Researchers identify traits linked to better outcomes in HPV-linked head and neck cancer

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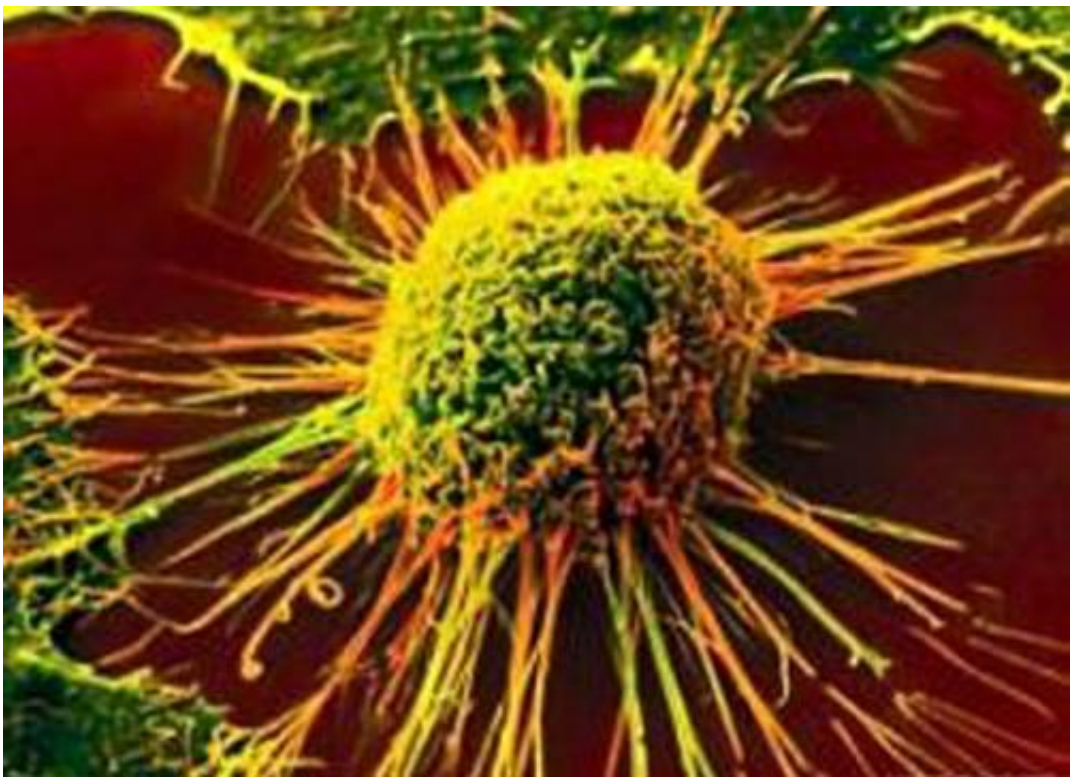

Using a new blood test that's in development, University of North Carolina Lineberger Comprehensive Cancer Center researchers identified characteristics that could be used to personalize treatment for patients with a type of head and neck cancer linked to HPV infection.

Researchers believe the findings, published in the journal *Clinical Cancer Research*, could help identify those patients with characteristics linked to improved treatment responses. They hope to tailor therapy for those patients to reduce their exposure to potential toxic side effects.

"Head and neck cancers that are caused by HPV infection tend to have a better overall outcome than head and neck cancers related to other factors like smoking and alcohol," said UNC Lineberger's Gaorav Gupta, MD, Ph.D., assistant professor in the UNC School of Medicine Department of Radiation Oncology. "There's been a lot of interest in exploring whether we can give less treatment to these patients and still achieve the same level of cure, while reducing the toxicities of treatment. The goal of this study was to investigate whether a blood test for circulating tumor HPV DNA can potentially be used to monitor the response of a patient's cancer to chemotherapy and radiation."

The researchers developed the test to detect levels of DNA in the blood from HPV-linked oropharyngeal squamous cell carcinoma tumors. Studies are ongoing to see if the test can be used to monitor patients' response to treatment with radiation and chemotherapy. In addition, the test has been licensed for commercial development to the company Naveris Inc.

In their latest work, researchers identified characteristics in patients that could be used to stratify and personalize treatment. They drew their findings from a study of the blood test results from 103 patients who were undergoing chemotherapy and radiation for HPV-linked oropharyngeal squamous cell carcinoma.

"What this means is that in the future, dynamic, real-time monitoring of circulating tumor HPV DNA in the blood during treatment may help us better personalize and select treatment—especially the level of radiation and chemotherapy we give the patient," said the study's first author,

UNC Lineberger's Bhishamjit S. Chera, MD, associate professor in the UNC School of Medicine Department of Radiation Oncology.

One characteristic that emerged from their study as a biomarker of a good outcome was a high level of circulating tumor HPV DNA in the blood before treatment. Since the finding seems counterintuitive, researchers plan to investigate why a high level of initial viral DNA in the blood would be linked to a better outcome.

"It may seem confusing at first, but we think it reflects how addicted the tumor is to HPV biology," Gupta said of the finding.

In addition, they found that patients who then rapidly cleared the circulating tumor DNA from their blood were more likely to have improved outcomes. Patients who were able to clear more than 95 percent of the DNA from their blood by day 28 of treatment were considered to have a favorable clearance rate. For 19 out of 67 patients with those two favorable biomarkers, they found that none had persistent or recurrent disease.

"When we put these two factors together, meaning if someone had a lot of HPV DNA and it cleared quickly, we didn't observe any failures of treatment in our cohort," Gupta said.

Conversely, they found that cancers with low levels of circulating DNA from tumors at the outset—or less than 200 copies of HPV DNA per milliliter—and with unfavorable clearance of HPV DNA after treatment had a higher risk of recurrence. That risk was even worse when combined with other risk factors such as an extensive history of smoking.

Researchers at UNC Lineberger are planning to open a clinical trial in which patients are stratified to receive different levels of therapy based

on real-time monitoring of circulating tumor HPV DNA. The planned trial, which will be led by Colette Shen, MD, assistant professor in the UNC School of Medicine Department of Radiation Oncology, will include patients with a smoking history and who are currently not eligible for reduced intensity treatment. By using circulating tumor HPV DNA monitoring during treatment, the investigators hope to identify patients who may be safely spared the additional toxicities of full intensity treatment.

More information: Bhishamjit S. Chera et al, Rapid Clearance Profile of Plasma Circulating Tumor HPV Type 16 DNA during Chemoradiotherapy Correlates with Disease Control in HPV-Associated Oropharyngeal Cancer, *Clinical Cancer Research* (2019). DOI: 10.1158/1078-0432.CCR-19-0211

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