EFFECTS OF LOW DOSE RADIATION AND RADIATION COUNTERMEASURES ON INFECTION BY SPACEFLIGHT ANALOGUE CULTURED *SALMONELLA* USING 3-D BIOMIMETIC HUMAN TISSUE MODELS

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While both microgravity and radiation are major biological stressors associated with the spaceflight environment, their cumulative impact on host-pathogen interactions and infectious disease risks are rarely considered. This is critical to address, since the cumulative effects of these stressors during spaceflight may result in unexpected negative impacts on crew health and performance that neither condition alone would predict, thus limiting the ability to develop effective countermeasures. Previously, we showed that both spaceflight and spaceflight analogue culture increased the virulence and pathogenesis-related characteristics of the foodborne pathogen, *Salmonella* Typhimurium (*S.* Typhimurium), which is responsible for disqualification of food destined for the International Space Station and *Salmonella* spp. have been found aboard NASA spacecraft. Recently, we demonstrated that spaceflight-analogue culture of *S.* Typhimurium increased its ability to infect 3-D biomimetic human intestinal tissue models. In a separate study, we showed low dose radiation damaged our 3-D intestinal models. The primary objective of this proposal is to evaluate the possibility that low dose radiation will exacerbate the already increased bacterial pathogenicity of *S.* Typhimurium observed following spaceflight analogue culture. In addition, we will determine the impact of a radiation countermeasure to provide protection against both radiation and pathogen-induced tissue damage and inflammation.

Hypothesis: The already enhanced infection potential of spaceflight analogue cultured *S.* Typhimurium will be further exacerbated when used to infect host cells exposed to low dose radiation and this enhanced pathogenicity can be mitigated by a radioprotective compound. **Aims**: 1. Characterize the impact of spaceflight-analogue culture on the ability of *S.* Typhimurium to infect 3-D biomimetic intestinal tissue models before and after exposure to low dose radiation. 2. Evaluate the ability of the radioprotective compound, EC-18, to protect 3-D intestinal models from low dose radiation, *S.* Typhimurium infection, and the cumulative impact of these stressors.

Significance: Current infectious disease risk assessments for spaceflight do not consider the potential for increased susceptibility to infection and disease resulting from exposure to low dose radiation, which is a critical consideration. This study will provide key evidence to determine if exposure to low dose radiation may be a factor in astronaut susceptibility to infection during long duration exploration missions and the impact of selected countermeasures to mitigate that risk to crew health. We have completed infection studies of the 3-D biomimetic intestinal tissue models and are currently analyzing the data.