Introduction: Exploration of deep space will result in long term protracted exposures to microgravity and space radiation. Our current understanding of the fundamental mechanisms of response to these stressors on biological systems and human health remain limited. Current radiation risk estimates for crewed space flight are based predominantly on human epidemiology data following low linear energy (LET) radiation exposures. These data are scaled to the radiation types and fluences commonly encountered in space through the application of radiation quality factors and dose, dose rate modification factors. NASA and the scientific community acknowledge the limitations of this approach, however appropriate data on the radiation quality dependence for high energy, high atomic number ions (HZE) such as those found in space are currently unavailable making for large uncertainties in risk estimates. The majority of data available do not mimic the complex exposure scenarios found in deep space where the effects of both microgravity and radiation contribute to the response, therefore studies beyond low earth orbit (LEO) utilizing the deep space gateway platform will provide a wealth of new scientific information.

Space Radiation Environment: The general climate of galactic cosmic radiation (GCR) varies fairly predictably on an 11-year cycle, however solar particle events (SPEs) are unpredictable, both in character and timing. Episodic SPEs can be managed by providing sufficient shielding, but GCRs are always present and their energy spectra extend to very high energies with sufficient intensity such that shielding cannot eliminate all potential hazards. Both SPEs and GCR contain protons and heavier nuclei (HZE particles). Despite being present in relatively low abundance, HZE particles have a high ionization potential and will be the main contributors to risk [1],[2]. Animal studies indicate that HZE nuclei are more biologically effective than low LET radiation. For example the relative biological effectiveness (RBE) factors comparing \( \gamma \)-rays with HZE ions in mice or rats for skin tumors indicate values as high as 25-40 [3]. Furthermore, tumors appear to develop earlier after high-LET radiation than after low LET [4]. This short latency and increased effectiveness observed for HZE ions compared with sparsely ionizing radiations suggests that the scaling currently used in risk assessment approaches may be insufficient to define critical radiation quality effects.

Uncertainties in predicting risk from space radiation exposures: NASA currently models risk using the double detriment life-table for an average population [4],[5],[6]. This latter model is based primarily on epidemiological studies of the Japanese A-bomb survivors and is “scaled” using a radiation-quality factor (Q) and a dose, dose rate effectiveness factor (DDREF) [7]. The A-bomb survivor data predicts risk largely based on colon dose [8]. These risk models do not explicitly account for the actual biological effects of radiation that lead to the increased health risk, and they do not account for potentially synergistic effects occurring due to the combined exposure to microgravity. The frontier of risk sciences is in developing integrated experimental and computational models of health consequences that embrace the underlying biology with as much mechanistic detail as experimentally and computationally tractable with realistic exposure condition inputs. Additionally, the choice of the biological model employed, whether it be cells grown in monolayers, 3D tissue cultures, or animals, must be robust and capable of addressing the most pressing questions identified for furthering deep space exploration.

The value of high throughput data collection and computational approaches: The biological responses observed following exposure to a relatively low level but protracted stress such as produced by the space environment can be both difficult to measure and evaluate. Mathematical models are useful for understanding the operating principles of complex biological networks under these conditions. They can be used to organize information, to uncover the relationships between measured biological variables, and to generate testable hypotheses [9],[10]. Mechanistic models have been developed for a few well-studied signaling and metabolic pathways. While these models are useful for understanding the operating principles of a particular pathway and to generate predictions about intervention targets, they are parameter intensive, and demand a level of knowledge that is currently unavailable for all but a few of the pathways within the cell. It is critical that data collected in deep space exploration can be utilized for model development and for relative risk evaluations. Data capable of being deposited into a structured database such as that provided via the GeneLab platform, will provide more power and greater efficiencies for science conducted in deep space.

The Importance of Radiation Monitoring: The biological responses induced by protracted low dose exposures to the deep space environment will be inhomogeneous in both their temporal and spatial distributions. Likewise the radiation field will have a variable energy
and spatial spectra. In order to correlate the induced biological responses the external environmental variables, we must have accurate characterization of the environment. Many radiation detection technologies currently available for exploration missions have substantial limitations, including the need for complex modeling to convert directional response to omni-directional dose and dose equivalent and estimation of the neutron contribution. Ames has developed an innovative compact dosimeter (Fig. 1) based on the tried-and-true tissue equivalent proportional counter (TEPC) technology. TEPCs have served as environmental monitors against which other dosimeters are compared and have been used extensively on the ISS, the Space Shuttle, high altitude balloons, and in aviation. However, current TEPCs, including those on the ISS as well as their ground-based counterparts, are not suitable for missions beyond LEO - they are too large, power intensive, and would saturate during a substantial solar event, at a moment when real-time dose information would be most urgently needed for the interpretation of biological responses.

The choice of dosimeter must account for limitations in mass, volume, and power expected on exploration missions. Time-PIX, TID, Liulin, and RaySure are very compact Si-based sensors employing various detection approaches. The advantages of the Si sensors are their small size and low power requirement. The disadvantages are their directionality and insensitivity to neutrons. Neutrons may contribute 30% of the dose equivalent depending on shielding and surface location.

The mini-TEPC was developed as part of a collaboration between NASA Ames and investigators at Texas A&M University and Colorado State University [11]. The challenge was to develop a TEPC that could satisfy the small size and low power requirements while also providing reliable dosimetry for the complex radiation environment in space, which includes steady-state GCR, highly variable and potentially very intense SPE radiation, and secondary neutrons. The mini-TEPC is compact, with low power requirements and a broad response spectrum (0.5 kg, 0.5 W, 300 cm², neutron sensitive, 0.2-1200 keV/µm LET response, and omni-directional). This characterization makes it a promising candidate dosimeter for human exploration missions. In addition, the mini-TEPC responds reliably to the wide range of dose rates possible during exploration missions. This is not the case for the TEPCs presently available, which would saturate at the high dose rates expected during a large SEP event. Biological data collected as part of deep space missions will be significantly more impactful when coupled with appropriate and complete dosimetric data.

**Conclusion:** Currently insufficient data exists to accurately predict fundamental biological responses induced in complex radiation and microgravity environment encountered in deep space, and to be able to translate such data to the determination of individual risk to crew. In this abstract we touch on several important areas of consideration in designing experiments for deployment in deep space, including the value of high-throughput and computational approaches and the importance of appropriate dosimetry to facilitate interpretation of induced biological responses.

**References:**


**Figure 1.** Compact TEPC for stand-alone applications. Serial data can interface through USB port.