



CRACKING YOUR CODE

From exonerating the wrongly accused to tracing genetic ancestry or even changing how we age, the future of DNA research is just beginning to unfold.

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On April 24, 2018, 72-year-old Joseph James DeAngelo, now known as the Golden State Killer, was apprehended and eventually charged with 13 counts of murder and 13 counts of attempted kidnapping, thanks to publicly shared genetic codes. No, DeAngelo didn't submit a sample to find out what percentage Italian he was, but a distant relative of his did take an at-home genetic test.

Using a crowdsourced online database, investigators found that the test taker's DNA partially matched DNA taken from evidence related to the serial killer. From there, the search was narrowed from a pool of millions down to a single family, eventually leading police to DeAngelo, who lived within miles of many of the attacks. This was the second time that law enforcement used this method to catch a perpetrator, and in the short amount of time since, at least 13 other suspected criminals have been identified in the same way. So even if you've personally never supplied your own DNA to an outside party, if your relatives have, this information can be used in a case involving you.

DNA is the hereditary material present in nearly all human cells and the cells of almost all other life forms. Composed of four nucleobases (biological compounds) in various sequences, it builds and maintains organisms — similar to the way letters of the alphabet are arranged to form words and sentences — and our understanding of it has come a long way since it was discovered in the 19th century.

The DNA molecule was initially isolated in 1869 by Swiss chemist Johann Friedrich Miescher, but it was University of Cambridge biologists Francis Crick and James Watson who first proposed the double-helix structure of DNA, in a 1953 issue of *Nature*. A few decades later, British geneticist Sir Alec Jeffreys made a breakthrough discovery that led him to develop DNA profiling. That technology came into wider use in 1986 and immediately helped authorities convict a man of two rapes and murders committed within the past three

years. Anyone who's watched *CSI*, *Forensic Files* or any other police procedural TV show in the past two decades has heard of the process, also known as DNA fingerprinting, and for criminal investigators it's now the gold standard for ascertaining innocence or guilt. Forensic experts extract DNA at crime scenes from samples of skin cells, blood, semen, saliva or other bodily fluids; the processed samples are then compared with those of a suspect, in the hope of getting a match and identifying the bad guy. (Of course, while the turnaround time is seemingly instant on *CSI*, real-world lab results can take days or weeks or the tests may never be processed at all.)

Conversely, DNA has also played an integral part in freeing people who have been wrongfully imprisoned. The Innocence Project, a nonprofit legal organization, uses the testing to exonerate innocent inmates serving sentences. To date, 350 people have been released thanks to those efforts.

TO YOUR HEALTH

These days, DNA evidence applies well beyond the courtroom. Every day thousands of Americans readily mail their own spit, cheek swabs or stool samples to companies like 23andMe, MyHeritage or AncestryDNA, hoping to learn more about their family history, hereditary traits or other burning issues of existence. And the competition for your spit is fierce. Open a magazine or change the TV channel and you'll likely encounter an advertisement for at-home genetic tests. People use such kits to pinpoint ethnic origins that might help explain their own pasta addiction or fondness for kilt wearing, to track down relatives or to verify that Fido is indeed a purebred (yes, dog DNA kits also exist). And, increasingly, companies are claiming that understanding your DNA profile can help further your own well-being.

Not surprisingly, some of those companies are located in the Bay Area. San Francisco-based Vitagene offers to analyze how ancestry affects personal nutrition and health, claiming that its methodology "leverages big data, machine learning, and the latest scientific research and technology" to devise a client-specific diet and fitness plan. Another company, GenoPalate, employs geneticists and registered dietitians to examine genetic profiles and give targeted nutritional advice. Most of these tests study DNA extracted from saliva; others, like San Francisco's uBiome, get a bit more intimate, studying mailed-in vaginal swabs and fecal samples to produce information about a customer's microbiome (the full genetic

complement of bacteria and other microorganisms in a body) and assess gut or vaginal health.

So is it worth it? In a 2018 *Women's Health* magazine interview, Dr. Leo Treyzon, a gastroenterologist at L.A.'s Cedars-Sinai Medical Center, says that while uBiome and other purveyors of at-home testing kits can help people take their health into their own hands, the data provided isn't very insightful yet. "In 2018 we can look at your gut and give you data on it, but the research on what you can actually do with those results isn't actually there," he maintains.

