Bacteria and other microbes are all around us, even living inside our bodies. Most are harmless; some are essential for life. Others can infect a person and may cause a disease, but not always.

“It’s a very dynamic dance between the host that gets infected and the pathogen that infects the host in terms of who wins,” says microbiologist Cheryl Nickerson, professor of life sciences at the Biodesign Institute at Arizona State University. “It’s like a high-stakes poker game.”

To better understand that dynamic dance, Nickerson has been studying these interactions in the absence of one constant for life on Earth—gravity. “It’s amazing how powerful the force of gravity can be,” she says, “in preventing us from observing key cellular responses important for microbial virulence (disease-causing potential).

Since first being funded by NASA in 1998, while at Tulane University, Nickerson (http://sols.asu.edu/people/cheryl-nickerson) and her colleagues have conducted experiments both in a simulated microgravity environment in the lab and in the spaceflight environment on Space Shuttle and International Space Station (ISS) missions. This work is unraveling the complex cellular and molecular responses of both pathogen and host and may have translational Earth benefits.

A Master Switch for Virulence

Infectious disease is a significant health problem in the United States and globally. The major food-borne bacterial pathogen Salmonella, for instance, causes some 1.2 million Americans to sicken each year, resulting in about 19,000 hospitalizations and 380 deaths, according to the U.S. Centers for Disease Control and Prevention. In Nickerson’s early NASA-sponsored research, she discovered that this pathogen becomes more virulent after culture in the microgravity environment of spaceflight or time in a bioreactor that simulates that environment. The finding has major implications for anyone headed into space.

But what was happening inside the pathogen that made it more virulent? To find out, Nickerson’s team compared gene expression in Salmonella cultures grown during spaceflight with otherwise identical controls on Earth. They discovered that in microgravity culture, genes important for the virulence of Salmonella were not being regulated as when this same organism is grown on Earth. The activity of about one-third of those genes was controlled by a single “master switch,” a small protein called Hfq.

In addition to controlling virulence, Hfq is known to regulate ion response pathways. Armed with that information and other knowledge, “we had a clue that if we changed the salt concentration in the culture medium in which we grew Salmonella, we might be able to turn off that increased virulence,” Nickerson recalls. When her team did that, the bacteria lost their extra disease-causing ability in response to spaceflight culture. Such research could lead to the development of effective countermeasures that could, for instance, reduce or prevent the impact of severe food poisoning.

Hfq is not unique to Salmonella. This master switch can be found in many other pathogens and the Nickerson team showed that this switch also controlled the spaceflight and spaceflight-analogue response of Pseudomonas aeruginosa, a bacterium that causes urinary tract, lung, eye, and wound
Nickerson turned to a well-studied organism that is a frequent human stand-in for research—a tiny nematode worm called *Caenorhabditis elegans*. In January 2015, she and her colleagues, including Mark Ott of the Johnson Space Center and John Alverdy of the University of Chicago, sent a small cadre of these worms up to the ISS, where astronauts infected them with *Salmonella*.

The infections were monitored in real time using video imaging downlinked to Nickerson’s team. Other samples were fixed for subsequent gene expression and immune response profiling upon return to Earth. Some worms were also given phosphate as a nutritional countermeasure in an attempt to protect against the infection. The team simultaneously performed the same set of experiments on the ground under otherwise identical conditions to provide a control, so they will be able to tease out the effects of the microgravity environment on the infection process. Nickerson needed five years to prepare for the experiment—one of the most complex biological experiments ever done in space—and the data is currently being analyzed back on Earth.

Nickerson’s work has already yielded important discoveries and new tools for studying human health and disease. For example, her lab has used NASA microgravity analogue bioreactors to develop advanced three-dimensional models of human tissues that closely mimic those in the body. She has shown that these models respond to challenge with pathogens, toxins, and drugs in key ways that reflect the process in the body, and cannot be observed using traditional cell culture approaches.

The spaceflight environment enables scientists to conduct biomedical research in ways that are not possible on Earth. Such studies have become more important than ever, Nickerson says, because right now, in the war between humans and the microbes that can harm us, microbes and the infectious diseases they cause are on the winning side.

**For additional information, contact:** Space Life and Physical Sciences Research and Applications Division, National Aeronautics and Space Administration [http://www.nasa.gov/directorates/heo/slprsa/](http://www.nasa.gov/directorates/heo/slprsa/)

May 2015