GAPS MASTERCLASS

MODULE 4

Genetics & MTHFR

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The Legal Part

Please note that much of this guide is based on my understanding and training as a Nutritional Therapy and GAPS Practitioner, as well as personal experience . I make every attempt to ensure accuracy of the content, I take no responsibility for errors or omissions.

You should use this information as you see fit, and at your own risk.

Nothing in this guide is intended to replace common sense, legal or other medical advice, it is meant to inform the reader. Apply it to your own set of circumstances with care.

Any health recommendations are based on my experience as a GAPS Practitioner and of those I trust. Any recommendations are from sources that I would use for my own family or clients but I make no guarantees about the service or rates you will receive from these providers.

I think you will receive great value from this guide. Please email me at melanie@honestbody.com with any errors or incorrect links so that I can update the materials.

Welcome to:

MASTERCLASS MODULE 4

In this workbook we will be discussing:

1. Genetics 101
2. What goes wrong in our genetics
3. Epigenetics & supporting your genes
4. Methylation & MTHFR Mutations
5. How to test your genes

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TERMS

Terms you need to know for this module:

- **amino acids** - a class of carbon, oxygen, nitrogen, and hydrogen-based compounds that are the building blocks of the body, combining to form proteins
- **phosphate** - a naturally occurring form of phosphorus
- **wild type** - the prevailing gene or characteristic seen in individuals in normal conditions
- **SNP (single nucleotide polymorphism)** - a variation in a single base pair in a sequence of DNA (will interchangeably be referred to as a polymorphism, mutation, or variation)
- **phenotype** - an observable characteristic
- **genotype** - the genetic makeup that gives rise to a particular observable characteristic
- **23andMe** - a direct-to-consumer, saliva-based genetics test intended to establish ancestry lines through genetic analysis

INTRO TO PERSONAL GENETICS

People tend to either be completely fascinated or completely frightened of the thought of genetics playing a larger role in health decisions. My hope is, at the very least, is that by the end of this lesson- you'll be able to make an informed decision about whether personal genetics testing is right for you.

And personal genetics? What is it? Aren't all genetics "personal"? This term may be new to you and, in fact, it's very new to all of us. It refers to a type of testing that reveals changes in our chromosomes or genes. This kind of testing was not possible before the completion of the Human Genome Project in 2003. The Human Genome Project was a

labor of love (and science!) by a group of very smart people, who enabled us to read the entire genetic "handbook" of how our bodies are put together. Pretty amazing stuff.

Genetic Testing Overview

Genetic testing can be done in a number of ways: through bodily fluids, such as blood, saliva, or amniotic fluid, or through tissue, such as a skin swab or biopsy. Entire chromosomes can be evaluated, or we can "zoom in" to examine the genetic material contained within the chromosomes. Personal genetics testing is generally designed to be as non-invasive as possible... a blood draw, at worst, but generally just a little vial filled with your saliva, sent to a company like 23andMe for analysis.

So, why would anyone want to have this kind of testing done? Well, the revelations that it can provide about ancestry can be pretty motivating for some people. It can also uncover predispositions to certain conditions or diseases. This may sound frightening, but my hope is that by the time you're done with this module, you'll feel empowered by the idea of genetic testing because it will enable you to fend these conditions off before they ever happen! Or, if you've already found yourself dealing with one of these unfortunate conditions, with the help of a knowledgeable practitioner, you may be able to identify some subtle adjustments to your nutrition and lifestyle that will make all the difference on your road to wellness.

I'm talking this genetic thing up, but, oh boy, there are some down sides. Let's put on the brakes for a minute and examine the cons of genetic testing.

- **First of all, as far as sciences go, it's a newborn baby! Researchers are learning new things every day, yet there is so much that we are**

still light years away from understanding. One of the most gaping holes is in uncovering how our genetics are interacting with our food, with the world around us, and with the communities of microbial DNA within us. To drive that last point home, the genetic material contained within our bodies that is actually our own is outnumbered by 100 to 1 by bacterial DNA! The study of the "talking" that happens between the genes of various microorganisms is only just beginning to be done, but the winner of this talking contest seems to be clear. Here's hoping that the bacteria doing the talking have some good things to say!

- **It may open the door for pharmaceutical companies to use genetic findings as a convenient excuse to coerce masses of people to take drugs unnecessarily, or for people to be driven by fear to have other "preventative", but risky medical interventions.**

- **For those of us (which probably means most of us) who do not appreciate the complicated relationship that exists between our genes and all of the other factors influencing our health (diet, lifestyle, and environmental factors, etc.)- that genes, alone, are not the authors of our destiny- these genetic revelations can be a source of anxiety, or may create a general feeling of helplessness. These feelings are stressful, and when I bring up "lifestyle and environmental factors", the biggest one of all is S-T-R-E-S-S.**

- **One of our major concerns about personalized genetics should be this: that we- you, me, all of us- as a society and as individuals, will hide behind our genetics, throw our hands in the air, and become a victim of the theory that we are inherently broken. A "broken" person is free to excuse themselves from any personal responsibility to treat our bodies like the temples that they are.**

While some genetic syndromes may be devastating, generally speaking, our genetics are very much not our destiny. Genetic variations are

better described as “personality traits”, and the combination of them make us who we are by determining how we respond to our various environment, creating either a state of ill-health or one of harmony and balance.

So, wait a minute - What makes up this “environment” that I keep referring to and why is it important? It’s important for a few categories of reasons. The first category is more obvious and is what I’ve been referring to... what kind of burden these factors are putting on the “translation” of your genetic code, that is happening every second of every day. For instance, you are genetically not that great at metabolizing a certain chemical, predisposing you to certain types of cancer. So, stay away from that chemical. Duh.

