TEST PATIENT

TEST PHYSICIAN

DR JOHN DOE

GUa d`Y HYghBUa Y

Sex::
DUHY Collected: 00-00-0000...

111 CLINIC STF 99H

111 H9GH'ROAD TEST SUBURB @AB =8: 00000000 UR#:0000000

```7@=B*=*7`GI 6I F6`J*=*7`' \$\$\$



E: info@nutripath.com.au A: PO Box 442 Ashburton VIC 3142

# Healthy Weight DNA Insight®







#### SCIENTIFIC STRENGTH RATING SYSTEM

The genetic markers and studies selected for this report represent the best and most recent genetic research in diet, nutrition, exercise, weight-related health conditions and medication response. Some research can be described as stronger than others based on the size of the population studied and whether the outcome has been replicated. Due to the current state of scientific research on the genetics of diet, exercise and nutrition, most of the studies referenced in your report are based on individuals of Caucasian ethnicity. While we all have the same genes, there are genetic and non-genetic factors in different ethnicities that might yield different outcomes for non-Caucasian populations. Your report includes a star system (in applicable sections), described below, to rate the strength of the research evidence for the genetic marker and the associated result. The star rating is not applicable for your health conditions and drug response sections. However, the genetic markers and studies used to report these conditions are based on the most accepted scientific information in the field.

***	Results derived from a large study of approximately 2,000 or more people, with at least one additional study showing the same results (replication study).
****	Results derived from a moderately-sized study of at least 400 people, with or without a replication study.
****	Small study of less than 400 people in some cases, with other small replicated studies. Results in this category are preliminary, but pass our criteria for statistical significance.
****	Results in this category should be considered extremely preliminary.



DIET



Eat a diet low in carbohydrates, particularly refined carbohydrates, instead of a low fat, Mediterranean or other diet.



You have a higher than average genetic risk for elevated LDL (bad) cholesterol. You should limit your saturated fat intake and avoid foods containing trans or hydrogenated fats to help reduce this risk.



Your genetics are associated with an increased likelihood of regaining weight after losing it, so it is particularly important for you to continue with your genetically appropriate diet after losing weight.



Carbohydrates are not just in pasta and bread, but are sometimes in foods you don't expect. Be sure to review nutritional labels for carbohydrate content.



Your genotype is associated with increased benefits from polyunsaturated fats. Replace saturated and trans (hydrogenated) fats, such as butter, lard and margarine, with polyunsaturated fats, such as vegetable oil, nuts, seeds, as well as some fish, in your diet.



#### **NUTRITIONAL NEEDS**

#### 9 Genetic Markers Tested



You have a genetic variant associated with lower levels of folic acid. Good sources of folate include vegetables, fruits, whole grains, legumes, as well as fortified foods and vitamin supplements.



You have a genetic variant associated with lower vitamin B6 levels. Be sure your diet includes foods rich in vitamin B6, such as dark green leafy vegetables, whole grains, legumes, poultry, fish and eggs.



You have a genetic variant associated with lower vitamin B12 levels. Be sure your diet includes foods rich in vitamin B12, such as meat, fish, poultry and milk products. You can also obtain B12 from fortified foods and vitamin supplements.





Continue a vigorous exercise regimen after losing weight. You have genes that are associated with an increased chance of gaining weight back.



If you do not exercise currently, start slow and exercise regularly. Starting too hard and too fast can lead to injury, pain or frustration.



#### METABOLIC HEALTH

40 Genetic Markers Tested



You have a higher than average genetic likelihood for elevated LDL cholesterol levels. Regular monitoring of your cholesterol by your physician is recommended.



Your genetic profile shows a higher than average likelihood for decreased HDL (good) cholesterol. HDL levels can sometimes be improved through aerobic exercise and a healthy diet.



You have a higher than average genetic likelihood for elevated triglyceride levels. Therefore, regular monitoring by your physician is recommended. You can help manage triglyceride levels by maintaining a healthy weight, reducing saturated fat and sugar intake, and increasing your consumption of omega-3 fatty acids (fish or seafood).



#### HEALTH CONDITIONS & MEDICATION RESPONSE

33 Genetic Markers Tested



Based on your results, modifications to your diet, lifestyle or medication may be appropriate. Discuss with your physician.

YOUR MATCHING DIET	TI ]
Matching Diet Type p. 7	LOW CARB DIET
Response To Monounsaturated Fats p. 10	NEUTRAL
Response To Polyunsaturated Fats p. 10	INCREASED BENEFIT
Omega-6 And Omega-3 Levels p. 11	TYPICAL
EATING BEHAVIOR TRAITS	Ø
Snacking p. 13	TYPICAL
Satiety - Feeling Full p. 13	TYPICAL
Eating Disinhibition p. 13	LESS LIKELY
Food Desire p. 14	TYPICAL
Sweet Tooth p. 14	TYPICAL
NUTRITIONAL NEEDS	
Vitamin B2 p. 16	STAY BALANCED
Vitamin B6 p. 17	OPTIMIZE INTAKE
Vitamin B12 p. 17	OPTIMIZE INTAKE
Folate - Folic Acid p. 18	OPTIMIZE INTAKE
Vitamin A p. 19	OPTIMIZE INTAKE
Vitamin C p. 20	STAY BALANCED
Vitamin D p. 20	STAY BALANCED
Vitamin E p. 21	STAY BALANCED
EXERCISE	8
Endurance Training p. 24	ENHANCED BENEFIT
HDL (Good) Cholesterol Response To Exercise p. 25	NORMAL BENEFIT
Insulin Sensitivity Response To Exercise p. 25	ENHANCED BENEFIT

Weight Loss-regain p. 28  Metabolism p. 29  Adiponectin Levels p. 29  METABOLIC HEALTH FACTO  Elevated LDL Cholesterol p. 31  Decreased HDL Cholesterol p. 32	NORE LIKELY TO GAIN WEIGHT BACK NORMAL
Metabolism p. 29  Adiponectin Levels p. 29  METABOLIC HEALTH FACTO  Elevated LDL Cholesterol p. 31  Decreased HDL Cholesterol p.	POSSIBLY LOW
Adiponectin Levels p. 29  METABOLIC HEALTH FACTO  Elevated LDL Cholesterol p. 31  Decreased HDL Cholesterol p.	POSSIBLY LOW
METABOLIC HEALTH FACTO Elevated LDL Cholesterol p. 31 Decreased HDL Cholesterol p.	ORS 👽
Elevated LDL Cholesterol p. 31  Decreased HDL Cholesterol p.	
Decreased HDL Cholesterol p.	ABOVE AVERAGE
The state of the s	
	ABOVE AVERAGE
Elevated Triglycerides p. 33	ABOVE AVERAGE
HEALTH CONDITIONS	•
Diabetes, Type 2 p. 35	AVERAGE RISI
Osteoarthritis p. 36	AVERAGE RISI
Venous Thrombosis p. 36	TYPICAL RISI
MEDICATION RESPONSE	
Clopidogrel Metabolism p. 38	ULTRARAPII METABOLIZER
Simvastatin-induced Myopathy p.	INCREASED RISI
	TYPICAL SENSITIVIT





#### DIET MATCHING DIET TYPE

Your diet has been selected by looking at many genetic variants associated with how people respond to the different macronutrients (proteins, fats and carbohydrates) in their food<sup>1,2,3,4,5,6</sup>. Your genetic risk profiles for metabolic health factors were also evaluated to determine your recommended diet<sup>7,8</sup>. Together, your genetic results suggest which one of the following diets may be best for you: "Low Fat," "Low Carb," "Mediterranean" or a "Balanced Diet." It is highly recommended to discuss any change in your diet plan with your health care provider.

#### YOUR DIET RECOMMENDATIONS

- ✓ Eat a diet low in carbohydrates, particularly refined carbohydrates, instead of a low fat, Mediterranean or other diet.
- ✓ You have a higher than average genetic risk for elevated LDL (bad) cholesterol. You should limit your saturated fat intake and avoid foods containing trans or hydrogenated fats to help reduce this risk.
- ✓ Your genetics are associated with an increased likelihood of regaining weight after losing it, so it is particularly important for you to continue with your genetically appropriate diet after losing weight.
- ✓ Carbohydrates are not just in pasta and bread, but are sometimes in foods you don't expect. Be sure to review nutritional labels for carbohydrate content.
- ✓ Your genotype is associated with increased benefits from polyunsaturated fats. Replace saturated and trans (hydrogenated) fats, such as butter, lard and margarine, with polyunsaturated fats, such as vegetable oil, nuts, seeds, as well as some fish, in your diet.

#### ▶ YOUR RESULT ◀

#### **LOW CARB DIET**

Your genotype is associated with weight loss or other health benefits from a diet lower in carbohydrates.

#### **VOUR RELATED GENES**

in in the second		
Gene Tested	Your Genotype	Scientific Strength
ADIPOQ-rs17300539	G/G	****
APOA2-rs5082	T/T	****
FTO-rs9939609	T/A	****
KCTD10-rs10850219	G/G	****
LIPC-rs1800588	C/C	****
MMAB-rs2241201	C/C	****
PPARG-rs1801282	C/C	****
AND MODE		

AND MORE...

#### ▶ YOUR RESULT ◀ LOW CARB

Non-starchy vegetables, high-quality proteins and

#### LOW FAT

Lean proteins, fiber-rich vegetables, grains and fruits, and healthy fats

#### BALANCED

Balance of healthy fats, carbohydrates and proteins

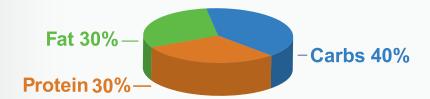
#### **MEDITERRANEAN**

Fish, monounsaturated fats. and low glycemic, high fiber vegetables, fruits, grains and legumes

#### DIET

#### LOW CARB DIET

A carbohydrate-controlled diet limits the amount of carbohydrates you consume. Foods rich in carbohydrates include breads, cereals, grains, rice, starchy vegetables, fruit, as well as milk and yogurt. More importantly, a carbohydrate-controlled diet plan focuses on non-starchy vegetables, healthy fats, as well as high-quality protein foods. Although this diet plan limits carbohydrates, it does not completely exclude them. Refined and processed foods should be avoided in order for healthier, nutrient-dense carbohydrates to fit into your daily intake. Concentrate on strongly colored fruits and vegetables with bold flavors. For your protein intake, incorporate legumes, fish (and other seafood), lean chicken, and limit your red meat consumption to about 3 ounces or less, 2 to 3 times per week. Regarding fats and oils, it's best to choose vegetable fats and to minimize your intake of animal fats. Processed and highly refined foods, trans fats, as well as added sugars, should be avoided. Most popular low-carbohydrate diets consist of a weight loss phase, which is very low in carbohydrates and is followed by a maintenance phase that manages carbohydrates.



#### Low Carb Diet: Key Aspects

#### Fruits and Vegetables

- ➤ Bright colors, bold flavor.
- ➤ Consume a variety of colors.
- ➤ Try to eat 9 servings of fruits and vegetables per day.
- ➤ Leafy green veggies are optimal.
