



Pioneering at-home genetics testing kits unravel the mysteries of the double helix as they shed light on ancestry.

By Julie Vallone

BRAVE NEW WORLD

In December of last year, Jason Caldwell and his three Latitude 35 teammates got into a small boat and rowed 3000 miles across the Atlantic. One of the few people on the planet with the stamina to make the trip more than once, Caldwell had entered the same competitive race the year before; he knew just how grueling it could be. In his previous attempt he had embarked with three teammates but due to illness and injury, two of them had to be evacuated at the 600-mile mark. Still, Caldwell and his sole teammate completed the remaining 2,400 miles on their own and somehow managed to finish in 11th place.

Caldwell, however, was determined to win. Looking for anything that would give his team the edge, he happened to bump into a partner of Vitagene, a company that uses personalized test results to help its clients achieve their health and fitness goals. Caldwell was intrigued, and Vitagene saw the dividends in joining forces with him in his quest. The company arranged for teammates to send in blood and DNA samples and, based on their genetic tests, reciprocated with packs of vitamins tailored to the needs of each team member.

Throughout the race, Caldwell and team took the vitamins as directed, stayed healthy throughout the ordeal and ultimately finished in first place. They also set the world record, beating the previous time by 11 hours. Today, Caldwell credits Vitagene as a key component of the team's victory: "Not only were the vitamins a big factor of our success, but also the way they packaged them made it easy for us to take them under extreme conditions," says Caldwell.

San Francisco-based Vitagene is just one of a growing number of DNA testing companies now revolutionizing the industry. Some provide direct-to-consumer genetic information to anyone at reasonable cost; others require a doctor's prescription. Both types unravel ancestral, medical and physical mysteries that have challenged us down through the ages, most commonly from traces of mucous and saliva.

Getting your medical, personal health and ancestry DNA analyzed usually works like this: You order a kit, which contains a tube that you can spit into or a swab to use on your inner cheek. You send your DNA back to the company, and a few weeks later, the company notifies you that your results are ready. Results are usually available online. Depending on the service you use, you can learn whether you're a carrier of a certain disease, how to design the most effective your nutritional and fitness regimen and where in the world your ancestors came from. That list of offerings is sure to expand in the near future. The personalized DNA testing space has quickly grown in popularity, with millions of people signing up as it becomes increasingly affordable, explains Vitagene founder and CEO Mehdi Maghsoodnia.

"Ten years ago, I did my genetic test for \$5,000. Now it's \$99, and it's even getting cheaper. It will probably hit something like the \$50 range in a couple of years," he said. His company's website offers the AncestryDNA Test that, for \$99, includes "a DNA test kit and a detailed report with ancestry and tailored recommendations for diet, fitness and supplementation."

23andMe, which came onto the personal genomics scene back in 2006, was the first direct-to-consumer genetic testing kit that promised to inform users about genetic predispositions for more than 90 different traits, from baldness to cancer. In 2013, the company ran afoul of the FDA, which was concerned that

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- ANNE WOJCICKI, 23ANDME

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- JASON CALDWELL, THIRD FROM LEFT, AND LATITUDE 35 TEAM

BEN DUFFY

23andMe was dispensing health-related data that could be inaccurate or had the potential to be misinterpreted by customers. At that time, the company was offering reports on over 200 diseases and conditions.

"When the FDA declared that genetic info about your health characteristics was a medical diagnostic, that required a different way of presenting the information," says Stanford Professor Emeritus Doug Brutlag, who has researched and taught courses on personal genetics for decades.

Brutlag explained that there are some genetic variations in the DNA sequence that cause a disease, and others that are simply associated with a disease, but they don't necessarily cause it. Unaware of that distinction, DNA testing clients can misinterpret the results, and some do. The FDA demanded more clarity and fewer prognoses.

"It's important that people know what is the chance they can come down with a disease, how much of the disease is genetic, and how much was based on environmental factors," he explained. To illustrate, Brutlag, who is a diabetic, said that while he has a gene for diabetes, the reason he got it was environmental. "The environment in my case was predominantly a place called McDonald's." For that reason, Brutlag believes it is important for people to have their results interpreted by a genetic counselor or

other medical professional.

