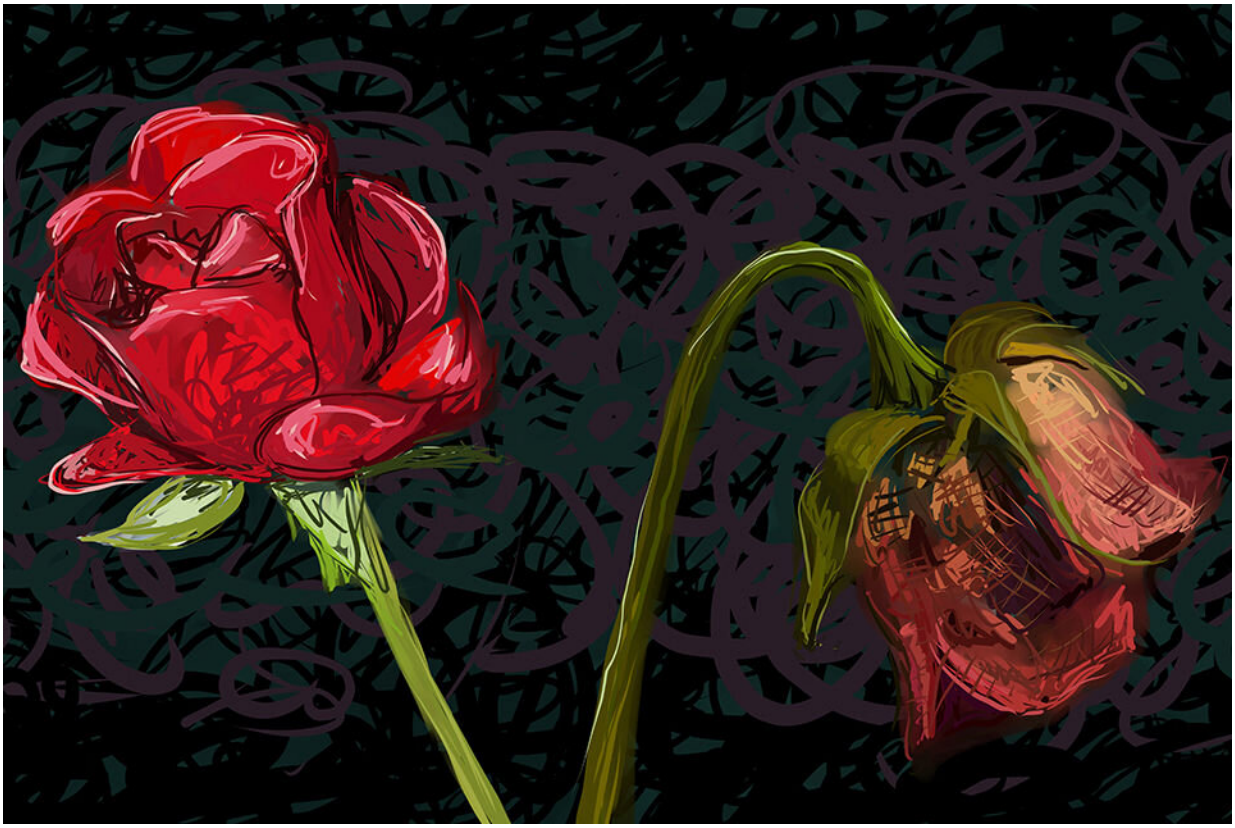
MedicalXpress

Exposure to pollutants, increased free-radical damage speeds up aging

June 21 2021



A new study by WVU School of Medicine researcher Eric Kelley suggests that unrepaired DNA damage can increase the speed of aging. Kelley and his colleagues genetically modified mice to remove a crucial DNA-repair protein from some of their stem cells. Without this protein, the mice were unable to fix damaged DNA accrued in their immune cells. By the time the genetically modified mice were 5 months old, they resembled a regular two-year-old mouse. For context, a two-year-old mouse is similar in age to an 80-year-old human. Credit: Aira Burkhart/WVU

Every day, our bodies face a bombardment of UV rays, ozone, cigarette smoke, industrial chemicals and other hazards.

