



# Your Genetic Report

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# Recommendation Summary

## RECOMMENDATION FOR Metabolic: General

**You have lower levels of adiponectin and altered leptin binding**, slowing your metabolic rate and encouraging adipogenesis, the formation of fat from food. You also have **increased ghrelin** stimulating hunger and food seeking behaviour with an increased risk of weight gain, particularly when consuming saturated fats and refined carbohydrates. However, you have a normal thermogenic rate (burning of fat for fuel) helping to slightly moderate weight gain.

**You require 3 meals a day, with no snacking, leaving 5 to 6 hours in between meals.** You do not need to move to intermittent fasting, but you can if you wish. You may have water, coffee and tea (caffeinated or **caffeine free**) with a small amount of milk or milk substitute but nothing over 25 to 30 calories in between meals. If you wish a latte or similar beverage, it must be at the meal. **You also need to keep saturated fats and simple refined sugars very low in the diet.** (this exact number is calculated by carb and fat genes)

**TMC (Tri Metabolic Control) by Signature Supplements**– 2 caps twice a day 30 mins or more before meals for 4 weeks to significantly reduce ghrelin, increase adiponectin and regulate leptin, boosting the metabolism as well as significantly reducing hunger and food cravings, allowing you to stick to your genetic diet with ease. Then rotate this in 1 week out of every 4 to 6 weeks.

## RECOMMENDATION FOR Carbohydrates

**You are sensitive to carbohydrates.** You make more insulin to carbohydrates, destabilizing blood sugars much more readily significantly increasing weight gain upon carbohydrate consumption. You do not produce many inflammatory substrates in your GI tract following carbohydrate consumption, helping to reduce the impact on the bowel and stomach. However you can stimulate cancerous pathways when consuming too many carbohydrates.

**Keep grains, starches, fruits or alcohol (see list of these carbohydrates to moderate below) to a maximum of 2 meals per day**, where the physical size of the carbohydrate is 2/3rd the physical size of the protein for 8 weeks. Do not use sweets as your carbohydrate on a regular basis, save that as a treat.

**Keep healthy, non starchy vegetables as your main carbohydrate source.** (See the unlimited vegetable list provided to you )

### **Carbohydrates to moderate:**

Grains: breads, pastas, rice, corn, popcorn, quinoa, legumes, muffins, crackers etc

Starches: potato, sweet potato, yam, squash, carrot, beets, turnip etc

Fruits: all fruits except the tomato, berries are the best choice

Alcohol: wine, spirits, beer etc

Sweets: cakes, pastries, cookies, candy, soda pop, hot chocolate etc

**TMC by Signature Supplements (note leptin, adiponectin and ghrelin regulate insulin)** 1 capsule 30 minutes before meals for 8 weeks if blood sugars are unstable. Please double the dose if metabolic section requires this.

## RECOMMENDATION FOR Protein

You are best with 3 meals a day and no snacking. Leave 5 to 6 hours in between meals with only the fluids such as water, coffee or tea with a small amount of milk or milk substitute. Do not add sugar to those beverages. Do not consume anything over 25-30 calories in between meals to maintain your hormonally balanced metabolism.

You need the lowest amount of complete protein out of all codings. **You require 0.6 to 0.8 grams of protein per kilogram of body weight** divided by 3 to calculate the amount of protein you need per meal. Eg. A 165 lb individual is 75 kg. That would be equal to approximately 18 grams of protein per meal. This should come from complete protein, which as a vegetarian is limited. See your attached p

Please note: Other food groups such as vegetables, legumes, nuts and seeds also contain incomplete protein. For instance 1/2 cup of almonds contains 15 grams of protein, 1/2 cup of lentils contains 9-11 grams of protein and 1 cup of broccoli contains 3 grams of protein. Most people consume approximately 20 grams of protein per day through these other non full protein sources. The amount of complete protein above is and should be, in addition to these other incomplete protein sources.

As we age, we require more protein. If you are menopausal, or over 55 yrs of age, please add 0.2 grams of protein per kilogram of body weight.

If you are exercising more than 2.5 hours per day, then add in 0.3 to 0.4 grams of protein per kilogram of body weight to compensate for the increased muscle breakdown.

### **Ideal protein sources for a vegetarian include:**

Pure Paleo Protein Powder by Designs for Health (animal byproduct)

Dream Protein by Promedics (whey)

Raw Protein by Garden of Life (plant based)

Protein Powder by Good Protein (plant based)

Egg whites

Greek Yogurt - check your dairy genes

Cottage Cheese - check your dairy genes

Non GMO tofu products

Tempeh

Soy Milk

Edamame Beans

Quinoa - also a carb

Buckwheat- also a carb

Hemp seeds

Chia seeds

Hummus ( with tahini in it)- also a carb

Black bean pasta or edamame pasta

Power Slice Bread by Dimpflmeier or Keto Fiberlicious by Grainsfield or UnBun Bread

## RECOMMENDATION FOR Fats

Upon the consumption of saturated fats, you release slightly more ghrelin, the hunger hormone, which can increase food seeking behaviour and food cravings, especially for energy dense foods such as sweets and fats. In addition, your body readily increases the size and number of fat cells, a process known as adipogenesis. These metabolic effects are greatly stimulated and enhanced only when consuming more than 22 grams of saturated fat per day.

Treatment is to **reduce dietary intake of saturated fats to less than 22 grams per day**. Some simple changes that can be made to lower saturated fat intake and maintain poly and mono unsaturated fats include consuming almonds and walnuts over most other nuts, using olive or avocado oil and eliminating coconut oil, and consuming more poultry and fish versus red meat. Below is a chart comparing saturated fat levels in several common foods.

### Food Source | Saturated Fat

1 tbsp MCT oil	14 grams
1 oz or 28 grams raw almonds	1 gram
1 oz walnuts	1.7 gram
1 oz cashews	2.5 grams
1 oz macadamia nuts	3.5 grams
3 oz grilled salmon	2.1 grams
3 oz chicken skinless breast	2.2 grams
3 oz beef	3.5 grams
1/2 cup of 2% cottage cheese	2 grams
1/2 cup of 0% cottage cheese	0 grams
3/4 cup 0% greek yogurt plain	0 grams
3/4 cup 2% greek yogurt	3.5 grams
1 oz cheddar cheese	9.4 grams
1 oz brie	8 grams
1 large egg	2 grams
1 oz milk chocolate	5 grams
1 oz dark chocolate	9 grams
1 tbsp of olive oil	1.9 grams
1 tbsp of canola oil	1 gram
1 tbsp of coconut oil	13 grams

**Soluble and insoluble fiber by any brand**– 1 scoop per day in water at a meal with higher saturated fat to bind the fat to the fiber for excretion and prevent absorption of the fat.

## RECOMMENDATION FOR

## Dairy

You have normal lactase persistence. Your small intestinal cells have retained the ability to continue to produce lactase, the enzyme to break down lactose in dairy products.

**You do not need to stay away from dairy products.**

Keep in mind this does not mean you may not have a dairy sensitivity to the proteins casein and whey in dairy. Avoid dairy if you experience symptoms when consuming it.

## RECOMMENDATIONS FOR

## Dopamine

**You make less dopamine and produce fewer dopamine receptors** to bind this lower concentration of dopamine. **You also clear dopamine out quickly**, decreasing the length of time dopamine has to stay bound into a receptor and have an effect.

This greatly increases the risk for addictive type behaviours such as gambling, over training in sports, eating, and shopping, doom scrolling. You may also have a greater desire for fattier foods such as chips, cheese, nuts and alcohol.

This combination of genes is associated with seeking out more pleasure or reward, whether from food, sex or extreme supports. It requires “greater highs” to “satisfy” the brain.

You also may find holding focus and concentration for prolonged periods of time difficult.

To help increase dopamine production naturally you can take **Dopamine Booster by Signature Supplements** - 2 capsules twice a day empty stomach (30 minutes or more before food or 2 hours or more after food).

When craving a food or behaviour try one minute of jumping jacks or similar exercise to boost dopamine quickly and naturally and help cut through the craving.

**Regular exercise, according to your genetics is key to maintain balanced dopamine levels.**  
**Moderate stress through deep breathing, meditation, diet and your stress hormone genes.**

**You produce lower levels of the DAT protein. This decreases the transportation of dopamine to its target tissues entirely independent of how much dopamine you are making or supplementing with.** Boosting with dopamine naturally or pharmaceutically without increasing the transportation of dopamine leads to a toxic buildup of unused dopamine. This can easily stimulate dopaminergic endotoxicity and the conversion of dopamine into adrenaline. Increasing transportation of dopamine is crucial for you.

**Dopamine Delivery by Signature Supplements** - 2 caps twice a day for 8 weeks on an empty stomach (30 mins or more before food or 2 hours or more after) and then reduce to 1 cap twice a day.

## RECOMMENDATION FOR Serotonin

**You make the normal amount of serotonin**, particularly in the intestines, where most of the serotonin is produced, and your transportation of serotonin out of the bowel to its target tissues is normal. However, **your clearance of serotonin is slightly faster**, decreasing the length of time serotonin can remain in a receptor exerting its effect. With this is also a faster clearance of stress hormones is equally fast decreasing their ability to further impair serotonin production.

This genotype combination can slightly increase the risk for depression, low moods, waking at 5 am or early morning waking, gastro-intestinal bloating, IBS symptoms, muscle pain and swelling, and food cravings, particularly for chocolate or sweets.

**5HTP by Genestra**- 1-2 caps twice a day with food. Alternatively, you can boost brain serotonin levels with **High Potency Rest Reset by Signature Supplements** if your sleep section also requires this - 2 caps at 8:30 pm (where melatonin will breakdown into serotonin right where it is needed).

Regular exercise, according to your genetics is key to maintain balanced serotonin levels. Moderate stress through deep breathing, meditation, diet and your stress hormone genes.

## RECOMMENDATIONS FOR

## Short Term Stress Response

**You produce the normal amount of ACTH from the pituitary and cortisol from the adrenal glands for each stressor.** You also have the normal number of hypothalamic receptors for mineralocorticoids to help shut off the HPA axis and return the nervous system to the quiet parasympathetic side.

However, **you produce a higher level of FKBP5**, the binding protein that regulates glucocorticoid binding and sensitivity, impairing negative feedback regulation of the HPA axis. This is the most important gene in the stress section for it indicates that your nervous system has a very difficult time turning off further production of the stress hormones even well after the stressor is resolved.

In addition, your clearance of stress hormones through your COMT gene is slow, allowing for a prolonged binding and action of the stress hormones in the nervous system.

All of this increases the risk of anxiety depression, PTSD, hyperactivity, panic attacks and exaggerated emotional responses.

Cortisol, like inflammation can turn over 90% of genes to their adverse position independent of how you treat those other genes. Cortisol also increases the production of the inflammatory cytokines IL6 and TNF $\alpha$  by up to 76%. This inflammation then triggers the HPA stress axis directly further stimulating these genes and more cortisol production making this section crucial to treat.

This inflammatory response not only aggravates all inflammatory conditions such as arthritis or irritable bowel syndrome, but it also inflames all neural tissues, blocking the binding of good neurotransmitters such as dopamine and serotonin, independent of how much neurotransmitter you make or we supplement with.

Cortisol and the stimulation of these genes also inhibits the production of digestive enzymes by 88%, forcing the deposition of acids into the stomach when you eat. These acids not only irritate and inflame the lining of the stomach and bowel, but they cut the food at the incorrect place, making the food appear "foreign" to the immune system in the bowel, forcing it to mount an inflammatory immunoglobulin response against it. This not only impairs the absorption of the food, but creates significant gas and bloating to food randomly.

This may be contributing to your increase in food sensitivities.

Cortisol inhibits the production of melatonin as it does not want you to enter into stage 4 deep sleep, decreasing the quality of sleep and thus impairing all healing.

Cortisol can easily decrease the rate of the metabolism from 92% down to 35%, independent of diet and exercise.

**Sereniten Plus by Pure Encapsulations or Stress Reset by Signature Supplements-** 2 capsules twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) for 8-10 weeks and then reduce to 1 capsule twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) increasing as needed for periodic stressors that occur.

Deep breathing and meditation.

Exercise according to your exercise genes.



You make significantly less glutamic acid decarboxylase, the enzyme responsible for breaking down glutamate, the most abundant excitatory neurotransmitter in the brain and central nervous system into GABA, an inhibitory neurotransmitter that helps calm the nervous system. **This leads to much higher glutamate levels and significantly reduced GABA production** within the central nervous system increasing the risk of anxiety, depression, sleep disturbances and muscle spasticity, seizures and CNS excitation.

**GABA Reset by Signature Supplements** – 2 caps twice a day empty stomach (30 mins or more before food or 2 hours or more after) for 8 weeks and then reduce to 1 cap twice per day empty stomach.

## RECOMMENDATION FOR Long Term Stress Response

You produce the normal amount of corticotropin releasing hormone (CRH) from your hypothalamus for each stressful event you encounter. This helps return your central nervous system back to the parasympathetic side, the quiet side, with greater ease following a stressful event. You also have the normal amount of CRH receptors with which to maintain parasympathetic stimulation.

**However, you produce a high level of FKBP5**, the binding protein that regulates glucocorticoid binding and sensitivity, impairing the negative feedback regulation of the HPA axis and keeping your nervous system stuck for longer periods of time in the sympathetic stress side. This is the most important gene in the stress section for it indicates that your nervous system has a very difficult time turning off further production of the stress hormones even well after the stressor is resolved.

In addition, your clearance of stress hormones through your COMT gene is slow, allowing for a prolonged action of the stress hormones in the nervous system, augmenting the above effects.

All of this allows the central nervous to get “stuck” in the sympathetic side with great ease, increasing risk of anxiety depression, PTSD, hyperactivity, panic attacks and exaggerated emotional responses.

Cortisol, like inflammation can turn over 90% of genes to their adverse position independent of how you treat those other genes. Cortisol also increases the production of the inflammatory cytokines IL6 and TNF $\alpha$  by up to 76%. This inflammation then triggers the HPA stress axis directly further stimulating these genes and more cortisol production making this section crucial to treat.

**Sereniten Plus by Pure Encapsulations or Stress Reset by Signature Supplements** 2 capsules twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) for 6-8 weeks after completing treatment for your short term stress response and then reduce to 1 capsule twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) increasing as needed for periodic stressors that occur.

Deep breathing and meditation.

Exercise according to your exercise genes.

## RECOMMENDATION FOR Cardiovascular

You have approximately equal distribution of fast and slow twitch fibers in your muscles. Fast twitch fibers enable one to sprint, and slow twitch fibers allow one to perform endurance exercises. As you have a mix between the two, you are best designed for a combination of moderated sprints and longer slower endurance.

You also have an increased blood flow in large quick bursts to the muscle during exercise and a better control of sodium-potassium regulation within the cells. In addition, you have more beta-2 adrenergic activity with increased bronchodilation with short intense exercise. Both of these effects further moderate your exercise style slightly towards faster sprints or HIIT (High Intensity Interval Training).

Because of your increased risk of injury with High Intensity Training, it is important to follow recommendations in your Injury and susceptibility section and avoid any start-stop exercises such as soccer.

Note: This is for cardiovascular exercise, not weight training. Your resistance or weight training style is in the next section. It is very possible to code for the opposite style of workout for weight training depending on your genes.

**You are better with 1.5 to 2 minute intervals at 70-75% capacity, with 45 second recovery intervals at 40% capacity for 45-50 minutes twice a week. Alternating with a consistent cardiovascular workout for 45-60 minutes at about a 60% capacity twice a week.**

## RECOMMENDATION FOR Resistance Training

You are designed for medium weights, medium repetition resistance training. You produce the normal amount of angiotensin converting enzyme or ACE, and thus have a good flush of blood volume over the muscle body during exercise, with adequate control of your sodium potassium pumps for repair from exercise. This allows you to increase the amount of weight used during exercise.

The variant C coding for the INSIG2 gene is associated with an increased in subcutaneous weight fat deposition in both men and women, which is increased when performing heavy weight, fewer repetition resistance training. This is even more prominent in men. However, your G/C position decreases the effect of weight gain with heavy weights slightly, and also allows you to slightly increase the amount of weight used.

**You are designed for moderate weight, moderate repetition (10-14 reps) per exercise resistance training. You can take small 30 second breaks in between exercise. You would do best to perform exercises that recruit more than one muscle group at a time.** Eg, with medium weights perform a shoulder press from a squat position, standing up at the same time as you perform your shoulder press to engage both the legs (with no weights) and the arms in one exercise. Repeat for 10-14 repetitions, with a small break between each repetition if needed. **Aim for sets of each exercise 2 to 3 times a week.**

Note: These recommendations are for resistance or weight training exercise style, not cardiovascular exercise. Your cardiovascular exercise style is in the section above. It is very possible to code for the opposite style of workout for these two sections.

## RECOMMENDATION FOR

## Injury Susceptibility and Prevention

**You have a significant increased risk of injury when exercising, especially when performing high intensity interval training, stop-start sports or lifting heavy weights.** You produce an increased amount of metalloproteases, the enzymes that are involved in the breakdown and remodelling of collagen (especially collagen type 1, 11, 1V, 1X and X) as well as increasing the breakdown of the main components of connective tissue, the proteoglycans, fibronectin, laminin and elastin, greatly compromising not just the strength but also the elasticity and resistance of tendons under stress or during exercise. **You also produce more than the normal amount of IL6**, a potent inflammatory substrate when you exercise, augmenting inflammation in the tendons and joints as well as increasing weight gain.

However, you do produce more collagen type 1 protein helping to increase the strength and integrity of your collagen type 1, the main collagen type in most tendons and ligaments.

Treatment: Warming up with a walk before exercise is key to increase the blood flow and oxygen into muscles so that they are more flexible and can stretch with greater ease when you do exercise, decreasing the pressure and stress on the attached tendons. Avoid plyometrics and stop-start sports such as soccer as much as possible. Use K-tape around the Achilles tendon or any weaker joint to support the muscles and increase proprioception and nerve firing to the muscle. This once again will allow the muscle to function with greater response, decreasing the stress placed on the tendons. Always ice after exercise.

**Resveratrol Extra by Pure Encapsulations**- 1 capsule twice a day empty stomach (30 minutes or more before food or 2 hours or more after) to reduce the excess production of MMPs and IL6. After 6 weeks this can reduce to 1 per day. Look to Neural Repair or TMC and see if they are also needed, for they will contain Resveratrol and cross cover here, decreasing the need to add in another pill.

**Arthroben by Designs for Health** - .1 scoop per day in water empty stomach.

## RECOMMENDATIONS FOR General

You have the normal production of human leukocyte antigen, part of the histocompatibility complex family, capable of triggering allergenic, asthmatic and immune responses. When a foreign body, such as a virus, bacteria or allergen enters the body, it is able to decipher self versus non-self and does not mount an immune reaction against your own body tissues through the T-cells, decreasing inflammation and tissue damage

No treatment is needed.

You produce slightly more than the normal amount of interferon through this gene. This can increase the general inflammatory response throughout the body, but more importantly can augment the production of interleukins, inflammatory cytokines and the synthesis auto-antibodies, throwing the immune response into “overdrive”.

This coding also decreases the ability of the immune system to see a pathogen when it first enters the body, delaying the time it takes to mount a response to it, increasing the severity of the infection.

This coding is associated with a slight increased risk of inflammatory bowel disease, ulcerative colitis, and several autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and multiple sclerosis.

Stress and chronic infections or cancer can downgrade this response, lowering the immune response rather than increasing it. In this case the T-cytotoxic cells, anti-inflammatory cytokines, macrophages and interleukin response would be low.

If you do not have any of the above disease, nor experience frequent inflammatory flares in the bowel or skin, then you do not necessarily need to treat these gene, for you most likely are not expressing this gene. If you are presently experiencing one or more of these conditions or have more frequent inflammatory reactions in the bowel or skin then treatment is **Moducare (by Moducare)** 1 capsule a day empty stomach (30 minutes or more before food or 2 hours or more after).

If you have a personal or family history of cancer or frequent infections treatment is **Immune Modulator by Signature Supplements** - 3/4 tsp in water or 4 caps on an empty stomach daily. Take this twice a day if you presently have cancer and add **Immune Booster by Signature Supplements** - 1 cap per day. If you are heterozygote or variant for the CYP1A2 gene increase DIM by 1 cap per day or increase cruciferous veggies to balance the effect of curcumin in the Immune Booster on CYP1A2.

## RECOMMENDATION FOR Inflammation

**You produce the normal amount of the inflammatory cytokine TNF $\alpha$ . However, you produce increased levels of IL6.** Elevated IL6 stimulates higher TNF $\alpha$  production independent of genetic coding, creating a cyclic pro-inflammatory response in the body. This not only prolongs the healing from any injury or infectious disease, but also greatly contributes to several conditions such as obesity, diabetes, osteoporosis, arthritis, and mood disturbances.

Inflammatory cytokines easily cross the blood brain barrier stimulating the HPA axis and stress response even in the absence of a stressor. In response, the nervous system further stimulates the production of these inflammatory substrates, creating a cyclic stress-inflammatory response that must be treated.

Inflammation, like cortisol can trigger over 90% of genes to their adverse position independent of treatment, once again making this section crucial to treat.

Inflammation can mutate hormone and neurotransmitter receptors, altering their shape so that substrates cannot bind into them and mount a response, independent of the amount of available hormone or neurotransmitter.

**Glutathione Complex by Signature Supplements** - 2 caps twice a day empty stomach (30 minutes or more before food or 2 hours or more after for 4 weeks and then reduce it to 2 caps a day thereafter.

Please check your detox genes as you may already be taking these supplements and you do not need to duplicate this. Curcumin or turmeric can also reduce both TNF $\alpha$  and IL6, but as it is contra-indicated for CYP1A2 C/C, leaving glutathione and NAC as a better choice.

## RECOMMENDATION FOR Phase 1

You produce the normal amount **phase 1 detoxification enzyme cytochrome P450 1A2**. not too much and not too little. This is very balanced place to be for this genes. **However, you produce less CYP3A4 enzymes.** These enzymes are crucial for the metabolism of xenobiotics in the body. They modify both exogenous and endogenous compounds from the environment and in the body in order to prepare them for phase 1 detoxification (clearance of the toxin out of the body).

Slower CYP3A4 activity is associated with a slower clearance of hormones, estrogen in particular, as well as several xenobiotics. This gene is particular active in women.

