One electron could be key to furture drugs that repair sunburn

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Researchers who have been working for nearly a decade to piece together the process by which an enzyme repairs sun-damaged DNA have finally witnessed the entire process in full detail in the laboratory.

What they saw contradicts fundamental notions of how key biological molecules break up during the repair of sunburn – and that knowledge could someday lead to drugs or even lotions that could heal sunburn in humans.

In the *Proceedings of the National Academy of Sciences*, the Ohio State University researchers and their colleagues confirm what was previously known about the enzyme photolyase, which is naturally produced in the cells of plants and some animals – though not in mammals, including humans. The enzyme repairs DNA by tearing open the misshapen, damaged area of the DNA in two places and reforming it into its original, undamaged shape.

But the enzyme doesn't break up the injury in both places at once, as researchers previously suspected from theoretical calculations. Instead, it's a two-step process that sends an electron through the DNA molecule in a circuitous route from one breakup site to the other, the new study revealed.

The research was led by Dongping Zhong, the Robert Smith Professor of Physics and professor in the departments of chemistry and biochemistry at Ohio State.

Zhong and his team literally shed light on the process in the laboratory using a laser with a kind of strobe effect to take super-fast measurements of the enzyme in action.

What they saw surprised them.

The two key chemical bond sites broke up one after the other – the first in just a few trillionths of a second, and the next after a 90-trillionths-of-a-second delay.

The reason? The single electron ejected from the enzyme – the source of energy for the breakup – took time and energy to travel from one bond site to the other, tunneling along the outer edge of the ring-shaped damage site.

Also, it turns out that for the enzyme taking the long way around is the most efficient way for the electron to do the job, Zhong explained.

"The enzyme needs to inject an electron into damaged DNA -- but how?" he said. "There are two pathways. One is direct jump from the enzyme across the ring from one side to the other, which is a short distance. But instead the electron takes the scenic route. We found that along the way, there is another molecule that acts as a bridge to speed the electron flow, and in this way, the long route actually takes less time."

Now that they have revealed how the enzyme actually works, the researchers hope that others can use this knowledge to create synthetic photolyase for drugs or even lotions that can repair DNA.

Ultraviolet (UV) light damages DNA by exciting the atoms in the DNA molecule, causing accidental bonds to form between the atoms. 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.

The dimer in question is called a cyclobutane pyrimidine dimer, and it is shaped like a ring that juts out from the side of the DNA.

For those organisms lucky enough to have photolyase in their cells, the enzyme absorbs energy from visible light – specifically, blue light – to shoot an electron into the cyclobutane ring to break it up. The result is a perfectly repaired strand of DNA.

That's why photolyase-carrying insects, fish, birds, amphibians, marsupials, and even bacteria, viruses and yeast are all protected from cancer-causing UV rays from the sun. Meanwhile, humans and all other mammals lack the enzyme, and so are particularly vulnerable to UV.

A synthetic form of photolyase could make up for our enzymatic shortfall. But Zhong's group will leave that discovery to other researchers; they have now set their sights on photoreceptors – the proteins that absorb light and initiate signaling for many biological functions.

Provided by The Ohio State University