

DNA's repair system studied in hopes of better cancer treatments

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For a human cell, this is a scary world. Each of the 60 trillion or so cells in the average person's body is damaged tens of thousands, perhaps a million, times a day, scientists say.

The results can be deadly.

Ultraviolet rays from the sun, smoking, harmful chemicals, moldy peanuts, certain diseases, genetic accidents and simply growing old can cause mutations, additions, subtractions, swaps and reversals that jumble the long strings of DNA that control a cell.

Even breathing can create mischief. As cells take in oxygen to make energy from food, hazardous byproducts are created that can corrupt DNA.

An injured cell can run amok, reproducing wildly and spreading through the body, causing cancer, blindness, anemia, premature aging or other misfortunes.

Fortunately, evolution has developed an elaborate biochemical system that detects and repairs damaged DNA. If the repair system can't fix the mistake, it signals the cell to commit suicide.

"Without effective DNA repair, life as we know it could not exist," Zvi Livneh, a biochemist at Israel's Weizmann Institute of Science, wrote in the Feb. 18 issue of EMBO Journal, a publication of the European

Molecular Biology Organization.

With DNA damage playing such an important role in cancer, scientists are eager to understand how DNA corrects such damage in hopes of improving their ability to diagnose and treat the dread disease. In [cancer cells](#), for example, it's best if the DNA repair cycle fails so the cells can't replicate themselves.

Dr. Alan D'Andrea, a radiology professor at Harvard Medical School, founded a firm called The DNA Repair Co. in Cambridge, Mass., which is developing personalized cancer therapies.

The big international drug company Sanofi Aventis spent \$500 million in April to acquire the rights to an enzyme that's involved in repairing DNA damage. The drug would prevent cancer cells from repairing the DNA that's damaged during treatment with chemotherapy or radiation.

Nuclear radiation, such as that created by the 1986 accident at Chernobyl, Russia, "snaps the DNA backbone as easily as we might break a hair," according to a report from the European Integrated DNA Repair Project, a multinational scientific attack on the problem. "One break is sufficient to kill a cell."

At a weeklong DNA repair conference last winter in Ventura, Calif., scientists discussed what conference leaders called "major advances (in a) rapidly expanding field."

For example, Wei Yang, a molecular biologist at the National Institutes of Health in Bethesda, Md., reported on the latest techniques to recognize damaged DNA. She compared the task to "finding needles in a haystack."

Leona Samson, a biological engineer at the Massachusetts Institute of

Technology in Cambridge, works with yeast cells, which also suffer DNA damage, like all living organisms.

"To our surprise, we have identified hundreds of responsive genes" linked to DNA repair, Samson reported on her Web site.

DNA errors are a factor in aging as well as in cancer, which primarily affects the elderly.

"A number of recent research advances place DNA repair squarely at the crossroads of cancer and aging," the European repair-project scientists declared.

Here's how DNA repair works:

When a cell divides, it goes through a series of steps called the cell cycle. Checkpoints exist at several points in the cycle to make sure that there are no mistakes in the 3 billion chemical units that make up DNA. If there are none, it's OK for the cell to divide.

If something is wrong with the DNA, however, the cycle halts until the cell can be fixed or eliminated.

The [DNA repair](#) kit contains a rich variety of tools. Their use depends on the type of damage.

If only a single DNA unit, called a "base," has mutated, special enzymes -- proteins that facilitate biochemical reactions -- can restore the correct base.

If a longer stretch of DNA is corrupted, different enzymes loosen the tightly wound strings of DNA -- the famous "double helix" -- to let the repair crew gain access to the spoiled part. The enzymes then clip out a

patch around the trouble spot and synthesize a fresh batch of DNA to replace it.

If an entire strand of DNA is broken, certain genes encode proteins that can stitch the broken ends back together. That's the case with genes known as BRCA-1 and BRCA-2; if those genes are damaged, for instance, a woman is more likely to get breast cancer.

ON THE WEB

An animated view of the DNA cell cycle: tinyurl.com/ym8alq

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