

Version 1.3.0

**Personalized Nutrition & Fitness Genome Report**

(MicroArray Report)

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### *DNA UNLOCKED® Personalized Nutrition & Fitness Genome Report*

##### *INTRODUCTION*

***Congratulations! You have now taken an important step to take control of your health.***

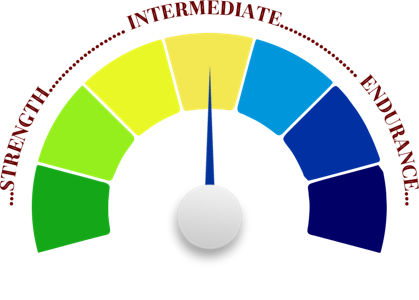
*With the* ***DNA UNLOCKED® Personalized Nutrition & Fitness Genome Report*** *we have analyzed and interpreted vital parts of your genome to give you insights about your nutrition and ﬁtness traits. With this knowledge you and your healthcare providers, dieticians/nutritionists or ﬁtness trainers could personalize your diet or ﬁtness routine.*

*Explore your results in good health!*

##### *HOW TO USE THIS GUIDE*

*You have the control of using this guide to learn about whatever aspect of your Nutrition & Fitness genome that you wish. You can read the entire guide or skip to the sections that you are most interested in to gain valuable insights about your Nutrition & Fitness traits. Each section will display the relevant data in an easy to understand format with your result, an interpretation, summary and recommendation when indicated.*

*The conditions or traits in this report are often multigenic or multifactorial, so your predisposition likelihood or relative risk (relative to the average risk in the population) will be given to you and you may be classiﬁed as (low risk, intermediate risk, or high risk) which will be indicated by a "risk meter" as shown below.*

**

*In addition, for these multigenic or multifactorial diseases or traits, the scientiﬁc strength of each polymorphism or variant analyzed is indicated using a 5 star rating system*  *and is factored in to the genetic risk score. The scientiﬁc strength is based on 4 factors of evidence that contribute to the strength.* ***1.*** *The size of the research study (i.e. how many people enrolled in the study)* ***2.*** *the power of the association (power with genome wide signiﬁcance of 5 x 10-8 and less)* ***3.*** *the eﬀect size (i e size of the odds ratio)* ***4.*** *and whether the results were replicated.*

##### *HOW TO USE THIS GUIDE*

*For traits that are aﬀected by metabolism possible results may include poor metabolizer, intermediate metabolizer, normal metabolizer, rapid metabolizer, or ultra-rapid metabolizer as shown below. When possible, an interpretation and recommendations given, as well as, dosage / side eﬀect warning.*



**ULTRARAPID METABOLIZER RAPID METABOLIZER NORMAL METABOLIZER**

**INTERMEDIATE METABOLIZER**

**POOR METABOLIZER**

*Icons are used throughout the report/guide in order to make things clear and to easily navigate through the information. These icons include:*

 Your results  The Science

 Recommendations  Populations studied

Table of Contents link (click icon to be taken back to the report Table of Contents)

##### *DISCLAIMER*

*This report can be used by the individual being tested to gain insights about his or her DNA makeup and how it is related to his or her wellness traits (not considered clinical in nature). It is highly recommended to review these results with a qualiﬁed health care professional, nutritionist and/or ﬁtness trainer. This test was developed, and its performance characteristics determined by the testing laboratory. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA) or any other regulatory agency. The laboratory and its partners are regulated under CLIA as qualiﬁed to perform high-complexity testing. Although actionable insights may be gained from this test/report, this test/report is to be regarded as investigational or for research only, and it does not take the place of recommendations set by your healthcare provider, nutritionist or ﬁtness trainer.*

*Although this test is a comprehensive test that genotypes and analyzes many parts of your genome (approximately 730,000 data points using microarray technology that tests coding and intergenic or non- coding regions of your genome) this test does have limitations. Also, please keep in mind that the analysis and interpretation were performed at the best of our abilities using the current up-to-date scientiﬁc knowledge, but as the scientiﬁc knowledge changes there may be changes to your report/results and the way it should be interpreted. We will make every eﬀort to notify you of such changes in the future as science catches up, but there are no guarantees and you may use this report/guide today at your own risk. We will not be held liable for any errors presented in this report (due to limitations of the technology or for any other reason) or actions you or your healthcare provider, nutritionist or ﬁtness trainer may decide to take based on the results of this report/guide. For more information about the limitations of this test see the "Limitations section" at the end of this report/guide.*

*If you have any questions about this report/guide or wish to speak to a representative, please email us at* [*info@tovanahealth.com*](mailto:info@elseemedicine.com) *.*

##### *SAMPLE INFORMATION*

**Healthcare Provider:** {{Case\_OwnerDepartment}}

**Specimen Type:** {{Case\_MainSample\_SourceName}}

**Sample ID:** {{Case\_patient}}

**Report Date:** {{Date}}

##### *DEMOGRAPHICS*

Name: DOB:

{{Patient\_Name}}

Sex: {{Patient\_Gender}}

**Paternal Ancestry:** {{Patient\_PaternalAncestry}}

**Maternal Ancestry:** {{Patient\_MaternalAncestry}}

##### *MEDICAL AND SURGICAL HISTORY SUMMARY*

Not reported.

##### *FAMILY HISTORY*

Not reported.



# *SECTION 1*

## *Nutrition & Diet Genomics*

BACK TO TOC

**In this section, you will gain insights about the best nutrition and diet practices based on your genotype (genetic makeup) for various gene variants (DNA changes) associated with vitamins, minerals, eating habits, metabolism and food sensitivities.**

#### YOUR RESULTS AT A GLANCE

***Click on a trait link to be taken to the detailed trait results.***

|  |  |  |
| --- | --- | --- |
| **CARDIOMETABOLIC HEALTH** | |  |
| **Trait Your Result** | |
| Caﬀeine Metabolism | **{{caffeine\_metabolism\_interpretation}}** |
| T2D Risk / Whole Grains & Fiber Beneﬁts | **{{t2d\_risk\_interpretation}}** |
| Omega-3 and Omega-6 Levels | **{{omega3\_and\_omega6\_level\_interpretation}}** |
|  | | |

|  |  |  |
| --- | --- | --- |
| **FOOD REACTIONS & TASTE PERCEPTION** | |  |
| **Trait Your Result** | |
| Lactose Intolerance | **{{lactose\_intolerance\_interpretation}}** |
| Bitter Taste Perception | **{{bitter\_taste\_perception\_interpretation}}** |
|  | | |

|  |  |  |
| --- | --- | --- |
| **NUTRITIONAL NEEDS & NUTRIENT METABOLISM** | |  |
| **Trait Your Result** | |
| Vitamin B2 (Riboﬂavin) | **{{vitamin\_B2\_interpretation}}** |
| Vitamin B12 (Cobalamin) | **{{vitamin\_B12\_interpretation}}** |
| Vitamin C (Ascorbic Acid) | **{{vitamin\_C\_interpretation}}** |
|  | | |

**CARDIOMETABOLIC HEALTH**

#### Caﬀeine Metabolism

Caﬀeine is a stimulating substance found naturally in many plants and is added to food,beverages and medicines. Caﬀeine has many metabolic eﬀects including stimulating the nervoussystem, which can give you a boost of energy and make you feel alert.

Caﬀeine can have many additional beneﬁts including:

 increase your metabolic rate and the burning of fat

 ergogenic eﬀects, such as increase in stamina, physical performance, cut post-workout muscle pain and decrease your recovery time

 lead to improvements in physical performance by increasing adrenaline and release of fatty acids from the breakdown of fat that your body can use as fuel.

 serve as a source of nutrients including riboﬂavin, manganese, niacin, pantothenic acid, potassium, and magnesium

 may lower the risk of type 2 diabetes, stroke, depression, Parkinson's disease,

Alzheimer's disease and dementia

 is protective for the liver and can lower the risk of cirrhosis  lower the risk of colorectal and liver cancer

Caﬀeine can have negative eﬀects as well if you consume too much, including upset stomach, heartburn, dehydration, anxiety, shakiness and it can increase your heart rate and blood pressure. Genetic polymorphisms (variants) in certain genes can aﬀect the way the body metabolizes caﬀeine, and thus inﬂuence the number of cups of coﬀee or quantity of caﬀeine an individual should have per day.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *CYP1A2* | rs2472300 | A | AA, GA | **GG** |  |
| rs762551 | A | AA, CA | **AA** |  |
| rs2472299 | G | GG, GA | **GG** |  |
| rs2069526 | G | GG, GT | **TT** |  |
| rs12720461 | T | TT, TC | **CC** |  |
| rs28399424 | T | TT, TC | **CC** |  |
| rs2472304 | A | AA, AG | **GA** |  |
| *CYP1A1-CYP1A2* | rs2472297 | T | TT, TC | **CC** |  |
| rs2470893 | T | TT, TC | **CC** |  |
| *AHR* | rs6968554 | A | AA, AG | **AG** |  |
| rs10275488 | T | TT, TC | N/A |  |
| *NRCAM* | rs382140 | A | AA, AG | **GG** |  |

N/A = Data Not Available

 Your Risk:

***Report***

**{{caffeine\_metabolism\_interpretation}}** of caﬀeine.

**{{caffeine\_metabolism\_result}}** to consume more cups of coﬀee per day.

 Recommendations:

Caﬀeine can have many beneﬁts, but also some negative eﬀects if too much is consumed, so consuming the right amount of caﬀeine is the key to getting the beneﬁts. The general recommendations are to consume a moderate amount of caﬀeine (up to 400 mg of caﬀeine per day) which is about 1-2 cups of coﬀee a day. Prior to exercise/sports activity current guidelines recommend ingestion of 3-9 mg/kg approximately 60 min prior to exercise.

Based on your genotype further personalized recommendations include:

* {{caffeine\_metabolism\_recommendation}}.
* Avoid drinking coﬀee or caﬀeine at night-time so that it does not aﬀect your sleep.
* If you ever feel negative eﬀects of caﬀeine, such as dehydration, shakiness, anxiety, or elevated heart rate/blood pressure, notify your doctor and adjust your caﬀeine intake.

**The Science:** Caﬀeine is primarily metabolized in the liver, almost exclusively by cytochrome P450 enzymes, into araxanthine, theophylline, and theobromine. There is inter-individual variability in the metabolism of caﬀeine and its eﬀects, based on genetic variations in these enzymes. One of these enzymes, the CYP1A2 (or cytochrome P450 1A2) enzyme, has been extensively studied, and was shown to be responsible for up to 95% of all caﬀeine metabolism. For individuals that are carriers of the slow metabolizer genotype, research has shown that there is greater risk of non-fatal myocardial infarction (heart attack), so coﬀee consumption should be limited to no more than 1 cup per day.

There are multiple haplotypes (i.e. genotype combinations) for the *CYP1A2* gene, and each haplotype may be more prevalent in one population compared to the others. Multiple studies have shown that individuals of the \*1F haplotype, i.e. carriers of the rs762551 AA genotype, are rapid metabolizers of caﬀeine. As a result, these individuals can degrade caﬀeine and clear caﬀeine metabolites faster from the blood and would require more caﬀeine per day to respond and have the same eﬀects of caﬀeine intake as slow metabolizers. In fact, it was shown that individuals who are fast metabolizers tend to drink more cups of coﬀee per day. The \*1F haplotype is also considered a CYP1A2 enzyme inducer of other drugs (i.e. causes increased metabolism of other drugs/medications a person may be taking and result in reduced biologic activity of the drug).

**Caﬀeine Metabolizer Status**: In general, individuals who are homozygous or heterozygous for the

\*1F genotype are considered **ultra-rapid or rapid metabolizers** respectively, those that are homozygous for the \*1A genotype are **normal metabolizers**, those that are heterozygous for the

ancestral \*1A genotype are considered **intermediate metabolizers**, and those that are homozygous for all other genotypes are considered **slow metabolizers**.

In general, Europeans have an increased carrier rate of the rapid metabolizer \*1F haplotype, whereas among the Emirati Arab population, it has been shown that most of the population are carriers of the ancestral normal metabolizer \*1A haplotype. Arabs in this region are very rarely slow metabolizers of caﬀeine.

Another intergenic region **between the *CYP1A1* and *CYP1A2* genes** was found to be associated with caﬀeine consumption. The **rs2472297 T allele and rs2470893 T allele** were both found to increase caﬀeine consumption by a nominal amount per day. This eﬀect may be due to greater clearance of caﬀeine due to higher CYP1A1 or CYP1A2 enzymatic activity.

