Scientists get first glimpse at how plants, most animals repair UV-damaged DNA

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For the first time, researchers have observed exactly how some cells are able to repair DNA damage caused by the sun's ultraviolet (UV) radiation. The Ohio State University study revealed how the enzyme photolyase uses energy from visible light to repair UV damage.

This enzyme is missing in all mammals, including humans, although all plants and all other animals have it. Greater understanding of how photolyase works could one day lead to drugs that help repair UV damage in human DNA.

In the online edition of the Proceedings of the National Academy of Sciences, Dongping Zhong and his colleagues report experimental evidence of what scientists have long suspected -- that visible light excites the photolyase molecule and boosts the energy of electrons in its atoms. This in turn enables the enzyme to inject an electron into the DNA molecule at the UV damage site temporarily to perform repairs.

They also report something that was unexpected: Water plays a key role in the process, by regulating how long the donated electron stays inside the damage site before returning to the photolyase molecule.

Scientists believe that all placental mammals lost the ability to make this enzyme some 170 million years ago, said Zhong, an assistant professor of physics and adjunct assistant professor of chemistry and biochemistry at Ohio State.

That's why humans, mice, and all other mammals are particularly vulnerable to cancer-causing UV rays from the sun. But the rest of the animal kingdom – insects, fish, birds, amphibians, marsupials, and even bacteria, viruses and yeast – retained a greater ability to repair such damage.

Since the 1940s, scientists have been trying to understand how the DNA in plants and some animals can be damaged by UV light, and then – seemingly – repaired by visible light. In the 1960s, they identified the enzyme that was responsible for the repair, and named it photolyase, but they didn't know exactly how the enzyme worked.

By the 1980s, scientists proposed a mechanism for photolyase – that it donated an electron to damaged DNA – but nobody could prove it. The reaction happened too fast to be seen with normal laboratory tools.

Scientists also knew that the enzyme formed a tiny water-filled pocket to host the damage site within a cell nucleus, said Zhong. But until his latest series of experiments, nobody knew how water affected the reaction.

The Ohio State researchers mixed photolyase with UV-damaged DNA, and hit the mixture with a kind of blue strobe light to simulate the energy that it would receive from visible light.

Because the light pulses lasted less than a trillionth of a second, the researchers were able to make a very fast series of measurements to follow how the chemical reaction evolved over time.

They assembled their measurements together like a series of stop-motion photographs to reveal the individual steps of UV repair.

Zhong explained the damage and repair processes this way: When a UV photon strikes a portion of DNA, the atoms in the DNA molecule

become excited. Sometimes an accidental bond forms between them. The bond is called a photo-lesion, and can lead to a kind of molecular injury called a dimer. Dimers prevent DNA from replicating properly, and cause genetic mutations that lead to diseases such as cancer.

In cell nuclei that contain photolyase, the enzyme forms a water-filled pocket with the right shape and size to accommodate the dimer for the repair. Normally, the enzyme wouldn't be able to reach the dimer, which is hidden inside the coiled DNA molecule, Zhong said. But electrical interactions between the DNA molecule and the enzyme cause the portion of the DNA that contains the dimer to flip outwards from the coil and into the pocket.

Then, when a photon of visible light hits the pocket, the enzyme becomes excited, and expels one of its own electrons into the dimer, which forces a rearrangement of the atoms in the DNA.

“From our work, we see that in less than a billionth of a second, the damaged DNA bases can recover their original form and the dimer will be gone, as if the UV damage never occurred,” Zhong said. But even within that short time, there's a danger of the donated electron jumping back to the photolyase enzyme before the repair is done.

Zhong's work has revealed how the water in the pocket performs a critical function at this point.

When the photolyase enzyme becomes excited, it jostles the water molecules, and that motion within the pocket delays the electron's exit from the dimer until just after the repair is done.

As far as scientists can tell, photolyase's only function is to repair DNA, and it's very good at it. The enzyme harnesses energy from the visible portion of sunlight to repair UV damage in plants and animals with 90

percent efficiency.

“Unfortunately, during evolution, mammals lost this enzyme,” said Zhong. “So we humans have more of a chance of getting skin cancer than an insect or a frog.”

Scientists would like to develop drugs that use photolyase's mechanism to repair UV damage in human skin, but they've had trouble with the first steps – replicating the photolyase reaction in the laboratory, and fully understanding it. Zhong hopes his latest study will change that.

“Maybe now that we know how light, enzyme, and water work together to control the timing, we can modulate this function and mimic what nature does,” he said. “We want to understand why this timing is so perfect.”

Zhong conducted this study with graduate students Ya-Ting Kao and Chaitanya Saxena and research associate Lijuan Wang, all of Ohio State, and Aziz Sancar of the University of North Carolina at Chapel Hill School of Medicine.

Source: Ohio State University