Science Translational Medicine Podcast

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Host – Annalisa VanHook
Hello, I'm Annalisa VanHook. Welcome to the *Science Translational Medicine* Podcast for June 24th, 2015. In this show, I'll be speaking with Dr. Nishant Agrawal of the Johns Hopkins University School of Medicine about his new study on detecting tumor DNA in the blood and saliva of patients with head and neck cancers.

Head and neck cancers are among the most common types of cancer worldwide, and they're becoming more common. Unfortunately, this cancer is still difficult to detect and treat, and there are no reliable biomarkers for following the progress of patients through therapy.

The group of Nishant Agrawal and Bert Vogelstein at the Johns Hopkins University School of Medicine has now shown that tumor DNA can be detected in the blood and saliva of patients with head and neck cancers, and that this DNA can be used for genetic analysis and possibly even for predicting relapse.

Here now is Dr. Agrawal to tell us more.

Interviewer – Annalisa VanHook
Dr. Agrawal, thanks for joining us.

Interviewee – Nishant Agrawal
Thank you, Annalisa.

Interviewer – Annalisa VanHook
How prevalent are head and neck cancers? And how treatable are they?

Interviewee – Nishant Agrawal
Squamous cell carcinoma can occur in the lining of the digestive tract, skin, and lung. So, if you look at all of these different sites where squamous cell carcinoma can arise, it's a relatively common cancer. Head and neck squamous cell carcinoma occurs in the oral cavity, pharynx, and larynx, and we refer to those as mucosal head and neck squamous cell carcinoma. So, mucosal head and neck squamous cell carcinoma is the seventh most common cancer worldwide and occurs in more than approximately 500,000 patients each year and about 50,000 patients in the United States. The major risk factors for this cancer are tobacco use, HPV (or human papillomavirus), and alcohol use. And head and neck cancer are generally associated with a poor 5-year overall survival of only approximately 50%.

The general treatment is a combination of surgery, radiation, and chemotherapy. As head

and neck oncologists, we have excellent outcomes for early-stage cancers—that is, stage I and stage II—and also cancers at any stage that are associated with the human papillomavirus. However, the prognosis is generally worse for advanced-stage head and neck cancers not associated with HPV. In this study, we evaluated tumors that are HPV-negative and HPV-positive, including tumors of the oral cavity, oropharynx, larynx, and hypopharynx.

Interviewer – Annalisa VanHook
In your study, you show that tumor DNA can be detected in the blood and saliva of some patients with head and neck cancers. How accurate is your detection method, and how do the blood and saliva samples compare in terms of accuracy?

Interviewee – Nishant Agrawal
The overall sensitivity when we combine saliva and plasma is 96%, with a specificity of nearly 100%. Regardless of site, stage, and HPV status, the sensitivity remained greater than 86% and ranged from 86 to 100% when both saliva and plasma were available and analyzed. The overall sensitivity for saliva alone is 76% compared to 87% for plasma alone. The specificity remains nearly 100%, but the sensitivity does appear to be dependent on site, stage, and HPV status when saliva and plasma are evaluated independently. To highlight some of the results, for saliva, tumor DNA was found in 100% of patients with oral cavity cancers. For the oropharynx, larynx, and hypopharynx, plasma appeared to be preferentially enriched compared to saliva, with detection rates ranging from 86 to 100%.

Interviewer – Annalisa VanHook
Does your test rely on knowing the mutation pattern that's in the tumors in the patients? Or can you diagnose new tumors in new patients with these tests?

Interviewee – Nishant Agrawal
So, in our current study, the HPV status and/or the somatic mutation status of the primary tumor was necessary. So we did identify these changes in the primary tumor. But however, going forward and for future studies, we've developed a panel that would obviate the need for sequencing of the primary tumor. So, you know, we think that this is a panel that will be generally applicable for patients with head and neck cancer going forward.

Interviewer – Annalisa VanHook
How would you envision your test being used in the clinic?

Interviewee – Nishant Agrawal
So, the exact indications are really yet to be defined and probably evolving, but we do think that there's a role for tumor DNA detection in screening, early detection, monitoring, and surveillance. So, in terms of screening and early detection, we envision high-risk patients being screened by their primary care physicians, dentist, or even, let's say, at a baseball game. And we think this is all possible since we are able to provide a panel of genes that are most commonly mutated in head and neck squamous cell

carcinoma, including HPV.

In terms of monitoring and surveillance, the current imaging methods really make assessment of response to treatment and differentiation between progression versus treatment effect very challenging. So, as clinicians, our decision making is significantly compromised because there is no accurate monitoring method. So we're forced to be reactionary and respond when disease burden is greater, when the tumor becomes palpable or visible by physical examination or imaging. So, our scheme to use tumor DNA as a biomarker can be used to dynamically monitor disease burden throughout the life cycle of the tumor, allowing oncologists and clinicians to act in the present instead of the past. And actually, in fact, our preliminary data from patients with follow-up samples after treatment suggests that detection of tumor DNA could provide a clinically meaningful lead time.

Interviewer – Annalisa VanHook
How close is your test to being ready for clinical use?

Interviewee – Nishant Agrawal
So, realistically, tumor DNA detection in our assay is probably a few years away. But, you know, I think we're going to continue to press forward and work hard. We do still need to improve our test performance by modifying our saliva collection method to increase how robust it is, increasing the volume of plasma, and optimizing our gene panel. And then, ultimately, we'll still have to validate our findings in a larger study before it is used clinically.

Interviewer – Annalisa VanHook
Dr. Agrawal, thanks for joining us.

Interviewee – Nishant Agrawal
Thank you so much, Annalisa.

Host – Annalisa VanHook
That was Dr. Nishant Agrawal of the Johns Hopkins University School of Medicine. You can check out his paper in the June 24th issue of *Science Translational Medicine* by going to our website at stm.sciencemag.org.

I'm Annalisa VanHook and thanks for listening!

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