Signiﬁcant evidence of association was also found at the intergenic SNP **rs382140** near the ***NRCAM* gene**, a gene which is expressed in the brain and implicated in vulnerability to addiction. The **risk A allele** was associated with more coﬀee consumption in the large study of European ancestry individuals.

The ***AHR* gene** codes for a transcription factor that helps regulate xenobiotic chemical metabolizing enzyme genes such as the *CYP1A1* gene. Among the risk alleles that were discovered in the *AHR* gene is the **A allele** of the **rs6968554 SNP** and the **T allele** of the **rs10275488 SNP**.

It should be noted that medications/drugs, epigenetic, and environmental factors, such as smoking (which induces caﬀeine clearance), can aﬀect CYP1A2 enzymatic activity as well. In addition, polymorphisms in the *CYP1A2* and other genes not detected in this assay may also aﬀect an individual's caﬀeine metabolism.

**Populations studied:** Emirati, Egyptian, Turkish, Japanese, Korean, Chinese, European, African, Ethiopian, Costa Rican

#### T2D Risk / Whole Grains & Fiber Beneﬁts

Whole grains contain the entire grain, which includes the bran and germ,therefore have more nutrients. Some examples of whole grains include whole wheat, oats, faro,cornmeal and foods made from these grains like bread, cereal and pasta.

Eating whole grains provides many important health beneﬁts:

 Excellent source of many nutrients including ﬁber, B vitamins, folate, iron, magnesium and selenium.

 Whole grains can help you have regular bowel movements.

 Dietary ﬁber from whole grains may help improve blood cholesterol levels and lower the risk of heart disease, stroke, obesity and type 2 diabetes.

 Dietary ﬁber from whole grains can make you feel full, so you eat less calories and help can help manage weight.

Gene-diet interactions have been shown to aﬀect the risk of diseases such as type 2 diabetes.Studies have shown that consumption of whole grains and foods with low glycemic load and glycemic index(i.e. low insulin demand) can modify the genetic risk of type 2 diabetes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *TCF7L2* | rs12255372 | T | TT, TG | **GT** |  |

 Your Risk:

**{{t2d\_risk\_interpretation}}** of type 2 diabetes (when not on a whole grain/ﬁber diet).

**Increased beneﬁt** when on whole grain and ﬁber diet at preventing diabetes and lowering cholesterol.

Recommendations:

* Eat more whole grains throughout the day- check the ingredient list for foods you buy and look for 100% whole wheat, oats/oatmeal, brown rice, popcorn, whole rye or other whole grains listed as the ﬁrst ingredient.
* Also try eating brown rice instead of white, whole grain pasta instead of regular white pasta, try oatmeal for breakfast and snack on air popped popcorn instead of chips!

**The Science:** The ***TCF7L2* gene** is considered the strongest type 2 diabetes (T2D) locus identiﬁed in the genome, and evidence suggests itplays an important role in insulin synthesis, processing, and

secretion. Variations or polymorphisms in this gene have been shown to impaired insulin synthesis, processing, and secretion and thus raise type 2 diabetes risk. Studies have shown that a high-quality carbohydrate diet like that found in whole grains & ﬁbers can modify the risks of these geneticvariants. One such variant, the **rs12255372 T allele** was shown to be associated with greater risk of type 2 diabetes, especially when an individual has high glycemic load and glycemic index (i.e. high insulin demand) due to poor diet. Lowering the insulin demand by eating whole grain carbohydrates helps to decrease the eﬀects of this risk allele (genetic marker) and genotype. In another study, whole grain diet was suggestive in having greater eﬀects of lowering HbA1c (measure of glucose over 3 months), total cholesterol and other anthropomorphic measures in individuals with the **GT** or **TT** genotype compared to individuals that are not on a whole grain diet. The beneﬁt of whole grain and ﬁber diet was also observed with the **GG genotype**, with even greater eﬀects at modifying diabetes measures. Other genetic and environmental factors can also have an important impact on risk of type 2 diabetes and should be considered.

**Populations studied:** European, Mexican

#### Omega-3 and Omega-6 Levels

Omega-3 and omega-6 fats are both "polyunsaturated fats" (or PUFAs), which have been shown to have beneﬁcial eﬀects on heart health, as well as, allergies, mental health, cognitive development and mortality. Our bodies need both fats but do not make either of them, so we must get them from food. It is good to maintain a 1:1 ratio of omega-6 to omega-3 fats so be mindful of what you eat, especially if you follow a western diet which has high levels of omega-6. Omega-6 has pro-inﬂammatory eﬀects and too much omega-6 fats can be bad for you. Some of the eﬀects of too much omega-6 include increase in blood pressure, blood clots that can cause heart attack and stroke, and can cause your body to retain water.

These essential polyunsaturated fats can be found in fatty ﬁsh like salmon, mackerel, albacore tuna, trout and sardines, as well as plant foods like ﬂaxseeds, walnuts, chia seeds, plant-based oils (canola, soy, corn, saﬄower and soybean oil). Eating the right amount of these polyunsaturated fats may have heart healthy beneﬁts including lowering blood pressure, controlling blood sugar and slowing the buildup of plaque in arteries. Consuming too much of these foods can lead to weight gain because they are high in calories, so portion control is important. Polymorphisms (variants) of genes encoding enzymes in the metabolism of PUFAs contribute to plasma concentrations of fatty acids and may aﬀect an individual's dietary requirements of these fats.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *FADS1* | rs174538 | A | AA, AG | **AA** |  |
| *ELOVL2* | rs3734398 | C | CC, CT | **TT** |  |
| *NOS3* | rs1799983 | T | AA, AC | **GG** |  |

 Your Risk:

1. **{{omega3\_and\_omega6\_level\_interpretation}}** of decreased omega-6 and omega-3 plasma concentration.
2. **{{omega3\_and\_omega6\_level\_result}}** of triglyceride reduction with omega-3 intake.

 Recommendations:

Based on your genotype data you have an {{omega3\_and\_omega6\_level\_recommendation}} of decreased omega-6 and omega-3 plasma concentration, as such it is important to include these polyunsaturated fats as part of your diet, especially to replace unhealthy fats like butter, lard and other solid fats. Here are some more tips below.

* + Eat ¼ cup of walnuts for a snack. But be sure to keep your portion small, as nuts are high in calories.
  + Replace some meats with ﬁsh. Try eating at least 2 meals with ﬁsh per week.
  + Sprinkle ground ﬂax seed on your meal.
  + Add walnuts or sunﬂower seeds to salads (try 1 tablespoon per person).
  + Cook with corn or saﬄower oil instead of butter and solid fats.
  + Check food labels and be sure not to eat more than one serving in a sitting.
  + You may also beneﬁt from taking ﬁsh oil supplements as a good source of EPA and DHA omega-3.
  + Consult with your doctor or dietician/nutrition specialist for further recommendations.

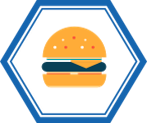
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Age (years)** | **Omega-3 AI (g/day)** | | **Food Sources of Omega-3** | **g (grams)** |
| ≥ 19 (male) | 1.6 | | Flaxseed oil, 1 tbsp | 7.26 |
| ≥ 19 (female) | 1.1 | | Chia seeds, 1 ounce | 5.06 |
| AI: Adequate Intake Sources: NIH | | | English walnuts, 1 ounce | 2.56 |
| Flaxseed, whole, 1 tbsp | 2.35 |
| Salmon, Atlantic, wild, cooked, 3 ounces | 1.57 |
| **Food Sources of Omega-6** | | **g (grams)** | Canola oil, 1 tbsp | 1.28 |
| Flaxseed oil, 1 tbsp | | 8.5 | Sardines, canned in tomato sauce, drained, 3 ounces | 1.19 |
| Canola oil, 1 tbsp | | 1.3 | Soybean oil, 1 tbsp | 0.92 |
| Flaxseed, whole, 1 tbsp | | 2.2 | Mayonnaise, 1 tbsp | 0.74 |
| English walnuts, 1 tbsp | | 0.7 | Sea bass, cooked, 3 ounces | 0.65 |
|  | | | Edamame, frozen, prepared, ½ cup | 0.28 |
| Shrimp, cooked, 3 ounces | 0.24 |

**The Science:** It was shown in one study that the **rs174537 SNP** in the ***FADS1* gene,** that is involved in polyunsaturated fatty acid metabolism, accounted for 18.6% of the additive variance of arachidonic acid (AA), an omega-6, polyunsaturated fatty acid. The **T allele** was shown to be associated with signiﬁcant decrease in the arachidonic acid (AA) plasma concentration and a marginal decrease in omega-3 EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) concentrations as well. In the same *FADS1* gene, other studies have shown the **rs174538 A allele** to also be associated with decreased omega-3 EPA levels.

In a large study the **rs3734398 C allele** in the ***ELOVL2* (elongase) gene** was found to have a signiﬁcant increase in omega-3 EPA and DPA levels and a decrease in omega-3 DHA levels. This may be due to a less eﬃcient activity of elongase protein resulting in decreased elongation (or conversion) of EPA to DHA.

Finally, the interaction of nitric oxide synthase enzyme directed by the ***NOS3* gene** with omega-3 fat has been shown to impact an individual's triglyceride levels. Individuals who are carriers of the **rs1799983 A** allele can be signiﬁcantly more successful at reducing triglyceride levels with dietary intake/supplementation of omega-3 fatty acids. If there is inadequate intake of omega-3 in these individual's, then triglyceride levels may increase which can have negative eﬀects on the body like obesity, and impaired blood circulation leading to heart problems.

**Populations studied:** European, Singaporean Chinese, African, Hispanic



**FOOD REACTIONS & TASTE PERCEPTION**

**Lactose Intolerance**

People with lactose intolerance are unable to fully digest the lactose sugar in milk and milk containing dairy products. Lactose intolerance is usually caused by the deﬁciency of lactase, a digestive enzyme produced in the small intestine that the body needs to digest lactose. People with true lactose intolerance may develop signs and symptoms including: diarrhea, nausea or vomiting, abdominal cramps, bloating and gas. In the most common form of lactose intolerance, known as primary lactose intolerance, the body produces enough lactase in childhood needed to digest milk for nutrition, but the production of lactase drops sharply by adulthood. This form of lactose intolerance was shown to be genetically determined and is most common in people of African, Asian, Hispanic and American Indian descent. It is believed that anevolutionary advantage in certain European populations evolved to allow for persistence of Lactase (i.e. the ability to digest lactose persists into adulthood) to obtain additional nutrition from milk and dairy foods. This ability is sometimes seen in non-European populations as well depending on the individuals genotype.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *MCM6* | rs4988235 | G | CC | **..** |  |
| rs182549 | C | GG | **CC** |  |

 Your Risk:

**{{lactose\_intolerance\_interpretation}}.** Based on your genotype you have a typical likelihood to be lactose intolerant.

Recommendations:

{{lactose\_intolerance\_recommendation}}

**The Science:** Lactase persistence is a heritable autosomal dominant condition and has been strongly correlated with several single nucleotide polymorphisms (SNPs or variations in the genome) located in a regulatory region in the intron of the ***MCM6* gene**, about 14kb upstream of the lactase gene (*LCT* gene) in various populations. Individuals that do not have persistence of the lactase enzyme are considered lactose intolerant (i.e. they do not produce enough of the enzyme to digest lactose). Studies show that individuals with the **CC genotype in the rs4988235 polymorphism** are more likely to lack the lactase enzyme and be lactose intolerant.Those with the CT or TT genotype are more likely to have persistence of the lactase enzyme and are less likely to be lactose intolerant. Similarly, individuals with the **GG genotype in the rs182549 polymorphism** are more likely to lack the lactase enzyme and be lactose intolerant. Whereas individuals with the GA or AA genotype are more likely to have persistence of the lactase enzyme and are less likely to be lactose intolerant. It should be noted that other polymorphisms or variants may play an important role in the persistence (or deﬁciency) of the lactase enzyme in other (non-European) ethnic populations.

