The Effects of Smoking on Head and Neck Cancer Reveal Treatment Target

After finding a protein that smoking affects to drive head and neck cancer, investigators hope manipulating it will prove beneficial.

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After discovering that cigarette smoking impacts a particular protein in a way that drives the growth of head and neck cancer squamous cell carcinoma (HNSCC), researchers hope that by manipulating that protein they can better fight the cancer.

Cigarette smoking is associated with a higher risk of HNSCC, at least in part because it alters cell metabolism to promote the growth of the cancer.

Publishing their findings in Molecular Cancer Research, investigators led by Ubaldo Martinez-Outschoorn, MD, an associate professor in the department of medical oncology at Thomas Jefferson University in Philadelphia, built on their previous research that found that HNSCC tumors thrive when supported by noncancerous fibroblasts, cells that assist in maintaining the architecture of the tumors. The fibroblasts generate metabolic products that help deliver energy to the tumors and fuel their harmful growth.

In the new study, the investigators exposed fibroblasts to cigarette smoke and found that this increased a type of metabolism known as glycolysis, which produces the tumor-growth-fueling metabolites. Malignant cells also developed greater mobility and resistance to cell death—hallmarks of cancerous cells. In a mouse model, the smoke-exposed fibroblasts aided in the development of larger tumors. The scientists also found that smoke-exposed fibroblasts interact with other tumor-supporting tissues, including immune cells.

The study team identified a protein on tobacco-exposed fibroblasts that apparently drove these changes in cell metabolism. The researchers concluded that the protein, known as monocarboxylate transporter 4 (MCT4), is an important mediator of smoking's effect on cancer's aggressiveness. The investigators found ways to manipulate it, raising hopes of developing therapies to blunt the protein's effects.

With these findings, the study authors have set the stage for a clinical trial in which they will try to prevent cigarette smoke's impact on the metabolism of HNSCC tumors. They will assess the effects of the diabetes drug metformin on the metabolism of cancer cells, while the PD-L1

checkpoint inhibitor Imfinzi (durvalumab), they hope, will remove the signals that keep the immune system from going after such cells.

“We think metformin and durvalumab might have a synergistic effect on the cancer, where metformin slows the bad players, the cancer cells, and durvalumab grows the strength of the good players, the immune cells,” Joseph Curry,MD, an associate professor in the department of otolaryngology–head and neck surgery at Thomas Jefferson,said in a press release.

To read the study abstract, click here.
