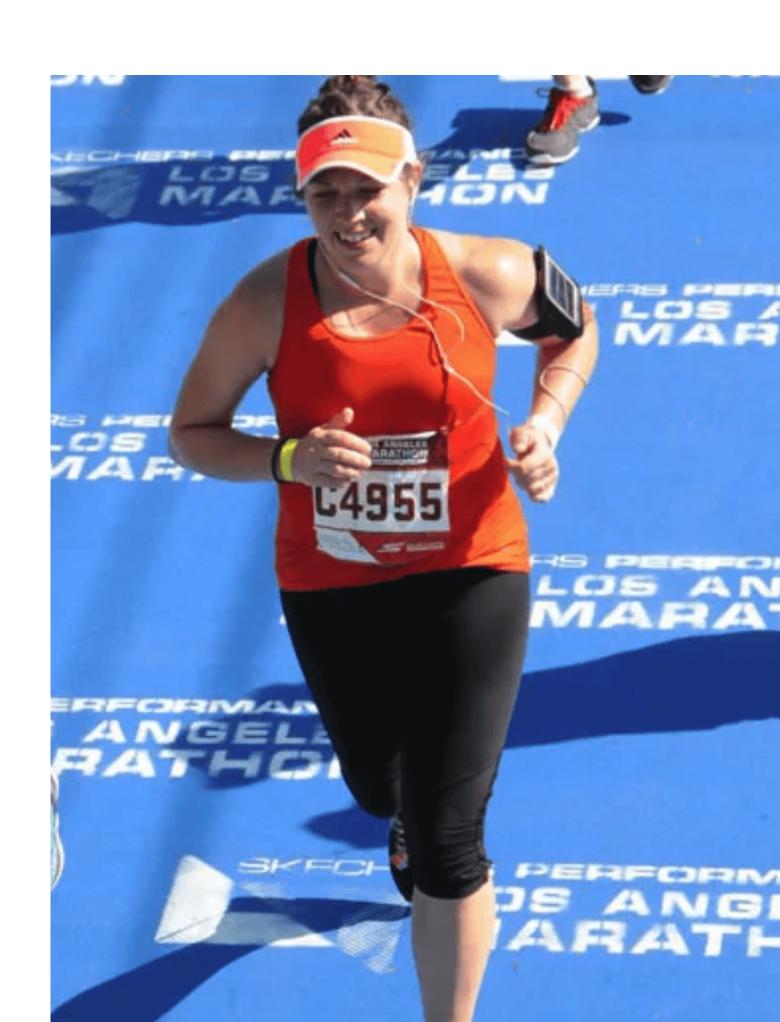
Genetic medical astrology? Nutrigenomic DNA tests: Can you prime your health by tailoring diet and exercise to your biology?

ne promise of genetic testing is that it can tell you more about the way you're built so that you can tailor your lifestyle to fit your biology," wrote Anne Machalinksi, an ex-marathon runner and mom of three kids, in an article in Self magazine a few years ago

Anne is a true believer. Since becoming a mother she had gotten out of shape, going from running a 5-minute mile to chugging her way around the track. Her exercise routine and diet plan were not working. She tried lifting weights to increasing vegetable intake to cutting down on alcohol, and experimented with various crash diet plans, all to no avail.

In frustration, Anne tried something that is becoming increasingly popular among the scientifically inclined amongst us; she got a DNA test, with a UK-based online company <u>FitnessGenes</u>, to come up with a tailored fitness and health plan.



Machilinksi running the 2016 LA Marathon.

FitnessGenes mapped 42 of her genes and their variants, known as alleles. According to the company, the tests revealed that her personal choice for weight loss—training for a marathon—was a bad one.

Because I have two copies of what some call a "sprint" allele on my ACTN3 gene, I can produce a protein found in fast-twitch muscle fibers. I also have two copies of an allele associated with power and strength on my ACE gene. Combined together, ... these findings mean that I'm naturally fast and strong, with muscles that recover quickly after a workout. If I want to decrease my body fat, [I was instructed], I should drastically cut down on long, slow endurance runs, which likely blunt my body's ability to use fat as an energy source. Instead, I should focus on getting in about five high-intensity, low volume strength and interval workouts per week.

Anne was an early adaptor of what its proponents believe is a life-changing technology.

"Developing personalized diet and exercise plans could well be one of the most important fitness revolutions of the 21st century," said Dan Reardon, CEO and co-founder of FitnessGenes.

Is that science speaking or the dubious plug of a still-unproven technology?

What's the science behind the promise?

Personal DNA plans are the promised land to treat many illnesses. Two decades after the Human Genome Project was completed, the market for over-the-counter DNA based products is booming. One of the hot categories has become known as "nutrigenomics" — the promise of better understanding how food and exercise can modify our predispositions to disease and immune functions.

Nutrigenomics, as its proponents call it, is a booming industry. Testing companies brought in more than \$170 million in revenue in 2018, according to Global Market Insights, driven in large part by direct-to-consumer genetic-testing companies including 23andMe and Ancestry.

