

Active Project (2015 - 2015)

# Prototype Biology-Based Radiation Risk Module Project

Center Independent Research &amp; Developments: JSC IRAD Program | Mission Support Directorate (MSD)



## ABSTRACT

Biological effects of space radiation and risk mitigation are strategic knowledge gaps for the Evolvable Mars Campaign. The current epidemiology-based NASA Space Cancer Risk (NSCR) model contains large uncertainties (HAT #6.5a) due to lack of information on the radiobiology of galactic cosmic rays (GCR) and lack of human data. The use of experimental models that most accurately replicate the response of human tissues is critical for precision in risk projections. Our proposed study will compare DNA damage, histological, and cell kinetic parameters after irradiation in normal 2D human cells versus 3D tissue models, and it will use a multi-scale computational model (CHASTE) to investigate various biological processes that may contribute to carcinogenesis, including radiation-induced cellular signaling pathways. This cross-disciplinary work, with biological validation of an evolvable mathematical computational model, will help reduce uncertainties within NSCR and aid risk mitigation for radiation-induced carcinogenesis.

## ANTICIPATED BENEFITS

### To NASA unfunded & planned missions:

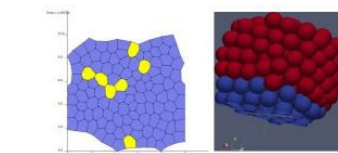
Space radiation effects and radiation risk mitigation are strategic knowledge gaps for the Evolvable Mars Campaign and are major limiting risks as defined by NASA's Human System Risk Board. Current radiation cancer risk estimates (NSCR) are associated with large uncertainties and there is a need for accurate biological models that can be used to characterize molecular mechanisms of radiation carcinogenesis (HAT #6.5a: Human GCR Radiation Protection). Our proposed work will help reduce uncertainties and mitigate the risk of radiation carcinogenesis by providing a prototype of a biology-based computational model for use along with the NSCR to generate an evolvable cancer risk assessment model. The use of novel

### 3D Organotypic Culture:



Organotypic model of human esophageal epithelium (A) Schematic diagram of a 3D organotypic culture showing individual layers. (B) Small-equivalent collagen/fibroblast base prior to epithelial seeding, shown in 24 mm transwell inserted into a 6-well plate. (C) H&E stained section of human esophagus (image from [www.histology.net/](http://www.histology.net/)). (D) H&E stained section of a formalin-fixed paraffin-embedded slice from a 16-day organotypic culture of normal human esophageal epithelial cells grown in our laboratory at JSC. (E) A section from a similar culture immunostained for the basal marker KRT14 (red) and the suprabasal differentiation marker KRT13 (green); nuclei are counterstained with DAPI (blue).

### Tissue Simulation with CHASTE



2D (left) and 3D (right) models of generic tissue simulated with CHASTE. The 2D vertex cells are confined in a  $10 \times 10$  square, whose cell cycles are regulated with a contact-inhibition model, with yellow cells in S phase and the blue in other phases, while the 3D spherical cells are in a 0.5-0.5-cube, and regulated with a Wnt signaling cell cycle model, with blue cells representing proliferative stem and transit cells and the red for differentiated cells.

Here are examples of the 3-D tissue cultures we will use to generate biological datasets for this project, and a tissue simulation with the software CHASTE.

## Table of Contents

Abstract . . . . .	1
Anticipated Benefits . . . . .	1
Detailed Description . . . . .	2
Technology Maturity . . . . .	2
Management Team . . . . .	2
U.S. Locations Working on this Project . . . . .	3
Details for Technology 1 . . . . .	4

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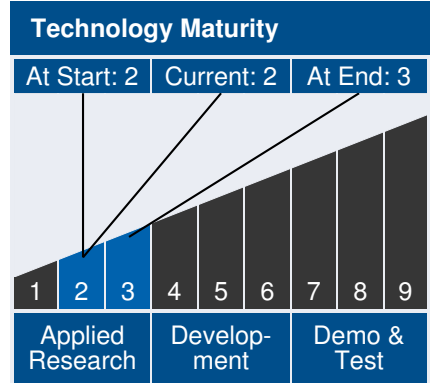
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3D models will also provide a low-cost avenue for testing nutritional and biomedical countermeasures, thereby providing risk mitigation strategies and enabling sustainable human exploration on planetary and other missions.

## DETAILED DESCRIPTION

We will utilize novel 3D models as ground testbeds for radiation effects in humans. We will compare radiation effects on normal human epithelial cells in standard 2D monolayer culture with 3D organotypic models in which morphological features, differentiation markers, and growth characteristics of a fully differentiated normal human tissue are more accurately represented. Markers of genotoxic damage and limited histological and cell kinetic parameters will be entered into a multiscale computational software CHASTE (Cancer, Heart And Soft-Tissue Environment) to simulate the tissue homeostasis and radiation response. Comparison of the results (population kinetics and proliferation indices) with the experimental results will provide a biological validation of the CHASTE model; we will formulate quantitative correlations between tissue specific parameters and the outcome of genotoxic effects.



