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Lower antioxidant level might explain higher skin-cancer rate in males

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Men are three times more likely than women to develop a common form of skin cancer but medical science doesn't know why. A new study may provide part of the answer.

Researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) have found that male mice had lower levels of an important skin antioxidant than female mice and higher levels of certain cancer-linked inflammatory cells.

The antioxidant, a protein called catalase, inhibits skin cancer by mopping up hydrogen peroxide and other DNA-damaging reactive-oxygen compounds that form during exposure to ultraviolet B light (UVB), a common source of sunburn and cancer-causing skin damage. Studies by others have linked low catalase activity to skin cancer progression.

The research is published online in the *Journal of Investigative Dermatology*.

The findings suggest that women may have more natural antioxidant protection in the skin than men, say study co-leaders Gregory Lesinski and Tatiana Oberyszyn, both of the OSUCCC – James.

"As a result, men may be more susceptible to oxidative stress in the skin, which may raise the risk of skin cancer in men compared to women,"

says Lesinski, an assistant professor of molecular virology, immunology and medical genetics and a member of the OSUCCC – James Innate Immunity Program.

The study also found that UVB exposure caused a unique inflammatory white blood cell population called 'myeloid-derived suppressor cells' to migrate from the bone marrow into the exposed skin. Furthermore, higher numbers of these cells moved into the skin of male mice than female mice.

"To our knowledge, we've shown for the first time that UVB exposure causes a migration of systemic myeloid-derived suppressor cells, and it suggests that these cells might be a novel source of UVB-induced immune suppression," says first author Nicholas Sullivan, a research scientist in the Oberyszyn lab in the Department of Pathology.

This, in turn, might mean that these UVB-induced inflammatory cells contribute to the genesis of skin tumors and perhaps other tumors rather than simply facilitating cancer progression, as generally thought, Sullivan notes.

Normally, the body mobilizes the suppressor cells to limit immune responses to infection, sepsis or trauma so that healing can begin, Lesinski says.

"However, in the cancer setting, repeated UV light exposure or after other chronic or repeated inflammatory stimuli, these cells persist and become immunosuppressive," he says. "They can render helpful immune cells such as T cells or natural killer cells unable to recognize and eliminate cancer cells in the skin."

Lesinski, Oberyszyn, Sullivan and their colleagues conducted the study using a strain of hairless mice that develops squamous cell carcinoma of

the skin – the second most common skin cancer in humans – when exposed to UVB.

The investigators also found that treating mice with topical catalase inhibited the migration of the suppressor cells into UVB-exposed skin, suggesting that the influx of these cells in males might be due to the relatively lower skin-catalase activity.

In fact, male mice with UVB-induced skin tumors had 55 percent more of the suppressor cells in the skin than did their female counterparts.

"This is the first report to our knowledge of a sex discrepancy in this group of inflammatory cells in tumor-bearing mice, and it suggests that our findings might translate to other types of cancer," says Oberyszyn, associate professor of pathology and a member of the OSUCCC – James Molecular Biology and Cancer Genetics Program. "Men face a higher risk of numerous types of cancers, and relatively higher levels of inflammatory myeloid cells might contribute to this susceptibility."

Provided by Ohio State University Medical Center