Personalized Medicine Will Fit You Like a Glove

The right patient. The right drug. The right dose.

Bringing this trio together is the mission of personalized medicine.

The Food and Drug Administration (FDA) is working to advance the science that will make that happen, says Elizabeth Mansfield, Ph.D, director of personalized medicine in the Office of In Vitro Diagnostics Device Evaluation and Safety in FDA's Center for Devices and Radiological Health.

FDA researchers are "assessing the new technologies that lead us to an entirely new approach to patients," says Mansfield. "They can let us know a lot more specifically what treatments will likely work for individual patients."

Scientists advanced the cause of personalized medicine with the decoding of the human genome, a genetic map of the body. They identified 20,000-25,000 human genes and the sequences of billions of chemical pairings within DNA—the building block of our genetic makeup.

"The human genome allowed us to learn and discuss a lot more," says Mansfield. "This is one person's genome, this is another's. What is the difference? What is abnormal and should be targeted? You can use the difference to assess how to treat a disease. What particular kind of drug will make a difference?"

A Focus With Deep Roots

In August 2011, FDA released its "Strategic Plan for Regulatory Science," an initiative that identified stimulating innovation in clinical evaluations and personalized medicine as among its priorities. Regulatory science is the science of developing new tools, standards, and approaches to assess the safety, effectiveness, quality and performance of FDA-regulated products.

Stephen P. Spielberg, M.D., Ph.D., FDA's deputy commissioner for medical products and tobacco, says personalized medicine dates back to "the dawn of medicine."

"Doctors always treat one patient at a time. If you go back to herbalists and even shamans, the goal was always to develop an individual approach," says Spielberg. "This is simply a continuation of what we've always done, but now using the remarkable tools of rapidly developing science."

Spielberg says the challenge in developing new drugs is "recognizing the huge human diversity in the causes of disease and in the response to medicines and other interventions. It's figuring out the true biological basis of diseases, increasing diagnostic precision, and developing and using medicines targeted at specific causes of disease."

He gives FDA's January 2012 approval of Kalydeco as an example of scientific research that led to an effective clinical

"DNA research has opened a door to individualized medical treatments."

trial and a medication that will help people identified as having a specific genetic condition.

Kalydeco treats patients who have cystic fibrosis, a life-threatening disease that causes lung infections and digestive problems. Specifically, the drug targets a genetic mutation found in 4 percent of people with cystic fibrosis and works to improve lung function and lead to beneficial weight gain. While the drug will only benefit about 1,200 patients, its development is "remarkable," Spielberg says, because it treats an actual cause of disease, not just the symptoms.

Genetic and biological science was used to identify the problem at the molecular level, to develop a medicine that targets that specific problem, and to identify patients with this mutation to participate in the clinical trial.

"This is a beautiful model of how these things can work together: Knowledge of the mechanism of disease, genomics, biology and a targeted clinical trial," Spielberg says. "It's an amazing example of the promise of personalized medicine."

From Theory to Practice

Genomic information has already been added to some drug labels to help health professionals identify patients who will most benefit from a drug and those at the greatest risk of an adverse drug reaction.

An example of such labeling is the anti-blood clotting Plavix. Patients with a certain genetic makeup do not metabolize the drug effectively, and therefore the drug may not be as effective in lessening their risk of heart attack or stroke.

For that reason, FDA directed that a boxed warning be added to the Plavix label informing healthcare professionals that there are tests to identify genetic differences in the way certain liver enzymes function in metabolizing the drug.

Mansfield gives cancer treatment as a model of how genetic tests are used. Cancer centers across the country are doing molecular profiling to look for genetic mutations in their patients. When mutations are found that are common in a certain kind of cancer, researchers work to develop a targeted treatment.

For example, FDA recently approved a melanoma drug called vemurafenib, intended for patients with tumors that have a mutation in a gene known as BRAF. FDA has also approved a genetic test to detect the gene mutation in patients. This test will identify those patients for whom the drug will be most likely to work.

Companion Diagnostics

Mansfield says companion diagnostics are among other tools used by researchers involved in personalized medicine.

Companion diagnostics are tests that help determine whether a patient should receive a particular drug therapy or how much of the drug to give.

One type of companion diagnostic looks for whether a patient has an excess of a gene or protein that would indicate whether a drug will hurt or help. The breast cancer drug Herceptin, for example, was approved with a companion test for this purpose.

Mansfield says it has become apparent over the last 10 years that producing "blockbuster" drugs that are approved for everyone, but may only benefit some patients, may not be as useful as creating more specifically targeted therapies.

"Nothing happens quickly," she notes. "But progress is coming."

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