DAVID KRANTZ

Nutrigenomics and Nutrigenetics

Using your DNA for better nutrition and health

You are reading this because you are interested to learn about how the science of nutrigenetics, nutrigenomics, and epigenetics can help *you* lose weight, sharpen your mind, boost your energy, and ensure the health of your children. First, I want to ask you a question.

How did humans figure out what to eat before we had diet books, food pyramids, and health experts?

Was it only by taste or ease of procurement? Or did traditional cultures observe the effects of how eating combinations of different food led to health vibrancy for both parents and offspring?

Now, let me ask you a second question. Why do you eat the way you do now?

Do you eat what you do because of taste, convenience, or cost? Do you eat what you grew up eating? Or, do you eat because you know that what you put in your body is providing the perfect building blocks for success?

OK, I get it, those are both pretty leading questions. But, if you're like I was a few years ago, you probably eat the things that simply taste good to you, that maybe you grew up eating, or that are quick and easy to prepare. Perhaps you pay attention to eating "healthy" things, but then that brings up the question "how do you know what is healthy for *you?*" For the first time in human history, we have instant access to nearly every food grown or made across the world at any time of year. And, for the first time in human history, commercial interests are vying for your food budget with little to no concern for long-term health effects. So, if you want to eat healthier, how do you know what to eat?

You could follow one of the *hundreds* of fad diet books written each year. But, when you get right down to it, none of those plans can possibly take into account your unique body, metabolism, and biochemistry. Those diets might work for some people

some of the time, but because of our unique differences, they just don't work for all people all the time. Traditional cultures eating traditional foods often had systems, such as Ayurveda or the Chinese 5 Element System, to determine what the appropriate nutrition was for the *individual.* The idea of a "food pyramid" or standard plan that should apply to everyone, is something relatively new. And, with the obesity epidemic getting worse every day, that approach clearly has failed. Is there a better way?

A resounding "Yes!" comes from the sciences of nutrigenomics, nutrigenetics, and epigenetics.

So, what are these things and how can they help you?

Nutrigenetics is the study of how to eat for your genes. There are tiny variations in each of our genetic codes that affects our individual metabolic response to nutrients. This knowledge can then be applied to develop personalized nutrition for people based on their individual genetic makeup. For instance, if you had a genetic variation that made it difficult to transport saturated fat in the body, we would alter the diet to include less saturated fat. Or, for someone who may have a genetic predisposition to have lower conversion from the inactive form of vitamin A (beta-carotene) to the active form of vitamin A (retinol), we would add foods high in retinol into the diet or supplement extra retinol to help offset the genetic predisposition. There are hundreds of variations that can give us clues to how to support your underlying biology.

Nutrigenomics is the study of how food and nutrients effect gene expression. Epigenetics is the study of how genes change their expression, or how the products of those genes are modified or regulated, in response to stimuli such as food. Genes can be "turned up" or "turned down" through a variety of different mechanisms and this can happen either before birth or during the course of life. Our genes are actually highly responsive to the environment, and are constantly assessing the signals our minds and bodies are receiving and creating. Nutrigenomics allows us to very precisely modify some of the most very basic layers of the human system in order to positively change the

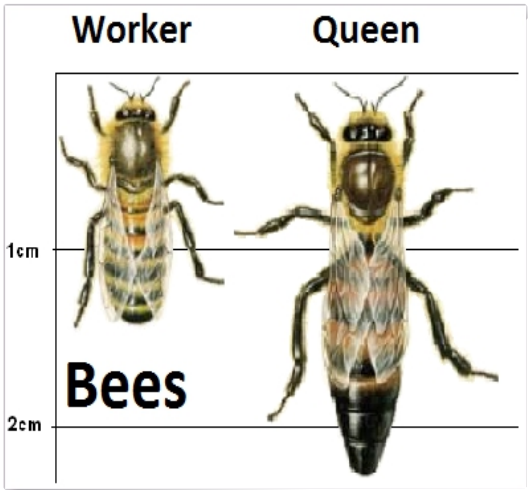
outcome of your genetic expression. For example, if you have a genetic variation or SNP (single nucleotide polymorphism) that predisposes you to have low adiponectin, an important hormone for hunger and satiety, we could add more monounsaturated fat into the diet as that has been shown to actually up-regulate or boost the expression of the gene that codes for adiponectin. Nutrigenomics is one of most exciting areas of research in science today.

