Youngevity Nutrigenetics Handbook

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Letter From Sanjeev Javia

One test, a lifetime of critical understanding – Youngevity Nutrigenetics revolutionizes the way individuals relate to their nutrition and dietary lifestyle. This simple test unlocks the power of Single-Nucleotide Polymorphisms (SNPs). These tiny alterations in DNA patterns can reveal underlying genetic tendencies and predispositions.

Youngevity Nutrigenetics **examines 35 different SNPs** to expose thousands of unique genetic combinations.

Youngevity Nutrigeneticsoffers insights into **6 major categories** of weight management and wellness.

- **General Health:** Some genes show a predisposition to increased health risks. These genes show correlations between diet and exercise that can affect certain cardiovascular functions.

- **Risk of Obesity:** Specific genes correlate to the buildup of fat tissue in the body. How much a person weighs and how that fat tissue is distributed in the body depends largely on individual genetic makeup. Knowing this information provides a better assessment of what size and weight is realistic.

- **Food Choices:** Certain genetic variations relate directly to food processing such as how the body reacts to fat, protein and carbohydrates. These variations, as well as an individual's eating habits combine to give an overall picture of how you will react to certain food groups.

- **Exercise & Activity:** Our bodies are made up of two kinds of muscles: slow and fast twitch. Each individual's genetics favors one over the other and this

information can direct you to the type of exercises you should employ to burn fat, regulate your blood pressure as well as your cholesterol levels.

- **Behavior & Motivation:** Some genetic inclinations determine how easy or difficult it is to make good choices concerning foods. When you know your genetic tendencies to cravings and food reactions, they can better manage situations where they may overeat.

- **Nutrients:** Some genetic markers show gaps in a patient's ability to process vitamins in a way that will maximize their ability to use them. Knowing where the deficiency is allows you to complement your diet with the nutrients you may be challenged with. Many nutrients help directly in weight loss and the metabolism of fat.

The information that you obtain from this test will change your life and the life of your children for generations to come!

Sanjeev Javia
"Do What You Can, When You Can, The Best You Can"

What's In Your "Genes"?

The Role Of Genetics On Nutrition

It's now been over two decades since the Human Genome project began and the human genome has been sequenced. Enormous amounts of resources in scientific, academic, and clinical have been spent, along with over $10 Billion, to better understand the human individuality of dietary preferences and health traits.

We have been inundated over the countless years of how best to live a long, healthy, vital life through various dietary lifestyles. Low carbohydrate, high protein, low fat, high fat, inflammatory based foods, alkalinity measures, all have surmounted to little stability and certainty of energy, proper weight, and optimal health. Living in these extremes may be many; however thriving in these extreme nutritional preferences is few. The vast majority of us perform not only best for the long term, but also with immediate results, with a more moderate and easier to follow approach. Understanding the role your genes play allows you to best optimize the nutritional environment around you so that you can better achieve your health goals.

Genetics of weight management

Where the study of nutritional genetics has made significant impacts in health is in the areas of weight loss. In the most advanced countries, such as Europe, where preventative medicine and lifestyle education is stressed, using genetic data to create nutritional plans has become the norm. Much of an individual's weight management success depends on the certainty they feel with their strategy and plan. Genetic data offers this hard evidence that not only allows a deep scientific proof of what is best for the individual but also the certainty that gives them the confidence that the recommendations are right for them.

Genetic tests such as YGY NutriGenetics can provide information that pertains to nutrient choices and weight management. For example; are there any issues with fat absorption or metabolism, insulin resistance, taste perception or even food addictions that result in constant cravings. Genetic information can help to focus and cut out a lot of the trial and error often involved in the nutrient choices you make from foods and supplements.

The "Evolution" Of Nutrigenetics

Understanding NutriGenetics

Nutrigenetics or Nutritional Genomics, is the field of study that examines the relationship between the nutrition, and specifically the nutrients in your food, and your genes. The relationship does not exclude itself to just the nutrients found in your foods, but also in various dietary supplements and non-food products containing nutrients. For the most part, each of us are similar in how we breakdown, process, and metabolize foods and their nutrients. However, there can be slight differences, that can cause impairments, that can cause these functions to be less optimal. Understanding your DNA, through the study of Nutrigenetics, helps you to optimize your nutritional lifestyle.

The Evolution Of Your Nutrient Genes

How you respond to the constant environmental factors that relate to your dietary and daily lifestyles is what surmounts to your overall health and wellness. As the various factors interact with your body, and more specifically your genes, you determine the responses which will dictate your overall health and performance.

For the most part, all of us respond to our dietary habits in a similar fashion. The fundamental processes that make up our food and nutrient metabolism is the same because 99% of our genetic make up is identical. However, there is that 1%. This 1%, although small, can lead to very large differences in how we will respond to our nutrition

and most importantly, the resulting of nutrition that is not aligned with our genetic make up.

Human health is the result of constant interaction between genes and environmental factors. The most significant environmental factors are our diets and daily lifestyles.

For example, descendants of hunting tribes are better-suited for high-protein diets while descendants of farming tribes are better-suited for high-carbohydrate diets.

These variations in food metabolism and nutritional requirements are the result of millions of years of evolution. As we evolved we also began to transition from one dietary lifestyle to another. The entire process of natural selection allowed us to better be suited for our environmental and dietary environment. All this evolution and transition created minor differences in all of us and although, for the most part, we will be similar to what foods and lifestyles that will create survival, the aligning to our differences allows for optimization.