- ➤ Limit store-bought fruit juice to 1/2 cup per day (no sugar or sweetener).
- ➤ Limit starchy vegetables.

#### Grains and Starchy Vegetables

- ➤ Avoid all refined grains.
- ➤ Use satisfying alternatives to grain, such as sweet potato, squash, mushrooms, and eggplant in moderation.
- ➤ Try quinoa.

#### Protein Foods

- ➤ Eat at least a 1/4 to 1/2 cup of legumes per day.
- ➤ Limit red meats.
- ➤ Eat fish or other seafood at least 2 to 3 times per week.
- ➤ Remove all visible fat and skin from meat, fish and poultry.
- Prepare meat by baking, broiling, steaming or poaching.
- ➤ Avoid frying meat.

#### Milk Products

- ➤ Plain Greek-style yogurt is optimal.
- ➤ Avoid milk products with added sugar.
- ➤ Limit cheese.

#### Fats and Oils

- ➤ Avoid hydrogenated and trans fats.
- ➤ Limit saturated fats.

#### General

Minimize or avoid added sugars and foods with added sugar. This is especially important if you are trying to lose weight or control your blood sugar levels, or if your triglyceride levels are elevated.

#### DIET

#### TYPES OF FAT IN YOUR DIET

Acting as an important part of any diet and a source of energy, fat provides flavor to your diet, but more importantly, it is a vital element in the absorption of fat-soluble vitamins such as vitamins A, D, E and K. The two major types of fat include saturated and unsaturated (polyunsaturated and monounsaturated) fats. In order for your body to function normally, you need to maintain a consistent and balanced supply of saturated and unsaturated fats. A third type of fats consists of hydrogenated fats, which are processed fats that are not found naturally, such as in margarine and fried fast foods. Hydrogenated fats may also contain trans fatty acids and are generally unhealthy and should be avoided.

#### SATURATED FAT

- ➤ Beef
- ➤ Lamb
- ➤ Lard
- ➤ Milk
- ➤ Cream
- ➤ Poultry (dark meat)
- ➤ Veal
- ➤ Pork
- ➤ Butter
- ➤ Cheeses
- ➤ Coconut oil
- ➤ Walnuts
- ➤ Almonds

- ➤ Evening
- ➤ Borage seed oil
- ➤ Nuts and seeds
- ➤ Poultry and

#### **UNSATURATED FAT**

Monounsaturated

➤ Avocados

➤ Extra virgin

olive oil

➤ Nuts

➤ Olives

- Polyunsaturated
- ➤ Cold water fish (e.g., salmon, herring, halibut, sardines.
- mackerel)
- ➤ Flaxseed
- ➤ Chia seed
- ➤ Pumpkin Seed
- primrose oil

- eggs

#### HYDROGENATED FAT

- ➤ Margarine (stick)
- ➤ Most fast foods
- ➤ Fried foods
- ➤ Hiahly processed foods
- ➤ Shortening
- ➤ Foods
- containing trans fats



## DIET RESPONSE TO MONOUNSATURATED FATS

Fat is an important part of any diet, and not all fats are bad. Monounsaturated fat is considered a healthy dietary fat found in avocados, olives, and some nuts, as well as oils, such as olive oil. The two possible outcomes for this test are "Increased Benefit" or "Neutral." Having an "Increased Benefit" from monounsaturated fat suggests you could benefit from eating foods containing monounsaturated fats. In general, it is best to avoid trans fats and limit saturated fat intake.

Genetic variants in two genes, ADIPOQ and PPARG, have been associated with a lower body weight in individuals when more than 13% of their calories come from monounsaturated fats<sup>5,6</sup>. This would be equivalent to a person on an 1,800-calorie diet consuming about 1 to 2 tablespoons of olive oil and a quarter cup of nuts each day as part of their total caloric intake. While the ADIPOQ study was done in a population of both men and women, the PPARG study was done only in women. There is not enough scientific evidence to support if the PPARG association is also true in men.

#### ▶ YOUR RESULT ◀

#### **NEUTRAL**

For people with your genotype, the amount of dietary monounsaturated fat you eat is not likely to affect your body weight. However, avoiding trans fats and substituting some saturated fats with monounsaturated fats is still recommended, as it has several health benefits.

## YOUR RELATED GENES Gene Tested Your Genotype Scientific Strength ADIPOQ-rs17300539 G/G ★★★ PPARG-rs1801282 C/C ★★★



## DIET RESPONSE TO POLYUNSATURATED FATS

Polyunsaturated fat is considered a healthy fat and is important for heart and brain function, as well as growth and development. Two types of polyunsaturated fats are omega-6 and omega-3 fats. Good sources of omega-6 fats include evening primrose and borage oils, as well as olives, nuts and poultry. Additionally, good sources of omega-3 fats include fish and seafood, as well as flaxseed, walnuts, hemp seeds, and dark green leafy vegetables.

The two possible outcomes in this report are "Increased Benefit" or "Neutral." Having an "Increased Benefit" from polyunsaturated fat means you should try to eat foods containing polyunsaturated fats. In general, it is best to avoid trans fats and minimize saturated fats. One study in women has shown that those with a certain genetic variant in the PPARG gene tend to have a lower body weight when they consume more polyunsaturated fats than saturated fats<sup>6</sup>. This association has not been studied in men.

#### ▶ YOUR RESULT ◀

#### **INCREASED BENEFIT**

People with your genotype who have a diet that includes more polyunsaturated fats, rather than saturated fats, tend to have a lower body weight, compared to those who do not.

YOUR RELATED GENES		
r Scientific ype Strength		
****		



## DIET OMEGA-6 AND OMEGA-3 LEVELS

Polyunsaturated fats (PUFAs) in our diet are composed of omega-3 and omega-6 fatty acids, both of which are recommended by the American Heart Association (AHA) for good heart health. Long-chain PUFAs are provided by our diet, but can also be synthesized in our bodies starting from the precursor essential fatty acids, linoleic acid (LA, omega-6) and alpha-linolenic acid (ALA, omega-3). Both omega-3 and omega-6 fats are processed in the body by the same enzyme complex<sup>9</sup>. The major dietary sources of omega-3 fatty acids include foods, such as flaxseed and walnuts, as well as fish oils and fish such as salmon. Processed foods often contain high levels of omega-6, while healthy sources of omega-6 include evening primrose and borage oils, as well as olives, nuts and poultry. Historically, the ratio of omega-6 to omega-3 fats in the diet was maintained close to a healthy 1:1, while in the current Western diet it is estimated to be about 15:1<sup>10</sup>.

In recent genome-wide association studies that included over 10,000 people, it was found that those with the C/C or C/T genotypes at a variant in the FADS1 gene, which codes for one of the enzymes involved in processing omega-3 and omega-6 fats, had "Decreased" blood levels of arachidonic acid (AA), a long-chain omega-6 fat, as well as eicosapentaenoic acid (EPA), a long-chain omega-3 fat. On the other hand, those with a T/T genotype had "Typical" levels of these two omega-fats<sup>11,12</sup>. Since both AA and EPA are precursors of biologically important metabolites, those with a "Decreased" outcome should increase their dietary intake of both omega-3 and omega-6 fatty acids. However, considering the current skewed ratio of omega-6:omega-3 fats, it is recommended that people monitor the intake of omega-6 fats from processed foods, while increasing their intake of omega-3 fats.

#### ▶ YOUR RESULT ◀

#### **TYPICAL**

People with your genotype were found to have typical blood levels of an important omega-6 fat and an important omega-3 fat.

#### 





## EATING BEHAVIOR TRAITS SNACKING

Snacking can be a healthy or unhealthy behavior. Snacking on balanced foods, containing healthy fats, lean protein, fiber and low glycemic index carbohydrates, in small portions, throughout the day can help control hunger cravings and reduce total caloric intake, while snacking on junk food can have negative health effects. Genetic markers associated with snacking behavior include variants in the receptor for leptin, an essential hormone for the regulation of food intake. The possible results in this report are "Typical" and "Increased." If you receive the "Increased" result, you may want to curtail the negative effects of snacking by choosing healthy snacks, eating slowly and reducing the size or calories of snacks. People with the G/G genotype in a leptin receptor (LEPR) genetic marker were more likely to show "Increased" snacking behavior in the same study. This association has not been studied in men.

#### ▶ YOUR RESULT ◀

#### **TYPICAL**

Your genotype is not associated with extreme snacking behavior.

#### YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
LEPR-rs2025804	A/G	****



## EATING BEHAVIOR TRAITS SATIETY - FEELING FULL

Satiety can be described as the feeling of fullness after you eat. The FTO (fat mass and obesity-associated) gene is known to be an important factor that predisposes a person to a healthy or unhealthy level of body weight<sup>17</sup>. The two possible outcomes in this report are "Difficulty in Feeling Full" and "Typical." People who experience "Difficulty in Feeling Full" tend to eat more without feeling satisfied. To help manage this outcome, you could increase the amount of fiber in your diet and balance meals and snacks throughout the day. Examples of foods high in fiber include whole wheat bread, oatmeal, barley, lentils, black beans, artichokes, raspberries, and peas. In a 2008 study, the A/A genotype at rs9939609 in the FTO gene was associated with "Difficulty in Feeling Full" Although this study was done in children, there is preliminary data to support that the association also holds true in adults<sup>19</sup>.

#### ▶ YOUR RESULT ◀

#### **TYPICAL**

People with your genotype tend to feel full after a meal.

#### YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
=TO-rs9939609	A/T	****



## EATING BEHAVIOR TRAITS EATING DISINHIBITION

Eating disinhibition describes the tendency to eat more than normal in response to a stimulus, such as a tasty food or in situations that trigger overeating (e.g., emotional stress or specific social situations). In a 2010 study, the T allele of rs1726866 was "More Likely" to be associated with eating disinhibition in women<sup>20</sup>. The C/C genotype at the same marker was "Less Likely" to be associated with eating disinhibition. There is not enough scientific evidence yet to determine if this association also holds for men.



#### ▶ YOUR RESULT ◀

#### LESS LIKELY

Your genotype is not associated with an increase in susceptibility for eating disinhibition.

#### YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
TAS2R38-rs1726866	C/C	****



## EATING BEHAVIOR TRAITS FOOD DESIRE

Although there is no objective method to quantify someone's feeling of hunger or liking for a particular type of food, behavioral scientists have devised techniques to measure an individual's motivation to consume food and compare it with that of others. This measurement, called the reinforcing value of food<sup>21</sup>, describes how much effort an individual is willing to put forth to get access to food. The reinforcing value can be determined through a series of tests in a laboratory setting. In each of those tests, the individual being tested is asked to complete a task in exchange for a small portion of his or her favorite foods. The task of the initial test is easy, so the food is not difficult to win. As the tests continue, the task gets more and more difficult until, at some point, the participant feels that the food is no longer worth the effort and decides to guit. This experiment tells us that early guitters, when compared with late quitters, are low in food reinforcement. Using this technique, a 2007 study<sup>13</sup> identified a genetic component in food reinforcement. Among people who were considered obese, those who had a specific variant (T allele) of the genetic marker rs1800497 had an "Increased" likelihood to make more effort to obtain their favorite foods and eat more of them. In contrast, the C/C genotype was associated with "Typical" levels of food reinforcement.

