# Me, My Genes and Us

## - Personal Experiences With Gene Tests, and Some Sociological Observations

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**Abstract**
I'm here to talk about my own personal experiences with genetic tests. As a journalist, I got the opportunity to take a personal genetic test from the decodeme website in order to write about this new service for Danish newspapers. So, although I am a theoretical biologist by training, my task will be to take the perspective of the consumer and to convey some of the thoughts and feelings people may have when deciding to take one of these personal genetic tests offered by different companies. Some of the questions I want to try to answer are: What do these tests tell us right now? What do they do to us? And what kind of social expectations might be created around this brave new world of genomics?

The main learning points I want to put forward are threefold: First, the genetic tests on the internet are currently not very useful, neither for the consumer, nor for the health care system. Second, the perceived usefulness of genetic tests will also in the future continue to be low for the consumer, mainly because of the counterintuitive concepts of probability on personal health. And third: The coming social and governmental changes will be much bigger than the changes in health care and prevention. One of the consequences, for instance, will be an alliance between researchers and patients/consumers, whom will build up strong pressures on the health care system, which itself will lag behind the scientific developments.

### Ordering and understanding a genetic test

A small scraping from my mouth was enough. I sent the sample to Iceland, and after two weeks, I could log into a website and read about my DNA, my ancestry, my appearance and my genetic mutations. I could also download a 30MB file with more than one million number plate-like codes, called SNP's, listing my most common DNA variations. They show what makes me genetically unique, and tell, where I have inherited what from my parents, and how my DNA is different from other people's DNA.

It was like being scared and reassured at the same time. But most of all, it was a fascinating experience. The ability to check my genes online and keep up with the latest research, linking disease with SNP's, is almost addictive. When I drank milk, smoked or had a pain in the knee - immediately I checked what my SNP's says: And yes, I have the mutation that makes me break

down lactose and I can therefore digest milk. And no, I have no particular tendency to become nicotine dependent, and I even have a reduced risk of lung cancer (This is good, a little devil inside me thinks, because then I can continue to smoke). And yes, the arthritis my grandmother had might also become part of my future.

It turns out that my risk of getting cancer, asthma or sclerosis is lower than in general, but I will have to prepare myself to the possibility of getting old mans diabetes (rs7903146 - TT), Alzheimer's disease (rs4420638 - AG) or become blind (rs1329428 - GG), but most probably I will die from a heart attack (rs10116277 - TT). I can also see that my SNP rs7495174 has the initials AA, and that the SNP rs12913832 has GG. The vast majority of people with this combination have, like me, blue eyes. I can also compare my DNA to other peoples DNA. I compare with Bantu people, with Bedouins and Mayans. But I have clearly most in common with the French and Scots.

**Where the difficulties start**

But then the problems started. When looking at my gene profile, what struck me most about the results was that they were so boring. All numbers fluctuate around a relative genetic risk of 1.0 – which is defined as the average of the population in question. So the first lesson was the following: **SNP's don't seem to say much**. Whether I had a probability of 0.92 or 1.14 – the usefulness of such numbers seemed close to nil.

It is as if there is a paradox here: Everybody says that physical and psychological traits are to a high degree heritable - but my individual genes are not very informative. What does it mean that my relative risk of getting lung cancer is 0.82? And getting arthritis 1.43? Either I'll get it, or I won't. The probability of a single event is a meaningless concept for me. The problem is the following: It might very well be that genes can cause diseases, but SNP's just associate you with them. **Lesson: Association is not causation.**

The next question was: Which numbers should I ignore? Which ones should I worry about? And which ones could I be sure would manifest themselves at one point? Again: not easy. Although the absolute risk might seem more relevant, it also is not very useful. What does it mean that my risk of getting Alzheimer is increased from six percent to 10.5 percent? That I just can ignore it? That I should get checked? That I'll have to shoot myself in the head when I get 60? **Lesson: There is a real danger of getting hung up on numbers, even though they mean nothing.**

My family history is definitely more useful. I know that my grandmother had arthritis and my other grandmother got type 2 diabetes. For these two diseases there are elevated risks for me too, and suddenly these numbers make more sense. Although the absolute lifetime risk of arthritis is only 1.4 percent, I feel – because of my family history – that my risk of getting arthritis is much higher than, say, Alzheimer, of which there is a much higher absolute risk but no family history! **Lesson: The value of a genetic scan means less than knowing the disease history of your family.**