The "Thrifty" Genes

When food sources were limited during the hunter-gather years, almost 3 million years ago, we developed a human genome that developed "thrifty genes". These genes were incredibly beneficial due to the every changing landscape of food scarcity and abundance. There was more scarcity than abundance, therefore these genes promoted the efficient food utilization, fat deposition, and rapid weight gain when there was an abundance of food, preparing for a likely chance of food shortage. This delicate process was advantages to us 3 million years ago.

Further genetic advantages developed a couple hundred thousand years ago when we began to domesticate plants and animals. Although food was more readily available, significantly reducing the chance of survival during low production years, the variety of diet became less diverse. In addition, crops and livestock were regionally dependent due to climate and environments, hence genetic variations suited for regional diets evolved.

The most dramatic transition of the human diet occurred within the last century. Industrialized food production made all kinds of food available in excess at extremely low prices. Since then, overeating has become an epidemic, especially in affluent Western countries. The advances of modern technology have also led to an increase in sedentary lifestyles and overall lower energy expenditure. This combination has resulted in rapid weight gain among human populations.

Regardless of these dietary changes, the human genome has remained almost the same over the last 100 years. The 200 or so "thrifty genes" that were once

advantageous are incompatible with modern diets and has caused use to be plagued by a variety of health concerns.

Importance Of Your Genetic MakeUp

- Understand your body's response to the basic types of nutrients (carbohydrates, saturated, monounsaturated and polyunsaturated fatty acids)
- Review of a number of important health factors, such as genetic predisposition to obesity, inadequate nutrition, triglyceride and blood sugar levels, bone density, etc.
- Calculation of the genetic risk for lacking the most important vitamins and minerals
- Based on your genetic makeup, an assessment of many other features, such as metabolic characteristics, exposure to oxidative stress, perception of taste and smell, and other factors that influence diet and lifestyle.
- Choosing the correct dietary and nutraceutical supplements to help support your health goals
- Establishment of dietary guidelines and lifestyle guidance based on the findings from personal genetic makeup

Key Terms

Chromosome - a rod-like form of the DNA molecule containing many hundreds or thousands of genes. The nucleus contains 22 autosomal chromosome pairs as well as one pair of sex chromosomes. In addition to the DNA molecule, there are proteins (mainly the histones) around which the DNA wraps. Such wrapping and further transformation result in a tightly formed chromosome taking up much less space than in an unfolded form.

Chromosome (sex) - there are two types of chromosomes: X (female) and Y (male). Women have two X chromosomes in a pair (XX) while men have an X and a Y

chromosome (XY); the Y chromosome is inherited only from the father and its presence in the fetal development results in the creation of a male child.

DNA molecule - a molecule found in the cell nucleus that carries instructions for the creation of an organism. The human DNA, constructed from four different nucleotides, has a form of a double helix, meaning that two complementary DNA strands wind around each other. Complementary means that nucleotide C always pairs with G and A always with T.

Gene - the code in a DNA sequence which carries information for protein formation. Genes are passed on from parents to children and give all the information needed for the formation and development of an organism.

Genome - the entire DNA found in the cell nucleus that contains all autosomal chromosomes and both sex chromosomes.

Phenotype - the visible characteristics of an individual, such as the hair colour, as well as the presence or absence of disease. The expression of a phenotype is influenced by the genotype as well as the individual's environment.

SNP (Single Nucleotide Polymorphism) - a DNA sequence marker, formed by one nucleotide substitution (e.g. A→ C) at a specific point. It represents a variation in the genetic code which may be different in different people. These small variations, however, may be very numerous for there are 30 million SNPs in a human genome. This very variability dictates the phenotype differences among individual people. Research in this area was fuelled by the finding that certain SNPs are linked with or more prevalent in certain diseases or traits. The results of these studies (association studies) form a theoretical background for the services that GenePlanet provides.

Epigenetics - is the study of heritable changes in gene expression (active versus inactive genes) that does not involve changes to the underlying DNA sequence — a change in **phenotype** without a change in **genotype** — which in turn affects how cells read the genes. Epigenetic change is a regular and natural occurrence but can also be influenced by several factors including age, the environment/lifestyle, and disease state.

What Your Gene's "Talk" About

Satiety & Satiation

Low Satiety/Satiation is the inability to feel fullness after a meal and/or not respond quickly to when your body has had enough. If you have low satiety, you have a tendency to overeat. About 13-15% people in the normal population and 49-55% in the overweight and obese populations have low satiety. More than 50 genes have been reported to regulate satiety in humans including FTO and MC4R.

What causes low satiety?

Low satiety can be genetic. About 50 genes that regulate satiety in humans have been reported, of which FTO and MC4R are the two best known examples.

How many people have a low satiety?

About 49-56% of people have mild low satiety and 13-15% have severe low satiety. The percentage of those with severe low satiety is higher in overweight and obese (49-55%) populations.

What are common eating behaviors of people with low satiety?

People with low satiety tend to eat larger portions, eat more energy-dense, high-fat, high-sugar foods, and continue eating even after meals. Consequently, people with low satiety eat 10% more calories per meal than people with normal satiety.

What can I do to lose weight?

If you experience low satiety, you should pay close attention to your portion sizes and food choices. Smarter food choices can help you avoid energy-dense and nutrition-sparse foods while portion control keeps your meals at sensible sizes. Consume foods and nutritional aids, such as dietary supplements, that have high fiber and high protein. Eat foods with greater bulk, such as uncooked vegetables, also pause between eating.