#### ▶ YOUR RESULT ◀

#### **TYPICAL**

Your genotype is not associated with an increased desire or willingness to put forth additional effort to obtain your favorite foods.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
ANKK1/ DRD2-rs1800497	C/C	****



## EATING BEHAVIOR TRAITS SWEET TOOTH

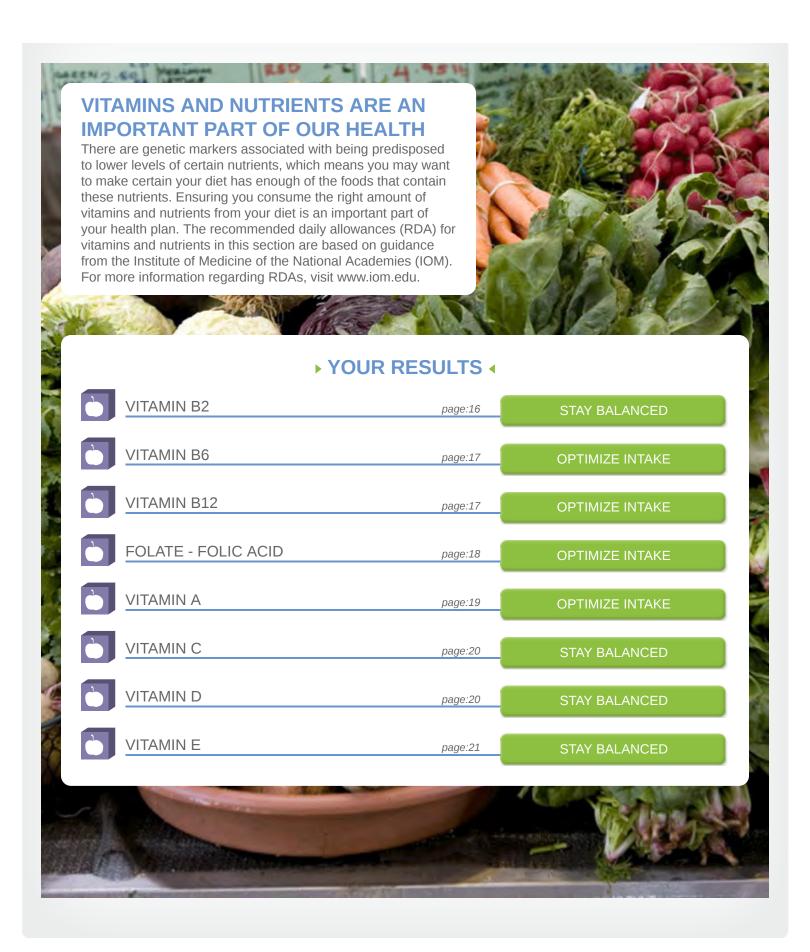
Craving sweet foods is sometimes described as having a "sweet tooth." The possible outcomes in this report are "Increased" or "Typical." If your genotype shows an "Increased" likelihood to eat lots of sweets, try choosing fruit as a healthy sweet alternative to sugary foods or soda. Be sure to follow your diet as some diet plans, such as the low carbohydrate diets, significantly limit the amount of sugar you can eat. Sweet foods can include healthy foods, such as fruits, or unhealthy foods like candy and sweetened beverages. People with the C/T and T/T genotypes showed an "Increased" likelihood to eat more sweets and sugary foods, while people with the C/C genotype were more likely to have a "Typical" intake of sugary foods<sup>22</sup>.

#### ▶ YOUR RESULT ◀

#### **TYPICAL**

People with your genotype tend to eat an average amount of sugary foods.

YOUR RELATED GENES			
Gene Tested	Your Genotype	Scientific Strength	
SLC2A2-rs5400	C/C	****	



#### YOUR NUTRITION RECOMMENDATIONS

- ✓ You have a genetic variant associated with lower levels of folic acid. Good sources of folate include vegetables, fruits, whole grains, legumes, as well as fortified foods and vitamin supplements.
- ✓ You have a genetic variant associated with lower vitamin B6 levels. Be sure your diet includes foods rich in vitamin B6, such as dark green leafy vegetables, whole grains, legumes, poultry, fish and eggs.
- ✓ You have a genetic variant associated with lower vitamin B12 levels. Be sure your diet includes foods rich in vitamin B12, such as meat, fish, poultry and milk products. You can also obtain B12 from fortified foods and vitamin supplements.





#### NUTRITIONAL NEEDS VITAMIN B2

Vitamin B2, or riboflavin, is a central component of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), both of which serve as cofactors of several critical enzymes involved in the electron transport chain, as well as in the metabolism of carbohydrates, fats and proteins<sup>23</sup>. Vitamin B2 is found in a variety of foods including milk, cheese, green leafy vegetables, legumes, beans, lean meats and fortified grains. Individuals with the T/T genotype at a variant in the MTHFR gene are likely to have increased levels of homocysteine, which are a risk factor for cardiovascular disease and stroke<sup>24,25,26</sup>. Levels of homocysteine were highest in T/T individuals with low riboflavin or vitamin B2 levels, and further, riboflavin supplementation was found to reduce homocysteine levels in these individuals<sup>27,28</sup>. Thus, individuals with the T/T genotype should "Optimize Intake" of vitamin B2 by eating foods rich in vitamin B2. On the other hand, vitamin B2 levels are likely to have a relatively small impact on homocysteine levels in people with the C/T or C/C genotypes, and hence, they should "Stay Balanced" and maintain a healthy diet.

#### ▶ YOUR RESULT ◀

#### STAY BALANCED

In people with your genotype, riboflavin levels have a relatively small impact on levels of homocysteine. Elevated levels of homocysteine are a risk factor for heart disease. You should maintain a healthy diet.

## YOUR RELATED GENES Gene Tested Your Genotype Scientific Strength MTHFR-rs1801133 C/T ★★★★



Vitamin B6, also called pyridoxine, helps your body's neurological system to function properly, promotes red blood cell health, and is involved in sugar metabolism ("http://ods.od.nih.gov/factsheets/vitaminb6/"). Vitamin B6 is found naturally in many foods, including beans, whole grains, meat, eggs and fish. Most people receive sufficient amounts of vitamin B6 from a healthy diet, and B6 deficiency is rare in the United States.

The genetic marker rs4654748 in the NBPF3 gene (near the ALPL gene) has been found in multiple studies to be associated with reduced levels of vitamin B6, possibly due to faster than normal clearance of this vitamin from the bloodstream<sup>29,30</sup>. Individuals with a C/C or C/T genotype had lower levels of B6 than those with the T/T genotype. Therefore, if your genotype is C/C or C/T, you will get a result of "Optimize Intake." If your genotype is T/T, it is suggested that you "Stay Balanced" and maintain a healthy diet. The studies we report observed associations between vitamin levels and particular genotypes; however, that does not mean that your levels are out of balance. You should ensure that you are eating a healthy diet and discuss this result with your physician. The recommended intake of vitamin B6 for most adults is 1.3 to 1.7 milligrams per day.

#### ▶ YOUR RESULT ◀

#### **OPTIMIZE INTAKE**

People with your genotype are more likely to have lower blood levels of vitamin B6. You may optimize your intake of vitamin B6 by paying attention to your diet and eating foods rich in vitamin B6.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
NBPF3-rs4654748	C/C	****



#### NUTRITIONAL NEEDS VITAMIN B12

Vitamin B12 plays an important role in how your brain and nervous system function. It helps to keep red blood cells healthy and is a critical component for synthesis and regulation of your DNA<sup>31</sup>. Vitamin B12 is found naturally in foods of animal origin including meat, fish, poultry, eggs and milk products. A healthy diet will typically provide sufficient B12, although vegetarians, vegans, older people, and those with problems absorbing B12 due to digestive system disorders may be deficient. Symptoms of vitamin B12 deficiency can vary, but may include fatigue, weakness, bloating, or numbness and tingling in the hands and feet. The recommended intake for adults is 2.4 micrograms per day.

Multiple genetic studies have identified a marker in the gene FUT2 as being associated with lower levels of B12 in the blood<sup>30,32,29</sup>. This effect may be due to reduced absorption of B12 in the gut<sup>30</sup>. People with G/G or A/G genotypes are recommended to "Optimize Intake" because they may have lower levels of B12. Eating foods rich in vitamin B12 can promote healthy levels of B12, especially for those over the age of 50. People with the A/A genotype should "Stay Balanced" and maintain a healthy diet. The studies we report observed associations between vitamin B12 levels and particular genotypes; however, that does not mean that your levels are out of balance. You should ensure that you are eating a healthy diet and discuss this result with your physician.

#### ▶ YOUR RESULT ◀

#### **OPTIMIZE INTAKE**

People with your genotype are more likely to have lower blood levels of vitamin B12. You may optimize your intake of vitamin B12 by paying attention to your diet and eating foods rich in vitamin B12.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
FUT2-rs602662	G/G	****



Folate is found in many foods, such as green leafy vegetables like chard or kale, as well as beans, lentils, fruits and fortified grains. This nutrient plays a role in protein metabolism, as well as DNA repair<sup>33</sup>. Folate can lower the blood level of homocysteine, a substance linked to cardiovascular disease at high levels<sup>34</sup>. Diets rich in folate have been associated with reduced risk of cardiovascular disease<sup>35</sup>. Folate is particularly important early in pregnancy for preventing some birth defects<sup>33</sup>. For this reason, pregnant women or women intending to become pregnant are advised an elevated recommended daily intake of 600 micrograms of folate. The recommended intake of folate for most adults is 400 micrograms per day.

A relatively common variant in the MTHFR gene, known as C677T (rs1801133), has been associated with lowered folate and elevated homocysteine levels in the blood<sup>34</sup>. Hence, people with a T/T or C/T genotype should "Optimize Intake" of folate. People with the C/C genotype should "Stay Balanced" and maintain a healthy diet. The studies we report observed associations between vitamin levels and particular genotypes; however, that does not mean that your levels are out of balance. You should ensure that you are eating a healthy diet and discuss this result with your physician.

#### ▶ YOUR RESULT ◀

#### **OPTIMIZE INTAKE**

People with your genotype are more likely to have lower blood levels of folate and higher blood levels of homocysteine. Foods rich in folic acid are recommended for you.

## YOUR RELATED GENES Gene Tested Your Genotype Scientific Strength MTHFR-rs1801133 C/T ★★★★



Vitamin A is a nutrient that describes a number of related compounds, including retinol, retinal, and retinoic acid. Vitamin A is critical for numerous functions in the body, including healthy vision, immune system action, bone growth, reproduction, and the proper regulation of gene expression<sup>36,37,38,39</sup>. The recommended intake of vitamin A for most adults is 700 to 900 micrograms per day.

Much of the vitamin A found in your body is derived from beta-carotene, a nutrient found in some plants and foods, such as pumpkin, carrots, sweet potatoes and spinach. A genetic study has found that vitamin A conversion from beta-carotene is impaired in women carrying variants of the BCMO1 gene<sup>40</sup>. This association has not been studied in men.

