How it Works: Genetic Testing in Lung Cancer

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Hi, my name is Kurtis Davies and I'm the lead assay development scientist in the Colorado Molecular Correlates Laboratory and instructor in the Department of Pathology at the University of Colorado Anschutz Medical Campus.

This video is going to talk about how genetic tests work. And in past videos I've discussed basic cancer cell biology, including driver mutations and how they lead to activated proteins that result in unregulated tumor cell growth. And I've also discussed how targeted therapies are now available that directly target these activated proteins. But, as I mentioned in previous videos, to receive these new targeted therapies, it must be determined whether or not certain mutations exist in certain genes in your tumor cells. In this video, I'm going to describe how the genetic tests work that determine if these mutations exist in an individual's tumor sample.

So, to perform these tests that look for the gene mutations doctors must first obtain DNA from your tumor cells. This usually involves using chunks of tumor that have been surgically removed or smaller tumor samples called biopsies that are obtained by sticking a needle-like instrument directly into the tumor.

Alternatively, tumor cells are known to excrete really small amounts of DNA directly into the bloodstream. And there are exciting new approaches that use this DNA that is found in the blood for the test. So by doing it this way, you don't need an invasive procedure like surgery or a biopsy; you just need a blood draw. And this is called the liquid biopsy approach.

So once the material is obtained, whether it be surgically removed tumor, tissue biopsy, or a liquid biopsy from a blood draw, the DNA is extracted and then submitted to some kind of analysis to determine whether certain mutations exist in certain genes in the DNA from the tumor cells. The various testing platforms work via one way or another determining the sequence of DNA in certain genes to determine if certain mutations exist in the sample.

A few years ago, in lung cancer it was sufficient to test only a few genes for these mutations, specifically genes called EGFR and ALK and more recently ROS1. It was sufficient to just test these three to guide clinical decision-making. This is because these were the only genes that, if mutated, could be directly targeted with available targeted therapies.

However, there has been a very dramatic increase over the past couple years in the number of genes and the number of mutations within these genes that we know can be attacked with targeted therapies. In many cases, these recently

identified mutations are targeted with drugs off label or drugs that have not yet been approved but are being investigated in clinical trials. But regardless, if the mutations are identified in your tumor, then there may be an option to tailor a therapy that works specifically to target that specific mutation.

So due to the large number of known targetable mutations, the approaches for genetic testing have been changing pretty dramatically over the past several years. Whereas before it was sufficient to use tests that only looked at one gene at a time, because there were only a few genes that we really cared about, now more and more doctors are submitting tumor samples to test that can look at multiple genes simultaneously.

In a recently developed testing platform often referred to as next generation sequencing, or NGS, has really facilitated this approach. And now there are many NGS-based tests that look at dozens to hundreds, even thousands, of genes all in a single test. So you're getting a much more complete picture of what, at the genetic level, is making the cancer cells grow.

Since our understanding of lung cancer genetics is expanding, and the number of approved drugs or drugs in clinical trials is also expanding, many lung cancer doctors now feel that it's important to do genetic testing beyond just a few standard genes, so beyond just EGFR, ALK, and ROS1. They really want a much more complete picture of what is going on at the genetic level in the tumor cells, so they might be able to find a specific targeted therapy tailored specifically to the patient's genetic makeup within their tumor.