Enzyme System

When there is a lack of enzymes, the body cannot utilize the nutrients it needs. This triggers fat storage and stimulates the appetite, causing weight gain and food cravings. Although enzymes are often associated with digestion, this is not their only function. Enzymes are complex proteins that facilitate hundreds of activities throughout the body. They are responsible for the use of vitamins and minerals, the regulation of hormones, and the health of the immune system. Enzymes also play an important role in detoxification, a vital component of weight loss. Even basic activities like breathing and talking rely on the presence of metabolic enzymes.

It's important to understand that most of society no longer functions in a way that's conducive to proper enzyme and digestive function.

Activing Metabolism

Low metabolism or metabolic rate, causes your body to expend less energy than normal on maintaining its basic functions like breathing, temperature, and your heart rate. A low basal metabolic rate normally leads to weight gain because your energy intake outweighs your low energy expenditure. More than 18% men and 25% women in the US have a low metabolism. Variations in the ADIPOQ and UPC2 genes are associated with increased risk for low metabolism.

What causes low metabolism?

Low metabolism has been linked to both genetic and environmental factors. People with certain risk variants of genes involved in converting carbohydrates and lipids into energy.

Medical conditions, such as hypothyroidism and anemia, or use of certain medications, such as beta-blockers (i.e. propranolol) and pain relievers (i.e. methadone), can also cause low metabolism. Over-consumption of foods including broccoli, cauliflower, tofu, soy milk, strawberries, pears and peaches can lower metabolism, as can deficiencies of nutrients such as iron and vitamin C.

How many people have low metabolism?

It is unclear how many people have a low metabolism. In the United States, 9.2% adults have been diagnosed with hypothyroidism; this number is greater for women aged 50 or older. Anemia affects about 14% men and 30% women worldwide and is caused by iron deficiency, which can lead to low metabolism.

What do people with low metabolism have in common?

People with low metabolism experience many symptoms related to lack of energy, the most common being: fatigue, low heartrate, heightened sensitivity to cold, and dry skin, brittle fingernails, thinning hair and even hair loss.

What can I do to lose weight?

If you have a low metabolism, you can manage your weight by exercising and eating metabolism-boosting foods.

Emotional Eating (Appetite Suppression)

Emotional eating is when you eat for reasons besides hunger. It is driven by genes involved in the reward system in your brain. About 40% of people experience emotional eating and about 3.5% of women and 2% of men are diagnosed with binge eating disorder, a severe type of emotional eating, at some point in their life. Variants of DRD2 and OPRM1 genes are associated with increased risk for emotional eating and binge eating disorder.

What causes emotional eating?

Emotional eating is driven by the brain's reward system; it remembers when you enjoy particular foods and seeks them out during times of emotional stress. These foods, called trigger foods, act like drugs by eliciting positive emotional responses and fostering cravings.

Malnutrition can also trigger mood swings and emotional eating. It causes the brain to send the body a signal that it needs food to fulfill a nutritional need. However, most people do not understand what their bodies are trying to tell them and turn to familiar foods to try to satisfy their cravings. This is particularly harmful for those who regularly eat high-fat and high-sugar foods because their diets are high in calories but low in nutrients. The result is a vicious cycle of continued malnutrition, mood swings, emotional eating, and weight gain.

People with risk variants of certain genes involved in the brain reward system, such as DRD2 and OPRM1, are more likely to be emotional eaters. Those with both DRD2 and OPRM1 risk variants have the greatest risk for binge eating disorder.

How many people experience emotional eating?

About 40% of all people have experienced emotional eating. In general, women are more susceptible to emotional eating than men. About 3.5% of women and 2% of men are diagnosed with binge eating disorder at some point in their life.

What are the eating behaviors of people with emotional eating?

People who exhibit emotional eating behaviors typically enjoy energy-dense snacks such as nuts, dried fruits, cakes, pastries and biscuits. Each emotional eater has their own personal trigger foods. When combined, emotional eating and low satiety can turn a small snack into a full-blown calorie bomb; what starts as one cookie can easily become a whole box.

What should I do to control emotional eating?

See if you are lacking key nutrients in your diet. Identifying what nutrients you are lacking, you can follow the tips provided to correct your nutrition imbalance.

Next, take basic steps to manage your emotional eating episodes. Do not buy or keep your trigger foods in your home. Instead, pre-portion out healthy snacks in small bags or containers and eat those instead when you feel any cravings. This way you can cut down on calories and boost your mood at the same time.

Gene Responsibility

FTO

Much of weight gain can be caused by overeating, which leads to overweight and obesity in a long run. Unfortunately, we are genetically predisposed to overeating. The genes which were once beneficial to our ancestors during food shortages are now liabilities in today's environment of food excess. To date, over 50 obesity risk genes have been identified.

The fat mass and obesity–associated gene, FTO, was the first obesity risk gene identified by genome wide association studies. While the molecular mechanism of the FTO gene is not well understood, epidemiological studies and animal models have confirmed its function in the hypothalamus of brain, an area responsible for the regulation of appetite and satiety. Appetite is the desire to eat while satiety is the sensation of fullness after eating. In general, people with low satiety continue to have an appetite to eat while people with a high satiety lose their appetite after meals. Studies

also conclude that the FTO gene does not play any role in basal metabolic rate or any other type of energy expenditure.

People with FTO risk variants are more likely to overeat due to low satiety. Eating behaviors associated with a low satiety include: 1) eating larger portions (more calories) ; 2) preferring calorie-dense foods that are high in fat and sugar, such as biscuits, cakes, pastries, cheese, fatty meats, etc.; 3) enjoying palatable foods (mostly appetizers, desserts and snacks) after already having eaten a meal; and 4) snacking more frequently.

For carriers of FTO risk variants, satiety control should be the first priority for weight management.