Epigenetics

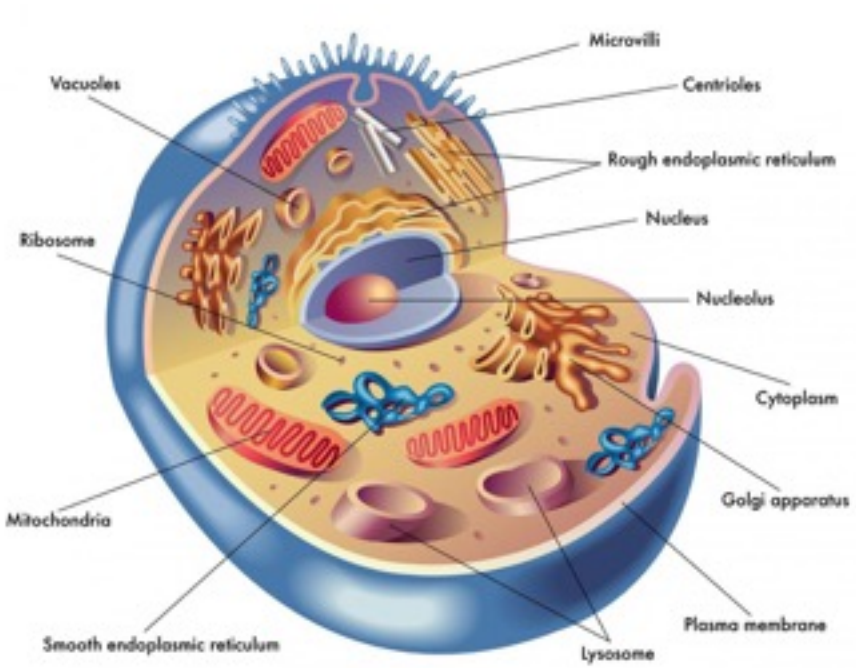
The other category has a fancy name that you may or may not have heard before - Epigenetics. This is a big deal and we have just barely scratched the surface of its impact on human disease. Epigenetics literally means “above genetics”, and is the process by which our genes (or parts of our genes) are turned on and off. So, if a our DNA contains a particular mutation that is determined not to be advantageous to us, a healthy body should be able to switch that gene off, like putting duct tape over the mouth of someone who is saying nasty things and really getting on your nerves. This can mean the difference between getting almost any disease or not! The body does this “switching off” largely through a process called methylation. Lots more on that later. In the mean time, here is a list of factors that strongly influence this epigenetic switch:

Diet	Environmental chemicals	Stress
Physical activity	Hormone imbalances	Smoking

Medications	Trauma	Pollution
Aging	In utero environment	Lack of oxygen
Sleep	Dysbiosis	Inflammation

GENETICS 101

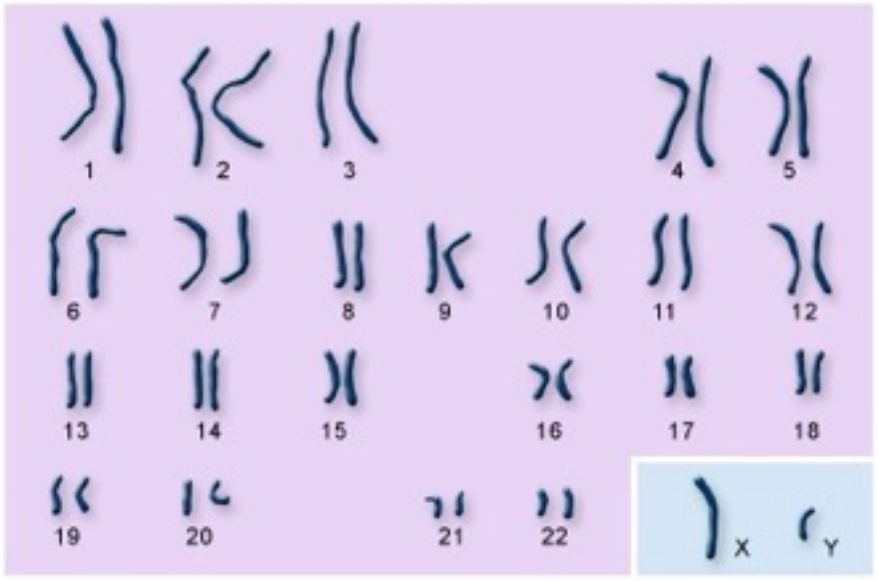
Let's begin by zooming our microscope way out... Our bodies are made of cells. That isn't really big news. Now, let's jog your grade school memory back to what those cells look like on the inside.



Most importantly here, notice the nucleus (this is where the DNA is contained), ribosomes (these make the RNA), and mitochondria (they contain their own special DNA). Fun fact: Scientists have hypothesized that our mitochondria may have evolved from special bacteria, explaining why they have their own DNA. Imagine that! Bacteria

actually living inside of our cells, creating the energy that our bodies run on!