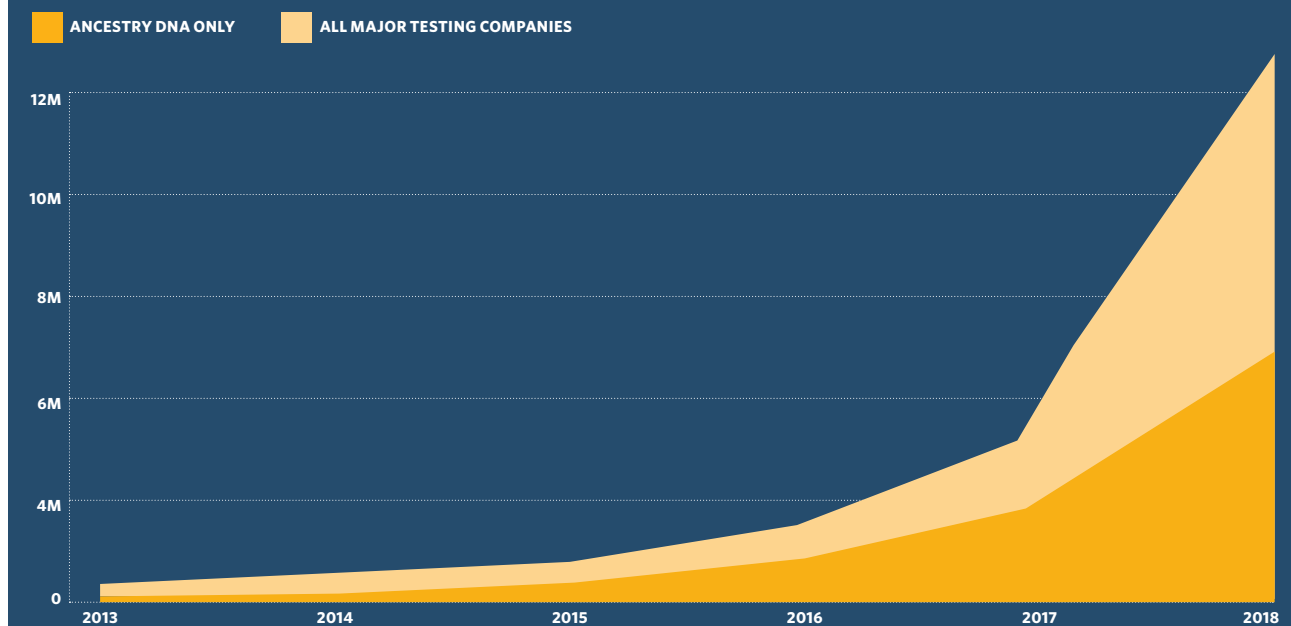
Even so, DNA products keep appearing on the market. In October 2018, Mountain View-based 23andMe gained an advantage over its competition when the FDA approved a test it uses that examines how the body processes medications, including drugs addressing depression. (Before then, the company was already offering screenings for some of the genes involved in Alzheimer's, Parkinson's and breast cancer, in addition to ancestry-tracing services.) The day after that green light, the FDA seemed to backpedal, stressing that patients and their doctors should not make treatment decisions based on such testing in lieu of medical lab work and exams.

WHO OWNS YOUR DNA?

Regardless of whether you've mailed anyone a sample, there's a good chance you're already part of a genetic database, or at least part of you is. According to a February 2018

A RISING TREND

Total number of people tested by consumer genetics companies, in millions.



ISOGG, LEAH LARKIN, COMPANY REPORTS

article in *MIT Technology Review*, more than 12 million Americans have taken a direct-to-consumer DNA test, a number that by now has undoubtedly multiplied since the recent winter holidays. AncestryDNA claims to have “shattered” its November records thanks to Black Friday and Cyber Monday sales and says its kits were Amazon’s best-selling non-Amazon-branded product on Cyber Monday for the second year in a row.

Yet as the quantity of shared genetic information has grown, so have concerns about what’s done with it. Crowdsourced online databases like GEDmatch, DNA.Land and Open Humans, where users can anonymously upload DNA test results, present privacy issues. Also, test results, for all the interesting insights they yield, can also present data that aren’t always clear, and as with most new scientific and technological strides, it can take time for laws to catch up. Control of that info is another issue: In July 2018 the internet exploded when British pharmaceutical company GlaxoSmithKline gained an exclusive right to mine 23andMe’s customer data for drug development purposes. The arrangement was legal, though: after you drop that tube in the mail the testing companies own it, and while there are some restrictions, the range of permitted uses is murky. Most famously, police used GEDmatch to capture

the Golden State Killer and the NorCal Rapist, but data from genetic material has many other possible applications.

And while test results can clue you in to your familial or ethnic lineage, they can’t confirm that you’re 100 percent Italian. “Autosomal [numbered DNA] ethnicity estimates really tell us ethnicity from about 500 years ago,” says Colleen Greene, a genealogist who teaches a graduate genealogy course in the School of Information at San Jose State University. “People often do not understand that and get confused, because they know their ancestors lived in, say, Ireland, 150 years ago.” Ethnicity testing can be pretty accurate geographically — good at indicating if your ancestors came from Southern Europe or West Africa — but if you’re trying to boil it down to a percentage, the results are more iffy. Since each company gets a different sample of your genome, findings can vary significantly from one kit to another; “in addition to these differing snapshots, testing companies also use different algorithms to analyze those snapshots, different reference populations to compare data, and different categories for grouping ethnicities,” adds Greene.

USER BEWARE

And ultimately, some people may not be glad to get the whole story. For instance, while many adoptees have successfully

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sought and found biological parents or relatives through at-home DNA tests, that doesn’t always lead to happiness: numerous online forums attest to unwelcome discoveries, from men learning their children were not their biological offspring to people startled to hear of half-siblings whose existence they’d had no reason to suspect. Users of 23andMe and AncestryDNA are cautioned about this risk of unanticipated information and are offered the opportunity to opt in or out of learning about close genetic matches. Both companies also train their customer service representatives in ways to communicate with clients who are disturbed after receiving unexpected news.

