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Researchers Have Plan For Genetic Eye Tests Ignored by Industry

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Researchers discovered in 1997 one of the genes that cause Leber's congenital amaurosis, a rare retinal condition that affects about one in 50,000 Americans, leaving them blind from birth. The assumption was that a genetic test to help diagnose patients with the disease would soon follow.

But now, six years later, there isn't a commercially available genetic test in sight. Not for that gene. Not for several others linked to the same problem. Not for the vast majority of more than 90 other genes researchers have found that, when defective, account for a variety of disorders that progressively or abruptly steal people's vision.

Why no tests? Mainly because the diseases are rare -- and represent a potential market far too small for a company to make money selling a test.

Yet, in the gold-rush atmosphere that has characterized the deciphering of the genetic code, companies and academic institutions scramble to patent almost anything that comes out of a DNA-sequencing machine. Chances are somebody owns at least a piece of these genes.

"There's all this intellectual property out there now stuffed in file drawers," says Edwin M. Stone, professor of ophthalmology at the University of Iowa College of Medicine in Iowa City. The result, he says, is a bottleneck that prevents doctors from obtaining and sharing with patients information that could benefit their lives. Dr. Stone aims to unplug the bottleneck.

It's a larger issue than you might think. More than 6,000 diseases individually afflict fewer than 200,000 people, the threshold for rare diseases under federal law. Collectively, perhaps one in 10 Americans has one, prompting Dr. Stone to say: "Rare diseases are common."

Once a gene or culprit mutation is discovered, a test for it is easy to develop. Dr. Stone and colleague Val C. Sheffield, both Howard Hughes Medical Institute investigators at the university, have been running gene tests on their eye patients for a decade as part of their research program. Other academic centers do the same. Even though there aren't yet cures for the myriad eye disorders the doctors treat, gene tests still offer useful information.

For example, some people with retinal degeneration are still driving in their 70s while others are blind by age 20. Knowing early in life which mutation you have could enable you to make smart decisions about the future. Gene tests also can help determine whether an affected person's relatives are at risk or whether women in a family are likely to pass on the disorder to their children.

"If you're going to try to tell people what to expect as they get along in life, it's going to be incredibly

important to know precisely which genes they have," says Richard G. Weleber, an ophthalmologist and molecular geneticist at Oregon Health & Science University, Portland. But unless tests are available, "people with rare diseases are going to be left behind."

Which brings us to Dr. Stone's plan. He and Dr. Sheffield now offer genetic tests for eye diseases as a clinical service of the university rather than as a research project, but with an important caveat: No one -- neither the university nor those who "own" the genes through patents -- can make any money from the tests.

So far, tests for about 20 different genes are available. By doing them at cost -- currently $160 to $975 per test -- and without paying hefty licensing and royalty fees, the scientists hope to keep the price affordable enough to assure patient access to the tests.

What do those who hold patents to the genes say? Before launching the service earlier this year, the scientists paid $20,000 for a search to track down the owners of the 26 genes. It turned up 72 different owners, ranging from academic medical centers to large pharmaceutical companies.

Letters went out informing the patent holders of the scientists' strategy for offering the tests. So far, 12 have responded. None has opposed the idea, a few support it and most others want more information. Meanwhile, the tests are available.

While a public-relations black eye surely awaits anyone who tries to enforce a patent that would deny testing to a blind patient, Dr. Stone and others believe federal legislation akin to laws encouraging development of drugs for rare diseases is needed to ensure the tests are available.

The stakes are getting higher. Gerald Chader, chief scientific officer of Foundation Fighting Blindness in Owings Mills, Md., says genetic tests are crucial to the next big advance in blindness research: clinical trials for new drug-based and gene-based therapies now in the pipeline that hold the promise to cure some forms of blindness.

Two years ago, University of Pennsylvania researchers inserted a gene into the eye of a dog named Lancelot who was blind from a mutation in a gene called RPE65. Now the dog can see. The same gene is one of several associated with the blinding Leber's congenital amaurosis. Human trials could begin within the next five years.

That has Dr. Stone working on another project: In collaboration with other eye researchers nationwide, he is looking for Leber's patients to test for RPE65. With a potential treatment on the horizon, "We want to find as many people as we can who have what the dog has," he says.

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