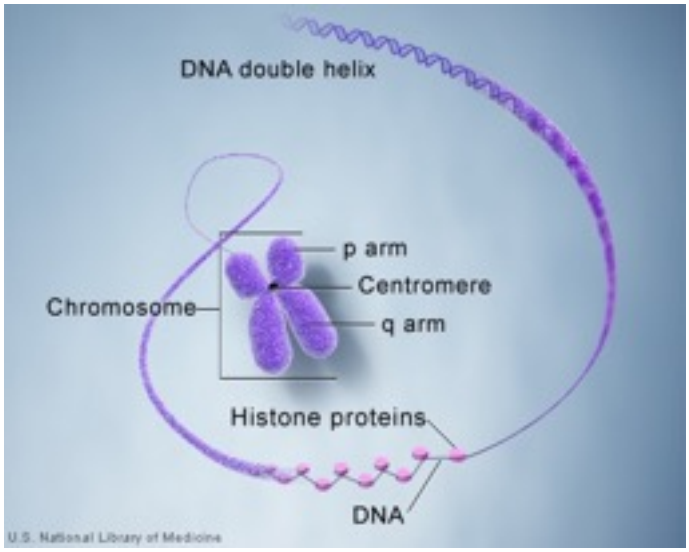
Let's imagine we've taken a ride on our own Magic School Bus inside this human cell. Like royalty nested on thrones, safely inside the castle walls, our genetic material is housed deep inside the nucleus. Residing here are 46, or 23 pairs, of chromosomes. It's actually 21 pairs + 2 sex chromosomes (2 X's for a girl, and X + Y for a boy). We inherit half of these chromosomes from our mother (the left half of the pair, for instance) and half from our father (the right half of the pair).



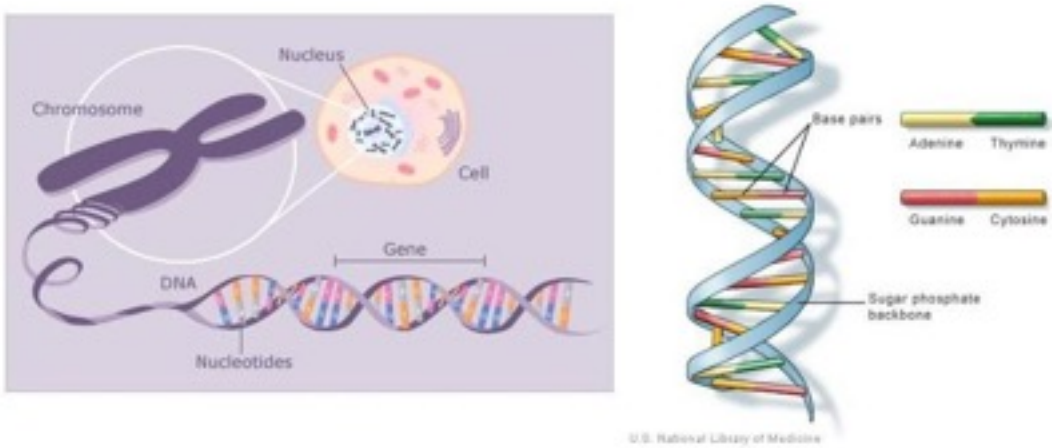
U.S. National Library of Medicine

When the body needs to create a new cell, it must reproduce this genetic material so that the newbie has its own copy. This is done by RNA, which is made by the little blob-shaped structures called ribosomes (in the image #1, above), in a process that looks something like a game of "Telephone". The RNA carries a copy of the DNA, in its own "RNA language" to the new cell.

Now let's zoom in a little further. What do these chromosomes actually contain? What do they look like on the inside?



The image above shows a pair of chromosomes, attached in the middle by something called a centromere, causing them to form their characteristic "X" shape. Each part of the chromosome can be further defined as a long arm (p arm) or a short arm (q arm). Each arm is packed full of genetic material, or DNA, that has been wound up for maximum storage and safe-keeping. Let's unwind this DNA a little further.



Shaking the kinks out of a length of DNA, we can see that it is arranged in a beautiful double spiral formation, known as a double helix. The purple, spiral part is known as the "backbone" and is made of sugar and phosphate. The colorful rungs of the ladder are where the genetic code is actually held. These are called DNA base pairs. They are always comprised of particular amino acids- adenine (A), thymine (T), cytosine (C), and guanine (G). These base pairs are like turtledoves, ideally mating for life. A only has eyes for T. C has fallen hard for G. It is the job of these little love birds to lay out a plan for every process that happens within the body...

I'm going to say something here that is very important, so TAKE NOTE! When I say "every process that happens within the body", I want you to hear the word enzyme. Enzymes are little proteins (long strings of amino acids) that are at the root of of nearly everything that keeps us alive. They are responsible for breaking down food and putting the nutrients back together into something that our bodies can use. The build things up and break things down, step by step, like little worker bees. Our bodies make these enzymes. How? Genes.

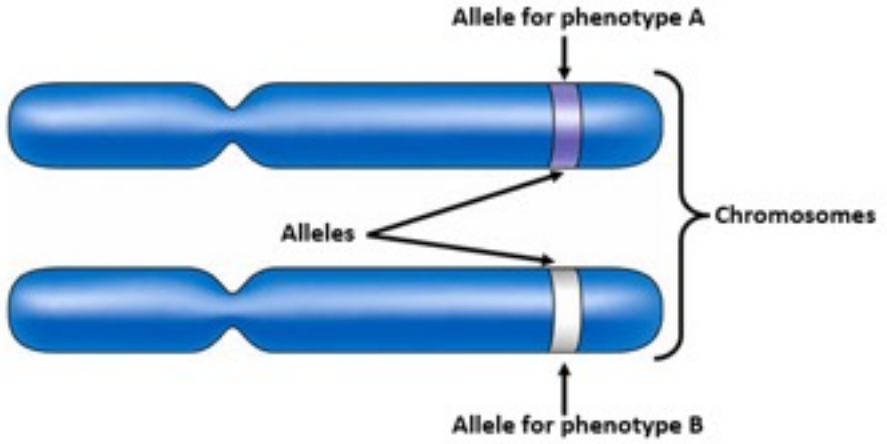
Let's come back to those images above. What, in all of this tangled up mess of genetic material, constitutes a gene?