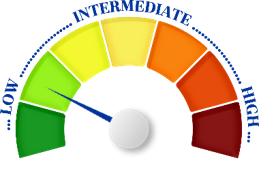
**Populations studied:** European, Mexican

#### Bitter Taste Perception

Bitterness or bitter taste is one of the ﬁve taste sensations and is one that humans are particularly sensitive to. Bitter taste is described as sharp, strong, or disagreeable in ﬂavor, but when combined with other ﬂavor elements, it can provide dimension and balance. Compounds that have an alkaline pH, such as baking soda, often have a bitter ﬂavor. Some foods that are considered bitter are dark, leafy green vegetables (e.g. broccoli, Brussel sprouts, kale), grapefruit, bitter melon, mustard greens, olives, cocoa (or dark chocolate), dark coﬀee, and citrus peels.

Some people can sense the bitter taste of food more than others. This means that one person might ﬁnd a food to be more bitter tasting than someone else, even if it is the same food. This ability to detect bitterness is thought to have evolved as a defense mechanism to protect us from toxic plants and other substances, which often taste bitter. It is known that our ability to taste bitterness is inherited in adominant fashion, but some individuals are born with two recessive alleles (versions of the gene) andare not able to taste bitterness of certain compounds or chemicals. Your ability to taste bitterness may aﬀect the way you experience certain foods and thus your dietary choices and your health.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *TAS2R38* | rs713598 | G | CC or CG (Taster) GG (Non-Taster) | **CC** |  |
| rs1726866 | A | GG or AG (Taster) AA (Non-Taster) | **GG** |  |
| rs10246939 | C | TT or CT (Taster) CC (Non-Taster) | **TC** |  |

 **Your Risk:**

**{{bitter\_taste\_perception\_result}} to be a Bitterness Non-Taster**

 **Recommendations:**

**Your genetic risk to be a bitterness non-taster is {{bitter\_taste\_perception\_recommendation}}** and you are more likely to be a bitterness taster.

* + Avoid excessive salt use. As a bitterness taster you may have an increased preference for salty foods to mask the bitter taste in those foods. As such, you should limit your salt intake to avoid the negative health eﬀects of salt, such as hypertension, if consumed excessively over time.
  + You should also maintain a diet rich in vegetables to avoid a negative impact on your health (if little or no vegetables are consumed), such as increased risk for colon cancer.

**The Science:** The ability to taste the bitterness of the chemical compounds, propylthiouracil (PROP) and phenylthiocarbamide (PTC) can be mostly explained by variations in the *TAS2R38* gene that codes for a bitter taste receptor on the tongue. Being a bitter taster is considered a dominant trait. This means that you need only one copy of the "bitter taster" allele (version) in the *TAS2R38* gene to taste the bitterness, whereas if you have two copies of the "non-taster" allele you will not taste the bitterness of PROP or PTC. Despite the strong inﬂuence of the *TAS2R38* gene on bitter taste perception, we humans have about 30 genes that code for bitter taste receptors. Each receptor can interact with several compounds, allowing people to taste a wide variety of bitter substances. Also, an individual's sensitivity may change over time, and some people may ﬁnd that they can taste PROPR or PTC on some days, but not on other days. In certain populations (mainly European), it has been shown that being a PROP or PTC taster may protect an individual from cigarette smoking due to the bitter compounds present in tobacco smoke.

**Populations studied:** European, African American, Brazilian



**NUTRITIONAL NEEDS & NUTRIENT METABOLISM**

**Vitamin B2 (Riboﬂavin)**

Also known as Riboﬂavin, Vitamin B2 works with the other B vitamins and is important for body growth and red blood cell production. It also helps turn the food you eat into the energy you need.

Although it is rare, Riboﬂavin deﬁciency can happen if you do not get enough riboﬂavin in the foods you eat. People who follow a vegan diet, pregnant and breastfeeding women and those diseases or hormonal disorders are at risk for deﬁciency too. Riboﬂavin deﬁciency can cause skin disorders, sores at the corners of your mouth, swollen or cracked lips and hair loss.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *MTHFR* | rs1801133 | A | TT (High) or CT | **GA** |  |

 Your Risk:

**{{vitamin\_B2\_result}}** of Riboﬂavin deﬁciency

 Recommendations:

You have an {{vitamin\_B2\_recommendation}} of Vitamin B2 deﬁciency based on your genotype data. It is good to eat a diet with adequate amounts of Vitamin B2.

* + Vitamin B2 is found in many foods which can help prevent and treat deﬁciencies. Some of the best sources of vitamin B2 are eggs, lean meats, low-fat milk, green vegetables (such as asparagus, broccoli and spinach), fortiﬁed cereals, bread and grain products.
  + Supplements is likely not necessary because your riboﬂavin levels are likely only moderately low, but speak with your doctor about further testing and supplements as needed.

|  |  |  |  |
| --- | --- | --- | --- |
| **Age (years)** | **RDA (mg/day)** | **Food Sources of Vitamin B2** | **mg (milligrams)** |
| 14-18 (male) | 1.3 | Beef liver, pan fried, 3 oz | 2.9 |
| 14-18 (female) | 1.0 | Breakfast cereals, fortiﬁed with 100% of the DV  of riboﬂavin, 1 serving | 1.7 |
| 14-18 (pregnant) | 1.4 |
| 14-18 (lactating) | 1.4 | Oats, instant, fortiﬁed, cooked with water, 1  cup | 1.1 |
| ≥ 19 (male) | 1.3 |
| Yogurt, plain, fat free, 1 cup | 0.6 |
| ≥ 19 (female) | 1.1 |
| Eggs, cooked, 2 large | 0.4-0.5 |
| ≥ 19 (pregnant) | 1.4 |
| Milk, 2%, 1 cup | 0.5 |
| ≥ 19 (lactating) | 1.4 |
| Beef, tenderloin steak, boneless with fat  trimmed, grilled, 3 oz | 0.4 |
| Sources: NIH | |
| Almonds, without shell, 1/4 cup | 0.3-0.4 |

**The Science:** MTHFR or methylenetetrahydrofolate reductase is an enzyme that uses riboﬂavin (vitamin B2) and other B vitamins as cofactors to process folic acid (folate) and helps to convert the amino acid homocysteine to another amino acid, methionine. Methionine is used by the body to make proteins and other important compounds. When the MTHFR enzyme is not functioning properly levels of folic acid and the co-factor riboﬂavin is reduced, while levels of homocysteine in the blood are elevated because it cannot be converted to the much-needed amino acid methionine. The elevation of homocysteine in the blood can have negative adverse eﬀects such as heart disease, stroke, and high blood pressure (hypertension). The resulting reduced folic acid is also a risk factor for neural tube defects in pregnancy.

There have been numerous studies that have shown the ***MTHFR* 677C>T (rs1801133) polymorphism** results in reduced MTHFR enzyme activity, and homozygotes of this polymorphism (i.e. individuals who have a **TT genotype**) were associated to have decreased folic acid, decreased riboﬂavin, and increased homocysteine levels putting them at risk for cardiovascular disease and other health risks. Studies have shown that for at risk individuals with the TT genotype, supplementation with vitamin B2 can reduce the levels of homocysteine by as much as 22% and even more (by ~40%) in individuals deﬁcient in vitamin B2. It was also shown that intake of vitamin B2 (as little as 1.6 mg/day) in individuals with the TT genotype can signiﬁcantly reduce blood pressure by as much as13.4 mmHg systolic and 7.5 mmHg diastolic.

**Populations studied:** European

#### Vitamin B12 (Cobalamin)

Vitamin B12 is important to keep your nerve and red blood cells healthy and helps breakdown the protein that you eat so your body can use it for other functions.

Vitamin B12 deﬁciency occurs when the body does not get enough B12 from food or has a diﬃcult time absorbing B12. This is more common in older adults, those following vegetarian or vegan diets or those with digestive disorders. Symptoms of B12 deﬁciency can include anemia (low blood cells), loss of balance, numbness or tingling, weakness or fatigue and poor memory. It has been shown in several studies that genetic variations or polymorphisms serves as an independent risk factor for low vitamin B12 blood serum levels or deﬁciency.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *FUT2* | rs602662 | G | GG or AG | **GA** |  |
| rs492602 | A | AA or AG | **AG** |  |
| *FUT6* | rs3760775 | G | GG or TG | **GG** |  |
| *CUBN* | rs1801222 | A | AA or AG | **GG** |  |

 Your Risk:

**{{vitamin\_B12\_result}}**of lower blood serum vitamin B12 levels or deﬁciency based on the available genotype data.

 Recommendations:

Based on your genotype, you have an {{vitamin\_B12\_recommendation}} of being deﬁcient in vitamin B12 if you do not maintain a source of vitamin B12 in your diet. Eating foods with vitamin B12 can help prevent and treat deﬁciencies.

* + Vitamin B12 is highest in animal foods such as meat, poultry, shellﬁsh, eggs and dairy.
  + Some fortiﬁed breakfast cereals (where vitamins are added) also have B12 as do some nutritional yeasts.
  + For some, including those following vegetarian and vegan diets, people with digestive issues and older adults- supplements may be needed. Speak to your doctor or healthcare provider to determine what is best for you.
  + The Recommended Dietary Allowance (RDA) for vitamin B12 is set at 2.5 micrograms/day for nonsmoking, nonpregnant women and for nonsmoking men to achieve suﬃcient levels of vitamin B12 in the blood.

|  |  |  |  |
| --- | --- | --- | --- |
| **Age (years)** | **RDA (mcg/day)** | **Food Sources of Vitamin B12** | **mcg (micrograms)** |
| 4-18 | 2.4 | Clams, cooked, 3 oz | 84.1 |
| 14-18 (pregnant women) | 2.6 | Liver, beef, cooked, 3 oz | 70.7 |
| 14-18 (lactating women) | 2.8 | Breakfast cereal, fortiﬁed with 100% DV for  vitamin B 12, 1 serving | 6 |
| ≥ 19 | 2.4 |
| ≥ 19 (pregnant women) | 2.6 | Trout, rainbow, wild, cooked, 3 oz | 5.4 |
| ≥ 19 (lactating women) | 2.8 | Salmon, sockeye, cooked, 3 oz | 4.8 |
| Sources: NIH | | Tuna ﬁsh, light, canned in water, 3 oz | 2.5 |
| Egg, cooked, 2 large | 1.5-1.6 |
| Breakfast cereals, fortiﬁed with 25% of the  DV for vitamin B12, 1 serving | 1.5 |
| Beef, top sirloin, broiled, 3 ounces | 1.4 |
| Cottage cheese, 1 cup | 1.1-1.5 |

**The Science:** There are multiple factors that contribute to variations in B vitamin levels in humans and genetics plays an important role to inﬂuence these levels.

Fucosyltransferases encoded by the *FUT* genes have been shown to inﬂuence vitamin B12 concentrations. One mechanism for this is by adding fucose to maintain the intestine cell surface glycan structure and their metabolism, thereby mediating the hosts interaction with intestinal microbiota inﬂuencing its composition. Well studied polymorphisms in the *FUT2* gene have shown strong associations with vitamin B12 levels. The G allele of the rs602662 and the A allele of the rs492602 polymorphism are two such variations that confer risk for B12 deﬁciency. Diﬀerences in Another SNP (single nucleotide polymorphism) rs3760775 positioned intergenic 5'-upstream of the *FUT6* gene, was also strongly associated with vitamin B12 levels, with the A allele shown in the study to cause an increase in B12 levels (and thus the G allele is considered the risk allele for B12 deﬁciency).

The protein expressed by the ***CUBN*** gene forms a receptor complex responsible for vitamin B12 uptake in the ileum of the small intestine. There have been a number of studies that have shown that variants or polymorphisms in the ***CUBN*** gene are associated with vitamin B12 deﬁciency. In one of these studies, the reference **A allele** of the ***CUBN* 1041A>G (rs1801222) polymorphism** was associated with a decrease in vitamin B12 levels and individuals who have one or two copies of the A allele (i.e. with an **AA or AG genotype**) tend to also have increased homocysteine levels as a result of B12 deﬁciency, putting them at risk for cardiovascular disease (such as ischemic stroke).

**Populations studied:** European, African, Indo-European, Dravidian

***Sample ID: {{Case\_patient}}***

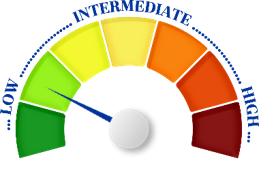
***- CONFIDENTIAL REPORT -***

#### Vitamin C (Ascorbic Acid)

Vitamin C is (or L-ascorbic acid) is an essential part of the human diet needed for growth and repair of tissues in all parts of the body. Vitamin C is used to heal wounds, repair and maintain parts of bones and teeth and works to block cell damage.

