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Take Control of Your Health

Unlocking Personalized Health: Navigating the Unique Terrain of Nutritional Individuality

Analysis by Dr. Joseph Mercola | March 03, 2024

STORY AT-A-GLANCE

- Recent advances in genetic sequencing bring us one step closer to being able to optimize health based on a person's unique genetic mutations
- Polymorphisms that affect your metabolic pathways can alter your individual nutrient requirements
- The ideal approach to health can be likened to a double-layered cake, with universally recognized practices forming the base layer, such as consuming whole foods and staying active, while the other layer pertains to unique individual factors
- Understanding your genetic idiosyncrasies is crucial for optimizing health beyond common guidelines
- Foods that would be most helpful in hitting your nutrient targets include egg yolks, liver, oysters, clams and unfortified nutritional yeast

In this interview, Chris Masterjohn, who has a Ph.D. in nutritional sciences from the University of Connecticut,[1] and I discuss nutritional individuality, and how to assess your own personal nutritional needs.

While there are many opinions about which diet might be best, not all diets are ideal for everyone. There are exceptions to every rule, and only you can figure out whether a given recommendation is right for you.

As noted by Masterjohn, Roger Williams is the "father" of this field. He documented how the biochemistry of different people resulted in different nutritional needs.

> *"For example, one thing that he probably would've recognized about me is that my eyes are light blue. I've got greater UV destruction of retinol inside the eye, so I'm likely to require a higher amount of vitamin A,"* Masterjohn says.
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> *"I think there were many people, in between then and now, who have tried to come up with ways to determine, should you eat high carbs, should you eat low-carb, and all these different things. But I think we are now entering the realm where we can get a lot more precision on the hundreds of ways, really thousands of ways, that we are different. There are a lot of nuances that we are just now being able to come to.*
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> *It really takes a lot of work to get incredible precision, but we can now start thinking about things that people can self-experiment with at home, such as how different metabolic pathways might be altered, and why you might need to get most of your nutrients at levels that occur in a whole food, but maybe another person needs a lot of extra riboflavin, and another needs a lot of extra thiamine.*
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> *And, if either one of those people do the opposite, they're going to wind up in a lot of trouble. So, I think we are now at the place where we want to start getting deeper into the precision that's becoming available."*

Precision Technologies

One of the major technological advances we've seen over the last year is that whole genome sequencing has become affordable enough to be applied at mass scale. For example, the Regeneron Genetics Center recently completed sequencing 1 million exomes,[2] which approximates whole genome sequencing.

What they discovered is that there's an enormous variety of genetic mutations, so-called polymorphisms. So much so that the average person has one or two super-rare

mutations shared by only a few other people. And Masterjohn suspects that may be an underestimate. “I think it's really three to five,” he says.

> *“Before whole genome sequencing became affordable at mass scale ... what people were doing to try to understand their DNA was something like 23andMe or Ancestry, and then often running those through third party reports,”* Masterjohn says.
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> *“Those are extremely limited in what they're testing, because they're only capturing a couple hundred thousand out of the millions of variations. But way more importantly than that, the snip chip test, the methodology that they're using, loses all of its accuracy when you're looking for something that is present in fewer than 1 in 1,000 people.*
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> *The test is dependent on the stats that you get from large numbers of people ... The reason that this is important is because what whole genome sequencing has taught us is that each person is most impacted by somewhere around one to five super-rare genes that they have. This means the older testing from 23andMe is not giving you anything accurate at that level.*
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> *So, the way we should think about our health is kind of like a double layered cake — you've got one layer of the things that everyone should be doing ... There are certain things that everyone would agree on, like eating mostly whole foods, make sure that you're meeting all the basic requirements for your nutrients ... stay active, get outside, get sunshine, et cetera.*
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> *But then there's this other layer. Things that are unique to me are going to be extremely unique to me, because I've got a small handful of mutations ... and [few or no other people are] going to have the same ones that I have.*
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> *And that, I think, is where you can unlock the [next] big step ... None of it invalidates the things that we should all be doing ... exercise and eating a healthy diet, but it does make us able to say, ‘Alright, I've done everything that I can, I've achieved 7 out of 10 for my health, how do I get to 10 out of 10? I think*

understanding those deep idiosyncrasies is how to unlock that last mile of the run.'"

The Role of Epigenetics

The human body has approximately 23,000 genes and each gene can produce a variety of proteins. In all, there are about 14 million polymorphisms, or sites of variation. This is in part what allows to produce 100,000 different proteins.

