

# DNA sequencing set to go beyond researchers

By Erin Allday

Stanford scientists are planning to comb through the complete genetic makeup of 100 people with unexplained hereditary conditions or "mystery" diseases, hoping for answers that have long been elusive for some patients and

► **In Business:** Genome sequencing technology is not yet reliable or affordable, a study says. **CI**

may even guide treatment.

At the very least, scientists say, the in-depth analyses will contribute to broader understanding of the complex ties

between DNA and health.

The work is a pilot project that marks the first time Stanford has made whole genome sequencing — a process that unveils a person's complete DNA map — available to patients outside of a research setting.

At Stanford "hospital we

were starting to ask, 'At what point do we jump into this?'" said Euan Ashley, co-director of the new Clinical Genomics Service at Stanford. "We're finally at the point people have been talking about for years. We think the future is here and it's time to jump in."

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## Weather

Clear.  
Highs: 65-75  
Lows: 41-52

**D6**



## 'Mystery' diseases to get DNA testing

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The project is open only to hand-selected patients whom doctors believe may benefit from whole genome sequencing. And while scientists say they're excited to start looking at the bedside applications of DNA sequencing, they're sensitive to the limitations of their work.

Several of the scientists who are most involved in the clinic were authors on a paper — published Wednesday in the *Journal of the American Medical Association* — that pointed out some of the major costs and scientific barriers to making whole genome sequencing widely available.

### Costs less than \$1,000

The technology may be more affordable now than ever — when done for research, whole genome sequencing can cost under \$1,000 — but there are still questions about its accuracy and usefulness for the public at large.

People might learn they're at increased risk for certain common diseases like diabetes or Alzheimer's. But more than likely, they'll find out they have thousands of unique genetic mutations that doctors and scientists don't yet understand.

"Whole genome sequencing is not ready for primetime," said Dr. Tom Quertermous, one of the study authors,

along with Ashley. "People talk a lot about how cheap it is, how it's going to change everything, how we can integrate it into a patient's medical record. But that's completely not the case."

Still, he and other scientists believe there are people who might benefit from full sequencing, and the program at Stanford is one step toward figuring out who those patients might be.

Whole genome sequencing may even be a cost-effective test for some patients, said UC Berkeley geneticist Steven Brenner. He's not familiar with the Stanford program, but Brenner said similar projects at other institutions, which used a somewhat simpler test called whole exome sequencing, have solved diagnostic mysteries that had stumped doctors for years.

"Sequencing has become a tool with great power that can give insight," Brenner said. "It's not a cheap test, but compared to the clinical workup patients have already been through, it's really quite remarkable. Undoubtedly there are cases where genome or exome sequencing can be quite a useful tool."

Genetic testing as a whole has taken off in the past decade. The most common use is in testing for genetic mutations, such as the BRCA gene that's associated with breast cancer, in patients who are



Sam Wolson / Special to The Chronicle

**Euan Ashley, co-director of the Clinical Genomics Service that is conducting the pilot project at Stanford hospital, says: "We think the future is here and it's time to jump in."**

thought to be at risk. Scientists have discovered dozens of specific genetic mutations that are now well known to be associated with conditions like cancer or certain hereditary illnesses.

### Complex undertaking

Whole genomic sequencing, though, is a far more complex and difficult undertaking. It requires mapping out a person's entire genetic code and identifying the tens or even hundreds of thousands of variations that make the patient unique.

At this time, at least, it's not productive to do such sequencing on patients unless doctors have some reason to believe they'll find something useful, scientists say. At Stanford, doctors hope they've

identified groups of patients who may benefit.

One group is infants with unexplained diseases that seem likely to have a genetic cause. In many cases those babies are eventually diagnosed, but often only months or years later. A whole genome analysis may unveil unique genetic mutations that help define the disease earlier. That could, in turn, point doctors toward possible drug treatments, or at least give parents some peace of mind.

Stanford scientists also will look at adult patients who may have hereditary conditions for which doctors haven't been able to identify a specific genetic mutation. If scientists can find a mutation that may be the cause, they can use that information to look for the

same mutation in other family members.

Eric Evans of Los Altos believes that an inherited, deadly heart condition called cardiomyopathy runs in his family. His father and several of his father's brothers died in their 40s, although doctors were never able to say for sure what brought on the heart attacks that killed them.

### Living with uncertainty

People with cardiomyopathy often don't know they have the condition until their heart has started to behave erratically. There are several known genetic causes of cardiomyopathy, but Evans never tested positive for any of those mutations.

So Evans, who is 43, has lived with uncertainty — not knowing if his father and uncles died of cardiomyopathy, or whether he was fated to develop it too. Late last month, he joined the Stanford pilot program for whole genomic sequencing. He'll find out the results this month.

"If they find something, it would help me make lifestyle choices — like diet, exercise, maybe medicine as well — that would help prevent the onset of the disease," Evans said.

He decided years ago not to have children, in case he carries a genetic mutation. In that regard, he said, "I've already made my choice, so the outcome doesn't matter as much to me now. But it's better to know than not."

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