

# CHANGING THE FACE OF CANCER RESEARCH

Biomarker technology is quickly gaining ground in the biopharmaceutical industry as a tool to increase efficacy, improve quality, minimize unnecessary side effects and reduce costs. When used in conjunction with advanced technologies — mutation assays and digital pathology — biomarkers are ushering in a new era of cancer research that pushes the envelope in personalized medicine.

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CHRISTOPHER UNG, Vice President, Strategic Business & Operations, Oncology, at TMD, a Quintiles Central Laboratory, explains how advances in biomarker technology are ushering in a new era of cancer therapy development.

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## MUTATION ASSAYS AND BIOMARKERS

In 2008, researchers made a breakthrough when studying the KRAS gene — a molecular triggering gene that transforms a protein implicated in several types of cancers. They identified a mutation within this gene as a negative predictor for well-known oncology treatments, particularly with regard to a class of drugs called EGFR inhibitors. This data proved to be compelling, as patients with this mutation have little chance of responding to most drugs. About 35 to 40 percent of colorectal cancer patients have these mutations, and hence will not respond to many existing therapies. By excluding these patients, researchers can spare them any potential side effects and focus their efforts on developing targeted therapies for patients with the standard form of the KRAS gene.

Today, the KRAS mutation assay is a valuable oncology test used to detect solid tumor mutations, which can identify the genomic changes that occur in each patient's cancer and help researchers find the optimum individual treatment plan. Recently, the American Society of Clinical Oncology and the National Comprehensive Cancer Network recommended that all patients with metastatic colorectal cancer be tested for mutations to the KRAS gene. Mutation assays and biomarkers are the cornerstones of personalized medicine and targeted therapies.

The KRAS breakthrough was an example of a molecular marker that involved a real-time polymerase chain reaction (PCR) technology and the ability to extract DNA from tissue. Today, researchers are using biomarkers in two important ways. The first is to select and target particular patients, screening the population that might respond to the investigative therapy. By using these screens, researchers provide therapies to patients who may receive the most benefit.

The second way researchers are using biomarkers is through pharmacodynamic (PD) biomarkers, which help assess efficacy. Normally when giving a drug to a patient for a particular cancer, researchers and trial sponsors can now understand how the drug is working earlier in the process. Biomarkers give researchers the ability to study a particular protein and understand if or how a therapy has a biological effect on the patient, based on how the protein is expressed.

Similarly, additional genomic tests can help not only in predicting prognosis, but potentially guide cancer treatment decisions as well. The Lung Metagene Predictor test developed at Duke University Medical Center, for example, identifies patients who are at high-risk for lung cancer recurrence. Testing patients for this signal may allow physicians to prescribe a course of therapy that is appropriately aggressive or conservative depending on the predicted risk of recurrence.

## DIGITAL PATHOLOGY

In addition to mutation assays, another technology transforming biomarker research is digital pathology. This technology enables researchers to look at digital images from any investigative site worldwide. This technology will eliminate issues associated with transporting and storing human tissue and make sample images available instantly.

In essence, this technology allows a researcher to use his or her computer as a microscope. Through this new form of digital pathology, scientists can view an image of an entire tissue section, scanned directly from the original glass slide, and zoom in as far as 40X — all remotely with just a computer. From any location on the globe, scientists can view the specimen down to the cellular level and view the morphology of the assay.

By transferring these high-resolution images, researchers will no longer need to ship physical specimens, which is particularly beneficial in countries that prohibit the export of human tissue. These high-resolution images can be transmitted efficiently across the globe over secure networks. Ultimately, it allows investigators, scientists and clinicians to view these specimens and collaborate in real time.

## TRANSFORMING CANCER RESEARCH

Overall, these advanced biomarker technologies can produce better response rates to oncology drugs, while minimizing toxicity in patients. By increasing efficacy and screening out patients who likely will not respond to a particular drug, researchers can greatly advance patient care and the treatment of cancer, while reducing costs associated with unnecessary therapies.

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In addition, by refining biomarker capabilities, researchers can embark on the next step of patient treatment: understanding how to combine therapies. Through combinations — for example, chemotherapy plus a targeted therapy or two targeted therapies — researchers can truly begin treating patients via personalized medicine. Rather than viewing a patient simply as a “breast cancer” patient or “colon cancer” patient, and then subjecting them to the typical course of chemotherapeutic and targeted therapeutic cocktails, researchers can identify the right combination of drugs to treat each individual patient, often in a more cost-effective and time-effective manner.

This is an exciting time for cancer research, and the industry as a whole is truly committed to getting the best cancer treatment to the patient. Optimal outcomes, increased efficacy, decreased risk and reduced side effects for patients are all at the heart of personalized medicine. Through biomarkers and related technologies, cancer researchers are pioneering the next generation of treatments that will improve and save lives over the next 50 years.