MCM6

All mammals are born with the ability to digest lactose, a sugar abundant in milk for the nourishment of newborns until weaning. Lactose itself cannot be absorbed by the intestine and must be broken down into absorbable sugars (glucose and galactose) by lactase anchored on the surface of the small intestine epithelial cells. Lactase (also called lactase-phlorizin hydrolase (LPH) in humans) is encoded by the lactase gene (LCT) on human chromosome 2 (2q21). Regulation of the lactase gene, and therefore the ability to digest lactose, is actually found in an adjacent gene called MCM6 (minichromosome maintenance complex component 6).

The expression of lactase in the small intestine usually declines gradually after weaning resulting in adult mammals gradually losing the ability to digest lactose. Some humans continue to have normal lactase expression (called Lactase Persistence, LP), and can enjoy milk and other dairy foods into adulthood, while others have an insufficient level of lactase to digest dairy foods properly. For those people, dairy products cause indigestion (so called lactose intolerance) because undigested lactose stimulates fast growth of gas-producing gut bacteria.

DRD2

Emotional eating is driven by emotional cues like depression, anxiety, happiness, sadness, and boredom rather than hunger. By engaging in emotional eating, we are subconsciously seeking comfort or pleasure from food.

Emotional eating can lead to weight gain for people who also have a low satiety. In severe cases, it can lead to binge eating, also known as compulsive eating. Binge eating is a subtype of emotional eating. When emotional eating is out of control over what or how much an individual eats, it becomes binge eating disorder. About 3.5% of women and 2% of men in the United States are diagnosed with binge eating disorder at some point in their life.

Emotional eating is mainly regulated by the reward systems in the brain. The four aspects of the brain reward system: motivation (wanting), outcome (liking), memory (learning) and habituation (adapting) determine how a cue (food, drug, money, promotion etc.) is perceived, liked, memorized, expected or even forgotten.

The rewarding properties of foods, mainly the palatability, act like addictive substance (such as alcohol or marijuana) in the reward system of human brain to produce the feeling of pleasure. Palatability is the overall attractiveness of a food judged by its flavor, taste and texture. In human population, sweet (i.e., high-sugar) and high-fat diets are generally considered palatable. Although most people like fatty and sugary foods to various levels, not all of us are “sweet tooth”. Some people are rather indifferent to the tasty pleasures of life. The difference is explained in part by the genetic variations in the emotional eating genes. And there are many of them. The DRD2 and OPRM1 genes are two better understood ones.

The DRD2 gene is a key player in the dopamine neuronal circuits. Dopamine is the “feel good” neurotransmitter that motivates people for pleasure. Low level of dopamine is often blamed for depression related conditions. The OPRM1 gene, on the other hand, is a key play in the opioid neuronal circuits. Activation of the opioid neuronal circuits leads to the production of dopamine. Activities of the opioid system also determine how much you enjoy the pleasure. These neuronal circuits interact with each other and with other neuronal circuits to produce an overall “reward value” of a food. This “reward value” influences eating behaviors. An imbalanced activity among various neuronal circuits often leads to emotional eating. People suffering from binge eating disorder appear to be highly active in both the dopamine and the opioid systems.

A variation in the DRD2 gene results in a reduced dopamine function in the brain. People carrying this variation have an increased risk for addiction disorders as well as increased risk for obesity. In these individuals, palatable foods are used as passive compensatory means for the decreased dopamine activity during emotional eating. In other words, they have to eat more to get the same satisfaction (“reward value”) from the foods.

ADIPOQ

If you are overweight or obese, you have probably tried to burn off the extra fat by increasing exercise and physical activity with varying degrees of success. It turns out that not all of us can achieve the same amount of weight loss with the same amount of exercise. The reason behind this could be attributed to what kind of ADIPOQ gene you have.

The ADIPOQ gene instructs fat cells on how to make the hormone adiponectin. This hormone travels through your blood to your muscle and liver cells where it starts burning fat and triggering glucose utilization processes. By doing so, it promotes energy consumption. Therefore, a higher level of adiponectin in blood makes weight loss easier and reduces your risk for type 2 diabetes.

Two variants of the ADIPOQ gene cause cells to make less adiponectin. One is associated with a 20% reduction in adiponectin levels and the other with a 40% reduction. Decreased adiponectin levels leads to less efficient fat burning, less glucose utilization, and a greater risk of becoming overweight, obese, and developing type 2 diabetes. What is striking about these two variants is that many people carry at least one of them: up to 26% of the general population carries the variant associated with 20% reduction while up to 59% carries the variant associated with 40% reduction. These people likely have more difficulty losing weight.

LIPC

The *LIPC* gene provides instructions for making an enzyme called hepatic lipase. This enzyme is produced by liver cells and released into the bloodstream where it helps with the conversion of fat-transporting molecules called very low-density lipoproteins (VLDLs) and intermediate-density lipoproteins (IDLs) to low-density lipoproteins (LDLs). The enzyme also assists in transporting molecules called high-density lipoproteins (HDLs) that carry cholesterol and triglycerides from the blood to the liver, where the HDLs deposit these fats so they can be redistributed to other tissues or removed from the body. Hepatic lipase helps to keep these fat-transporting molecules in balance by regulating the formation of LDLs and the transport of HDLs. Normally, high levels of HDL (known as "good cholesterol") and low levels of LDL (known as "bad cholesterol") are protective against heart disease.

ADLH2

The Asian flush, sometimes called the “Asian glow,” refers to a common reaction to alcohol among East Asians. This facial flushing was found to be a result of a deficiency of a liver enzyme called ALDH2. This finding was revealed in a 1981 article in *Lancet*.

