THE $1,000 GENOME

< Doctors Sift Through Patients' Genomes To Solve Medical Mysteries

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DAVID GREENE, HOST:

New technology has made it faster and cheaper to analyze a person's entire genetic code. As a result, more and more doctors are starting to decipher their patients' genetic blueprints to help diagnose and treat them. In part three of our series, The $1,000 Genome, NPR's Rob Stein explores how some patients are already being helped by this process known as genetic sequencing.

ROB STEIN, BYLINE: Sara Terry's first clue that something was wrong with her son, Christian, came just three weeks after he was born.

SARA TERRY: We went to check on him, just like any parents go and check on their kids, just to make sure they're breathing. And we found him in his crib, and he wasn't breathing. He was blue.

STEIN: Sara and her husband were horrified. They rushed their baby to the hospital.

TERRY: And we took him to the ER, and at that point, we found out he had a bunch of

medical problems.

STEIN: Christian survived, but that terrifying night was the beginning of a long, frustrating odyssey, six years of going from doctor to doctor to doctor.

TERRY: He has developmental delay and low muscle tone. He's smaller for his age than most kids. He has sleep apnea that kind of comes and goes. He had a heart murmur, which resolved on its own when he was about one. And he is behind a little bit in school.

STEIN: The Terrys got every test every specialist could think of. This was before what doctors call whole genome sequencing was really an option. And not one of the doctors could tell them what was wrong with Christian.

TERRY: With a child who goes undiagnosed, you don't know how to treat it, and you don't know, maybe, what their life expectancy is, or what you can expect from this child or how you can push them, or what you can do with them. So it can be very difficult. And you don't know if you're doing everything you can for them.

STEIN: The Terrys finally ended up at the Baylor College of Medicine in Houston. A doctor there told them about something they'd never heard of.

TERRY: She said there's a new test called whole genome sequencing, and it tests for every genetic syndrome that we know to test for. Pretty much, it looks at everything, and if this is something you want to do, we can do it. And, of course, we said we would love to do it.

STEIN: So, they sent off Christian's sample for testing and waited. Until now, genetic tests only scanned small parts of someone's DNA, like the parts carrying genes that can cause Alzheimer's or Huntington's or breast cancer. Whole genome sequencing spells out the entire genetic code - the whole thing, all three billion letters. At Baylor,

where the Terrys brought Christian, Arthur Beaudet heads the genetics department.

ARTHUR BEAUDET: For those of us in the field, it is sort of a holy grail. We now have the ability to get very complete genetic information about individuals and interpret in the context of whatever problems they may have.

STEIN: Not long ago, it took hundreds of scientists years and billions of dollars to do this on just one genome. But the technology has gone crazy. Now a few lab techs using high-speed sequencing machines can unravel anyone's DNA for just thousands of dollars in just weeks - sometimes even days, maybe hours.

BEAUDET: To me, it's a spectacular advance. It changes everything, in the sense that we really begin to understand, at an individual patient level, exactly which gene is altered, and we can begin to think about ways to intervene.

STEIN: So far, doctors are using sequencing mostly on two kinds of patients. The first are patients like Christian, with mysterious illnesses no one can seem to sort out. Les Biesecker studies sequencing at the National Institutes of Health.

LES BIESECKER: Any patient who has one of these rare diseases will tell you about the misery and the agony of this process, which is going from doctor to doctor, undergoing test after test after test, and sometimes at the end of that odyssey, you still don't have an answer. And it's a miserable process for patients to go through.

STEIN: The great hope of sequencing is that someday, no one will ever have to go through that kind of misery again. The second big group of patients getting their genes sequenced is cancer patients, like Jamie Zweig. He's been fighting esophageal cancer for more than two years. Doctors at the Mayo Clinic sequenced his cancer to see if they could target treatment at the precise genetic mutations that caused his tumors. What they discovered was that his cancer was vulnerable to a drug no one had ever considered, a drug designed to treat breast cancer.

JAMIE ZWEIG: I feel much more on the track of beating the disease than being subject to the disease.

STEIN: This is all very new, but it's becoming more and more common. Jonathan Rothberg heads a company that makes sequencers. He says he's starting to get calls from cancer centers all around the country.

JONATHAN ROTHBERG: Physicians now want to use sequence in the same way that they had used X-rays, MRI and CAT scan. They want to use it as a normal part of the practice of treating cancer patients.

STEIN: But Hank Greely says not so fast. He's a bioethicist at Stanford. He says a lot has to be worked out before whole genome sequencing is used widely.

HANK GREELY: We'll have to worry when you're sequencing a kid with an unknown syndrome and also checking the parents to see what he inherited from which of his parents. That can be really medically useful, but we have to worry about: How accurate is the sequencing? How good is our interpretation? And how well are we conveying an accurate message to the patients?

STEIN: It's far from clear how often sequencing will yield truly definitive, useful information. Right now, for the most part, it won't be much help at all. And here's the danger: scary but vague results will send patients down long, frightening dead ends filled with lots of tests and useless treatments that themselves could be dangerous and expensive. Another fear is this: Doctors could easily discover something they weren't even looking for. So one of the questions, according to Harvard geneticist Robert Green, is whether doctors should even be looking for other stuff.

ROBERT GREEN: A huge question in front of the genetics community right now is: If you do sequencing for one purpose, what is your obligation to look and to report on findings elsewhere in the genome?

STEIN: While the experts try to sort all that out, whole genome sequencing is starting to be done at more and more hospitals. Sara Terry remembers the day doctors called with the results of sequencing Christian.

TERRY: I was just kind of speechless. And I just kind of sat there for a little while thinking: Am I dreaming? Like, did I really just get a phone call? We were just so happy to have a diagnosis and to know that they'd found what we had been searching for all these years.

STEIN: Doctors discovered Christian has something rare. They call it a Noonan syndrome-like condition. Christian is now six. There's no miracle drug that will cure him. But his mother says the diagnosis helps a lot. Their doctors know they can safely give him shots to help him grow. Sara and her husband know he won't suddenly develop some fatal complication. And now they know that it's not likely to show up again if they try to have more kids.

TERRY: This has made such a huge difference in our lives. I just can't even tell you. We are just so relieved.

STEIN: Rob Stein, NPR News.

(SOUNDBITE OF MUSIC)

GREENE: Next week, our series continues. We'll learn what happens when the process of genetic sequencing hits the market. That's here on MORNING EDITION, from NPR News.