Q&A: Michael Pellini on Cancer Diagnostics

Foundation Medicine's chief executive lays out the practicalities of delivering genomic-based advice

In June, Foundation Medicine of Cambridge, MA, will launch nationally a commercial service that will combine next-generation sequencing (NGS) of about 200 genes with integrated clinical, therapeutic, and clinical trial information, helping oncologists understand each patient's cancer at the level of its molecular blueprint. Michael Pellini, MD, chief executive officer, discussed the company's role with *Cancer Discovery*'s Eric Bender.

What's the overall challenge in molecular diagnostics?

There's a tremendous amount of excitement over targeted therapeutics and the opportunity for patient-specific therapy, but the bottom line is that even with a handful of targets and a handful of approved therapies today, we're already seeing confusion in the marketplace. Oncologists must figure out what tests to order, what to do when they get many individual reports back from various labs, and how to synthesize all this information.

We've hit the tip of the iceberg. Based on our internal assessment of what's happening inside the pharmaceutical world, there are more than 500 targeted compounds in clinical development today. Those 500 compounds are targeting more than 140 genomic alterations. We're going to see an almost exponential growth in the number of targeted therapeutics that will be used and a similar growth in the number of molecular tests that need to be ordered.

If you are an oncologist who is a subspecialist at an academic center and you see one type of patient all day long, you may know exactly what tests to order, exactly what therapeutics to give based on the results, and exactly what clinical trials are available. However, if you are a community oncologist and you see 30 patients a day, most with different tumor types, it's extremely difficult, if not impossible, to get your arms around all that data.

Also, keep in mind that we are simply running out of tissue on which to perform so many individual tests. The current diagnostic testing system is not time-, tissue-, or cost-efficient. It has to change for many reasons.

What's your company's role?

At Foundation Medicine, we're focused on translating into clinical practice this deluge of molecular information that's about to hit. We say let's take a comprehensive picture of the molecular blueprint of each patient's cancer and let the tumor tell us what's important, and then oncologists can use their training to select therapeutics to hit those molecular changes that are the key drivers.

This is a statement that would have been ridiculous to make even 2 years ago because the technology was not ready for prime-time use in typical clinical specimens. We have perfected this approach so that it can be performed on routine, paraffin-embedded specimens.

Our molecular pathology report provides clinically actionable information linked to the genomic alterations identified in the patient sample. For example, the oncologist will get access to information regarding targeted therapies as well as potential clinical trials that hit those targets, together with the appropriate references from the literature.

"Let's take a comprehensive picture of the molecular blueprint of each patient's cancer and let that tumor tell us what's important, and then oncologists can use their training to select therapeutics to hit those drivers," says Michael Pellini.

How do you choose which genes to test?

Our test is driven by clinically actionable information. If an alteration of a gene is targeted by a drug that's on the market, it's in our test. If it's targeted by a drug that's in a clinical trial somewhere, it's in our profile. If there is exciting work being done in a specific target and we have reason to believe that at some point in the next couple of years a therapeutic agent targeting that genetic alteration will hit clinical development, then we'll include that gene as well.

In the first pass, we had approximately 200 genes in the test. By the middle of the year the number will be closer to 300. Depending on the progress that's being made within the pharmaceutical world, the test will be updated every 1 to 2 years, as necessary.

Eventually I'm sure that we'll move into the world of whole-exome and whole-genome sequencing, but there's just no need to do that right now.

What level of coverage does your sequencing provide?

In the clinical world, it's critical to have exquisite sensitivity and specificity for every test. With NGS, one of the ways that you achieve a very high level of sensitivity and specificity is by ramping up the number of times you sequence each molecule (called "coverage"). It sounds easy to do, but it's actually very difficult to ramp up the coverage with routine clinical specimens that are typically small, paraffin-embedded tissue. We originally stated that we would achieve an average coverage of 500×. In the first 200 patient samples that we ran through our laboratory, the average coverage was over 1,100×.

Will oncologists buy in?

Our laboratory was CLIA [Clinical Laboratory Improvement Amendments] certified in the fourth quarter of last year. Since that time, we've been accepting cases that have been coming to us through word of mouth, which has resulted in a few dozen clinical cases arriving at our laboratory every week. Acceptance from academic oncologists was somewhat expected, but the early positive reaction from community oncologists has been extremely gratifying. The oncologists who have ordered our tests are coming back time and time again. ■