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T cell channel could be targeted to treat head and neck cancers

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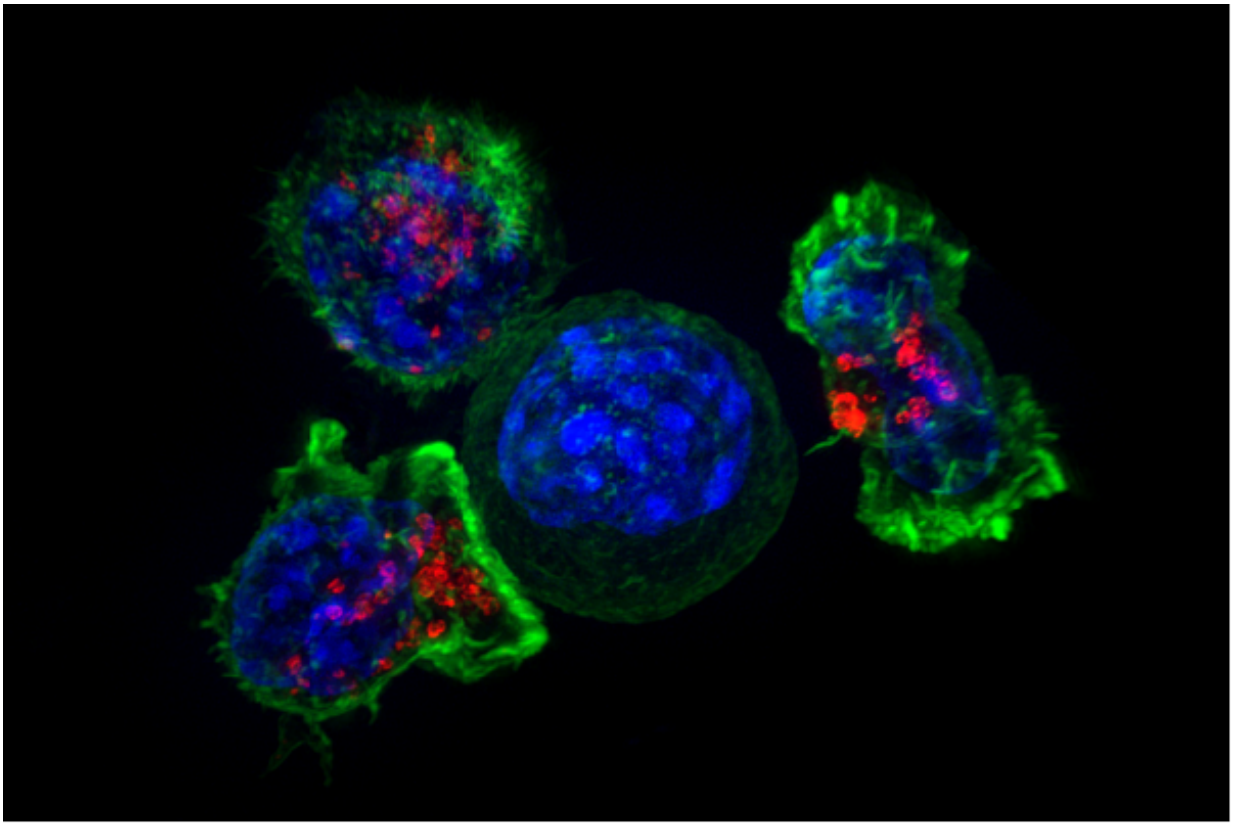

Killer T cells surround a cancer cell. Credit: NIH

Researchers at the University of Cincinnati (UC) have discovered that an ion channel, active within T cells (white blood cells), could be targeted to reduce the growth of head and neck cancers.

This research, which was reported this month in *Cancer Research*, shows that defective Kv1.3 channels, which regulate calcium ions (Ca2+) presence in T cells, and Ca2+ abnormalities in tumor infiltrating lymphocytes—cells that attack and kill cancer cells—may contribute to the inability of the immune system to fight off head and neck cancers.

By regulating their expression at the cellular level and using the body's own immune response to fight the tumor cells, patients with these cancers could have better, more effective outcomes.

"Head and neck squamous cell carcinoma is the sixth most common type of cancer, with a 5-year survival of 50 percent," says Laura Conforti, PhD, professor in the Department of Internal Medicine at the UC College of Medicine, a researcher within the UC Cancer Institute and corresponding author on the study. "The heterogeneity of these tumors, the complex anatomy of the head and neck region and the proximity of these tumors to several vital organs and structures present a challenge in conventional treatment options of these cancers.

"Immunotherapies aimed to boost the immune system to fight cancer cells are showing promising results in this group of patients."

Conforti says that to survive and spread, tumors create a cozy microenvironment where they often go unrecognized by the immune system.

"The extent to which CD8+ cells, a type of T cell capable of killing cancer cells, infiltrate the head and neck tumor affects disease progression and responsiveness to therapy," she says. "Also, how well CD8+ lymphocytes function within the confines of the tumor microenvironment determines their ability to eradicate cancer cells, and in the case of head and neck solid tumors, tumor infiltrating lymphocytes have multiple functional defects, decreasing their ability to work

correctly."

"The function of CD8+ lymphocytes depends on Ca2+, which is controlled by ion channels. In particular, Kv1.3 ion channels regulate Ca2+ influx into T cells. In this study, we assessed the role of Kv1.3 channel and Ca2+ fluxes on these lymphocytes' function in head and neck cancer," she adds.

Conforti says that her team, led by Ameet Chimote, PhD, research associate in the Division of Nephrology and Hypertension, used tumor samples and blood from 14 patients with head and neck cancers to analyze how Kv1.3 effected the function of tumor infiltrating T lymphocytes.

They found a 70 percent reduction in functional Kv1.3 channels in tumor infiltrating lymphocytes as compared to the blood T cells, which was accompanied by a decrease in Ca2+ levels and reduced ability to attack and kill cancer cells.

"Overall our data showed that suppression of Kv1.3 channels in these lymphocytes, the cells that fight off cancer, contribute to their decreased function, raising the possibility that this channel may be used as a potential marker of functionally competent T cells that have infiltrated the tumor mass," Conforti says. "These findings are particularly timely as a recently published study in *Nature* proposes these channels as potential new target for immunotherapy in cancer. The authors in this study reported that overexpressing these channels in an animal model with cancer lead to increased survival.

"Further studies are needed on this T cell channel to find out more about its effects on head and neck cancer and ways we can target it to improve outcomes."

More information: A. A. Chimote et al. Kv1.3 channels mark functionally competent CD8+ tumor infiltrating lymphocytes in head and neck cancer, *Cancer Research* (2016). DOI: 10.1158/0008-5472.CAN-16-2372