Consuming too little vitamin C can lead to deﬁciency. Symptoms can include low blood cells, bleeding gums, diﬃculty ﬁghting infections, swollen joints and weak teeth.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *SLC23A1* | rs33972313 | T | TT or CT | **CC** |  |

 Your Risk:

**{{vitamin\_C\_result}}** of lower blood serum vitamin C levels or deﬁciency based on the available genotype data.

 Recommendations:

Based on your genotype, you have a {{vitamin\_C\_result}} of being deﬁcient in vitamin C if you do not maintain a source of vitamin C in your diet.

* + Make sure you consume a balanced diet that includes sources of vitamin C to decrease the risk of long-term adverse health eﬀects of vitamin C deﬁciency.
  + Eating foods with vitamin C can help prevent and treat deﬁciencies. Fruits and vegetables are the best sources of vitamin C including citrus fruits (oranges and grapefruit), red and green pepper and kiwi.
  + Other fruits and vegetables, such as broccoli, strawberries, cantaloupe, potatoes and tomatoes have vitamin C too.
  + The **Recommended Dietary Allowance (RDA)** for vitamin C is set at **75 mg/day** for nonsmoking, nonpregnant women and at 90 mg/day for nonsmoking men to achieve suﬃcient levels of vitamin C in the blood.

Smokers need to consume 35 mg/day more dietary vitamin C to make up for vitamin C depletion caused by smoking. A Tolerable Upper Intake Level of 2,000 mg/day is recommended for adults by the National Institute of Health in the US and Institute of Medicine of the National Academies. Although high levels of vitamin C from supplements or medical prescriptions are generally harmless for most individuals, some people do have adverse reactions.

|  |  |  |  |
| --- | --- | --- | --- |
| **Age (years)** | **RDA (mg/day)** | **Food Sources of Vitamin C** | **mg (milligrams)** |
| 14-18 (male) | 75 | Red pepper, sweet, raw, ½ cup | 95 |
| 14-18 (female) | 65 | Orange juice, ¾ cup | 93 |
| 14-18 (pregnant women) | 80 | Orange, 1 medium | 70 |
| 14-18 (lactating women) | 115 | Grapefruit juice, ¾ cup | 70 |
| ≥ 19 (male) | 90 | Grapefruit, ½ medium | 65 |
| ≥ 19 (female) | 75 | Kiwi fruit, 1 medium | 64 |
| ≥ 19 (pregnant women) | 85 | Green pepper, sweet, raw, ½ cup | 60 |
| ≥ 19 (lactating women) | 120 | Broccoli, cooked, ½ cup | 51 |
| Sources: NIH | | Strawberries, fresh, sliced, ½ cup | 49 |
| Brussels sprouts, cooked, ½ cup | 48 |
| Tomato juice, ¾ cup | 33 |
| Cantaloupe, ½ cup | 29 |
| Cabbage, cooked, ½ cup | 28 |
| Cauliﬂower, raw, ½ cup | 26 |
| Potato, baked, 1 medium | 17 |
| Tomato, raw, 1 medium | 17 |

**The Science:** Humans are unable to produce vitamin C (L-ascorbic acid) due to a series of loss-of function mutations in the gulonolactoneoxidase (GULO) locus. As a result, vitamin C needs to be acquired from dietary sources. Vitamin C deﬁciency has been shown to be the cause of scurvy and complex chronic diseases, such as cardiovascular diseases, due to the contributions of vitamin C as an antioxidant and in the synthesis of biological entities such as hormones and collagen. Active transport of vitamin C into the cell is achieved by co-transporter proteins, one of which is produced by the ***SLC23A1* gene** that is responsible for the absorption of dietary vitamin C in the intestines and its reabsorption in the kidneys. It has been found that individuals with the **T risk allele in the rs33972313 SNP** found in exon 8 of the *SLC23A1* gene are likely to have lower circulating levels of Vitamin C due to a conformational change or protein failure, impairing the activetransport of the vitamin.

**Populations studied:** European



# *SECTION 2*

## *Fitness Genomics*

BACK TO TOC

**In this section, you will gain insights about how your alleles (genotypes) in certain genes aﬀect your ﬁtness and physical activity. This includes exercise motivation and behavior; your body’s ability to recover from exercise and whether you are more prone to injury; what type of exercise/training is ideal for your body; and predisposition to various physiological responses to exercise.**

#### YOUR RESULTS AT A GLANCE

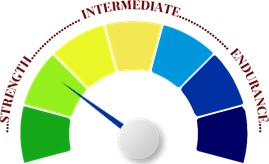
***Click on a trait link to be taken to the detailed trait results.***

|  |  |  |
| --- | --- | --- |
| **FITNESS** | |  |
| **Trait Your Result** | |
| Exercise Behavior | **{{exercise\_behavior\_interpretation}}** |
| Power and Strength | **{{power\_and\_strength\_interpretation}}** |
| Endurance / Endurance Training | **{{endurance\_training\_interpretation}}** |
| Pain Sensitivity | **{{pain\_sensitivity\_interpretation}}** |
| Achilles Tendon Injury / Tendinopathy | **{{achilles\_tendon\_injury\_interpretation}}** |
| Muscle Fatigue & Cramping | **{{muscle\_fatigue\_and\_cramping\_interpretation}}** |
| Aerobic Capacity (VO2max) | **{{aerobic\_capacity\_interpretation}}** |
| Blood Pressure Response to Exercise | **{{blood\_pressure\_response\_to\_exercise**  **\_interpretation}}** |
| Weight - BMI Response to Exercise | **{{bmi\_response\_to\_exercise\_interpretation}}** |
|  | | |

### *POWER/STRENGTH VS. ENDURANCE PERFORMANCE*

In humans, there seems to be an evolutionary mediated tradeoﬀ between power/strength and endurance phenotypic traits, so that an individual is inherently predisposed toward performance in either power/strength or endurance exercises/sports. Biologically, endurance performance requires sustained muscular contraction over a long period of time and is dependent on aerobic pathways (requiring oxygen for energy), whereas power/strength performance requires high-speed and forceful muscle contraction and is dependent on the anaerobic pathways (not requiring oxygen for energy).

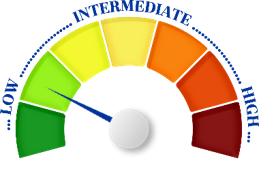
**Based on your genotype data you are predisposed to having a somewhat enhanced power and strength performance compared to endurance performance.**

****

#### Exercise Behavior

Exercise behavior or the time spent on leisure-time physical activity has been established to be heritable (i.e. inﬂuenced by genetic factors) to some degree. Being physically active on a routine basis can have many health beneﬁts including helping to lower high blood pressure, lower blood sugar, improve cholesterol levels, improve mood, improve energy, and even help prevent cancer. Some people have a harder time to start or maintain regular physical activity due to genetic factors, environment, psychological or socioeconomic barriers.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *LEPR* | rs12405556 | T | TT | **GG** |  |
| *Intergenic* | rs10252228 | G | GG | **AG** |  |

Your Risk: {{exercise\_behavior\_result}}

 **Recommendations:**

Based on your genotype from the available genomic data, your behavior to start and continue to be physically active is greater than average, but other factors play a role as well, so your actual exercise behavior may vary. Changing behavior can be a diﬃcult task, but there are steps you can take to achieve this.

To achieve and maintain a regular exercise routine you may try various techniques, such as:

* Get professional help and advice from a professional/personal trainer. Add a social component to exercise by exercising with a friend or in a group. Perhaps you can start your own exercise group in your community, such as a walking or running group, if one does not exist.
* Enroll in a gym or exercise class on a set schedule. Try to be physically active for at least 3 days per week.
* Set small weekly or monthly achievable goals in your exercise routine. Once you have achieved a goal, continue setting new goals to maintain and improve your physical activity and exercise behavior.

**The Science:** Research has shown that genes involved in the pathway related to the hypothalamic regulation of the energy balance plays a role in an individual's voluntary exercise behavior. One of

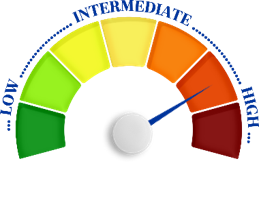
these genes is the ***LEPR* (leptin receptor) gene**, which has been linked to obesity and type 2 diabetes mellitus as well due to polymorphisms (or variations) that reduce leptin binding to the leptin receptor protein (LEPR). Studies have shown that individuals with the **TT genotype** at **rs12405556** of the *LEPR* gene are less likely to be physically active by at least 5% than those with the GG or GT genotype. Another polymorphism, **rs10252228**, located in the **intergenic region** between the *NPSR1* and *DPY19L1* genes was signiﬁcantly associated with leisure-time exercise behavior in another large population study. It should be noted that other variants in the genome, and possibly in the mitochondrial DNA which is involved in energy expenditure, may play an important role in exercise behavior as well.

**Populations studied:** European (American and Dutch), Pima Indians

#### Power and Strength

Muscle strength and power have an important inﬂuence on functional abilities and exercise or sports performance. Both environmental stimuli (i.e. nutrition, training) are important contributing factors to muscle strength and power, and genetic factors have also been shown to have an important impact on these traits. Except for improving athletic performance, building and maintaining muscle strength and power has multiple health beneﬁts including decreasing the risk of osteopenia or osteoporosis (bone disease) and cardiovascular disease (such as coronary artery disease or heart attack).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *ACTN3* | rs1815739 | C | CC | **CC** |  |
| *HIF1A* | rs11549465 | C | CC | **CC** |  |
| *ACVR1B* | rs2854464 | A | AA | **AG** |  |
| *AGT* | rs699 | G | CC | **AG** |  |
| *AMPD1* | rs17602729 | G | CC | **GG** |  |
| *NOS3* | rs1799983 | G | GG, GT | **GG** |  |
| *UCP2* | rs660339 | G | CC, CT | **GG** |  |

Your Risk: {{power\_and\_strength\_result}}

 **Recommendations:**

{{power\_and\_strength\_recommendation}}.

* Maintaining an exercise regimen which includes power- or strength-based activities could have beneﬁts to your health (e.g. bone and heart health).
* You may want to get help and advice from a exercise training professional/personal trainer to determine the activity that is best for you especially if you are a beginner.
* Always consult with your doctor or healthcare provider before beginning any exercise program.

**The Science:** Research has shown that the **T allele** at the **rs1815739 polymorphism** in the ***ACTN3***

**gene** can lead to decreased levels or deﬁciency of the α-actinin-3 protein (a protein important in

maintaining the myoﬁbrillar array within the muscle ﬁbers) and can impair muscle strength/power and performance. Individuals with the **TT genotype** at this position were shown to have altered type-2 muscle ﬁbers (fast twitch muscle ﬁbers) morphology (appearance) and both decreased power and strength, as well as sprinting ability. This genotype is not typically found in high performance power/strength athletes, who were found to possess a **CC genotype** instead. In addition, research has shown that when an individual has an **rs1815739 CC genotype** in the ***ACTN3* gene** and also has the **rs11549465 CC genotype** in the ***HIF1A* gene** (that codes for a transcription factor that regulates the activity of other genes in response to hypoxia or decreased oxygen, so that the body can still produce energy) are more likely to excel in power/strength related sports such as sprinting.

Individuals homozygous for the **rs2854464 A allele (i.e. AA genotype)** in the ***ACVR1B* gene** also showed increased strength (~2% in dynamic knee extensor strength) compared to the GG or AG genotypes.

Other studies have shown that the **C allele at rs699** in the ***AGT* gene** results in more angiotensin and angiotensin II levels, a skeletal muscle growth factor favoring strength- and power-related performance. For this reason, power and strength athletes (e.g. throwers, jumpers, sprinters) are more likely to be carriers of the **CC genotype** as opposed to the TT or TC genotype.

The ***AMPD1* gene**, is important in skeletal muscle energy metabolism during exercise, and the **T allele** at the **rs17602729 polymorphism** results in deﬁciency of the AMPD protein, causing impaired AMP metabolism that produces muscle fatigue, weakness and cramping. It has been shown that soccer players, who are considered power/strength sprinters possess the **C allele** and **CT genotype** at signiﬁcantly higher frequency, than compared to endurance runners. Another study showed that the **T allele** was underrepresented (i.e. low frequency) in power-oriented athletes compared to controls.

