Can Online Genetic Testing Predict the Future?

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We bank, shop, and make friends online, so why not access our genetic profiles online? That's the business model for Navigenics.com, deCODEme.com, and 23andMe.com — personalized medicine in the digital age. In fact, the principals behind these three start-ups see online direct-to-consumer genotyping and risk assessment as the driver for new models of consumer-physician interaction, medical research, and preventive healthcare.

"I'm convinced that in the next 3 to 5 years, every college-educated person in the world will have a genetic profile," declares Kari Stefansson, MD, DrMed, president, CEO, and cofounder of deCODE Genetics in Reykjavik, Iceland, the parent company of deCODEme.

TRANSITION PERIOD

The pitch is directed to consumers, but all three Web sites keep providers in the loop. Navigenics, in Redwood Shores, Calif., includes access to genetic counselors and engages the physician community on its website with pages entitled "Integrating our service into your practice" and "What we tell your patients." Similarly, 23andMe features open letters to scientific and medical communities, and deCODEme cautions customers to "seek the advice of your physician ... with any questions you may have regarding the genetic aspects of a medical matter."

Disclaimers positioned discreetly at the bottom of their Web pages remind visitors that the service provided by 23andMe "is for research and educational use only"; "Navigenics does not provide medical advice, diagnosis or treatment"; and "The de CODEme.com website is for informational purposes only and should NOT be used for medical decision making." Customers are asked to agree to a dense legal "service agreement and informed consent" document before parting with $985 for the services of deCODEme or $399 for 23andMe. Navigenics charges $2,500 for its Health Compass product, which includes such services as a whole-genome scan and round-the-clock access to genetic counselors.

If this comes off as a bit schizophrenic — disclaimers coupled with an invitation to take a bite out of the apple from the tree of genetic knowledge — it's because this is all brand new, and caution is the watchword. Stefansson sees this as a "transition period" in which vendors are figuring out how to market their services while regulators are figuring out how to direct them. Some states have laws that don't permit residents to obtain certain information about genetic risk provided by genotyping services; otherwise, few, if any, regulations apply — yet.

"The regulations are unclear and evolving," says Matt Crenson, content manager for 23andMe, headquartered in Mountain View, Calif. "They were designed for a different kind of genetic testing. I'm even hesitant to say that what we do is testing, because customers don't go into this with any one question they expect to have answered."

Amy DuRoss, vice president for policy and business affairs at Navigenics, says her company discussed industry standards with, and solicited input from, key stakeholders —including its competitors, when entering the market. "We recognized a need for industry guidance to lay the foundation for standards and to protect consumer interests."

THIS IS COMPLICATED

One measure of these start-ups is the stature of the principals behind them. 23andMe is the brainchild of biopharmaceutical executive Linda Avey and healthcare investor Anne Wojcicki, wife of Google cofounder Sergey

deCODEme's Web site touts the company as a pioneer in human genetics that has analyzed DNA from over 300,000 people worldwide.

Someone whose results show higher risk for a disease may never get it. "To me, the information is a nonstarter," says genetic counselor Beth Peshkin.

Brin. The name comes from the 23 pairs of chromosomes that compose the human genome. Investors include Google, Genentech, and tech guru Esther Dyson.

Geneticist Dietrich Stephan, PhD, and prostate cancer specialist David Agus, MD, founded Navigenics, backed by venture capital firms Kleiner Perkins Caufield & Byers, Mohr Davidow Ventures, and Sequoia Capital. 23andMe and Navigenics have corralled a stable of illustrious advisors from prestigious research institutes and universities.

deCODEme's claim to fame is that its parent company has identified many of the genes and genetic variants associated with an increased risk of disease. These discoveries are incorporated into the deCODEme genetic scan, according to Stefansson, a board-certified neurologist and neuropathologist who was on the University of Chicago, Harvard University, and Beth Israel Hospital in Boston staffs before cofounding deCODE in 1996.

"When customers select deCODEme, they're buying from the guys who discovered some of the genetic variants that 23andMe and Navigenics present," says Stefansson. "Our competence in human genetics is unsurpassed."

EDUCATIONAL AND INFORMATIONAL

After customers hit the "buy" button on one of these sites and enter their payment data, they get a test kit in the mail for submitting their DNA as a saliva sample or a buccal swab. A few weeks later, an e-mail notifies them that their password-protected results are available on the Web site.

Results are based on one-letter DNA variations (single nucleotide polymorphisms, or SNPs). All three vendors will conduct an overall assessment of your genome and an analysis of your SNPs relative to published research on SNPs known to be associated with common diseases.

For example, Navigenics lists, among many other conditions, Alzheimer's disease, breast cancer, type 2 diabetes, heart attack, lung cancer, lupus, macular degeneration, multiple sclerosis, and obesity under "Conditions we cover."

Estimated disease risks come with many qualifications, however. For example, an SNP may be associated with a disease, but so may one or more still unidentified SNPs or gene mutations. Environmental factors also influence risk. Also, someone whose results show a higher risk for a disease may never get it, and someone with a lower risk already may have the disease or may get it one day.

Beth Peshkin, senior genetics counselor at the Lombardi Comprehensive Cancer Center of Georgetown University Medical Center, makes a distinction between testing for SNPs and testing for gene mutations known to be associated with such diseases as breast cancer or Huntington's disease. Right now, a highly predictive test for hereditary breast and ovarian cancer is available only from the company holding patents on the BRCA 1 and BRCA2 genes.

"In the adult genetics arena, the most common testing being done is for breast, ovarian, and colon cancer susceptibility, and unlike the tests being offered by companies like Navigenics, 23andMe and deCODEme, these are highly predictive genetic tests," says Peshkin. "SNPs may be associated with increased or decreased risk of disease, but in many cases, these are very minimal changes in risk, like a 15 percent increase in risk, which is not enough to impact medical management. That number sounds high, but when you calculate the percent increase in risk, it is very small."

Crenson, at 23andMe, concedes Peshkin's point. "We're aware that the information we provide is more educational and informational," he says. "I certainly wouldn't take medical action based on the information in my account."

But Stefansson, for one, disagrees.

"Many of these variants confer risk that is greater than the risk of heart attack when you are in the top quintile of cholesterol," he says. "Forget that they are genetic variants; look at them as risk factors we can measure. And there are all kinds of things that can be done to diminish the genetic risk. This is bound to have a tremendous impact on how we switch from interventional to preventive medicine."

Peshkin maintains that SNP data cannot be properly interpreted in the absence of a family history: "The danger of interpreting this information without context of family history is that people who have a family history and test negative for gene alterations may be falsely reassured."

Navigenics says it includes only conditions that are "actionable," meaning prevented, detected early, or treated.

Peshkin thinks that for many consumers, "Spending that [money] on a gym membership that's actually used may be more valuable than spending it on getting information that we don't know how to interpret."

Elissa Levin, director of Navigenics' genetic counseling program, has a different viewpoint. "Knowing that they are potentially predisposed to certain conditions may be the push people need to engage in their own health," she says. "They are gaining insight into how to make better health choices about screening, diagnosis, and prevention."

Stefansson, for his part, is convinced that services like deCODEme will be heavily subscribed. "I think [genetic tests] are going to conquer the world within the next 3 to 5 years, and we are fighting for our share of that."

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