I'll start here- three rungs of a ladder, or base pairs, in a row comprises a "codon". This is a region of DNA that gives instructions to the body to produce a particular amino acid. There are, however, some codons that are known as "non-coding". These regions don't contain information about what amino acid to produce, but are equally important. They give instructions about when to start or stop a particular process... or sometimes they contain information that something we haven't been able to figure out yet.

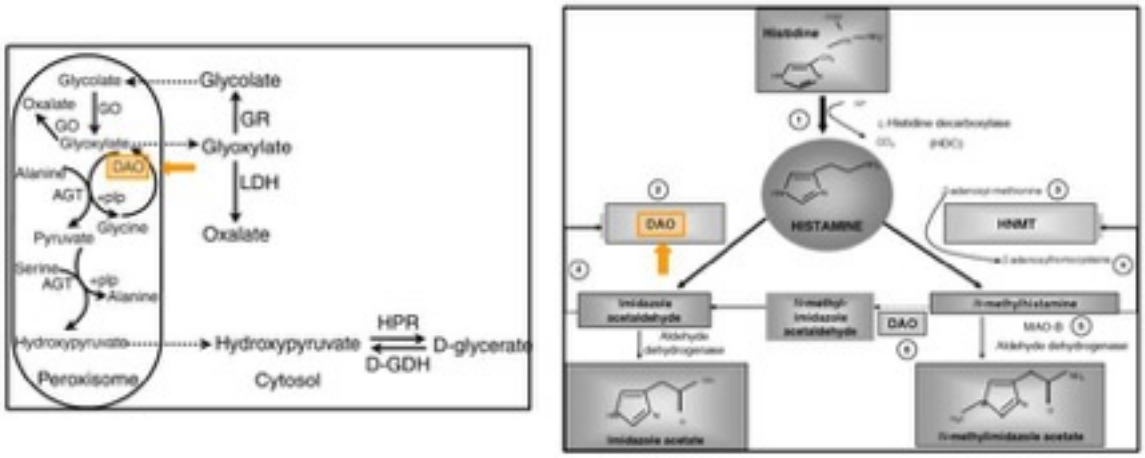
Anywho, a *gene* held within this mass of packed-in double helix, can be seen as a region between "start" codons and "stop" codons. Like a computer program, the body will give specific instructions:

1. Start
2. Make **X** protein
3. Now make **Y** protein
4. Attach **X** protein to **Y** protein
5. Stop
6. Start
7. Make **A** protein
8. And so on...

Playing into this instruction booklet are 2 different sets of information. Remember, we are made both of our mother and father- and both of their genetic contributions will have something to say about how our bodies function. Rewind back to the beginning of our little lesson. Remember how our chromosomes come in pairs (Thanks, Mom. Thanks, Dad.)? Well, in roughly similar areas on each of those chromosomes lie corresponding pairs of genes. These corresponding genes are called alleles. Here's a little visual (of two chromosomes that are not being held together by a centromere) to clear that one up for you a little:



Now, to get a particular function done in the body, many genes function together in a pathway. These can get pretty complicated, with one gene sometimes playing a role in many different pathways. The following is an example of the diamine oxidase gene (DAO). It functions to break histamine down, as well as to produce the amino acid, glycine... and this isn't even all it does!



Do you see what I mean? Yikes. So complicated, yet also not. Amid the chaos there is a humbling sense of order... But now is not the time to wax philosophical. It's time to talk about what it means for a gene to be mutated.

When Things Go Not Quite "Right"

In order to understand what "not quite right" is, we should start by exploring what "normal" is. I use the term "normal" very loosely, as it doesn't really even exist! We all have genetic mutations of one type or another. They make us each the special person that we are. That said, we will define "normal" as something called the wild type. This doesn't have anything to do with crazy parties or exotic animals. It is simply the genetic allele or characteristic (phenotype) that is seen in the majority of a healthy population.

Now we can start putting some of our newfound genetics knowledge to work! A genetic mutation occurs when a DNA base (those C's, G's, A's, and T's) has gone wonky. At some point, something went awry and caused C to switch to a T, or something of that sort. Remember, this is important because it affects the codon > which affects the amino acid produced > which affects the function of an enzyme.

Now, mistakes do happen and our bodies are anything but stupid. They have a backup plan. This backup plan is a built-in system that accommodates for these piddly mistakes by listing out some possible variables in the X codon = X amino acid equation. It says, "Ok... I see that you didn't do things exactly as I expected. Instead of "Turn right", you spelled "Trn rite". I will still turn right, though. Despite the fact that you didn't spell that correctly, I still catch your drift."

Because of this back up plan, and because some of the genetic instructions- though valuable- are not critical, some mutations may not make much difference at all in how our bodies function. Sometime, however, the mutations are a little more confusing- Instead of "Turn right" or "Trn rite", the instruction is "Turn light". Wait, what? You want me to turn a light on? Sometimes things can really get lost in translation. Or the mutation may occur at a really critical place in the gene- like a recipe for baking a cake that never tells you to turn the oven on, add the main ingredient, or get the cake OUT of the oven!

Depending on where the variation (or mutation) has occurred and if it actually changed which amino acid was produced, that particular genetic instruction manual could be changed in different ways or not much at all. Mutations that cause changes there to be a change in the amino acid often cause the enzyme to be a slightly (or very) weird shape. Enzymes are three-dimensional structures with an "active site". These active sites are like keyholes that fit various cofactors, like vitamins and minerals. Cofactors are not just luxuries for our little enzyme vehicles, like heated seats or rear view mirror air fresheners.

