I get by with help from my friends: Maintaining immune cells in head and neck cancer

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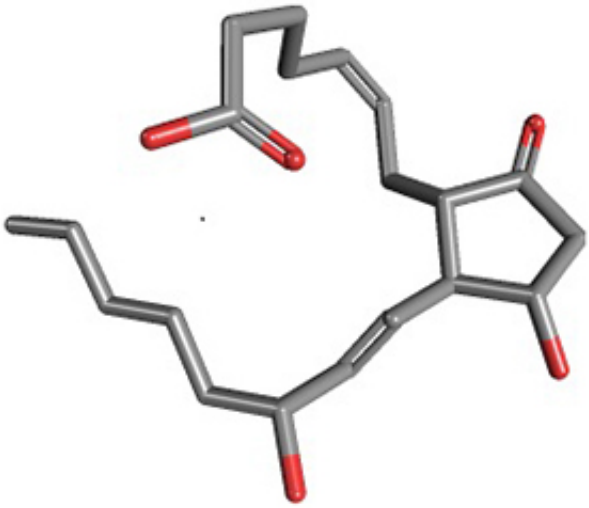

Prostaglandin E2. Credit: National Center for Biotechnology Information. PubChem Compound Database; CID=5280360

In an article published September 22, 2016 in *Frontiers in Immunology*, researchers at the Medical University of South Carolina (MUSC) and the Ralph H. Johnson VA Medical Center report that inhibiting prostaglandin production slows the progression of premalignant lesions to head and neck squamous cell carcinoma (HNSCC). Preclinical studies showed that treatment of premalignant lesions with indomethacin, a

nonsteroidal anti-inflammatory drug (NSAID) similar to aspirin, increased the presence of immune cells and lessened tumor burden.

Cancers of the head and neck begin with lesions in the oral cavity, including the larynx, pharynx, throat, lips, mouth, salivary glands, and nasal passages. Although the incidence of HNSCC has been on the decline over the past several decades, the National Cancer Institute reports that approximately 3% of all cancers in the U.S. result from HNSCC, with men being diagnosed twice as often as women. Treatment for HNSCC includes surgical removal and chemo-radiation treatment; however, these interventions often fail, and patients have a five-year survival rate of only 50%. It is critical to determine better treatment options for HNSCC patients.

One way researchers at MUSC are trying to improve the treatment of HNSCC is by enhancing the body's own immune system to attack the tumor.

"There's a lot of effort to stimulate immune reactivity using immunotherapy. The problem with that is cancer can protect itself against the immune defenses. Head and neck cancer is notorious for that," said immunologist M. Rita Young, Ph.D., senior author for this study, who holds a dual appointment at MUSC and the Ralph H. Johnson VA Medical Center.

As an immunologist, Young has been working on addressing this problem by studying how the immune system affects tumor progression. Previous work from her laboratory has shown that the composition of immune cells within premalignant lesions differs from that within HNSCC. Significantly, as premalignant cells develop into HNSCC, the immune environment switches from stimulatory/inflammatory to immunosuppressive. This change in the tumor microenvironment prevents the immune system from combating the cancer. Prostaglandin

may be an important mediator of this switch.

M. Rita Young, Ph.D., is senior author on the *Frontiers in Immunology* article. She is professor of otolaryngology and professor of medicine at the Medical University of South Carolina and the associate chief of staff for research and development at the Ralph H. Johnson VA Medical Center. Credit: Medical University of South Carolina

The current study used a novel mouse model of HNSCC to determine how inhibition of prostaglandin affects tumor progression. Mice with premalignant lesions were given indomethacin, an NSAID that inhibits the production of prostaglandin. Indomethacin treatment increased the presence of immune cells at the lesion site and led to a systemic

activation of the immune system. Specifically, there was an increase in both Th1-associated cytokines (IL-2 and IFN-γ) as well as Th2-associated cytokines (IL-10). This activation of the immune system reduced the progression of premalignant lesions to HNSCC.

Future studies in this area will be focused on maintaining a strong immune presence in pre-malignant lesions for patients. If studies in humans bear out these preclinical findings, further research using more specific prostaglandin inhibitors in combination with other immunomodulatory compounds could provide a better treatment regimen to prevent the formation of HNSCC.

"Immunotherapy should be considered as a treatment strategy for premalignant lesions before they progress to cancer. We can detect them. Why not treat them?" said Young. Furthermore, these intervention strategies may be able to help prevent smaller, as yet undetectable lesions from progressing to HNSCC.

This work provides strong evidence that treatment of premalignant lesions with indomethacin reduces the tumorigenicity of HNSCC. A better understanding of the mechanisms by which the immune system combats early-stage cancer could lead to improved clinical outcomes in HNSCC, and potentially, other types of cancer as well.

"If we can be more persistent and focused on finding premalignant lesions before they become malignant, simple therapies might be beneficial," said Sara Johnson, Ph.D., a postdoctoral fellow at MUSC and a co-author on the article.

More information: Sara D. Johnson et al, Indomethacin Treatment of Mice with Premalignant Oral Lesions Sustains Cytokine Production and Slows Progression to Cancer, *Frontiers in Immunology* (2016). DOI: 10.3389/fimmu.2016.00379

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