Now, while highly individualized health care is possible based on genetic variations, I believe we should consider the role of epigenetics as well. The fact that you have a unique genome doesn't mean that you must get genetic testing to optimize your health. As explained by Bruce Lipton, Ph.D., genetic expression is primarily determined by epigenetic factors.

Epigenetics refers to changes in gene expression that do not involve alterations to the underlying DNA sequence. Epigenetic modifications occur through various mechanisms such as DNA methylation, histone modification and non-coding RNA regulation, just to name a few. In short, epigenetic factors play critical roles in the development of disease, disease susceptibility, and responses to environmental factors without directly changing the DNA sequence itself.

For example, the level of carbon dioxide (CO_2) in your body modulates histone, which in turn modulates the expression of the DNA. For clarification, histones are proteins found in eukaryotic cell nuclei that play a crucial role in the packaging and organization of DNA.

Their main biological function is to package DNA into compact structures called nucleosomes, which are the fundamental units of chromatin. Histones help regulate gene expression by controlling access to the DNA strand, which can either promote or inhibit transcription.

Histones also undergo various post-translational modifications, such as acetylation, methylation, phosphorylation and ubiquitination, which can alter the structure of

chromatin and influence gene expression. These modifications can act as signals for other proteins to bind to chromatin and regulate gene activity. So, overall, histones are essential for maintaining the structural integrity of chromosomes and regulating gene expression in eukaryotic cells.

My argument is that if you have a unique anomaly, it's not necessarily a "fatal flaw" that requires special workarounds. There may be epigenetic mechanisms that can bypass or attenuate the mutation, and CO_2 might be one of those ways, by modulating histone.

Counterargument: Epigenetic Influence Is a Narrow One

Masterjohn disagrees, commenting:

> *"Genetics has a stronger impact on how each of us are different, and epigenetics has a stronger impact on, for example, if you have a unique problem — when in your life does it onset, and what is the power to resolve it?*
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> *It really doesn't have that much of an impact on how individual we are, because the types of epigenetic regulations are relatively narrow. So, you could say, for example, psychological stress is going to impact your epigenetics ...*
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> *Everyone's trauma can be very, very unique in terms of the experience of it, and what the content of it was. But there's not that many different types of stress response to trauma in the body. So, the resulting epigenetics are largely narrow ...*
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> *I'm not implying that we know everything there is to know. I'm implying that we've learned some things that are valuable. So, when I say 'genetic,' [do not read] that as genetic determinism. If anything, I would argue against genetic determinism, because the point is to find the points of actionability.*
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> *If something's actionable, then by definition it's not deterministic, because your action is changing it. So, I'm not talking about determinism, I'm talking about uniqueness.*

There are valuable things that we've learned very recently about the skew of genetic mutations in people that have actionable implications, which means there are nuances you can add to how you do things to optimize and maximize your health.

Obviously, these things interact, but epigenetics, I don't think, add as much to the uniqueness as genetics do, because we can all get stressed, but generally stress is quite similar in what it's doing. There's a handful of stressors that we can experience, psychological, and emotional work, metabolic, not eating enough, exercising too much. There's a bunch of them, but they're relatively small.

Whereas, if you look at the skew of big bottlenecks in metabolic pathways, you're looking at 30-ish essential nutrients that could be altered. You're looking at three major macronutrients that could be altered, and you're looking at combinations that come from those. You're really looking at thousands of possible individual bottlenecks that have maybe dozens to hundreds of implications of how you could uniquely tailor your diet."

Working With Polymorphisms in Real Life

As an example, Masterjohn discovered that he has a riboflavin-responsive mutation, and he's heterozygous for it. In a heterozygous individual, the two alleles (alternate forms of a gene) for a particular trait are different. Infants who are homozygous for it — where the two alleles are identical — have a near-100% infancy death rate.

Giving these infants riboflavin supplementation drives that death rate down to 10%. As a result, he suspected that his riboflavin requirement might be higher than normal and, indeed, taking 75 milligrams of riboflavin each day abolished his seasonal allergies. "I have not had any allergies since I did that," he says.

