Who's Your Daddy?

The perils of personal genomics.

By Daniel Engber

Daniel Engber (@danengber) is a columnist for ***Slate***.

http://www.slate.com/articles/health_and_science/science/2013/05/paternity_testing_personal_genomics_companies_will_reveal_dna_secrets.single.html#pagebreak_anchor_2

First Jackie learned her brother Alex was her uncle. Then things got a little weird.

In the spring of 2012, the 34-year-old and her older sibling (their names have been changed) spit a few milliliters of saliva into plastic tubes and shipped them off to 23andMe, a personal genomics company, for consumer-grade scans of their DNA. Their family has a long history of cancer, alcoholism, and bipolar disorder, and Jackie, who happens to work for a biomedical research lab, wanted to learn all she could about her health risks and propensities.

Alex wasn't quite so into it. Jackie is curious by nature, the kind of person who's always asking questions. ("You never, ever, *ever* know anything for sure," she tells me. "As a kid, I was always saying, 'How do I know the sky is really blue?' ") Her brother's just the opposite: a military man with little time for facts that don't bear directly on his mission goals. Growing up, she called him "Robot," because he's so even-keeled and self-sufficient. When they both got emails saying that their genome data could be viewed online, Alex didn't open his.

The two agreed to look over their reports together, though. Meeting at their mother's place, they logged into 23andMe.com and checked the hints about their health and heritage that had been extracted from their genomes. None of what they found was so surprising or distressing, at least until they reached a screen that promised access to "close relatives" who might be in the system. Opting in, the siblings learned a fact about themselves that would have been disturbing, were it not so obviously in error: Jackie had an uncle, the software told them—an Uncle Alex.

When Jackie wrote about the glitch on the 23andMe message board, she got a quick reply: That's not an error, another user wrote; it means that you and Alex are more distantly related than you think. The scientists in Jackie's lab agreed: Full siblings have about one-half their DNA in common, as do parents and their children. But the genome scan must have showed that she and Alex share one-fourth of their DNA instead. That proportion could imply that two samples came from a niece and her uncle, or from a girl and her grandfather. But it could also mean that Jackie and Alex were half-siblings—that they shared one parent but not the other.

Alex, who is eight years older than his sister, refused to believe the news. When Jackie called him to explain what the "uncle" thing was all about, he snapped at her. She'd never seen the "Robot" so angry or distraught. "Mom did not cheat on Dad," he said. "It's a data-entry mistake. You're crazy!" But for Jackie, something had begun to click. She and her brother had never looked that much alike, and their personalities were opposite. Their parents had been separated for 20 years, and Jackie was never close with the man she'd always called her dad. Though he lived just 10 minutes down the road, they rarely talked at all. When she had a baby last year, he didn't even come to visit.

Jackie had sent in her DNA to learn something new about herself but ended up more confused than ever. That night, she went to her mother's house and heard about a one-night stand with a much older man, her biological father, now dead for many years. When she got home that night she went to the bathroom to wash off her makeup. "I didn't recognize myself," she says. "I looked in the mirror and thought, who is this person?"

Last December, 23andMe announced that it would be cutting prices for its genome scans. The 7-year-old company reduced the cost from $299 to $99, in the hopes of building a database of 1 million users by the end of 2013. (They're one-quarter of the way there.) If that happens, how many of those clients will find themselves in the same dismaying situation as Jackie and her brother?

The study of false fatherhood, or nonpaternity, has turned up a wide variety of answers. University of Oklahoma anthropologist Kermyt Anderson says that measured rates of nonpaternity vary quite dramatically depending on the group of people being tested. Among those men who are quite confident of their status as biological fathers—the ones who volunteer their families for genetic studies of inheritance, for example—Anderson found a rate of nonpaternity of roughly 1.7 percent. At minimum, he says, 1 in 60 dads raises children that don't belong to him.