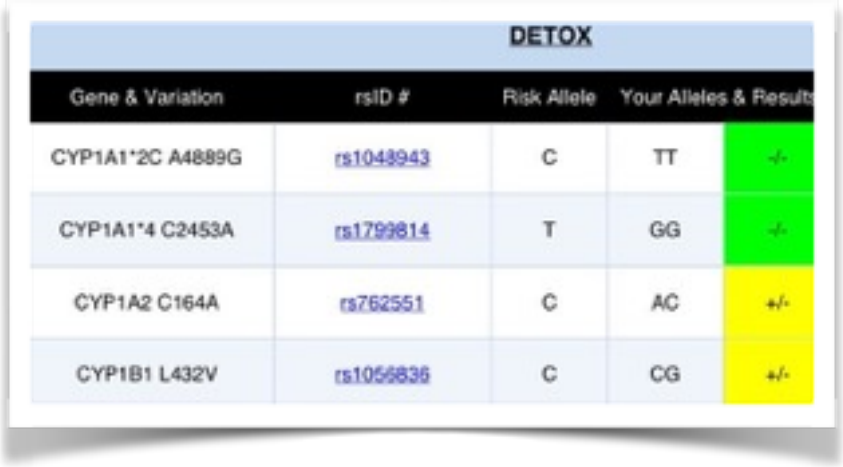
They are the keys in the ignition, required to even start the thing! So, when a misshapen enzyme happens along, it doesn't bind with these cofactors as easily, making more difficult to get that particular pathway snapping along, the way it should.

For example, in the gene known as COMT, in the H62H variant, there was a DNA base change at codon 62. Thankfully, this mutation did not change the instructions significantly enough to change amino acid produced (Histidine is still histidine. Phew.). That said, the mutation still slowed the catechol-o-methyltransferase enzyme function down a little, but not by much. In contrast, in a different mutation of the COMT gene- the V158M variation- at codon 158, there was a DNA base mutation that caused the body to produce the amino acid methionine instead of valine. Now we've done it. This really slowed enzyme function down... And for this person, it could mean being more sensitive to pain, more vulnerable to stress, a tendency toward anxiety.

These DNA base mutations aren't the only kind of genetic mishaps that we are capable of. Others types of genetic errors can actually be more serious. I won't go into much detail about these because personal genetics testing generally only covers DNA base mutation. Generally speaking, these affect larger areas of a chromosome- maybe even the whole thing. They include things like insertions (where genetic material from one chromosome is inserted into a different chromosome), deletions (where some genetic material is missing altogether, trisomies (when there are 3 copies of an entire chromosome, rather than 2), monosomies (when there is only a single copy of a chromosome, rather than a pair), etc.

Genetic Mutation Shorthand

If you should decide to order a genetics panel, the result will look something like this:



DETOX				
Gene & Variation	rsID #	Risk Allele	Your Alleles & Result	
CYP1A1*2C A4889G	rs1048943	C	TT	-/-
CYP1A1*4 C2453A	rs1799814	T	GG	-/-
CYP1A2 C164A	rs762551	C	AC	+/-
CYP1B1 L432V	rs1056836	C	CG	+/-

This may be gibberish to you, which is okay. Hopefully you spend your days (except maybe this day) doing things much more fulfilling than learning about genetic jargon. I'll give you a quick rundown on the various ways that this report represents a single genetic mutation, or SNP. SNP is pronounced "Snip" and is an acronym for single nucleotide polymorphism. It's a crazy looking term, but just means that one of those darn DNA bases got screwed up.

First, in both Allele columns, a "risk allele" is defined and your alleles are reported. You can see if you had 0, 1, or 2 copies of the risk allele. Risk allele generally is referring to a changed DNA base, and just means that it's been found to cause something other than a wild type phenotype (or characteristic). This "other than" may fall anywhere on a spectrum from very undesirable to actually conferring a health benefit, depending on the gene and mutation.

Given your risk allele status- Did you have any copies? One copy (heterozygous)? Two copies (homozygous)?- you may or may not have had one of those pesky amino acid changes. This change is reported out in the first column as something like "CYP1A1 A4889G" or "CYP1B1 L432V". Scientists can be hard-headed, so this can get a little random. Hang with me.

Sometimes this format refers to the change in the DNA base. When this is the case, it would mean something like, "At position 4,889 in the CYP1A1 gene, the adenine DNA base was mutated to guanine". Other times, this format is telling us about how the mutated DNA base resulted in an amino acid change. In this case, the number tells us the codon where the DNA base mutation occurred. The letters tell us if/what the resulting amino acid change was. So, "At codon 432 in the CYP1B1 gene, the amino acid known as leucine was changed to one called valine". Whoops.

Epigenetic Oversight

Let's come back to why this thing called epigenetics is so important. It's the science behind nature versus nurture. And as it turns out, it's both nature and nurture. Just for emphasis, I'll show this list of factors influencing epigenetics again. It's really that critical.

