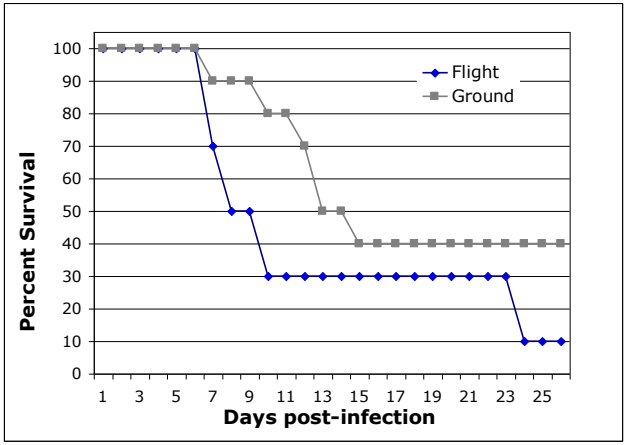
Spaceflight-Induced Changes in Microbial Virulence and the Impact to the Host Immune Response

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Introduction

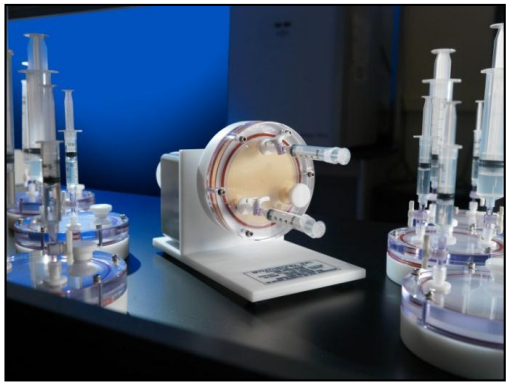
- Over the past 50 years, microorganisms have displayed unexpected responses relevant to infectious disease when grown in spaceflight and spaceflight analogues, including changes in final cell concentration, biofilm production, stress resistance, antibiotic sensitivity, gene expression, and virulence.
- Seminal studies demonstrated that the foodborne pathogen, *Salmonella enterica* serovar Typhimurium, increased its virulence and pathogenesis-related characteristics in response to both spaceflight and spaceflight analogue culture[1,2,3].
- Since those experiments, alterations in the pathogenesis-related characteristics of other pathogens have been documented in response to growth in these environments[4,5,6], and a recent study has demonstrated an increase in virulence of *Serratia marcescens* cultured during spaceflight[7]. However, our overall knowledge of which microorganisms will alter their virulence in response to spaceflight and spaceflight analogue culture remains very limited.

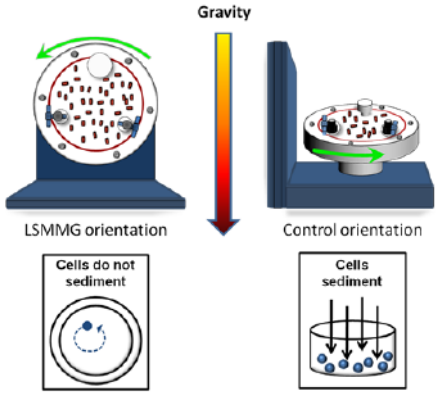


Decreased time to death in mice infected with flight *S.* Typhimurium as compared with identical ground controls[2]

Experimental Design

- Using bacteria that are cultured in both the spaceflight analogue Rotating Wall Vessel (Synthecon) and control conditions, this study will:
  - **Aim 1: Characterize the effect of spaceflight analogue culture on microbial pathogenesis-related stress responses and *in vitro* host-pathogen interactions.** Analysis will include microbial stress responses as well as colonization and viability following pathogen challenge of three-dimensional (3-D) tissue co-culture models containing immune cells.
  - **Aim 2: Characterize the effect of spaceflight analogue culture on the virulence potential of pathogenic microorganisms.** Changes in virulence will be assessed using a mouse model of infection.
- We selected obligate and opportunistic pathogens that are medically important and have been or are likely to be found aboard spacecraft, including *Streptococcus pneumoniae*, *Salmonella enterica* serovar Enteritidis, *Pseudomonas aeruginosa*, *Burkholderia cepacia,* and enterohemorrhagic *Escherichia coli* (EHEC).





Progress and Significance

- Progress
  - Initial characterization of spaceflight analogue culture on microbial growth kinetics, stress responses, and in vitro infection of 3-D cell cultures is underway for the five selected pathogens.
- Significance
  - This information will provide critical understanding into the impact of microgravity on potential alterations in microbial virulence and associated infectious disease risk to crew health during spaceflight missions.
  - In addition to protecting crew health, this knowledge leads to better use of crew time, up mass, and other mission resources as well as facilitate the use of new approaches, such as pick and eat crops.
  - This study complements a parallel immunological study investigating the impact of these spaceflight analogue cultured microorganisms on astronaut blood (PI: Crucian)

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