**Wrong or only premature?**

The gene profile from the decodeme website clearly states that not all risk factors are included. This is important, because science is far from having found all the genetic associations for any of the investigated diseases. Take a look at the following table:

| Trait | Relative genetic risk (May 2008) | Relative genetic risk (December 2008) |
|---|---|---|
| Age-related Macular Degeneration | 1.35 | 0.53 |
| Celiac Disease | 0.34 | 0.32 |
| Colorectal Cancer | 0.98 | 0.87 |
| Crohn's Disease | 0.92 | 0.88 |
| Obesity | 1.05 | 0.77 |
| Prostate Cancer | 0.85 | 0.64 |
| Psoriasis | 0.69 | 0.79 |
| Restless Legs | 1.38 | 1.26 |
| Type 2 Diabetes | 1.20 | 1.25 |

The table shows the time-dependency of the risks which have changed because of new evidence of associations. They are clearly changing the risk estimates in unpredictable ways. And probably this will continue for some years to come. What does it mean? Clearly consumers of the tests won't say, that they get healthier when their relative risk numbers decrease, but they will be fair to say, that the numbers are premature, if not utterly wrong.

According to statistician John Ioannidis from Tufts University, the first association studies usually show great effects. But soon after, when other researchers verify the results and new SNP's get included into the calculation, the strength of the associations is diminished. Often to such a degree that the effect becomes minimal and can be neglected. Even worse, Ioannidis believes that the vast majority of results are plainly wrong. Rather than measuring an effect, the tests measure a bias, e.g. a distortion of data due to lack of information from what is not yet included. One has to remember that only 1 million SNP's are investigated, which means that we know nothing about 2,999 million SNP's waiting to be analyzed. **Lesson: Incomplete genetic data can lead to wrong conclusions about your health status.**

Also, the more SNP's you will find in the long run, there is a chance that the numbers will get closer and closer to the average relative risk of 1.0. Thus, the only way to verify the claims of the utility of the genome scans are to make large randomized studies, where participants not only get scanned all of their DNA, but also are followed through their life, so that you can correlate the genetic data with their behaviour, eating habits and lifestyle. The data would also have to be correlated with environmental and social factors. Only then it will be possible to achieve a safe separation between genetic and non-genetic factors underlying the development of diseases. (As James Watson said at a recent conference, where researchers investigated his genome: "We'll see if any of it adds five minutes to my life span,") **Lesson: Genetic data, isolated from lifestyle and environmental data, is not very informative.**

**What will other people do with this information?**

Will other people be more sensible than I in interpreting their genes? Let's hope so. At one point last summer I lured my half-brother to take the same test at decodeme. When I asked him what he had learned from the results, he said "nothing". He felt cheated. When I told him about this conference he said "tell Kari that I want my money back".

Why so? Let's take an example: His results said that he to 77 % might be bald – even though we both have the same mother. But he is NOT bald. His conclusion was that the test must be wrong! He wasn't quite able to accept the difference between a statement about probability, and a prediction about himself: When reading that he is lactose intolerant, he said "but I drink milk and I digest it. So the test must be wrong!" And when reading that he has a less probability of restless legs than I have, he said "but I have more restless legs than you. The test must be wrong!" This is an important reason why personal genomics might have some problems of finding a broad audience. Causation is easy to understand and to make useful. Association is not.

Even I have started stupidly to speculate about, what's in it for me. I like to brag about my Churchill gene when smoking a big cigar in a bar here in Denmark (It is still allowed to smoke in some public places in DK), because my genes (wrongly) suggest to me that I'll not get lung cancer. But there are many other ways in which people can use this type of information for their own benefit. They can use it to improve doping results, to make decisions about their offspring (positive and negative eugenics) or deny moral responsibility ("blame no me, but my genes"). **Lesson: People will make an equal amount of wrong and right conclusion with regard to their genetic profile.**

**Social concerns**

Most public concerns have dealt with the question of unpleasant knowledge: What if I learned I was likely to die young? Or what if I have passed on a rogue gene to my daughter? Many have also questioned the potential abuse from governments, insurance companies and employers, who could use such information against them in the future. But probably the opposite situation will be even more common: People will go to their employer or their university and say: Hey, look at my Sioux gene; I am three percent Native American, so please give me my scholarship, and my casino money! Or they'll say, hey, I am seven percent Jew, please let me get Israeli citizenship (for what ever reason that is). In general, they will try to take advantage for their own benefit.

Also, with genetic test results in hand, parents may feel tempted to wave it in the child's face and say, "Your destiny is here. You have the Usain Bolt gene! Two copies of the ACTN3 gene! You have to go to sports training, not to these stupid drama lessons!" And too many children might have to fight the burden of hopeful parents, and run away, or commit suicide. In conclusion: As long as genetic tests are as tentative as they are right now, they become modern horoscopes. And horoscopes tend to be abused. **Lesson: The number of social abuses could very well be equal the number of social benefits.**

Other important social concerns on the emergence of genetic testing are the following:

- *Self-knowledge implies knowledge about kin*.

