tumors are derived from epithelial cells, the results from this proposal will make important contribution to the mechanism of HZE particle-induced carcinogenesis and therefore, providing valuable information for estimating the risk of space radiation-induced carcinogenesis and for further protection from such risk.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The results from this proposed work will reveal the important role of p63 in HZE particle-induced human epithelial cell transformation. Since the majority of human tumors (more than 90%) are derived from epithelial cells, the results from this proposal will make an important contribution to the understanding of how low doses of HZE particles can promote carcinogenesis and, therefore, provide valuable information for estimating the risk of space radiation-induced carcinogenesis and for further attempting to reduce such risk.
Task Progress:	During the first year of this grant, we have confirmed the important role of p63 in HZE particle radiation-induced human epithelial cell transformation. We have published two articles discovering the roles of TGFbeta/Smad pathway in HZE particle radiation induced tissue/cell damage. To investigate the two pathways, p63-JAG1/Wnt4-Myc and p63-CD95-JNK-Jun, proposed in our hypothesis, we have irradiated the p63 down-regulated human epithelial cells or up-regulated fibroblasts with low doses of HZE particles. Materials for the detection of the components in these two pathways have been prepared. We are expecting to obtain our preliminary data in a short period of time. In the fall we will investigate the possible crosstalk of p63 and p53 in TGFbeta/Smad signaling pathway. ED. NOTE (December 2015): Per Space Radiation Element Manager L. Simonsen, PI Dr. Minli Wang moved from Universities Space Research Association in 2014; the study is now inactive.
Bibliography Type:	Description: (Last Updated: 12/09/2015)
Articles in Peer-reviewed Journals	Wang M, Saha J, Cucinotta FA. "Smad7 foci are present in micronuclei induced by heavy particle radiation." Mutation Research. 2013 Aug 30;756(1-2):108-14. Epub 2013 Apr 30. http://dx.doi.org/10.1016/j.mrgentox.2013.04.011 ; PubMed PMID: 23643526 , Aug-2013
Articles in Peer-reviewed Journals	Wang M, Saha J, Hada M, Anderson JA, Pluth JM, O'Neill P, Cucinotta FA. "Novel Smad proteins localize to IR-induced double-strand breaks: interplay between TGFß and ATM pathways." Nucleic Acids Res. 2013 Jan;41(2):933-42. http://dx.doi.org/10.1093/nar/gks1038 ; PubMed PMID: 23221633 , Jan-2013
Articles in Peer-reviewed Journals	Saha J, Wang M, Cucinotta FA. "Investigation of switch from ATM to ATR signaling at the sites of DNA damage induced by low and high LET radiation." DNA Repair. 2013 Dec;12(12):1143-51. http://dx.doi.org/10.1016/j.dnarep.2013.10.004 (Originally reported in August 2013 as "in press" as of August 2013.) , Dec-2013