



## Seattle's Genelex sees if the genes fit

By Luke Timmerman

*Seattle Times business reporter*

Making a buck off DNA has never been easy. Howard Coleman has been trying nearly 20 years. First came paternity testing, then criminal forensics. Later on, family ancestry.

But now Coleman, the chairman of Seattle-based Genelex, thinks he has found a moneymaker with mass consumer appeal: genetic testing for susceptibility to bad drug reactions.

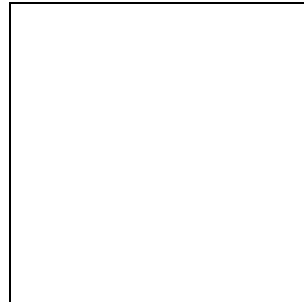
In recent months, the heart problems connected to pain relievers Vioxx and Celebrex have raised public awareness about drug side effects, and inquiries about Coleman's testing have increased. The problem of adverse reactions is vast, and so is the business opportunity. More than 100,000 Americans die every year from bad reactions to prescription drugs, and 2.1 million suffer serious damage from side effects, according to the Journal of the American Medical Association. Adverse drug reactions are at least the sixth-leading killer in America.

One factor is genetics. If a patient's liver enzymes are slow to break down a drug, it could build up in the body and cause serious side effects. Tiny variations in a person's DNA can affect those enzymes. But most doctors don't examine patients' genetic profiles; instead, they prescribe medications through trial and error.

Coleman says much of the trouble can be avoided if doctors do genetic testing before they write a prescription. If, say, a depressed patient needs Prozac, and the doctor knows the patient metabolizes drugs poorly, a lower dose might be prescribed or a different medication recommended. Coleman, a savvy promoter, has been cited by Oprah, Reader's Digest and The Associated Press for work on the drug-reaction test. He says that with simple genetic tests already available, and more sophisticated ones on the way, the time is coming when virtually everyone will be tested before their doctor writes a prescription.

"It's an important piece of information that doctors don't have now about their patients," Coleman said.

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TOM REESE / THE SEATTLE TIMES

Genelex's Howard Coleman says that with simple tests already available from companies such as his, and with sophisticated ones on the way, eventually all patients will be tested for susceptibility to a drug reaction before a doctor writes a prescription.

His company offers consumers, for \$600, a blood test for the most common enzymes involved in drug metabolism, which they can share with their doctors.

Coleman has been pitching it for five years, but it was a tough sell until recently, with just over 1,000 sales since introduction.

Since the pain relievers Vioxx and Celebrex made headlines for links to heart problems, Coleman says, his company has been getting up to 30 calls a day about the genetic tests. It's a mixed blessing: Genelex's tests cannot measure enzymes that break down Vioxx but can tell if a person metabolizes Celebrex poorly.

This year, tests for adverse drug reaction could account for a third of Genelex revenue but, Coleman said, "we're not talking big dollars yet."

He isn't the only one trying to get a share of the new market. A handful of other small companies offer tests on a limited basis, as does the highly regarded Mayo Clinic.

As a small company, Genelex does not plan to go down the difficult road of winning Food and Drug Administration certification for its test. It doesn't have the cash for long-term clinical trials to prove that patients using its test are better off.

To succeed, Coleman needs to convince doctors they need the information and hope it captures the imagination of the public.

David Veenstra, an associate professor of pharmacy at the University of Washington, said he thinks companies like Genelex are onto something, but many barriers are in the way.

There have not been enough large clinical trials that show patients are better off when drugs are prescribed in sync with their genetic profile.

Insurance companies typically do not pay for the tests, partly because of the lack of evidence.

Also, environmental factors, such as whether a patient smokes, may have just as much to do with how the patient metabolizes drugs as genetics.

And doctors may still not know how to interpret the information. There is no road map for what to do if a patient metabolizes Prozac poorly: change the dose, change the drug, or rethink certain drug combinations.

### **Genetics play a role in drug metabolism**

Here are popular classes of drugs metabolized by two common liver enzymes, CYP2D6 and CYP2C9. Tiny genetic variations can alter these enzymes, affecting how quickly the drugs are absorbed and processed. **Genelex**, a small Seattle company, is offering genetic tests to spot those variations.

Antidepressants

Antipsychotics

Antiseizure medications

Blood thinners

Beta blockers

Pain relievers

Chemotherapy drugs

Source: **Genelex**, Roche, Food and Drug Administration

Doctors would have to change their prescribing habits and learn a complex new field of genetic analysis.

Perhaps most importantly, Veenstra said, clear-cut answers to the questions about genetic testing likely aren't coming soon.

Diagnostics companies don't have enough money to run definitive clinical trials for that information, he said. Even a hot new genetic chip from Roche and Affymetrix, hailed by the FDA as the first of its kind for adverse-drug-reaction testing, doesn't have that sort of evidence backing it up.

Big pharmaceutical companies have the money, but they don't have an incentive to run trials to support genetic testing, Veenstra said, because the knowledge could whittle down the size of their markets.

Plus, as Coleman points out, no one is marching in the streets demanding patients get genetically screened.

"There is no organized constituency for adverse drug reactions, like the American Cancer Society is for cancer," he said.

Still, Veenstra said, "This is a nice concept with a lot of potential."

For now, some anecdotal evidence is trickling in; some positive, some mixed. Marilyn Sturtevant, a fibromyalgia patient from Peoria, Ill., who takes several medications, said she took the Genelex test after a near-fatal reaction to the antibiotic Cipro.

The test was inconclusive. Cipro is metabolized by an enzyme Genelex couldn't test for, and Sturtevant's other enzymes were normal. But she learned Cipro can inhibit a certain drug-metabolizing enzyme, which could cause problems for her other medications. Dr. Marsha Cain, a psychiatrist in Federal Way, said the information can be complicated to interpret, but she has become an advocate.

Based on Genelex's test, she has made some decisions to reduce doses and switch medications, Cain said. So far, the patients are responding well.

Mark Rogge, vice president of preclinical development at Seattle-based ZymoGenetics, said his company is working hard to determine which types of patients might have bad reactions in clinical trials of its drugs.

If the Vioxx and Celebrex debacle offers a lesson, Rogge said, it is that drug companies must know which patients should and should not be taking its drugs.

"This is definitely where science is going and where medicine needs to go," Rogge said.

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