Those with a result of "Optimize Intake" may bypass this effect by consuming adequate amounts of preformed vitamin A. which can be found in fortified milk and breakfast cereals, as well as in multivitamins containing retinyl palmitate or retinyl acetate<sup>41,42</sup>. People who receive a "Stay Balanced" outcome should maintain a healthy diet. An additional outcome in this report is "Inconclusive." which means that there was not enough scientific evidence to determine how your genotype relates to the efficiency of converting beta-carotene to vitamin A. The study we report observed associations between vitamin A levels and particular genotypes. However, that does not mean that your levels are out of balance. You should eat a healthy diet and speak with your physician before making specific changes to your dietary regimen.



#### ▶ YOUR RESULT ◀

#### **OPTIMIZE INTAKE**

People with your genotype are likely to have a reduced efficiency in converting beta-carotene into vitamin A. Therefore, you may have a reduced level of vitamin A in your blood.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
BCMO1-rs7501331	T/T	****
BCMO1-rs12934922	A/T	****



Vitamin C, or L-ascorbic acid, must be acquired from dietary sources, as humans are unable to synthesize it. Some dietary sources of vitamin C include lemons, oranges, red peppers, watermelons, strawberries and citrus juices or juices fortified with vitamin C. While a severe deficiency of vitamin C ultimately leads to scurvy, variations in vitamin C levels have also been associated with a wide range of chronic complex diseases, such as atherosclerosis, type 2 diabetes and cancer<sup>43</sup>. These associations are thought to result from a contribution of vitamin C as an antioxidant, as well as its role in the synthesis of collagen and various hormones. After ingestion, the vitamin C in one's diet gets transported across the cell membrane via transport proteins, one of which is SLC23A1. A recent study of over 15,000 people found that the A allele of a variant in SLC23A1 was associated with decreased levels of circulating vitamin C<sup>44</sup>. Therefore, if your genotype is A/A or A/G, you will get a result of "Optimize Intake." People with a G/G genotype should "Stay Balanced" and maintain a healthy diet.

#### ▶ YOUR RESULT ◀

#### STAY BALANCED

Your genotype is not associated with lower blood levels of vitamin C. You should maintain a healthy diet.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
_C23A1-rs33972313	G/G	****

SL



### *NUTRITIONAL NEEDS*VITAMIN D

Vitamin D is important for the absorption and utilization of calcium, which is beneficial for maintaining good bone health<sup>45</sup>. Exposure to sunlight is an important determinant of a person's vitamin D level, since there are few natural dietary sources of vitamin D. While sunscreen use blocks skin production of vitamin D, excessive sun exposure is a risk factor for skin cancer and related conditions, and is not recommended. Dietary sources of vitamin D include some fatty fish, fish liver oils, and milk or cereals fortified with vitamin D. The recommended intake of vitamin D for most adults is 600 IUs per day. About 115 IUs of vitamin D is found in one cup of vitamin D-fortified, non-fat, fluid milk.

Multiple genetic studies have identified a variant in the GC gene that codes for the vitamin D-binding protein that is associated with decreased blood levels of 25-hydroxyvitamin D, which is the major circulating form of vitamin D<sup>46,47</sup>. People with the G/G or G/T genotype at this genetic marker may be susceptible to lower blood vitamin D levels due to reduced ability to transport vitamin D in the body. Therefore, these people may need to "Optimize Intake" of vitamin D. People with a T/T genotype are advised to "Stay Balanced" and maintain a healthy diet. The studies we report observed associations between vitamin D levels and certain genotypes; however, that does not mean that your levels are out of balance. You should eat a healthy diet and speak with your physician before making specific changes to your dietary regimen.

#### ▶ YOUR RESULT ◀

#### STAY BALANCED

Your genotype is not associated with lower levels of vitamin D (plasma 25-hydroxyvitamin D levels). However, other factors, such as diet and exposure to sunlight, play an important role in regulating levels of vitamin D in blood.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
GC-rs2282679	T/T	****

SEX: FEMALE ACC #: F7715014 DATE: NOV 12, 2015



**NUTRITIONAL NEEDS** 



PAGE 21



#### NUTRITIONAL NEEDS VITAMIN E

Vitamin E is a group of eight antioxidant molecules, of which alpha-tocopherol is the most abundant in the body. Vitamin E functions to promote a strong immune system and regulates other metabolic processes<sup>48,49</sup>. The recommended intake of vitamin E for most adults is 15 milligrams per day. Note that synthetic varieties of vitamin E found in some fortified foods and supplements are less biologically active. Sources of naturally-occurring vitamin E in foods are vegetable oils, green leafy vegetables, eggs and nuts.

One study of 3,891 individuals found that people with the A/A or A/C genotypes at an intergenic marker, rs12272004, near the APOA5 gene, had increased plasma levels of alpha-tocopherol<sup>50</sup>. Therefore, they should "Stay Balanced" and maintain a healthy diet. This is good news since increased vitamin E levels are associated with decreased frailty and disability in old age<sup>51</sup>. People with the C/C genotype were not associated with increased levels of alpha-tocopherol, and hence they would need to "Optimize Intake" of vitamin E through the increased intake of foods rich in vitamin E. Keep in mind, however, that most adults normally do not take in adequate amounts of vitamin E on a daily basis<sup>52</sup>, so keeping an eye on your vitamin E intake is good advice for anyone. The studies we report observed associations between vitamin E levels and certain genotypes; however, that does not mean that your levels are out of balance. You should eat a healthy diet and speak with your physician before making specific changes to your dietary regimen.

#### ▶ YOUR RESULT ◀

#### STAY BALANCED

Your genotype is associated with increased alpha-tocopherol levels, which is one compound that makes up vitamin E. You should maintain a healthy diet to stay balanced.

YOUR RELATED GENES			
Gene Tested Your Scientific Genotype Strength			
INTERGENIC- rs12272004	A/C	****	

#### NUTRIENTS, WEIGHT MANAGEMENT AND GENETICS

New studies continue to emerge that demonstrate links between nutrients and genetics that show benefits in health and weight loss. Some of the benefits that scientists observe in relation to genes are listed below.

Important: The genes and associated benefits listed below are not part of your genetic test. The content on this page is informational.



NUTRIENT/FOOD	POTENTIAL HEALTH & WEIGHT LOSS BENEFITS	ASSOCIATED GENE(S)
Resveratrol	Weight Loss, Decrease Weight Gain	SIRT1, PPARA, PPARG, ER
Polyphenols (tea)	Decrease Weight Gain	PPARG
Conjugated Linoleic Acid (CLA)	Fat Burning, Weight Loss	PPARA, PPARG
Ispoprenols (farnesol)	Weight Loss	PPARA, PPARG
Abietic Acid	Weight Loss	PPARG
Capsaicin (Hot Pepper)	Weight Loss, Anti-inflammatory	PPARG
Phytol (Chlorophyll)	Weight Loss	PPARA
Auraptene (Citrus)	Weight Loss	PPARA, PPARG
Isohumulone (Hops)	Weight Loss	PPARA, PPARG
Guggulsterone (Gugle)	Weight Loss	Farnesoid X Receptor
Soy/Genistein	Weight Loss	Steroid Receptors: Estrogen, Androgen, Progesterone
Diosgenin	Weight Loss	Steroid Receptors: Progesterone
Ginseng	Weight Loss	Steroid Receptors: Estrogen
Hyperforin	Weight Loss	Pregnane X Receptor
Alpha-lipoic Acid	Reduction of Overeating	AMPK Inhibitor
Anthocyanins (Pigment)	Overall Health Benefit	Adiponectin
Licorice LFO (Polyphenols)	Overall Health Benefit	FA synthase
Pomegranate Extract (Lenolenic Acid)	Overall Health Benefit	b-oxidation/PPARA

## EXERCISE HAS LONG BEEN SHOWN TO PROVIDE MANY HEALTH BENEFITS

Studies have shown a link between genetics and exercise, and how people respond to exercise for weight loss and other health benefits. A few examples of this link include the ACE and ACTN3 genes and the association with elite athlete status, as well as the LPL gene and its connection to the loss of body fat in response to exercise. A summary of your results is listed below.

#### **▶ YOUR RESULTS ◄**

ENDURANCE TRAINING

page:24

ENHANCED BENEFIT

3º

HDL (GOOD) CHOLESTEROL RESPONSE TO EXERCISE

page:25

NORMAL BENEFIT

R

INSULIN SENSITIVITY RESPONSE TO EXERCISE

nage:2

**ENHANCED BENEFIT** 



#### YOUR EXERCISE RECOMMENDATIONS

- ✓ Continue a vigorous exercise regimen after losing weight. You have genes that are associated with an increased chance of gaining weight back.
- ✓ If you do not exercise currently, start slow and exercise regularly. Starting too hard and too fast can lead to injury, pain or frustration.





## EXERCISE ENDURANCE TRAINING

Endurance training is generally used to describe exercise that is done for a longer duration with moderate intensity. Most people can benefit from a combination of endurance, high intensity and resistance exercises. Some people have genetic markers that are associated with "Enhanced Benefit" from endurance training, while others will gain "Normal Benefit." The studies that were used to calculate your result tested responses to a 20-week endurance training program<sup>53,54,55</sup>. This result can be used to help tailor your exercise routine. Always consult your physician or health care provider before beginning any exercise program.

#### ▶ YOUR RESULT ◀

#### **ENHANCED BENEFIT**

Endurance training may provide enhanced health benefits to people with your genotype.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
LIPC-rs1800588	C/C	****
LPL-rs328	C/C	****
PPARD-rs2016520	A/A	****
PPARD-rs2016520	A/A	***



### EXERCISE

#### HDL (GOOD) CHOLESTEROL RESPONSE TO EXERCISE

One of the health benefits of exercise can be the improvement of your cholesterol. HDL cholesterol is known as the good cholesterol, and having more HDL is beneficial. Most people can improve their HDL levels by exercising. In the Heritage Family Study, people with the A/G and G/G genotypes were more likely to have an "Enhanced Benefit" in their HDL levels by exercising<sup>55</sup>. People with "Normal Benefit" may also increase their HDL levels by exercising, but may not experience an enhanced effect.

#### ▶ YOUR RESULT ◀

#### NORMAL BENEFIT

Your genotype is associated with a typical increase in HDL (good) cholesterol in response to a 20-week endurance training program.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
PPARD-rs2016520	A/A	****



## EXERCISE INSULIN SENSITIVITY RESPONSE TO EXERCISE

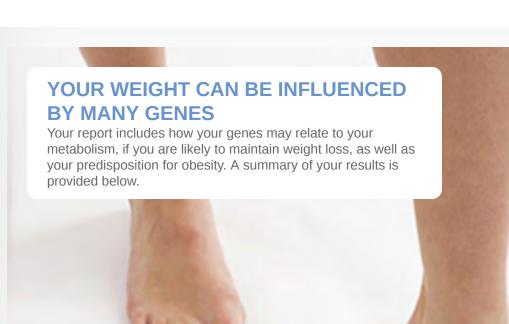
Insulin sensitivity is a good thing. Insulin in your body helps control your response to glucose, commonly known as sugar. Having an increased insulin sensitivity means that the body has a better ability to process sugar. The opposite of insulin sensitivity is called insulin resistance, which is linked to obesity and type 2 diabetes. Most people have a beneficial response to exercise, resulting in increased insulin sensitivity. According to a study, people with C/C or C/T genotypes, at a marker in the LIPC gene, showed an "Enhanced Benefit," compared to those with a T/T genotype<sup>54</sup>. Although people with T/T genotypes are likely to gain "Less Benefit" in insulin sensitivity from exercise training, exercise remains important in many other aspects of their health.