Here are some examples of nutrigenomics and epigenetics in action:

The Queen Bee's Royal Diet

All bees that live in a hive together are technically genetically identical. Their base DNA code is exactly the same except for a small amount of random mutations. So, what causes the distinction between the queen bee and the rest of the workers? The queen is much larger and is the only bee in the colony that can reproduce.

The answer is epigenetics and nutrigenomics. The queen bee is the only one in the hive that gets to eat royal jelly, which has a very different set of nutrients than the honey that the other bees eat, including phenyl-butyrate, a chemical known as an HDAC inhibitor. This causes a drastic change in the epigenetic markers that turn up and down different genes. Methylation and acetylation are types of epigenetic marks that "turn up" or "turn down" the expression of a gene like a dimmer switch. In worker bees, the ovary genes are highly methylated and turned off. In the queen bee, the royal jelly causes the ovary genes to *de-methylate* and allows her to reproduce, grow larger, and adopt a very different set of behavioral traits. The gene known as DNMT3 has been isolated as the main gene involved in the process.



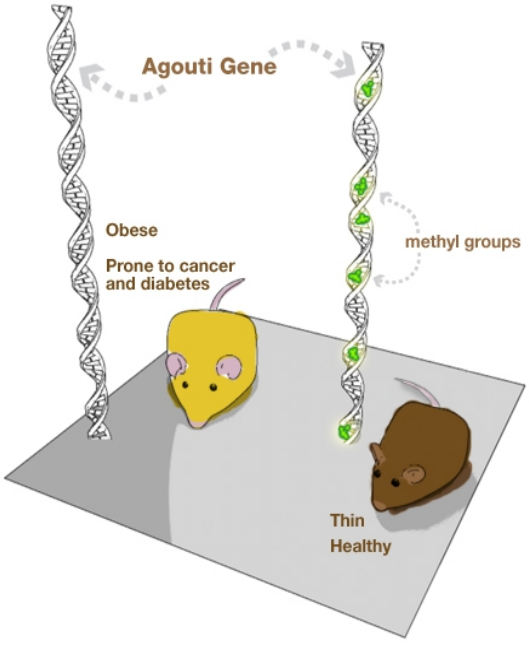
New research also suggests that what queen bees *don't eat* also plays a major role in ovary development. A compound known as p-coumaric acid is found abundantly in the fermented pollen that worker bees eat, but not in royal jelly. Researchers were able to determine that bees raised on a p-coumaric laden diet had smaller ovaries, and that royal jelly has a protective effect against the effects of p-coumaric acid. So, it seems that the combination of receiving the correct foods, and avoiding the incorrect foods, is what makes a queen bee.

Both of these bees are genetically identical. They also were both were *born* with the exact same epigenetic marks and methylation pattern. Their diet is what creates the change in the epigenome that results in the differences you see here. This is nutrigenomics is action. Would you rather be a queen bee or worker bee?

The Agouti Gene in Mice

Epigenetic patterns are also passed down from parent to offspring. It's our genes' way of making sure that we are prepared to respond to the environment that our parents' genes sensed during conception and pregnancy.

Laboratory experiments in mice show how impactful a mother's diet is in shaping the epigenome of her offspring. All mammals have a gene called agouti. When a mouse's agouti gene is completely unmethylated (and allowed to express itself highly), its coat is yellow and it is obese and prone to diabetes and cancer. When the agouti gene is methylated (as it is in normal mice), the coat color is brown and the mouse has a low disease risk. Fat yellow mice and skinny brown mice are genetically identical. However, the fat yellow mice are different because they have a gene that is epigenetically "stuck to the on position."

