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Task Description:

POSTDOCTORAL FELLOWSHIP
Risk of infection is a problem anywhere on Earth, but can be an emergency during spaceflight. Spaceflight has profound effects on microbial characteristics, including altering virulence of dangerous pathogenic organisms. Furthermore, studies in recent years have established that the human immune system is dysregulated during spaceflight, which alters astronauts' risk of acquiring infectious diseases during flight. The current proposed research would create a new assessment tool that not only measures the risks of pathogens detected in flight, but also considers alterations in host and environmental factors. We hypothesize that using machine learning, we can create a predictive risk assessment tool that considers spaceflight-induced changes to host and pathogen in the context of a flight environment, based on previous changes in microbial populations, current pathogen ecology, and host immunologic profiles unique to flight. This tool will not only aid in future microbial surveillance and response, but also on the implementation of countermeasures and planning of protocols for disease prevention, diagnosis, and treatment during long-term missions. We propose to address our hypothesis with the following three aims:

Aim 1: Characterize the historical pathogen population aboard the International Space Station (ISS) to create a spaceflight microbiome signature.

Aim 2: Translation of molecular approaches to microbial monitoring to clinically relevant risk profiles.

Aim 3: Define the infection-specific risks developed in astronauts to create a spaceflight host signature.

The data acquired from these studies will finally bridge the gap between surveillance data and risks of infection based on clinical relevancy of factors from both host and pathogen. The risk assessment tool developed from this research will have wide applications, as it can be incorporated into a software program to monitor infection risks in spacecraft and terrestrial facilities, including hospitals, schools, and airports.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

To our knowledge, this is the first attempt to assess the historical microbial environment on the International Space Station (ISS). The findings of Aim 1 have important impacts to microbial monitoring and risk mitigation for infectious disease on the ISS. Importantly, this assessment has provided a baseline for the "normal" microbial environment. This baseline can be applied to retrospective analysis of clinical issues experienced by crew, future microbial monitoring analysis and response, and risk assessment by combining these applications. Additionally, the finding that pathogens with the potential to cause sepsis and urinary tract and skin/wound infections have been more frequently detected over time, with a greater increase in recent years, suggests that the risk of contraction of these types of infections may have risen. Further, monitoring of this trend may suggest the need for improvements in and/or increased frequency of disinfection techniques on the ISS, which may abrogate this increase and prevent such infections.
The spatial assessment of the ISS microbial populations also produced some high-impact findings. While it was not surprising to find the lower-use modules like the Bigelow Expandable Activity Module (BEAM) were infrequent homes to the potential pathogens, it was interesting to uncover that the Columbus module was the location with the highest number of samples positive for potential pathogens in almost every category (excluding urinary tract pathogens, which were most found in Node 3 and resistant pathogens, which were most found in the U.S. lab). Additionally, Node 1 was among the areas with the highest frequency for foodborne pathogen detection, which has the greatest clinical relevance, as this is the location for food preparation and consumption.

It is important to remember that many of the pathogens in these clinical categories can also be members of a healthy human's skin flora. So, while the detection of potential pathogens in the air or on surfaces of the ISS does illuminate risk for infection, that risk must be balanced against the expectation of detecting many of these bacteria after surfaces have been touched by crew. This balance will be much easier to maintain with access to the historical microbial environment of the ISS, as we now know how long and how frequently these potential pathogens have been detected. Efforts to improve disinfection can be compared back to this microbial profile to assess success.

This profile also served as the input for Random Forest (RF) assessment to use machine learning to investigate trends and relationships among the data from the last 20 years. RF analysis revealed that machine learning can be used to categorize pathogens and introduce microbes that may have a relationship to these potential pathogens. Those relationships may be linked to environmental conditions that improve the success of the growth of these microbes and potential pathogens. Conditions like these could be manipulated to reduce risk of infection. Additionally, the microbes associated with the potential pathogens can be added to a "watch list" for further investigation. As we have seen, spaceflight conditions can alter pathogen virulence factors, so it may be worth watching these non-pathogenic microbes for any changes induced by spaceflight as a future direction of this work. This illustrates just one of the applications of the findings from machine learning analysis of the ISS environment microbial profile. This innovative approach to microbial monitoring may help with risk assessment, investigations of spaceflight conditions for microbes, and/or response to detection of potential pathogens in space. The potential for this approach will be further characterized as the molecular monitoring and host immune profiles are completed in Aims 2 and 3.