#### ▶ YOUR RESULT ◀

#### ENHANCED BENEFIT

Your genotype is associated with enhanced insulin sensitivity in response to exercise.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
LIPC-rs1800588	C/C	****



#### **▶ YOUR RESULTS ◆**

OBESITY page:28 AVERAGE

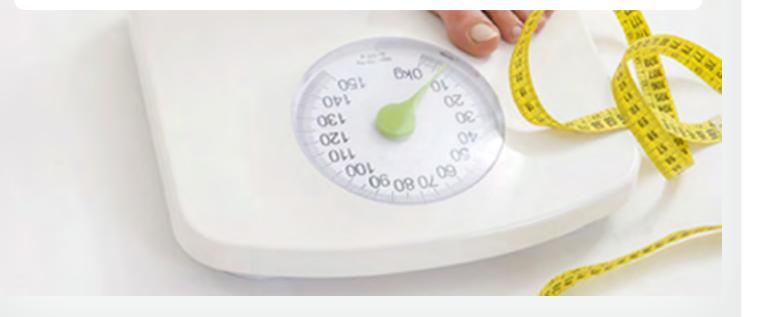
WEIGHT LOSS-REGAIN

page:28

MORE LIKELY TO GAIN WEIGHT
BACK

METABOLISM page:29 NORMAL

ADIPONECTIN LEVELS page:29 POSSIBLY LOW





**Actual Weight** 

Weight: 140 lbs Height: 5' 6"

#### **Normal**

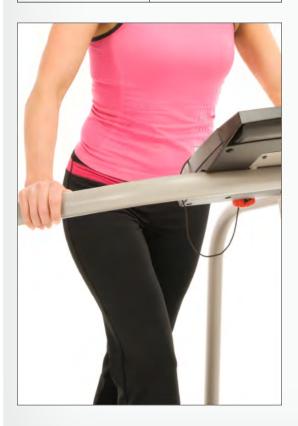
BMI body mass index

22.6

-	
Category	BMI range - kg/m2
Underweight	Less than 18.5
Normal	from 18.5 to 24.9
Overweight	from 25 to 29.9
Obese	from 30 to 34.9
Clinically Obese	from 35 to 39.9
Extremely Obese	40 or greater

Body mass index (BMI) is a measure of body fat based on height and weight that applies to adult men and women. BMI is usually represented in kg/m2. Your BMI was calculated using your survey responses for weight and height. If your BMI is not listed here, you may not have completed those responses in the survey.

Your actual weight is a result of a combination of factors including lifestyle, environment and genetics. Your Obesity Index result is a measure of your likelihood, based on genetics, to have a BMI over 35 (clinically or extremely obese). Since your weight is affected by many factors, it is possible for your Obesity Index result to be very different than your actual weight. The important point is that the genetics of obesity do not lead to an inevitable outcome. Many people have a choice of managing lifestyle to counteract genetics. For example, some people that are of normal weight BMI can have an Obesity Index of above average or high. This example is commonly seen in someone who is controlling diet, nutrition, eating behaviors and/or exercise to manage their body weight. The opposite can also be true. Some people who have an actual BMI in the obese categories can have an Obesity Index of average, below average or low. This case can sometimes be explained by lifestyle choices, environment or other health factors that have led a person to become obese without having the genetics associated to obesity.





## YOUR BODY AND WEIGHT OBESITY

Obesity is influenced by both genetic and environmental factors. Approximately 40 to 70% of an individual's susceptibility to obesity is inherited<sup>56</sup>. When someone reaches a body mass index (BMI) of 30 to 35 (clinically obese) or above 40 (morbidly obese), genetic factors with strong effects are likely to be involved. There are 2 possible outcomes of this test: "Average" and "Above Average". An "Above Average" outcome does not mean that you are obese, it only means that you have a higher than average genetic likelihood for a high BMI.

Your genetic predisposition to obesity is determined from your genotypes at variants in the FTO (fat mass and obesity associated) and MC4R (melanocortin-4 receptor) genes. The association of these genes to obesity is well-established. The MC4R gene is expressed in the brain's hunger center and is involved in regulating energy balance<sup>57</sup>. Rare mutations in the MC4R gene have been shown to cause a rare, inherited form of obesity. FTO is less well-understood, but is also believed to be important for controlling feeding behavior and energy balance<sup>58</sup>. Your test result includes common variants that have been confirmed in many large genetic studies (including multiple studies of over 38000 individuals) to be associated with a predisposition for high BMI and/or obesity<sup>17,59,60,61,62</sup>. However, as lifestyle also has a considerable impact on obesity, you can mitigate your risks by eating a proper diet, exercising and reducing stress<sup>63,64</sup>.

#### ▶ YOUR RESULT ◀

#### **AVERAGE**

Your genetic profile indicates an average predisposition for being overweight.

YOUR RELATED GENES		
Gene Tested Your Scientific Genotype Strength		
FTO-rs9939609	A/T	****
MC4R-rs17782313	T/T	****



## YOUR BODY AND WEIGHT WEIGHT LOSS-REGAIN

There are genes associated with the tendency to gain weight back after a person loses weight, and there are genes that protect a person from weight regain. In one study, people with the G/G genotype at a marker in the ADIPOQ gene were "More Likely to Gain Weight Back," while people with other genotypes were more likely to show "Weight Loss Maintained" 165. It is best after losing weight to maintain a healthy diet, exercise and nutrition plan to keep the extra pounds off and support long-term health.



#### ▶ YOUR RESULT ◀

## MORE LIKELY TO GAIN WEIGHT BACK

You may have difficulty keeping weight off after losing weight.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
ADIPOQ-rs17300539	G/G	****



## YOUR BODY AND WEIGHT METABOLISM

Metabolism describes the way your body burns energy (calories) and tends to have a strong correlation to managing your weight. Resting metabolism is how your body burns energy while at rest. People with a "Fast" metabolism can sometimes eat more food with little exercise and not gain weight. People with a "Normal" metabolism tend to require average amounts of food intake and average amounts of exercise to maintain weight. A genetic marker in the leptin receptor (LEPR) is associated with interactions in your brain that trigger how and when you burn energy. People with a C/C genotype tend to have an increased resting metabolic rate, or "Fast" metabolism, while people with C/G or G/G genotypes are not associated with an increased resting metabolic rate; therefore, they have a "Normal" metabolism<sup>66</sup>. However, having this genetic variant is only one of many other genetic and non-genetic factors that contribute towards your metabolism. Exercise is a common method of increasing your metabolism.

#### ▶ YOUR RESULT ◀

#### **NORMAL**

Your genotype is associated with a normal resting metabolic rate.

#### YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
LEPR-rs8179183	G/G	****



## YOUR BODY AND WEIGHT ADIPONECTIN LEVELS

Adiponectin is a hormone that is produced by fat cells and functions in the body to trigger your liver and muscles to get energy from fat<sup>67</sup>. Higher levels of adiponectin are considered good for weight loss and health<sup>68</sup>. Your health care provider can test your adiponectin levels. If you have low levels, losing weight may be a good way to increase your adiponectin levels<sup>67</sup>. A variant in the adiponectin gene (ADIPOQ) is associated with adiponectin levels. People with A/A or A/G genotypes were associated with "Possibly Low" levels of adiponectin, while those with the G/G genotype had "Typical" levels<sup>69</sup>.

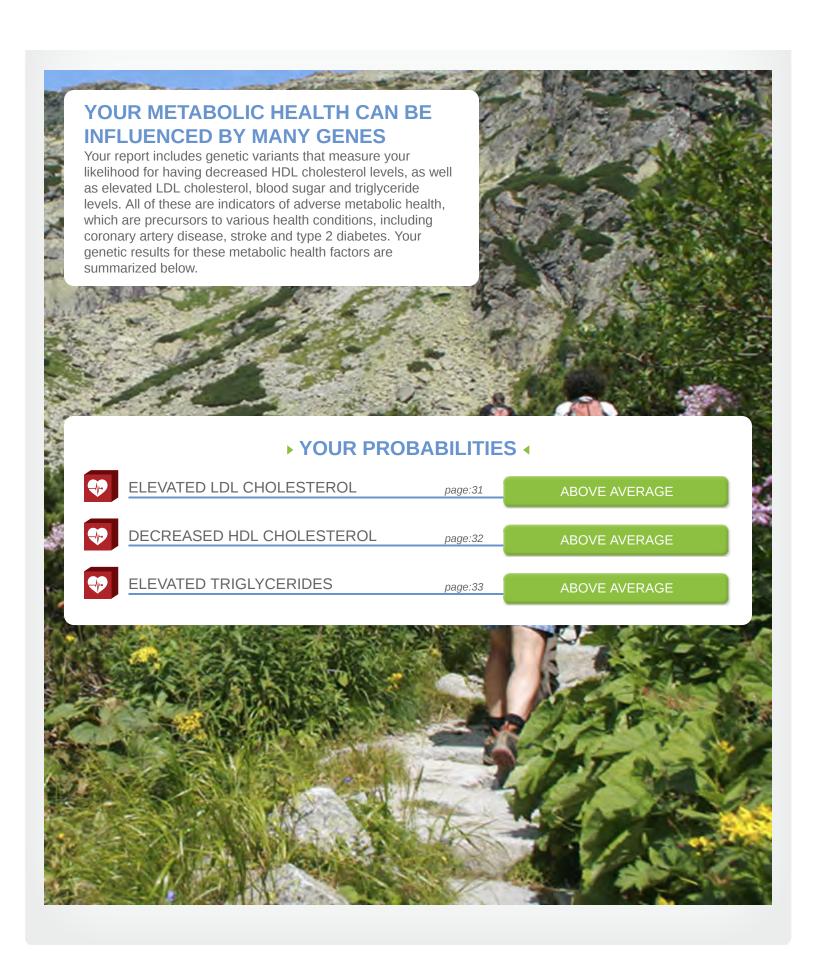
#### ▶ YOUR RESULT ◀

#### **POSSIBLY LOW**

Your genotype is associated with lower adiponectin levels.

#### YOUR RELATED GENES

Gene Tested	Your Genotype	Scientific Strength
ADIPOQ-rs17366568	A/G	****



#### YOUR HEALTH RECOMMENDATIONS

- ✓ You have a higher than average genetic likelihood for elevated LDL cholesterol levels. Regular monitoring of your cholesterol by your physician is recommended.
- ✓ Your genetic profile shows a higher than average likelihood for decreased HDL (good) cholesterol. HDL levels can sometimes be improved through aerobic exercise and a healthy diet.
- ✓ You have a higher than average genetic likelihood for elevated triglyceride levels. Therefore, regular monitoring by your physician is recommended. You can help manage triglyceride levels by maintaining a healthy weight, reducing saturated fat and sugar intake, and increasing your consumption of omega-3 fatty acids (fish or seafood).





