

We can read your DNA ... but how well can we understand it?

What would you do if a genetic analysis showed you carried a mutation that increased your risk for breast cancer? [Angelina Jolie's choice to undergo a dramatic double mastectomy](#) in the face of this information fueled headlines.

As Carolyn Johnson notes in a recent piece for the Boston Globe, “the public tends to see DNA as holding almost-mystical power.” Jolie’s story is just the highest-profile example of the way DNA testing is permeating our society.

Johnson brings up another example:

On paper, Dr. Robert C. Green should be worried. An analysis of his DNA flagged a rare mutation in a gene linked to a condition that causes facial deformities at birth. But Green only has to look in the mirror to know that he does not have the disorder, [Treacher Collins syndrome](#).

“Most likely this is not a meaningful mutation,” the Brigham and Women’s Hospital geneticist said, pulling up alarming photos on his computer screen of people with the condition. “I know this, but imagine if you’re a pregnant woman and someone reported that mutation out to you about your baby. Can you imagine?”

And here’s the crux of her piece, and something that will be ever more important to remember as cheap sequencing and the rising tide of genetic awareness brings more and more people face-to-face with the messy truth of their genomes:

Green’s experience shines a light on an important truth about DNA: The facts about your genes are not necessarily facts about you.

The fact is, even geneticists are not able to make one-to-one connections between isolated mutations and a person’s medical fate. There is a huge amount of interpretation involved; every scientist and doctor might be reading the same letters but they are not getting the same message. Johnson explains:

In 2012, [Boston Children’s Hospital sponsored the CLARITY challenge](#), a competition to identify the genes causing mysterious diseases in three separate children by crunching raw DNA from their families. The teams did not all come up with the same results.

“If you give a genome to 27 different labs, you will often get different answers,” [Heidi Rehm, chief laboratory director of the Partners HealthCare Laboratory for Molecular Medicine] said. Her group won the CLARITY competition.

One slide Rehm uses when she is giving talks shows how widely these interpretations vary. Three genomics laboratories cataloged all the genetic variants they knew that were linked to developmental disorders called RASopathies.

Theoretically, these results should largely overlap. But the labs didn’t agree on what 53 of those genetic variants meant. And a portion of those interpretations were wildly divergent. For example, one lab asserted there wasn’t enough information to know what a genetic variant meant, while another said it was definitely pathogenic.

Of course, beyond the fact that labs are struggling to interpret the information from DNA analysis, there’s the fact that your health itself is also an interpretation. Any effect your genes might have is going to be modified by its environment, which in this case includes everything from other genes, to your diet, your habits, to your literal, physical surroundings. Very, very few diseases are the direct and immediate result of mutation, and very rarely can we look at a genome and say: “There, THIS mutation is the problem!”

I’ll let Johnson’s conclusion stand on its own:

The genome carries powerful information about disease risk and can be an important tool in unraveling disease, and techniques and databases are already being improved. But the pace may not be as fast as the embrace of DNA as a medical tool. Scientists see a day of reckoning ahead.

“There’s going to be a massive awareness of what we don’t know and the discrepancies about what people are saying about things,” Rehm said. Then, she said, the problems will be fixed.

Read Carolyn Johnson’s full article at the Boston Globe: “Scientists hoping to ease interpretation of the DNA ‘book of life’”

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Additional Resources:

- [“Angelina Jolie fallout: Should counseling be required with DNA screenings?”](#) Jon Entine | Genetic Literacy Project
- [“Angelina Jolie’s Preventive Mastectomy Increased Breast Cancer Awareness But Didn’t Educate Public About Determining Risk,”](#) Matthew Mientka | Medical Daily
- [“From Volunteers, a DNA Database,”](#) Albert Sun | New York Times