### Fiscal Year:
FY 2015

### Project Title:
NSCOR: Space Radiation and Gastrointestinal Cancer: A Comprehensive Strategy for Risk Assessment and Model Development

### PI Name:
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### Division Name:
Human Research

### Program/Discipline--Element/Subdiscipline:
HUMAN RESEARCH--Radiation health

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### Project Type:
GROUND

### Solicitation:
2014-15 HERO NNJ14ZSA001N-NSCOR Radiation

### Start Date:
04/15/2015

### End Date:
04/14/2020

### Performance Goal Text:
Considering the high spontaneous incidence of gastrointestinal (GI) cancer and higher incidence of premalignant
## Task Description:

Considering the high spontaneous incidence of gastrointestinal (GI) cancer and higher incidence of premalignant colonic polyps, an even modest increase by space radiation exposure could have a significant effect on astronauts’ health risk estimates during and after long-duration manned space flights. However, there is substantial uncertainty for GI cancer risk estimation from space radiation due to the lack of in vivo human data. This proposal addresses the category in the current solicitation involving ‘new approaches’ towards ‘mechanistic understanding’ of GI cancer risk using ‘new biological models’ for ‘studies of radiation quality and dose-rate effects’ in relation to ‘individual radiation sensitivity’.

The overarching goal of the current proposal is to specifically investigate cellular and molecular hypothesis driven mechanisms in relevant mouse models that will contribute to carcinogenic risk estimates of GI cancer after exposure to space radiation beams prioritized in the current solicitation. We have chosen high priority HZE beams. Since maximal effects have already been seen with 28Si ions, this will be a priority and we will extend to lower Z at similar energy using 16O and 4He ions. Having found modest effects in some studies with protons and considering the importance of assessing the effects of mixed beams, we will take advantage of the availability of the sequential field proton/56Fe (6.2/150 keV/µm) beam to start to represent the mixed particle radiation in space. We will consult with NASA on beam prioritization and consider the Galactic Cosmic Ray (GCR) Simulator as the study progresses. Specifically, this proposal seeks to determine incidence and grade as well as identify molecular perturbations and target cells associated with intestinal and gastric (stomach) tumors through monitoring of changes in the tumor number, histology, gene expression, metabolome, and in the genome of the proposed model system after exposure to these space-radiation beams.

We are proposing four complementary Aims (and projects) that will have a common objective to develop a more reliable GI cancer risk prediction model. 1] Quantitatively assess GI tumorigenesis in mouse models of GI cancer and collect samples for qualitative analysis (Project 1), 2] Dissection of the signaling events and consequences in gastrointestinal cells of the persistent effects of space radiation (Project 2), 3] Characterization of radiation-induced neoplastic events in normal diploid human colonocytes (Project 3), 4] Development of systems biology (Project 4A) and mathematical modeling (Project 4B) approaches for GI cancer risk assessment.

## Rationale for HRP Directed Research:

## Research Impact/Earth Benefits:

## Task Progress:

New project for FY2015.

## Bibliography Type:

Description: (Last Updated: 03/05/2019)