## METABOLIC HEALTH FACTORS ELEVATED LDL CHOLESTEROL

Low-density lipoprotein (LDL) is the type of cholesterol that can become dangerous if you have too much of it. Like gunk clogging up your kitchen drain, LDL cholesterol can form plaque and build up in the walls of your arteries. This can make your arteries narrower and less flexible, putting you at risk for conditions like a heart attack or stroke. Optimally, LDL levels should be less than 100 mg/dl. Near-optimal levels range from 100 to 129 mg/dl and borderline high from 130 to 159 mg/dl. A score greater than 160 mg/dl is high and greater than 190 mg/dl is very high. Your physician can measure your cholesterol levels.

A genetic result of "High" or "Above Average" does not mean you have elevated LDL cholesterol levels, but tells you that you may have a genetic propensity for elevated LDL cholesterol levels. On the other hand, a result of "Low" or "Below Average," tells you that you have a lower than average genetic likelihood for elevated LDL cholesterol levels. However, you could still develop problems with your LDL levels as a result of your diet and other factors. This report is based on genetic variants studied in over 19,000 individuals. A genetic result of "High" means that you share a similar genetic profile with individuals from the Framingham Heart Study who had elevated LDL cholesterol levels measuring, on average, above 139 mg/dl with approximately 25% of individuals measuring above 160 mg/dl<sup>7</sup>. A genetic result of "Above Average" means that you share a similar genetic profile with individuals measuring, on average, above 130 mg/dl LDL with approximately 17% of individuals measuring above 160 mg/dl LDL cholesterol7. A genetic result of "Average" means that you share a similar genetic profile with individuals measuring, on average, near-optimal LDL cholesterol levels. Diet plays an important part in LDL levels. Processed foods and foods high in trans fat contribute to elevated LDL levels.

#### ▶ YOUR PROBABILITY ◀

#### ABOVE AVERAGE

You share a similar genetic profile with individuals who exhibit borderline-high LDL cholesterol levels. Therefore, you have a higher than average likelihood for elevated LDL (bad) cholesterol levels.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
ABCG8-rs6544713	C/T	****
APOB-rs515135	G/A	****
CELSR2-rs12740374	G/G	****
HMGCR-rs3846663	C/T	****
HNF1A-rs2650000	A/C	****
INTERGENIC- rs1501908	G/G	****
LDLR-rs6511720	G/G	****
MAFB-rs6102059	C/T	****
NCAN-rs10401969	T/T	****
PCSK9-rs11206510	T/T	****



## METABOLIC HEALTH FACTORS DECREASED HDL CHOLESTEROL

High-density lipoprotein (HDL) cholesterol is known as good cholesterol, because high levels of HDL cholesterol seem to protect against heart attack, while low levels of HDL cholesterol (less than 40 mg/dL) increase the risk of heart disease<sup>70</sup>. While multiple mechanisms are known to account for this, the major one is thought to be the role of HDL in transporting excess cholesterol away from the arteries and back to the liver, where it is passed from the body<sup>71</sup>. Your HDL cholesterol can be measured with a simple blood test. In men, typical HDL cholesterol levels range from 40 to 50 mg/dl. In women, female hormones cause typical HDL cholesterol levels to range from 50 to 60 mg/dl; however, after menopause there is a tendency for decreased HDL cholesterol levels. Foods containing trans fats can lower HDL cholesterol levels, which is unhealthy. Cholesterol levels should be monitored by your physician.

A genetic result of "High" or "Above Average" does not mean you have decreased HDL cholesterol levels, but tells you that you may have a high propensity for decreased HDL cholesterol levels. On the other hand, a result of "Low" or "Below Average," tells you that you have a lower than average propensity for decreased HDL cholesterol levels. Our genetic testing is based on genetic variants studied in over 19,000 individuals. A result of "High" means that you share a similar genetic profile with individuals from the Framingham Heart Study who had decreased HDL cholesterol levels measuring, on average, below 46 mg/dl with approximately 37% of individuals measuring below 40 mg/dl. On the other hand, a result of "Above Average" means that you share a similar genetic profile with individuals measuring, on average, below 50 mg/dl HDL cholesterol with approximately 30% of individuals measuring below 40 mg/dl HDL cholesterol?

#### ▶ YOUR PROBABILITY ◀

#### **ABOVE AVERAGE**

You share a similar genetic profile with individuals exhibiting decreased HDL cholesterol levels. Therefore, you have a higher than average likelihood for decreased HDL cholesterol levels.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
ABCA1-rs1883025	G/G	****
ANGPTL4-rs2967605	G/G	****
CETP-rs247616	C/C	****
FADS1-rs174547	T/T	****
GALNT2-rs4846914	A/G	****
HNF4A-rs1800961	C/C	****
KCTD10-rs2338104	C/C	****
LCAT-rs2271293	A/G	****
LIPC-rs10468017	C/C	****
LIPG-rs4939883	T/T	****
LPL-rs12678919	A/A	****
PLTP-rs7679	C/T	****
TTC39B-rs471364	A/A	****
ZNF259-rs964184	C/G	****



## METABOLIC HEALTH FACTORS ELEVATED TRIGLYCERIDES

Triglyceride is the chemical term for fat as it is stored in your body. People with elevated triglycerides are at risk of conditions, such as coronary artery disease or type 2 diabetes. Having higher triglycerides is often associated with poor lifestyle choices, such as lack of exercise, excessive alcohol consumption, cigarette smoking, excessive refined carbohydrate consumption and being overweight. A normal triglyceride score is under 150 mg/dl. Triglyceride levels in the range of 150 to 199 mg/dl are defined as borderline high, with over 200 mg/dl considered high and over 500 mg/dl very high. Your triglyceride levels can be monitored by your physician.

A result of "High" or "Above Average" does not mean you have elevated triglyceride levels, but tells you that you may have a propensity for elevated triglycerides levels. On the other hand, a genetic test result of "Low" or "Below Average," tells you that you have a lower than average likelihood for elevated triglyceride levels. The genetic test is based on genetic variants studied in over 19,000 individuals. A genetic result of "High" means that you share a similar genetic profile with individuals from the Framingham Heart Study who had elevated triglyceride levels measuring on average above 150 mg/dl with approximately 31% of individuals measuring above 200 mg/dl<sup>7</sup>.

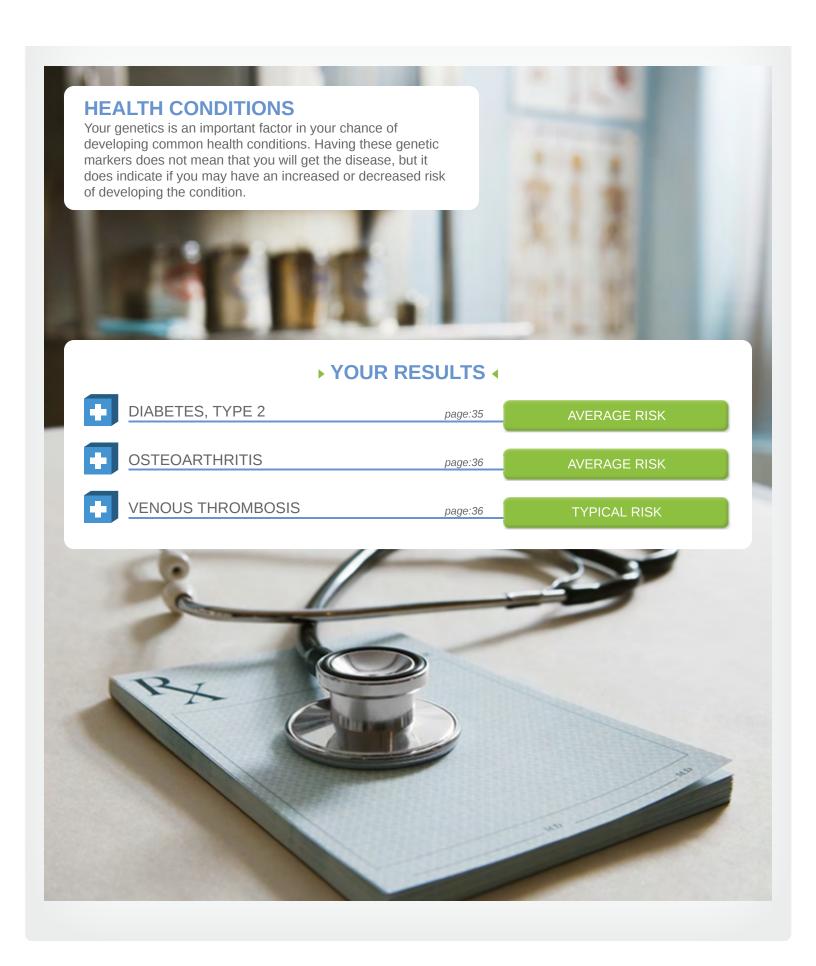


#### ▶ YOUR PROBABILITY ◀

#### **ABOVE AVERAGE**

You share a similar genetic profile with individuals who exhibit borderline-high triglyceride levels. Therefore, you have a higher than average likelihood for elevated triglyceride levels.

YOUR RELATED GENES		
Gene Tested	Your Genotype	Scientific Strength
ANGPTL3-rs10889353	A/C	****
APOB-rs7557067	A/A	****
FADS1-rs174547	T/T	****
GCKR-rs1260326	C/T	****
LPL-rs12678919	A/A	****
MLXIPL-rs714052	T/T	****
NCAN-rs17216525	C/C	****
PLTP-rs7679	C/T	****
TRIB1-rs2954029	A/A	****
XKR6-rs7819412	A/A	****
ZNF259-rs964184	C/G	****





Type 2 diabetes (T2D) is a chronic disease in which there are high levels of sugar (glucose) in the blood. T2D is the most common form of diabetes. Symptoms of the disease include persistent thirst, frequent urination, hunger, fatigue, weight loss, itchy skin and blurry eyesight among others. If you have T2D your body does not respond efficiently to insulin, the hormone responsible for regulating sugar levels in the body. It is estimated that up to 75% of T2D risk is caused by obesity. Obesity also results in a state of insulin resistance whereby target organs for insulin action do not respond efficiently to take in glucose from the blood. Obesity is responsible for much of the increase in T2D that is seen world-wide. Type 2 diabetes (T2D) can be prevented. The two most important risk factors for T2D are obesity and lack of physical activity<sup>72,73,74,75</sup>. Watch your weight and get plenty of exercise.

A genetic result of "increased risk" or "above average risk" does not mean that you have the disease, or will get the disease, but rather that you have a predisposition to developing the disease. A result of "average risk" indicates that the likelihood of developing the disease is similar to the overall population. Our test outcome is determined using genetic laboratory results in conjunction with the patient's self-reported ethnicity.

#### ▶ YOUR RESULT ◀

#### **AVERAGE RISK**

Based on your genetic profile you have an average likelihood for developing type 2 diabetes.