**avoid caffeine or one at most, increase raw cruciferous vegetables** as much as possible, and **DIM and Detox (By Pure Encapsulations)** 2 caps twice a day empty stomach (30 minutes or more before food or 2 hour or more after) for 2 weeks, repeating this twice a year to help support phase 1 detoxification.

## RECOMMENDATION FOR Phase 2

**You have slightly slower phase 11 detoxification pathways.** Phase 11 enzymes are responsible for catalyzing the conjugation of many toxic compounds, carcinogens and medications. Slower activity with less enzyme production through these genes increases inflammation, cellular damage and can allow toxic substrates to act as pre-carcinogens.

Slower SOD2 or Mitochondrial Superoxide Dismutase decreases the natural protection of the mitochondria and DNA from oxidative damage.

**However, you do have normal activity in the GSTP1 gene helping to prevent cellular damage from oxidative inflammation and an accumulation of some toxic pre-carcinogens in body tissues.** You also have normal NQO1 enzymes increasing the removal of partially oxidized quinone molecules as well as of exogenous toxins such as benzene, a carcinogen found in laundry detergents, pesticides, smoke, and household and industrial cleaners decreasing the risk of inflammation, tissue damage and cancers.

**Glutathione Complex by Signature Supplements** - 2 caps twice a day empty stomach (30 minutes or more before food or 2 hours or more afterwards) for 4 weeks and then reduce to 1 cap twice per day. Increase back up if exposed to heavy toxins.

**Consume an abundance of raw cruciferous vegetables.**

**Keep well hydrated- 0.5oz/ lb of body weight.**

## RECOMMENDATIONS FOR

## Vitamins, Minerals and Methylation: General

### B6

You have a slightly faster clearance of Vitamin B6 via altered production of the hormone NBPF3 – neuroblastoma breakpoint member 3. This can increase the risk of anxiety, depression, muscle cramps or spasms, skin conditions, and the metabolism of carbohydrates and lipids in the body.

**P5P -Any Brand** 1 capsule(50mg) a day with food or 1 capsule of **Pure Genomics Multivitamin (Pure Encapsulations)** per day with food. You should also increase foods rich in vitamin B6 such as fish, poultry, pork, brown rice, eggs, dark green vegetables.

### Folic Acid

You produce the normal amount of the enzyme methylenetetrahydrofolate reductase that is key for metabolizing inactive dietary folate or folic acid into its active form methyl-folate.

Maintain foods rich in folate such as eggs, asparagus, legumes, broccoli, brussels sprouts and dark leafy greens.

### Zinc

You have normal transportation of zinc inside and outside of the cells. Low levels of zinc are associated with many chronic conditions such as cardiovascular disease, allergies, chronic infections and cancers. Zinc plays an important role in the processing, storage and secretion of insulin greatly increasing the risk of obesity and type 2 diabetes.

Maintain foods high in zinc such as legumes, nuts, seeds and dairy (if genetically you can handle dairy). During times of infection or illness you can take 25mg of **Zinc Citrate-Any Brand** per day with food.

### B12/ Bifidobacterium

Your production of the enzyme fucosyltransferase 2 which is involved in the absorption of vitamin B12 through the gut normal. However, you produce less 5-methyl-tetrahydrofolate-homocystein S-methyltransferase, or methionine synthase, and less methionine synthase reductase altering both the degradation and recycling of B12. All of this leads to slightly lower B12 levels in the body with a slight increased risk for higher homocysteine levels, increased migraines, and potential for several neurological diseases.

More importantly, you have far less Bifidobacterium growth in your gut, with greater potential for gastro-intestinal upset, inflammation and reduced immunity.

**Adenosyl/Hydroxy B12 (Pure Encapsulations)** 1 capsule per day with food or **Tricobalamin (Designs for Health)** 1 cap per day with food, OR 1 capsule of **Pure Genomics Multivitamin (Pure Encapsulations)** per day with food. It is very important that you do not start this until after the 8 weeks and come off any supplement with methyl B12 in it now.

**HMF Intensive Probiotic (Genestra/Seroyal)** – 2 per day with food.

Or **Bifido PB30 (Vita Aid)**- 2 per day with foods

### Vitamin A

You have very low conversion of beta carotene into its active vitamin A carotenoid form. The conversion rate may be lowered by as much as 60%. Vitamin A is needed for a strong immune response, particularly with T-cell and lymphocyte regulation. It is also a key vitamin involved in pregnancy, the prevention of visual deterioration and aging of the eyes. Vitamin A is required for red blood cell formation, the transportation of hemoglobin and subsequently oxygen around the body. Finally Vitamin A is also a key component in the normal growth of skin, hair and nails.

Boosting levels is important to help support all of the above body functions.

**Vitamin A (Pure Encapsulations)** 10 000 IU = 3000mcg – 1 capsule per day with food or 1 capsule of **Pure Genomics Multivitamin (Pure Encapsulations)** per day with food. Increasing foods rich in Vitamin A is also useful. Those foods include spinach, broccoli, sweet potato, beef, red peppers and cod.

### Vitamin C

You have normal absorption of vitamin C from the diet, through the bowel and into the blood. This transportation of vitamin C is key for the strength and rapidity of immune reactions, especially the anti-viral response. Vitamin C helps to inhibit the replication of a virus that has entered the body, and thus reduce the impact of the infection on the body. Vitamin C also plays a key role in collagen repair and synthesis, both in the skin and in the joints, promotes healthier hair and nails, and strengthens our mucosal membranes, especially in our gastro-intestinal tract.

Maintain foods high in vitamin C such as brussel sprouts, spinach, tomato, citrus fruits, turnip and cauliflower.

### Vitamin D

You have a normal production of the vitamin D binding protein aiding in the delivery of vitamin D to its target tissues.

Vitamin D binds into over 300 000 receptors in the body, affecting areas such as bone and muscle metabolism, collagen remodeling, production of immune cells, regulation of blood sugars and plays a role in the growth of cancers.

**Vitamin D (Pure Encapsulations)** – 1000 IU per day with food, especially in colder climates where sun exposure is low. Follow your vitamin D levels and increase or decrease the dose as needed.

## RECOMMENDATION FOR Estrogen

You have a significantly higher production of cytochrome 17A1 enzyme with a faster conversion of pregnenolone into DHEA, ultimately increasing your production of estrogen. You also have a poor conversion of this estrogen into the 2-OH protective form, the form that is protective against receptor stimulation, cellular proliferation and cancer. However, your conversion of some of your estrogen into the 4-OH form, the most carcinogenic form of estrogen is quite low, helping to decrease the risk of estrogenic effects in the body.

This combination can slightly increase your risk of fibroids, endometriosis, cysts, breast, prostate and colon cancer. These are very important genes to consider if you are on or thinking about hormone replacement therapy, whether that be natural, bio-identical or pharmaceutical.

**DIM by Signature Supplements** – 1 capsule per day empty stomach (30 minutes or more before food or 2 hours or more after) for 6 weeks.

For menopausal symptoms. add in **Menopause Management by Signature Supplements** - 2 caps twice a day empty stomach until symptoms have dissipated and then reduce to 1 cap twice a day. This product regulates kisspeptin and NeuroKinin B, the safe and effective way to regulate hot flashes.

Increase raw cruciferous vegetables such as broccoli, brussel sprouts and kale, all of which contain DIM, diindolymethane to reduce 4-OH estrogen.

Avoid charred barbecued foods which increase the activity through these genes.

Maintain a normal body weight as these genes are stimulated by obesity. Check your metabolic and dietary genes for guidance.

## RECOMMENDATION FOR Testosterone

You have an increased production of the enzyme 5 alpha-reductase leading to a higher conversion rate of the less active form of testosterone into the more potent form dihydrotestosterone. However you produce the normal amount of sex hormone binding globulin, decreasing the amount of active testosterone available to circulate and bind into and activate testosterone receptors.

This can slightly increase the risk of PCOS and menstrual irregularities in women.

**Test dihydrotestosterone levels first, and most importantly, match the above symptoms with family and personal health history before starting supplemental treatment.** These are two genes that may not have been turned on yet in the body and unlike reducing 4-OH estrogen, lowering testosterone when it is not needed can result in fatigue, decreased libido and other such symptoms.

If supplemental treatment is needed **Testo-Protect by Signature Supplements**– 2 capsules a day empty stomach (30 minutes or more before food or 2 hours or more after).

Keep stress hormone levels balanced and maintain an ideal weight, for stress and obesity stimulate these genes. Look at your stress hormone, metabolic and dietary genes for guidance.

## RECOMMENDATION FOR Sleep: General

You produce very little cryptochrome 1 protein that could block the functioning of the clock gene and deregulate many circadian patterns. This helps to regulate sleep patterns, allowing you to fall asleep with greater ease and transition for one stage of sleep into another maximizing the amount of time spent in the healing and healthy stages of sleep.

You also produce the normal clock protein helping to maintain regular circadian rhythms. This leads to more evening sedation helping to fall asleep with more ease. It also helps to prevent more frequent waking throughout the night increasing both the quality and quantity of sleep, subsequently improving overall health and stress levels.

**Rest Reset by Signature Supplements** – 1capsule at 8:30 pm during times of stress. Make sure to take follow treatment plan in your stress section.

Avoid caffeinated beverages in the later half of the day.

Increase exercise in the morning.

## RECOMMENDATION FOR Thyroid: General

**You produce the normal amount of your main thyroid enzyme deiodinase-2 (DIO2)** helping to convert your thyroid hormone FT4 (thyroxine) into its active form FT3 (triiodothyronine) in your peripheral tissues. In addition, you also produce the normal amount of your secondary thyroid converting enzyme deiodinase-1 (DIO1) aiding in maximal conversion of T4 into T3.

**However, you do produce a slightly higher amount of the protein Phosphodiesterase 8B** that breaks down cAMP, one of the main signalling regulators in the thyroid, helping to maintain normal TSH levels.

All of these variables very slightly increase the risk of hypothyroidism, decreased energy, increased weight gain and adrenal disorders. **Before considering supplementation, test thyroid levels to see if you need support.**

**Thyroid Reset by Signature supplements** 1 capsule a day empty stomach (30 minutes or more before food or 2 hours or more after) .

Consider talking with your health care practitioner about using desiccated T3 for further treatment if needed.

## RECOMMENDATIONS FOR Longevity: General

**You produce lower levels of Beclin1**, the protein that helps to regulate autophagy and the clearance of damaged debris within tissues. This allows for easy stimulation of PI3K pathways involved in cellular turnover, growth and differentiation of tissues and is associated with an increased risk of cancer and inflammatory diseases. You will have a slightly more difficult and longer time getting into autophagy when following a fasting mimicking diet or intermittent fasting. This makes it much more important that you follow the dietary protocols closely.

**Autophagy Activator by Signature Supplements** - 1 cap before bed and increases to 2 caps when doing a fasting mimicking diet to stimulate all autophagy pathways. Take 2 caps daily if you have a chronic inflammatory disease or a neurological disorder.

AND

**Neural Repair by Signature Supplements**- 1 cap twice a day empty stomach for 8 weeks and then reduce to 1 per day.

Look to your SIRT6, ATG16L1, BDNF and IRS1 genes as well for they also play large roles in autophagy.

If you have a personal or family history of cancer or frequent infections treatment is **Immune Modulator by Signature Supplements** - 3/4 tsp in water or 4 caps on an empty stomach daily. Take this twice a day if you presently have cancer and add **Immune Booster by Signature Supplements** - 1 cap per day. If you are heterozygote or variant for the CYP1A2 gene increase DIM by 1 cap per day or increase cruciferous veggies to balance the effect of curcumin in the Immune Booster on CYP1A2.

Please check BECN1 for alternate dosing. Use whichever dose is higher for greater protection.

Please check ATG16L1 for alternate dosing. Use whichever dose is higher for greater protection.

If your weight is normal, follow your genetic diet above and introduce a cycle of fasting mimicking diet 4 times a year for the first year and then twice a year thereafter. If you are 25lbs or more above your ideal weight then introduce the fasting mimicking (FMD) diet once a month for 3 months and then twice a year thereafter.

Fasting Mimicking nutritional plan - 700 calories per day for 5 days.

Guidelines are as follows:

16 grams of protein per day for FTO TT, 18 grams of protein per day for FTO TA, and 20 grams of protein per day for FTO AA. Use a protein powder for this protein source. Be sure to minus the protein sources below when calculating the protein powder portion.

Unlimited lettuce (not spinach or kale), cucumber, and mushrooms. Use only olive oil, salt, pepper, lemon and spices on salad.

2 cups of broccoli and/or cauliflower and/or zucchini - this is approximately 5 grams of protein

10 almonds or 12 olives (this is approximately 3 grams of protein)

Please check ATG16L1 for dosing as well.

You produce the normal amount of SIRT6 helping to slow many of the processes involved in aging and increasing the rate of repair of damaged tissue. Higher levels of SIRT6 are associated with decreased frailty and lower progression of several chronic diseases. SIRT6 helps to slow many of the mechanisms involved in aging from inflammation and DNA repair to glucose metabolism and autophagy.

No Supplemental treatment is needed. Increase food based flavonoids and luteolins such as celery, broccoli, berries, apple skins and chrysanthemum flowers. Do not intake high levels of catechins such as green tea as they inhibit SIRT6 production.



You produce the normal amount of FOXO3 slowing the rate of aging. Lower levels of FOXO3 are associated with decreased DNA repair, altered immunity, decreased tumor suppression, increased inflammation and slower stem cell production and activity. Your higher levels of FOXO3 help to moderate the risk of several age-related diseases.

No treatment is needed but Increasing foods rich in astaxanthin such as salmon, trout, krill and shrimp is also helpful.

**You produce significantly less ATG16L protein decreasing the strength of autophagy pathways in the body.** This increases the risk of several cancers, auto-immune disorders, neurological disorders, and all inflammatory bowel disorders. ATG16L protein is inhibited by mTOR and PI3K stimulation. mTOR and PI3K pathways are greatly stimulated by increased protein and inhibited by resveratrol. You will have a much more difficult and longer time getting into autophagy when following a fasting mimicking diet or intermittent fasting. This makes it much more important that you follow the dietary protocols closely.

Treatment: **Autophagy Activator by Signature Supplements** - 2 caps a day before bed for 8 weeks and then reduce to 1 cap per day. Increase back to 2 caps per day when doing a fasting mimicking diet to stimulate all autophagy pathways. Take 2 caps daily if you have a chronic inflammatory disease or a neurological disorder.

AND

**Neural Repair by Signature Supplements**- 1 cap twice a day empty stomach for 8 weeks and then reduce to 1 per day.

If you have a personal or family history of cancer or frequent infections treatment is **Immune Modulator by Signature Supplements** - 3/4 tsp in water or 4 caps on an empty stomach daily. Take this twice a day if you presently have cancer and add **Immune Booster by Signature Supplements** - 1 cap per day. If you are heterozygote or variant for the CYP1A2 gene increase DIM by 1 cap per day or increase cruciferous veggies to balance the effect of curcumin in the Immune Booster on CYP1A2.

Please check BECN1 for alternate dosing. Use whichever dose is higher for greater protection.

Please check BECN1 for alternative dosing. Use whichever dose is higher for greater protection.

If your weight is normal, follow your genetic diet above and introduce a cycle of fasting mimicking diet once a month for 2 months and then 4 times a year for the first year and then twice a year thereafter. If you are 25lbs or more above your ideal weight then introduce the fasting mimicking (FMD) diet once a month for 4 months and then 4 times a year for the first year after and then twice a year thereafter.

Fasting Mimicking nutritional plan - 700 calories per day for 5 days.

Guidelines are as follows:

16 grams of protein per day for FTO TT, 18 grams of protein per day for FTO TA, and 20 grams of protein per day for FTO AA. Use a protein powder for this protein source. Be sure to minus the protein sources below when calculating the protein powder portion.

Unlimited lettuce (not spinach or kale), cucumber, and mushrooms. Use only olive oil, salt, pepper, lemon and spices on salad.

2 cups of broccoli and/or cauliflower and/or zucchini - this is approximately 5 grams of protein

10 almonds or 12 olives (this is approximately 3 grams of protein)

Look to your BECN1, SIRT6, BDNF and IRS1 genes as well for they also play large roles in autophagy.



You produce the normal levels of BDNF helping to maintain the integrity and maximal repair of your neural tissues as you age. Lower BDNF is associated with increased memory loss, dementia and Alzheimer's as well as decreased focus and concentration. Low BDNF can also increase the rates of depression and anxiety. Your higher levels of BDNF help to reduce the rate of brain aging and associated ailments.

No treatment is needed.

Avoid high levels of sugars which lowers BDNF and increase exercise which greatly stimulates BDNF (look to your exercise genes for guidance).

### RECOMMENDATION FOR

## Cholesterol: General

You produce the normal amount of the PCSK9 protein that binds to LDL receptors and breaks them down. This allows the liver to maximally clear LDL from the body, managing blood levels of LDL, the bad cholesterol and reducing the risk of familial hypercholesterolemia and cardiovascular disease.

However you have fewer LDL receptors with which to carry the cholesterol into the cell from the bloodstream to be broken down. This also greatly increases the risk of familial hypercholesterolemia and cardiovascular disease.

**Red Yeast Rice Extract by AOR** - 2 caps twice a day empty stomach before bed for 8 weeks and then reduce to 2 caps before bed.

# Report

## METABOLIC

### Metabolic: General

MC4R

rs17782313

The MC4R gene codes for the proteins that make up the Melanocortin-4 receptor in the hypothalamus of the brain. This receptor has a central role in satiety and controlled food intake. When stimulated by the agonist neuropeptide alpha-MSH (alpha melanocyte stimulating hormone) it reduces hunger, improves sensitivity to satiety signals, promotes meal termination and increases metabolism, fat burning and thermogenesis. The MC4R receptor, therefore, plays a pivotal role in the control of food intake, energy expenditure and weight homeostasis.

Mutations in the structure of the MC4R receptor have a profound impact on hunger, food intake, energy metabolism and adiposity. Animals with MC4R receptor mutations show hyperphagia, delayed meal termination and reduced sensitivity to satiety feedback peptides such as CCK. They also demonstrate metabolic abnormalities including reduced insulin sensitivity, impaired thermogenesis and lowered overall metabolic rate. Similar findings are seen in humans with a number of mutations of varying effect and penetrance associated with obesity and metabolic syndrome.

The melanocortin system is interesting in that it is one of the few neuroendocrine systems that have a natural antagonist, in this case AgRP (Agouti-Related Peptide). This messenger binds to the receptor and turns it off, which results in hunger, food seeking behaviour, lowered metabolism and weight gain.

**Normal Allele: T Variant Allele: C**

**You are: CT**

**Key Characteristics of the Variant Allele:**

- Each C allele is associated with an 8% increase in obesity.
- CC's can increase body weight by up to 43% independent of diet and exercise.
- Decreased satiation of appetite.
- Increased food seeking behaviour and desire to snack.
- Increased association with emotional overeating.
- Greater stress-related cravings for processed foods.
- Rapid weight gain on antidepressants and antipsychotics.
- Increased insulin resistance and a 14% increase in risk for type-2 diabetes.
- Hypogonadism
- Decreased libido

ADIPOQ

rs17366568

The ADIPOQ gene codes for the 244-amino acid protein Adiponectin, circulating in high concentrations in the blood of genetically normal individuals. Adiponectin is a bioactive, fat cell-derived hormone (adipokine) produced primarily in adipose tissue. It is also processed in smaller quantities in bone marrow, the cardiovascular system, the liver and muscle mass. It increases insulin sensitivity partially by suppressing glucose production, as well as increasing fatty acid oxidation and regulating glucose and insulin levels. It regulates healthy fat storage while preventing accumulation of lipids in other tissues (liver, muscle, arteries etc.) and has a strong cardio-protective role.

Adiponectin inhibits damaging inflammatory pathways, increasing endothelial NO (Nitrous Oxide) production and inhibiting oxidative stress. Adiponectin deficiency is associated with increased damage during cardiac ischemic events.

Reduced fat mass or weight loss increases adiponectin, promoting glucose and fatty acid uptake into adipocytes. Adiponectin reduces the production of cholesterol and glucose by the liver to help control metabolic syndrome. Overall it has a profound effect on the storage and use of fat as an energy source and extensive research indicates that it prevents the development of metabolic syndrome disorders such as diabetes. Circulating levels are significantly lower in patients with obesity, diabetes, hypertension and coronary artery disease and research shows that adiponectin can reverse insulin resistance and will likely provide a novel treatment approach for Type 2 diabetes.

This ADIPOQ gene codes for the production of adiponectin **during weight loss**, as opposed to during weight maintenance or when you deviate from your genetic dietary program.

**Normal Allele: G Variant Allele: A**

**You are: GG**

**Key Characteristics of the Variant Allele:**

- Lower circulating adiponectin during weight loss
- Slower rate of weight loss
- Increased overall weight gain and BMI
- Unstable blood sugars, insulin levels
- More food cravings
- Food cravings disappear or lessen with calorie deprivation
- Weight loss increases with calorie deprivation

ADIPOQ

rs17300539

The ADIPOQ gene codes for the 244-amino acid protein Adiponectin, circulating in high concentrations in the blood of genetically normal individuals. Adiponectin is a bioactive, fat cell-derived hormone (adipokine) produced primarily in adipose tissue. It is also present in smaller quantities in bone marrow, the cardiovascular system, the liver and muscle mass. It increases insulin sensitivity partially by suppressing glucose production, as well as increasing fatty acid oxidation and regulating glucose and insulin levels. It regulates healthy fat storage while preventing accumulation of lipids in other tissues (liver, muscle, arteries etc.) and has a strong cardio-protective role.

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This ADIPOQ gene codes for the production of adiponectin **during weight maintenance** or when deviating from your genetic dietary program.

**Normal Allele:** A **Variant Allele:** G

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Regains weight easily after weight loss
- Yo-yo dieter.
- More unstable glucose and insulin during weight maintenance
- Increased weight and BMI
- Increased food cravings during weight maintenance.
- Symptoms decrease with caloric restriction.

ADRB2

rs1042714

The ADRB2 gene, or the beta-2 adrenergic receptor is widely expressed in most cell types and is the primary target of catecholamines (stress hormones) during the stress response. It plays a significant role in a myriad of responses from controlling heart rate to blood pressure, mood, food cravings, response to exercise and energy balance in the metabolism.

The ADRB2 receptor regulates the metabolism through the stimulation of both thermogenesis (conversion of fat into heat for energy) and in lipid mobilization or breakdown for fuel. The variance in the gene is greatly associated with increased obesity, BMI and lipogenesis (formation of fat from food). The effects are greatly augmented with the consumption of sugars and fats.

