

## **A Cancer Vaccine Taps the Role of HPV in Head and Neck Cancer**

Recent research shows a common factor among one-fifth of all head and neck cancers, and specifically, almost 70 percent of all oropharyngeal cancers: the human papillomavirus (HPV). Once a cell is infected with the virus, HPV works to transform the normal cell into a cancer cell. Now, scientists are using that mechanism to fight the very cancer it causes.

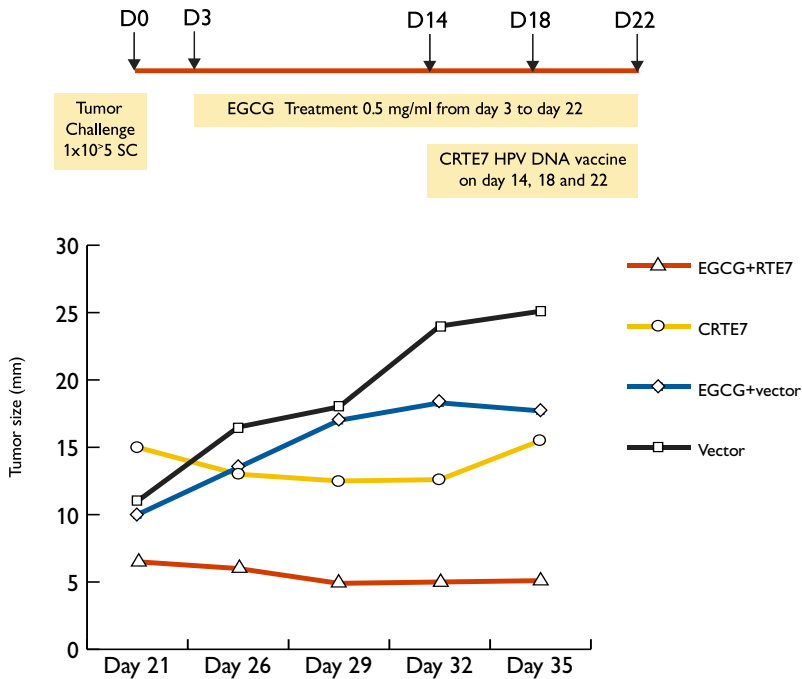
Johns Hopkins researchers are developing a novel, multimodality treatment regimen for HPV-associated tumors that consists of a mild chemotherapeutic agent, epigallocatechin-3-gallate (the active ingredient in green tea), plus a DNA vaccine that enhances the immune system's ability to recognize and kill HPV-infected cells. In preclinical animal models, the combination of the DNA vaccine and epigallocatechin-3-gallate (EGCG)

was found to reduce the tumor burden or decrease the number of HPV-associated cancer cells. It works by enhancing the immune system's already vital role in controlling HPV infections.

“An HPV vaccine made of DNA triggers a rapid response of immune cells that target HPV and helps the immune system kill cells infected by the virus,” explains Sara I. Pai, assistant professor of otolaryngology—head & neck surgery. “Because normal cells do not contain HPV DNA, the therapy would be delivered only to the HPV-transformed cancer cells.”

At the same time, the EGCG induces apoptosis (cell death) within the cancer cells. “Since the immune system is already primed by the DNA vaccine, we are able to broaden the response to other tumor-specific proteins/peptides released by the dying cancer cells,” she says. In preclinical models, the combination treatment led to an

**Combined HPV DNA vaccination and oral EGCG treatment generated synergistic antitumor therapeutic effects compared with monotherapy alone.**



For the tumor treatment experiments, C57BL/6 mice (five per group) were inoculated subcutaneously with  $1 \times 10^5$  HPV tumor cells per mouse. Three days after tumor inoculation, mice were vaccinated with the CRTE7 HPV DNA vaccine. Mice received a booster of CRTE7 HPV DNA vaccine with the same dose every four days after the first vaccination for a total of three vaccine administrations. EGCG was given in the drinking water at a concentration of 0.5 mg/mL at the start of the vaccination and continued for 18 days. Tumor volumes were measured and recorded twice per week for eight weeks following immunization. Tumor treatment experiments were repeated three times to generate reproducible data. The graph demonstrates that those mice receiving the combination of EGCG + CRTE7 HPV DNA vaccine (as depicted by the triangles) have the smallest tumor size as compared to animals receiving no treatment (squares), EGCG alone (diamonds), or CRTE7 HPV DNA alone (circles).

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enhanced tumor-specific immune response and enhanced antitumor effects, resulting in a higher cure rate than either the vaccine or EGCG alone.

The research, Pai says, exemplifies a new approach to treating cancer. Patients are traditionally treated according to where the cancer occurs. This new approach looks at what is causing the patient to develop the cancer—in this case, HPV—and then aims treatment at that uniquely identified cause.

“We’re introducing targeted immunotherapy for patients with HPV-associated cancers,” she says. “It’s the concept of providing treatment tailored specifically to the individual and his or her disease process. We’re excited to be participating in this novel research.”

If the vaccine proves effective, it can serve as adjuvant therapy, generating long-lasting, circulating immune cells in the body that can recognize and destroy microscopic cancer cells to prevent local-regional or metastatic recurrence of disease.