The chemical breakdown of alcohol happens primarily in the human liver and is facilitated by two major enzymes: alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH).

The defective ALDH2 allele is called ALDH2*2; it is separated from its active counterpart, ALDH2*1 by a single point mutation (G-A transition at the DNA level; the A allele at rs671=ALDH2*2). This mutation substitutes lysine (K) for glutamic acid (E) and reduces the enzyme's ability to convert acetaldehyde, a metabolic byproduct of alcohol, into acetate. Flushing is a result of an accumulation of acetaldehyde in the blood that causes dilation of the capillaries.

Acetaldehyde is a carcinogen in humans. Research has shown that facial flushing when drinking is indicative of ALDH2 deficiency, which can increase the risk of developing esophageal cancer by six to ten times. The "Asian flush" can disappear for some people later in their lives, especially if they continuously "practice" drinking. Regardless, heavy alcohol consumption still is associated with higher risk for esophageal and other types of cancers for anyone who has ever experienced the "Asian flush."

APOA2

Scientists showed that the APOA2 gene can significantly affect how a person's body reacts to what they eat. Only people who had a certain version of this gene AND ate a lot of saturated fats gained extra weight. So at least in this case, nature and nurture both play a role in body weight.

More specifically, scientists looked at how two different versions of the APOA2 gene affected a person's body mass index (BMI). BMI is usually a pretty good estimation of a person's body fat and is calculated using a person's height and weight. A BMI of 18.5 to 24.9 is "normal". Below 18.5 is underweight. A BMI of 25 up to 30 is overweight while over 30 is obese.

When people were on a diet high in saturated fats, those with one version of APOA2 had a higher BMI than people with the other version. But when people were on a diet low in saturated fats, it didn't matter what version they had. BMIs were essentially the same.

These results show that a person's APOA2 gene can affect his or her weight -- at least when they eat a lot of saturated fat.

MTHFR

Folate, also known as vitamin B9, is a water-soluble B vitamin. The synthetic version is called folic acid. Folate primarily exists in green leaves while folic acid is mainly found in supplements and fortified foods.

Folate is needed to make the building blocks of DNA and proteins. It is also required for the conversion of a “bad” amino acid, homocysteine, into an essential one, methionine. This conversion reaction is responsible for the methylation reactions (of DNA, RNA, protein, lipids, etc.) that are important for the cell to decide which genes to switch on and off (Fig.1)

When cells lack folate, the conversion of homocysteine to methionine is impaired. This may lead to hyperhomocysteinemia (high blood homocysteine) and disturbed DNA synthesis and/or DNA methylation reactions. Hyperhomocysteinemia exists in about 5% of the general population and is associated with increased risk for cardiovascular disease and many other disorders. Disturbed DNA synthesis and methylation cause DNA mutations and altered gene expression which can lead to birth defects and various cancers. Furthermore, folate deficiency causes anemia, a condition which occurs when there is insufficient hemoglobin in red blood cells to carry enough oxygen to cells and tissues.

MTHFR (methylenetetrahydrofolate reductase) is a key enzyme for folate metabolism (Fig.1). It catalyzes the irreversible conversion of one form of folate 5, 10-methylentetrahydrofolate (5, 10-MTHF) to another form 5-methyltetrahydrofolate (5-MTHF). This conversion is required to make homocysteine to methionine.

Reduced enzyme activity associated with these variants can be compensated for by increasing folate intake. People who carry one or more of these variants should strictly follow the DFE (Dietary Folate Equivalent) recommended by the Institute of Medicine of the National Academy of Sciences, USA available here. In addition to folate intake, variant carriers also need to make sure they get adequate vitamin B2, B6 and B12 which are all cofactors for enzymes involved in the different steps of folate metabolism (Fig.1).

Methionine restriction is recommended for risk variant carriers to reduce homocysteine accumulation and limit the effects of reduced MTHFR activity. Since dietary methionine is mostly found in animal proteins and folate is mainly found in vegetables, methionine restriction calls for vegetarian-orientated diets. In vegetarian diet regimens, a vitamin B12 supplement is strongly recommended since it is primarily found in animal products.

BCMO1

People with variations in the BCMO1 gene may require more vitamin A, particularly in the form of retinol found in foods from animal sources. BCMO1 is the gene that encodes

for an enzyme that converts plant-based carotenes (vitamin A precursors) to retinol that can be used by our cells. People that carry the T allele at rs12934922 and the T allele at rs7501331 have a BCMO1 enzyme that is about 60% less active than those who carry A and C alleles at these same positions. Individuals with the reduced convertor genotypes have elevated levels of carotenes and may be at risk for active vitamin A deficiency. Therefore, it is important for people that carry low-converting alleles to consume more animal-sourced vitamin A to prevent vitamin A deficiency.

CMO1

Carotenoids are currently investigated regarding their potential to lower the risk of chronic disease and to combat vitamin A deficiency in humans. These plant-derived compounds must be cleaved and metabolically converted by intrinsic carotenoid oxygenases to support the panoply of vitamin A-dependent physiological processes. Two different carotenoid-cleaving enzymes were identified in mammals, the classical carotenoid-15,15′-oxygenase (CMO1) and a putative carotenoid-9′,10′-oxygenase (CMO2). To analyze the role of CMO1 in mammalian physiology, here we disrupted the corresponding gene by targeted homologous recombination in mice. On a diet providing β-carotene as major vitamin A precursor, vitamin A levels fell dramatically in several tissues examined. Instead, this mouse mutant accumulated the provitamin in large quantities (*e.g.* as seen by an orange coloring of adipose tissues). Besides impairments in β-carotene metabolism, CMO1 deficiency more generally interfered with lipid homeostasis. Even on a vitamin A-sufficient chow, *CMO1*$^{-/-}$ mice developed a fatty liver and displayed altered serum lipid levels with elevated serum unesterified fatty acids. Additionally, this mouse mutant was more susceptible to high fat diet-induced impairments in fatty acid metabolism. Quantitative reverse transcription-PCR analysis revealed that the expression of peroxisome proliferator-activated receptor γ-regulated marker genes related to adipogenesis was elevated in visceral adipose tissues. Thus, our study identifies CMO1 as the key enzyme for vitamin A production and provides evidence for a role of carotenoids as more general regulators of lipid metabolism.