As this gene functions through the sympathetic nervous system, variant coding is also associated with higher levels of anxiety, panic attacks or increased anger and stress eating.

**Normal Allele:** C **Variant Allele:** G

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Increased sensitivity to carbohydrates and saturated fats
- Slower metabolic rate
- Decreased weight loss with endurance exercise
- Increased BMI
- Increased serum lipids
- Increased blood sugars and insulin
- Increased blood pressure
- Increased production of inflammatory cytokines (TNF and IL10)
- Altered leptin production and thus increased food cravings and slower metabolism
- Decreased thermogenesis
- Loose more weight on calorie reduced diet.

PPARG

rs1801282

Peroxisome proliferator-activated receptor gamma (PPAR-gamma) plays a central role in fatty acid and glucose metabolism as well as in fat storage and insulin sensitivity. It is found mostly in adipose tissue, but is also seen in the vascular endothelium, colon and in macrophages.

The receptor is the target for the TZD (thiazolidinediones) class of diabetic medications. The gene product has several different metabolic functions and has thusly been coined the master regulator of adipocyte biology. It works by modifying the transcription of a number of genes involved in glucose and lipid metabolism, fat cell differentiation and energy balance.

PPARg also has an anti-inflammatory effect on the endothelial cells of the cardiovascular system and reduces the development of atherosclerosis. Its effect on inflammation may be even more widespread with some studies indicating an association with conditions such as rheumatoid arthritis. PPARg inhibits the expression of inflammatory cytokines such as TNF-a and IL-6, and directs the differentiation of immune cells towards anti-inflammatory phenotypes. Both synthetic and natural PPARg activators are currently under investigation for their potential as anti-inflammatory agents.

PPARg is shown to be an important factor in fat cell differentiation. The process of adipogenesis involves the development of adipocyte precursor cells into functioning fat cells capable of filling them with lipids and expressing adipokines such as leptin and adiponectin. It has also been shown to promote the browning of white fat, a beneficial process that increases metabolism and fat burning and combats obesity.

**Normal Allele: C Variant Allele: G**

**You are: CC**

**Key Characteristics of the Variant Allele:**

- Lower BMI
- Improved insulin sensitivity
- Reduced risk of Type 2 diabetes.
- Worse on a high fat and high carbohydrate diet
- Significant cumulative effect when combined with FTO, ADIPOQ, MC4R and ADRA SNPS.
- Good response in weight loss with caloric reduction.
- Have greater health benefits from exercise.
- Lower heart disease risk.
- Higher risk of complications in patients that develop diabetes
- Increased weight gain, if the individual becomes overweight.

FTO  
rs9939609

FTO, the Fat Mass and Obesity-Related Protein, colloquially known as the “Fatso” gene, codes for the enzyme alpha-ketoglutarate-dependent dioxygenase. It was one of the first metabolic genes identified, and research into its clinical and lifestyle implications is extensive.

Approximately 42% of Caucasians, 5% of Africans and 21% of Asians carry the risk allele (A). This risk allele in large scale population studies accounts for an overall 1% increase in BMI and a 22% increased risk of obesity, *independent of* diet and exercise. However, the effect is significantly worse if an FTO-A individual consumes a low protein, high saturated fat or high calorie diet as the expression of the A allele is further enhanced with such nutrition.

The variant allele A is associated with alterations in 3 main metabolic hormones. The first is elevated ghrelin production. Ghrelin is our hunger hormone, and elevated levels cause increased food cravings, especially for energy dense foods such as sugars and saturated fats.

The second is adiponectin (see ADIPOQ genes), a hormone that increases insulin sensitivity and fatty acid oxidation and regulates both insulin and glucose levels thereby preventing the accumulation of lipids in the body. Reduced levels promote glucose and fatty acid uptake into fat cells, increase metabolic syndrome and obesity.

The third is leptin, our satiety hormone that reduces hunger and food seeking behaviour. Leptin decreases lipogenesis, the formation of fat and increases triglyceride hydrolysis and fatty acid oxidation. Leptin also helps to stimulate thermogenesis, or the browning of white fat to increase weight loss. Leptin resistance which is seen more frequently in the variant A allele leads to increased fat stores, food cravings, particularly after 6 pm and the inability to use fat as a fuel source.

The variant allele also has reduced levels of the proteins IRX3 and IRX5. These proteins promote the formation of unhealthy white fat over beneficial, fatty acid burning, brown fat by a factor of 5.

All of these variables are altered by the amount of protein, sugars and saturated fats consumed. Each genotype requires a specific amount of protein to control the hormone production.

**Normal Allele: T Variant Allele: A**

**You are: TT**

**Key Characteristics of the Variant Allele:**

- Increased production of Ghrelin, the “hunger hormone”.
- Decreased Adiponectin, increased fat storage.
- Reduced Leptin sensitivity, increased food cravings.
- Reduced levels of proteins IRX3 and IRX5, decreased brown fat formation.
- Increased insulin and glucose.
- Decreased thermogenesis.
- Increased obesity and BMI.

RECOMMENDATION FOR

**Metabolic: General**

**You have lower levels of adiponectin and altered leptin binding**, slowing your metabolic rate and encouraging adipogenesis, the formation of fat from food. You also have **increased ghrelin** stimulating hunger and food seeking behaviour with an increased risk of weight gain, particularly when consuming saturated fats and refined carbohydrates. However, you have a normal thermogenic rate (burning of fat for fuel) helping to slightly moderate weight gain.

**You require 3 meals a day, with no snacking, leaving 5 to 6 hours in between meals.** You do not need to move to intermittent fasting, but you can if you wish. You may have water, coffee and tea (caffeinated or **caffeine free**) with a small amount of milk or milk substitute but nothing over 25 to 30 calories in between meals. If you wish a latte or similar beverage, it must be at the meal. **You also need to keep saturated fats and simple refined sugars very low in the diet.** (this exact number is calculated by carb and fat genes)

**TMC (Tri Metabolic Control) by Signature Supplements**– 2 caps twice a day 30 mins or more before meals for 4 weeks to significantly reduce ghrelin, increase adiponectin and regulate leptin, boosting the metabolism as well as significantly reducing hunger and food cravings, allowing you to stick to your genetic diet with ease. Then rotate this in 1 week out of every 4 to 6 weeks.

## DIET

## Carbohydrates

GIPR  
rs2287019

GIPR or gastric inhibitory polypeptide receptor, also called glucose-dependent insulinotropic polypeptide, is an important peptide hormone that is synthesized in the duodenum and small intestine and binds to glucose-dependant insulinotropic peptide receptors or GIP's after a meal rich in carbohydrates.

GIPRs are abundant in a variety of tissues including the pancreas, adipocytes, brain and stomach, and thus GIP signalling is involved in a variety of pathways linked to obesity, insulin resistance and type 2 diabetes.

Some of the major roles of GIPR include the inhibition of gastric acid secretions and gastrin release, but more importantly stimulates insulin release in the presence of elevated glucose following carbohydrate consumption. The variant T allele of this gene presents with higher blood glucose levels and impaired insulin secretion following carbohydrate ingestion increasing the risk of obesity and diabetes.

**Normal Allele:** C **Variant Allele:** T**You are:** CC**Key Characteristics of the Variant Allele:**

- Increased GIPR production and activity.
- Increased insulin resistance
- increased glucose levels
- increased obesity
- increased abdominal fat
- increased BMI
- increased risk of Type 2 Diabetes

TCF7L2

rs7903146

TCF7L2 or transcription factor 7 like 2 is a gene that alters the expression of other genes that control insulin after the consumption of carbohydrates and saturated fats (but mostly carbohydrates). It is involved in the Wnt signalling pathway, a group of signalling transduction pathways that pass signals into cells via their surface receptors.

This is known as the largest risk factor gene for glucose regulation, insulin production as well as inflammation in the colon upon the consumption of carbohydrates. Variance (T allele) within this gene greatly increases blood glucose and insulin levels significantly increasing weight and BMI. It also has impaired beta cell function (pancreatic cells that release insulin) following carbohydrate consumption further impacting weight and blood glucose regulation.

This is one of 2 TCF7L2 SNPS reported to be associated with type 2 diabetes. Both have equal power (92% correlation) to estimate the risk of T2DM.

**Normal Allele:** C **Variant Allele:** T

**You are:** CT

**Key Characteristics of the Variant Allele:**

- Increased weight, BMI following carbohydrate consumption and saturated fat intake.
- Altered glucose and insulin levels
- Increased risk of type 11 diabetes by 2-fold for homozygote variants and heterozygotes have a 1.4 fold increase.
- Increased risk for metabolic syndrome.
- Increased abdominal adiposity
- Increased colon cancer

IRS1

rs2943641

Insulin receptor substrate 1 (*IRS1*) is a ligand of the insulin receptor tyrosine kinase and is central to the insulin receptor signal transduction pathway. *IRS1* is the major protein initiating the stimulation of glucose transport in both muscle and adipose tissue. In addition, this protein plays a key role in the insulin signalling through body tissues. Deregulation in *IRS1* expression and function has been reported in insulin-resistant states such as obesity and type 2 diabetes.

More specifically, the *IRS1* gene makes the protein IRS-1 that binds to insulin and IGF-1 receptors. This binding then causes phosphorylation which then in turn activates a multitude of signalling pathways, many of those involving glucose and insulin regulation.

Variance within this gene cause an increase in glucose uptake contributing to obesity, type 2 diabetes, insulin resistance and triglyceride formation upon carbohydrate consumption.

*IRS1* is also involved in the PI3K pathway. PI3K or phosphatidylinositol 3-kinase is part of a family of enzymes involved in cellular functions such as cellular growth, proliferation, differentiation, and motility, all of which are turned on in cancer. This specific pathway of PI3K and IRS-1 is involved in insulin and glucose insensitivity of cancerous tumours as well as altered benefits of calorie restriction on the tumours.

**Normal Allele:** T **Variant Allele:** C

**You are:** CT

**Key Characteristics of the Variant Allele:**

- Increased *IRS1* protein production.
- Increased insulin resistance
- Increased glucose levels
- Increased obesity
- Increased risk of Type 11 Diabetes
- Increased risk of Metabolic Syndrome
- Increased risk of cancers – colorectal, lung, prostate and breast

## RECOMMENDATION FOR Carbohydrates

**You are sensitive to carbohydrates.** You make more insulin to carbohydrates, destabilizing blood sugars much more readily significantly increasing weight gain upon carbohydrate consumption. You do not produce many inflammatory substrates in your GI tract following carbohydrate consumption, helping to reduce the impact on the bowel and stomach. However you can stimulate cancerous pathways when consuming too many carbohydrates.

**Keep grains, starches, fruits or alcohol (see list of these carbohydrates to moderate below) to a maximum of 2 meals per day**, where the physical size of the carbohydrate is 2/3rd the physical size of the protein for 8 weeks. Do not use sweets as your carbohydrate on a regular basis, save that as a treat.

**Keep healthy, non starchy vegetables as your main carbohydrate source.** (See the unlimited vegetable list provided to you )

### **Carbohydrates to moderate:**

Grains: breads, pastas, rice, corn, popcorn, quinoa, legumes, muffins, crackers etc

Starches: potato, sweet potato, yam, squash, carrot, beets, turnip etc

Fruits: all fruits except the tomato, berries are the best choice

Alcohol: wine, spirits, beer etc

Sweets: cakes, pastries, cookies, candy, soda pop, hot chocolate etc

**TMC by Signature Supplements (note leptin, adiponectin and ghrelin regulate insulin)** 1 capsule 30 minutes before meals for 8 weeks if blood sugars are unstable. Please double the dose if metabolic section requires this.

## DIET

## Protein

FTO  
rs9939609

FTO, the Fat Mass and Obesity-Related Protein, colloquially known as the “Fatso” gene, codes for the enzyme alpha-ketoglutarate-dependent dioxygenase. It was one of the first metabolic genes identified, and research into its clinical and lifestyle implications is extensive.

Approximately 42% of Caucasians, 5% of Africans and 21% of Asians carry the risk allele (A). This risk allele in large scale population studies accounts for an overall 1% increase in BMI and a 22% increased risk of obesity, *independent of* diet and exercise. However, the effect is significantly worse if an FTO-A individual consumes a low protein, high saturated fat or high calorie diet as the expression of the A allele is further enhanced with such nutrition.

The variant allele A is associated with alterations in 3 main metabolic hormones. The first is elevated ghrelin production. Ghrelin is our hunger hormone, and elevated levels cause increased food cravings, especially for energy dense foods such as sugars and saturated fats.

The second is adiponectin (see ADIPOQ genes), a hormone that increases insulin sensitivity and fatty acid oxidation and regulates both insulin and glucose levels thereby preventing the accumulation of lipids in the body. Reduced levels promote glucose and fatty acid uptake into fat cells, increase metabolic syndrome and obesity.

The third is leptin, our satiety hormone that reduces hunger and food seeking behaviour. Leptin decreases lipogenesis, the formation of fat and increases triglyceride hydrolysis and fatty acid oxidation. Leptin also helps to stimulate thermogenesis, or the browning of white fat to increase weight loss. Leptin resistance which is seen more frequently in the variant A allele leads to increased fat stores, food cravings, particularly after 6 pm and the inability to use fat as a fuel source.

The variant allele also has reduced levels of the proteins IRX3 and IRX5. These proteins promote the formation of unhealthy white fat over beneficial, fatty acid burning, brown fat by a factor of 5.

All of these variables are altered by the amount of protein, sugars and saturated fats consumed. Each genotype requires a specific amount of protein to control the hormone production.

**Normal Allele:** T **Variant Allele:** A

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Increased production of Ghrelin, the “hunger hormone”.
- Decreased Adiponectin, increased fat storage.
- Reduced Leptin sensitivity, increased food cravings.
- Reduced levels of proteins IRX3 and IRX5, decreased brown fat formation.
- Increased insulin and glucose.
- Decreased thermogenesis.
- Increased obesity and BMI.

## RECOMMENDATION FOR Protein

You are best with 3 meals a day and no snacking. Leave 5 to 6 hours in between meals with only the fluids such as water, coffee or tea with a small amount of milk or milk substitute. Do not add sugar to those beverages. Do not consume anything over 25-30 calories in between meals to maintain your hormonally balanced metabolism.

You need the lowest amount of complete protein out of all codings. **You require 0.6 to 0.8 grams of protein per kilogram of body weight** divided by 3 to calculate the amount of protein you need per meal. Eg. A 165 lb individual is 75 kg. That would be equal to approximately 18 grams of protein per meal. This should come from complete protein, which as a vegetarian is limited. See your attached p

Please note: Other food groups such as vegetables, legumes, nuts and seeds also contain incomplete protein. For instance 1/2 cup of almonds contains 15 grams of protein, 1/2 cup of lentils contains 9-11 grams of protein and 1 cup of broccoli contains 3 grams of protein. Most people consume approximately 20 grams of protein per day through these other non full protein sources. The amount of complete protein above is and should be, in addition to these other incomplete protein sources.

As we age, we require more protein. If you are menopausal, or over 55 yrs of age, please add 0.2 grams of protein per kilogram of body weight.

If you are exercising more than 2.5 hours per day, then add in 0.3 to 0.4 grams of protein per kilogram of body weight to compensate for the increased muscle breakdown.

### **Ideal protein sources for a vegetarian include:**

Pure Paleo Protein Powder by Designs for Health (animal byproduct)

Dream Protein by Promedics (whey)

Raw Protein by Garden of Life (plant based)

Protein Powder by Good Protein (plant based)

Egg whites

Greek Yogurt - check your dairy genes

Cottage Cheese - check your dairy genes

Non GMO tofu products

Tempeh

Soy Milk

Edamame Beans

Quinoa - also a carb

Buckwheat- also a carb

Hemp seeds

Chia seeds

Hummus ( with tahini in it)- also a carb

Black bean pasta or edamame pasta

Power Slice Bread by Dimpflmeier or Keto Fiberlicious by Grainsfield or UnBun Bread

## DIET

## Fats

FABP2

rs142649876

Fatty acid binding protein 2 is one of a group of proteins that plays a key role in the absorption and intracellular transport of long chain fatty acids. It is produced primarily in the small intestines and is encoded by the FABP2 gene. Fatty acids are the building blocks of lipids or fats and are classified according to the number of carbon atoms in their chains or tails. Long chain fatty acids are those with 14 or more carbon atoms. They are also classified according to the number of hydrogen bonds into saturated, monounsaturated or polyunsaturated. These fats can be found in foods as variable as dairy fat, coconut oil, olive canola and safflower oil, fish oils, nuts and avocado. They include both healthy and unhealthy fats with the nutritional value determined by a number of structural factors including length and saturation.

Fatty acids are key for energy production (ATP production). When compared to other macronutrients such as carbohydrates or proteins, fatty acids yield the most APT on an energy per gram basis. This is why fatty acids are the foremost storage form of fuel in humans, animals and to a lesser extent plants.

The variant A allele has twice the affinity for long chain fatty acids and therefore increases their absorption and processing. This results in increased fatty acid oxidation leading to insulin resistance and increased risk of type 11 diabetes.

G/G – no increased sensitivity to saturated fats and sugars

G/A – moderate sensitivity to saturated fats and sugars – approximately 25%

A/A – approximately double the sensitivity to saturated fats and sugars.

**Normal Allele: G Variant Allele: A**

**You are: GG**

**Key Characteristics of the Variant Allele:**

- Increased weight gain + BMI with > 53 grams of saturated fats and/or refined sugars per day.
- Increased glucose levels.
- Increased insulin resistance.
- Increased risk of Type 2 diabetes
- Increased risk of hyperlipidaemia in Type 2 (but NOT Type 1) diabetes
- Increased fatty acid uptake and delivery to tissue – by 2 fold
- Lower HDL
- Higher total cholesterol
- All above turned on when consuming > 53 grams of saturated fat and/or refined sugars.

FTO  
rs9939609

FTO, the Fat Mass and Obesity-Related Protein, colloquially known as the “Fatso” gene, codes for the enzyme alpha-ketoglutarate-dependent dioxygenase. It was one of the first metabolic genes identified, and research into its clinical and lifestyle implications is extensive.

Approximately 42% of Caucasians, 5% of Africans and 21% of Asians carry the risk allele (A). This risk allele in large scale population studies accounts for an overall 1% increase in BMI and a 22% increased risk of obesity, *independent of* diet and exercise. However, the effect is significantly worse if an FTO-A individual consumes a low protein, high saturated fat or high calorie diet as the expression of the A allele is further enhanced with such nutrition.

The variant allele A is associated with alterations in 3 main metabolic hormones. The first is elevated ghrelin production. Ghrelin is our hunger hormone, and elevated levels cause increased food cravings, especially for energy dense foods such as sugars and saturated fats.

The second is adiponectin (see ADIPOQ genes), a hormone that increases insulin sensitivity and fatty acid oxidation and regulates both insulin and glucose levels thereby preventing the accumulation of lipids in the body. Reduced levels promote glucose and fatty acid uptake into fat cells, increase metabolic syndrome and obesity.

The third is leptin, our satiety hormone that reduces hunger and food seeking behaviour. Leptin decreases lipogenesis, the formation of fat and increases triglyceride hydrolysis and fatty acid oxidation. Leptin also helps to stimulate thermogenesis, or the browning of white fat to increase weight loss. Leptin resistance which is seen more frequently in the variant A allele leads to increased fat stores, food cravings, particularly after 6 pm and the inability to use fat as a fuel source.

The variant allele also has reduced levels of the proteins IRX3 and IRX5. These proteins promote the formation of unhealthy white fat over beneficial, fatty acid burning, brown fat by a factor of 5.

All of these variables are altered by the amount of protein, sugars and saturated fats consumed. Each genotype requires a specific amount of protein to control the hormone production.

**Normal Allele:** T **Variant Allele:** A

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Increased production of Ghrelin, the “hunger hormone”.
- Decreased Adiponectin, increased fat storage.
- Reduced Leptin sensitivity, increased food cravings.
- Reduced levels of proteins IRX3 and IRX5, decreased brown fat formation.
- Increased insulin and glucose.
- Decreased thermogenesis.
- Increased obesity and BMI.

APOA2

rs5082

The APOA2 gene encodes for apolipoprotein A2, which is the second most abundant high-density lipoprotein in the body (Apolipoprotein A1 is the most prevalent). Apolipoproteins A1 and A2 are the major protein components of high-density lipoproteins or HDL's, the "good cholesterol" that removes excess bad cholesterol (LDL) from the blood and reduces atherosclerosis and cardiovascular disease risk.

APOA2 influences the regulation of several key enzymes in lipoprotein metabolism including hepatic lipase. It also affects cholesterol ester transfer proteins, phospholipid transfer proteins, serum glucose, free fatty acid and insulin levels. Of great importance is that it plays a significant role in modulating the body's response to dietary saturated fat.

The association between the variant allele of the APOA2 gene, high BMI and a high fat diet is one of the strongest examples of gene-diet interactions. A mean increase in BMI of 6.2% is seen in C/C (or G/G) versus C/T (A/G) or T/T (A/A) individuals when consuming equally high amounts of saturated fat exceeding 22 grams per day. This association is of particular importance in societies with abundant food and food high in fat content (such as a typical western diet).

**Normal Allele: A Variant Allele: G**

**You are: GG**

**Key Characteristics of the Variant Allele:**

- Reduced APOA2 transcription
- Increased BMI when consuming a high saturated fat diet (>22g per day)
- Increased visceral body fat and waist circumference.
- Increased hunger and desire for energy dense foods resulting from increased ghrelin levels.
- Lower efficiency of fat absorption following a meal.
- Faster clearance of fats from the bloodstream.
- Lower levels of cholesterol, triglycerides, cholesterol-HDL ratio.
- Lower risk of cardiovascular disease.
- No apparent association with Type-2 diabetes

## RECOMMENDATION FOR Fats

Upon the consumption of saturated fats, you release slightly more ghrelin, the hunger hormone, which can increase food seeking behaviour and food cravings, especially for energy dense foods such as sweets and fats. In addition, your body readily increases the size and number of fat cells, a process known as adipogenesis. These metabolic effects are greatly stimulated and enhanced only when consuming more than 22 grams of saturated fat per day.

Treatment is to **reduce dietary intake of saturated fats to less than 22 grams per day**. Some simple changes that can be made to lower saturated fat intake and maintain poly and mono unsaturated fats include consuming almonds and walnuts over most other nuts, using olive or avocado oil and eliminating coconut oil, and consuming more poultry and fish versus red meat. Below is a chart comparing saturated fat levels in several common foods.

