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## Power tools for the gene age / New test can help doctors in prescribing medications

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One day a doctor might hold off on prescribing you a drug until your genes get the once-over in a device made by Affymetrix.

The Santa Clara company that pioneered the use of the gene chip - - a DNA-scanning system for genetic research -- is now the first to adapt such technology for the diagnosis of individual patients.

Doctors will soon be able to order a test to find out whether patients have unusual gene variations that predict whether they'll suffer bad reactions to certain drugs.

The diagnostic chip can reveal whether patients clear drugs from their systems too quickly or too slowly. Too fast, and the normal dose is too low to do much good. Too slow, and the drug builds up in the bloodstream at potentially dangerous levels.

The AmpliChip CYP450, developed by Roche for use on Affymetrix systems, is the first diagnostic test approved by the Food and Drug Administration that belongs to the class of gene-scanning tools called DNA microarrays.

The FDA approval in January was a milestone that Robert Lipshutz had expected from the day he started work at Affymetrix in 1993, a year after the company started.

The company's fledgling gene chips were already showing the potential to accelerate research to find the genes that can cause disease.

Once those troublesome genes were identified, the logical next step was a diagnostic test to see if an individual patient carried the trait, said Lipshutz, now senior vice president of Affymetrix's diagnostics division.

In the early 1990s, he and other company executives expected that diagnostic gene chips could eventually guide treatment or warn patients to avoid other risk factors. This approach to individualized treatment based on the particular genetic traits of each patient is now known as pharmacogenomics.

The idea got a boost when the government gave Affymetrix a big grant in 1994 to develop handheld diagnostic devices for doctors, Lipshutz said. The company worked up promising prototypes, but the time was not ripe. The research community had not yet nailed down enough ways to test for genetic differences that would be clearly useful in medical practice.

"The challenge you had was, what questions would you ask, and was the marketplace ready?" said Lipshutz.

Things changed about three years ago when Affymetrix and Roche started planning a wide-ranging effort to commercialize Roche's genetic tests on Affymetrix chips. Affymetrix now has

other collaborations to develop diagnostics with Veridex LLC, a division of Johnson & Johnson, and with the Institut Curie in Paris.

Affymetrix had decided early on to leave it to partners such as Roche to find the genes linked to disease and establish each gene's worth as a guide to treatment decisions, Lipshutz said. As the manufacturer of gene chips and their scanners, Affymetrix would ensure that its partners' tests would give reliable results when used in diagnostic labs.

The approval of the AmpliChip CYP 450 test was a huge event for Affymetrix, said Steven Bodovitz, principal at the San Francisco consulting firm Bioperspectives. "Diagnostics is a really important growth area for them if it works out."

At this point, the entire diagnostics market is \$20 billion to \$25 billion, Bodovitz said, a fraction of the \$200 billion to \$300 billion spent annually on prescription drugs. Of the total diagnostics market, only a small subset is devoted to molecular diagnostic products that test for biological molecules like genes, he said.

Although other genetic tests are in use, they're not based on DNA microarrays. They include tests for cystic fibrosis, certain cancer-related genes and genetic variations in disease-causing microorganisms.

Bodovitz said the complexity of biology could make it hard to develop more gene chip tests that show a clear relationship between a genetic pattern and a drug effect.

Lipshutz agrees that any new test must prove its value in medical practice.

"You can't just be adding costs to the medical system," he said.

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