An example: I am a carrier of the hemochromatosis allele (having the combination A;G in the SNP rs1800562) which is found in 5-10 percent of Caucasian populations. (A;A) homozygotes have a 85 percent risk of developing hemochromatosis, a disorder whose symptoms include cirrhosis of the liver, diabetes, hypermelanotic pigmentation of the skin, and heart failure. Me having one A means that there is no small risk that one of my family members are homozygote, and since this disease is easy to treat but difficult to diagnose (and since some of them seem to have skin problems), I have told them that they should get a blood test for hemochromatosis. But this is not always a prudent thing to do. They might not want to know. They might not want me to know. They might just be

plainly annoyed by me bothering them or knowing something about them. **Lesson: Knowing your own genes creates a non-trivial responsibility towards your family members.**

- *Segmentation, social tagging and discrimination vs. health, pension, and insurance governance*
From a governmental point of view, population genetic profiling will be very useful. Health, insurance, and pension authorities will be able to make targeted preventive regulations against detrimental traits and, conversely, create proper incentives in order to harvest beneficial traits. But this only applies for benevolent democracies. Recently though, we have learned how fragile democracies and their institutions can be. In most cases politicians on this planet give a higher priority to the protection of the nation-state rather than to individual and human rights. It is therefore not clear, whether protective laws (like the Genetic Information Non-discrimination Act, GINA, in the U.S.) in all situations will hinder abuses of segmentation, genetic tagging and discrimination. **Lesson: Exposed genomes need stronger legal rights, extending beyond national borders.**

- *Multiculturalism vs. social norms*
The manipulation and selection of genetic profiles will magnify social inequality. Even strong regulations won't hinder this in the long run. It will lead to an even more segmented civil society. The dangers are obvious: We will have to accept that some social norms apply only to some of us. Others have the right to marry their cat, to have children with their mutants, have special rights and treat each other in a way we sometimes think is inhumane. It could undermine civil cohesion and create new types of human groups who no longer want to share the community's future. Equal rights could risk being replaced by cultural clans with odd customs, inequality before the law and unequal opportunities. **Lesson: The possible disruption of civil coherence needs to be checked with plenty of education and information.**

But you could also imagine a more positive scenario: a scenario where we learn to understand the difference between diversity and inequality, the difference between identity and the norm. A clarification of the limits of personal rights and social demands could also have the advantage that we start to think about an extension of the Universal Declaration of Human Rights, so that it becomes really universal and includes all possible variants of our species and their relatives. L**esson: Whether the ongoing DNA revolution will result in greater tolerance, or whether it will result in greater bigotry and intolerance, is still an open question.**

**Conclusion**
Let's try to review the lessons pushed forward in this talk:

- SNP's don't seem to say much.
- Association is not causation.
- There is a real danger of getting hung up on numbers, even though they mean nothing.
- The value of a genetic scan means less than knowing the disease history of your family.
- Incomplete genetic data can lead to wrong conclusions about your health status.
- Genetic data, isolated from lifestyle and environmental data, is not very informative.
- People will make an equal amount of wrong and right conclusion with regard to their genetic profile.
- The number of social abuses could very well be equal the number of social benefits.
- Knowing your own genes creates a non-trivial responsibility towards your family members.
- Exposed genomes probably need stronger legal rights, extending beyond national borders.

- The possible disruption of civil coherence needs to be checked with plenty of education and information.
- Whether the ongoing genome revolution will result in greater tolerance, or whether it will result in greater bigotry and intolerance, is still an open question.

It is clear, that many of the negative ramifications of genetic testing stem from a lack of knowledge and unclear consequences. Therefore, the way ahead should have a primary focus on education, rather than on regulation. People who have grown up with the democratization of information will not tolerate paternalistic regulations that keep them from their own genomes, and early adopters will explore how this new information can best be used to manage our health. A good example in this direction is the PGP-consortium (www.personalgenomes.org/) which is a group of volunteers from the general public working together with researchers to advance personal genomics.

A cry for regulation might be as premature as the tests themselves. In addition, the health care system, as mentioned before, is experiencing a power grab from the general public. In many medical areas there is a new alliance between researchers and patients. This emerging alliance tries to push forward the quality of the health care system, which itself very often is unaware of new insights, and which is lagging behind the implementation of new treatments. This will be even more pronounced in the case of personal genomics. Most doctors only have had a single course in genetics, and the increasing speed of new insights and new technologies put a huge demand on the training of health care personnel.

In such a situation, every hand is needed. Instead of holding back and trying to keep the academic authority, medical professionals will have to become coaches of people, who themselves will be the experts of their disease. This requires a maximum of educational effort and a minimal but sufficient amount of governmental regulation, which in turn will have to extend beyond national borders and apply globally.