23andMe has since relaunched its service and revamped its products and protocol, and now offers two tests based on current FDA guidelines: one to discover ancestry (\$99), and the other that tests both ancestry and carrier status for certain diseases (\$199). Although genetic counseling is not required, 23andMe does recommend it. The site also features disclaimers indicating the tests aren't intended to diagnose a disease or assess your risk for developing it.

23andMe chief executive Anne Wojcicki says the company continues to work with the FDA in hopes of offering more medical information in the future. "People want health information they probably otherwise can't get from their physician, including information on conditions like Alzheimer's, Parkinson's and drug response. We see that there's tons of consumer interest in that area and it's just not out yet, and that's what we're working pretty hard to get," said Wojcicki at a recent Wall Street Journal live conference.

TESTING TO TAILOR NUTRITION

As one of the most prominent pioneers in the emerging science of nutritional genomics (a.k.a. nutrigenomics), Vitagene uses personal DNA testing to tell you how your body responds to certain

Should You Tell Your Family When You Test Positive?



When a DNA test result discloses that you are a carrier for a particular inherited disease, such as sickle cell anemia, Tay-Sachs disease or Wilson's disease, should you let family members know?

Absolutely, says a genetic counselor. This is one of the important ethical questions around DNA testing that Lisa Moss has encountered in her nine years as a licensed, Certified Genetic Counselor for Palo Alto Medical Foundation. She believes it's important for people to understand the family issues before they get tested.

"People should know that if you test positive, your siblings are now at risk, your children are at risk and you may have inadvertently disclosed that one of your parents has this genetic change," she explains. "It's important to talk to

your family to let them know you're doing this. And it's crucial to share your results with your family members."

Moss acknowledges that this isn't always easy. In some cases, patients refuse to share the information with their family. In others, family members just don't want to know, and patients are just honoring their wishes. But in Moss's view, not telling family members leaves them at a disadvantage, because they could use the information to get tested themselves, make decisions on their own parenting choices and take the steps needed to protect their own health.

"You can do this test for your own health," says Moss, "but you need to recognize that it can impact many more people."

foods. It also uses genetic information to specify your optimal exercise program and vitamin regimen.

"We are not doing what 23andMe is doing," explains Maghsoodnia. "We don't go into disease predispositions. We are very focused on wellness and nutrition, and trying to tell you what to do to stay healthy."

Maghsoodnia started the company because he believed in the value of the wellness perspective—a preventative model based in using DNA testing to maintain good health through personalized nutrition and fitness. He was also frustrated that the wellness

information had become so confusing for consumers and wanted to create a clear, targeted solution.

"There are over 80,000 health products out there on the shelf, and the average consumer is getting bombarded with mixed messages," says Maghsoodnia. "On any given day, you can read an article that says, 'Everyone should be taking Vitamin D.' Then you read another article that says, 'Vitamin D increases your chance of cardiac arrest in certain genetic dispositions.' So the consumer is extremely confused: Should I be taking it or shouldn't I be taking it?"



SHIVANI NAZARETH, COUNSYL

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FROM TOP: SHUTTERSTOCK; COURTESY OF COUNSYL

Vitagene empowers customers with actionable information about how they can improve their health, based on nutritional predispositions and deficiencies.

"We go into detail about what people should and shouldn't be taking. For instance, we say things like, 'You should be taking only 30 mg of vitamin D and a 100 mg of iron. You shouldn't be taking vitamin K.'"

Vitagene is also partnering with high-quality supplement companies to create customized monthly vitamin packs for its customers, based on the DNA results, just as it did for the Latitude 35 rowing team.

"We send you pills that are personalized to you. If we said you should take a multivitamin without vitamin K, we'll send you one without vitamin K. And you'd actually get it cheaper than you would on the retail shelf," Maghsoodnia explains.