One of the things that you can look at is — if you develop a hypothesis around it, and you test it — what is the outcome? With regard to riboflavin, it affects Complex 1 in the

mitochondrial electron transport chain. Masterjohn explains:

> *"The gene [affected] is ACAD9, and ACAD9 is a moonlighting protein that fulfills two functions. One is in fatty acid oxidation, and one is as a chaperone to assemble mitochondrial respiratory chain complexes ... If you look at the case reports, it's usually Complex 1 that's deficient, but sometimes it's Complex 2.*
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> *I also had a respiratory chain assay from a cheek swab that, interestingly enough, did not show that I had a deficiency of anything, but it did show that my Complex 2 was way higher than my Complex 1. This is not consistent with disease, but it is consistent with the fact that I have a mutation that decreases Complex 1.*
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> *I've found that super valuable, where, if I can predict, from a biochemical pathway, that this going to feed into Complex 1 more, or Complex 2 more, I can consistently show that the things that feed into Complex 2 lower my resting lactate, and the things that feed into Complex 1 raise my resting lactate.*
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> *That happens to be a very good leading indicator of a health effect. So, for example, I found that generally if something increases my lactate and I ignore it, it's going to wind up shortening my sleep. Whereas, if I remove the things that increase my resting lactate, and I take the things that decrease my resting lactate, generally, that improves other things I track, such as my sleep."*

Trial and Error

In the interview, Masterjohn also provides another personal example relating to high-dose biotin supplementation gone wrong. Based on past symptoms, lab work and genetic testing suggesting his biotin recycling was poor, he started taking 10 mg of biotin per day.

By the end of one month, his focus was severely impaired, he kept dropping things and was easily angered. "I was in a conversation where the stress of the conversation would otherwise have been very trivial, but I got so angry that I screamed so hard that I saw

flashing lights," he said. "The only time I've ever experienced that in the past has been through physical stress. I've never gotten angry and had that happen."

Once he stopped taking the biotin, all these symptoms vanished. In the end, he concluded that the biotin supplementation had worsened the respiratory chain issue caused by the riboflavin-responsive mutation. He comments:

> *"So, look, if you are content with just eating well and exercising well, and everything's going well, and you're not trying to optimize and you're not trying to fix a problem, then fine, whatever. But no one needs to be on 10 milligrams of something that the requirement is 30 micrograms of, unless they have a very unique need for that.*
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> *There is a very severe homozygous biotin-related disease where this one mutation was considered an absolute death sentence in infancy. No one had ever said, 'Maybe more than the traditional 10 milligrams of biotin for a genetic disorder in biotin metabolism is needed.'*
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> *Then, someone decided, 'I've got one of these girls who has this mutation, she's supposed to die any minute now, I'm going to keep titrating the biotin up until her skin rash goes away.' So, they did that, and she wound up on 1.3 grams [1,300 mg] of biotin a day.*
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> *So, 10 milligrams gave me a neurological disorder, and 10 milligrams is insanely high compared to the 30 to 300 micrograms basal requirement is. She's on 1.3 grams instead of 10 milligrams, 130 times what I was on. But last time anyone published on her, she was alive at 13 years old, which is considered impossible according to the textbooks on this disorder ...*
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> *So, there is a need to experiment outside the boundaries of diagnosable diseases, and in the realm of optimization, but my point is, once you get into optimizing with things that are outside the realm of 'everyone should do this,' that's the point where you really want to take additional measures to test whether you are actually optimizing what you think you are.*

> *Fasting glucose, ketones and lactate ... are not going to pinpoint an exact issue, but just knowing whether you are overstressing your respiratory chain for one of 300 reasons is a huge thing to know ... So, if you put in biotin at 5 milligrams a day and your lactate goes from 0.7 to 2 millimoles per liter, you know that biotin overstresses your respiratory chain.*
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> *You don't know with exact precision about why, but you don't need to know that to say, that's too much biotin for me, that was an error in my optimization, and I'm going to pull back."*

Cover Your Basics First

Individual polymorphisms aside, one of the lifestyle strategies that applies to just about everyone is to get your basic micronutrients from whole foods. You're just not going to hit the recommended daily allowances from processed foods and junk food. Masterjohn recommends tracking your nutrient intake using an app like Cronometer, at least for a few weeks, to make sure you're hitting your targets.

> *"The foods that would be most helpful in hitting your nutrient targets would be egg yolks, liver, oysters, clams and unfortified nutritional yeast,"* he says.
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> *"If you hit those, you're pretty much hitting everything, but you are kind of missing some plant-centric nutrients like vitamin C. I think bell peppers are super useful, yellow, orange and red bell peppers, out of the foods that are in a standard grocery market in the Western world, have the highest vitamin C to carbohydrate ratio."*

Cronometer will also help you determine if you're eating too much linoleic acid (LA), which acts as a metabolic poison when consumed in excess. For more details, see "**Linoleic Acid — The Most Destructive Ingredient in Your Diet**."