#### **VOUR RELATED GENES** Gene Tested Your Genotype CDKAL1-rs10946398 CDKN2B-rs10811661 T/C ESR1-rs3020314 T/T FTO-rs8050136 A/C HHEX-rs1111875 G/G HNF1B-rs7501939 T/C IGF2BP2-rs1470579 A/C JAZF1-rs864745 A/G KCNJ11-rs5219 T/C KCNQ1-rs2237892 T/C MTNR1B-rs10830963 C/C NOTCH2-rs10923931 G/G PPARG-rs1801282 C/C SLC30A8-rs13266634 T/T TCF7L2-rs7903146 C/C WFS1-rs10010131 G/G



Osteoarthritis (OA) is a common joint disorder, which is due to aging and wear and tear on the joints. Genetics, age, estrogen use and bone density are all important systemic risk factors for OA. Obesity, joint injury, joint deformity, repetitive stress injuries, playing sports and muscle weakness affect the location and severity of OA. Family and twin studies suggest that approximately 40% to 80% of an individual's susceptibility to osteoarthritis is inherited<sup>76,77</sup>. There are also differences in the degree of heritability depending on the sex of the individual and on the location (e.g. hip or knee) of the affected joint. You cannot change your age, your parents or your fondness for sports, so the best way to reduce your risk of OA is to avoid obesity<sup>78</sup>. Eat a healthy diet<sup>79</sup> and include physical activity in your life to maintain your ideal body weight and keep yourself healthy<sup>63,64</sup>. If you stay slim, you will not only reduce your risk of OA in old age, you will also reduce your risk of type 2 diabetes, hypertension, cardiovascular disease, and other serious conditions<sup>80</sup>.

A genetic result of "increased risk" or "above average risk" does not mean that you have the disease, or will get the disease, but rather that you have a predisposition to develop the disease. A result of "average risk" indicates that the likelihood of developing the disease is similar to the overall population.

#### ▶ YOUR RESULT ◀

#### **AVERAGE RISK**

Based on your genetic profile you have an average likelihood of developing osteoarthritis.

YOUR RELATED GENES	
Gene Tested	Your Genotype
GDF5-rs143383	T/C
PTGS2-rs4140564	T/T



## HEALTH CONDITIONS VENOUS THROMBOSIS

Venous thrombosis (VT) is the formation of a blood clot in the veins that can potentially lead to thromboembolism (i.e., the blocking of a blood vessel by a portion of the clot that has broken away from it). The individual risk of venous thromboembolism (VTE) is determined by a complex interaction of genetic, circumstantial and environmental factors. Risk factors include immobility, surgery, trauma, cancer, hormonal therapy, pregnancy, advanced age and family history<sup>81,82</sup>. You can avoid the most common lifestyle risk factors for VTE, which are obesity, inactivity, cigarette smoking and long-haul air travel. Discuss other preventive measures with your physician especially if you are planning on having surgery.

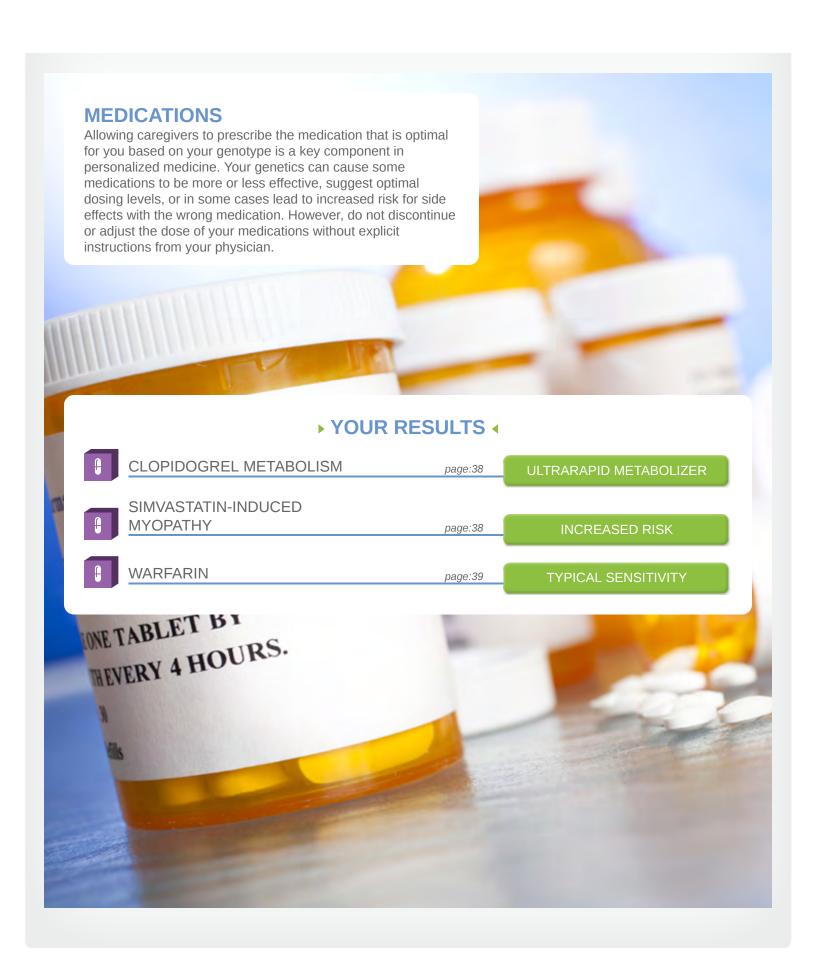
A genetic result of "increased risk" or "above average risk" does not mean that you have the condition but rather that you have a predisposition to developing the condition. A result of "typical risk" indicates that the likelihood of developing the VT is similar to the overall population. Our genetic testing is based on variants shown to be involved in a large proportion of patients with VT<sup>83,84,85</sup>. However, you should be aware that other genetic, environmental and life style factors can have a significant effect on the likelihood of developing VT.

#### ▶ YOUR RESULT ◀

#### TYPICAL RISK

Based on your genetic profile you have a typical likelihood for developing venous thrombosis.

YOUR RELATED GENES		
Gene Tested	Your Genotype	
F2-Prothrombin G20210A	G/G	
F5-Factor V Leiden	G/G	
MTHFR-rs1801133	C/T	





## MEDICATION RESPONSE CLOPIDOGREL METABOLISM

Clopidogrel (Plavix) is a drug used to inhibit the formation of blood clots in patients with coronary artery disease, peripheral vascular disease, and cerebrovascular disease. Our test uses genetic variants that determine how your body will process (i.e., metabolize) the drug and, therefore, will help your physician determine the best drug and dose regimen for you. If your result is "poor metabolizer" or "intermediate metabolizer" then the likelihood of an adverse event after cardiac angioplasty (e.g., stent implantation) is significantly increased<sup>86,87,88</sup> because you will not metabolize the drug very well and it will be less effective. Although our test uses the most common variants known to affect clopidogrel metabolism other variants may play a role in your specific case. Other factors known to influence clopidogrel include obesity so keeping a healthy weight can help you have the best outcome when under a clopidogrel regimen.

#### ▶ YOUR RESULT ◀

#### ULTRARAPID METABOLIZER

Based on your genetic results you are an ultrarapid metabolizer of clopidogrel.

YOUR RELATED GENES		
Tested Your Genotype		
285 G/G		
893 G/G		
8560 C/T		
9504 A/A		
1556 T/T		
7013 C/C		
2267 G/G		



### MEDICATION RESPONSE SIMVASTATIN-INDUCED MYOPATHY

Simvastatin is a member of the statins, a class of cholesterol-lowering drugs whose major potential adverse effect is skeletal muscle toxicity. Approximately 5% to 10% of patients taking statins experience muscle pain<sup>89</sup>. A small portion of patients, (1.5% to 5.0%) may develop more severe symptoms indicating muscle degradation (myopathy)<sup>89</sup>. In rare cases (0.1 to 0.2 cases per 1,000 person-years), severe muscle damage leads to acute, potentially lethal kidney failure<sup>89,90</sup>. A result of "increased risk" should be discussed with your physician to guide the choice of drug and drug dosing. A result of "typical risk" indicates that the likelihood of adverse effects due to simvastatin is similar to the overall population. Our test uses the genetic variant most commonly associated with statin-caused muscle damage. However, rarer variants may also affect the likelihood of statin-related complications. In addition to genetic effects, your risk of simvastatin-induced myopathy varies with your age, gender, body mass index, ethnicity and other clinical factors<sup>91</sup>.

#### ▶ YOUR RESULT ◀

#### **INCREASED RISK**

Based on your genetic profile you have an increased likelihood of developing a myopathy in response to simvastatin.

YOUR RELATED GENES	
otype	



Warfarin is the most frequently used oral anticoagulant worldwide, prescribed for indications such as venous thrombosis, pulmonary embolism, atrial fibrillation and cardiac valve replacement. Warfarin is highly efficacious, but its narrow therapeutic window and large interindividual dosing variability lead to a high incidence of adverse events<sup>92,93</sup>. Customizing initial warfarin dose based on genetic results may decrease your risk of bleeding complications and may reduce the time required to achieve a stable, therapeutic effect<sup>94,95,96</sup>. A result of "Substantially Increased Sensitivity" or "Increased Sensitivity" should be discussed with your physician for decisions around initial drug dosing. A genetic result of "Typical Sensitivity" indicates that probably standard doses of warfarin are appropriate for you. However, consult your physician for appropriate drug dosing and potential drugdrug interactions.

▶ YOUR RESULT ◀

#### TYPICAL SENSITIVITY

Based on your genetic profile you have an average sensitivity to warfarin

YOUR RELATED GENES		
Gene Tested Your Genotype		
CYP2C9-rs1057910	A/A	
CYP2C9-rs1799853	C/C	
CYP2C9-rs9332131	A/A	
VKORC1-rs9923231	G/G	

- 1. Ordovas JM et al. Dietary Fat Intake Determines The Effect Of A Common Polymorphism In The Hepatic Lipase Gene Promoter On High-density Lipoprotein Metabolism: Evidence Of A Strong Dose Effect In This Gene-nutrient Interaction In The Framingham Study. *Circulation* **106**, 2315-21 (2002).
- 2. Junyent M et al. Novel Variants At KCTD10, MVK, And MMAB Genes Interact With Dietary Carbohydrates To Modulate HDL-cholesterol Concentrations In The Genetics Of Lipid Lowering Drugs And Diet Network Study. *The American Journal Of Clinical Nutrition* **90**, 686-94 (2009).
- 3. Sonestedt E et al. Fat And Carbohydrate Intake Modify The Association Between Genetic Variation In The FTO Genotype And Obesity. *The American Journal Of Clinical Nutrition* **90**, 1418-25 (2009).
- 4. Corella D et al. APOA2, Dietary Fat, And Body Mass Index: Replication Of A Gene-diet Interaction In 3 Independent Populations. *Archives Of Internal Medicine* **169**, 1897-906 (2009).
- 5. Warodomwichit D et al. ADIPOQ Polymorphisms, Monounsaturated Fatty Acids, And Obesity Risk: The GOLDN Study. *Obesity (Silver Spring, Md.)* **17**, 510-7 (2009).
- 6. Memisoglu A et al. Interaction Between A Peroxisome Proliferator-activated Receptor Gamma Gene Polymorphism And Dietary Fat Intake In Relation To Body Mass. *Human Molecular Genetics* **12**, 2923-9 (2003).