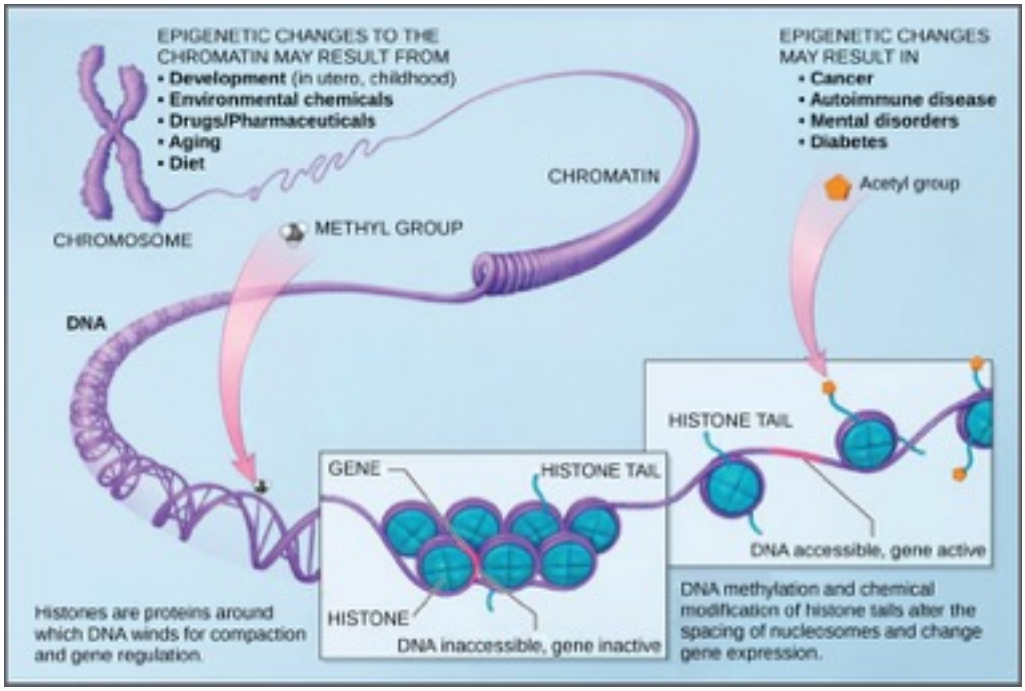
Diet	Environmental chemicals	Stress
Physical activity	Hormone imbalances	Smoking
Medications	Trauma	Pollution
Aging	In utero environment	Lack of oxygen
Sleep	Dysbiosis	Inflammation

We can do extensive analysis of our entire genome, understand every genetic predisposition that we have, but we cannot forget that these genes are not our destiny. Through careful tending, our genetic garden can blossom into something beautiful.

We can literally change the course of history by providing our children with a better genetic code (and giving them the health & lifestyle know-how to practice their own good gardening skills!).

On the flip side, we can turn a good genetic code into a pile of garbage, passing this dump heap down to our children and even our grandchildren. Study after study has shown that malnourishment, trauma, anything that causes a change to our epigenome, **will affect our grandchildren even more than it does ourselves or our children**. It is the ultimate legacy.

I won't spend a lot of time on this because it gets pretty technical, but here's a visual of how it works. In short, methylation... and to a lesser extent acetylation.



METHYLATION

The "M" Word

What is methylation and why are we focusing on it so much? Methylation is simply the act of a "methyl group" (or a group of one

carbon and three hydrogen atoms) attaching itself to an enzyme in your body. When this methyl group attaches to an enzyme, the enzyme can do its job. This is a vital process that occurs in all cells of your body. I've covered its role in epigenetics, but what else does it do? It turns out that it's actually essential for a number of critical processes in the body.

Methylation is responsible for:

- **Cellular repair:** Synthesis of nucleic acids (the raw ingredients of DNA and RNA), needed to produce and repair DNA and RNA.
- **Protecting cell membranes:** Critical to the production of phosphatidylcholine, the main building block of all cell walls in the body. Without proper levels, cell membranes become damaged and weak, making them more susceptible to harmful substances and not quite as good at transporting nutrients into and out of the cell.
- **Protecting DNA and RNA:** Unprotected DNA is susceptible to damage by viruses, bacteria, heavy metals, solvents, and other environmental toxins.
- **DNA regulation:** Turns genes on and off, affecting the expression of your genes.
- **Healthy immune system function:** Formation and maturation of red blood cells, white blood cells, and platelet production.
- **Histamine breakdown:** A methyl group binds to histamine, causing the histamine to break apart.
- **Glutathione production:** Stimulation of the body's primary antioxidant and detoxifier. Glutathione prevents the accumulation of toxins in the body and protects us from oxidative stress, which also leads to premature aging.
- **Neurotransmitter production:** Makes and breaks down various neurotransmitters, such as epinephrine, dopamine, serotonin, and melatonin.
- **Detoxification:** This includes both internally produced hormones and the hormone-like chemicals we are exposed to externally, as well as any other drug, heavy metal, or toxin.

- **Energy production:** Essential to the production of many of the substances required to keep mitochondria producing proper amounts of ATP, our body's form of usable energy.
- **Myelination of nerves:** Myelin is the coating that covers and protects our nerves. It is made of fatty acids and amino acids that require methylation for their production.
- **Immune function:** Specifically, the production of T cells. T cells are needed to regulate the action of B cells. B cells are responsible for antibody production. Therefore, an excess can lead to an increase in allergic and/or autoimmune responses. Our bodies also use methylation to silence the expression of a virus as it buries itself in our DNA.
- **Cancer cell elimination:** This is a scary thought, but the potential for tumor development exists in our bodies at all times. Methylation is used both to produce the immune cell that kill these cancer cells and/or to regulate the cell's gene expression (turning it off). Hooray for methylation.
- **Production of certain nutrients:** CoQ10, carnitine, creatine, and ATP (the body's usable form of energy).

The MTHFR Genetic Defect

I titled this section "The MTHFR Genetic Defect" to keep you on your toes. There isn't ever just a single way that a gene can mutate. It's a real mutation jungle out there. The amount of mutations that a single gene can have would make your head spin. The thing is, because of what we discussed earlier in this lesson- they're not all important. Researchers spend a lot of time determining which mutations actually are important.

