Repair Shops for Broken DNA

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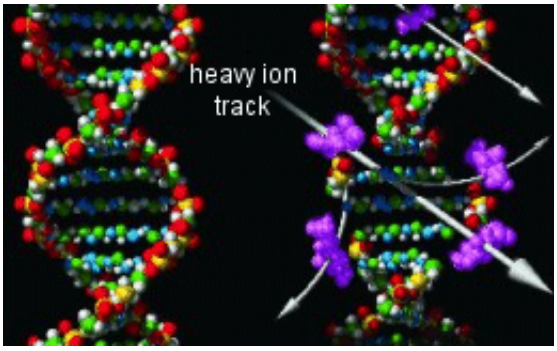

An artist's concept of DNA battered by space radiation.

A stray bullet rips through the command center, blowing holes in vital equipment and damaging the data archives. Repair teams spring into action. The damage must be patched up quickly or the control systems could go haywire. It's literally a matter of life or death, and a decision must be made: try to fix the damage in place, or move the broken parts to the repair shop.

This is a drama that unfolds every day in the microscopic world inside the cells of astronauts. High-speed particles of space radiation zip through an astronaut's body. Occasionally, one of these particles will strike and break a strand of DNA. Because DNA carries a cell's genetic information and directs its behavior, broken DNA can make a cell grow out of control and even lead to cancer.

Fortunately, cells have teams of repair enzymes that try to fix this

damage. Scientists have long thought that these enzymes always go to the site of injury and fix the DNA damage in place. But new research by Francis Cucinotta, the Chief Scientist for NASA's Space Radiation Program at the Johnson Space Center, and his colleagues suggests that cells might sometimes move broken DNA to special "repair shops" instead.

It's a new and controversial idea, Cucinotta says. "Scientists just didn't discuss this idea before. People assumed that the repair just happened right there where the damage occurred." And indeed, the research shows that some strands of DNA are repaired on the spot. Others, however, are relocated.

What's the difference? "I think it is the most damaged DNA that gets relocated," says Cucinotta.

If so, this relocation system might provide a way for scientists to distinguish between minor repairs and major ones. While cells can often fix minor DNA damage successfully, they sometimes botch major repairs. That can make the cell even more prone to becoming cancerous, so selectively blocking the relocated repairs could force a severely damaged cell to self-destruct rather than attempt to fix itself, thus keeping the astronaut healthier overall. "It may be better to let some cells die off that have been damaged," Cucinotta says.

To simulate space radiation, a team led by Sylvain Costes of the Lawrence Berkeley National Laboratory exposed human cells grown in the lab to one of three radiation types: gamma rays, X-rays, and high-energy iron nuclei generated in the particle accelerator at NASA's Space Radiation Laboratory, a part of the Brookhaven National Laboratory in Upton, New York.

These iron nuclei closely resemble cosmic rays, the most dangerous form

of space radiation and the most difficult kind to protect astronauts from. The experiments using iron nuclei provided the clearest evidence that cells might be moving broken DNA to repair centers. These high-speed particles blaze straight-line paths through cells. So spots of damage caused by a single iron nucleus should be along that straight path.

Yet that's not the pattern that Costes and his colleagues found when they analyzed images of real cells taken 10 minutes after the cells were irradiated. By attaching fluorescent molecules to some of the repair enzymes, the scientists could see green, glowing spots in the cells wherever DNA was being fixed. Rather than staying along the line where the damage occurred, these glowing spots seemed to congregate at other places within the cells.

"Often, we saw repairs happening near the boundary between the dense area containing all the chromosomes and the surrounding, emptier regions," Cucinotta explains.

Cells might move damaged portions here because it's easier, he suggests. DNA repair involves dozens of different enzymes. Rather than trying to gather all these enzymes at the damage site, it might be more efficient for cells to keep all these enzymes in discrete locations near the chromosomes and bring injured DNA to them.

"It's more likely to be an accurate repair that way," Cucinotta says. The transport mechanism that cells would use to move the DNA around remains unknown.

While the idea of DNA repair shops is fairly new, it's not without precedent. When bacteria duplicate their chromosomes, they do so by passing the DNA through a place in the cell called the origin of replication rather than sending the copy-machine enzymes to wherever the DNA happens to be.

If future research supports the repair-shop idea, the discovery could help NASA cope with the health threat posed to astronauts by radiation.

For one, understanding this relocation and repair system would let researchers improve computer programs they use to estimate space radiation health risks. Also, better knowledge of cells' repair mechanisms could potentially reveal new molecular targets for drugs that would someday improve astronauts' tolerance to radiation. And that would make the occasional bullet--or cosmic ray--a bit less alarming.

Source: Science@NASA