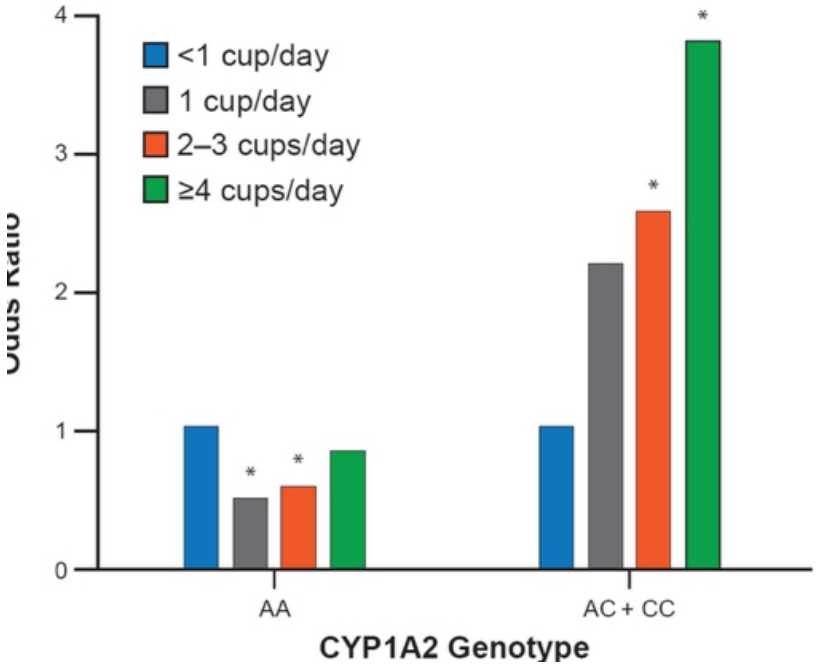


When scientists fed fat yellow mother mice a diet rich in extra methyl groups (the raw material needed to methylate and turn off genes) their offspring turned out thin, healthy, and brown coated. The base genome between parent and offspring couldn't account for these rapid generational changes, but the epigenome can. More and more amazing research is coming out almost daily detailing the mechanisms that allow for highly complex control over the expression of our genes.

Caffeine Genes and Cardiovascular Risk

Ever seen how many contradictory studies there are about coffee? You can find hundreds of articles saying that coffee is beneficial and equal number saying it's harmful. Well, the most recent studies have shown that it varies depending on your genes. Without controlling for genetics in earlier studies, you can imagine why the statistics might be all over the place.

A single nucleotide variation in the CYP1A2 gene drastically changes the risk of heart attack and high blood pressure from caffeine intake. This gene codes for a liver enzyme that is involved in the breakdown and metabolism of caffeine. In the graph below, you can see how drastic a difference this variation makes. The “AA” or “fast metabolizer” genotype actually has a lower risk of cardiovascular problems with greater daily coffee intake. On the other hand, the “AC” and “CC” or “slow metabolizer” genotypes have dose-related risk of cardiovascular issues with caffeine intake.



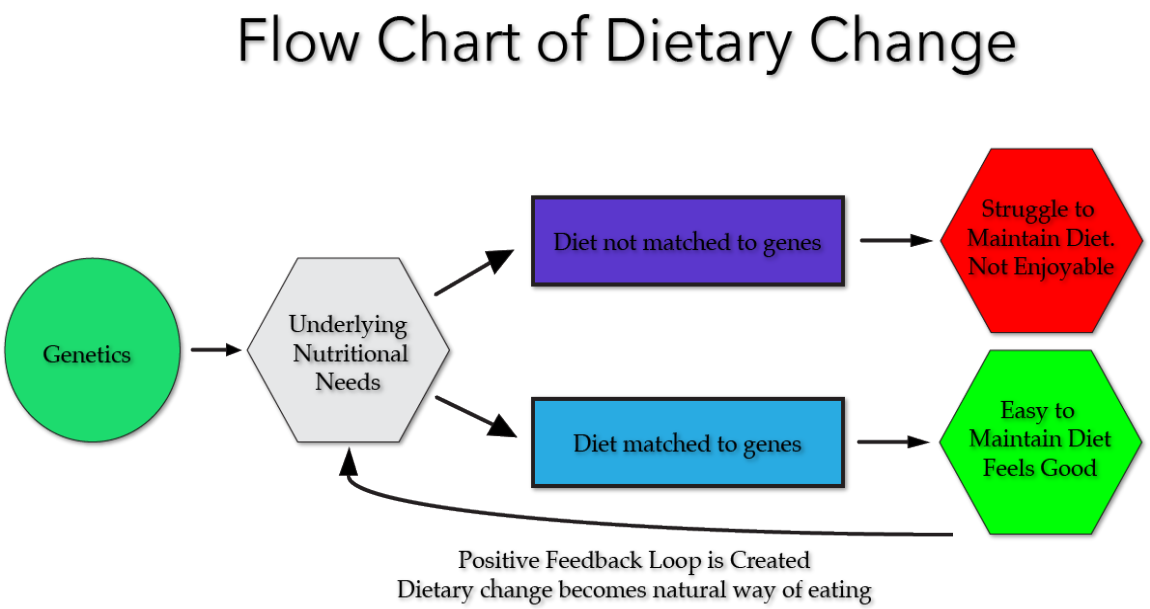
So, for someone with an “AC” or “CC” genetic variation, it would be wise to limit caffeine intake. However, for someone with an “AA” variation, drinking coffee is actually a great idea! This is nutrigenetics in action. By understanding how our underlying base genetic code influences our response to a certain substances, we can modify our habits to best support our genome.