The **G allele rs1799983 polymorphism** in the ***NOS3* gene** has also been shown at greater frequency in power-athletes compared to controls or endurance athletes. The greater production of NO (nitric oxide) in individuals with the **GG** or **GT genotype**, allows for increased blood supply, hypertrophy of the muscles, as well as greater skeletal muscle glucose uptake, and may serve as a scientiﬁc explanation for this association.

Finally, with respect to the ***UCP2* gene rs660339 polymorphism**, there is a greater **C allele** frequency in elite power athletes compared with controls, but this was only a small study and should be considered preliminary.

Although genetic polymorphisms contribute to an individual's ability to excel in power/strength vs. endurance performance sports other factors such as gene-gene interactions, environmental, and epigenetic factors are also important contributors.

**Populations studied:** European, Greek, African, Israeli

#### Endurance / Endurance Training

Endurance performance is a complex trait subject to both genetic and environmental factors. Research has shown that the likelihood of excelling in endurance performance exercise/sports is polygenic and depends on the number of endurance-related alleles an individual possesses in a number of diﬀerent genes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *ADRB3* | rs4994 | G | CT | **AA** |  |
| *ADRB2* | rs1042713 | A | AA, AG | **AA** |  |
| *GSTP1* | rs1695 | G | GG, GA | **AA** |  |
| *NFIA-AS2* | rs1572312 | G | CC | **GG** |  |
| *TSHR* | rs7144481 | C | CC | N/A |  |
| *RBFOX1* | rs7191721 | G | GG | **AG** |  |
| *PPARGC1A* | rs8192678 | C | GG, GA | **CC** |  |
| *UCP2* | rs660339 | A | TT | **GG** |  |
| *PPARD* | rs2267668 | A | AA | **AA** |  |
| rs1053049 | T | TT | **TT** |  |
| *GALNTL6* | rs558129 | G | GG | **AA** |  |
| *ACTN3* | rs1815739 | T | TT | **CC** |  |

Your Risk: {{endurance\_training\_result}}

N/A = Data Not Available

 **Recommendations:**

{{endurance\_training\_recommendation}}

* Maintaining an exercise regimen which includes endurance activities could have beneﬁts to your health (e.g. heart health).
* You may want to get help and advice from a exercise training professional/personal trainer to determine the activity that is best for you especially if you are a beginner.
* Always consult with your doctor or healthcare provider before beginning any exercise program.

**The Science:** β-Adrenergic receptors (βARs) are stimulated by naturally occurring catecholamines that have metabolic and cardiovascular eﬀects. The β3AR coded for by the ***ADRB3* gene** is present and functional in the human heart and the **C allele** of the **rs4994 polymorphism** has been found in higher frequency among endurance performance athletes compared to controls. As such, individuals with the **CT genotype** are considered to have a predisposition to endurance performance. In addition, there is suggestive evidence that the **rs1042713 A allele** in the ***ADRB2* gene** encoding for the β2AR may associate with endurance performance.

One study showed that individuals with the **rs1695 G allele** in the ***GSTP1* gene** has greater improvements in cardiorespiratory ﬁtness (i.e. aerobic capacity or VO2max, maximum ventilation or VEmax) and changes in fat-free mass. As such, individuals with a **GG** or **GA genotype** beneﬁt more

from aerobic/endurance training and can achieve a higher aerobic capacity (VO2max).

Elevated VO2max (a measure of your maximal aerobic capacity) is a favorable trait to have for aerobic ﬁtness and endurance related sports. In general, as your aerobic ﬁtness increases, your VO2max increases and endurance athletes have a high VO2max. Research has shown that the favorable allele for increased VO2max and endurance performance is the **rs1572312 C allele** in the ***NFIA-AS2* gene** and

individuals with the **CC genotype** have the greatest potential for aerobic capacity and endurance advantage. Similarly, the **rs7144481 C allele** in the ***TSHR* gene** and the **rs7191721 G allele** in the ***RBFOX1* gene** were associated with greater aerobic capacity and found in greater frequency in elite endurance athletes compared to controls.

The PPARGC1A protein is expressed in high levels in cells with abundant mitochondria and, consequently, with a predominant oxidative metabolism as during endurance performance. It has been shown that there is an absence of the **rs8192678 A allele** in the ***PPARGC1A* gene** in endurance athletes compared to sprinters (power/strength athletes). As such, **GG** and **GA genotypes** are expected in endurance performance athletes, whereas the AA genotype is expected in sprinters.

In the ***UCP2* gene rs660339 polymorphism**, there is a greater **T allele** frequency in elite endurance athletes compared with controls.

The PPARδ protein coded by the ***PPARD* gene** is involved in the metabolism of free fatty acids and carbohydrates and is thus believed to control the energy supply to skeletal muscles via both the aerobic and anaerobic pathways. Signiﬁcant associations have been found between polymorphisms (variations) in the *PPARD* gene and athleticism. The **rs2267668 G allele** and the **rs1053049 C allele** are underrepresented (i.e. at lower frequency) in all athletes compared to non-athlete controls. For people who are considered strength-endurance athletes (who utilize mixed aerobic/anaerobic energy production) and whose main sporting event durations ranging from 5 to 30 minutes at moderate to high intensity, the rs1053049 C allele might be speciﬁcally unfavorable.

One study showed that the **rs558129 T allele** in the ***GALNTL6* gene** was signiﬁcantly less frequent in endurance athletes compared to ethnic-matched controls.

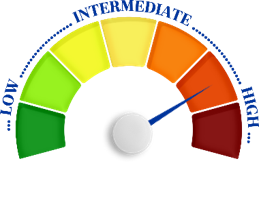
As opposed to power/strength performance athletes, the **rs1815739 T allele** in the ***ACTN3* gene** is considered an endurance genetic marker.

**Populations studied:** European, Israeli, Russian, Japanese, Australian, African

#### Pain Sensitivity

Pain is an uncomfortable feeling that serves as a warning sign that something is wrong in your body, such as tissue damage. Pain begins when particular nerve endings are stimulated sending a signal to the brain which can be mild to severe in degree. Some people are more sensitive to pain than others, which can be related to enzyme activity and number of pain receptors present. Individuals with increased pain sensitivity, are less tolerant to pain, and as a result will not be able to perform physical activity, such as exercise, at a certain intensity or for prolonged periods due to increased level of discomfort from pain. Studies have shown an association of pain sensitivity with variations in the *COMT* gene.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *COMT* | rs4680 | A | AA, GA | **AA** |  |

Your Risk: {{pain\_sensitivity\_result}}

 **Recommendations:**

{{pain\_sensitivity\_recommendation}}

* Practice deep breathing exercises to relax yourself.
* Practice positive thinking that will get your focus oﬀ the pain. For example, if you are walking or running and feel discomfort in your muscles because of increased pain, try shifting your focus on the beneﬁts of exercise to your health and motivate yourself. Meditation can also help.
* Exercise more frequently. Exercise releases endorphins, which can decrease your pain perception and not feel as much pain during physical activity. Moderate- to vigorous-intensity aerobic exercise training has been shown to increase ischemic pain tolerance.
* Exercising in a group or with a friend can help motivate you and releases endorphins that can increase your pain tolerance.
* Set small achievable goals and in your exercise routine and a timeframe to achieve those goals. Once you have achieved a goal, continue setting new goals to improve your physical activity.
* Monitor the levels of pain during exercise or physical activity. Assign a number of pain severity from a scale 0 to 10 (0 being pain free and 10 being the worst pain). When you increase your

physical activity you may feel discomfort, soreness and pain, but this should improve as you are more active. If, however, your pain level consistently reaches a level of 7 or higher, you should stop, decrease the intensity of the exercise, change the exercise, or consult with your doctor to avoid injury. You may also wish to consult with a trainer or someone who is knowledgeable in proper exercise techniques.

**The Science:** The ***COMT* gene** codes for the catechol-O-methyltransferase (COMT) enzyme that metabolizes catecholamines (e.g., dopamine, epinephrine, and norepinephrine) of glial cells and postsynaptic neurons in the central nervous system and other tissues. Studies have shown that decreased COMT enzyme activity results in increased pain sensitivity. The **G to A polymorphism** (i.e. amino acid change from valine to methionine) at **rs4680** in the ***COMT* gene** reduces COMT enzyme thermostability and activity. Individuals with an **AA genotype** were shown to exhibit a 3 to 4-fold reduction of enzyme activity and decrease in the breakdown of catecholamines. This leads to increased pain sensitivity (and lower pain tolerance) when exposed to mechanical or thermal stimulation, such as exercise.

**Populations studied:** Multi-ethnic

#### Achilles Tendon Injury / Tendinopathy

Achilles tendinopathy (AT) is a common overuse injury caused by repetitive energy storage and release with excessive compression that can lead to a sudden injury, or even cause rupture of the Achilles tendon. AT is one of the most substantial injuries aﬀecting athletes, associated with delayed recovery or inability to return to competition.

The Achilles tendon is the biggest and strongest tendon in the human body that connects the calf muscles at the lower to the heel bone. It allows you to extend your foot or point your toes. Straining the tendon by overuse and overload above the physiological limit can cause micro-trauma and eventually inﬂammation of the tendon sheath, degeneration, or a combination of both. Without the minimum time for recovery of the tendon, this can lead to a tendinopathy.

Some risk factors for AT that can lead to tendinopathies include overuse, lack of ﬂexibility, poor circulation, gender (more common in men), endocrine or metabolic factors and genetic factors.

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| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *MMP3* | rs679620 | C | GG | **TT** |  |
| *COL11A1* | rs3753841 | A | TT, CT | **GG** |  |
| rs1676486 | G | CC, CT | **AA** |  |
| *COL11A2* | rs1799907 | T | TT, AT | N/A |  |
| *TNC* | rs13321 | C | CC, CG | N/A |  |
| rs2104772 | A | AA, AT | N/A |  |

Your Risk: {{achilles\_tendon\_injury\_result}} **{{achilles\_tendon\_injury\_image}}**

N/A = Data Not Available

 **Recommendations:**

{{achilles\_tendon\_injury\_recommendation}}

Some actions you can take to prevent tendinopathy is:

* To stretch your calf muscles and Achilles tendon consistently in the morning, before exercise and after exercise to maintain good ﬂexibility.
* To increase duration of your warm up and cool down periods before and after exercise.
* To strengthen your Achilles tendon. Your doctor or physical therapist can help you get started with a suitable exercise (e.g. toe-raise exercises) and move on to more challenging exercises as you heal and get stronger.
* To wear appropriate shoes with shock absorbing insoles which could have a preventive eﬀect on Achilles tendinopathy. A podiatrist may also make further recommendations for appropriate shoes or supportive devices.
* To avoid physical activities that will strain the tendon, such as those requiring a surge of energy or overextension of this tendon (e.g. uphill running).
* To massage the tendon to help with breakdown of scar tissue, stimulate blood ﬂow and promote healing and stretching of the calf muscles.

**The Science:** Matrix metalloproteinase proteins (MMPs) are critical to ligament homeostasis and integrity. In preliminary studies, it has been shown that polymorphisms (variants) within the matrix metalloprotein 3 or ***MMP3* gene** can signiﬁcantly modify the risk of tendinopathy (tendon injury). The **G allele** of **rs679620** and **GG genotype** was signiﬁcantly associated with risk of Achilles tendinopathy.

Type XI (type 11) collagen which is important in collagen ﬁbril assembly, is also expressed in the developing tendons. Polymorphisms (variants) in the genes that produce the collagen ﬁbrils can potentially alter the mechanical properties of the collagen and predispose someone to tendon injury. One study has shown that individuals with the **TCT allele combination** of the **rs3753841 (in *COL11A1*), rs1676486 (in *COL11A1*), rs1799907 (in *COL11A2*) polymorphisms** are at 8.8% increased risk of having chronic Achilles tendinopathy or injury.

In the ***TNC* gene** the **A allele** of the **rs2104772 polymorphism** and the **C allele** of the **rs13321 polymorphism** were found to have an association with Achilles tendinopathy as part of a 3 allele haplotype.

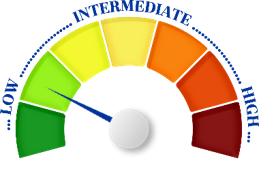
**Populations studied:** European, South African, Australian

#### Muscle Fatigue & Cramping

Muscle fatigue is when the muscle feels weak, painful and tired. A muscle cramp is a sudden and involuntary contraction of one or more of your muscles. Muscle cramps can be severely painful and can make it temporarily impossible to use the aﬀected muscle and continue sports or exercise activities.