Of the at least fifty known variants to the MTHFR gene, the two primary ones are known as C677T and A1298C.

MTHFR is a gene that holds instructions for the production of an enzyme called methyl-tetrahydrofolate reductase. This gene is only one in a pathway of genes and enzymes involved in the process of methylation- BUT- this one occurs at a critical point in the process (like the instruction that says, "Hey, dummy! Take the cake out of the oven so that you don't burn the house down!") where the substance known as a "methyl group" is added to the vitamin known as folate, creating a new substance called "methylfolate". Both SNPs mentioned above, but particularly the C677T SNP, may cause a deficiency of methylfolate in your body. Big whoop. Who needs methylfolate, anyway? Take a look at the list above, of the things that methylation does in your body and tell me again that you don't need it. I dare you. When methylation slows down, your resistance to infections and pathogens decreases, you have less protection against free radical damage in your body, and many other things- all which can lead to an increase in the amount of toxins in your body.

About 45-50 percent of caucasians carry the at least one copy of the C677T mutation. This percentage may rise even higher for those of French, Spanish, Italian, Asian, or Mexican origin. Remember from earlier, heterozygous means that you carry 1 copy of the mutation. Homozygous means that you carry 2. The more copies, the more significantly it will affect enzyme function. While this is all still a very new science, it seems to shake out something like this:

MTHFR A1298C Heterozygous = 20% loss of function
MTHFR A1298C Homozygous = 40% loss of function
MTHFR C677T Heterozygous = 40% loss of function
MTHFR C677T Homozygous = 75% loss of function
A combination of one C677T and one A1298C defects (sometimes called "compound heterozygous") = 40% loss of function

So what does this mean for you? Hopefully nothing... but maybe something. These particular gene mutations (and to a lesser extent,

some other genes in the methylation pathway) can increase your risk of a number of serious health conditions. At the risk of sounding like broken record, I'll say this again- Your genes are not your destiny- but, sometimes they help to explain how we've gotten ourselves into a bummer of a situation, and paint a clearer picture of the path to digging ourselves out of the hole. Not every individual with mutations in this pathway will have one of the health conditions that listed out below. The mutation may be a critical predisposing factor, but without a sufficient environmental or infectious "triggers", you may still be able to count yourself among the healthy. So, keeping in mind that most conditions are the result of a number of factors, MTHFR and other methylation pathway genetic defects are tied to a wide variety of conditions:

Autism	**Down's syndrome**	**Addictive behaviors**
Frequent miscarriages	**Male and female infertility**	**Blood clots**
Depression	**Anxiety**	**Schizophrenia**
Bipolar disorder	**Fibromyalgia**	**Chronic fatigue syndrome**
Chemical sensitivity	**Parkinson's disease**	**Irritable bowel syndrome**
Stroke	**Cleft palate**	**Tongue tie**
Migraines	**High homocysteine levels**	**Breast cancer**
Atherosclerosis	**Low T or NK cells**	**Alzheimer's**
Multiple sclerosis	**Heart attack**	**Methotrexate toxicity**
Nitrous oxide toxicity	**Histamine intolerance**	**Diabetes**
Chronic Viral Infections	**Cancer**	**Seizure disorders**
Insomnia	**Bipolar disorder**	**Allergies**
Spina Bifida/Neural Tube Defects	**Autoimmune disorders**	**Hashimoto's or hypothyroidism**
Autoimmune disorders	**ADD or ADHD**	**Dementia**
Neuropathy	**Lyme disease***	

**Methylation isn't the cause of Lyme disease, but explains why some people are much more prone to becoming chronically ill from it than others.*

Letting Your Genetics Be Your Guide

If our genetic code is a worthy instruction manual for something as wonderful as our bodies on the inside, it should be good enough for us to use on the outside as well, to make better diet and lifestyle choices for ourselves.

When you've been battling an array of health issues for some time, trying to figure this stuff out for yourself can make your head spin. You may find a great benefit in the guidance of a professional, trained in nutrition and holistic care. They can help you understand things like, why can't I tolerate this GAPS-friendly food when other people can? Why do I have trouble sleeping after I've been on the computer when it doesn't bother my husband at all? Why do I seem to be more debilitated by stress than my friends? They can help to guide you through a targeted supplementation program that addresses your individual needs, taking both nature and nurture into account. Sometimes a nutrient (like methylfolate) that would seem to be beneficial from a genetic standpoint for someone with an MTHFR defect, can prove to worsen the situation if things like inflammation, stress, and dysbiosis are not dealt with first.

I've focused mostly on methylation and MTHFR defects in this lesson because in its oversight of our epigenetics, it has earned a special place among genes. But, as part of a full genetics panel, you'll receive information about many more genes. Here is a very abbreviated list of some of the heavy-hitters and their functions:

Gene	Function
GIF	Formation of a substance known as intrinsic factor, critical to the absorption of B12
HNMT	Breaks down histamine inside cells

Gene	Function
DAO	Breaks down histamine outside of cells
COMT	Breaks down epinephrine, norepinephrine, dopamine, and estrogen
MAO	Breaks down serotonin, melatonin, epinephrine, and norepinephrine
HLA	Various HLA genes predispose to various types of allergies and autoimmune conditions
GST	Transfers glutathione to a free radical, protecting our cells from destruction
FUT2	Determines the amount of “attachment sites” you have for bacteria, both good and bad

What Interferes With Methylation?

