Scientists find how sun-damaged DNA is fixed

By Mike Lafferty
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The Ohio State team's discovery could lead to the creation of drugs to repair human skin.

Somewhere in the climb up the evolutionary tree, humans and other mammals lost a key ability to repair DNA damaged by sunlight. Plants, bacteria, frogs, insects and every other species of animal have this power.

Now, Ohio State University scientists have shown how it works.

This development, like uncovering a lost secret, could lead to the creation of drugs and other therapies, particularly skin creams, to repair damaged DNA, said biophysicist Dongping Zhong, leader of the research team.

A reduced capacity to repair DNA makes mammals more at risk, he said.

"We have more of a chance of getting (skin) cancer than an insect," Zhong said.

Genetic material is damaged when ultraviolet radiation in sunlight breaks chemical bonds in the DNA molecule. That allows parts of the molecule to form odd combinations called dimers.

These dimers cause sunburns and can lead to cancer.

This is not to say that we can't repair our sun-damaged DNA. In humans and other mammals, the damage is contained to half of the DNA molecule. The intact half usually can repair its mate.

Nearly every other organism, however, has the additional fix-it system.

The mechanism, thought to have been lost by human ancestors 170 million years ago, involves photolyase, a chemical that was good at protecting organisms living under an early Earth sky when there was little UV-absorbing ozone.

Photolyase molecules roam the cell nucleus looking for damaged DNA, Zhong said. Once a damaged area is spotted, the molecule goes to work when it is struck by a photon of sunlight.

The Ohio State scientists report in the online edition of the *Proceedings of the National Academy of Sciences* that the energy in the photon excites the molecule, which in turn expels an electron that is taken up temporarily by the damaged DNA. This electron fixes the DNA by forcing it to realign its atoms properly.

JAY LaPRETE | FOR THE DISPATCH

Dongping Zhong, a biophysicist at Ohio State University, and other researchers used a laser to observe the abilities of a DNA-repair molecule that doesn't exist in mammals.

"Light is both the poison and remedy," said Bern Kohler, an Ohio State chemist who studies the formation of dimers and their role in cancer.

Kohler is familiar with the research but is not a member of Zhong's team.

The Ohio State team made its own highly purified DNA for its experiments. A special laser illuminated a sample of genetic material to observe and precisely time the results.

"In less than one-billionth of a second, the damaged DNA recovers and the dimer is gone," Zhong said.

Zhong and graduate student Ya-Ting Kao also learned that water plays a vital role in controlling the reaction. It keeps the electron in the DNA long enough for the repair to be accomplished before it returns to the photolyase molecule.

Understanding the process should help develop therapies to repair damaged DNA, Kohler said. One need is a treatment for those with xeroderma pigmentosa, a disorder that keeps people from repairing their dimers, he said.

They have high skin-cancer rates and must stay out of the sun.

A possible treatment might use stem cells genetically reprogrammed with the missing gene that creates photolyase, Zhong said.

Before that happens, photolyase might be added to tanning lotions or sun blockers, provided that scientists can figure out a way to get it into skin cells, Zhong said.

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