Anderson also went through data from companies that make their money testing for paternity. The men who send off DNA for these commercial tests presumably have cause to be suspicious. These men should have the highest incidence of nonpaternity, Anderson says. When he checked the research on this population, he found a median rate of close to 30 percent.

The true number across the U.S. population likely falls between these two extremes, but while it's often said that 10 percent of fathers are raising someone else's child, this interpolation isn't quite supported by the facts. The best summations of the data figure an overall prevalence of nonpaternity at more like 2 or 3 percent. One analysis from 2008 looked at several dozen studies going back to the 1890s and found an average rate of 3.1 percent, but also hinted that the numbers might be declining over time (possibly in concert with increasing contraceptive use).

Which is all to say that the expanded 23andMe database may include as many as 30,000 customers like Jackie (3 percent of 1 million) who have gone their whole lives without knowing that their father doesn't share their genes. Even now, among the 250,000 people who have already been genotyped by the company, one might expect that 6,000 or 7,000 were unwittingly involved in cases of nonpaternity. Some of these people have sent off their saliva and gotten back a secret that changed their families forever, for better or for worse.

The rise of personal genomics has not created this phenomenon, of course. Nonpaternity results can arise even in the course of routine medical testing. What happens if a doctor sees that a baby's blood type could not have come from its father? (If the baby's is AB and the father's turns up O, the doctor knows that something is amiss.) In the last few decades, the medical establishment has decided that these findings should be concealed, to protect the mother's privacy and avoid unnecessary harm.

Those who seek that information can get it elsewhere. As of 2011, you can buy an over-the-counter, mail-in paternity test in every state. (The kit costs about $30, plus $129 for analysis.) But these customers know exactly what they're getting into. When people sign up for a service such as 23andMe, they may have no idea that a family secret is about to be exposed.

23andMe does take some steps to warn its users of the risks. The top question on the company FAQ is "What unexpected things might I learn?" and the answer mentions that "genetic information can also reveal that someone you thought you were related to is not your biological kin. This happens most frequently in the case of paternity." The terms of service specify that "once you obtain your Genetic Information, the knowledge is irrevocable," and that "you may learn information about yourself that you do not anticipate" and "may provoke strong emotion."

Yet it's also true that the chances of discovering a case of nonpaternity through 23andMe, and the relative significance of that discovery, far outweigh almost every other finding that the service can provide. Much of what the scan can tell you is perfectly trivial. Do you have the genes for blue eyes or red hair? (For a first approximation, try looking in the mirror.) Do you have the genes for tasting bitterness in Brussels sprouts? (Maybe, but who cares?)

After Steven Pinker signed up for 23andMe, he wrote in the *New York Times Magazine*, "For all the narcissistic pleasure that comes from poring over clues to my inner makeup, I soon realized that I was using my knowledge of myself to make sense of the genetic readout, not the other way around."

Other data points from your personal genomic scan will be more suggestive than deterministic. The test might tell you that you're at a somewhat heightened risk for diabetes or arthritis, but it can be hard to know which bullet points are based on solid science, and which are based on single studies with unconvincing correlations. I asked the company's senior research director Joanna Mountain which genome data would have the most real-world significance for customers, and she named four: Major risk factors for Parkinson's disease, Alzheimer's, a form of heart disease called TTR-related cardiac amyloidosis, and breast and ovarian cancer. (The latter are similar to the risk factor discovered by Angelina Jolie. 23andMe reports on three well-studied variants of the BRCA gene, but there are hundreds of others that may be associated with cancer.)

These are serious conditions, and the risks conferred by certain gene variants appear to be severe. With breast cancer, for example, the relevant mutations may increase the risk of getting the disease from about 13 percent to 60 percent. In Parkinson's, the risk goes up from about 1 or 2 percent to 74 percent. The gene for cardiac amyloidosis can increase the risk of heart failure among elderly African-Americans from 15 percent to 38 percent. Having two copies of the Alzheimer's gene might boost your risk of that disease by a factor of 11.