There are now dozens of niche companies making nutrition-based claims, from modes to hyperbolic. DNAWeekly, a blog put together a list of what it claims are 10 of the best known companies pushing genebased weight loss strategies. A company called My Toolbox Genomics promises the moon:

Nutritional test screens over 50 different genes to tell you everything you need to know about your diet. Our report showed which foods our test taker should be adding to or removing from their diet, not only to lose weight but also to increase overall health.

Customers are clicking away in massive of numbers. <u>April Summerford</u>, a women's fitness coach, spent hundreds of dollars on at-home DNA tests to curate the perfect diet plan for herself, and is a true believer.

"I've been able to biohack my way to feeling better through what, I think, is the future of wellness," <u>said</u> April, who believes that a broad plan for good health is not effective anymore and a curated personalized

map is the solution.

And yet the accuracy of the promised claims and gains remains a grey area.

Nature v Nurture

As any geneticist would tell you, we are a product of nature and nurture. Genetics alone do not determine our traits as the environment around us plays a vital role in regulating our genetic expression. For example, genetic traits such as height or intelligence might be inherited but environmental factors such as malnourishment during pregnancy or after and harsh living conditions impact outcome. Understanding these external impacts on our genetic expression can provide us with tools to control the negative impact and boost the positive.

Looking at the specific relationship between nutrition and genetics, the genetic variability within us can be translated into the differences we may have in nutritional processes such as metabolism, absorption and excretion. And these differences then contribute to our nutritional requirements.

For example, a person who suffers from <u>celiac disease</u>—a hereditary disorder —cannot consume gluten (a common protein found in wheat, rye and barley) without triggering a serious auto-immune response. This is because, for them, gluten causes the body to attack the small intestines which then interferes with proper nutrient absorption in the body.

For a person living with celiac disease, awareness of nutrition and how specific food choices can impact their health is crucial in minimizing long term health problems. With one in 100 people worldwide living with celiac disease, understanding such intricacies between what we eat has become even more important.

In this broad context, <u>personalized medicine</u> (which is not the same as an at-home DNA nutritional test) can be extremely helpful.

"It embraces this idea that despite all of us being 99.9% the same, there is that 0.1% that truly determines how you respond to the world around you," <u>notes</u> Dr. Yael Joffe, founder and chief science officer of 3X4 Genetics.

As he correctly notes, it's the 0.1% variation between us that allows us to react differently to similar situations from a drug reaction to efficacy of medicine. The goal of personalized medicine, therefore, is to customize medical decisions for an individual person tailored to their needs to create better health outcomes.

The challenge is: How do you translate this factoid into a personalized nutritional plan? That's a lot trickier.

Disease susceptibility linked to multiple genes and complex environmental factors

Companies such as <u>Habit</u>, <u>DNAfit</u> and <u>Nutrigenomix</u> all offer DNA-based nutritional recommendations using genetic testing to identify genes for weight loss, eating habits and more. They collect your DNA from a cheek swab or a saliva sample. They then generate a

<u>report</u> that details which specific gene variations in that person are "associated" with celiac disease, sensitivity to fats, lactose intolerance and more. Next come recommendations on diet and lifestyle changes to improve health, supposedly gleaned from the DNA analysis.



Credit: Habit

"Associated" is the key word here, as critics of these tests point out. Genes are almost never cause-and-effect linked to an outcome, in the way, say, one gene is 100% predictive of getting Parkinson's disease or specific genes are linked to breast or ovarian cancer. There are an estimated 7,300 so-called Mendelian single-gene linked disorders, which are rare and usually inherited.

So, a nutritional genomic test can be reliable if done to test monogenic diseases such as <u>galactosemia</u> that affects how the body processes a simple sugar called 'galactose'. This sugar is commonly found in many foods and if the disease is left undiagnosed, a person can suffer from feeding difficulties, lack of energy, loss of weight and more serious complications. In cases such as this, a genetic test can be really valuable in diagnosing a disorder, offering predictive and accurate results.

There are many pitfalls t trying to analyze complex health factors and nutrition impacts using genetics. Many companies focus on macronutrients such as metabolism of lipids and carbohydrates. For that they use FTO (fat mass and obesity associated) genetic variants. The FTO gene variant is universally considered as one of the variants that has an association with our BMI.

However, outside of this one gene, nearly <u>900 other gene variants</u> also exist that have a phenotypic association with BMI. One identified variant (or even a few) cannot explain a person's genetic predisposition to weight loss.

But many DNA test companies try to circumvent the hard science by claiming to offer DNA-linked insights not just for monogenic but also for complex diseases such as obesity, which is likely caused but multiple

genes and complex lifestyle factors.

For example, Personal Diagnostics, a UK based company supplies at-home DNA kits including an 'obesity risk DNA test.' In this test, the company analyzes 4 'fat genes' to assess susceptibility to weight gain, influences on BMI and blood lipids. The test claims it encourages better management of diet through curated health insights which in turn will prevent diseases such as diabetes, blood pressure and cardiovascular diseases linked with obesity. But the evidence for such grandiose claims is not clear.