Rigorous physical activity and overuse of the muscle can cause muscle fatigue and/or cramping. Some other causes fatigue and cramping include buildup of lactic acid in the muscles, lack of minerals and electrolytes your muscles need, dehydration, holding a position for a prolonged period, or sudden activity without proper warmup. Some individuals are genetically more at risk of developing muscle fatigue and cramping, but there are other environmental, nutritional, and physical factors involved as well.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *AMPD1* | rs17602729 | A | TT | **GG** |  |

Your Risk: {{muscle\_fatigue\_and\_cramping\_result}}

 **Recommendations:**

{{muscle\_fatigue\_and\_cramping\_recommendation}}

Some important recommendations to prevent muscle fatigue and cramps are:

* Always stay well hydrated (i.e. drink ﬂuids) before and during exercise or sports activities.
* Maintain a healthy diet rich in vitamins and minerals or take a supplement if needed.
* If you are a competitive sports athlete or exercising for a prolonged duration (usually over 60 minutes), you may want to use sports drinks that contain minerals/electrolytes and carbohydrates to help prevent cramps and give you energy. However, you should not use sports drinks regularly when you are not engaged in sports. These drinks are high in calories, sugar and sodium, and can have detrimental eﬀects on your health (e.g. obesity, diabetes, high blood pressure) if taken too much.
* Static stretching (i.e. extending and holding your arms, legs or other body parts to a point of tension and holding that position for some duration) is best to do after exercise or sports activity. Research has shown that doing this type of stretching before a workout can reduce muscle strength and performance. On the other hand, dynamic stretching is ideally done before a workout and it involves a concise range of motion meant to mimic the movement we make during rigorous exercise.

**The Science:** The ***AMPD1* gene**, is important in skeletal muscle energy metabolism during exercise, and the **T allele** at the **rs17602729 polymorphism** results in deﬁciency of the AMPD protein, causing impaired AMP metabolism that produces muscle fatigue, weakness and cramping. This may explain why soccer players, who are considered power/strength sprinters are more likely to possess the **C allele** and **CT genotype** and thus less prone to muscle fatigue and muscle cramps. Although an individual's genetics may inﬂuence the likelihood of muscle fatigue/cramps, other factors such as blood supply, dehydration, and mineral/electrolyte levels play an important role as well. People with certain medical conditions (e.g. myopathy, neuropathy, diabetes or thyroid disorder) are also at risk for greater muscle fatigue, weakness and cramping.

**Populations studied:** Multi-ethnic

#### Aerobic Capacity (VO2max)

VO2max (measured in ml/kg/min) is the measurement of an individual's maximal aerobic capacity or the maximum amount of oxygen that an individual can utilize during intense, or maximal exercise. The better an individual is at using oxygen, the faster and/or longer the person will be able to run or be engaged in an exercise activity. An individual's VO2max level can vary depending on gender, age, body composition, medical conditions/current health, genetics and level of physical activity.

Elevated VO2max is a favorable trait to have for cardiorespiratory/aerobic ﬁtness and endurance related sports. In general, as your aerobic ﬁtness increases, your VO2max increases and so does your endurance, which is why elite endurance athletes (e.g cross- country skiers, long-distance/marathon runners, soccer players, rowers, and bicyclists) have a high VO2max.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *PPARGC1A* | rs8192678 | C | GG, GA | **CC** |  |
| *NFIA-AS2* | rs1572312 | G | CC, CT | **GG** |  |
| *TSHR* | rs7144481 | C | CC, CT | N/A |  |
| *RBFOX1* | rs7191721 | G | GG, GA | **AG** |  |
| *GSTP1* | rs1695 | G | GG, GA | **AA** |  |

Your Risk: {{aerobic\_capacity\_result}}

N/A = Data Not Available

 **Recommendations:**

{{aerobic\_capacity\_recommendation}}

* To increase your cardiorespiratory ﬁtness and VO2max (aerobic capacity) you should start or continue in an endurance training program. Training programs will vary from individual to individual and depends on the sport you are interested in.
* You should consult with your doctor before starting any training program or sports activity especially if you have a medical condition.

**The Science:** The PPARGC1A protein is a regulator in energy metabolism and is expressed in high levels in cells with abundant mitochondria and, consequently, with a predominant oxidative metabolism as during endurance performance. It has been shown that there is an absence of the **rs8192678 A allele** in the ***PPARGC1A* gene** in endurance athletes compared to sprinters (power/strength athletes). As such, **GG and GA genotypes** are expected in endurance performance athletes who have high VO2max levels or aerobic capacity.

Research has shown that the favorable allele for increased VO2max and endurance performance is the **rs1572312 C allele** in the **NFIA-AS2 gene** and individuals with the **CC genotype** have the greatest potential for aerobic capacity and endurance advantage. Similarly, the **rs7144481 C allele** in the ***TSHR***

**gene** and the **rs7191721 G allele** in the ***RBFOX1* gene** were associated with greater aerobic capacity

and found in greater frequency in elite endurance athletes compared to controls.

Another study showed that individuals with the **rs1695 G allele** in the ***GSTP1* gene** has greater improvements in cardiorespiratory ﬁtness (i.e. aerobic capacity or VO2max, maximum ventilation or VEmax,) both at baseline and following endurance training. As such, individuals with a **GG** or **GA**

**genotype** beneﬁt more from aerobic/endurance training and can achieve a higher aerobic capacity

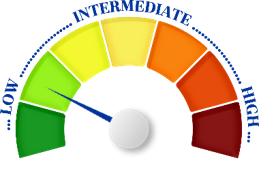
(VO2max).

**Populations studied:** European, Russian, Israeli

#### Blood Pressure Response to Exercise

High blood pressure or hypertension, is a common condition in which the long-term force of the blood against your artery walls is high enough, that it can cause health problems over- time, such as a heart attack or stroke. There are several risk factors for developing primary (essential) hypertension which include age, race, family history, decreased physical activity, smoking, high salt intake, poor diet, excessive alcohol intake, stress and certain chronic conditions. Genetics also plays a role in risk for developing high blood pressure and certain genes have been shown to exert a blood pressure response to exercise or physical activity. Some individuals will genetically have a higher risk of blood pressure increase during exercise and may not respond as well to exercise as others to bring down their blood pressure. These individuals may need a diﬀerent exercise regimen as other "typical responders".

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *EDN1* | rs5370 | T | TT, GT | **GG** |  |
| rs2070699 | C | CC, CG | N/A |  |
| *NET* | rs2242446 | C | CC, CT | **TT** |  |

Your Risk: {{blood\_pressure\_response\_to\_exercise\_result}}

 **Recommendations:**

{{blood\_pressure\_response\_to\_exercise\_recommendation}}

* Maintain a good exercise routine or enroll in a training program for maximal beneﬁts.
* Start or maintain other healthy lifestyle choices such as, low salt diet, stop or cut down on smoking, limit alcohol consumption, start relaxing techniques to cut down stress (other than smoking, eating or drinking alcohol), and eat a healthy diet rich in fruits and vegetables to achieve a good nutritional status.
* Consulting with a nutritionist and exercise specialist can also be helpful in changing lifestyle and initiating weight loss.
* If your blood pressure is consistently elevated (>130 mmHg systolic/ >80 mmHg diastolic) despite good exercise, good diet and lifestyle choices, speak to your doctor or healthcare provider about the best treatment options to achieve normal blood pressure levels.

**The Science:** Individuals with a low cardiorespiratory ﬁtness level who are carriers of the **rs5370 T allele** in the ***EDN1* gene** have a higher risk of hypertension and their blood pressure (systolic blood pressure and pulse pressure) will not respond well to a 20-week endurance training program. Furthermore, when combined with the **C allele** of the **rs2070699 SNP** in a 2-SNP haplotype the risk for high blood pressure and poor blood pressure response to exercise/ﬁtness among low ﬁt individuals increases even further.

The presynaptic norepinephrine (NE) transporter (*NET*) mediates synaptic clearance and recycling of NE, and deﬁciency of *NET* has been linked to elevated blood pressure, heart rate, and catecholamine concentrations. In one study it was found that common polymorphisms (variants) in the ***NET* gene** that reduces the expression of *NET* (i.e. lower *NET* levels present) results in higher blood pressure during exercise. Speciﬁcally, the **rs2242446 C allele** was associated with an elevated blood pressure response during exercise, which can lead to future adverse cardiovascular outcomes including hypertension.

**Populations studied:** European, Russian, Israeli

#### Weight - BMI Response to Exercise

Human obesity deﬁned as a BMI or body mass index of 30 kg/m2 is caused by a complex interplay of genes and environment. The prevalence of obesity and its co-morbidities has increased during the last few decades and excess body weight is now a major public health problem. Although the reason for the increase in obesity prevalence has been largely attributed to lifestyle or environmental factors (such as poor diet or lack of physical activity), genetic factors also play an important role in the susceptibility to obesity. Maintaining a physically active lifestyle is important for all individuals in preventing weight gain and has other health beneﬁts. Studies have shown that in individuals with certain genetic risk factors for obesity, physical activity can signiﬁcantly mitigate the genetic risk of increased BMI that could lead to obesity.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *FTO* | rs8050136 | A | AA | **CA** |  |

Your Risk:{{bmi\_response\_to\_exercise\_result}}

**Recommendations:**

{{bmi\_response\_to\_exercise\_recommendation}}

* Speak to your doctor or health care provider about the beneﬁts of exercise and the exercise regimen that is appropriate for you.
* Maintain a good exercise routine or enroll in a training program for maximal beneﬁts.
* Consulting with a nutritionist and exercise specialist can also be helpful in changing lifestyle and initiating weight loss.

**The Science:** Common variants (i.e. polymorphisms or DNA variations) of the ***FTO*** (fat mass and obesity-associated) gene have consistently been found to be associated with obesity-related traits in humans. The *FTO* gene is highly expressed in the hypothalamus, which is known to regulate energy homeostasis. Evidence has shown that *FTO* risk variants are associated with increased energy intake and several studies have shown that physical activity (resulting in energy expenditure) can modify the genetic eﬀects of the *FTO* gene variants that give rise to increased risk of obesity.

The **A** allele at the **rs8050136 polymorphism** of the ***FTO* gene** is considered an obesity-related risk allele, and individuals with the AA genotype are at signiﬁcantly increased risk for increase in BMI and obesity. In several studies, including two large meta-analysis studies each involving over 200,000 individuals of various ancestries, the eﬀect of the *FTO* gene risk allele and genotype is attenuated by as much as 27%-30% in physically active individuals compared to inactive individuals. As such, these individuals are considered good responders to physical activity, and the importance of moderate to increased intensity physical activity should be stressed in these individuals to help prevent the risk of obesity and its associated risks.

**Populations studied:** Pan-ethnic



# *SECTION 3*

## *Other traits and interesting facts*

BACK TO TOC

**In this section, you will gain insights about the best nutrition and diet practices based on your genotype (genetic makeup) for various gene variants (DNA changes) associated with vitamins, minerals, eating habits, metabolism and food sensitivities.**

#### YOUR RESULTS AT A GLANCE

***Click on a trait link to be taken to the detailed trait results.***

|  |  |  |
| --- | --- | --- |
| **ADDITIONAL TRAITS** | |  |
| **Trait Your Result** | |
| Wet vs. Dry Earwax, Sweating and Body Odor | **{{wet\_vs\_dry\_earwax\_interpretation}}** |
| Hair Loss and Baldness (Androgenic Alopecia) | **{{hair\_loss\_and\_baldness\_interpretation}}** |
| Dental Caries | **{{dental\_caries\_interpretation}}** |
| Sleep Depth (Deep Sleep) | **{{sleep\_depth\_interpretation}}** |
| Warrior vs. Worrier | **{{warrior\_vs\_worrier\_interpretation}}** |
|  | | |



***Please note, we were only able to provide analysis/interpretation for the listed traits based on the available data. Your results may change as more scientiﬁc data becomes available to include in the analysis.***

#### Wet vs. Dry Earwax, Sweating and Body Odor

Earwax is a yellowish, waxy material that is produced by the sebaceous gland in the ear canal inside the ear. It functions to clean, lubricate, and protect the lining of the ear canal by repelling water, trapping dirt, and making sure insects, fungi, and bacteria do not get through and harm the eardrum. Depending on an the genotype in the *ABCC11* gene, an individual may have dry or wet earwax and may or may not sweat excessively. Colostrum secretion found in breast milk may also be aﬀected in females.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *ABCC11* | rs17822931 | A for dry wax G for wet wax | AA - dry wax GG or GA - wet wax | **CC** |  |

Your Result: {{**wet\_vs\_dry\_earwax\_result**}}

**Recommendations:**

* If you have earwax impacted in your ear, it can be eliminated with drops, water irrigation, and instruments used by doctors, audiologists, or trained technicians.
* Removal of earwax by a trained professional is the best method of getting troublesome wax out. Over-the-counter drops work well for small amounts of wax. Prescription drops may be needed if earwax buildup is a recurring problem.
* DO NOT use a Q-tip (cotton swab), paper clip, or a hairpin to remove the wax. Doing so puts you at risk of pushing the wax farther in the ear canal or causing trauma to the lining of the ear canal or ear drum leading to bleeding or infection.
* Consult with your doctor or healthcare provider about safe options available to reduce sweating and body odor.