Given the stakes, 23andMe tries to protect its users. To check your status as a carrier for the genes in question, you must confirm that you're prepared to know the truth and understand the consequences. Even so, the actual risk of carrying these genes is very low. Just 0.013 percent of the population carries the relevant mutations predisposing them to breast and ovarian cancer, for example. (Among Ashkenazi Jews, it's 2 or 3 percent.) One or 2 percent of people will turn out to have the major risk factor for Alzheimer's, and the gene for cardiac amyloidosis matters most to African-Americans, among whom the rate is still just a few percent.

So the chances that you're carrying these genes—the risk that you're at a heightened risk for one of these diseases—tops out at 2 or 3 percent, even in the ethnic groups that are most heavily afflicted. That's directly comparable to the risk of nonpaternity, except when it comes to nonpaternity, we're not talking about people who are merely "carriers" of a twisted gene. If your father's not your father, that's the end of the story. It's not a risk factor; it's a fact.

23andMe asks for two layers of consent before it shows family relationships. First, users are given the chance to turn off the "relative finder" function, which shows relations as close as second cousins. Less than 1 percent of the site's customers choose to opt out. The rest are given the chance to click through to see their "close relatives," and about 40 percent proceed. It's the people in this latter group who may uncover a case of nonpaternity.

This quirky system shows the difficulties that arise in managing genomic data. It used to be that people chose to learn about themselves or not, and doctors helped determine which bits of information were appropriate for each of us to know. Now we're heading for a place where secrets flow more freely, where wise consumers must play defense with the facts.

A certain gene might increase the risk for a certain kind of cancer; that's easy to assimilate. But what about the data points that tell us how we fit in with our families? And how does this relate to our changing sense of what it means to have a family at all? "We are living in an awkward interval where our ability to capture the information often exceeds our ability to know what to do with it," said NIH director Francis Collins last summer, in an interview with Gina Kolata of the *New York Times*. Science is getting personal. Medicine is getting personal. Information is getting personal. That means each of us will have to figure out a personal approach to the swelling stream of data. At some point, all of us may have to decide: Do I want to know the truth or not? Am I a Jackie or an Alex?

As time went by, Jackie found some satisfaction in her newfound knowledge. Her lack of closeness with her father wasn't from some failing on his part or on hers, she thought; it wasn't cause for guilt or shame or disappointment. It was only nature. Their relationship had been doomed by mismatched nucleic acids. "I didn't connect with my dad, and now it makes sense," she says. "It's fine. It is what it is."

Jackie doesn't plan to tell her father what she knows. There's no point in hurting him, she says. If they were closer, maybe they would need to have a conversation; but then again, if they were closer, the truth might be more painful still. For now, she's decided not to bring it up, and she won't mention it again to her brother Alex or her mom.

She's been searching for descendants of her biological father, though, and reaching out to his relatives on Facebook and Ancestry.com. A distant cousin passed along a family history that her grandfather, Emmet, typed out in 1964, after five years spent sifting through state archives and church registers. The painstaking document traces Jackie's ancestors back to Norway across 17 generations—an early analog to her own project of self-discovery done through spit analysis and social media. "His attitudes sound just like mine," she says, referring to Emmet's urge to look into his background. "I can tell you that before this whole experience, I would have told you that I believed more in nurture than nature, but since then I've seen how strong nature is."

Some people seem to have this inborn curiosity, a need to dig into their pasts. (A future version of 23andMe might tell you if you're the type of person who would be interested in 23andMe!) Now those people have a better tool for excavation—and when 1 million customers start to pick away, they're sure to tap a heavy vein of secrets.

If this is good or bad it's hard to say. Near the bottom of his history, Emmet jotted down some thoughts that Jackie says she shares exactly: "Many people when discussing genealogy comment that we should let the sleeping dead lie," he wrote almost 40 years ago, "and the other cliché heard so frequently is the warning to be careful lest you turn up a horse thief. The trouble with the first saying is that the sleeping dead just don't lie; something of them is with each of us, dormant or dominant."