washingtonpost.com

'Superbugs' Could Benefit Humans

Zero Gravity and Radiation Produce Powerful Microbes

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Tuesday, September 25, 2007; A03

Truth or fiction?

¿ A high school student gains superpowers after being bitten by a radioactive spider.

¿ An electron beam meant to clean up a bioterrorism site transforms a mild-mannered microbe into a life form able to withstand radiation doses hundreds of times stronger than would kill a person.

¿ Altered by the absence of gravity, an everyday bacterium aboard a spacecraft mutates into a highly lethal bug that poses a surprise threat to astronauts.

Okay, Spider-Man is still fiction. But a pair of independent studies has brought the other two scenarios to life.

The twin tales of menacing mutants are stark reminders of the microbial kingdom's immense versatility -- and of the inadvertent biological transformations that can be wrought by human activities.

But they also point to potential new therapies for cancer and infectious diseases that otherwise might never have been identified.

"When we push the frontier and push biological systems to their limits to see what they can do, that's often when we get the breakthrough insights," said Cheryl Nickerson, a microbiologist at Arizona State University in Tempe, whose experiment led to the creation of lethal bacteria on a recent space shuttle mission -- in fully sealed containers, she emphasized.

That experiment, flown aboard the shuttle Atlantis
last fall, was the first to test in true weightlessness a curious observation: In conditions mimicking microgravity on Earth, bacteria undergo changes that make them more deadly.

That virulence could pose real risks to astronauts, but those earlier findings were obtained under artificial conditions whose medical relevance remained uncertain. They came from a device resembling a small Ferris wheel, which gently swishes bacteria upward in a liquid medium and so gives them the sensation of weightlessness. Scientists call it a low-shear environment, because the bacteria do not fall through the liquid but remain suspended, as though floating in outer space.

If real weightlessness also increases bacterial virulence, then space food might need to be better screened for pathogens and stronger antibiotics might be needed to treat infections in space.

In Nickerson's experiment, astronaut Heidemarie Stefanyshyn-Piper grew salmonella bacteria, which can cause food poisoning, and preserved them for subsequent tests upon the shuttle's return.

Back on Earth, the space-grown bugs were fed to mice. They proved to be nearly three times as likely to cause disease and about twice as deadly as they were before the flight, the team reports in this week's online edition of the Proceedings of the National Academy of Sciences, released yesterday.

Tests found 167 genes that were either more or less active in the shuttle bugs than in their earthbound counterparts -- including many under the control of a single genetic regulator called Hfq.

"This is really the first time that, under actual conditions of outer space, increased virulence and specific changes in gene regulation have been demonstrated," said A.C. Matin, a molecular biologist at the Stanford medical school.

The finding is worrisome because spaceflight is known to suppress astronauts' immune systems, Matin said. Unfortunately, he added, NASA
has cut funds for studies of this safety issue, a decision he equated to "playing Russian roulette with people in space."

The work offers potential benefits for non-astronauts, too, Nickerson said. Tissues that are relatively isolated from the fluidic turbulence of the body's interior, including parts of the gastrointestinal and urinary tracts, are low-shear environments, it turns out -- perhaps explaining why infections there are often hard to treat. Nickerson suspects that drugs designed to act on Hfq could offer a new approach to fighting such infections.

A second study, described in the October issue of Radiation Research, involves single-cell organisms known as archaea, which share some traits of bacterial and human cells.

It started at the Idaho Accelerator Center at Idaho State University in Pocatello, where scientists are developing a device that shoots extremely high-energy beams of electrons capable of killing every kind of known microbe.

They hope to make a portable device that can quickly make an area safe after a bioweapon attack.

Scientists have long been aware that some bacteria are remarkably resistant to radiation. The most resilient of all, *Deinococcus radiodurans*, grows happily while basking in gamma-ray doses of 5,000 grays, hundreds of times as high as a common *E.coli* bacterium can handle. (One gray is the amount of radiation in about 5,000 chest X-rays.)

To see if that represents a natural limit of what a cell can handle, Linda C. DeVeaux of Idaho State, Shiladitya DasSarma of the University of Maryland Biotechnology Institute in Baltimore and co-workers took cultures of an archaeon called *Halobacterium* and exposed it to the 20 million-electron-volt Idaho beam four times over four months.

"We zapped the hell out of them," DeVeaux said.

The mutant microbes that survived that experiment are unfazed by doses exceeding 11,000 grays, putting them well into first place for radiation hardiness among actively replicating organisms.

But the achievement is about more than a place in the Guinness World Records book, DasSarma said. Tests have revealed the molecular mechanism that appears to grant the new mutants much of their hardiness -- a mechanism that, in a weaker form, protects and repairs DNA in human cells, too.

With that target identified, there is hope of developing medicines that enhance those natural mechanisms in human cells. Supplied to healthy tissues, they could minimize "collateral damage" in cancer patients who get radiation therapy.

Such drugs may also someday protect astronauts from the high radiation doses they would receive during prolonged spaceflights, DasSarma said. More controversially, he added, the work suggests that halobacteria or other microorganisms can survive cataclysmic radiation events in space and still land alive on Earth aboard meteorites.

John R. Battista, a microbiologist at Louisiana State University in Baton Rouge, said blasting bugs with beams and studying their genes "offers an entirely new approach to studying radio-resistance in organisms."

That is important, he said, because although halobacteria are not known to cause disease, some medically threatening microbes may share their capacity to adapt when stressed -- something biodefense beamers would want to know before they start mopping up.