So, how new is this?

Well, in a sense it's a very new approach to health, and in another, its something that traditional cultures have been doing for thousands of years just without the understanding of the genetic mechanisms. The ability to look deeply at the human genome, and compare our genetic variations to traits and outcomes has only been possible since the human genome was mapped in the early 2000's. Since then, the research has exploded, and we're now at a place where there is robust data that can be used to truly help people. But, traditional cultures have been looking at what foods and practices create the optimal genetic expression in their offspring for hundreds of generations, they just didn't have the language for it, or the precision we have now.

Think of nutrigenomics and nutrigenetics as the art of *creating* health. The science is clear – most of us are not at the mercy of some uncontrollable descent into degeneration as we age. There are clear steps to increasing longevity, improving body composition, and optimizing cognitive health. Ancient cultures did the best they could with observation, and now we're rediscovering the art of creating health with individualized precision and the tools and techniques to accelerate the process.

We have the means to know what your body needs on the deepest levels. These tools provide a template to go beyond healthy to optimal. These precision genetic tools allow us to move away from "dieting" and toward sustainable and delicious eating habits that simply become part of everyday life. Feeding your body the nutrition it *wants* from the ground up makes it easy to sustain those eating habits. It's a positive feedback loop.



How do nutrigenomics and nutrigenetics work?

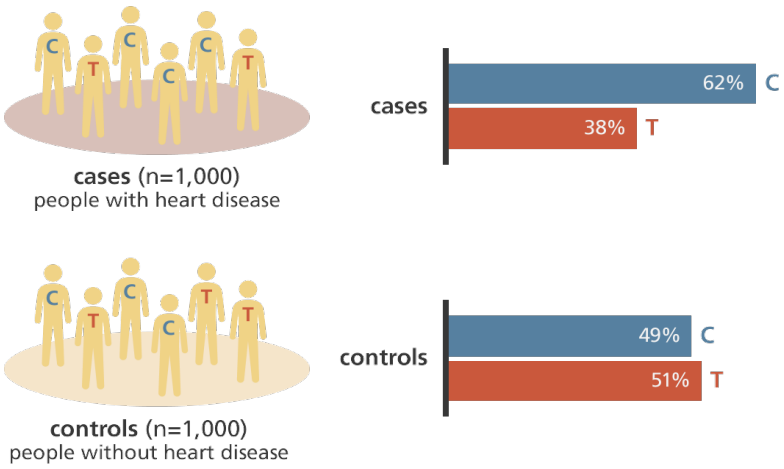
Our DNA code is built out of pairs of four different molecules called nucleotides. Adenine, thymine, cytosine, and guanine. They're abbreviated by the letters A, T, C, and G. These letters are arranged in specific patterns that act as an instruction manual to create different proteins, which create the sum total of our biochemistry. We each have 3 billion of these letters in our DNA, and 99% of that code is the same from person to person. The 1% that differs between us gives us our unique differences. Its easy to imagine how different color eyes, skin, or hair can be related to genetic variations. Those are only the differences that show up on the surface, so imagine just how many subtle differences there are in the different biochemical pathways that are responsible for the way we react to different foods and nutrients *inside* the body.