### Food Source | Saturated Fat

1 tbsp MCT oil	14 grams
1 oz or 28 grams raw almonds	1 gram
1 oz walnuts	1.7 gram
1 oz cashews	2.5 grams
1 oz macadamia nuts	3.5 grams
3 oz grilled salmon	2.1 grams
3 oz chicken skinless breast	2.2 grams
3 oz beef	3.5 grams
1/2 cup of 2% cottage cheese	2 grams
1/2 cup of 0% cottage cheese	0 grams
3/4 cup 0% greek yogurt plain	0 grams
3/4 cup 2% greek yogurt	3.5 grams
1 oz cheddar cheese	9.4 grams
1 oz brie	8 grams
1 large egg	2 grams
1 oz milk chocolate	5 grams
1 oz dark chocolate	9 grams
1 tbsp of olive oil	1.9 grams
1 tbsp of canola oil	1 gram
1 tbsp of coconut oil	13 grams

**Soluble and insoluble fiber by any brand**– 1 scoop per day in water at a meal with higher saturated fat to bind the fat to the fiber for excretion and prevent absorption of the fat.

## DIET

# Dairy

MCM6

rs4988235

MCM6 is the gene that controls whether or not the LCT gene produces lactose. The MCM6 gene provides instructions for making part of the MCM complex, a group of proteins that form a helicase. A helicase is a group of enzymes that binds to and remodels DNA.

There is a specific DNA sequence within the MCM6 gene that controls the regulation or expression of a nearby gene called LCT, the lactose gene, which provides instructions for making lactase to breakdown lactose. The MCM6 gene controls the turning on or off of the LCT gene and thus the production of lactase.

Lactose cannot be broken down in the small intestines nor absorbed through the GI tract in its whole form. It must be broken down or digested by lactase into glucose and galactose.

Undigested lactose can cause a myriad of symptoms from gas, bloating, abdominal pain to diarrhea and nausea.

Lactose intolerance is the result of a deficiency of lactase, and there are 4 main types. Primary lactose intolerance occurs with age, where there is a natural decrease in enzyme production. This type of intolerance does not cause damage to the gastro-intestinal tract. Secondary lactose intolerance is due to injury in the small intestines such as infection, celiac or IBS. Developmental lactose intolerance can occur in premature infants, and often improves with age or time. And the rarest form, congenital, whereby little to no lactase is made right from birth.

**Normal Allele:** A **Variant Allele:** G

**You are:** AA

**Key Characteristics of the Variant Allele:**

- Decreased lactase persistence.
- Decreased lactase production from childhood into adulthood.
- Increased lactose intolerance.
- Increased gas, bloating and nausea.

## RECOMMENDATION FOR

## Dairy

You have normal lactase persistence. Your small intestinal cells have retained the ability to continue to produce lactase, the enzyme to break down lactose in dairy products.

**You do not need to stay away from dairy products.**

Keep in mind this does not mean you may not have a dairy sensitivity to the proteins casein and whey in dairy. Avoid dairy if you experience symptoms when consuming it.

## NEUROTRANSMITTERS

# Dopamine

COMT  
rs4680

COMT or Catechol-O-methyltransferase is an important enzyme produced by the COMT gene that degrades or metabolizes several catecholamines including dopamine, adrenaline and noradrenaline (epinephrine and norepinephrine), along with estrogens and certain drugs. This enzyme adds a methyl group that is donated by SAMe (S-adenosylmethionine) and is thus also a major methylation gene.

COMT is extremely active in the prefrontal cortex, the area in the brain that is responsible for cognitive behaviour, decision making, personality expression, learning, addictions and moderating much of social behaviour.

Increased COMT activity decreases the binding and activity along with increasing the clearance of dopamine, adrenaline, noradrenaline, and catechol estrogens by almost 50%.

With respect to the clearance of dopamine through this gene, the normal allele is considered the adverse position, for it has a faster clearance of dopamine.

**Normal Allele:** G **Variant Allele:** A

**You are:** AG

**Key Characteristics of the Variant Allele:**

- Decreased COMT activity.
- Increased dopamine leading to less addictive behaviour, less food cravings.
- Increased pleasure responses following a stimuli.
- Increased anxiety due to higher stress hormone levels
- Often called the Worrier (as opposed to the G allele referred to as the warrior).
- More obsessive-compulsive behaviours.
- Increased fear response associated with PTSD.

DRD2/ANKK1  
rs1800497

This is a second important dopamine receptor that stimulates dopaminergic pathways involved in reward, learning, motivation and pleasure. It has an additive effect with other dopamine genes such as DRD2.

Dopamine is our calming, reward and addictive brain messenger. DRD2 codes for the number and efficacy of dopamine receptors that you have and thus satisfaction felt from life, behaviours, food and alcohol. Together with DRD2, these genes play significant roles in the development of ADHD, ADD, schizophrenia, depression, learning and addictive behaviours such as over eating, gambling, alcoholism and shopping. This gene with its reward and addictive nature, also plays a large role in satisfaction from food, volume of food consumed and food choices.

This gene and DRD2 are also major genes in all demyelinating diseases such as Parkinson's and MS.

This gene plays a large role in positive or negative energy picked up off of others or in the environment, and how easily you let go of things. When stressed, or with genetically higher cortisol, adrenaline or noradrenaline, the production and binding of dopamine is impaired and/or blocked accentuating all the above ailments and diseases.

There are several dopamine receptors on the kidney, and abnormal coding for this gene alters the RAS system, increasing bloating, edema and blood pressure.

**Normal Allele:** G **Variant Allele:** A

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Reduced DRD2 receptors
- Reduced dopamine activity
- Less pleasure derived from events.
- Frequent excitement seeking behaviour or with greater intensity.
- Increased addictions
- Food cravings for fattier foods such as chips, cheese, nuts and wine.
- Increased learning disorders ...ADD, ADHD

DRD2  
rs6277

DRD2 or the dopamine receptor D2 is a crucial dopamine receptor that stimulates dopaminergic pathways involved in reward, learning, motivation and pleasure.

Dopamine is our calming, reward and addictive brain messenger. DRD2 codes for the number and efficacy of dopamine receptors that you have and thus satisfaction felt from life, behaviours, food and alcohol. Low dopamine expression or activity greatly increases the risk for ADHD, ADD, schizophrenia, depression, learning and addictive behaviours such as over eating, gambling, alcoholism and shopping. It also plays a large role in satisfaction from food, volume of food consumed and food choices.

DRD2 also controls the activity of adenylyl cyclase, the enzyme that converts ATP into cyclic AMP, contributing to the regulation of substrates inside cells.

It is also a major genes in all demyelinating diseases such as Parkinson's and Multiple Sclerosis.

This gene plays a large role in positive or negative energy picked up off of others or in the environment, and how easily you let go of things. When stressed, or with genetically higher cortisol, adrenaline or noradrenaline, the binding of dopamine to these receptors can be partially or fully blocked accentuating all the above ailments or diseases.

There are several dopamine receptors on the kidneys, and abnormal coding for this gene alters the Renin Angiotensin System (RAS), increasing bloating, edema and blood pressure.

**Normal Allele:** A **Variant Allele:** G

**You are:** AG

**Key Characteristics of the Variant Allele:**

- Reduced DRD2 receptors
- Reduced dopamine activity
- Less pleasure derived from events.
- Frequent excitement seeking behaviour or with greater intensity.
- Increased addictions
- Food cravings for fattier foods such as chips, cheese, nuts and wine.
- Increased learning disorders ...ADD, ADHD

DAT1

rs463379

DAT1 or the dopamine transporter gene, is also known as the sodium-dependant dopamine transporter or SLC6A3. This gene produces the protein DAT which moves dopamine across the cell membrane by coupling it with sodium ions. This then stimulates the reuptake of dopamine, ultimately effecting the amount of dopamine bound into a receptor and subsequent dopaminergic activity.

DAT1 is particularly active in the central nervous system, primarily in the areas that make up the dopaminergic circuits including the striatum and nucleus accumbens.

Low levels of DAT are associated with ADD, ADHD, bipolar disorder, clinical depression, eating disorders and substance abuse.

**Normal Allele:** C **Variant Allele:** G

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Low DAT protein production.
- Low dopamine transport.
- Low dopaminergic activity independent of the amount of dopamine present.
- Increased risk of ADD and ADHD
- Increased risk of addictive behaviours, food or substance abuse.
- Increased depression, bipolar and other mood disorders.

## RECOMMENDATIONS FOR

## Dopamine

**You make less dopamine and produce fewer dopamine receptors** to bind this lower concentration of dopamine. **You also clear dopamine out quickly**, decreasing the length of time dopamine has to stay bound into a receptor and have an effect.

This greatly increases the risk for addictive type behaviours such as gambling, over training in sports, eating, and shopping, doom scrolling. You may also have a greater desire for fattier foods such as chips, cheese, nuts and alcohol.

This combination of genes is associated with seeking out more pleasure or reward, whether from food, sex or extreme supports. It requires “greater highs” to “satisfy” the brain.

You also may find holding focus and concentration for prolonged periods of time difficult.

To help increase dopamine production naturally you can take **Dopamine Booster by Signature Supplements** - 2 capsules twice a day empty stomach (30 minutes or more before food or 2 hours or more after food).

When craving a food or behaviour try one minute of jumping jacks or similar exercise to boost dopamine quickly and naturally and help cut through the craving.

**Regular exercise, according to your genetics is key to maintain balanced dopamine levels.**  
**Moderate stress through deep breathing, meditation, diet and your stress hormone genes.**

**You produce lower levels of the DAT protein. This decreases the transportation of dopamine to its target tissues entirely independent of how much dopamine you are making or supplementing with.** Boosting with dopamine naturally or pharmaceutically without increasing the transportation of dopamine leads to a toxic buildup of unused dopamine. This can easily stimulate dopaminergic endotoxicity and the conversion of dopamine into adrenaline. Increasing transportation of dopamine is crucial for you.

**Dopamine Delivery by Signature Supplements** - 2 caps twice a day for 8 weeks on an empty stomach (30 mins or more before food or 2 hours or more after) and then reduce to 1 cap twice a day.

## NEUROTRANSMITTERS

# Serotonin

TPH2

rs4570625

TPH2 is the gene that produces the enzyme tryptophan hydroxylase that converts the essential amino acid tryptophan into 5-HTP, the precursor to serotonin.

Tryptophan must enter the body through diet. We cannot synthesize this on our own. Tryptophan is naturally high in foods such as nuts, cheese and red meat.

Serotonin has many different functions in the body. The most well-known is with mood. Serotonin in the brain helps to regulate anxiety, depression and overall mood. Low levels are associated with depression, brain fog and decreased focus.

As serotonin is primarily found in the stomach and intestines it is obvious that it plays a crucial role in regulating peristalsis and thus the control of bowel movements. Low levels of serotonin are greatly associated with nausea, alternating constipation and diarrhea, gas, bloating and IBS.

Serotonin is also the precursor to melatonin, one of our sleeping hormones. Low levels are associated with difficulties sleeping.

**Normal Allele: G Variant Allele: T**

**You are: GG**

**Key Characteristics of the Variant Allele:**

- Low moods
- Depression
- Anxiety
- Difficulties sleeping
- Waking at 5 am
- IBS, bloating, gas and irregular bowel movements
- Increased muscle myalgia and fatigue

MAOA  
rs77905

The *MAOA* gene provides the instructions for making an enzyme called monoamine oxidase A. This enzyme is part of a family of enzymes that breaks down molecules called monoamines through a chemical reaction known as oxidation. Specifically, monoamine oxidase A is involved in the breakdown of the neurotransmitters serotonin, epinephrine, norepinephrine, and dopamine.

Signals transmitted by serotonin regulate mood, emotion, sleep, and appetite. Epinephrine and norepinephrine control the body's response to stress. Dopamine transmits signals within the brain to produce smooth physical movements and regulate focus, concentration and addictive behaviours.

Monoamine oxidase A also helps break down monoamines found in the diet. It seems to be particularly important in the breakdown of excess tyramine, which is found in cheese and other foods.

With the gene, the normal allele G has increased enzymatic activity, thus a faster clearance serotonin and dopamine.

**Normal Allele:** G **Variant Allele:** A

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Note: This information is for the normal allele, yet lowers serotonin activity.
- Faster breakdown and clearance of serotonin and dopamine
- increased depression and decreased motivation
- Faster breakdown of epinephrine and norepinephrine
- Decreased anxiety and panic disorders

5-HTTLPR

rs11867581

5-HTTLPR is a serotonin transporter gene that is responsible for the re-uptake of serotonin. Serotonin is a key neurotransmitter in both the central and peripheral nervous systems that helps regulate mood, sleep, bowel function, food cravings, depression and the stress response.

The normal G allele is called the "long version" or "L" and is associated with normal transportation and production of serotonin from the bowel, where most of our serotonin is made, to its target tissues.

The variant A allele, also called the "short version" or "S", is associated with far less serotonin production and transportation from the bowel.

Low serotonin activity through this gene leads to exaggerated emotional responses by increasing amygdala firing. The amygdala is the gland in the brain largely responsible for synthesizing emotions and preparing an appropriate emotional reaction. These emotions are augmented further following a childhood trauma or event, easily increasing the risk of PTSD, depression and heightened prolonged stress responses. Low serotonin transportation can make it difficult to let go of smaller day to day events, causing one to ruminate for prolonged periods of time.

**Normal Allele:** G **Variant Allele:** A

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Decreased serotonin production and transportation out of the intestines.
- Decreased uptake serotonin into target tissue.
- Increased depression.
- Difficulties letting go of past events.
- Increased PTSD
- Heightened reactions to stress.

## RECOMMENDATION FOR Serotonin

**You make the normal amount of serotonin**, particularly in the intestines, where most of the serotonin is produced, and your transportation of serotonin out of the bowel to its target tissues is normal. However, **your clearance of serotonin is slightly faster**, decreasing the length of time serotonin can remain in a receptor exerting its effect. With this is also a faster clearance of stress hormones is equally fast decreasing their ability to further impair serotonin production.

This genotype combination can slightly increase the risk for depression, low moods, waking at 5 am or early morning waking, gastro-intestinal bloating, IBS symptoms, muscle pain and swelling, and food cravings, particularly for chocolate or sweets.

**5HTP by Genestra**- 1-2 caps twice a day with food. Alternatively, you can boost brain serotonin levels with **High Potency Rest Reset by Signature Supplements** if your sleep section also requires this - 2 caps at 8:30 pm (where melatonin will breakdown into serotonin right where it is needed).

Regular exercise, according to your genetics is key to maintain balanced serotonin levels.  
Moderate stress through deep breathing, meditation, diet and your stress hormone genes.

## NEUROTRANSMITTERS

## Short Term Stress Response

COMT  
rs4680

COMT or Catechol-O-methyltransferase is an important enzyme produced by the COMT gene that degrades or metabolizes several catecholamines including dopamine, adrenaline and noradrenaline (epinephrine and norepinephrine), along with estrogens and certain drugs. This enzyme adds a methyl group that is donated by S-adenosylmethionine (SAMe) and is thus also a major methylation gene.

COMT is extremely active in the prefrontal cortex, the area in the brain that is responsible for cognitive behaviour, decision making, personality expression, learning, addictions and moderating much of social behaviour.

Increased COMT activity decreases the binding and activity along with increasing the clearance of dopamine, adrenaline, noradrenaline, and catechol estrogens by almost 50%.

With respect to the clearance of dopamine through this gene, the normal allele is considered the adverse position, for it has a faster clearance of dopamine.

**Normal Allele:** G **Variant Allele:** A

**You are:** AG

**Key Characteristics of the Variant Allele:**

- Decreased COMT activity.
- Increased dopamine leading to less addictive behaviour, less food cravings.
- Increased pleasure responses following a stimuli.
- Increased anxiety due to higher stress hormone levels
- Often called the Worrier (as opposed to the G allele referred to as the warrior).
- More obsessive-compulsive behaviours.
- Increased fear response associated with PTSD.

FKBP5

rs3800373

FKBP5 is also known as FK binding protein 5. This protein is a member the immunophilin protein family, which helps to regulate protein folding, immunoregulation and most importantly regulates glucocorticoid binding and sensitivity.

Binding of FKBP5 to the glucocorticoid receptor reduces cortisol-binding capacity leading to impaired negative feedback regulation of the HPA (Hypothalamic-Pituitary-Adrenal) axis leading to a prolonged stress response. It also produces an augmented stress reaction both emotionally and physically. This in turn heightens the HPA axis creating a cyclic stimulation of the central nervous system ultimately increasing the risk of anxiety, panic disorders, depression and other mood disorders.

**Normal Allele:** C **Variant Allele:** A

**You are:** AC

**Key Characteristics of the Variant Allele:**

- Increased FKBP5 expression
- Loss of negative feedback in the HPA axis
- Increased anxiety
- Prolonged short-term stress response- easier to get “stuck” in stress loop.
- Increased depression
- Increased PTSD, especially from childhood memories.

NR3C2

rs5522

NR3C2 or nuclear receptor subfamily 3 group C member is a mineralocorticoid receptor (MR) which plays a key role in the activation of the body's stress pathway, the HPA or hypothalamic-pituitary-adrenal axis. It determines the sensitivity of the stress response.

Stress activates the HPA axis, resulting in the release of corticosteroids which bind to 2 receptors in the brain, the MR receptor encoded by this gene, and the glucocorticoid receptor (GR). Stress hormones, especially cortisol, have a very high affinity for these MR receptors, altering the sensitivity and activity of the HPA axis.

When cortisol binds into an MR, it induces a negative feedback loop within the HPA axis, inhibiting stimulation of the stress pathway. The greater the number of active MR receptors, the greater the negative feedback in the HPA axis, reducing the stimulation of the HPA axis. The variant C allele is associated with fewer MR receptors, and less negative feedback. This results in an increased physiological stress response, elevated depressive and anxious symptoms, increased HPA stimulation with less initiating stressors and loss of negative feedback with reduced cortisol-induced MR gene expression.

This variant C allele also increases the amount of ACTH produced by the hypothalamus, which stimulates the HPA axis to produce more cortisol.

The variant C allele is also associated with decreased focus, concentration, hyperactivity, impulsivity and increased ADD and ADHD. !

**Normal Allele:** T **Variant Allele:** C

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Fewer mineralocorticoid receptors
- Decreased negative feedback in the HPA axis
- Increased plasma ACTH
- Increased cortisol
- Increased depression
- Increased anxiety and hyperactivity
- Increased ADD/ADHD

GAD1

rs2241165

GAD1 is a gene that increases the production of glutamic acid decarboxylase, the enzyme responsible for converting glutamate, the most abundant excitatory neurotransmitter in the brain and central nervous system into GABA, an inhibitory neurotransmitter that helps calm the nervous system.

Glutamate plays a major role in learning, memory, energy levels and mood regulation. It also increases neuroplasticity allowing the brain and body to adapt to changing environments. However, chronic stress or poor GAD1 function increase glutamate release beyond normal leading to increased CNS excitation and decreased neuroplasticity.

GABA exerts its primary function in the synapses between the neurons of most CNS inhibitory pathways. Low levels of GABA are associated with many psychiatric illnesses from anxiety and autism to schizophrenia, as well as physical ailments such as seizures, tremors and sleep disorders.

**Normal Allele:** C **Variant Allele:** T

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Low glutamic acid decarboxylase.
- Low GABA and high Glutamate levels.
- Increased anxiety and depression.
- Increased restlessness or “feeling on edge.”
- Difficulty concentration.
- Sleep disturbances.
- Increased muscle fasciculations, seizures and tremors.

## RECOMMENDATIONS FOR

## Short Term Stress Response

**You produce the normal amount of ACTH from the pituitary and cortisol from the adrenal glands for each stressor.** You also have the normal number of hypothalamic receptors for mineralocorticoids to help shut off the HPA axis and return the nervous system to the quiet parasympathetic side.

However, **you produce a higher level of FKBP5**, the binding protein that regulates glucocorticoid binding and sensitivity, impairing negative feedback regulation of the HPA axis. This is the most important gene in the stress section for it indicates that your nervous system has a very difficult time turning off further production of the stress hormones even well after the stressor is resolved.

In addition, your clearance of stress hormones through your COMT gene is slow, allowing for a prolonged binding and action of the stress hormones in the nervous system.

All of this increases the risk of anxiety depression, PTSD, hyperactivity, panic attacks and exaggerated emotional responses.

Cortisol, like inflammation can turn over 90% of genes to their adverse position independent of how you treat those other genes. Cortisol also increases the production of the inflammatory cytokines IL6 and TNF $\alpha$  by up to 76%. This inflammation then triggers the HPA stress axis directly further stimulating these genes and more cortisol production making this section crucial to treat.

This inflammatory response not only aggravates all inflammatory conditions such as arthritis or irritable bowel syndrome, but it also inflames all neural tissues, blocking the binding of good neurotransmitters such as dopamine and serotonin, independent of how much neurotransmitter you make or we supplement with.

Cortisol and the stimulation of these genes also inhibits the production of digestive enzymes by 88%, forcing the deposition of acids into the stomach when you eat. These acids not only irritate and inflame the lining of the stomach and bowel, but they cut the food at the incorrect place, making the food appear "foreign" to the immune system in the bowel, forcing it to mount an inflammatory immunoglobulin response against it. This not only impairs the absorption of the food, but creates significant gas and bloating to food randomly.

This may be contributing to your increase in food sensitivities.

Cortisol inhibits the production of melatonin as it does not want you to enter into stage 4 deep sleep, decreasing the quality of sleep and thus impairing all healing.

Cortisol can easily decrease the rate of the metabolism from 92% down to 35%, independent of diet and exercise.

**Sereniten Plus by Pure Encapsulations or Stress Reset by Signature Supplements-** 2 capsules twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) for 8-10 weeks and then reduce to 1 capsule twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) increasing as needed for periodic stressors that occur.

Deep breathing and meditation.

Exercise according to your exercise genes.



You make significantly less glutamic acid decarboxylase, the enzyme responsible for breaking down glutamate, the most abundant excitatory neurotransmitter in the brain and central nervous system into GABA, an inhibitory neurotransmitter that helps calm the nervous system. **This leads to much higher glutamate levels and significantly reduced GABA production** within the central nervous system increasing the risk of anxiety, depression, sleep disturbances and muscle spasticity, seizures and CNS excitation.