LA intake above 10% is highly likely to cause problems. Ideally, you want to keep it well below 5%. If your LA intake has been high, make sure you're getting enough vitamin E, as it protects PUFAs from lipid peroxidation.

In other words, vitamin E protects your cells from the damage caused by LA and other PUFAs. And you don't need much. According to Masterjohn, 0.6 mg of vitamin E per gram of PUFAs in your diet is all you need to protect against the damage.

Make Sure You're Getting Enough Collagen

A subset of the whole food recommendation is to make sure you're getting enough collagen. Homemade beef bone broth is an ideal source, and using a pressure cooker, you can whip up bone broth in as little as two to four hours.

> *"Generally speaking, one of the important metrics is the methionine-to-glycine ratio in the diet, and if you optimize around that, the rule of thumb is you want to eat all the bones and collagenous tissue that would be associated with the meat that you're eating,"* Masterjohn says. *"I find it super easy to do that if I cook a chicken in the Instant Pot, and then I take the meat off and throw the bones back in."*

The devil's in the details though. When cooking broth, you want to make sure the bones are as organic as possible, as the bones of animals raised in concentrated animal feeding operations (CAFOs) tend to be contaminated with heavy metals, which leach out during cooking.

Some bones are also better sources of collagen than others. Chicken feet and the knuckle bones (knee joint) of cows are particularly high in collagen and are therefore excellent choices for making bone broth. As a general rule of thumb, Masterjohn recommends getting 10 to 15 grams of collagen for every 100 grams of non-collagen animal protein.

> *"If you eat a more plant-based or shellfish-based diet, your methionine-to-glycine ratio starts to look a lot like what it would look like if you ate an animal diet, nose to tail. So, the degree to which you need to think about drinking bone broth is very dependent on how much meat you're eating. You want to think about it a lot more when you're eating a lot more [red] meat."*

A large portion of collagen is made up by **glycine, which has many important health benefits**. Interestingly, one easily recognized symptom of glycine deficiency is an overly reactive startle reflex. If you're easily startled, you're probably deficient in glycine.

Polymorphisms and Gut Function

As noted by Masterjohn, polymorphisms can also affect your gut function and even the makeup of your gut microbiome. So, while probiotics such as Akkermansia are important, addressing any underlying mitochondrial dysfunction caused by polymorphisms may be even more foundational.

> *"I've seen some amazing cases where someone has small intestinal bacterial overgrowth (SIBO) and then they supplement with high dose thiamine and it just disappears,"* he says.
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> *"That example is a case where they stumbled into it by luck, but they fixed a major reason for their own idiosyncratic mitochondrial dysfunction. And then that became apparent as the dominant driver of the microbiome.*
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> *Before I was talking about how, generally, if I feed Complex 2 versus Complex 1, my lactate goes down and my health goes up. One of the things that happens when I really know I'm optimizing around that is, a) I effortlessly lose body fat at a very high caloric intake, and b) I start having two perfect bowel movements a day.*
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> *The issue is, how fast can you figure out the idiosyncratic bottleneck and fix it? And does it conflict with the damage that's done to your gut? So, for example, if you really should be on a high-starch diet for some reason, but now you've wrecked your microbiome such that eating a high-starch diet feeds the wrong microbes, then you might have some chicken-and-egg type of stuff to figure out.*
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> *And then, there might be other times where literally all you need is 2,000 milligrams of thiamine, and it's like a miracle, and you don't really have that*

conflict. Then, of course, there are all kinds of permutations of gray areas in between those two polarities.

Basically, what I would do is, I would look for and fix the underlying bottleneck, and then I would be borrowing from the basic principles of the GAPS diet, bone broth, et cetera, on an as-needed basis, to try to make sure that you're not eating foods that are irritating, and you are eating foods that are healing for the gut. I do think glutamine has a particularly significant role in gut healing as well, alongside glycine and bone broth."

More Information

In closing, Masterjohn comments:

> *"Do the low hanging fruit. Then, when you really want to optimize, the next thing — after you've really got [the basics] on lock — I think that's where it's time for some self-experimentation. It really helps to know a little bit about biochemistry, and do some testing like glucose, ketones, lactate, do some tracking micronutrients in Cronometer and so on.*
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> *If you subscribe to my newsletter, I talk about this stuff all the time. So, if you ever want to jump down the optimization rabbit hole with me, my newsletter is where to start that."*

You can subscribe to his newsletter and find loads more information on **Masterjohn's Substack**.

Sources and References

- [1] Kresser Institute Chris Masterjohn PhD Bio
- [2] Regeneron.com