Single Nucleotide Polymorphisms

Each one of those 3 billion pairs of A's, T's, C's, and G's has a specific location it occupies within a gene. This allows us to compare one person's genome to another person's genome and make note of where the differences exist. The 1% of nucleotides that differ from one person to another are called “single nucleotide polymorphisms” or “SNPs” for short. These are simply substitutions of one letter for another with for example, a C instead of a T in a person's code. They are inherited and are not mutations, but rather variations. These tiny genetic differences can have a major impact on a number of different factors from the way we metabolize different nutrients, to how we synthesize neurotransmitters, to how we respond to light, to our hormone production, to our likelihood to develop disease, to our muscle growth, to our sleep quality, and beyond.

Genome-Wide Association Studies and Gene Specific Candidate Studies

So how do we know what these variations actually mean in real life? Genome-Wide Association Studies (GWAS for short) involve taking a group of people with a specific condition or trait and comparing their genome to a control group of people who don't have that condition or trait. If they find there are specific SNPs that appear significantly more often in the trait-related group than the control group, it is likely that there is a correlation between that SNP and the condition or trait. For example, in the chart to the left, you can see that the C version of this specific allele appears more often in the



group with heart disease. It is important to note that correlation does not necessarily equal causation, but this type of study allows further investigation into the genetic reasons for the difference in outcome. Sometimes, there are very specific reasons we can understand why a SNP produces an outcome, and other times it is simply correlation without a specific cause. Understanding the cause allows us to use precise and targeted interventions to modify the outcome, which is what I focus on.

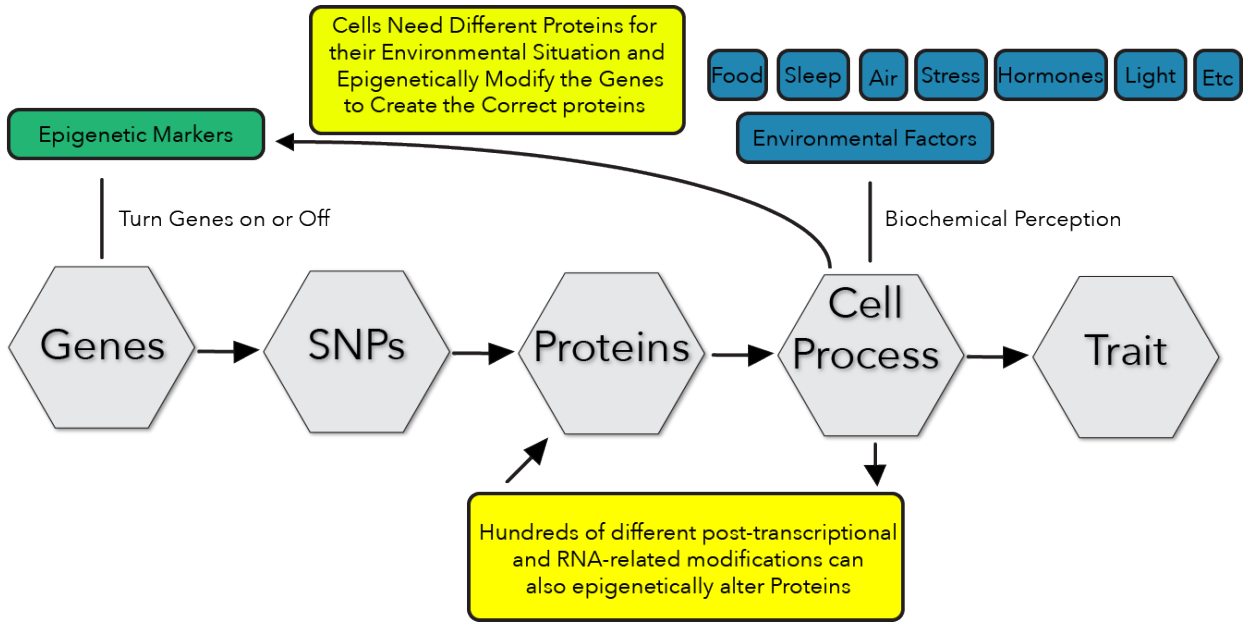
Gene Specific Candidate Studies are similar to GWAS but start with a target gene, rather than a trait or condition. Instead of comparing the whole genome of two groups of people, they select a specific gene that they believe might cause a different outcome between the two groups. For example, if a study examines the genetic basis for vitamin D deficiency, they might choose to look at only the differences in the Vitamin D Receptor gene. This often allows for researchers to better understand the cause of a trait of condition beyond just the correlation.