**GABA Reset by Signature Supplements** – 2 caps twice a day empty stomach (30 mins or more before food or 2 hours or more after) for 8 weeks and then reduce to 1 cap twice per day empty stomach.

## NEUROTRANSMITTERS

## Long Term Stress Response

COMT  
rs4680

COMT or Catechol-O-methyltransferase is an important enzyme produced by the COMT gene that degrades or metabolizes several catecholamines including dopamine, adrenaline and noradrenaline (epinephrine and norepinephrine), along with estrogens and certain drugs. This enzyme adds a methyl group that is donated by S-adenosylmethionine (SAMe) and is thus also a major methylation gene.

COMT is extremely active in the prefrontal cortex, the area in the brain that is responsible for cognitive behaviour, decision making, personality expression, learning, addictions and moderating much of social behaviour.

Increased COMT activity decreases the binding and activity along with increasing the clearance of dopamine, adrenaline, noradrenaline, and catechol estrogens by almost 50%.

With respect to the clearance of dopamine through this gene, the normal allele is considered the adverse position, for it has a faster clearance of dopamine.

**Normal Allele:** G **Variant Allele:** A

**You are:** AG

**Key Characteristics of the Variant Allele:**

- Decreased COMT activity.
- Increased dopamine leading to less addictive behaviour, less food cravings.
- Increased pleasure responses following a stimuli.
- Increased anxiety due to higher stress hormone levels
- Often called the Worrier (as opposed to the G allele referred to as the warrior).
- More obsessive-compulsive behaviours.
- Increased fear response associated with PTSD.

CRHR1

rs242939

Corticotropin releasing hormone receptor 1 or CRHR1 is the receptor that binds CRH, corticotropin releasing hormone, stimulating the HPA (hypothalamic-pituitary-adrenal) axis, pushing the nervous system to the sympathetic stress side.

The main function of CRH is to stimulate the pituitary to produce and release ACTH, which in turn stimulates the adrenals to produce cortisol, adrenaline and noradrenaline. The C allele or variant allele has a higher number of CRH receptors to bind CRH continually stimulating the stress response and is thus associated with increased anxiety, depression, and mood disorders.

The subsequent increase in production of stress hormones from this SNP are also significantly linked to obesity, IBS and IBS-like symptoms, asthma and increased blood pressure.

**Normal Allele:** T **Variant Allele:** C

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Increased CRH receptors
- Increased binding of CRH
- Increased stimulation of the HPA axis
- Increased anxiety
- Increased depression
- Increased obesity and unstable blood glucose levels.
- Increased bloating, gas and irregular bowel movements.

FKBP5

rs3800373

FKBP5 is also known as FK binding protein 5. This protein is a member the immunophilin protein family, which helps to regulate protein folding, immunoregulation and most importantly regulates glucocorticoid binding and sensitivity.

Binding of FKBP5 to the glucocorticoid receptor reduces cortisol-binding capacity leading to impaired negative feedback regulation of the HPA (Hypothalamic-Pituitary-Adrenal) axis leading to a prolonged stress response. It also produces an augmented stress reaction both emotionally and physically. This in turn heightens the HPA axis creating a cyclic stimulation of the central nervous system ultimately increasing the risk of anxiety, panic disorders, depression and other mood disorders.

**Normal Allele:** C **Variant Allele:** A

**You are:** AC

**Key Characteristics of the Variant Allele:**

- Increased FKBP5 expression
- Loss of negative feedback in the HPA axis
- Increased anxiety
- Prolonged short-term stress response- easier to get “stuck” in stress loop.
- Increased depression
- Increased PTSD, especially from childhood memories.

## RECOMMENDATION FOR Long Term Stress Response

You produce the normal amount of corticotropin releasing hormone (CRH) from your hypothalamus for each stressful event you encounter. This helps return your central nervous system back to the parasympathetic side, the quiet side, with greater ease following a stressful event. You also have the normal amount of CRH receptors with which to maintain parasympathetic stimulation.

**However, you produce a high level of FKBP5**, the binding protein that regulates glucocorticoid binding and sensitivity, impairing the negative feedback regulation of the HPA axis and keeping your nervous system stuck for longer periods of time in the sympathetic stress side. This is the most important gene in the stress section for it indicates that your nervous system has a very difficult time turning off further production of the stress hormones even well after the stressor is resolved.

In addition, your clearance of stress hormones through your COMT gene is slow, allowing for a prolonged action of the stress hormones in the nervous system, augmenting the above effects.

All of this allows the central nervous to get “stuck” in the sympathetic side with great ease, increasing risk of anxiety depression, PTSD, hyperactivity, panic attacks and exaggerated emotional responses.

Cortisol, like inflammation can turn over 90% of genes to their adverse position independent of how you treat those other genes. Cortisol also increases the production of the inflammatory cytokines IL6 and TNFa by up to 76%. This inflammation then triggers the HPA stress axis directly further stimulating these genes and more cortisol production making this section crucial to treat.

**Sereniten Plus by Pure Encapsulations or Stress Reset by Signature Supplements** 2 capsules twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) for 6-8 weeks after completing treatment for your short term stress response and then reduce to 1 capsule twice a day empty stomach (30 minutes or more before food, or 2 hours or more after) increasing as needed for periodic stressors that occur.

Deep breathing and meditation.

Exercise according to your exercise genes.

## EXERCISE

## Cardiovascular

ACTN3

rs1815739

ACTN3 is a gene that codes for the production of the alpha actin 3 protein, one of the main proteins that form the fibers that are responsible for generating the explosive powerful contractions during sprints or HIIT (High Intensity Interval Training) style exercise. If the protein filaments which make up the muscle fiber contain a higher percentage of actin protein, then a stronger, more dense muscle fiber is formed, capable of performing more explosive contractions with decreased risk of injury.

C allele individuals have more actin 3 protein producing more fast twitch fibers, with thicker myelin sheaths around their nerves and faster nerve impulses from the brain to the muscle for quick powerful responses fuelled by short bursts of ATP. C/C allele individuals are the sprinters and are designed for true HIIT exercise.

T allele individuals have little to no actin 3 protein, and thus have few fast twitch fibers. Instead they have an abundance of slow twitch fibers for endurance sports and workouts. The T allele individual does not have the physical capability to sprint or perform HIIT style exercises. If they do they will increase the production of creatine kinases, a measurement of muscle breakdown and inflammation, along with cortisol, our body's stress hormone, for doing the wrong type of exercise for your body is a physical stressor.

**Normal Allele:** C **Variant Allele:** T

**You are:** CT

**Key Characteristics of the Variant Allele:**

- Unable to produce adequate Actin 3 protein
- Fewer fast-twitch fibers for sprinting or intervals
- Abundance of slow twitch fibers for endurance sports
- Better oxidative muscle metabolism over long periods of time
- Increased inflammation and DOMS (delayed onset muscle soreness) with HIIT.

ADRB2 EX  
rs1042713

The beta-2 adrenergic receptor is one of 7 members of the adrenergic receptor family. Similar to the other members, ADRB2 specifically binds and is activated by catecholamines.

This ADRB2 receptor is abundantly expressed in bronchial smooth muscle cells leading to bronchodilation, in the cardiac myocytes and vascular smooth muscle cells causing increased rate and force of heart contractions and vasoconstriction when stimulated.

The alpha adrenergic is the primary receptor for vasoconstriction, yet the beta receptor also has significant vascular effects. Unlike the alpha receptor, the beta receptor has far greater differences in the metabolic rate, metabolic responses and sudden cardiac events in response to exercise and stress.

The A allele is associated with far fewer ADRB receptors and thus less vasoconstriction and bronchodilation, particularly under stress or during intense exercise. Thus, the A allele is much better with longer slower endurance workouts. They have a lower resting cardiac output due to a reduced stroke volume (amount of blood pumped by the left ventricle of the heart in one contraction). This combined with a lower blood pressure and increased VO2Max (volume of oxygen per unit of time that an individual uses during exercise or exertion) makes them the ideal marathon runner.

**Normal Allele:** G **Variant Allele:** A

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Fewer beta-2 adrenergic receptors
- Less vasoconstriction, lower blood pressure
- Higher peak oxygen consumption, increased VO2Max
- Better with endurance training or sports.
- Worse with sprints or HIIT (less bronchodilation with short intense exercise)

ACE

rs4343

Ace is the gene that produces the enzyme angiotensin converting enzyme or "ACE" to transform angiotensin I into angiotensin II. Angiotensin II is a vasoconstrictor that increases blood pressure, which in turn influences blood flow, sodium potassium pumps and the metabolism within the muscle.

Angiotensin II also acts upon nerves to increase the sensation of thirst and desire for salt to encourage the release of ADH (anti-diuretic hormone) from the pituitary and noradrenaline from sympathetic nerves. It also stimulates the adrenals to increase the production of aldosterone, increasing sodium retention and leaching potassium from the kidneys. The kidneys in response increase water reabsorption to increase blood volume and pressure. The end game of all of these responses is to increase the blood pressure and blood flow as well as the delivery of nutrients through the body.

A allele individuals produces far less ACE, decreasing the control of plasma sodium and potassium and thus the regulation of blood volume and pressure. As HIIT (High Intensity Interval Training) exercise is far more reliant on quick muscle reactions, it requires more blood flow in short bursts of which the A allele cannot produce. This is one reason why the A allele does not do well with HIIT exercise. They are far better with longer slower endurance, even more so at altitude. Similarly, if they attempt eccentric exercises (an exercise where the action of the muscle also lengthens it, for example the descend of a bicep curl) with increased weights the decreased blood flow across the muscle has been shown to increase creatinine kinase (CK) levels, a measurement of muscle inflammation and breakdown, far more than the G allele. Thus, the style of resistance of weight training they need is similar to their cardiovascular workout – endurance or multiple reps with lower or lighter weights.

**Normal Allele: G Variant Allele: A**

**You are: GG**

**Key Characteristics of the Variant Allele:**

- Produces less ACE for sprints or HIIT exercises.
- Better with endurance
- Better at altitude exercising compared to G allele
- Increased creatine kinase and inflammation.
- Inflammation worse with eccentric exercises, heavy weights, sprints or HIIT.
- Better is endurance resistance training – multiple reps, light weights, little to no breaks.

## RECOMMENDATION FOR Cardiovascular

You have approximately equal distribution of fast and slow twitch fibers in your muscles. Fast twitch fibers enable one to sprint, and slow twitch fibers allow one to perform endurance exercises. As you have a mix between the two, you are best designed for a combination of moderated sprints and longer slower endurance.

You also have an increased blood flow in large quick bursts to the muscle during exercise and a better control of sodium-potassium regulation within the cells. In addition, you have more beta-2 adrenergic activity with increased bronchodilation with short intense exercise. Both of these effects further moderate your exercise style slightly towards faster sprints or HIIT (High Intensity Interval Training).

Because of your increased risk of injury with High Intensity Training, it is important to follow recommendations in your Injury and susceptibility section and avoid any start-stop exercises such as soccer.

Note: This is for cardiovascular exercise, not weight training. Your resistance or weight training style is in the next section. It is very possible to code for the opposite style of workout for weight training depending on your genes.

**You are better with 1.5 to 2 minute intervals at 70-75% capacity, with 45 second recovery intervals at 40% capacity for 45-50 minutes twice a week. Alternating with a consistent cardiovascular workout for 45-60 minutes at about a 60% capacity twice a week.**

## EXERCISE

## Resistance Training

INSIG2

rs7566605

INSIG2 or insulin induced gene 2 produces a protein that when activated alters lipid synthesis and stimulates fatty acid synthesis. Its expression is downregulated by insulin and by exercise in certain individuals.

The INSIG2 gene is associated with obesity and increased BMI and how that is affected by resistance training. Each Allele responds metabolically differently to weight training, and that effect is slightly augmented between sexes.

**Normal Allele:** G **Variant Allele:** C

**You are:** CG

**Key Characteristics of the Variant Allele:**

- Higher baseline of subcutaneous fat especially in women.
- Women have less weight loss with high weight low repetition resistance training.
- Men can easily gain weight with high weight low repetition resistance training.
- Both sexes are better with high repetition resistance training.
- Better results making the resistance training like a cardiovascular workout.

ACE

rs4343

Ace is the gene that produces the enzyme angiotensin converting enzyme or "ACE" to transform angiotensin I into angiotensin II. Angiotensin II is a vasoconstrictor that increases blood pressure, which in turn influences blood flow, sodium potassium pumps and the metabolism within the muscle.

Angiotensin II also acts upon nerves to increase the sensation of thirst and desire for salt to encourage the release of ADH (anti-diuretic hormone) from the pituitary and noradrenaline from sympathetic nerves. It also stimulates the adrenals to increase the production of aldosterone, increasing sodium retention and leaching potassium from the kidneys. The kidneys in response increase water reabsorption to increase blood volume and pressure. The end game of all of these responses is to increase the blood pressure and blood flow as well as the delivery of nutrients through the body.

A allele individuals produces far less ACE, decreasing the control of plasma sodium and potassium and thus the regulation of blood volume and pressure. As HIIT (High Intensity Interval Training) exercise is far more reliant on quick muscle reactions, it requires more blood flow in short bursts of which the A allele cannot produce. This is one reason why the A allele does not do well with HIIT exercise. They are far better with longer slower endurance, even more so at altitude. Similarly, if they attempt eccentric exercises (an exercise where the action of the muscle also lengthens it, for example the descend of a bicep curl) with increased weights the decreased blood flow across the muscle has been shown to increase creatinine kinase (CK) levels, a measurement of muscle inflammation and breakdown, far more than the G allele. Thus, the style of resistance of weight training they need is similar to their cardiovascular workout – endurance or multiple reps with lower or lighter weights.

**Normal Allele: G Variant Allele: A**

**You are: GG**

**Key Characteristics of the Variant Allele:**

- Produces less ACE for sprints or HIIT exercises.
- Better with endurance
- Better at altitude exercising compared to G allele
- Increased creatine kinase and inflammation.
- Inflammation worse with eccentric exercises, heavy weights, sprints or HIIT.
- Better is endurance resistance training – multiple reps, light weights, little to no breaks.

## RECOMMENDATION FOR Resistance Training

You are designed for medium weights, medium repetition resistance training. You produce the normal amount of angiotensin converting enzyme or ACE, and thus have a good flush of blood volume over the muscle body during exercise, with adequate control of your sodium potassium pumps for repair from exercise. This allows you to increase the amount of weight used during exercise.

The variant C coding for the INSIG2 gene is associated with an increased in subcutaneous weight fat deposition in both men and women, which is increased when performing heavy weight, fewer repetition resistance training. This is even more prominent in men. However, your G/C position decreases the effect of weight gain with heavy weights slightly, and also allows you to slightly increase the amount of weight used.

**You are designed for moderate weight, moderate repetition (10-14 reps) per exercise resistance training. You can take small 30 second breaks in between exercise. You would do best to perform exercises that recruit more than one muscle group at a time.** Eg, with medium weights perform a shoulder press from a squat position, standing up at the same time as you perform your shoulder press to engage both the legs (with no weights) and the arms in one exercise. Repeat for 10-14 repetitions, with a small break between each repetition if needed. **Aim for sets of each exercise 2 to 3 times a week.**

Note: These recommendations are for resistance or weight training exercise style, not cardiovascular exercise. Your cardiovascular exercises style is in the section above. It is very possible to code for the opposite style of workout for these two sections.

## EXERCISE

## Injury Susceptibility and Prevention

MMP3  
rs679620

MMP's or matrix metalloproteinases are involved in the breakdown of extracellular matrix proteins and tissue remodeling. They are particularly active in arthritis as well as joint and tissue repair. The expression of the MMP3 gene is regulated at the transcription level, where the promoter region responds to stimuli such as growth factors, cytokines and injury.

The variant C allele is associated with increased enzyme production and thus increased degradation of collagen types 1, 2, 4, 1X and X. The C allele also has increased breakdown of the main components of connective tissue: the proteoglycans, fibronectin, laminin and elastin, greatly compromising not just the strength but the elasticity and resistance of tendons under stress.

The degradation and resulting inflammation have further damaging effects by activating other MMP's such as 1, 7 and 9 in the GI tract, skin, bones and joints.

This combined effect leads to increased tendinopathies, higher overall inflammation, weaker tissue and increased risk of injury.

**Normal Allele:** T **Variant Allele:** C

**You are:** CT

**Key Characteristics of the Variant Allele:**

- Increased MMP3 production
- Increased activation of other MMP's
- Increased inflammation.
- Increased degradation of collagen
- Increased degradation of elastin, fibronectin, proteoglycans and laminin
- Increased risk of tendinopathies and collagenous injury

IL6

rs1800795

IL6 or interleukin 6 acts as an inflammatory cytokine or substrate that is stimulated under several conditions such as fever, injury, infections, exercise, stress and obesity. Its main role within the immune system is to stimulate the production and recruitment of neutrophils and consequently B-cells to increase inflammation and help the immune system attack an invading pathogen.

In the cardiovascular system IL6 increases inflammation in the blood vessels and stimulates the production of TNF $\alpha$  (tumor necrosis factor alpha) and CRP (C-Reactive Protein), two other inflammatory substrates.

IL-6 is also an important mediator of fever and acute phase immune responses. It is capable of crossing the blood brain barrier to initiate the synthesis of prostaglandins increasing body temperatures or fevers. However, the increased inflammation in the brain can inflame and mutate neuronal receptors, greatly increasing the progression mood disorders. Its mechanism for increasing depression and other mood disorders is by IL6 alterations in BDNF (brain derived nerve factor), which is responsible for “repairing” damage and inflammation to neural tissue and receptors. Without this repair, important hormones such as serotonin and dopamine are unable to bind into their receptors and regulate mood.

It is also secreted in the osteoblasts (bone cells) to stimulate osteoclastic or bone breaking activity, along with abnormal scarring in joints and increased risk of tendinopathies and arthritides.

IL-6 is also produced in adipose tissue increasing adipogenesis, slowing the metabolic rate. The increased inflammation inside the adipose tissue as a result of elevated IL6 also impairs the production of adiponectin which in turn destabilizes blood sugar levels increasing the risk of diabetes.

Those with higher levels of IL6 post operatively have far less favourable outcomes, especially cardiovascular surgery, due to the IL-6 induced rise in CRP and subsequent increased cardiac inflammation.

**Normal Allele:** C **Variant Allele:** G

**You are:** CG

**Key Characteristics of the Variant Allele:**

- Increased IL6 production.
- Increased inflammation.
- Increased bone and joint inflammation, degradation and tendonopathies.
- Increased obesity and diabetes.
- Increased blood sugars.
- Increased risk of depression or mood disorders.
- Increased risk of osteoporosis.
- Decreased favourable outcome following surgery or cardiac disease.

**COL1A1**  
**rs1800012**

COL1A1 is a gene that codes for collagen type 1 production. Collagen is a rope like-structure that is made of 3 chains. Type 1 collagen is comprised of 2 alpha-1 chains and one alpha-2 chain.

Type 1 collagen is the major component of the fibrils, a building block of collagen and cartilage, accounting for 85% of them.

The allele coding for COL1A1 may seem a little backwards as the C allele, the variant allele, has increased collagen type 1. This may seem strange that the variant has the beneficial property here, but it evolved through time to help us. This increased production of collagen increases the strength and resilience of tendons and ligaments in order to decrease the risk of tendon tears while running and hunting.

The A allele individual has added benefits of tendon strength as they have altered ratios of alpha 1 and 2 chains in their collagen, favouring the alpha 1, the stronger of the 2 chains, and increasing the tensile strength of tendons and ligaments further.

**Normal Allele: A Variant Allele: C**

**You are: CC**

**Key Characteristics of the Variant Allele:**

- Increased collagen type 1 production.
- Decreased risk of tendon tears.
- Increased alpha 1 chain ratio in the collagen.
- Able to perform more powerful explosive exercise with decreased risk of injury.
- Note this is the variant allele although it is the advantageous allele.

## RECOMMENDATION FOR

## Injury Susceptibility and Prevention

**You have a significant increased risk of injury when exercising, especially when performing high intensity interval training, stop-start sports or lifting heavy weights.** You produce an increased amount of metalloproteases, the enzymes that are involved in the breakdown and remodelling of collagen (especially collagen type 1, 11, 1V, 1X and X) as well as increasing the breakdown of the main components of connective tissue, the proteoglycans, fibronectin, laminin and elastin, greatly compromising not just the strength but also the elasticity and resistance of tendons under stress or during exercise. **You also produce more than the normal amount of IL6**, a potent inflammatory substrate when you exercise, augmenting inflammation in the tendons and joints as well as increasing weight gain.

However, you do produce more collagen type 1 protein helping to increase the strength and integrity of your collagen type 1, the main collagen type in most tendons and ligaments.

Treatment: Warming up with a walk before exercise is key to increase the blood flow and oxygen into muscles so that they are more flexible and can stretch with greater ease when you do exercise, decreasing the pressure and stress on the attached tendons. Avoid plyometrics and stop-start sports such as soccer as much as possible. Use K-tape around the Achilles tendon or any weaker joint to support the muscles and increase proprioception and nerve firing to the muscle. This once again will allow the muscle to function with greater response, decreasing the stress placed on the tendons. Always ice after exercise.

**Resveratrol Extra by Pure Encapsulations**- 1 capsule twice a day empty stomach (30 minutes or more before food or 2 hours or more after) to reduce the excess production of MMPs and IL6. After 6 weeks this can reduce to 1 per day. Look to Neural Repair or TMC and see if they are also needed, for they will contain Resveratrol and cross cover here, decreasing the need to add in another pill.

**Arthroben by Designs for Health** - .1 scoop per day in water empty stomach.

## IMMUNITY

## General

HLADQB1  
rs7775228

The HLADQB1 gene belongs to a group of MHC (major histocompatibility complex) genes that provide the instructions for making proteins on the surface of specific immune cells, which in turn triggers an immune response. This response then triggers a variety of inflammatory, allergenic and asthmatic reactions.

The variant C allele is associated with increased allergies to benign substrates and augmented asthmatic reactions.

The HLA complex, also called human leukocyte antigen, helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses, bacteria and allergens. For this reason this gene is involved in the initiation and progression of several autoimmune conditions such as celiac disease and Multiple Sclerosis.

**Normal Allele:** T **Variant Allele:** C

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Increased HLA production
- Increased inflammation
- Increased risk of asthma
- Increased risk of allergies
- Increased risk of celiac disease
- Increased risk of irritable bowel syndrome
- Increased risk of auto-immune disorders.

