

Research team discovers new method to test for oral cancer

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Oral cancers and precancerous mouth lesions are considered especially difficult to diagnose early and accurately.

For one, biopsies are expensive, invasive, stressful for the patient and can lead to complications. They're also not feasible if repeated screenings of the same lesion are required.

A team of researchers, led by a clinician scientist at the Case Western Reserve University School of Dental Medicine, has discovered a noninvasive, low-cost test to detect oral cancer, monitor [precancerous lesions](#) and determine when a biopsy is warranted.

Their findings, published in the journal *Cell Reports Medicine*, are based on a scoring system linked to the levels of two proteins in cells brushed from suspicious oral lesions of patients at [dental clinics](#) or the ear, nose and throat department at University Hospitals (UH).

One of the proteins (human beta defensin 3 or hBD-3) is expressed at high levels in early-stage oral cancer, while the second (hBD-2) is low or unchanged.

The ratio of hBD-3 to hBD-2 in the lesion site—over the ratio of the two proteins on the opposite, normal site—generates a score, called the beta defensin index (BDI).

A score above a predetermined threshold implies cancer; anything below does not. Determining the levels of the proteins and quantifying the BDI is done routinely in a lab.

The BDI was independently validated using identical protocols at CWRU/UH, University of Cincinnati Medical Center and West Virginia University School of Dentistry.

"When we first discovered hBD-3, we saw it acted as a 'good guy,' involved in wound-healing and killing microbes," said Aaron Weinberg, chair of the Department of Biological Sciences at the Case Western Reserve School of Dental Medicine and the study's lead researcher.

"When we found it was regulated the same way certain cells grow uncontrollably, we started studying hBD-3 in the context of oral cancer."

"Imagine our surprise when this Dr. Jekyll turned out to be Mr. Hyde," he said.

"We found it was not only promoting [tumor growth](#) but was overexpressed in the early stages of the disease, while another member, hBD-2, wasn't changing. This difference in levels of expression of the two proteins compared to the opposite side in the same patient led us to examine the BDI's ability to distinguish cancer from benign lesions."

Weinberg credits School of Dental Medicine instructor Santosh Ghosh for navigating the BDI scoring process.

Head and [neck cancer](#) (HNC), of which oral cancer is about 90%, is the seventh-most prevalent malignancy in the world, and developing countries are witnessing a rise in its incidence. HNC makes up about 5% of all cancers worldwide and 3% of all malignancies in the United States, according to the National Institutes of Health.

There are about 640,000 cases of HNC per year, resulting in about 350,000 deaths worldwide, mainly in socioeconomically disadvantaged populations and underserved communities.

The study's lab-based approach, which is now patented, can reduce biopsies in primary care clinics by 95% because it can tell clinicians who actually needs a biopsy, said Weinberg, also secondarily appointed in the Departments of Pathology and Otolaryngology at the Case Western Reserve School of Medicine. The test can also be used in developing countries where [oral cancer](#) is rampant and pathology services are questionable or lacking, he said.

The positive data from the lab-based approach has inspired the development of a point-of-care (POC) device in collaboration with Umut Gurkan, the Wilbert J. Austin Professor of Engineering at the

Case School of Engineering. The POC diagnostic approach measures the protein ratio and could be used directly in a clinic, providing results within half-hour.

Working through Case Western Reserve's Technology Transfer Office, a patent for the device is pending, setting up possible manufacturing and clinical validation as a next step.

More information: Beta Defensin Index (BDI): A Functional Biomarker For Oral Cancer Detection, *Cell Reports Medicine* (2024). DOI: [10.1016/j.xcrm.2024.101447](https://doi.org/10.1016/j.xcrm.2024.101447). [www.cell.com/cell-reports-medi ... 2666-3791\(24\)00070-3](https://www.cell.com/cell-reports-medicine/2666-3791(24)00070-3)

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