Plant carotenoids are an important dietary source of vitamin A (retinol and its esters) and the sole source of vitamin A for vegetarians. The first step in the conversion of dietary provitamin A carotenoids to vitamin A is the cleavage of the central carbon 15,15′-double bond in carotenoid substrates. This reaction is catalyzed by the cytoplasmic enzyme carotenoid 15,15′-monooxygenase (CMO1)[8](previously termed *β*-carotene 15,15′-monooxygenase) in the epithelial cells of the small intestinal mucosa

(1,2). The most common carotenoid substrate for CMO1 is *β*-carotene, which is cleaved by the enzyme to form 2 molecules of retinal (retinaldehyde). The retinal formed is further converted to retinol and subsequently to retinol esters in the epithelial cells of the intestinal mucosa and then transported in chylomicrons to the liver, the main organ for vitamin A storage. Importantly, numerous studies have shown that a substantial amount of the absorbed dietary carotenoids are not cleaved by the CMO1 enzyme in the human intestine, suggesting that the CMO1 enzyme is saturated during normal dietary conditions. Carotenoids that escape the CMO1 enzyme are also incorporated into chylomicrons together with other lipids and the majority of carotenoids circulating in the blood are associated with low and high density lipoprotein particles and hence are taken up in tissues via the LDL receptor. CMO1 has been shown to be highly expressed in the epithelial cells of a variety of extraintestinal tissues, which suggests that the enzyme may constitute a back-up pathway for vitamin A synthesis during times of insufficient dietary intake of vitamin A. An important feature of the enzyme is that only 1 unsubstituted *β*-ionone ring half-site is required for efficient 15,15′-double bond cleavage; hence, in addition to *β*-carotene, there are ~50 additional known provitamin A carotenoids found in nature that can each form 1 molecule of retinal.

COMT

The *COMT* gene provides instructions for making an enzyme called catechol-O-methyltransferase. Two versions of this enzyme are made from the gene. The longer form, called membrane-bound catechol-O-methyltransferase (MB-COMT), is chiefly produced by nerve cells in the brain. Other tissues, including the liver, kidneys, and blood, produce a shorter form of the enzyme called soluble catechol-O-methyltransferase (S-COMT). This form of the enzyme helps control the levels of certain hormones.

In the brain, catechol-O-methyltransferase helps break down certain chemical messengers called neurotransmitters. These chemicals conduct signals from one nerve cell to another. Catechol-O-methyltransferase is particularly important in an area at the front of the brain called the prefrontal cortex, which organizes and coordinates information from other parts of the brain. This region is involved with personality, planning, inhibition of behaviors, abstract thinking, emotion, and working (short-term) memory. To function efficiently, the prefrontal cortex requires signaling by neurotransmitters such as dopamine and norepinephrine. Catechol-O-methyltransferase helps maintain appropriate levels of these neurotransmitters in this part of the brain.

CYP1A2

The **CYP1A2** gene encodes a member of the cytochrome p450 family of proteins, which metabolize nutrients and drugs. One well known substrate of CYP1A2 is caffeine; individuals who carry one or more CYP1A2*1C alleles are "slow" caffeine metabolizers, whereas carriers of the variant CYP1A2*1F are "fast" caffeine metabolizers. The same amount of caffeine will therefore tend to have more stimulating effect on CYP1A2 slow metabolizers than on CYP1A2 fast metabolizers.

CYP1A2 can also be stimulated or inhibited by numerous medications and food-drug interactions. Fluoroquinolones, for example, are both metabolized by, and inhibit, the CYP1A2 enyzyme. This can slow the breakdown of caffeine, for example, leading to caffeine overstimulation. Conversely, smoking is a well-known activator of CYP1A2 (especially the CYP1A2*1F form), resulting in faster breakdown of drugs metabolized by CYP1A2 and the possibility of insufficient drug concentrations in the body to yield much therapeutic benefit.

FUT2

The role of genetics and our health is a rapidly evolving field of study and interest, and researchers continue to produce breakthroughs in understanding this relationship. New developments continue to emerge regarding the role of our genetics and the functionality of our gut flora microbes.

Recent research has identified a key gene that influences gut bacteria in a major way. This gene is known as FUT2, or fucosyltransferase 2. Genetic mutations in FUT2 has shown to be a link towards decreases in bifidobacterium, a key, beneficial microbial colony that lines the gut. Additionally, research shows that FUT2 mutations are strongly associated with Crohn's Disease, an inflammatory and autoimmune bowel condition.

FUT2 is involved in the formation of an immune complex known as the H antigen. FUT2 forms a sugar-polymer known as oligosaccharide. Oligosaccharides become food for gut flora. FUT2 regulates the expression of certain "blood-group antigens", and as such directly influence bowel flora concentrations. Approximately 20% of the population have FUT2 gene mutations.