**The Science:** The ABCC11 protein helps transport small molecules across apical membranes such as those in apocrine secretory cells. The **rs17822931 SNP** (single genetic alteration), also known as c.538G>A or G180R variant, in the ***ABCC11* gene** determines wet vs dry earwax as well as sweat production, and it is also associated with lipid secretion.

Individuals with an **AA genotype** are more prone to having dry ear wax. Individuals with a **GG** or **GA genotype** are likely to have **wet ear wax**. People with dry ear wax may be more at risk of having cerumen impaction and infections but this is not an absolute fact.

Women with the **AA genotype** have also been shown to have **no or low apocrine colostrum secretion** from their mammary gland in the breasts (67% risk) compared to the GG or GA genotype

individuals. This could have implications on breastfeeding (volume of breast milk produced).

Finally, studies have shown that individuals with **GG** or **GA genotypes** have a **greater tendency for sweating and body odor** (aka osmidrosis or bromohydrosis) causing these people to use more deodorant or sometime opt to have their axillary apocrine glands removed surgically if their condition is severe. Therefore, individuals who have the AA genotype do not need to be subject to the chemicals of deodorant use and its associated costs, and can avoid a surgical procedure.

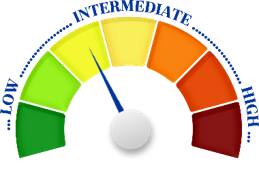
**Populations studied:** East Asians commonly have the recessive AA genotype (80-90%) whereas Europeans and Africans commonly have the GG or GA genotypes. The frequency of ear wax type among other populations in the world including other parts of Asia and the Middle East is mixed.

#### Hair Loss and Baldness (Androgenic Alopecia)

Hair loss is a physical trait that can begin to occur at any age in adult males and the prevalence is known to increase with age. There is a known strong genetic component to hair loss that can predispose a person to more severe and earlier hair loss than the average population risk. Hair loss is sometimes referred to as male pattern baldness or in medical terms androgenetic alopecia, which is considered the most common form of hair loss in men. Studies have shown that when male pattern baldness occurs at an early age or prematurely there is an increased risk for cardiometabolic disease, (e.g. coronary artery disease, elevated cholesterol levels, hypertension, hyperinsulinemia, insulin resistance, metabolic syndrome) and prostate cancer.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *AR* | rs6152 | G | GG | N/A |  |
| *EDA2R* | rs1385699 | T | TT or TC | **TT** |  |
| *Intergenic* | rs2180439 | C | CC or TC | **TT** |  |

N/A = Data Not Available

Your Result: {{hair\_loss\_and\_baldness\_interpretation}}

 **Recommendations:**

DHT(dihydrotestosterone), the main biological cause of hair shrinking and hair loss, can be suppressed with the proper intervention to slow down or even stop the hair loss process if caught early enough.

* Some studies suggest that regular cardiovascular exercise, such as aerobic work-out, can maintain healthy testosterone levels and thus protect against hair loss.
* Diet modiﬁcation to a low fat, low sugar and low-calorie diet can also prevent hair loss.
* Quitting to smoke, if you are a smoker, can also have signiﬁcant positive eﬀects to slow the rate of hair loss.
* Consult with your doctor about a potential underlying medical condition, such as abnormal thyroid hormone levels, that may be aﬀecting your hair.
* Get screened regularly by your dermatologist (who may use the Hamilton-Norwood Scale to monitor hair loss (see the Hamilton-Norwood scale below for your reference) and ask him/her for

recommendations about treatments that can help prevent further hair loss or slow down its progression.

* Treatments may include:
  1. natural supplements, such as saw palmetto, that blocks the conversion of testosterone into DHT (dihydrotestosterone). Lowering DHT levels may slow down hair loss.
  2. Minoxidil (Rogaine™ and Regaine™) is an over-the-counter FDA approved topical medication (applied to the scalp area once per day), that is eﬀective in treating hair loss and can be combined with other treatments.
  3. Finasteride (Propecia™) is another FDA approved medication that can be prescribed by your doctor to help slow the rate of hair loss.
  4. certain shampoos may also be recommended to protect against hair loss.
* Speak to your doctor for more detailed recommendations that is right for you.

**The Science:** Individuals aﬀected by male pattern baldness are inheriting hair follicles with a genetic sensitivity to Dihydrotestosterone (DHT) which is a by-product of testosterone that shrinks hair follicles. Hair follicles that are sensitive to DHT begin to miniaturize, shortening the lifespan of each hair follicle aﬀected. Over time, after continuous exposure to DHT, these aﬀected follicles stop producing hair.

Variants (DNA changes) or SNPs in the *AR* gene coding for the androgen receptor protein located on the X chromosome, has been shown to be highly indicative of the risk of developing male pattern baldness. The risk allele in the **rs6152 SNP is G**, but other polymorphisms contribute signiﬁcantly to male pattern baldness. **Another risk allele is T, in the rs1385699 SNP** of the ***EDA2R* gene** produces a protein that can cause activation of the androgen receptor protein *AR* gene that increases the risk for hair loss. Both these SNPs are located on the X chromosome, which means it mostly aﬀects males, however, baldness may also occur in females that are homozygous for the **rs6152 GG** genotype and are harboring additional SNPs risk alleles required for baldness.

The Norwood Hamilton Scale

The Norwood Hamilton Scale is a way to measure the extent of male pattern baldness, and is the generally accepted standard when describing hair loss in general.

|  |  |
| --- | --- |
|  | **Stage 1** - There is minimal or no recession of the hairline. |
|  | **Stage 2** - Triangular and typically symmetrical areas of recession at the front temporal area. Hair loss remains ahead of a line several centimeters in front of the ears. Hair falls and may become less dense in the central front part of the scalp. Initial signs of baldness are becoming evident. |
|  | **Stage 3** - This represents the minimal extent of hair loss suﬃcient to be considered as baldness according to Norwood. There are deep symmetrical recession at the temples that are bare or only sparsely covered by hair. In Type III vertex, the hair loss is primarily from the vertex with limited recession of the frontotemporal hairline that does not exceed the degree of recession seen in Type III. The crown is added since it'â€™'s a common occurrence with age. |
|  | **Stage 4** - Recession at the front temporal areas is more severe than stage 3. There is a decisive lack of hair on the crown. A band of moderately dense hair extending across the top separates the two areas of hair loss between front temporal and crown. This band bridges between the hair covered areas on the side of the head. |
|  | **Stage 5** - At stage 5 hair loss at the vertex region is still separated from the front temporal region but the division is much less distinct. The band of hair extending across the crown is noticeably narrower and thinner. Hair loss at the vertex and front temporal regions are larger. When viewed from above, stages 5 to 7 show the remaining hair at the sides and back as a distinct horseshoe shape. |
|  | **Stage 6** - The bridge of hair that once crossed the crown is now gone with only sparse hair remaining. The front temporal and vertex regions are now joined into one area. Hair loss on the  sides has extended further. |
|  | **Stage 7** - This stage is the most severe form of hair loss and only a narrow band of hair in a horseshoe shape remains on the sides and back of the scalp. This hair is usually not dense and may be quite ﬁne. At the back of the neck the hair is sparse with a semi-circle over both ears  present. |

**Populations studied:** In general, the prevalence of male pattern hair loss is higher and starts at an early age in Caucasians than in the Asian population.

#### Dental Caries

Dental caries is the breakdown of teeth due to acids made by bacteria and is the most common chronic disease worldwide. It is inﬂuenced by the interaction of genetic and environmental factors, including dietary habits.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *AJAP1* | rs3896439 | A | AA, GA | **GA** |  |

**Your Result: {{dental\_caries\_interpretation}}**of dental caries in the maxillary mid-dentition teeth.

 Recommendations:

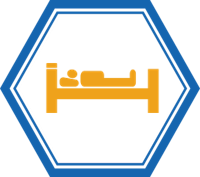
{{dental\_caries\_recommendation}}

* Maintaining a good dental hygiene is important.
* Consult with your dentist regarding the best treatment and preventive measures for your dental health.

**The Science:** One study found associations in genes thought to be involved in craniofacial, salivary gland, and tooth development. One of the signiﬁcant associations found was the **rs3896439 polymorphism** in the upstream un translated region of the ***AJAP1*** gene. The *AJAP1* gene encodes a protein that interacts with another protein involved in tooth development. The variation at rs3896439 aﬀects the maxillarymid dentition tooth surface

**Populations studied:** European

#### Sleep Depth (Deep Sleep)

Stage 3 sleep, also known as deep sleep, slow-wave sleep, or delta sleep, is an important part of our sleep cycle and health. In this stage of sleep your muscles relax and you breathe at a slower rate slow; this sets the stage for growth and healing. Some features of deep sleep include: decreased blood pressure, increased blood ﬂow to the muscles, tissue repair and growth occurs, the bodies energy is recharged and the pituitary gland releases human growth hormone.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *ADA* | rs73598374 | A | AA, GA | **GG** |  |

 Your Result: {{sleep\_depth\_result}}

Recommendations:

* Consuming caﬀeine during the daytime may help you sleep better.
* Make sure you also do not stay up too late and lose sleep, because you will feel more tired the following day.

**The Science:** ADA (or adenosine deaminase) is considered an important enzyme involved in homeostatic regulation of sleep. Individuals who possess an **A allele in the rs73598374 SNP of the *ADA* gene** (i.e. c.22G>A variant or G to A change in the DNA at position 22) are likely to have decreased ADA (adenosine deaminase) enzyme activity in erythrocytes and lymphocytes, promoting adenosine accumulation in sleep regulatory areas and a more pronounced homeostatic drive. This polymorphism has been associated with more intense (deeper) sleep as evidenced by higher sleep EEG spectral power. It has also been associated with higher sleep eﬃciency, longer slow wave sleep duration and amplitude, and fewer reports of awakenings. The alpha-amylase activity in saliva is increased as well, indicating greater sleep drive (or sleep pressure), in individuals with an A risk/eﬀect allele.

Individuals with the **A risk/eﬀect allele** have also been shown to have more feeling of tiredness after sleep deprivation (i.e. after not getting enough sleep).

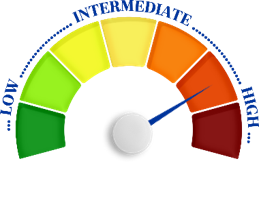
It was also shown that consumption of caﬀeine the day prior to sleep in AA or GA individuals has been linked to better sleep quality than GG homozygous individuals.

**Populations studied:** European, Brazilian

#### Warrior vs. Worrier

Human behavior and personality is complex and is usually a result of multiple genes and environmental inﬂuences. Certain genes play a more signiﬁcant role in aﬀecting neuronal networks in the brain that contribute in causing certain behaviors, including how individuals respond to diﬀerent stimuli or stressors. Some individuals indeed are more like "warriors" and have a higher tolerance for aversive or negative stimuli/stressors, whereas other individuals are more like "worriers" with a lower tolerance for stressor but have an advantage in memory and attention-related tasks.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Gene analyzed** | **SNPs/Loci analyzed** | **Risk or eﬀect variant** | **Risk or eﬀect genotypes** | **Your results** | **Scientiﬁc Strength/ Impact** |
| *COMT* | rs4680 | A | AA, GA | **AA** |  |

**Your Result: {{warrior\_vs\_worrier\_result}}** based on your genotype in the *COMT* gene. This means that you may have less tolerance for negative stimuli and stressful situations (and perhaps have more anxiety) but are better in memory and attention tasks.