IRF5

rs4728142

IRF5 is a member of the interferon regulatory factor or IRF family of immune substrates. It is a group of transcription factors with a wide variety of roles, including virus-mediated activation of interferon, T-cell activity, modulation of cellular growth, differentiation, apoptosis, and immune system activity.

IRF5 acts as a molecular switch or trigger that controls whether macrophages will promote or inhibit inflammation. When this activity is overly stimulated, it can easily increase the initiation of several auto-immune and inflammatory conditions.

Blocking the production of IRF5 in macrophages may help treat a wide range of autoimmune diseases. Conversely, boosting IRF5 levels might help treat people whose immune systems are weak, compromised, or damaged. IRF5 seems to work either by interacting with DNA directly, or by interacting with other proteins that then control which genes are switched on.

However, under stress, prolonged infections or diseases, IRF5 activity is downgraded leading to a compromised immune response. Boosting the activity of IRF5 and the immune response then becomes necessary.

This gene when over active is associated with general inflammatory response within the immune system, ulcerative colitis, scleroderma, RA, SLE, MS, Parkinson's and other autoimmune conditions. When under activated it is associated with chronic immune deficiency, frequent infections, and a poorer cancer response.

**Normal Allele:** G **Variant Allele:** A

**You are:** AG

**Key Characteristics of the Variant Allele:**

- Increased IRF expression.
- Increased interferon production
- Increased interleukin production
- Increased inflammatory cytokine production
- Increased risk of inflammatory auto-immune conditions.
- Increased risk of inflammatory bowel disease.

## RECOMMENDATIONS FOR General

You have the normal production of human leukocyte antigen, part of the histocompatibility complex family, capable of triggering allergenic, asthmatic and immune responses. When a foreign body, such as a virus, bacteria or allergen enters the body, it is able to decipher self versus non-self and does not mount an immune reaction against your own body tissues through the T-cells, decreasing inflammation and tissue damage

No treatment is needed.

You produce slightly more than the normal amount of interferon through this gene. This can increase the general inflammatory response throughout the body, but more importantly can augment the production of interleukins, inflammatory cytokines and the synthesis auto-antibodies, throwing the immune response into “overdrive”.

This coding also decreases the ability of the immune system to see a pathogen when it first enters the body, delaying the time it takes to mount a response to it, increasing the severity of the infection.

This coding is associated with a slight increased risk of inflammatory bowel disease, ulcerative colitis, and several autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and multiple sclerosis.

Stress and chronic infections or cancer can downgrade this response, lowering the immune response rather than increasing it. In this case the T-cytotoxic cells, anti-inflammatory cytokines, macrophages and interleukin response would be low.

If you do not have any of the above disease, nor experience frequent inflammatory flares in the bowel or skin, then you do not necessarily need to treat these gene, for you most likely are not expressing this gene. If you are presently experiencing one or more of these conditions or have more frequent inflammatory reactions in the bowel or skin then treatment is **Moducare (by Moducare)** 1 capsule a day empty stomach (30 minutes or more before food or 2 hours or more after).

If you have a personal or family history of cancer or frequent infections treatment is **Immune Modulator by Signature Supplements** - 3/4 tsp in water or 4 caps on an empty stomach daily. Take this twice a day if you presently have cancer and add **Immune Booster by Signature Supplements** - 1 cap per day. If you are heterozygote or variant for the CYP1A2 gene increase DIM by 1 cap per day or increase cruciferous veggies to balance the effect of curcumin in the Immune Booster on CYP1A2.

## IMMUNITY

## Inflammation

IL6

rs1800795

IL6 or interleukin 6 acts as an inflammatory cytokine or substrate that is stimulated under several conditions such as fever, injury, infections, exercise, stress and obesity. Its main role within the immune system is to stimulate the production and recruitment of neutrophils and consequently B-cells to increase inflammation and help the immune system attack an invading pathogen.

In the cardiovascular system IL6 increases inflammation in the blood vessels and stimulates the production of TNF $\alpha$  (tumor necrosis factor alpha) and CRP (C-Reactive Protein), two other inflammatory substrates.

IL-6 is also an important mediator of fever and acute phase immune responses. It is capable of crossing the blood brain barrier to initiate the synthesis of prostaglandins increasing body temperatures or fevers. However, the increased inflammation in the brain can inflame and mutate neuronal receptors, greatly increasing the progression mood disorders. Its mechanism for increasing depression and other mood disorders is by IL6 alterations in BDNF (brain derived nerve factor), which is responsible for “repairing” damage and inflammation to neural tissue and receptors. Without this repair, important hormones such as serotonin and dopamine are unable to bind into their receptors and regulate mood.

It is also secreted in the osteoblasts (bone cells) to stimulate osteoclastic or bone breaking activity, along with abnormal scarring in joints and increased risk of tendinopathies and arthritides.

IL-6 is also produced in adipose tissue increasing adipogenesis, slowing the metabolic rate. The increased inflammation inside the adipose tissue as a result of elevated IL6 also impairs the production of adiponectin which in turn destabilizes blood sugar levels increasing the risk of diabetes.

Those with higher levels of IL6 post operatively have far less favourable outcomes, especially cardiovascular surgery, due to the IL-6 induced rise in CRP and subsequent increased cardiac inflammation.

**Normal Allele: C Variant Allele: G**

**You are: CG**

**Key Characteristics of the Variant Allele:**

- Increased IL6 production.
- Increased inflammation.
- Increased bone and joint inflammation, degradation and tendonopathies.
- Increased obesity and diabetes.
- Increased blood sugars.
- Increased risk of depression or mood disorders.
- Increased risk of osteoporosis.
- Decreased favourable outcome following surgery or cardiac disease.

## TNFA rs1800629

TNFA or tumor necrosis factor alpha is cell-signalling protein (cytokine) involved in systemic inflammation. It is also one of the key inflammatory markers involved in cellular growth and in the acute phase of immune reactions. It is expressed in a variety of cells including T and B cells, natural killer or NK cells, mast cells, macrophages, fibroblasts and dendritic cells. TNFA modulates several process within these cells such as differentiation, cellular remodelling, tissue adhesion and more.

Its primary role is to regulate other immune cells to produce a strong immune reaction. It is able to induce fevers, apoptosis or cell death, increase inflammation, inhibit viral replication and much more. However, when we produce too much, or if it is activated for a long period of time, it can stimulate other inflammatory and immune responses with too much strength.

TNFA is activated in response to a diversity of stimuli such as inflammation (production of cytokines), allergic reactions, stress and infections. Its primary role is to orchestrate a myriad of immune cells and the mediators, such as MMP's, IL-1 and IL-6 to inflame or stimulate the inflammatory pathways. Thus it is one of the major players in asthma, hives, allergies, irritable bowel syndrome, colitis, psoriasis and arthritis.

TNFA is also involved in wound healing, collagenous development, and angiogenesis.

The TNFA gene is closely linked to the trigger of autoimmune disorders due to its geographical proximity to all the HLA class 1 and 2 genes on the chromosomes. Thus elevated TNFA or expression of this gene can initiate and increase progression of most autoimmune diseases.

**Normal Allele:** G **Variant Allele:** A

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Increased TNFa production.
- Increase inflammation.
- Increased risk of allergies.
- Increased risk of asthma.
- Increased risk of psoriasis and other inflammatory skin conditions.
- Increased risk of heart disease.
- Increased risk of irritable bowel syndrome, colitis and other inflammatory bowel conditions.
- Increased risk of arthritis.

## RECOMMENDATION FOR Inflammation

**You produce the normal amount of the inflammatory cytokine TNF $\alpha$ . However, you produce increased levels of IL6.** Elevated IL6 stimulates higher TNF $\alpha$  production independent of genetic coding, creating a cyclic pro-inflammatory response in the body. This not only prolongs the healing from any injury or infectious disease, but also greatly contributes to several conditions such as obesity, diabetes, osteoporosis, arthritis, and mood disturbances.

Inflammatory cytokines easily cross the blood brain barrier stimulating the HPA axis and stress response even in the absence of a stressor. In response, the nervous system further stimulates the production of these inflammatory substrates, creating a cyclic stress-inflammatory response that must be treated.

Inflammation, like cortisol can trigger over 90% of genes to their adverse position independent of treatment, once again making this section crucial to treat.

Inflammation can mutate hormone and neurotransmitter receptors, altering their shape so that substrates cannot bind into them and mount a response, independent of the amount of available hormone or neurotransmitter.

**Glutathione Complex by Signature Supplements** - 2 caps twice a day empty stomach (30 minutes or more before food or 2 hours or more after for 4 weeks and then reduce it to 2 caps a day thereafter.

Please check your detox genes as you may already be taking these supplements and you do not need to duplicate this. Curcumin or turmeric can also reduce both TNF $\alpha$  and IL6, but as it is contra-indicated for CYP1A2 C/C, leaving glutathione and NAC as a better choice.

## DETOXIFICATION

# Phase 1

### CYP1A2 rs762551

CYP1A2 is the gene that codes for phase 1 detoxification enzyme Cytochrome 1A2. CYP1A2 is part of the cytochrome P450 group of enzymes. Despite there being over 50 members of this family of enzymes, 6 of them metabolise 90% of drugs, with CYP1A2 and CYP3A4 being the most prominent ones. This enzyme is crucial for the metabolism of xenobiotics in the body. It modifies exogenous and endogenous compounds from the environment and the body in order to prepare them for phase II detoxification (clearance of the toxin out of the body). CYP1A2 also catalyzes many pharmaceutical drugs, often altering their efficacy. This is particularly true of medications such as Ciprofloxacin, fluvoxamine and amiodarone.

It also determines how your body specifically handles, metabolizes and clears cigarette smoke, caffeine and acetaminophen, as well as peppermint and echinacea.

CYP1A2's activity is slowed by caffeine, acetaminophen, turmeric or curcumin, amiodarone, cimetidine, ciprofloxacin and fluvoxamine, as well as charcoaled meats. Conversely it is sped up by tobacco, phenobarbital, carbamazepine, peppermint, echinacea and raw cruciferous veggies.

When toxins are modified into phase 1 substrates through this and many other CYP genes, they are frequently converted into more inflammatory, more damaging products on the body, increasing the necessity for a strong phase 2 detoxification pathway.

CYP1A2 is also the key enzyme in the etiology of breast cancer and is involved in the activation of aromatic and heterocyclic amines, polycyclic aromatic hydrocarbons and the production of beneficial 2-OH estrogen. Reduced CYP1A2 activity increases the risk of breast cancer.

**Normal Allele: A Variant Allele: C**

**You are: AC**

**Key Characteristics of the Variant Allele:**

- Known as the slow metabolizer.
- Decreased CYP1A2 production
- Decreased phase 1 detoxification
- Increased TNFa (an inflammatory cytokine)
- Increased cardiovascular disease and heart attacks.
- Worse with caffeine.
- Worse with high doses of curcumin or turmeric.
- Increased risk of colon cancer and colorectal polyps with BBQ'd meats.
- Increased risk of breast cancer.
- Increased inflammation

CYP3A4

rs2740574

Cytochrome 3A4 is one of the most abundant phase 1 cytochrome P450 enzymes. It is found in high concentration in the liver and small intestines where its main function is to metabolize approximately 50% of pharmaceutical medications, especially oral contraceptives. The CYP3A4 gene is also greatly expressed in the prostate, breast, stomach and colon.

CYP3A4 activity is increased by phenobarbital, phenytoin, rifampicin, St John's Wort and glucocorticoids (stress hormones) and is inhibited by many antibiotics such as erythromycin, as well medications and foods such as verapamil, prednisone, goldenseal and grapefruit.

CYP3A4 also contributes to the detoxification of bile acids, and steroid hormones.

**Normal Allele:** C **Variant Allele:** T

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Decreased enzyme production.
- Slowed phase 1 detoxification.
- Often require lower doses of pharmaceuticals due to slower clearance of them.
- Increased risk of breast, prostate and colon disease.

## RECOMMENDATION FOR Phase 1

You produce the normal amount **phase 1 detoxification enzyme cytochrome P450 1A2**. not too much and not too little. This is very balanced place to be for this genes. **However, you produce less CYP3A4 enzymes.** These enzymes are crucial for the metabolism of xenobiotics in the body. They modify both exogenous and endogenous compounds from the environment and in the body in order to prepare them for phase II detoxification (clearance of the toxin out of the body).

Slower CYP3A4 activity is associated with a slower clearance of hormones, estrogen in particular, as well as several xenobiotics. This gene is particular active in women.

**avoid caffeine or one at most, increase raw cruciferous vegetables** as much as possible, and **DIM and Detox (By Pure Encapsulations)** 2 caps twice a day empty stomach (30 minutes or more before food or 2 hour or more after) for 2 weeks, repeating this twice a year to help support phase 1 detoxification.

## DETOXIFICATION

## Phase 2

SOD2  
rs4880

SOD2 or Mitochondrial Superoxide Dismutase is a manganese-dependant enzyme that binds superoxide by-products of oxidative phosphorylation and converts them into hydrogen peroxide and diatomic oxygen. This is the main enzyme that protects the mitochondria and DNA from oxidative damage.

SOD exists in 3 forms, SOD1, 2 and 3. SOD1 is mostly found within in cell cytoplasm, nucleus and membrane lumen. SOD2 are located in the mitochondrial matrix, and 3 is mostly found extracellularly or outside the cell.

When mitochondria, the powerhouses of our cells, produce energy, they produce superoxide (and ROS) as a by-product. Superoxide is inflammatory and damaging and requires SOD2 to convert it into less damaging by-products (hydrogen peroxide and diatomic oxygen).

Decreased SOD2 activity is associated with premature aging, cancers, increased inflammatory diseases and motor neuron diseases.

**Normal Allele:** A **Variant Allele:** G

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Decreased enzyme production.
- Decreased clearance of all ROS.
- Increased inflammation.
- Increased risk of cancers.
- Decreased energy.

GSTP1

rs1695

Glutathione-S-Transferase P is a member of the Glutathione-S-transferase (GST's) family of enzymes that are key players in detoxification (Phase 2) by catalyzing the conjugation of many toxic compounds, carcinogens and cytotoxic medications with reduced glutathione in order to neutralize and clear them from the body. Reduced activity in the GSTP1 gene can easily lead to increased cell damage from oxidative inflammation and an accumulation of toxic pre-carcinogens in the body tissues.

Glutathione is an important antioxidant which neutralizes reactive oxygen species, the major cause of oxidative stress and damage. While glutathione itself does a fairly good job at neutralizing many ROS, it often requires the action of GSTP1 to neutralize the more damaging xenobiotic ROS's. Xenobiotics are damaging substrates that are not normally produced in the body (not a metabolic bi-product) but rather are absorbed or ingested external substances such as herbicides, pesticides, polyaromatic hydrocarbons, estrogens and several medications.

**Normal Allele:** A **Variant Allele:** G

**You are:** AA

**Key Characteristics of the Variant Allele:**

- Reduced enzyme activity.
- Reduced clearance of xenobiotics.
- Increased intracellular damage and inflammation.
- Increased risk of breast cancers and other estrogen receptored cancers.
- Greater anti-oxidant activity with high cruciferous vegetable consumption over A Alleles.

NQO1

rs1800566

NQO1 is the gene that produces the enzyme known as NAD(P)H quinone dehydrogenase 1 in the NRF2 pathways of the body. This enzyme prevents redox reactions or transferring of electrons from quinones to inhibit the production of radical inflammatory substrates. Quinones are biologically active compounds that play a significant role in the production of ATP, the body's energy unit.

However, if quinones are not oxidized completely they can form reactive oxygen species (ROS) actually damaging the tissues themselves. NQO1 enzymes ensure that partially oxidized quinone molecules are fully oxidized and cleared from the body in order to protect the body's tissues against damaging inflammation.

NQO1 is involved in the binding and breakdown of exogenous toxins such as benzene, a carcinogen found in laundry detergents, pesticides, smoke, and household and industrial clearers.

NQO1 also clears out estrogens. AA variants are associated with increased risk of breast cancers and other estrogen sensitive tumours.

NQO1 is highly concentrated in blood vessels, protecting them from inflammation. It also plays a key role in activating vitamin K to ensure proper blood clotting and bone health.

**Normal Allele:** G **Variant Allele:** A

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Decreased enzyme production.
- Low levels of NQO1.
- Increased inflammation.
- Increased risk of breast, lung and colon cancers.
- Not as responsive to epirubicin, a chemotherapeutic drug.

## RECOMMENDATION FOR Phase 2

**You have slightly slower phase 11 detoxification pathways.** Phase 11 enzymes are responsible for catalyzing the conjugation of many toxic compounds, carcinogens and medications. Slower activity with less enzyme production through these genes increases inflammation, cellular damage and can allow toxic substrates to act as pre-carcinogens.

Slower SOD2 or Mitochondrial Superoxide Dismutase decreases the natural protection of the mitochondria and DNA from oxidative damage.

**However, you do have normal activity in the GSTP1 gene helping to prevent cellular damage from oxidative inflammation and an accumulation of some toxic pre-carcinogens in body tissues.** You also have normal NQO1 enzymes increasing the removal of partially oxidized quinone molecules as well as of exogenous toxins such as benzene, a carcinogen found in laundry detergents, pesticides, smoke, and household and industrial cleaners decreasing the risk of inflammation, tissue damage and cancers.

**Glutathione Complex by Signature Supplements** - 2 caps twice a day empty stomach (30 minutes or more before food or 2 hours or more afterwards) for 4 weeks and then reduce to 1 cap twice per day. Increase back up if exposed to heavy toxins.

**Consume an abundance of raw cruciferous vegetables.**

**Keep well hydrated- 0.5oz/ lb of body weight.**

## VITAMINS, MINERALS AND METHYLATION

## Vitamins, Minerals and Methylation: General

NBPF3

rs4654748

The NBPF3 or Neuroblastoma Breakpoint Member 3 is the gene that codes for the production of the hormone NBPF3, which in part regulates the clearance of vitamin B6.

Vitamin B6 acts as a coenzyme in many important reactions in blood, central nervous system (CNS), and skin metabolism. It is important in heme and nucleic acid biosynthesis and in lipid, carbohydrate, and amino acid metabolism. It also is a key player in the production of several neurotransmitters.

Low levels can cause peripheral neuropathy, anemia, depression or anxiety, muscle cramping, seborrheic dermatitis, glossitis, confusion, and EEG abnormalities.

**Normal Allele:** T **Variant Allele:** C

**You are:** CT

**Key Characteristics of the Variant Allele:**

- Altered NBPF3 production.
- Increased clearance of vitamin B6 in the body.
- Increased risk of mood disorders.
- Increased risk of depression and anxiety.
- Increased risk of obesity and high blood sugars.
- Increased muscle cramping and spasticity.

SLC23A1

rs6053005

This second vitamin C gene is also a vitamin C transporter gene responsible for aiding in the absorption of vitamin C from our diet, through the bowel and into the blood. The absorption of vitamin C from the blood to its target tissue requires these two sodium-dependent vitamin C transporters. RS33972313 is the more significant of the two, but they both play a significant role in the body's ability to obtain and use vitamin C.

Vitamin C is one of the most powerful anti-oxidative anti-inflammatories for all water-soluble tissues. It possesses antiviral properties to help support the immune system (especially within the intestines where 70% of our immunity resides), and is a crucial co-factor in the production of collagen in joints, helping to prevent joint wear and tear, as well as in the skin, reducing wrinkles.

It is also involved in protecting the integrity of mucous membranes and in the prevention of gastric and intestinal inflammatory conditions such as Crohn's and gastric ulcers.

**Normal Allele: T Variant Allele: C**

**You are: TT**

**Key Characteristics of the Variant Allele:**

- Increased risk of common cold
- Decreased overall immunity and prolonged infections
- Increased risk of heart disease
- Increased risk of stomach cancer
- Increased risk of Crohn's and other inflammatory bowel disease
- Decreased collagen production

**MTHFR**  
**rs1801133**

MTHFR genes produce an enzyme known as methylenetetrahydrofolate reductase that is key for metabolizing inactive dietary folate or folic acid into its active form methyl-folate. It is probably best known for its role in converting homocysteine, an important cardiac disease marker, into methionine. However, it is also a key player in a process known as methylation, an important reaction for several biological processes including production and breakdown of hormones, synthesis of DNA and detoxification.

Alterations in methylation can change how the body breaks down and recycles vitamins and minerals, impairs the production of neurotransmitters greatly affecting mood and behaviour, and impacts the recycling of cholesterol and pathways contributing to cardiovascular disease.

Homozygote variants AA's only have approximately 30% methylation activity, while heterozygotes have up to 65%.

It should still be noted that research associating health-related issues with MTHFR polymorphisms is still under investigation, and that people with very high homocysteine levels are rarely the result of MTHFR polymorphisms itself.

**Normal Allele: G Variant Allele: A**

**You are: GG**

**Key Characteristics of the Variant Allele:**

- low methylenetetrahydrofolate reductase.
- Increased risk of cardiovascular disease.
- Increased venous thrombosis.
- Depression
- Anxiety
- Migraines
- Altered drug metabolism through the liver.

## MTHFR rs1801131

This other MTHFR gene also produces the enzyme methylenetetrahydrofolate reductase, key for metabolizing inactive dietary folate or folic acid into its active form methyl-folate. Similarly, it is known for its role in converting homocysteine, an important cardiac disease marker, into methionine. However, it is also a key player in a process known as methylation, an important reaction for several biological processes including production and breakdown of hormones, synthesis of DNA and detoxification.

These two genes work in tandem together.

Alterations in methylation can change how the body breaks down and recycles vitamins and minerals, produces neurotransmitters greatly affecting mood and behaviour, and in the recycling of cholesterol and regulation of cardiovascular pathways.

Homozygote variants GG's only have 30% methylation activity, and heterozygotes have up to 65%.

It should still be noted that research associating health-related issues with MTHFR polymorphisms is still under investigation, and that people with very high homocysteine levels are rarely the result of MTHFR polymorphisms itself.

**Normal Allele:** T **Variant Allele:** G

**You are:** TT

**Key Characteristics of the Variant Allele:**

- low methylenetetrahydrofolate reductase production.
- low methylation rates
- Increased risk of cardiovascular disease
- Increased venous thrombosis
- Depression
- Anxiety
- Migraines
- Altered drug metabolism through the liver.

MTR

rs1805087

MTR is the gene that codes for the production of the enzyme 5-methyl-tetrahydrofolate-homocysteine S-methyltransferase, or methionine synthase for short.