Like 23andMe, Vitagene also includes an ancestry test, which provides detailed analysis of your ethnic makeup. Maghsoodnia says that unlike the vitamin and fitness testing, the ancestry information doesn't really include much actionable information, but it could well play a role in uncovering food sensitivities and giving insight into personal metabolism. For example, certain indigenous populations are genetically more susceptible to type 2 diabetes than others, even when eating nutritionally comparable diets to other groups. Scientists have also detected one gene variation that seems to enhance the health benefits of polyunsaturated fats, for example, giving people who possess it a bigger boost in good cholesterol when they eat a diet rich in plant oils.

GETTING TO THE ROOTS OF YOUR DNA

The fact that Ancestry.com now has the world's largest consumer database, with DNA from more than 3 million people, shows that personal interest in DNA extends well beyond health information. AncestryDNA, part of Ancestry.com, employs direct-to-consumer genetic testing to analyze your ethnic mix and global roots of your DNA. Customers looking for a more complete picture can sign up for Ancestry.com membership, and combine their genetic information with Ancestry's billions of historical records and millions of family trees. Ancestry.com currently has offices in Lehi, Utah and in San Francisco, and is expanding into several other cities around the globe.

Catherine Ball, chief scientific officer at Ancestry.com, was doing research on biological databases at Stanford when she was tapped to help create AncestryDNA. For her, it was a chance to apply her knowledge to a completely different field, and communicate with regular people (rather than just scientists or clinicians) about the meaning of their DNA.

"It was all about democratizing access to the genome," she said. "And wasn't that the promise of the Human Genome project, that it would change all our lives?" (That project spanned 13 years and was completed in 2003. It mapped all the human genes, enabling the use of DNA information to develop new ways to treat, cure, or even prevent thousands of human diseases.)

Ball said that for students of family history, having multiple lines of access is important. DNA information complements public records and other documents people find when building their family tree.

"Sometimes the document trail runs cold. In that case, the

COURTESY OF VITAGENE



MEHDI MAGHSOODNIA, VITAGENE

MAGHSOODNIA STARTED THE COMPANY BECAUSE HE BELIEVED IN THE VALUE OF LOOKING AT HEALTH FROM THE WELLNESS PERSPECTIVE—STAYING HEALTHY NOW TO AVOID PROBLEMS LATER. HE WAS INTERESTED IN USING DNA TESTING TO STAVE OFF SICKNESS AND DISEASE THROUGH PERSONALIZED NUTRITION AND FITNESS.

genetic hint is going to be super helpful. Sometimes there's just not a lot of written history about some details, and (we help) find commonalities that will be meaningful," says Ball.

And when it comes to uncovering meaningful stories with Ancestry, Ball says there are just too many to count. "Almost every person I talk to has a profoundly personal experience with it. For instance, I'm completely floored by friends of mine who are African American, and who, for the first time, can get a glimpse of their African history before their ancestors were enslaved."

PHYSICIAN-ORDERED DNA TESTING

While most direct-to-consumer DNA companies are focusing on non-medical genetic interpretations, many people are still looking to the industry to provide deeper medical information. According to Wojcicki, 23andMe is the only direct-to-consumer DNA testing company that can offer carrier status information (without the

involvement of a physician). However, there are many companies in the Bay Area that can offer detailed information on other disease predispositions and a host of other medical issues using a physician-ordered kit, paired with genetic counseling.

San Francisco-based Counsyl has distinguished itself by focusing on women's health conditions. Working with OBGyns and other physicians, Counsyl can scan for more than 100 hereditary diseases. Counsyl also advises women if they have a family history of breast, colon, ovarian and other cancers. Once a patient learns the information, Counsyl connects her to one of its 50 genetic counselors.

"We don't just dump data in patients' laps. We think it's really important for the patients, as well as the physicians, to understand what they can do with the data," says Shivani Nazareth, Director or Medical Affairs at Counsyl. "For instance, if a patient learns that they are at an increased risk of developing breast cancer, we want to make sure they know they're eligible for earlier screening,

Mixed Breed, Pure Science: Testing Your Canine Companion



Ever since we adopted Ozzie, our cocker spaniel mix, from the Santa Cruz County Animal Shelter, our family has wondered what comprised the "mix" portion of our pup. At times, this question has been the subject of a heated family debate.