Carriers of the FUT2 (fucosyltransferase 2) genetic mutations have been shown to have lower concentrations of the gut microbe, bifidobacterium, as well as a greater predisposition towards Crohn's Disease and elevated serum concentrations of Vitamin B-12. Interestingly, these FUT2 "non-secretors" appear to have a greater resistance

towards certain pathogenic infections such as H Pylori, as well as protection against certain viruses.

GC

The protein encoded by this gene belongs to the albumin gene family. It is a multifunctional protein found in plasma, ascitic fluid, cerebrospinal fluid and on the surface of many cell types. It binds to vitamin D and its plasma metabolites and transports them to target tissues. Alternatively spliced transcript variants encoding different isoforms have been found for this gene.

Vitamin D binding protein (DBP) is the major carrier protein of 25-hydroxyvitamin D (25(OH) D) in the circulation, where it may serve roles in maintaining stable levels during times of decreased 25(OH) availability and in regulating delivery of 25(OH) D to target tissues. Several genetic polymorphisms of DBP have been described that lead to phenotypic changes in the protein that may affect affinity, activity, and concentration. These polymorphisms have been linked with alterations in bone density in several populations. One of the mechanisms by which DBP may alter bone health involves regulating vitamin D bioavailability. DBP-bound vitamin is thought to be relatively unavailable to target tissues, and thus alterations in DBP levels or affinity could lead to changes in vitamin D bioactivity. As a result, functional vitamin D status may differ greatly between individuals with similar total 25(OH) D levels. Additionally, DBP may have independent roles on macrophage and osteoclast activation. This review will summarize recent findings about DBP with respect to measures of bone density and health

KCDT10

The family of potassium channel tetramerizationdomain (KCTD) proteins consists of 26 members with mostly unknown functions. The name of the protein family is due to the sequence similarity between the conserved N-terminal region of KCTD proteins and the tetramerization domain in some voltage-gated potassium channels. Dozens of publications suggest that KCTD proteins have roles in various biological processes and diseases.

MMAB

The *MMAB* gene provides instructions for making an enzyme that is involved in the formation of a compound called adenosylcobalamin (AdoCbl). AdoCbl, which is derived

from vitamin B12 (also known as cobalamin), is necessary for the normal function of another enzyme known as methylmalonyl CoA mutase. This enzyme helps break down certain proteins, fats (lipids), and cholesterol.

The MMAB enzyme is active in mitochondria, which are specialized structures inside cells that serve as energy-producing centers. Once vitamin B12 has been transported into mitochondria, the MMAB enzyme converts a form of the vitamin called cob(I)alamin to AdoCbl. Studies suggest that this enzyme may also deliver AdoCbl to methylmalonyl CoA mutase.

The MMAB encodes a protein that catalyzes the final step in the conversion of vitamin B(12) into adenosylcobalamin (AdoCbl), a vitamin B12-containing coenzyme for methylmalonyl-CoA mutase. Mutations in the gene are the cause of vitamin B12-dependent methylmalonic aciduria linked to the cblB complementation group. Alternatively spliced transcript variants have been found

NBPF3

The NBPF3 and ALPL gene encodes the major enzyme involved in the clearance of vitamin B6. One variant of the NBPF3 gene is associated with 12 to 18% lower vitamin B6 concentrations. About 52% of Caucasians, 44% of Asians and 89% of Africans carry this variant. For these people, sufficient vitamin B6 intake is particularly important.

This gene has been associated with decreased levels of Vitamin B6 (pyridoxine), an important part of brain function, glucose metabolism and heart health.

CYP2R1

The activation of vitamin D requires 25-hydroxylation in the liver and 1α-hydroxylation in the kidney. However, it remains unclear which enzyme is relevant to vitamin D 25-hydroxylation. Recently, human CYP2R1 has been reported to be a potential candidate for a hepatic vitamin D 25-hydroxylase. Thus, vitamin D metabolism by CYP2R1 was compared with human mitochondrial CYP27A1, which used to be considered a physiologically important vitamin D_3 25-hydroxylase. A clear difference was observed between CYP2R1 and CYP27A1 in the metabolism of vitamin D_2. CYP2R1 hydroxylated vitamin D_2 at the C-25 position while CYP27A1 hydroxylated it at positions C-24 and C-27. The K_m and k_{cat} values for the CYP2R1-dependent 25-hydroxylation activity toward vitamin D_3 were 0.45 μM and 0.97 min^{-1}, respectively. The k_{cat}/K_m value of CYP2R1 was

26-fold higher than that of CYP27A1. These results strongly suggest that CYP2R1 plays a physiologically important role in the vitamin D 25-hydroxylation in humans.

DHCR7

The *DHCR7* gene provides instructions for making an enzyme called 7-dehydrocholesterol reductase. This enzyme is responsible for the final step in cholesterol production in many types of cells. Specifically, 7-dehydrocholesterol reductase converts a molecule called 7-dehydrocholesterol to cholesterol.

Cholesterol is a waxy, fat-like substance that is produced in the body and obtained from foods that come from animals (particularly egg yolks, meat, poultry, fish, and dairy products). It has important functions both before and after birth. Cholesterol plays a critical role in embryonic development by interacting with signaling proteins that control early development of the brain, limbs, genital tract, and other structures. It is also a structural component of cell membranes and myelin, the fatty covering that insulates nerve cells. Additionally, cholesterol is used to make certain hormones and is important for the production of acids used in digestion (bile acids).

PPARG

Energy storage is a mechanism used by humans to deal with food excess. PPAR (peroxisome proliferator-activated receptor) genes are master regulators of this mechanism.