Now let’s talk a little about some things outside of our genetics that can further slow an already genetically sluggish methylation pathway. First at bat is cofactors. Remember, enzymes need cofactors the way a car needs keys, but also wheels, gas, an engine, etc. These nutrients are absolutely necessary to help make the methylation pathway run:

Zinc	**Vitamin B2 (riboflavin)**	**Magnesium**
Vitamin B6 (pyridoxine)	**Vitamin B12**	**Folate (from food or folinic acid)**

In a frustrating catch-22 situation, some health conditions that are associated with methylation defects may muck methylation up even more by decreasing the absorption (or cause a depletion) of the nutrients listed above:

Celiac disease	**Crohn’s disease**	**Irritable bowel disease**
Ulcerative colitis	**Lyme disease**	

And if that wasn’t enough, certain drugs may also rob us of these vital nutrients. Or they may prevent one of our poor little enzymes from functioning- or they may overwhelm the entire methylation cycle,

altogether. I'm likely preaching to the choir here, but in most cases, drugs are a really bad idea! Here is a list of drugs and nutrients to be leery of when you have genetic defects in the methylation pathway:

- **Folic acid** (in both vitamins & fortified foods). It is a synthetic form of folate that is not processed easily in the body, and may even block absorption of more natural, more useable forms. Stick with the natural forms like folinic acid, calcium folinate, and 5-methyltetrahydrofolate.

- **Folate-blocking or depleting drugs**, such as birth control pills or Methyltrexate.

- **Proton pump inhibitors** (Prilosec or Prevacid) or **antacids** (like Tums). They block vitamin B12 absorption. Grrr.

- **Nitrous oxide** (laughing gas). This is used as anesthesia in various dental and surgical procedures. Not such a laughing matter.

- **Corticosteroids or estrogen-containing drugs**. Your body uses methylation to break these hormones down, so you may end up with too many of them in your system.

- **Nutrients that deplete methyl groups**. This includes things like high-dose niacin, or the prescription versions called Slo-Niacin and Niaspan.

- **Cholesterol-binding drugs** (such as Cholestyramine and Colestipol). These drugs not only deplete vitamins A, D, E and K, but also reduce absorption of folate and cobalamin from your food!

- **Anti-seizure drugs**. *Please do not stop taking any of these without consulting your doctor! If you would like to wean off of them or find a better alternative, you'll need your physician's help.* The worst offenders

for people with methylation defects include carbamazepine, oxcarbazepine, phenytoin and valproic acid, as they block folate absorption.
- **Sulfa-containing drugs** (like Sulfamethoxazole and trimethoprim). These drugs inhibit an enzyme in the pathway that is responsible for creating methylfolate.

* Although all of these drugs cause a functional depletion of folate, if you are taking them, do not supplement with folic acid (or any other form of folate) without the approval of your physician and/or pharmacist. In some cases, supplementation may cause the drug not to be effective.

While we're on our listing-things-out roll, here are a few more random things that may interfere with the methylation cycle:

- **Drinking alcohol in excess**. This blocks the methylation pathway, which severely depletes glutathione stores and production. Hangover, anyone?
- **Green coffee bean extract and other high dose antioxidants**. These place a high demand on methylation pathway nutrients and may deplete them with long-term use.
- **Candida**. Candida actually releases a toxic metabolite that is identical to that of alcohol!
- **Stress or anxiety**. Being chronically stressed out can deplete our body of nutrients required for methylation AND cause an increase in the need for methylation due to stress-related tissue damage. Double whammy!
- **Inflammation caused by allergenic substances**. This is often due to one or more of those "Four Horsemen" - wheat, dairy, egg, and soy. It can sometimes also include environmental irritants such as molds, pollens, pet dander, and the like. The inflammation caused by these allergies creates oxidative stress, placing an undue burden on the methylation cycle.

What Can We Do To Help Methylation?

If you're feeling like there must be more that you can do to be positively glowing, despite these genetic mutations, you're right... I'll leave you with the following things that you can and should do, both to feel better and to stay well:

- **Filter chlorine, fluoride, and other contaminants** from your drinking, shower, and bath water.
- **Use an air purifier** in your home and office.
- **Eliminate carpets** from your home and install low VOC wood or tile flooring.
- **Avoid exposure to synthetic chemicals** with known toxicity.
- **Avoid heavy metal exposure**. Remove mercury amalgams with a trained biologic dentist. Avoid aluminum exposure in antiperspirants or cookware.
- **Avoid** cooking, drinking, storing and heating in any type of **plastic** container.
- **Drink at least 60 oz of filtered water** per day with sea salt and/or minerals (electrolytes) added.
- **Eat slowly and peacefully**, including some form of protein and/or fat with meals and snacks.
- **Avoid eating processed foods**. Eat whole foods with no added chemicals or preservatives.
- Get your **daily intake of leafy greens**, like kale, parsley, and arugula, which are loaded with natural folate that your body can more easily process.
- **Eat hormone-free, grass-fed** beef, organic pastured butter or ghee, and organic eggs.
- **Eliminate all forms of gluten** from your diet.
- **Eliminate or reduce dairy products** in your diet. If you tolerate dairy products, make sure that they are unpasteurized. Cultured dairy products and/or sheep or goat milk may be better accepted.

- In short, **decrease all sources of inflammation** in your body.
- Use **castor oil packs** over your abdomen to relieve pain.
- Do **coffee enemas** to help with inflammation and detoxification.
- **Several times per week**, include activities that support gentle detoxification, (infrared sauna, epsom salt baths, rebounding, dry brushing, stretching, appropriate levels of exercise, massage, sweating, etc.).

STEPS TO TAKE

Along with this workbook, I have put together a **QuickSheet** for you that will guide you in the genetic testing process, if you choose to do so. That QuickSheet can be downloaded by **clicking here**.

WHAT'S NEXT

In Module 5, we will cover the topic of thyroid health within the GAPS template.