

Researchers design drug to restore cell suicide in HPV-related head and neck cancer

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Researchers have discovered a new mechanism by which the human papilloma virus (HPV) causes head and neck cancer, and they have designed a drug to block that mechanism. Though further research is needed, the new agent might offer a safer treatment for these tumors when combined with a tapered dose of standard chemotherapy.

HPV-positive head and neck cancer has become three times more common since the 1970s, and it could reach [epidemic levels](#) in the future, say researchers at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) who led the study.

"We believe these findings will help meet the real need for more effective and safer therapy for a growing number of HPV-positive head and neck cancer patients," says principal investigator Dr. Quintin Pan, associate professor of [otolaryngology](#) at the OSUCCC – James.

The study was published in the journal *Oncogene*.

The research, which mainly used head and neck cancer cells, shows that a protein produced by the virus blocks a protein made by the [host cell](#). The [cell protein](#), called p300, regulates a gene called p53. This gene both controls cell division and protects the body against cancer by causing cells to die before they become malignant.

By blocking the cell protein, HPV forces the host cell to live instead of

die and to proliferate and form tumors.

The prospective new drug, called CH1iB, prevents the [viral protein](#) from binding with the cell protein. This restores the function of the p53 "tumor-suppressor" gene and triggers the death of the cancer cells.

"Our study revealed a new mechanism for p53 inactivation in HPV-positive head and neck cancer, and this allowed us to develop an agent that disrupts that interaction and reactivates p53 in HPV-positive head and neck cancer," Pan says. "Our pre-clinical studies show CH1iB can reactivate p53 and eliminate HPV-positive head and neck cancer cells."

Pan notes that the standard of care for HPV-positive head and neck cancer uses high-dose cis-platinum, a chemotherapy drug that causes serious side effects that are difficult for patients to tolerate. The drug's toxicity raises the need for safer therapy, and, although further testing is necessary, combining CH1iB with a low dose of cis-platinum might one day provide an alternative.

For this study, Pan and his colleagues used high-risk HPV-positive head and neck squamous cell carcinoma cells. Key technical findings include:

- The small-molecule inhibitor CH1iB inhibits the binding of the HPV E6 protein with the p300 cell protein;
- The binding of the CH1iB inhibitor with p300 reactivated p53 and dramatically potentiated the efficacy of cis-platinum in HPV-positive head and neck cancer cells.
- The combination of CH1iB and cis-platinum eliminated 91 percent of HPV16-positive head and neck [cancer cells](#); it also increased apoptosis by 984 percent and 443 percent compared with CH1iB and cis-platinum respectively alone.

"These results suggest that fewer cycles or a tapered dose of cis-platinum, along with a CH1 inhibitor, might be sufficient to effectively manage HPV-positive head and neck cancer patients and offer a better toxicity profile," Pan says.

"Taken together, our data suggest that we've discovered a novel approach for reactivating the p53 gene in HPV-positive [head and neck cancer](#) that may translate to other HPV-positive carcinomas."

More information: www.nature.com/onc/journal/vao.../abs/onc201325a.html

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