Two-faced gene: SIRT6 prevents some cancers but promotes sun-induced skin cancer

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A new study published in *Cancer Research* shows SIRT6—a protein known to inhibit the growth of liver and colon cancers—can promote the development of skin cancers by turning on an enzyme that increases inflammation, proliferation and survival of sun-damaged skin cells.

Previously considered protective, SIRT6 is part of a family of seven proteins called sirtuins that help regulate genomic stability and prevent some of the genetic flaws associated with aging. SIRT6 helps repair DNA damage, which can lead to cancer. This study, in the journal's October 15 issue, reveals its activity can vary from one tissue type to another.

"Although SIRT6 suppressed tumor growth in some cell types, we discovered that it encouraged cancer development in others, particularly in skin cells," said study author Yu-Ying He, PhD, assistant professor of medicine at the University of Chicago.

"We found more SIRT6 protein in sun-damaged squamous cell carcinoma cells than in healthy, sun-protected human skin," she said. "When we deleted SIRT6 from skin cells in mice, tumor development decreased."

To understand how SIRT6 contributed to the onset of skin cancer the researchers looked at its effects on COX-2, an enzyme responsible for inflammation. COX-2 also promotes cell proliferation and survival, however, two hallmarks of cancer cells. When the researchers increased expression of SIRT6, COX-2 became more abundant. When they inhibited SIRT6 expression, COX-2 levels decreased.

They also found that exposure to ultraviolet-B light, a cancer-causing component of sunshine, could trigger increased expression of SIRT6 in skin cells. This led to the production of COX-2, which contributed to the development of skin cancers.

"Our findings underscore a critical role for SIRT6 in the skin damage cause by ultraviolet light," He said, "This adds to our understanding of the mechanisms of skin carcinogenesis. It suggests that SIRT6 could provide a useful target for cancer prevention. We are searching for safe and effective ways to inhibit it."

Provided by University of Chicago Medical Center