Out of this world: New study investigates infection of human cells in space

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At 3:21 a.m. PDT on April 5, Biodesign's Cheryl Nickerson (center) and her team, including post-doctoral researchers Jennifer Barrila (right) and Shameema Sarker (left) will see their latest experiment launched into low earth orbit aboard the space shuttle Discovery on mission STS-131. Credit: Cheryl Nickerson, Biodesign Institute, Arizona State University

In a first-of-its-kind experiment, the unique conditions of spaceflight will be used to examine how cells remain healthy or succumb to disease, particularly in the face of stress or damage.

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Cheryl Nickerson and her team, including Jennifer Barrila and Shameema Sarker, will see their latest experiment launched into low earth orbit aboard the space shuttle Discovery on mission STS-131. The goals of the team's research are to provide fundamental new insight into the infectious disease process, and further undestanding of other progressive diseases, including immune disorders and cancer.

The knowledge gained from this work may eventually aid in the development of new treatments for infectious diseases, which remain a leading cause of human morbidity and mortality worldwide. Results of the current study will also be used to help mitigate infectious disease risks to the crew, who are particularly vulnerable to infection, due to reduced immune function during spaceflight missions.

"The key to this research" said Nickerson, a School of Life Sciences associate professor and researcher at Biodesign's Center for Infectious Diseases and Vaccinology, "is the novel way that cells adapt and respond to the unique microgravity environment of spaceflight. In response to microgravity, cells exhibit important biological characteristics that are directly relevant to human health and disease, including changes in immune function, stress responses, and virulence (infectious disease potential) that are not observed using traditional experimental approaches."

This is the third time that Nickerson and her ASU team have flown their NASA-funded experiments aboard a space shuttle. Their previous research on board Shuttles Atlantis and Endeavour were the first to show that spaceflight induces major changes in the gene expression and virulence of the food-born pathogen, Salmonella. These changes were due, at least in part, to the unique way extracellular fluid flows around the surface of cells—like water flowing over and around a pebble in a streambed. This physical perturbation of the cell surface caused by the surrounding fluid flow over it results in a low fluid shear force that induces unique cellular responses in both bacteria (like Salmonella) and human cells.

The current mission will be the first time that human cells will undergo infection by a pathogen in spaceflight. Specifically, this thirteen day experiment, called STL-Immune, will characterize the effect of microgravity on intestinal cellular responses before and after infection with the food-borne pathogen, Salmonella typhimurium. Results of this study will be analyzed in a collaborative effort between Nickerson's lab and that of her co-investigator Mark Ott, a researcher at NASA's Johnson Space Center, and his graduate student, Sarah Castro.

The goals of these experiments are twofold: a) to better understand the effect of spaceflight on human cells before and after infection with an invasive bacterial pathogen—information of vital importance for ensuring the safety of astronauts, and b) to gain insight into responses of human and pathogenic cells in their customary environment within the human body on Earth. These conditions, Nickerson explains, can sometimes bear intriguing similarities to those observed during spaceflight, though this effect is often masked by gravity in conventional, Earth-based experiments.

Disease-causing bacteria like Salmonella are capable of keenly sensing the environmental conditions they encounter during infection in their human or animal hosts, adjusting their virulence as conditions dictate. As they infect their hosts, bacteria use a battery of options to dodge attempts to destroy them. Nickerson's previous work showed that bacteria can use the Hfq protein to regulate their pathogenic responses to fluid shear. The Hfq protein is highly conserved in bacteria, meaning it is found among a wide array of species, and plays an essential role in the infection process.

Interestingly, human cells have their own version of the bacterial Hfq protein, call Sm proteins, which are involved in cellular differentiation and responses to stress, immune system function, and the production of tumors. The group hopes to determine if the Sm proteins also act as response regulators during spaceflight, like the Hfq protein does in bacteria.

The excitement of Nickerson and her team is palpable as the launch day approaches. "To actually look at the host-pathogen interaction in flight," she said, "is really taking the findings from our previous spaceflight research to a whole new level." This research holds important benefits and applications for mitigating infectious disease risks to the crew during spaceflight, and for the development of new strategies to combat disease for the general public on Earth.

Dr. Duane Pierson, Chief Microbiologist for the NASA Life Sciences Directorate, stresses the importance of Nickerson's foundational studies into host-pathogen behavior: "Dr. Nickerson's earlier studies produced landmark discoveries of increased virulence in bacteria during spaceflight. Her current investigation may yield even more discoveries of the fundamental processes of microbial infection of human cells in the space environment."

A more thorough understanding of the way pathogens and human cells interact in space may pave the way to new vaccines and therapeutics for a broad range of infectious diseases, as well as other afflictions affecting human populations. Additionally, the results will be used to fine-tune protocols affecting astronauts, helping to ensure they don't fall victim to heightened microbial virulence.

"While studying cells using traditional experimental conditions in the laboratory has taught us an enormous amount about how cells behave normally or develop disease," Nickerson said, "we are starting to realize just how much we've missed using these conventional approaches. Our work using the spaceflight platform for such studies has and will continue to advance our fundamental understanding of the disease process in cells and could lead to major advancements in human health."

Provided by Arizona State University