This exposure can lead to free-radical production in our bodies, which damages our DNA and tissues. A new study from West Virginia University researcher Eric E. Kelley—in collaboration with the University of Minnesota—suggests that unrepaired DNA damage can increase the speed of aging.

The study appears in the journal *Nature*.

Kelley and his team created genetically-modified mice with a crucial DNA-repair protein missing from their hematopoietic stem cells, immature immune cells that develop into white blood cells. Without this repair protein, the mice were unable to fix damaged DNA accrued in their immune cells.

"By the time the genetically-modified mouse is 5 months old, it's like a 2-year-old mouse," said Kelley, associate professor and associate chair of research in the School of Medicine's Department of Physiology and Pharmacology. "It has all the symptoms and physical characteristics. It has hearing loss, osteoporosis, renal dysfunction, visual impairment, hypertension, as well as other age-related issues. It's prematurely aged just because it has lost its ability to repair its DNA."

According to Kelley, a normal 2-year-old mouse is about equivalent in age to a human in their late 70s to early 80s.

Kelley and his colleagues found that markers for cell aging, or senescence, as well as for cell damage and oxidation, were significantly greater in the immune cells of genetically-modified mice compared to

normal, wild-type mice. But the damage was not limited to the immune system; the modified mice also demonstrated aged, damaged cells in organs such as the liver and kidney.

These results suggest that unrepaired DNA damage may cause the entire body to age prematurely.

When we are exposed to a pollutant, such as radiation for cancer treatment, energy is transferred to the water in our body, breaking the water apart. This creates highly reactive molecules—free radicals—that will quickly interact with another molecule in order to gain electrons. When these free radicals interact with important biomolecules, such as a protein or DNA, it causes damage that can keep that biomolecule from working properly.

Some exposure to pollutants is unavoidable, but there are several lifestyle choices that increase exposure to pollution and thus increase free radicals in the body. Smoking, drinking and exposure to pesticides and other chemicals through occupational hazards all significantly increase free radicals.

"A cigarette has over 10 to the 16th free radicals per puff, just from combusted carbon materials," Kelley said.

In addition to free radicals produced by pollutant exposure, the human body is constantly producing free radicals during a process used to turn food into energy, called oxidative phosphorylation.

"We have mechanisms in the mitochondria that mop free radicals up for us, but if they become overwhelmed—if we have over-nutrition, if we eat too much junk, if we smoke—the defense mechanism absolutely cannot keep up," Kelley said.

As bodies age, the amount of damage caused by free-radical formation becomes greater than the antioxidant defenses. Eventually, the balance between the two tips over to the oxidant side, and damage starts to win out over repair. If we are exposed to a greater amount of pollutants and accumulate more free radicals, this balance will be disrupted even sooner, causing premature aging.

The issue of premature aging due to free-radical damage is especially important in West Virginia. The state has the greatest percentage of obese citizens in the nation and a high rate of smokers and workers in high-pollution-exposure occupations.

"I come from an Appalachian background," Kelley said. "And, you know, I'd go to funerals that were in some old house—an in-the-living-room-with-a-casket kind of deal—and I'd look at people in there, and they'd be 39 or 42 and look like they were 80 because of their occupation and their nutrition."

Many West Virginians also have comorbidities, such as diabetes, enhanced cardiovascular disease, stroke and renal issues, that complicate the situation further.

Although there are drugs, called senolytics, that help to slow the aging process, Kelley believes it is best to prevent premature aging through lifestyle change. He says that focusing on slowing the aging process through preventive measures can improve the outcome for each comorbidity and add more healthy years to people's lives.

"The impact is less on lifespan and more on healthspan," he said. "If you could get people better access to healthcare, better education, easier ways for them to participate in healthier eating and a healthier lifestyle, then you could improve the overall economic burden on the population of West Virginia and have a much better outcome all the way around."

More information: Matthew J. Yousefzadeh et al, An aged immune system drives senescence and ageing of solid organs, *Nature* (2021). DOI: 10.1038/s41586-021-03547-7