Food provides us with building materials and energy for maintaining normal cellular and bodily function. When we overeat, excess food becomes excess energy which is converted into stored fat, ultimately leading to weight gain. When it is needed, stored fat is utilized as the major energy supply leading to weight loss. Three PPAR genes in the human body, PPARG, PPARA, and PPARD, control these processes.

The PPARG gene makes the protein PPARγ. The PPARA gene makes the protein PPARα. The PPARD gene makes the protein PPARδ.

In the presence of excess energy, PPARγ triggers its storage by promoting fat synthesis. PPARα promotes fat burning in the liver to release the stored energy. PPARδ (also known as PPARβ or PPARβ/δ) promotes fat synthesis in the liver while initiating fat burning in muscle. Interplay of these three PPARs, modulated by environmental factors such as food, exercise and medication, plays a critical role in regulating energy

storage and supply in the human body. In addition, PPARs are also involved in adipogenesis (fat tissue growth) and osteogenesis (bone tissue growth).

SLCA2

Researchers have found that people with a certain DNA difference in their SLCa2 gene ate more sugar than people with other versions. The researchers hypothesize that these individuals may have brains that are less sensitive to the amount of sugar in the blood. Which means they may need to eat more sugar to feel full.

The SLCa2 gene has the instructions for making the GLUT2 protein.

GLUT2's job is to move glucose, the sugar our bodies use for energy, into cells. Researchers have found that GLUT2 is involved in feeling full from blood sugar levels GLUT2 is found in the brain. The protein GLUT2 is involved in telling someone when he or she is full. Results suggest that one small change in GLUT2 causes some people to eat more sugar.

TAS2R38

This gene encodes a seven-transmembrane G protein-coupled receptor that controls the ability to taste glucosinolates, a family of bitter-tasting compounds found in plants of the Brassica sp. Synthetic compounds phenylthiocarbamide (PTC) and 6-n-propylthiouracil (PROP) have been identified as ligands for this receptor and have been used to test the genetic diversity of this gene.

The TAS2R38 gene allows us to sense a bitter taste which protects us from ingesting toxic substances, present in some vegetables, which can also affect the thyroid when ingested in large quantities.

Bitter taste perception plays key roles in human behavior and health. By shaping the attractiveness of food and other substances such as vegetables, coffee, cigarette smoke, and alchohol. Evolutionary, plants initially developed toxic compounds in order to prevent themselves from beging easting. As a response to that, humans as well as other animals evolved the ability to taste these toxins through bitter tastes. Having a

heighten sense of these compounds can allow individuals to either completely avoid the consumption of these plants, or at least learn to regulate intake.

RAS2R38

Researchers were able to identify two specific genetic variations--known as TAS2R13 and RAS2R38--that seemed to affect perceptions about the taste of the alcohol. Specifically, the genetic variants affected how bitter a person perceived the alcohol to be. The researchers also found that the more bitter a person perceived the alcohol to be, the less likely they were to drink it, and vice-versa.

Researchers have found that that people with variants of the bitterness gene may drink as much as 50 percent less than those without the genetic variant. In other words, people may be predisposed--or not--to liking alcohol.

Important Nutrients For Weight Management

Green Coffee Bean

Green coffee bean extract, produced from the green beans of the Arabica plant, is a relatively new ingredient to weight loss products that has been getting strong attention; even being featured on the Dr. Oz program. This attention is not unfounded, green coffee bean extract has a number of health benefits, in particular as a weight loss aid.

Green coffee bean contains polyphenols, including chlorogenic acids, which, like grape seed extract and green tea, have antioxidant that help the body neutralize harmful free

radicals. Research has also shown that the chlorogenic acid in green coffee bean has an antihypertensive effect on rats and humans that promotes normal blood pressure [1-3].

Unlike coffee beverages, green coffee bean extract is low in caffeine and is not a stimulant. Chlorogenic acids are also destroyed when coffee beans are roasted and their benefits are not available in coffee drinks.

Chlorogenic acids support the weight loss benefits of green coffee bean in a couple different ways. First, promote balanced blood sugar by inhibiting the release of glucose within the body. Secondly, chlorogenic acids boost the metabolic output of the liver, which burns more fat. This dual mechanism works to support lean body mass by hindering the absorption of fat and weight gain.

Plant Derived Minerals

Many modern scientific accomplishments are truly amazing and have changed our lives dramatically. However, the world's best scientists have not been able to stop the decline of minerals in top soil where our foods are grown. The effects of significantly fewer minerals in the food we eat are far-reaching. Many medical and nutritional experts say the lack of minerals is the very reason we are subjected to so many ailments and sickness including chronic and degenerative disease. Minerals are a basic necessity of the human body and if we lack even a few of them it can weaken our immune system and detrimentally affect our health. Since minerals are vital to good health, the question arises, what kind of minerals should we be supplementing with every day?

Many people, even at a young age, complain about being tired, fatigued and just downright worn out at the end of a day. Many complain about not being able to lose weight and keep it off even after trying numerous weight loss products.

Fermentation

If there is one “magic pill” out there for weight loss, it can only be fermented foods and drinks. Fermented foods, like cultured vegetables, and fermented drinks, like coconut water kefir or probiotic beverages, change the way our bodies digest food and absorb nutrients. The friendly microflora enhance the enzymatic power of foods and produce

valuable micronutrients that support the detoxification pathways of the body and mitigate the harmful chemicals and metals that are found in today's modern environment.

So not only are you cleansing on a cellular level with these healing foods and drinks, but you are building your immune system and balancing your hormones. The body is able to let go of excess fat that is no longer necessary to protect your organs from acidity.

Best of all, fermented foods and beverages reduce or eliminate cravings for sugar and processed foods.