This enzyme converts homocysteine into methionine with the aid of methyl B12 or methylcobalamine as a methyl donor to initiate this conversion. This ultimately affects the levels of B12 in the body via regulation and degradation.

The main purpose of the gene is to produce the methionine that then increases the production of SAMe or S-adenosylmethionine, one of the most important methyl donors for a myriad of enzymatic reactions in the body.

MTR works in conjunction with MTRR for its control and use of B12 in the body, and more importantly the production of SAM-e and the clearance of homocysteine.

**Normal Allele:** A **Variant Allele:** G

**You are:** AG

**Key Characteristics of the Variant Allele:**

- May have lower methylmalonate levels (intracellular B12)
- Increased risk of high homocysteine.
- Altered methylation cycles.
- Altered choline production.
- Altered folate metabolism.

SLC30A8

rs11558471

SLC30A8 is one of 10 zinc membrane transporter genes. They control the movement of zinc inside and outside of a cell and regulate its intracellular and cytoplasmic concentrations. These zinc transporters are also referred to as solute carrier 30's which control the efflux of zinc from the cytoplasm out of the cell and from the cytoplasm into the vesicles.

Zinc transporters typically act as zinc sensors, responding to zinc availability in order to maintain a homeostatic balance of intracellular zinc levels. Cellular homeostasis requires mechanisms that tightly control the uptake, storage, and distribution of zinc. This is managed through the coordinated actions of zinc transporters and metallothionein's.

Zinc is an essential trace element that plays a vital role in several biological processes and cellular homeostasis. Abnormal zinc signalling is associated with several chronic diseases such as type 2 diabetes, cancer, cardiovascular disease and Alzheimer's.

Zinc also has an important role in the processing, storage, secretion and action of insulin in response to changes in elevated glucose concentrations. Oral administration of zinc significantly improves glucose clearance by modifying zinc levels in the beta cells of the pancreas, as well as in the kidneys and other body tissues.

**Normal Allele:** A **Variant Allele:** G

**You are:** AA

**Key Characteristics of the Variant Allele:**

- Decreased regulation of intracellular zinc
- Increased glucose levels
- Decreased insulin sensitivity
- Increased risk of obesity
- Increased risk of type 2 diabetes
- Increased inflammation

FUT2

rs602662

FUT2 is a gene that produces an enzyme called Fucosyltransferase 2, which is a membrane protein involved in B12 absorption through the gut. The FUT2 gene enzyme is found in epithelial tissues, the gastrointestinal mucosa and the salivary glands.

Variant A allele individuals have increased enzyme activity, and thus increased or maximal vitamin B12 absorption. This may seem counter intuitive that the variant allele has the better B12 absorption, but it does come at a cost. For A alleles have poor microbial diversity and growth leading to increased intestinal upset, colitis and Crohn's. The low FUT2 expression impairs the proliferation and growth of Bifidobacterium in the bowel, a key probiotic for modulating digestion, immunity and hormonal production.

The normal G allele individuals have lower FUT2 production and thus lower plasma B12 levels.

**Normal Allele:** G **Variant Allele:** A

**You are:** AA

**Key Characteristics of the Variant Allele:**

- High FUT2 production.
- Maximal B12 absorption through the gut.
- Lower risk of pernicious anemia.
- Increased risk of Crohn's, colitis and bowel irregularity.
- Decreased growth and vitality of probiotics, especially Bifidobacterium.

BCOM1

rs12934922

This second vitamin A SNP codes for the production of an enzymes that converts beta carotene into the active form of Vitamin A, the carotenoids. Low vitamin A increases the risk of photoreceptor rhodopsin (regulators of light), and thus a more rapid decrease in night vision as you age.

Vitamin A is also used in the activation and suppression of several genes and their DNA transcription. Abnormal expression of this gene during pregnancy greatly increases the risk of birth defects.

Vitamin A is also required for normal functioning of the immune system (T-cells, lymphocytes), as well as maintenance of skin, hair, and mucosal membranes. Vitamin A is also needed to mobilize iron stores and help transport them to red blood cells, forming hemoglobin and helping to oxygenate the body.

Excess expression of the gene appears to have a carcinogenic effect through its activation of the P450 enzyme in the liver which then turns on retinoic signaling leading to increased cell proliferation.

People who carry the T allele for either the rs7501331 or rs12934922 have enzymes that are 60% less active those who have either the C or A alleles.

**Normal Allele:** A **Variant Allele:** T

**You are:** AT

**Key Characteristics of the Variant Allele:**

- Decreased conversion of beta carotene to vitamin A
- Reduced humoral and cellular immune response.
- Reduced mucous membrane integrity.
- Increased risk of macular degeneration
- Increased progression of vision loss

BCOM1

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People who carry the T allele for either the rs7501331 or rs12934922 have enzymes that are 60% less active those who have either the C or A alleles.

**Normal Allele:** C **Variant Allele:** T

**You are:** CT

**Key Characteristics of the Variant Allele:**

- Decreased conversion of beta carotene to vitamin A
- Reduced humoral and cellular immune response.
- Reduced mucous membrane integrity.
- Increased risk of macular degeneration.
- Increased progression of vision loss

## MTRR rs1801394

MTRR is the gene that codes for the enzyme methionine synthase reductase, which catalyzes the conversion of the inactive form methionine synthase (MTR) into its active form. It uses riboflavin (vitamin B2) as its main cofactor.

MTR is one of the methylation genes as it is involved in the re-methylation of homocysteine to methionine with cobalamin (vitamin B12) participating as its main cofactor. This reaction is of utmost importance as MTR plays a pivotal role in folate metabolism, methionine cycling and the regeneration of B12.

Altered enzymatic activity within the MTRR gene may be associated with hyperhomocysteinemia and altered choline metabolism. This occurs due to the reduced affinity for MTR thus less reactivation of MTR, possibly resulting in elevated homocysteine levels.

Individuals with this polymorphism may be at increased risk for neural tube defects. There is also an association between MTRR SNPs and brain and colon cancer. This is further impacted by the altered choline synthesis and breakdown seen in homozygote variants GG's.

**Normal Allele:** A **Variant Allele:** G

**You are:** GG

**Key Characteristics of the Variant Allele:**

- 4-fold less enzymatic activity.
- Increased risk of hyperhomocysteinemia.
- Increased risk of hypomethioninemia.
- Altered methylation rates.
- Increased risk of neural tube defects.
- Slower regeneration of B12
- Increased risk of B12 deficiency and/or use of B12 in the body.

SLC23A1

rs33972313

This gene is a vitamin C transporter gene responsible for aiding in the absorption of vitamin C from our diet, through the bowel and into the blood. The absorption of vitamin C from the blood to its target tissue requires these two sodium-dependent vitamin C transporters. RS33972313 is the more significant of the two, but they both play a significant role in the body's ability to obtain and use vitamin C.

Vitamin C is one of the most powerful anti-oxidative anti-inflammatories for all water-soluble tissues. It possesses antiviral properties to help support the immune system (especially within the intestines where 70% of our immunity resides), and is a crucial co-factor in the production of collagen in joints, helping to prevent joint wear and tear, as well as in the skin, reducing wrinkles.

It is also involved in protecting the integrity of mucous membranes and in the prevention of gastric and intestinal inflammatory conditions such as Crohn's and gastric ulcers.

**Normal Allele:** C **Variant Allele:** T

**You are:** CC

**Key Characteristics of the Variant Allele:**

- Increased risk of common cold
- Decreased overall immunity and prolonged infections
- Increased risk of heart disease
- Increased risk of stomach cancer
- Increased risk of Crohn's and other inflammatory bowel disease
- Decreased collagen production

GC

rs2282679

The GC gene encodes for the production of a vitamin D binding protein which affects both the delivery of vitamin D to its target tissues as well as the clearance of vitamin D metabolites.

Vitamin D or cholecalciferol does not have any significant biological activity and must be metabolized in the body to its active form calcitriol or 1-25-dihydroxycholecalciferol. This is a two-step process whereby cholecalciferol is hydroxylated into 25-hydroxycholecalciferol in the liver, and then converted into 1, 25-dihydroxycholecalciferol in the kidneys. This active version of vitamin D is now ready to bind into one of more than 300 000 vitamin D receptors in the body.

All of this transportation and activation is dependent upon this gene and your other vitamin D gene.

Vitamin D is involved in several important processes in the body, the most well-known being mineral metabolism and bone growth as it facilitates intestinal absorption of calcium, phosphate and magnesium ions used in bone metabolism. It also regulates a transcriptional regulator of bone matrix proteins used in both collagen synthesis and bone remodelling.

Vitamin D supplementation, along with dietary fiber, has been shown to reduce the development of colon polyps by 40%. It is also involved in the prevention of many types of cancers including prostate and colon, as it plays a prominent role in cell-to-cell communication. Supplementing infants with vitamin D has been shown to prevent the development of type 2 diabetes in adulthood by 88%.

**Normal Allele:** T **Variant Allele:** G

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Lower vitamin D binding protein.
- Decreased delivery of Vitamin D to target tissues.
- Increased clearance of Vitamin D metabolites.
- Increased risk of osteoporosis.
- Decreased bone remodelling following fractures.
- Increased risk of colon cancer and polyps.
- Increased risk of type 2 diabetes.

## RECOMMENDATIONS FOR

## Vitamins, Minerals and Methylation: General

## B6

You have a slightly faster clearance of Vitamin B6 via altered production of the hormone NBPF3 – neuroblastoma breakpoint member 3. This can increase the risk of anxiety, depression, muscle cramps or spasms, skin conditions, and the metabolism of carbohydrates and lipids in the body.

**P5P -Any Brand** 1 capsule(50mg) a day with food or 1 capsule of **Pure Genomics Multivitamin (Pure Encapsulations)** per day with food. You should also increase foods rich in vitamin B6 such as fish, poultry, pork, brown rice, eggs, dark green vegetables.

## Folic Acid

You produce the normal amount of the enzyme methylenetetrahydrofolate reductase that is key for metabolizing inactive dietary folate or folic acid into its active form methyl-folate.

Maintain foods rich in folate such as eggs, asparagus, legumes, broccoli, brussels sprouts and dark leafy greens.

## Zinc

You have normal transportation of zinc inside and outside of the cells. Low levels of zinc are associated with many chronic conditions such as cardiovascular disease, allergies, chronic infections and cancers. Zinc plays an important role in the processing, storage and secretion of insulin greatly increasing the risk of obesity and type 2 diabetes.

Maintain foods high in zinc such as legumes, nuts, seeds and dairy (if genetically you can handle dairy). During times of infection or illness you can take 25mg of **Zinc Citrate-Any Brand** per day with food.

## B12/ Bifidobacterium

Your production of the enzyme fucosyltransferase 2 which is involved in the absorption of vitamin B12 through the gut normal. However, you produce less 5-methyl-tetrahydrofolate-homocystein S-methyltransferase, or methionine synthase, and less methionine synthase reductase altering both the degradation and recycling of B12. All of this leads to slightly lower B12 levels in the body with a slight increased risk for higher homocysteine levels, increased migraines, and potential for several neurological diseases.

More importantly, you have far less Bifidobacterium growth in your gut, with greater potential for gastro-intestinal upset, inflammation and reduced immunity.

**Adenosyl/Hydroxy B12 (Pure Encapsulations)** 1 capsule per day with food or **Tricobalamin (Designs for Health)** 1 cap per day with food, OR 1 capsule of **Pure Genomics Multivitamin (Pure Encapsulations)** per day with food. It is very important that you do not start this until after the 8 weeks and come off any supplement with methyl B12 in it now.

**HMF Intensive Probiotic (Genestra/Seroyal)** – 2 per day with food.

Or **Bifido PB30 (Vita Aid)**- 2 per day with foods

### Vitamin A

You have very low conversion of beta carotene into its active vitamin A carotenoid form. The conversion rate may be lowered by as much as 60%. Vitamin A is needed for a strong immune response, particularly with T-cell and lymphocyte regulation. It is also a key vitamin involved in pregnancy, the prevention of visual deterioration and aging of the eyes. Vitamin A is required for red blood cell formation, the transportation of hemoglobin and subsequently oxygen around the body. Finally Vitamin A is also a key component in the normal growth of skin, hair and nails.

Boosting levels is important to help support all of the above body functions.

**Vitamin A (Pure Encapsulations)** 10 000 IU = 3000mcg – 1 capsule per day with food or 1 capsule of **Pure Genomics Multivitamin (Pure Encapsulations)** per day with food. Increasing foods rich in Vitamin A is also useful. Those foods include spinach, broccoli, sweet potato, beef, red peppers and cod.

### Vitamin C

You have normal absorption of vitamin C from the diet, through the bowel and into the blood. This transportation of vitamin C is key for the strength and rapidity of immune reactions, especially the anti-viral response. Vitamin C helps to inhibit the replication of a virus that has entered the body, and thus reduce the impact of the infection on the body. Vitamin C also plays a key role in collagen repair and synthesis, both in the skin and in the joints, promotes healthier hair and nails, and strengthens our mucosal membranes, especially in our gastro-intestinal tract.

Maintain foods high in vitamin C such as brussel sprouts, spinach, tomato, citrus fruits, turnip and cauliflower.

### Vitamin D

You have a normal production of the vitamin D binding protein aiding in the delivery of vitamin D to its target tissues.

Vitamin D binds into over 300 000 receptors in the body, affecting areas such as bone and muscle metabolism, collagen remodeling, production of immune cells, regulation of blood sugars and plays a role in the growth of cancers.

**Vitamin D (Pure Encapsulations)** – 1000 IU per day with food, especially in colder climates where sun exposure is low. Follow your vitamin D levels and increase or decrease the dose as needed.

## REPRODUCTIVE HORMONES

## Estrogen

CYP17A1

rs6162

Cytochrome 17A1 is a member of the cytochrome P450 family of enzymes that catalyzes or breaks down 17 alpha hydroxylase and 17, 20-lyase, to convert pregnenolone and progesterone into DHEA and androstenedione.

CYP17A1 enzymes are abundant in the endoplasmic reticulum of the adrenal glands and gonads regulating the production of mineralocorticoids, glucocorticoids, androgens and estrogens.

The activity of this enzyme is far greater for the conversion of pregnenolone into DHEA affecting estrogen levels than any other pathway. Polymorphisms of this gene result in disordered estrogen metabolism increasing the risk of endometriosis, polycystic ovarian syndrome (PCOS), cysts, fibroids and estrogenic cancers.

**Normal Allele:** A **Variant Allele:** G

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Increased enzymatic activity
- Increased estrogen levels
- Increased risk of infertility
- Increased risk of PCOS, cysts and fibroids
- Increased risk of estrogen receptored cancers especially in those treated with HRT.

CYP1A1  
rs2606345

Cytochrome 1A1 is phase 1 detoxification enzyme that increases oxidative metabolism of xenobiotics (BP-7,8-dihydrodiol-9,10-epoxide – a potent carcinogen and aromatic hydrocarbon found in cigarettes and charred meats) and many pharmaceuticals. These drugs and chemicals synthesize hemoprotein, of which CYP1A1 gene then catalyzes to provide electrons to stimulate many reactions in the body.

The variant allele has increased activity, and thus increased toxicity from these potent carcinogens.

CYP1A1 is also the major enzyme that converts estrogens into the 2 hydroxy (2-OHE) estrogen form, the form that is protective against estrogen receptored cancers by inhibiting their proliferation.

**Normal Allele:** A **Variant Allele:** C

**You are:** AC

**Key Characteristics of the Variant Allele:**

- Note this is the normal allele.
- Decreased enzymatic activity.
- Less conversion to 2-OH estrogen.
- Increased estrogen cellular proliferation.
- Increased risk of PCOS, fibroids, and estrogen receptored cancers.
- Decreased risk of breast, prostate and colon cancer through toxicity levels.

CYP1B1

rs1056836

CYP1B1 belongs to the cytochrome P450 family of phase II enzymes that catalyzes several drugs, procarcinogens, cholesterol, fats and steroids.

It is also the central enzyme that converts estrogen into the 4 hydroxy (4-OHE) form, the most proliferative and carcinogenic version of estrogen. Increased activity in this gene from toxic exposure to environmental pollutants, smoking, alcohol and pesticides further pushes estrogen to its 4-OH form greatly increasing the risk of breast, prostate, ovarian, colon, and several other cancers.

The gene activity is further augmented with increased adipose tissue as estrogen is stored inside the fat cells.

CYP1B1's activity and potency is deactivated by cruciferous vegetables, hydration, regular bowel movements, regular exercise and weight loss.

**Normal Allele:** C **Variant Allele:** G

**You are:** CC

**Key Characteristics of the Variant Allele:**

- Increased enzymatic activity.
- Increased production of 4-OH estrogens by three fold.
- Increased estrogen cellular proliferation.
- Increased risk of PCOS, fibroids, prostatic growth and cancers through estrogen binding.
- Decreased risk of breast, prostate and colon cancer through toxicity levels.

## RECOMMENDATION FOR Estrogen

You have a significantly higher production of cytochrome 17A1 enzyme with a faster conversion of pregnenolone into DHEA, ultimately increasing your production of estrogen. You also have a poor conversion of this estrogen into the 2-OH protective form, the form that is protective against receptor stimulation, cellular proliferation and cancer. However, your conversion of some of your estrogen into the 4-OH form, the most carcinogenic form of estrogen is quite low, helping to decrease the risk of estrogenic effects in the body.

This combination can slightly increase your risk of fibroids, endometriosis, cysts, breast, prostate and colon cancer. These are very important genes to consider if you are on or thinking about hormone replacement therapy, whether that be natural, bio-identical or pharmaceutical.

**DIM by Signature Supplements** – 1 capsule per day empty stomach (30 minutes or more before food or 2 hours or more after) for 6 weeks.

For menopausal symptoms. add in **Menopause Management by Signature Supplements** - 2 caps twice a day empty stomach until symptoms have dissipated and then reduce to 1 cap twice a day. This product regulates kisspeptin and NeuroKinin B, the safe and effective way to regulate hot flashes.

Increase raw cruciferous vegetables such as broccoli, brussel sprouts and kale, all of which contain DIM, diindolymethane to reduce 4-OH estrogen.

Avoid charred barbecued foods which increase the activity through these genes.

Maintain a normal body weight as these genes are stimulated by obesity. Check your metabolic and dietary genes for guidance.

## REPRODUCTIVE HORMONES

## Testosterone

SHBG  
rs6258

SHBG is the gene that produces the glycoprotein SBHG that binds to androgens, estrogens and other steroid hormones such as cortisol and progesterone. Approximately 44% of testosterone is tightly bound to SHBG, another 54% is bound to serum albumin and only 1 to 2% is free or unbound and thus biologically available to bind into a receptor and have an effect. Thus the bioavailability of testosterone is greatly influenced by the amount of SHBG.

DHT, the active form of testosterone binds to SBHG with about 5 times the affinity of testosterone, and about 20% the affinity of estradiol. Low levels of SHBG are associated with higher active testosterone activity and can increase the risk of prostate issues, acne and hair loss in men, and endometrial cancer, infertility, increased hair growth and acne in women.

**Normal Allele: C Variant Allele: T****You are: CC****Key Characteristics of the Variant Allele:**

- Lower levels of SHBG
- Increased levels of testosterone.
- Increased risk of prostatic issues, acne and hair loss in men.
- Increased risk of endometrial cancer, infertility, facial hair growth and acne in women.

SRD5A2

rs523349

SRD5A2 or steroid 5 alpha-reductase is an enzyme that converts the less active testosterone into its active and potent form dihydrotestosterone (DHT). This enzyme is extremely active in the ovaries, testes, prostate, skin and liver.

SRD5A2's activity is stimulated by stress as the adrenals produce testosterone precursors for the fight or flight response. It is also stimulated by obesity.

Up to 10% of testosterone is normally converted into DHT. The G allele has 30% more conversion, greatly increasing the risk of prostatic issues in men and fertility problems and polycystic ovarian syndrome (PCOS) and hirsutism in women.

Higher levels of DHT in both sexes can increase the risk of cystic acne and aggressive behaviour.

**Normal Allele: G Variant Allele: C**

**You are: CG**

**Key Characteristics of the Variant Allele:**

- Note this is the normal allele.
- Increased 5 alpha-reductase activity.
- Increased conversion of testosterone into dihydrotestosterone.
- Increased cystic acne.
- Increased prostate growth and cancer in men.
- Increased PCOS in women.
- Increased hair loss in both sexes.

## RECOMMENDATION FOR Testosterone

You have an increased production of the enzyme 5 alpha-reductase leading to a higher conversion rate of the less active form of testosterone into the more potent form dihydrotestosterone. However you produce the normal amount of sex hormone binding globulin, decreasing the amount of active testosterone available to circulate and bind into and activate testosterone receptors.

This can slightly increase the risk of PCOS and menstrual irregularities in women.

**Test dihydrotestosterone levels first, and most importantly, match the above symptoms with family and personal health history before starting supplemental treatment.** These are two genes that may not have been turned on yet in the body and unlike reducing 4-OH estrogen, lowering testosterone when it is not needed can result in fatigue, decreased libido and other such symptoms.

If supplemental treatment is needed **Testo-Protect by Signature Supplements**– 2 capsules a day empty stomach (30 minutes or more before food or 2 hours or more after).

Keep stress hormone levels balanced and maintain an ideal weight, for stress and obesity stimulate these genes. Look at your stress hormone, metabolic and dietary genes for guidance.

## SLEEP

## Sleep: General

CLOCK

rs1801260

Clock genes are components of the circadian clock that regulate circadian rhythms in the body and often referred to as the circadian pacemaker. Clock genes make a transcription factor or protein that moves from the cytoplasm to the nucleus of a cell, stimulating and regulating its internal patterns and rhythms. This is known as a positive feedback loop in the sleep rhythm.

Mutations (G allele on 23andme or C allele in many studies) in this gene result in a premature stop codon that inhibits the production of the CLOCK protein, significantly altering the circadian rhythms to where it is either arrhythmic or lengthens the circadian cycle. Homozygote mutations can entirely lose their circadian rhythm.

The clock genes control several biological rhythms and play an important role in the pathophysiology of aging. One of its most crucial jobs is in the regulation of sleep. Insomnia is a major characteristic of the G Allele. Due to the disruption in circadian patterns, alterations in falling asleep as well as waking in the early and middle stages of sleep are frequently seen. This is often combined with increased night-time energy levels, leading to difficulty falling asleep with subsequent reduced hours of sleep during the night.

