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Hartford Firm's Genetic Tests Help Identify Effective Antidepressants For Individual Patients

Genomas Says Personalized Prescription Analysis Reduces Trial And Error In Finding Right Drug

BY WILLIAM WEIR, bweir@courant.com

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From the age of 14, Connecticut resident Laura suffered from depression. For 26 years, she said, she was placed on "every kind of antidepressant you can name."

None worked. If a drug had any effect at all, it was negative — headaches, weight gain, nausea. Medications then were prescribed for the side effects, some of which had their own side effects.

Laura, who asked that her last name not be used with this story, eventually went through a DNA analysis developed by Genomas, a biomedical company in Hartford, that provides information on the genes responsible for metabolizing medications.

Of the 80 or so kinds of antidepressants available, only a handful were compatible with Laura's genetic makeup, said Dr. Gualberto Ruano, president of Genomas.

Laura was immediately tapered off her medications and switched to an antidepressant that the analysis predicted would work. Within weeks, she showed significant improvement.

One of the biggest stumbling blocks in treating depression is the hit-or-miss choice of medication. About 40 percent of patients don't respond to the first medication prescribed, Ruano said. Few have as difficult a time as Laura finding the right medication, but the trial and error process is still frustrating for those seeking treatment.

To that end, much hope is riding on pharmacogenetics, a field that offers the promise of "personalized medicine" by predicting a patient's response to specific medications based on their genetics. The medical establishment isn't ready to completely get behind the method, but early studies are encouraging.

Ruano's lab initially used the technology for patients selected by Hartford Hospital. In early 2010 Genomas, in partnership with the hospital and the Insitute of Living, developed an Internet portal that distributes and manages the information derived from the DNA analyses. Clinicians equipped with passwords now can access and use the information to treat patients.

With this wider access, 2,400 patients have had the DNA analysis. The numbers reflect the need for fast, accurate prescribing of antidepressants, Ruano said.

"In the last 10 years, mental health has been the top market for the pharmaceutical industry," he said. "Ten percent of the U.S. population is taking antidepressants; 25 percent of women between 45 and 55 are taking antidepressants."

An increase in diagnoses of eating disorders, autism and attention deficit hyperactivity disorder has increased the need for treatment for children and adolescents as well. Because of developmental and learning issues, doctors must take extra care in choosing medications for young patients.

"So there is this huge need" to improve how well drug therapy for mental illness and depression work, Ruano said.

The DNA analysis begins with either a blood sample or a swab of the inside of the mouth, and within two days, clinicians have a map of the specific enzymes in a patient that metabolize medications in the patient's liver.

Enzymes — proteins that trigger chemical reactions — are determined by our genes and can vary significantly. The enzymes that matter here belong to a group known as cytochrome P450 (CYP450). Hundreds of metabolic pathways belong to this group, but the Genomas test looks specifically at three that metabolize many medications.

Ruano compares the pathways to a network of freeways — each freeway being a gene coding for specific enzymes. To work properly, there should be two copies of each of these genes — or two lanes. If a patient is deficient in one gene (one or both lanes blocked), the body won't metabolize the drug properly. This typically mutes any positive effects from the drug, and also can produce negative side effects.

An overabundance of a particular gene (more than two open lanes), also will blunt the drug's effects.

The solution, Ruano explained, is to assess enzyme activity and then prescribe medication compatible with that enzyme activity. Ruano said patients will generally go the traditional route first, allowing their physician to prescribe a drug for their depression. If that doesn't work, a DNA analysis is done.

Jane Buckley, an advanced practice registered nurse at Integrated Psychiatric Services in North Haven, a facility that provides the DNA analysis, said the test costs about $1,200 and is covered by most insurance companies.

It was at the North Haven facility where Laura went for her DNA analysis. The final straw came after she was prescribed Abilify, a relatively new antidepressant. When it didn't work, the doctors increased the dosage and prescribed Ambien to help her sleep, which worsened matters. A few days after her test, a clinician called her.

"They told me to stop taking the medication immediately," she said. She was eventually prescribed Lamictal, a medication that the test indicated would be effective. She's happy with the result.

"All because of a DNA test, I feel better," she said. "I don't feel anxious."

James Potash, head of psychiatry at the University of Iowa Hospitals & Clinics, and a specialist in the genetics of depression, cautioned that it's too early to say that pharmacogenetics' moment has arrived, at least with regard to prescribing antidepressants.

He said questions about effectiveness remain to be answered and that he is wary about companies moving forward too quickly to provide the tests commercially.

"It creates the impression that these tests can deliver much more than they actually do," Potash said. "I think it's medically premature to capitalize on the hype surrounding

genetics."

Potash wasn't swayed by the two case studies — each focusing on a single patient with positive outcomes using DNA analysis — that Ruano and others published earlier this year.

"You need a large, randomized, placebo-controlled test, and in theory that kind of study could be done," Potash said. "I think genetics is powerful and important and may well deliver something really valuable, but we're not there yet."