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strategies for living life at your best

EDITED BY ADAM J. MARTIN

body

BREAKTHROUGH:
A genetic test
can improve your
odds of getting
the right drug and
dose on the first try.

[ADVANCES]

the right medicine for you

Will that prescription
get you better fast—
or not? A new test
can help you find out.

by Margie Patlak

IMAGINE TAKING medicine that creates a new problem instead of fixing the one you've already got. Amy Jackson (not her real name) is all too familiar with this nightmare. Her treatment history reads like a litany of medical mishaps: Soon after she started taking an antidepressant, her blood pressure shot up. To curb it, her doctor prescribed a beta-blocker, but it left her feeling light-headed. Then, following an unrelated surgery, the doctor treated her pain with codeine—which, instead of relief, gave her nausea and constipation.

That was the last straw. Jackson soon contacted David Flockhart, M.D., Ph.D., a clinical pharmacologist who researches how genes affect people's responses to drugs. She had seen him give a lecture and ►



STYLING: NICOLE SCHNEIDER, HAIR/MAKEUP: JANEY MARIE

PHOTOGRAPHY BY MICHAEL HEIKO

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thought he could help. She was right. Special testing conducted by Flockhart, who serves on a U.S. Food and Drug Administration (FDA) advisory committee for clinical pharmacology, revealed that a genetic quirk was preventing Jackson's body from making an enzyme needed to break down a number of frequently prescribed drugs, including Prozac, beta-blockers, and codeine. The medications were simply building up in her system and creating havoc. But now, thanks in part to Flockhart's work, Jackson scrupulously avoids medicines that could cause more problems than they solve, and she's had far fewer bad reactions since being tested.

Not many people are fortunate enough to learn what Jackson did. But that may soon change. A gene-screening test similar to Flockhart's recently hit the market, and another is on the way. Even though the tests have yet to be evaluated in large-scale clinical trials and the FDA hasn't approved them yet for widespread use, experts in the field, like Richard Weinshilboum, M.D., of the Mayo Clinic, expect them to become standard in doctors' offices sometime in the future. "For the vast bulk of patients, this will be an important factor for many drugs," Weinshilboum says. "We'll be able to actually individualize therapy

instead of just talking about it."

Already, he notes, the technology is being used to help treat childhood leukemia. Beyond that, millions more people might be good candidates for the tests. Roughly 8 percent of whites, 2 percent of African-Americans, and 1 percent of Asians have the same odd wiring as Jackson. And studies show that roughly two-thirds of the population have trouble with drugs for such common conditions as depression and high blood pressure, while only about a third get relief from medicines for asthma or migraines.

whether your body is capable of reacting properly to antidepressants, painkillers, certain antibiotics, and drugs for high blood pressure, asthma, high cholesterol, and diabetes. The screens also work for a number of over-the-counter drugs, such as antihistamines and pain relievers.

The maker of the test that's currently available says people who are especially prone to bad reactions are likely to benefit the most. Flockhart says that screening should also make sense for people who need antidepressants or other psychiatric medicines, as well as certain cancer drugs

Just a small blood sample can tell you whether antidepressants, painkillers, and antibiotics will be helpful, harmful, or useless.

So for many people, finding the right drug or dosage can take several trips to the doctor and cause annoying, if not life-threatening, delays in effective treatment. Indeed, bad reactions to drugs are among the top 10 causes of death in the United States.

The new tests might help people avoid such side effects and get better quicker by showing how (or if) they'll respond to certain medications even before they take them. Just a small blood sample can reveal

like tamoxifen (for breast cancer treatment and prevention)—all of which have to be taken for weeks before you know whether they work.

The tests may be new, but the science behind them isn't. Researchers have known since the 1950s that some people react badly to medication because their bodies don't produce enough enzymes to break down underlying chemicals. But these findings didn't create much of a stir until the 1990s, when technological advances and a massive effort to decipher the human genome let scientists zero in on the underpinnings of drug reactions.

Among the dividends: The Signature Genetics test, from Cherry Hill, New Jersey-based Seryx Inc. Introduced last year, it can red-flag potential problems with three-quarters of the 200 most-prescribed medications. The catch: It costs about \$600, and the price almost doubles if it reveals anomalies that warrant a detailed list of do's and don'ts for how illnesses should be treated.

The Swiss pharmaceutical company Roche recently developed a test that may cost hundreds of

which drugs work for you?

IF YOU WANT TO FIND OUT, call Seryx Inc. toll-free at 877-243-6384 to locate a doctor in your area who offers the Signature Genetics test. Caveat: The test costs anywhere from \$600 to \$1,100 and hasn't been embraced (not yet, anyway) by the medical establishment.

want more information?

Helpful sites that explain how your body reacts to medications:

- **National Institute of General Medical Sciences**
www.nigms.nih.gov/funding/medforyou.html
- **American Association for Clinical Chemistry**
www.aacc.org/pharmacogenetics
- **American Pharmacists Association**
www.aphanet.org/govt/policycomm2000/pharmacobackground.html



NO SILVER BULLET:
If your prescriptions
aren't doing their
job, your genes may
be the problem.

fast stat

You're not alone if common medicines give you trouble. Consider this: Roughly two-thirds of the population get no relief from asthma and migraine drugs.

cases, such as Jackson's, in which a defect is known to cause a dramatic difference in a person's response to a drug. But he thinks the genetic quirks worth identifying may be too rare to make testing useful. Plus, just because a person has a particular genetic profile, that's no guarantee she'll have trouble with a particular medicine. Even if there are genetic roadblocks in the way, Wedlund says, backup pathways that the body uses to break down medications may do the job just fine.

Flockhart, however, believes that these types of complaints are too dismissive. "The fact that there are other sources of variability [in drug response] doesn't mean you shouldn't use a tool that allows you to improve it," he says. Flockhart himself relies on lab research to support his belief in gene tests. And he notes that the European Agency for the Evaluation of Medicinal Products, one of Europe's FDA equivalents, already recommends drug-response testing for patients who need antidepressants and lists appropriate dosages depending on test results.

Researchers are continuing to hunt for proof that the technology

dollars less. The AmpliChip CYP450 covers about a quarter of all commercially available drugs, and Roche hopes to make it available in the United States by the end of 2004.

The tests do have their critics. "This is a gimmick," says the University of Kentucky's Peter Wedlund, Ph.D., another authority on the genetics of drug metabolism. "It's like buying the fanciest car on the road—you can do it if you've got the money and want to waste it. But I don't have much confidence that Signature Genetics is going to be very valuable." He thinks more studies need to show payoffs before the tests are put into practice. Seryx, for example, didn't conduct clinical

Not all experts believe in drug-response testing. But one of Europe's FDA-like organizations already recommends it.

studies before launching Signature Genetics. Instead, the company relies on already-published lab-based clinical research linking common genetic defects to drug-metabolism problems. But this research doesn't prove that those problems lead to troublesome symptoms. "It's silly to propose we start applying this," Wedlund says, "when we don't know how valuable it will be."

He doesn't deny there are clear-cut

can help you and your doctor make better decisions about your health. But in the meantime, know that Amy Jackson has all the evidence she needs. **B**

Longtime health writer Margie Patlak chronicled a promising new test for ovarian cancer in the December 2003 issue. Her work has also appeared in The Washington Post and the Los Angeles Times.