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Using GEP Test Results to Manage Patients

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I am Jason Rizzo. I'm a dermatologist and Mohs surgeon. I practice in Southwest Florida, Bonita Springs, and Naples, and I'm here to talk about GEP testing.

So GEP testing stands for gene expression profiling. And what that is, it's a molecular test that's performed on biopsy material. Typically, it's FFPE, formalin-fixed paraffin-embedded biopsy material. And what they do is they extract RNA from the biopsy and look at a panel of genes. This panel is different depending on the test and the condition, but the idea is that there's certain gene signatures that can provide additional molecular information on the biology of the disease process. This information is often prognostic or diagnostic. Perhaps the most common and well-known test would be DecisionDx-Melanoma, which is a prognostic GEP test for cutaneous melanoma. And what this does is it provides information based on the gene panel, can give you a score on the risk of this melanoma recurring or metastasizing, and that's based on the genetic profile of the tumor.

There are other prognostic tests for melanoma and for primary cutaneous squamous cell carcinoma. There are also diagnostic tests for melanoma where you use this to help make a diagnosis of melanoma. And the idea here would be that certain gene profiles or gene expression signatures are predictive of this being a melanoma rather than a benign melanocytic neoplasm.

So the whole concept is that you're doing a molecular test, which is giving you information looking at the genetic profile of a tumor, not just the mutations, but what genes are expressed, and looking at a panel of genes, the genes and the number of genes, and which genes are different depending on the test. But the idea is that there's information in the molecular biology of the disease process that this test can capture by looking at a gene expression profile. And these genes are expressed. It's not just a DNA mutation or a chromosomal rearrangement. It's actually a gene that is not only mutated, but read out into RNA, and that's what the assay looks at. So it's a gene expression profile test.

How do I use this test in my dermatology practice? Well, as a cutaneous oncology surgeon, a lot of these tests are in the melanoma and primary cutaneous squamous cell carcinoma space. So the prognostic tests can help me further profile my patients. We certainly know there are well-established clinical and pathological risk factors for predicting recurrence in metastasis in both cutaneous melanoma and cutaneous squamous cell carcinoma. But we also know that there's so many of these lesions, and that the way we currently stage these patients based on clinical and pathological features, has gaps. There's patients that have good clinical and path variables, but still have bad outcomes, and patients that have bad clinical and path variables that have good outcomes. And having additional information on the molecular biology of the tumor can help you get more personalized medicine and tailor your treatment, and also your follow-up as far as surveillance goes for your patients.

So a great example would be if you have a low-stage, let's say melanoma or squamous cell that comes back as a high-risk genetic profile, you can escalate the way you follow or manage that patient, whether that be you see them more frequently in terms of follow-up for clinical and nodal exams. And you can consider escalating care, things like sentinel lymph node biopsy, surveillance imaging, and/or adjuvant radiation therapy, depending on whether we're talking about cutaneous melanoma or a primary cutaneous squamous cell carcinoma.

And there's evidence to support ways to escalate that care. But conceptually the idea is that there's unique genetic differences in every tumor that may allow you to tailor care to that patient. So in the prognostic world, the care would be changed in the way that you surveil or manage that patient. In the diagnostic world, it may actually help you make a diagnosis. The analogy I would give is oftentimes when

there's difficult to diagnose melanocytic lesions, people do testing like CGH, or FISH, or even various levels of IHC looking at different proteins or genetic changes in the tumor that are more likely to be found in a melanoma rather than a benign tumor, like a benign Spitz tumor, or an atypical Spitz, or things like that. So this is another test that can look at the gene expression profile and it can look at a number of genes, and that can be ordered on top of the biopsy.

So I like GEP testing because for a couple of reasons. Number one, it looks at multiple signals, multiple genes. It's not just one gene, and it looks in multiple directions. It's not just the gene being up. The gene can be enriched or de-enriched because it's looking in the whole biopsy. It's looking at bulk RNA. So it's sampling a gene expression profile, looking at multiple genes that are either up-regulated, or down-regulated relative to normal. And it's looking at that signal not just in the tumor, but also in the tumor microenvironment and the biopsy itself.

So you're able to capture multiple biological pathways in multiple directions, and in my opinion, with a greater dynamic range than some of the standard tests that we use with standard histology, immunohistochemistry, CGH, and things like that. And in fact, an argument could be made this could be a complementary test, not necessarily even a competitive test to those. It can aid and be used in conjunction with them.

I just think it's really important people understand what the assay is looking at. I think a lot of people just hear gene expression profile, and that just sounds kind of very sciencey and maybe confusing. I think it's really powerful if you think of exactly what the assay is looking at. It's extracting RNA from the biopsy and it's looking at a panel of genes. And literally able to count through quantitative PCR, how many copies of this gene is expressed in this biopsy? What is in that biopsy? Your tumor, the tumor microenvironment, the immune cell interaction, the stroma, all those things are captured. And that signal is very powerful because it's looking at multiple pathways in multiple directions as I've mentioned before. That signal could be up-regulated or down-regulated. So if we're comparing that to other signals, we look at, how strongly does a protein stain under the microscope with H&E? How purple is it? How pink is it? How blue is it? Or how many copies of this chromosomal rearrangement is there?

Those are also equally interesting and powerful test. But this is going to add a level of molecular complexity that can really help give a more personalized approach to that patient's tumor biology. And that, to me, as someone with a scientific and medical background, is a very powerful tool.

So as I mentioned before, I am a dermatologist and Mohs surgeon, but I also do have a PhD in molecular genetics. So I spent a lot of time doing research both in the lab and in the clinic. And one of the things that I find most promising about GEP and other evolving molecular tests is we're actually starting to see the point where personalized medicine is now being realized in the clinic. These are molecular tests that use molecular information on the individual biology of your patient's disease, and translate it into something we can use an action on in clinic today. So I encourage all of our readers and users to go look at the literature. It is one thing to have a test; it's another thing to have a test that's in the clinic, and that with data and evidence that tells us how it can actually change the way we manage our patients. So the way we manage our patients can be anything from how frequently we see them, how aggressively we surveil them, how aggressively we treat them. And there's an increasing body of literature showing that using this to kind of refine treatment algorithms can make a difference on overall quality and quantity of life.

So that's to me as someone who is always in love with molecular genetics but frustrated by the pace of that getting into the clinic is really what it's all about. Being able to deliver personalized care to our patients, that ultimately helps everyone, helps the provider, helps the patient, and in the long run, helps the payer in the system because we can know who needs more care and ultimately maybe who needs less. So it's really a useful toolkit for us as clinicians to learn more about and find the ways that can help us move the needle in our practice.