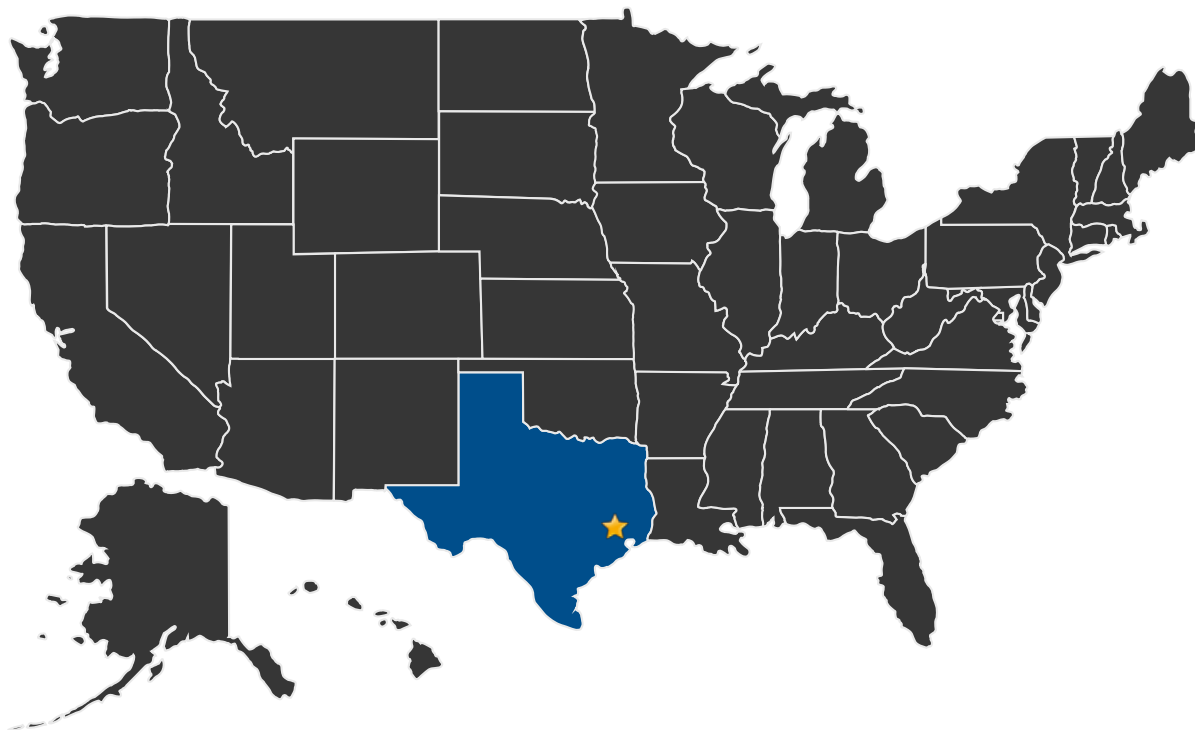
Management Team	
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## U.S. LOCATIONS WORKING ON THIS PROJECT



■ U.S. States With Work      ★ **Lead Center:**  
Johnson Space Center

### Other Organizations Performing Work:

- Universities Space Research Association Division of Life Sciences
- WYLE Integration Science & Engineering

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## DETAILS FOR TECHNOLOGY 1

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### Technology Title

Biology-Based Radiation Risk Assessment Module

### Technology Description

This technology is categorized as complex electronics software for ground scientific research or analysis

We will utilize novel 3D models as ground testbeds for radiation effects in humans. We will compare radiation effects on normal human epithelial cells in standard 2D monolayer culture with 3D organotypic models in which morphological features, differentiation markers, and growth characteristics of a fully differentiated normal human tissue are more accurately represented. Markers of genotoxic damage and limited histological and cell kinetic parameters will be entered into a multiscale computational software CHASTE (Cancer, Heart And Soft-Tissue Environment) to simulate the tissue homeostasis and radiation response. Comparison of the results (population kinetics and proliferation indices) with the experimental results will provide a biological validation of the CHASTE model; we will formulate quantitative correlations between tissue specific parameters and the outcome of genotoxic effects.

### Capabilities Provided

The prototype module will provide a biologically validated radiation risk assessment tool that can be used in conjunction with the epidemiology-based NASA Space Cancer Risk (NSCR) Model. This will help to reduce uncertainties within the NSCR.

### Potential Applications

A potential application for this technology includes being used operationally, with the NASA Space Cancer Risk Model, to predict "Safe Days" for astronauts. Another application includes being used a tool for ground-based scientific research on radiation risks.