In 2011, NASA named *Gattaca* as the most scientifically plausible science fiction film to date. Starring Ethan Hawke and Uma Thurman, the futuristic thriller (shot in part at the Marin County Civic Center) depicts a world where genetic engineering is used to perfect the human species. Hawke’s character dreams of space travel, but his genetically inferior status forbids it; undeterred, he buys the genes of a laboratory-engineered individual, takes on that person’s DNA identity and joins the space program.

Gattaca was released in 1997, but it took the federal government more than a decade to catch up with its topic. In 2008 Congress passed the Genetic Information Nondiscrimination Act, known as GINA. It bans use of genetic information in health insurance applications, preventing insurers from denying coverage or charging higher premiums based on someone’s genetic predisposition for someday developing a disease. The law also prohibits employers from using genetic information in making hiring, firing or other personnel decisions.

Still, a bill introduced in Congress could undermine those protections. House Resolution 1313 would let employers offer substantial health insurance discounts to employees who participate in a company-run wellness program that may include genetic screening; the law would let employers charge higher premiums to employees who opt out. In December 2017 the bill was brought to the House floor without committee review but hasn’t progressed since.

THE FUTURE IS NOW

Meanwhile, the future of genetics is looking more sci-fi than ever. This past November, Chinese scientist He Jiankui prompted a global outcry when he announced he’d successfully altered two babies’ genetic code by using a gene-editing technology called CRISPR. His claim has been met with skepticism, and the scientific community unequivocally

condemned Jiankui; the Chinese government suspended his research, and in December he was reportedly being sequestered under guard.

But legitimate gene-editing research is happening in our own backyard. “There are a number of labs here that are using the CRISPR technology,” says Kris Rebillot, director of communications at the Buck Institute for Research on Aging in Novato. “The Ellerby Lab is one key lab that’s working on Huntington’s disease and they’re trying to do gene replacement therapy.” CRISPR, genomics, and deriving stem cells from patients are just some of the technologies our researchers are using to learn more about the mechanisms of Huntington’s, Alzheimer’s, Parkinson’s and similar age-related neurodegenerative disease.

“There is the idea is that we all have two different ages,” says Eric Verdin, president and CEO at the Buck. “One, the chronological age, is how many years you have lived, and two, the biological age, is based on molecular and cellular health,” or more specifically, “Are you like the average population, or have you aged faster or slower?” Blood samples can help provide answers, though the research is still experimental. “We don’t really fully know what to do with these numbers,” Verdin says, “and it’s part of a whole change in the field of aging where we are trying to measure precisely how do people age.”

Curious about your biological age? There are spit-in-a-vial kits for that too, from companies like myDNAge or TeloYears. But researchers at the Buck hope their own work can point the way to a proactive, preventive-medicine approach to diseases brought on by aging — interventions that would prevent people from getting sick in the first place — and ways to track the effectiveness of treatments.

“The basic research of aging has been going on for close to 30 years, and we’re right at that transition where all of these discoveries are starting to be tested,” Verdin says. “There are a number of drugs that we know now increase health span and life span in animal models, and some of those are actually moving into the clinic as we speak. I would predict,” he adds, “that within 10 years we will have two drugs in the market that will be fighting the aging process.”

One of those drugs under development, now in its first phase of clinical trials, was incubated at the Buck, where the ultimate vision, Verdin says, centers on helping people “live better longer and live more gracefully and without diseases. Right now we associate aging with chronic disease, chronic conditions,” he says. “It doesn’t have to be this way.” So could a map to the fountain of youth be located inside each of us? If so, it’s for a quest that’s still underway. **M**

TOP GENETIC TESTING COMPANIES				
Service	What it's ideal for	Key feature	Cost	Where
23ANDME	Looking for long-lost relatives	Offers both ancestry and health results	\$99-\$199	23andme.com
ANCESTRYDNA	Looking for recent ancestors	Largest and most diverse database, low cost	\$99	ancestrydna.com
BASEPAWS	Cat breed and their risk for health conditions	Ancestry, personality traits, and diet recommendations	\$95	basepaws.com
HELIX	Specific tests for detailed insights	Offers over 35 DNA-powered kits and products	\$50-\$240	helix.com
LIVING DNA	Exact breakdown of ethnic makeup	Covers 80 different regions worldwide	\$99-\$159	livingdna.com
MYDNAGE	Estimating your biological age	Measuring the epigenetic modifications on your DNA instead of genetic marks	\$299	mydnage.com
UBIOME	Learning more about your gut and/or vaginal microbiome	Detecting microorganisms associated with specific infections	Free-\$399	ubiome.com
VITAGENE	People looking for a specific road map for their bodies	Customized fitness, vitamin and diet plan	\$99-\$149	vitagene.com
WISDOM PANEL	Dog breed and disease detection	World’s largest breed database, trait analysis and drug exercise testing	\$85-\$150	wisdompanel.com