Spit in a Cup: How Saliva Could Detect Oral Cancer Before Symptoms Arrive

Investigators with Baylor Scott & White Research and the Texas A&M University (TAMU) Baylor College of Dentistry have jointly launched a study to determine whether some metabolites in saliva can be used to detect oral cancer in early stages. Funded by a $200,000 Cancer Prevention and Research Institute of Texas (CPRIT) grant, the three-year pilot project could lead to new ways to spot the hard-to-diagnose disease that presents few symptoms.

As a metabolomics-based study, the research explores whether a person’s saliva contains biomarkers that flag oral cancer. By comparing healthy volunteers and those with oral inflammatory diseases with those diagnosed with oral cancer, researchers can assess biomarker levels in the latter group. If variances are found, physicians could someday use them for screening and even targeted treatment—finding and fighting cancer before symptoms develop and long before the tumor might be caught in a routine dental exam.

Urgent need for oral cancer screening

Usually associated with cancers of the mouth, tongue and pharynx, oral cancer is fairly rare, making up less than 5 percent of total malignancies. But statistics can seem grim—around 62 percent of patients survive five years after diagnosis. Compared to five-year survival rates for cancers of the breast (89 percent) and prostate (99 percent), oral cancer can be more deadly, mostly because it has few symptoms and is harder to detect until later, more aggressive stages.

“When people go to an oral hygienist, they often receive a thorough exam in the oral cavity to make sure there are no growths there,” said Teodoro Bottiglieri, PhD, right, director of the Center of Metabolomics at the Baylor Institute of Metabolic Disease. He is a co-investigator of this study alongside principal investigator, Yi-Shing Lisa Cheng, DDS, MS, PhD, below right, associate professor of diagnostic sciences with the TAMU-Baylor College of Dentistry. “But if they’re identifying them at that point, it’s already quite advanced. You really don’t want to wait until that point because the cancer can be aggressive.”

For this study, the researchers will focus on oral squamous cell carcinoma (OSCC), which comprises more than nine in 10 oral cancers. Currently, a clinical dental exam is the standard for detecting OSCC, but recent studies have indicated those exams fall short in effectively diagnosing the disease—thus the urgent need for these assessments.

Separating inflammation from cancer

Previous research found more than 100 biomarkers that could indicate OSCC, but those markers are also present in other dental problems. This study would be the first to distinguish OSCC from those common problems, which could help prevent false positives in the future.
“Almost all of the salivary biomarker research focuses on comparing the salivary components in cancer versus non-cancerous patients or healthy controls,” Dr. Cheng said. “But they really haven’t expanded to individuals who have common oral inflammatory diseases but do not have cancer. Often, inflammation presents when cancer cells are present in the mouth, so we’re trying to find the biomarkers that could distinguish between the two.”

Uptick in saliva diagnostics
Trends in saliva-based diagnostics have significantly increased over the past few years, resulting in FDA-approved tests for substance abuse problems and HIV. Additionally, a new initiative from President Obama and the National Institutes of Health aims to establish a database of patient tissue samples and bodily fluids (saliva included) to support precision medicine.

“I think people are paying more attention to what saliva can do in terms of being a diagnostic fluid, but there is still a long way to go,” Dr. Cheng said, adding that historically, saliva hasn’t been studied as much as other fluids, such as plasma, urine and blood. That said, it’s also more complex than those fluids, containing oral flora (microbes), digestive enzymes and proteins for lubrication purposes that blood doesn’t—which requires separation.

Complexities aside, researchers posit that we haven’t even scratched the surface of spittle’s potential. “We traditionally thought that the major function for saliva was digestion—which still holds true—but we now know its potential extends beyond digestion alone,” Dr. Cheng said.

Plus, with saliva and oral cancer—proximity can’t be overlooked.

“We could have chosen blood, we could have chosen urine, but we chose saliva because this was the obvious biological fluid that was closest to the target cancer,” Dr. Bottiglieri said.

Attacking cancer from two sides
Once Dr. Cheng’s team finalizes recruitment, including 180 participants spanning a range of diagnosis groups, Dr. Bottiglieri’s team will launch metabolic analysis. During that phase, he’ll focus on two unique, complementary approaches that each involve mass spectrometry, a technique that precisely identifies metabolites.

In a targeted approach, the team will study a panel of specific metabolites and amino acids, including vitamin B9 folate (women with low folate levels have shown an increased cancer risk). The untargeted approach, dubbed the “needle in a haystack” method, involves general analysis of over 400 metabolites that the team will map against a library of known compounds.

Each approach could yield valuable insights for both preventing and treating the disease.

“If we find metabolic targets, it will be useful as a diagnostic test but will also give us some information on which part of the metabolism is aberrant,” Dr. Bottiglieri said. “And that may lead to a potential target for treatment, so it’s a two-fold purpose.”

So how soon could we spit in a cup to detect cancer?
If results prove promising, a saliva-based cancer test could come within the decade—but not before large-scale clinical research to validate the data.

“This really is a pilot study,” Dr. Bottiglieri said. “And it will give us information on how best to go forward with a much larger study, because we can do a power analysis to see what the variability and data are like with these metabolites—since a lot of this methodology is very novel. But after a much larger trial, we’d be in a closer point where we would be able to say, ‘Yes, we have a good test.’"