Quantification and Reduction of Antibiotic-Resistant and Virulent Pathogens on Spacecraft

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The design and use of the human built environment (BE) imposes unique selection pressures on the microbial communities that are able to colonize and persist on indoor surfaces. As such, microbes in BEs exhibit an increase in genetic traits associated with antibiotic resistance, increased virulence, and elevated potential pathogenicity[1]. This is particularly true for indoor spaces that have low microbial community complexity, such as those that are more sealed from the outdoors and that are subject to frequent cleaning regimes[1,2]. For example, we know from our work in hospitals and in laboratory tests that available water, humidity and temperature levels play a strong role in the emergence of increased antibiotic resistance in bacterial populations[3,4], and it has been shown that low competition, resource-poor environments, such as those found on spacecraft, promote microbial proliferation and virulence[5–8].

This selection for increased pathogenicity in microbes poses specific and elevated risks for astronaut health, as spaceflight decreases host immune response[9–11]. Further, crew members are confined to spacecraft for extended periods of time, with a high rate of microbial exchange between individuals and surface materials, increasing the probability of transmission of potentially pathogenic bacteria to occupants[12]. Due to this increased risk of pathogen emergence and persistence in the BE and expanding space exploration programs, it has become increasingly important to consider the contribution and consequences of environment-driven genomic changes during spaceflight. Understanding these relationships will be critical in the optimization of future design[3,13] and operation of spacecraft, to promote crewmember health and 'healthy' microbial ecosystems[14].

We are only now beginning to fully study the microbes found on surfaces in the International Space Station (ISS) and quantify genetic changes in fungi and bacteria over time[7,15,16]. By combining these ongoing research efforts (e.g. Microbial Tracking 1-3 projects) with samples and data collected during the Artemis III mission, we can not only (i) further evaluate how spacecraft design and use influences the emergence, persistence, and transmission of pathogens, but we can also (ii) assess how spaceflight departure, moon landing, and return to Earth differentially alter the genetic traits that code for microbial phenotypes (e.g. antibiotic resistance and virulence) which negatively impact crew member health.

Finally, the Artemis III mission offers a compelling opportunity to bioengineer spacecraft microbial ecosystems by increasing community complexity through the reintroduction of bacteria with biological cleaners (i.e. active biological control). A recent study demonstrated that cleaning products containing food-grade spores of *Bacillus* bacteria actively reduced antibiotic resistance gene (ARG) abundance by up to 99% in healthcare settings[17]. Additional work has shown that biological cleaners reduced the abundance of pathogenic bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), by an average of 90% more than existing chemical cleaners[18,19]. It has been suggested that these cleaners competitively exclude bacteria that are well-adapted for survival in resource-poor environments (i.e., virulent pathogens[20]), and additional work has shown that *Bacillus* species are able to produce chemicals with antimicrobial properties on surface

materials [4,21]. This novel cleaning regime presents an easy, cost-effective way to reduce the incidence of infection and illness, and therefore, increase overall astronaut health as we continue to discover and explore the space beyond Earth.

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