Effects of smoking linked to accelerated aging protein

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A University of Iowa study is apparently the first to make a connection between a rare, hereditary premature aging disease and cell damage that comes from smoking. The study results point to possible therapeutic targets for smoking-related diseases.

The investigation found that a key protein that is lost in Werner's syndrome is decreased in smokers with emphysema, and this decrease harms lung cells that normally heal wounds. The findings appear in the Feb. 6 issue of the *American Journal of Respiratory and Critical Care Medicine.*

While people know that smoking is bad for health, not all the mechanisms by which smoke damages the body are fully understood, said Toru Nyunoya, M.D., assistant professor of internal medicine at the University of Iowa Carver College of Medicine and a pulmonologist with University of Iowa Hospitals and Clinics.

"Smoking can accelerate the aging process and shorten the lifespan by an average of more than 10 years. We focused on what happens within the lungs because of the similar aging effects, including atherosclerotic diseases and cancer, seen in people with Werner's syndrome and people who smoke," said Nyunoya, whose study was based in the lab of senior author Gary Hunninghake, M.D., University of Iowa professor of internal medicine and a researcher with the Iowa City Veterans Affairs Medical Center.

People with Werner's syndrome begin aging rapidly after adolescence and typically die from cancer or heart disease in their 40s or 50s. The condition is different from progeria (Hutchinson-Gilford syndrome), which causes even earlier premature aging and death at about age 13. Werner's syndrome affects an estimated one in 200,000 people in the United States and is more common in Japan, where up to one in 20,000 individuals are affected.

"Werner's syndrome involves a genetic mutation that causes a deficiency in what's known as Werner's syndrome protein. The protein normally helps repair DNA damage," Nyunoya said. "Smoking does not appear to cause the same mutation, but our study showed that it does decrease Werner's syndrome protein."

To reach that conclusion, the investigators compared lung fibroblasts (a type of cell) taken from nonsmokers without lung disease and patients with a heavy smoking history and severe emphysema. Fibroblasts from the smokers with emphysema had lost their ability to divide or grow, confirming that smoking habits cause cell aging. The cells also had lower levels of Werner's syndrome protein, compared to cells from nonsmokers.

The team also applied cigarette smoke extract to cultured lung fibroblasts taken from nonsmokers. They saw that Werner's syndrome protein expression was decreased, and the cells had lost their ability to repair wounds. In contrast, when the team caused the lung fibroblasts in petri dishes to overexpress Werner's syndrome protein, it had a protective effect and helped resist the damaging effects of cigarette smoke.

"Overall, our study may support efforts to target Werner's syndrome protein for use in developing treatments for smoking-related conditions such as emphysema," Nyunoya said.

The team will next use mouse models to further study the effects of smoking on Werner's syndrome protein.

Source: University of Iowa