"There is convincing evidence that common diet-related diseases are influenced by genetic factors, but knowledge in this area is fragmentary and few relationships have been tested for causality," wrote Ulf Görman in 2013, examining the ethics behind nutritional based genetic testing. "The evidence that genotype-based dietary advice will motivate appropriate behavior changes is also limited."

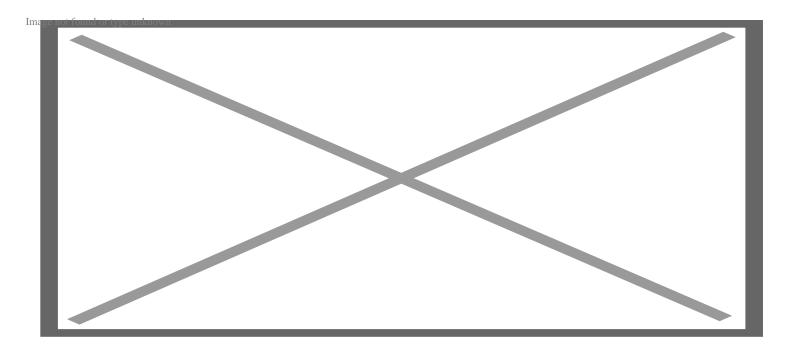
Genetic astrology: Upstart claims downplay their claims in small print

With the science behind the nutritional DNA testing still new and somewhat shaky, too much information and scientific jargon can confuse customers. While building up consumer expectations of discovering a DNA solution to their health concerns, companies often release complex or hazy information, leaving customers to try and figure out what is science and what is snake oil.

Concerns about the proliferation of junk science and over promising caught the eye of the FDA 10 years ago in a challenge to 23andMe, now the largest global <u>direct-to-consumer</u> (DTC) DNA testing company. The FDA was concerned that a test could give a false-positive or a false-negative based on a disease-linked association, prompting a patient to self-diagnose or treat herself, which in turn could create a bigger health risk.

"A direct-to-consumer test result may be used by a patient to self-manage, serious concerns are raised if test results are not adequately understood by patients or if incorrect test results are reported, the FDA highlighted when it temporarily banned 23andMe sales in 2012 in the US.

Since then, DTC companies have been able to protect themselves from liability for claims but adding disclaimers, such as the one displayed by DNAfit for its \$471 Circle Premium test.



In other words, buyer beware; this DNA-based advice could very well be of no value and may even provide misinformation.

Most mainstream scientists are dubious about nutrigenomics

Most scientists are not yet convinced the technology is ready for prime time.

"For complex traits such as diabetes, coronary artery disease or obesity where there are multiple genetic and environmental factors at play, genetic testing is less useful," <u>said</u> Heidi Rehm, chief genomics officer at the Center for Genomic Medicine at Massachusetts General Hospital.

Understanding complex disorders is just not that simple. Even with a scientific background, looking at the data released by DTC DNA companies can still be vague at best. According to David Mutch, nutritional biochemist at the University of Guelph in Canada:

Scientists working in the field, such as myself, would struggle [to evaluate the evidence behind personalized nutrition companies' products] because it's really a bit of a black box, and even for those companies that disclose what exactly they test for, you're still not entirely sure what science was used to get those particular variants onto their panel of variants that they're testing for.

Many scientists liken nutrition-based DTC genomics to little more than 'genetic astrology'. Fine print warnings that the data provided is not particularly reliable nor reassuring.

"I think it's unusual for us to think of scientific work that doesn't have legal and scientific standing, with the idea that we need to 'take this science with a grain of salt," says Jonathan Marks, a professor of anthropology at the University of North Carolina, Charlotte. "This probably the the wrong direction for the

scientific community to be leading the public in, if we're apprehensive about people <u>not taking science</u> <u>seriously enough</u>."

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23 geneticists from around the world wrote a <u>consensus statement</u> in 2016 in the *British Journal of Sports Medicine*, concluding that DTC DNA tests could not provide science-based guidance. Its key conclusion: Although this field has grown tremendously in recent years, the science is still in its earliest stages, and at the moment, tests relying on it hold no value.

One of the world's experts in this field, Claude Bouchard, director of the human genomics laboratory at Pennington Biomedical Research Center in Baton Rouge, has been unequivocal in his assessment of the claims emanating from this nascent field. After 40 years of research in this area, he is optimistic about the future but not so sanguine on the present.

"We've made a lot of progress in the last few decades," <u>Bouchard has said.</u> But as of today? "When it comes to these current genetic tests for fitness and performance, they have almost zero predictive power."

For an emerging science, nutrigenomics holds promise, and with time could yield insights that could be applied in our daily lives. But for now, much like crash diets and other fads, it is a closer to being a money-making, marketing gimmick—a fool's gold that a simple DNA test can tell you what to eat and how to lose weight, and like magic it will work. That's just not the case.

Mariam Sajid has a Master's degree from University of Nottingham, UK in molecular genetics and diagnostics and is passionate about improving medical communications that effectively translate scientific advancements to the public. Currently based in Pakistan, she works with digital healthcare companies in developing disease elimination programs for infectious diseases such as HIV and Hepatitis in lower-middle income countries. Follow her on twitter @mariamsajid00

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