With his similar markings, nonstop tail wagging, sweet nature and tendency to get really fat, I was almost sure he had the DNA of one of my favorite kinds of dogs, the Cavalier King Charles Spaniel. My daughter and husband had their doubts. Cavalier King Charles Spaniels are

sporting dogs who like to retrieve things. Ozzie retrieves nothing. Throw a ball at him, and he'll sit down and watch it go by, then look at you and wonder if you're maybe holding a treat.

To answer the question once and for all, I ordered an \$80 Mars Wisdom Panel DNA test kit for my dog. The small package I received a few days later included a simple DNA swab to rub against Ozzie's inner cheek, instructions on how to mark it so the Mars team could track it for his records, and a return postage box.

A few weeks after sending it in, I received an email from the Mars Veterinary Customer Care team telling me they had the results, and providing a link for me to access them on the Mars site.

So, according to Mars, here's the genetic makeup of Ozzie:

37.5 percent cocker spaniel

25 percent poodle (Poodle? Seriously? He's just not yappy like that.)

12.5 percent Chinese crested (What?! This dog breed looks like a cross between a Chihuahua and a Shetland pony, and nothing like Ozzie.)

25 percent mixed-breed groups that do not include Cavalier King Charles Spaniels.

"No Cavalier King Charles. Not a trace," I said with a sigh the next day to a fellow dog owner, who knew I had given our dog the test.

He looked at Ozzie, examining his gentle eyes, huge dog smile, and nonstop waggy tail. "OK," he said. "So now that you know, does it make you love him any less?"

Nope.

SHUTTERSTOCK

"WE WANT THIS TO BE MORE THAN JUST A SINGLE TRANSACTION. WITH A LOT OF DNA TESTING COMPANIES, YOU DO IT ONCE AND YOU'RE DONE. WITH US, BECAUSE WE'RE SEQUENCING SUCH A LARGE AMOUNT OF DATA, YOU CAN CONTINUE TO FIND NEW INSIGHTS AS NEW SCIENTIFIC DISCOVERIES ARE MADE."



more frequent mammograms and other preventative actions."

Counsyl also works with insurance companies, so they can advise people even before the DNA test on what treatments their insurance will cover. Moreover, insurance will usually cover all or part of the Counsyl test, but the out-of-pocket cost is \$349 (including genetic counseling).

Because it works with doctors, uses genetic counselors and runs its own lab, Counsyl, unlike 23andMe, is not currently regulated by the FDA. It is instead regulated by the Centers for Medicare and Medicaid services, which ensures their lab complies required standards.

Genos, also based in San Francisco, is similar to Counsyl in that it is physician-ordered. But rather than focus on parts of the DNA that relate to particular conditions or diseases, it tests the whole exome. Whole exome sequencing provides clients with information from 20,000 genes, and 50 times more data than most DNA testing companies. The cost is \$499.

Genos is also unique in that it gives people control of their data, which they can test over and over to answer any new question they have.

"We want this to be more than just a single transaction," says co-founder Mark Blumling, who graduated from Stanford with a BA in human biology, among other degrees.

"With a lot of DNA testing companies, you do it once and you're done. With us, because we're sequencing such a large amount of data, you can continue to find new insights as new scientific discoveries are made."

In addition, Genos runs studies with selected clients, and even compensates them \$50 to \$250 for the use of their data.

There are a lot of companies out there that monetize the genetic data they get from people, said Blumling, adding that Genos operates differently. "If we use your data, we want you to get some of the economic benefit."

He adds that participating in a study can be a virtuous cycle for clients. They're helping to drive new scientific discoveries that they, in the future, can benefit from, using the information to find new insights on their own DNA.

"It's a little bit like sequence now, discover forever," says Blumling. Today's payoffs may be remarkable, but tomorrow's revelations promise to be even more compelling and beneficial to us all. ■