1. Risk of infection is a problem anywhere on Earth, but can be an emergency during spaceflight. Spaceflight has profound effects on microbial characteristics, including altering virulence of dangerous pathogenic organisms. Furthermore, studies in recent years have established that the human immune system is dysregulated during spaceflight, which alters astronauts' risk of acquiring infectious diseases during flight. The current proposed research would create a new assessment tool that not only measures the risks of pathogens detected in flight, but also considers alterations in host and environmental factors. We hypothesize that using machine learning, we can create a predictive risk assessment tool that considers spaceflight-induced changes to host and pathogen in the context of a flight environment, based on previous changes in microbial populations, current pathogen ecology, and host immunologic profiles unique to flight. This tool will not only aid in future microbial surveillance and response, but also on the implementation of countermeasures and planning of protocols for disease prevention, diagnosis, and treatment during long-term missions. We propose to address our hypothesis with the following three aims:
Aim 1: Characterize the historical pathogen population aboard the ISS to create a spaceflight microbiome signature.

Aim 2: Translation of molecular approaches to microbial monitoring to clinically relevant risk profiles.

Aim 3: Define the infection-specific risks developed in astronauts to create a spaceflight host signature.

Task Progress:	2. The data acquired from these studies will finally bridge the gap between surveillance data and risks of infection based on clinical relevancy of factors from both host and pathogen. The risk assessment tool developed from this research will have wide applications, as it can be incorporated into a software program to monitor infection risks in spacecraft and terrestrial facilities, including hospitals, schools, and airports. To date, research efforts have focused on Aim 1. The historical pathogen population of the ISS environment, defined by samples from air and surfaces in/on the ISS and tested for bacterial and fungal growth, has been described. Importantly, this definition has been of a descriptive and clinically relevant nature, focusing on the presence of and changes in populations of potential pathogens that can cause harm to crewmembers during flight missions. The pathogen population results served as the baseline for a clinical-relevancy scoring system, which will be used throughout this project. This scoring system was designed to define known pathogens, potential/opportunistic pathogens, and harmless environmental microbes in the setting of the ISS. Importantly, potential/known pathogens were divided into categories based on the disease they are known to cause on Earth, including respiratory, urinary tract, foodborne/gastrointestinal, skin/wound, sepsis, and resistant (to host defense and/or antimicrobials) infections/diseases. The presence of these pathogens was described in a spatial and temporal way, to allow for visualization of the most clinically relevant pathogen populations over the course of the lifespan of the ISS and throughout the environment in which the astronauts live and work. The spaceflight microbiome signature has been constructed with the goal of using the signature in machine learning analysis. Briefly, metadata from microbial monitoring, including location of samples, culture/colony description/quantification, and species/genus of identified organisms were added to the clinical relevance scoring system to construct the metadata. Machine learning analysis has been applied to this metadata and comparisons across the data revealed the potential to use this analysis as a predictive tool for microbial load (pathogen presence and amounts over time), which demonstrates its value to risk assessment. 3. These findings are the results of the efforts for Aim 1 and represent the first prototype for the ISS environmental microbial signature tool. In addition, the description and clinical relevance of the historical pathogen population of the ISS environment helps define the risks to astronauts who live and work in this environment. These findings provide a benchmark for microbial population findings from future monitoring efforts, which can be used to inform planning and execution of countermeasures to address infection risk. 4. In the coming year, the focus of the efforts toward this project will be on Aims 2 and 3. First, implementation of molecular microbe monitoring into the ISS environmental microbiome signature, and/or translation of this monitoring into clinically relevant findings, will be completed. Second, the spaceflight host signature prototype will be constructed in a similar fashion to the microbial signature prototypes, but with host/astronaut immune/physiological changes induced by spaceflight. Together, the findings from these future efforts will be the products of this research and will be important contributions to the future of host/pathogen monitoring and response approaches during spaceflight.
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