The variant allele is also associated with increased weight gain and cholesterol. Within 4 days of sleeping 1 hour less per night, alterations in the production of leptin, ghrelin and cortisol ensue giving rise to 6% increase in obesity and a 30% alteration in insulin entirely independent of diet and exercise.

Not surprisingly, this SNP is also associated with behavioural problems ranging from depression to ADHD. Interestingly, The G allele is associated with insomnia and depression that varies greatly with seasonal changes in women, whereas in men, the depression is more year long and made worse with early morning waking.

Note: On 23andme the alleles are A and G, on many studies they are T (normal) and C (variant)

**Normal Allele: A Variant Allele: G**

**You are: AA**

**Key Characteristics of the Variant Allele:**

- Increased loss of positive feedback in the sleep loop.
- Increased stimulation/energy in the evening.
- Deregulation of circadian rhythms.
- Difficulties falling and staying asleep.
- Depression.
- Weight gain.
- Increased cholesterol.

CRY1

rs8192440

CRY1 is the gene that produces the protein cryptochrome 1, which blocks the activity of the clock genes deregulating the natural circadian rhythms. This is known as a negative feedback loop in the sleep rhythm. The CRY1 gene protein is a transcriptional inhibitor with a strong affinity for the activator proteins produced by the Clock and BMAL1 genes.

Circadian genes are involved in the regulation of all basic physiological processes in the human body. They control the expression of many genes localized in the heart, blood vessels, eyes and other organs and tissues. Their role is to ensure coherent and rhythmic protein synthesis which is critical for normal functioning in most body systems. Circadian disruption and loss of synchronization is associated with a decrease in the ability to adapt and maintain normal rhythms of processes. This is particularly true when it comes to sleep.

The variant G allele is associated with delayed sleep phase disorder (DSPD) whereby it lengthens the period of sleep phases and circadian molecular rhythms. Rather than cycling through stages 1 through 4 and REM in the normal 90-minute cycle, it may take 2.5 hours to transition from REM into stage 1, or from stage 1 into 2. This then leaves very few nighttime hours left to spend in stage 4 sleep, the most important healing stage of sleep.

G allele carriers have a very difficult time adapting to new time zones or shift work due to the altered timing of circadian patterns and delayed sleep cycles. This can quickly lead to chronic insomnia.

The G allele is highly correlated with manic depression, with a higher frequency of manic episodes rather than depressive ones.

Note in 23andme the alleles are G and A, in several studies they are C (normal) and T (variant)

**Normal Allele:** A **Variant Allele:** G

**You are:** AA

**Key Characteristics of the Variant Allele:**

- Increased cryptochrome 1 protein production.
- Increased negative feedback within the sleep loop.
- Delayed onset of sleep.
- Long transitions between stages of sleep.
- Difficulty adapting to time changes and shift work.
- Increased chronic insomnia.
- Increased weight gain.
- Increased cholesterol.

## RECOMMENDATION FOR

### Sleep: General

You produce very little cryptochrome 1 protein that could block the functioning of the clock gene and deregulate many circadian patterns. This helps to regulate sleep patterns, allowing you to fall asleep with greater ease and transition for one stage of sleep into another maximizing the amount of time spent in the healing and healthy stages of sleep.

You also produce the normal clock protein helping to maintain regular circadian rhythms. This leads to more evening sedation helping to fall asleep with more ease. It also helps to prevent more frequent waking throughout the night increasing both the quality and quantity of sleep, subsequently improving overall health and stress levels.

**Rest Reset by Signature Supplements** – 1capsule at 8:30 pm during times of stress. Make sure to take follow treatment plan in your stress section.

Avoid caffeinated beverages in the later half of the day.

Increase exercise in the morning.

## THYROID

## Thyroid: General

DIO2

rs12885300

The deiodinase 2 gene is the central gene controlling the production of our main active thyroid hormone T3 or triiodothyronine. The DIO2 gene encodes for an enzyme deiodinase that converts T4 (thyroxine) into its active version T3 (triiodothyronine) by removing an iodine atom from T4. This enzyme, deiodinase 2 (D2), is thought to be responsible for the majority of T3 production. It produces approximately 20 µg per day, that being 2/3rd of a healthy normal T3 production.

D2 is expressed in most tissues throughout the body especially with thyroid, brown fat, central nervous system, pituitary and skeletal muscle.

Carriers of the variant allele generally do not respond well to traditional T4 medications and require a combination therapy of T3 and T4.

The DIO2 enzyme is referred to as a selenoenzyme as it requires selenium and cysteine for optimal function.

**Normal Allele: C Variant Allele: T**

**You are: TT**

**Key Characteristics of the Variant Allele:**

- **Note this is the normal allele, but the one that carries the risk.**
- Lower deiodinase production and function.
- Lower levels of FT3 and FT4.
- Reduced FT3 and FT4 ratios.
- Increased thyroid disorders.
- Poor response to thyroid medications.
- Decreased energy levels.
- Unstable blood sugar levels.

PDE8B

rs4704397

Phosphodiesterase 8B is the protein encoded by this gene that catalyzes cAMP, a key signally regulator in the thyroid gland. It is in highest concentration in the thyroid (by 3-fold over any other location) but is also present in the adrenals, spinal cord, placenta and other regions of the brain.

PDE8B plays a significant role in the production of TSH. Increased PDE8B chemically destroys cAMP decreasing T3 and T4 production which in turn increases TSH production. It also alters adrenal function and insulin secretion.

**Normal Allele:** G **Variant Allele:** A

**You are:** AG

**Key Characteristics of the Variant Allele:**

- Increased PDE8B production and activity.
- Increased chemical destruction of cAMP.
- Increased TSH levels.
- Increased hypothyroidism.
- Increased thyroid adenomas.
- Increased adrenocortical tumors and Cushing's Syndrome.

DIO1  
rs2235544

Deiodinase 1 gene is a gene that plays a significant role in the activation of thyroid hormones and is the second most active gene responsible for the production of T3 in peripheral tissues. This protein is expressed predominantly in the liver and kidneys, but is also in the thyroid, adrenals and pituitary. Like the DIO2 gene, the DIO1 gene produces an enzyme deiodinase that removes the iodine atom from T4 (thyroxine) to make the more active hormone T3 (triiodothyronine). DIO1 is also involved in the degradation of both T3 and T4.

Healthy adults produce approximately 30 µg T3/day of which about 5 µg is secreted directly from the thyroid. The majority is produced outside of the thyroid by means of deiodination of T4 into T3. This gene produces another 5 µg per day.

The DIO1 enzyme is referred to as a selenoenzyme as it requires selenium and cysteine for optimal function.

**Normal Allele:** C **Variant Allele:** A

**You are:** CC

**Key Characteristics of the Variant Allele:**

- Lower deiodinase production and function.
- Lower levels of FT3 and FT4.
- Reduced FT3 and FT4 ratios.
- Increased thyroid disorders.
- Decreased energy levels.

## RECOMMENDATION FOR Thyroid: General

**You produce the normal amount of your main thyroid enzyme deiodinase-2 (DIO2)** helping to convert your thyroid hormone FT4 (thyroxine) into its active form FT3 (triiodothyronine) in your peripheral tissues. In addition, you also produce the normal amount of your secondary thyroid converting enzyme deiodinase-1 (DIO1) aiding in maximal conversion of T4 into T3.

**However, you do produce a slightly higher amount of the protein Phosphodiesterase 8B** that breaks down cAMP, one of the main signalling regulators in the thyroid, helping to maintain normal TSH levels.

All of these variables very slightly increase the risk of hypothyroidism, decreased energy, increased weight gain and adrenal disorders. **Before considering supplementation, test thyroid levels to see if you need support.**

**Thyroid Reset by Signature supplements** 1 capsule a day empty stomach (30 minutes or more before food or 2 hours or more after) .

Consider talking with your health care practitioner about using desiccated T3 for further treatment if needed.

## LONGEVITY

## Longevity: General

BECN1

rs10512488

Beclin 1 is a key protein produced by the BECN1 gene. This is one of the major genes involved in autophagy, a catabolic process that removes unnecessary, toxic or dysfunctional debris from within a cell through enzyme-dependant mechanisms. This process occurs naturally as an energy balancing mechanism during times of starvation. Autophagy is your body's way of clearing out damaged or dead tissue in an orderly fashion to allow for recycling of cellular components and "tuning up" of cellular pathways. The Beclin 1 protein is part of the PI3K complex (phosphatidylinositol-3-kinase), a complex that controls cellular turnover and growth of tissues. Beclin 1 triggers autophagy by binding to and inhibiting the PI3k pathways inducing autophagy. This gene plays an important role in many cellular processes including tumorigenesis, neurodegeneration, and apoptosis.

**Normal Allele:** G **Variant Allele:** A**You are:** AG**Key Characteristics of the Variant Allele:**

- Decreased Beclin1 production.
- Increased PI3K pathways.
- Increased cellular turnover, differentiation, and growth.
- Decreased lysosomal digestive enzyme activity.
- Decreased autophagy.
- Increased risk of many cancers.
- Increased risk of neurodegeneration.
- Increased risk of inflammatory diseases.

SIRT6

rs352493

SIRT6, or sirtulin 6, also known as the longevity gene, is one of the main genes responsible for efficient and effective DNA repair. SIRT6 belongs to the nicotinamide adenine dinucleotide (NAD+) dependant deacetylases and has a diverse role in aging, metabolism, and disease. It prolongs lifespan, regulates genomic stability, telomere integrity, transcription, and plays a key role in organizing proteins and recruiting enzymes that repair broken DNA. SIRT6 also regulates oxidative stress, neurodegeneration, glucose and fat homeostasis, inflammatory responses and autophagy, thus slowing the process of senescence

**Normal Allele:** T **Variant Allele:** C

**You are:** TT

**Key Characteristics of the Variant Allele:**

- Increased ROS production
- Decreased NRF2
- Increased rate of telomere shortening
- Decreased autophagy
- Decreased DNA repair
- Increased rate of aging
- Increased CV disease, lipid metabolism and heart failure

FOXO3

rs2802292

Forkhead box O3 protein (FOXO3) is a transcription factor involved in the regulation of several genes that control many cellular processes, including DNA repair, tumour suppression, immune function, and resistance to oxidative stress. Higher levels of FOXO3 are associated with longevity in both humans and animals by regulating cellular homeostasis, particularly with that of stem cells, and decreasing inflammation, a major contributing factor to all age-related diseases.

Several large studies have shown that variant for FOXO3 who produce higher levels of the FOXO3 transcription factor live longer. In fact, they are 2.75 times more likely to live to 95 years or older.

**Normal Allele:** T **Variant Allele:** G

**You are:** GG

**Key Characteristics of the Variant Allele:**

- *Note: this is the normal allele that carries the deleterious traits.*
- Decreased FOXO3 production..
- Decreased DNA repair.
- Decreased tumour suppression.
- Increased oxidative stress and inflammation.
- 2.75 times less likely to live to 95 or older and 26% increased risk of cardiovascular disease.
- Increased rate of aging.

ATG16L1

rs10210302

ATG16L1 or autophagy related gene 16L1 is the gene that provides the instructions for making a protein required for autophagy, the recycling of worn-out cell parts and clearing out of debris within a cell that is no longer needed. ATG16L plays a key role in many stages of autophagy including the autophagosome formation and recruitment of the lysosomes (enzymatic activity) needed for autophagy to take place, to the interaction with proteins and lipids that mediate the all autophagy related processes. ATG16L is present in most body tissues helping to clean and protect them, but is highly expressed in the colon, intestinal cells, leukocytes, and spleen which is why it is key in controlling bowel and immune disorders.

**Normal Allele: C Variant Allele: T**

**You are: TT**

**Key Characteristics of the Variant Allele:**

- Decreased ATG16L production.
- Increased PI3K pathways.
- Increased cellular turnover, differentiation and growth.
- Decreased lysosomal digestive enzyme activity.
- Decreased autophagy.
- Increased risk of many cancers.
- Increased risk of inflammatory bowel disease.
- Increased risk of immune disorders.

BDNF

rs6265

BDNF is a neurotrophic that is involved in the growth of new neurons, proliferation and expansion of existing neurons and the maintenance of synapses. It is known as the master molecule of the brain. When BDNF is released, it helps form synapses between neurons by increasing dendritic growth that wire those neurons together. This wiring then encourages more frequent firing down that neural pathway and subsequent consolidation of that thought or memory or process. In the brain, BDNF is most active in the hippocampus, forebrain and cortex, thus is essential for learning, mood and higher cognitive function and plays a key role in the prevention of age-related memory loss and dementia. In fact, higher levels of BDNF are associated with increased intelligence. In the peripheral nervous system, BDNF is most active in the retina, prostate, kidneys and motor neurons.

BDNF binds into 2 main types of receptors, Track B and LNGFR (low affinity nerve growth factor) receptors. When there is minimal damage to neural tissue, BDNF is produced and binds into the Track B receptor to repair the damage. When the damage is too great, BDNF binds into the LNGF receptor to stimulate apoptosis and cellular death to prevent spread and further damage to surrounding areas.

**Normal Allele:** C **Variant Allele:** T

**You are:** CC

**Key Characteristics of the Variant Allele:**

- Decreased BDNF production.
- Decreased neuronal and synaptic repair.
- Decreased dendritic growth,
- Decreased memory and increased risk of dementia and Alzheimer's.
- Increased depression and anxiety.
- Increased rate of aging.

## RECOMMENDATIONS FOR Longevity: General

**You produce lower levels of Beclin1**, the protein that helps to regulate autophagy and the clearance of damaged debris within tissues. This allows for easy stimulation of PI3K pathways involved in cellular turnover, growth and differentiation of tissues and is associated with an increased risk of cancer and inflammatory diseases. You will have a slightly more difficult and longer time getting into autophagy when following a fasting mimicking diet or intermittent fasting. This makes it much more important that you follow the dietary protocols closely.

**Autophagy Activator by Signature Supplements** - 1 cap before bed and increases to 2 caps when doing a fasting mimicking diet to stimulate all autophagy pathways. Take 2 caps daily if you have a chronic inflammatory disease or a neurological disorder.

AND

**Neural Repair by Signature Supplements**- 1 cap twice a day empty stomach for 8 weeks and then reduce to 1 per day.

Look to your SIRT6, ATG16L1, BDNF and IRS1 genes as well for they also play large roles in autophagy.

If you have a personal or family history of cancer or frequent infections treatment is **Immune Modulator by Signature Supplements** - 3/4 tsp in water or 4 caps on an empty stomach daily. Take this twice a day if you presently have cancer and add **Immune Booster by Signature Supplements** - 1 cap per day. If you are heterozygote or variant for the CYP1A2 gene increase DIM by 1 cap per day or increase cruciferous veggies to balance the effect of curcumin in the Immune Booster on CYP1A2.

Please check BECN1 for alternate dosing. Use whichever dose is higher for greater protection.

Please check ATG16L1 for alternate dosing. Use whichever dose is higher for greater protection.

If your weight is normal, follow your genetic diet above and introduce a cycle of fasting mimicking diet 4 times a year for the first year and then twice a year thereafter. If you are 25lbs or more above your ideal weight then introduce the fasting mimicking (FMD) diet once a month for 3 months and then twice a year thereafter.

Fasting Mimicking nutritional plan - 700 calories per day for 5 days.

Guidelines are as follows:

16 grams of protein per day for FTO TT, 18 grams of protein per day for FTO TA, and 20 grams of protein per day for FTO AA. Use a protein powder for this protein source. Be sure to minus the protein sources below when calculating the protein powder portion.

Unlimited lettuce (not spinach or kale), cucumber, and mushrooms. Use only olive oil, salt, pepper, lemon and spices on salad.

2 cups of broccoli and/or cauliflower and/or zucchini - this is approximately 5 grams of protein

10 almonds or 12 olives (this is approximately 3 grams of protein)

Please check ATG16L1 for dosing as well.

You produce the normal amount of SIRT6 helping to slow many of the processes involved in aging and increasing the rate of repair of damaged tissue. Higher levels of SIRT6 are associated with decreased frailty and lower progression of several chronic diseases. SIRT6 helps to slow many of the mechanisms involved in aging from inflammation and DNA repair to glucose metabolism and autophagy.

No Supplemental treatment is needed. Increase food based flavonoids and luteolins such as celery, broccoli, berries, apple skins and chrysanthemum flowers. Do not intake high levels of catechins such as green tea as they inhibit SIRT6 production.



You produce the normal amount of FOXO3 slowing the rate of aging. Lower levels of FOXO3 are associated with decreased DNA repair, altered immunity, decreased tumor suppression, increased inflammation and slower stem cell production and activity. Your higher levels of FOXO3 help to moderate the risk of several age-related diseases.

No treatment is needed but Increasing foods rich in astaxanthin such as salmon, trout, krill and shrimp is also helpful.

**You produce significantly less ATG16L protein decreasing the strength of autophagy pathways in the body.** This increases the risk of several cancers, auto-immune disorders, neurological disorders, and all inflammatory bowel disorders. ATG16L protein is inhibited by mTOR and PI3K stimulation. mTOR and PI3K pathways are greatly stimulated by increased protein and inhibited by resveratrol. You will have a much more difficult and longer time getting into autophagy when following a fasting mimicking diet or intermittent fasting. This makes it much more important that you follow the dietary protocols closely.

Treatment: **Autophagy Activator by Signature Supplements** - 2 caps a day before bed for 8 weeks and then reduce to 1 cap per day. Increase back to 2 caps per day when doing a fasting mimicking diet to stimulate all autophagy pathways. Take 2 caps daily if you have a chronic inflammatory disease or a neurological disorder.

AND

**Neural Repair by Signature Supplements**- 1 cap twice a day empty stomach for 8 weeks and then reduce to 1 per day.

If you have a personal or family history of cancer or frequent infections treatment is **Immune Modulator by Signature Supplements** - 3/4 tsp in water or 4 caps on an empty stomach daily. Take this twice a day if you presently have cancer and add **Immune Booster by Signature Supplements** - 1 cap per day. If you are heterozygote or variant for the CYP1A2 gene increase DIM by 1 cap per day or increase cruciferous veggies to balance the effect of curcumin in the Immune Booster on CYP1A2.

Please check BECN1 for alternate dosing. Use whichever dose is higher for greater protection.

Please check BECN1 for alternative dosing. Use whichever dose is higher for greater protection.

If your weight is normal, follow your genetic diet above and introduce a cycle of fasting mimicking diet once a month for 2 months and then 4 times a year for the first year and then twice a year thereafter. If you are 25lbs or more above your ideal weight then introduce the fasting mimicking (FMD) diet once a month for 4 months and then 4 times a year for the first year after and then twice a year thereafter.

Fasting Mimicking nutritional plan - 700 calories per day for 5 days.

Guidelines are as follows:

16 grams of protein per day for FTO TT, 18 grams of protein per day for FTO TA, and 20 grams of protein per day for FTO AA. Use a protein powder for this protein source. Be sure to minus the protein sources below when calculating the protein powder portion.

Unlimited lettuce (not spinach or kale), cucumber, and mushrooms. Use only olive oil, salt, pepper, lemon and spices on salad.

2 cups of broccoli and/or cauliflower and/or zucchini - this is approximately 5 grams of protein

10 almonds or 12 olives (this is approximately 3 grams of protein)

Look to your BECN1, SIRT6, BDNF and IRS1 genes as well for they also play large roles in autophagy.

You produce the normal levels of BDNF helping to maintain the integrity and maximal repair of your neural tissues as you age. Lower BDNF is associated with increased memory loss, dementia and Alzheimer's as well as decreased focus and concentration. Low BDNF can also increase the rates of depression and anxiety. Your higher levels of BDNF help to reduce the rate of brain aging and associated ailments.

No treatment is needed.

Avoid high levels of sugars which lowers BDNF and increase exercise which greatly stimulates BDNF (look to your exercise genes for guidance).

## CHOLESTEROL

# Cholesterol: General

LDLR

rs6511720

LDLR gene provides the instructions for making the proteins that form the LDL receptor. This receptor binds the low-density lipoproteins, the primary carriers of cholesterol into the blood. LDL receptors are on the outer surface of many cell types where they pick up circulating LDL from the bloodstream and transport it into the cell. Once inside the cell, LDL is broken down and then either used by the cell, stored or removed from the body. LDL receptors are particularly abundant in the liver to help remove excess cholesterol. It is important to note that statins do not work well to lower cholesterol in people with fewer LDL receptors.

**Normal Allele:** G **Variant Allele:** T

**You are:** GG

**Key Characteristics of the Variant Allele:**

- Note: This is the normal allele (G)
- Fewer LDL receptors.
- Less removal or clearance of cholesterol out of the body.
- Increased serum LDL levels.
- Increased risk of familial hypercholesterolemia.
- Increased risk of cardiovascular disease.

PCSK9

rs28942111

PCSK9 genes produces the protease called Proprotein Convertase, Subtilisin/Kexin type 9 which makes a protein that helps regulate cholesterol in the blood stream. It is expressed in the liver and kidney and helps regulate the production and degradation of the receptors that bind LDL cholesterol. The number of low-density lipoprotein receptors on the surface of the liver cells determines how quickly cholesterol is removed from the bloodstream. The higher the number of receptors, the faster the clearance of LDL cholesterol leaving lower levels in the bloodstream to cause ill effects. The PCSK9 protein breaks down the LDL receptor, decreasing LDL clearance, and elevating serum levels of LDL. Mutations in this gene are associated with familial high LDL cholesterol and atherosclerosis. It is important to note that statins are not very effective in people who produce higher levels of PCSK9.

**Normal Allele: T Variant Allele: A****You are: TT****Key Characteristics of the Variant Allele:**

- Increased PCSK9 production.
- Increased LDL receptor degradation.
- Decreased clearance of LDL.
- Increased serum LDL levels.
- Increased risk of familial hypercholesterolemia.
- Increased risk of cardiovascular disease.

## RECOMMENDATION FOR

**Cholesterol: General**

You produce the normal amount of the PCSK9 protein that binds to LDL receptors and breaks them down. This allows the liver to maximally clear LDL from the body, managing blood levels of LDL, the bad cholesterol and reducing the risk of familial hypercholesterolemia and cardiovascular disease.

However you have fewer LDL receptors with which to carry the cholesterol into the cell from the bloodstream to be broken down. This also greatly increases the risk of familial hypercholesterolemia and cardiovascular disease.

**Red Yeast Rice Extract by AOR** - 2 caps twice a day empty stomach before bed for 8 weeks and then reduce to 2 caps before bed.



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