Recommendations:

* {{warrior\_vs\_worrier\_recommendation}}

**The Science:** Catechol-O-methyltransferase (COMT) degrades the catecholamine neurotransmitters dopamine, epinephrine, and norepinephrine. The functional polymorphism in the ***COMT* gene rs4680 (val158met)** accounts for a decrease in COMT enzymatic activity. The low-activity **A allele (met158)** has been associated with improved working memory and attention-related tasks, but with less resilience against negative mood states or higher risk for anxiety-related behaviors. Individuals with **G alleles (val158)** have higher COMT enzymatic activity and thus may have improved dopaminergic transmission and Μ-opioid system activation giving these individuals a higher tolerance to emotional stress and to physical pain.

**Populations studied:** European, South African

### *Glossary of key terms*

**Cell** - a cell is the basic building block of life. Human cells contain a nucleus that contains the DNA, and membrane-bound organelles. It is estimated that an adult human body contains between 10 and 100 trillion cells. It is the Cells with speciﬁc functions are organized into tissues and organs that play a particular role in the body.

**Genome** - is the entire set of genetic instructions found in a cell. In humans, the genome normally consists of 23 pairs of chromosomes, as well as a small circular chromosome found in the cells' mitochondria. The genome contains approximately

3.1 billion bases of DNA sequence.

**DNA** - DNA stands for deoxyribonucleic acid (pronounced "dee OK si RAHY bo noo KLEY ik AS id") and is the chemical molecule that carries genetic instructions to produce all the proteins in living things. The DNA molecule consists of two strands with chemicals attached to them that wind around one another to form a structure known as a double helix. Each strand has a backbone consisting of phosphate groups and sugar (deoxyribose). Attached to each sugar is one of four bases, (A) adenine, (C) cytosine, (G) guanine, and (T) thymine. The bases pair with one another via hydrogen bonds (C with G, and A with T) forming the "rungs" of the DNA two strand "ladder." The sequence of base pairs along the backbones serve as instructions for assembling various protein and RNA molecules which play a particular function in the cells of the body.

**Gene** - the gene is the basic physical unit of inheritance. Each gene has a diﬀerent arrangement of DNA base pair sequence (i.e. denoted as ATGC base pair letters) that contains the code to making a protein or RNA molecule needed to specify a trait or perform a function in the body. Genes are arranged, one after another, on structures called chromosomes. A chromosome contains a single, long DNA molecule,

only a portion of which corresponds to a single gene. We inherit one chromosome (and gene versions) from each of our parents. We humans have approximately 22,000 protein coding genes arranged on our chromosomes. Chromosome (pronounced "KROH muh some") - our DNA is wound around proteins and packaged into chromosomes that can be seen under the microscope. Humans usually have 23 pairs of chromosomes, one pair from our father and one pair from our mother. 22 of the chromosome pairs are numbered, and called autosomes, and one pair is the sex chromosomes, X and Y. Chromosomes are like volumes in an encyclopedia. Each chromosome volume contains genes that serve as the pages of instructions to produce functional proteins in our body.

**Base pair** - a base pair is the combination of chemicals that make up the DNA code. There are 4 basic bases or chemicals, (G) guanine which pairs with

(C) cytosine, and (A) adenine which pairs with (T) thymine. The base pairs can be thought of as the "rungs" of the DNA double helix "ladder."

**Nucleotide (pronounced "noo KLEE oh tahyd")** - is the basic building block of nucleic acids, such as the RNA and DNA, which are made of long-chains of nucleotides. A nucleotide consists of a sugar molecule attached to a phosphate group and a nitrogen- containing base. The bases used in DNA are (A) adenine, (C) cytosine, (G) guanine, and (T) thymine. A bonds with T and G bonds with C to make up the DNA sequence.

**Variant and Mutation** - a variant is a variation or change in the persons DNA base pair chemicals. The variant can be small (e.g. single base pair change) or large (e.g. deletion or duplication of many base pair chemicals) Usually when the variant is pathogenic (i.e. disease-causing) it is also called a mutation. Variants can also be non-pathogenic (do not cause disease) and are considered benign.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ***Name: John Doe*** | ***Sex: M*** | ***DOB:*** | ***Sample ID: NF00001*** | ***Report*** |
| *Date: Jan 2nd, 2022* |  |  | ***- CONFIDENTIAL REPORT -*** | *DNA UNLOCKED V1.3.0* |

**SNP (pronounced "snip")** - stands for Single Nucleotide Polymorphism and is a type of polymorphism (i.e. disease-causing DNA change) that involves variation of a single base pair. SNPs in the human genome can correlate with disease, drug response, and other phenotypes. The genotype at a SNP is denoted as a two-letter base pair combination (e.g. GG, CT, TA etc.). Often SNPs are tagged with identiﬁcation numbers, known as RefSNP ID#s, assigned by NCBI (National Center for Biotechnology Information in the United States) and starts with an "rs" preﬁx followed by a number (e.g. rs6280).

**Polymorphism** - refers to one of two or more variants of a particular DNA sequence. The most common type of polymorphism involves variation at a single base pair, known as a SNV (Single Nucleotide Variant) or SNP (Single Nucleotide Polymorphism). Polymorphisms can also be much larger in size and involve long stretches of DNA.

**Genotype** - the genotype can refer to an individual's collection of genes or to the two alleles inherited for a particular gene (usually denoted as the two-letter combination of base pair at a particular locus, e.g. GG, CT, TA etc.). When the information encoded in the genes' DNA is expressed to make a protein or RNA molecules, the genotype is said to be expressed. The expression of the genotype contributes to the individual's observable traits, known as the phenotype.

**Phenotype (pronounced "FEE nuh tahyp")** - the outward expression of a person's genotype is called the phenotype. It is an individual's observable traits that can be largely determined by genetic factors (i.e. genotype) or by environment factors, or a combination of the two.

**Trait** - the term used to describe a distinguishing quality or characteristic that a person or other living organism has. In other words, a trait is something about you that makes you "you." Traits are determined by genes or the environment, or more

commonly by interactions between genes and environment. The genetic contribution to a trait is called the genotype. The outward expression of the genotype is called the phenotype.

**Protein** - are molecules composed of amino acid chains that are found in all living cells and are encoded by the DNA sequence of genes. Proteins play a variety of functions in the cell, including biochemical (enzymes), structural (cytoskeleton), mechanical (muscle), and cell signaling (hormones). Proteins are also an important part of the diet which contains essential amino acids the body needs.

**Enzyme** - An enzyme is almost always a protein and serves as a biological catalyst that speeds up the rate of a speciﬁc chemical reaction in the cell. A cell contains thousands of diﬀerent types of enzyme molecules, each involved in a speciﬁc chemical reaction. Like all protein molecules, enzymes are coded for by genes. Polygenic - is a term used referring to phenotypes or traits that are inﬂuenced by more than one gene or loci in the genome. Many polygenic traits are also inﬂuenced by the environment and are called multifactorial. Examples of polygenic traits include skin color, height, diabetes type 2, cholesterol levels, and certain nutrition and ﬁtness genetic traits.

**Mendelian inheritance (pronounced "men DEE lee uhn")** - is the inheritance pattern characteristic of organisms that reproduce sexually. This inheritance was described by the Austrian monk Gregor Mendel who performed crossing experiments on garden pea plants at his monastery during the middle of the 19th century. Mendel who introduced the idea of the gene and dominant and recessive traits is considered the father of genetics.

**Autosomal dominant** - with autosomal dominant inheritance, an individual only needs to inherit one copy of the abnormal gene (from either the father or mother) to develop the condition or be predisposed to developing the condition.

**Autosomal recessive** - with autosomal recessive inheritance, an individual needs to inherit abnormal copies of a gene from both parents to develop the condition. Parent's of the aﬀected individual are only considered carriers and are not aﬀected.

**X-linked inheritance** - is the mode of inheritance in which the abnormal gene is located on the X chromosome. Women have two copies of the X chromosome and men have one X and one Y chromosome, so disease causing variants on the X chromosome usually causes diseases that aﬀect men more severely than women.

**Carrier** - a carrier of a disease-causing variant/mutation will not be aﬀected by the disease, but can pass on the variant to his/her oﬀspring. If the sexual partner is also a carrier of the same disease (i.e. has a disease-causing variant in the same gene) the couple will have a 25% chance of having an aﬀected child in every pregnancy.

**Allele** - an allele is one of two or more versions of a gene or the surrounding non-coding DNA sequence. An individual inherits two alleles for each gene, one from each parent. If the two alleles are the same, the individual is homozygous for that gene. If the alleles are diﬀerent, the individual is heterozygous.

**Heritability** - Heritability is a measure of how well diﬀerences in people's genes account for diﬀerences in their traits. Heritability estimates range from 0 (or 0%) to 1 (or 100%). A heritability close to zero indicates that almost all the variability in a trait among people is due to environmental factors, with very little inﬂuence from genetic diﬀerences. A heritability close to one indicates that almost all of the

variability in a trait comes from genetic diﬀerences, with very little contribution from environmental factors.

Homozygous (pronounced "hoh muh ZAHY guhs")

* the term used when an individual inherits the same alleles for a particular gene (or surrounding non- coding sequence) from both parents. For example, when the genotype at a particular SNP location is GG, the individual is said to be homozygous at that location.

Heterozygous (pronounced "het er uh ZAHY guhs")

* the term used when an individual inherits diﬀerent alleles or versions of a particular gene (or surrounding non-coding sequence) from each parents. For example, when the genotype at a particular SNP location is GA, the individual is said to be heterozygous at that location.

**Benign** - the term used to indicate that a variant (DNA change) is not disease-causing. Note, a variant classiﬁed as benign can still inﬂuence the phenotype of a particular trait (such as a chronic disease trait).

**Pathogenic** - the term used to indicate that a variant (DNA change) is disease-causing. These types of variants disrupt the production or normal functioning of the protein being coded for by a gene.

**VOUS or VUS** - is an acronym that stands for "variant of uncertain (or unknown) signiﬁcance". This refers to an allele, or variant form of a gene, which has been identiﬁed through genetic testing, but whose signiﬁcance to the function or health of an individual is not known.

**TEST METHODOLOGY, LIMITATIONS, CONDITIONS/TRAITS LIST & REFERENCES**

###### Test Methodology:

*Genotyping method of DNA was done using Illumina iScan technology to capture regions of the genome that are within (i.e. exonic) and outside of the protein coding genes (i.e. intergenic). SNPs (Single Nucleotide Polymorphisms) or variants from the microarray data were used in the analysis to generate parts of this report. The sequencing, genotyping, alignment and variant calling of the data was performed at the Tovana Health laboratory located in 1445 North Loop West, Houston, TX 77008.*

###### Limitations:

*Absence of a causative variant(s) or SNPs (Single Nucleotide Polymorphisms) related to a trait by data obtained from microarray method does not exclude a genetic basis of the individual's condition/trait. Some types of genetic abnormalities may not be detectable with the technologies utilized for this testing. This test does not analyze mitochondrial DNA sequence or epigenetic changes of the genome. It is possible that the genomic region where a variant contributing to the trait/condition exists in the individual tested was not captured or accurately mapped to the reference sequence using the current technologies and therefore was not detected. Additionally, it is possible that a particular genetic change may not be recognized as the underlying cause of the trait due to incomplete scientiﬁc knowledge about the function of all genes in the human genome and the impact of variations in those genes. Variants in genes associated with the trait or thought to potentially relevant for the individual's analysis are included in this report. It should be noted that the heritability (i.e. the proportion that genetic variation contributes to the variance of a phenotypic trait) is only partial (< 100%) for the traits being analyzed. Lifestyle and other environmental factors contribute the variance of the trait as well and should be accounted for when interpreting these results.*

**General References:**

1. *Hindorﬀ LA, MacArthur J (European Bioinformatics Institute), Morales J (European Bioinformatics Institute), Junkins HA, Hall PN, Klemm AK, and Manolio TA. A Catalog of Published Genome-Wide Association Studies.*
2. *Online Mendelian Inheritance in Man, OMIM®. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), 2018. World Wide Web URL: https://omim.org/.*
3. *National Library of Medicine (US). Genetics Home Reference [Internet]. Bethesda (MD): The Library; 2013 Sep 16 [cited 2018 Mar 13]. Available from: https://ghr.nlm.nih.gov/.*