Epigenetic Modifications: Changing the Recipe

So you might be asking yourself, if 62% of the people in the above graphic have heart disease, why don't all of them same SNPs? While we can often identify a pattern, the human genome is a complex and dynamic multi-factoral system that is not necessarily linear. And, this is where epigenetics comes in. Just as the methylation marks changed the expression of the genes in the agouti mice and queen bee in the example above, there are 100's of possible ways beyond methylation to change the outcome of the gene SNP, and many different complex networks of interactions.

Our cells are in constant communication with the genome and use the epigenome to tell it how to respond the environment. Think of the genome as a recipe for a pie. It's just a list of instructions, not the actual pie. The epigenome is like the chef, who assembles the ingredients and bakes the pie. The cells are like the customers, who might give him feedback on how the pie tastes. After he gets feedback, he might decide to add some extra salt, bake the pie for longer, or add

some extra blueberries. The epigenetic modifications are like his notes written in the recipe. The important thing to remember, is that it acts as a feedback loop. As he gets a response from his customers, he modifies the recipe. This is how our genes respond and react to the signals they get from nutrients and other environmental factors to make sure the products they create are exactly what are cells need for their current situation. This is how nutrigenomics works. By inputting the right signals through food, nutrients, or herbs, we can instruct the epigenome to change the recipe so we get the result we want.



It's important to understand that through this process, we actually have more control over our health than previously thought. When I look at your SNPs, understand that what I tell you is not a prognosis. It's an opportunity to shift these factors in the direction of your choice. My approach is to help you better understand what your predispositions are so that you can take a precision approach to understand what tool or practice will most effectively shift you in a positive direction. Unlike what you may have come to expect from genetic testing, I'm here to find solutions and strategies for optimizing your genetic potential, rather than telling you about a fixed outcome.

So, by compiling your SNPs together, a fairly comprehensive picture of how you are genetically wired can be painted. Then by understanding these underlying factors,

nutrition and supplementation plans can be developed to epigenetically modify the outcomes of SNPs. Just like the queen bee in the above example, we can target specific genes with different nutrients or herbs that can turn on or off certain genes, or like in the caffeine example, we can modify your intake of substances to match the best outcome.

The Current State of Nutrigenomics and Nutrigenetics

How do I take advantage of this information?

Coaching vs Direct to Consumer Models

Right now, you can type in "genomic diet" to Google and find a number of services where you can upload your genetic data and get a report telling you what to eat or how to exercise. The problem with these direct to consumer models is that they fail to account for the individual. An algorithm just simply doesn't have the capacity to view you, the client, as a complex system of interactions and factors. Some of the top researchers in field are decrying these services as opportunistic and ineffective. Reducing the individual to data simply doesn't work. It's like diagnosing a disease without ever meeting the patient.

Working with a trained professional, either a coach or clinician, or doing the research yourself is important to get the full benefits of nutrigenomics and nutrigenetics. I'm not saying that you have to work with me, however, I do urge you to find someone who really understands this material to help you interpret it. When I look at an individual's genes, I look at over 300 SNPs that interact with each in complex ways. It is certainly possible to learn the information yourself, but for most people, it's a greater time investment than most want to commit to. I've purposely left much of the hard scientific details out of this report, but know that the full scope of nutrigenomics and nutrigenetics is quite vast and complicated. There are some fantastic resources out there for you to research on your own, but experts agree that having a guide is essential to getting the most out of this information.

Conclusion

Imagine a world where as soon as you were born, your parents could understand exactly what diet would support optimal health. While it might seem like science fiction, we are closer to that than you might think. The application of nutrigenomics and nutrigenetics holds great promise for the future, and its already here today. Eating for your genes has been practiced by traditional cultures for millennia. Now, we have the scientific tools to quantify these practices and deepen our understanding of how it works. If you're ready to upgrade yourself at the genetic level and pass on your health to future generations, gaining the knowledge is the first step.

To schedule a free 30 minute consultation and learn more about how epigenetics and nutrigenomics can help you thrive, click the picture below.

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