- 7. Kathiresan S et al. Common Variants At 30 Loci Contribute To Polygenic Dyslipidemia. *Nature Genetics* **41**, 56-65 (2009).
- 8. Dupuis J et al. New Genetic Loci Implicated In Fasting Glucose Homeostasis And Their Impact On Type 2 Diabetes Risk. *Nature Genetics* **42**, 105-16 (2010).
- 9. Glaser C et al. Genetic Variation In Polyunsaturated Fatty Acid Metabolism And Its Potential Relevance For Human Development And Health. *Maternal & Child Nutrition* **7 Suppl 2**, 27-40 (2011).
- 10. Simopoulos AP. The Importance Of The Omega-6/omega-3 Fatty Acid Ratio In Cardiovascular Disease And Other Chronic Diseases. *Experimental Biology And Medicine (Maywood, N.J.)* **233**, 674-88 (2008).
- 11. Tanaka T et al. Genome-wide Association Study Of Plasma Polyunsaturated Fatty Acids In The InCHIANTI Study. *PLoS Genetics* **5**, e1000338 (2009).
- 12. Lemaitre RN et al. Genetic Loci Associated With Plasma Phospholipid N-3 Fatty Acids: A Meta-analysis Of Genome-wide Association Studies From The CHARGE Consortium. *PLoS Genetics* **7**, e1002193 (2011).
- 13. Epstein LH et al. Food Reinforcement, The Dopamine D2 Receptor Genotype, And Energy Intake In Obese And Nonobese Humans. *Behavioral Neuroscience* **121**, 877-86 (2007).
- 14. Doehring A et al. Genetic Diagnostics Of Functional Variants Of The Human Dopamine D2 Receptor Gene. *Psychiatric Genetics* **19**, 259-68 (2009).
- 15. Eny KM et al. Dopamine D2 Receptor Genotype (C957T) And Habitual Consumption Of Sugars In A Free-living Population Of Men And Women. *Journal Of Nutrigenetics And Nutrigenomics* **2**, 235-42 (2009).
- 16. de Krom M et al. Common Genetic Variations In CCK, Leptin, And Leptin Receptor Genes Are Associated With Specific Human Eating Patterns. *Diabetes* **56**, 276-80 (2007).
- 17. Frayling TM et al. A Common Variant In The FTO Gene Is Associated With Body Mass Index And Predisposes To Childhood And Adult Obesity. *Science (New York, N.Y.)* **316**, 889-94 (2007).

- 18. Wardle J et al. Obesity Associated Genetic Variation In FTO Is Associated With Diminished Satiety. *The Journal Of Clinical Endocrinology And Metabolism* **93**, 3640-3 (2008).
- 19. den Hoed M et al. Postprandial Responses In Hunger And Satiety Are Associated With The Rs9939609 Single Nucleotide Polymorphism In FTO. *The American Journal Of Clinical Nutrition* **90**, 1426-32 (2009).
- 20. Dotson CD et al. Variation In The Gene TAS2R38 Is Associated With The Eating Behavior Disinhibition In Old Order Amish Women. *Appetite* **54**, 93-9 (2010).
- 21. Epstein LH et al. Food Reinforcement. Appetite 46, 22-5 (2006).
- 22. Eny KM et al. Genetic Variant In The Glucose Transporter Type 2 Is Associated With Higher Intakes Of Sugars In Two Distinct Populations. *Physiological Genomics* **33**, 355-60 (2008).
- 23. Powers HJ. Riboflavin (vitamin B-2) And Health. The American Journal Of Clinical Nutrition 77, 1352-60 (2003).
- 24. McNulty H et al. Homocysteine, B-vitamins And CVD. The Proceedings Of The Nutrition Society 67, 232-7 (2008).
- 25. Hustad S et al. The Methylenetetrahydrofolate Reductase 677C-->T Polymorphism As A Modulator Of A B Vitamin Network With Major Effects On Homocysteine Metabolism. *American Journal Of Human Genetics* **80**, 846-55 (2007).
- 26. Yazdanpanah N et al. Low Dietary Riboflavin But Not Folate Predicts Increased Fracture Risk In Postmenopausal Women Homozygous For The MTHFR 677 T Allele. *Journal Of Bone And Mineral Research : The Official Journal Of The American Society For Bone And Mineral Research* 23, 86-94 (2008).
- 27. Horigan G et al. Riboflavin Lowers Blood Pressure In Cardiovascular Disease Patients Homozygous For The 677C-->T Polymorphism In MTHFR. *Journal Of Hypertension* **28**, 478-86 (2010).
- 28. McNulty H et al. Riboflavin Lowers Homocysteine In Individuals Homozygous For The MTHFR 677C->T Polymorphism. *Circulation* **113**, 74-80 (2006).
- 29. Tanaka T et al. Genome-wide Association Study Of Vitamin B6, Vitamin B12, Folate, And Homocysteine Blood Concentrations. *American Journal Of Human Genetics* **84**, 477-82 (2009).
- 30. Hazra A et al. Genome-wide Significant Predictors Of Metabolites In The One-carbon Metabolism Pathway. *Human Molecular Genetics* **18**, 4677-87 (2009).
- 31. Zittoun J et al. Modern Clinical Testing Strategies In Cobalamin And Folate Deficiency. *Seminars In Hematology* **36**, 35-46 (1999).
- 32. Hazra A et al. Common Variants Of FUT2 Are Associated With Plasma Vitamin B12 Levels. *Nature Genetics* **40**, 1160-2 (2008).
- 33. Bailey LB et al. Folate Metabolism And Requirements. The Journal Of Nutrition 129, 779-82 (1999).
- 34. Yang QH et al. Prevalence And Effects Of Gene-gene And Gene-nutrient Interactions On Serum Folate And Serum Total Homocysteine Concentrations In The United States: Findings From The Third National Health And Nutrition Examination Survey DNA Bank. *The American Journal Of Clinical Nutrition* **88**, 232-46 (2008).
- 35. Voutilainen S et al. Low Dietary Folate Intake Is Associated With An Excess Incidence Of Acute Coronary Events: The Kuopio Ischemic Heart Disease Risk Factor Study. *Circulation* **103**, 2674-80 (2001).
- 36. Gerster H. Vitamin A--functions, Dietary Requirements And Safety In Humans. *International Journal For Vitamin And Nutrition Research*. *Internationale Zeitschrift Fur Vitamin- Und Ernahrungsforschung*. *Journal International De Vitaminologie Et De Nutrition* **67**, 71-90 (1997).
- 37. Semba RD. The Role Of Vitamin A And Related Retinoids In Immune Function. *Nutrition Reviews* 56, S38-48 (1998).
- 38. Dawson MI. The Importance Of Vitamin A In Nutrition. Current Pharmaceutical Design 6, 311-25 (2000).

- 39. Ross AC et al. The Function Of Vitamin A In Cellular Growth And Differentiation, And Its Roles During Pregnancy And Lactation. *Advances In Experimental Medicine And Biology* **352**, 187-200 (1994).
- 40. Leung WC et al. Two Common Single Nucleotide Polymorphisms In The Gene Encoding Beta-carotene 15,15'-monoxygenase Alter Beta-carotene Metabolism In Female Volunteers. *FASEB Journal : Official Publication Of The Federation Of American Societies For Experimental Biology* **23**, 1041-53 (2009).
- 41. Witschi JC et al. Preformed Vitamin A, Carotene, And Total Vitamin A Activity In Usual Adult Diets. *Journal Of The American Dietetic Association* **57**, 13-6 (1970).
- 42. Solomons NW et al. Plant Sources Of Provitamin A And Human Nutriture. Nutriture Reviews 51, 199-204 (1993).
- 43. Cahill LE et al. Vitamin C Transporter Gene Polymorphisms, Dietary Vitamin C And Serum Ascorbic Acid. *Journal Of Nutrigenetics And Nutrigenomics* **2**, 292-301 (2009).
- 44. Timpson NJ et al. Genetic Variation At The SLC23A1 Locus Is Associated With Circulating Concentrations Of L-ascorbic Acid (vitamin C): Evidence From 5 Independent Studies With >15,000 Participants. *The American Journal Of Clinical Nutrition* **92**, 375-82 (2010).
- 45. Holick MF. Vitamin D And Bone Health. The Journal Of Nutrition 126, 1159S-64S (1996).
- 46. Ahn J et al. Vitamin D-related Genes, Serum Vitamin D Concentrations And Prostate Cancer Risk. *Carcinogenesis* **30**, 769-76 (2009).
- 47. Wang TJ et al. Common Genetic Determinants Of Vitamin D Insufficiency: A Genome-wide Association Study. *Lancet (London, England)* **376**, 180-8 (2010).
- 48. Beharka A et al. Vitamin E Status And Immune Function. Methods In Enzymology 282, 247-63 (1997).
- 49. Morrissey PA et al. Optimal Nutrition: Vitamin E. The Proceedings Of The Nutrition Society 58, 459-68 (1999).
- 50. Ferrucci L et al. Common Variation In The Beta-carotene 15,15'-monooxygenase 1 Gene Affects Circulating Levels Of Carotenoids: A Genome-wide Association Study. *American Journal Of Human Genetics* **84**, 123-33 (2009).
- 51. Bartali B et al. Serum Micronutrient Concentrations And Decline In Physical Function Among Older Persons. *JAMA* **299**, 308-15 (2008).
- 52. Maras JE et al. Intake Of Alpha-tocopherol Is Limited Among US Adults. *Journal Of The American Dietetic Association* **104**, 567-75 (2004).
- 53. Garenc C et al. Evidence Of LPL Gene-exercise Interaction For Body Fat And LPL Activity: The HERITAGE Family Study. *Journal Of Applied Physiology (Bethesda, Md. : 1985)* **91**, 1334-40 (2001).
- 54. Teran-Garcia M et al. Hepatic Lipase Gene Variant -514C>T Is Associated With Lipoprotein And Insulin Sensitivity Response To Regular Exercise: The HERITAGE Family Study. *Diabetes* **54**, 2251-5 (2005).
- 55. Hautala AJ et al. Peroxisome Proliferator-activated Receptor-delta Polymorphisms Are Associated With Physical Performance And Plasma Lipids: The HERITAGE Family Study. *American Journal Of Physiology. Heart And Circulatory Physiology* **292**, H2498-505 (2007).
- 56. O'Rahilly S et al. Human Obesity: A Heritable Neurobehavioral Disorder That Is Highly Sensitive To Environmental Conditions. *Diabetes* **57**, 2905-10 (2008).
- 57. Tao YX. The Melanocortin-4 Receptor: Physiology, Pharmacology, And Pathophysiology. *Endocrine Reviews* **31**, 506-43 (2010).
- 58. Fawcett KA et al. The Genetics Of Obesity: FTO Leads The Way. Trends In Genetics: TIG 26, 266-74 (2010).
- 59. Loos RJ et al. Common Variants Near MC4R Are Associated With Fat Mass, Weight And Risk Of Obesity. *Nature Genetics* **40**, 768-75 (2008).

- 60. Willer CJ et al. Six New Loci Associated With Body Mass Index Highlight A Neuronal Influence On Body Weight Regulation. *Nature Genetics* **41**, 25-34 (2009).
- 61. Meyre D et al. Genome-wide Association Study For Early-onset And Morbid Adult Obesity Identifies Three New Risk Loci In European Populations. *Nature Genetics* **41**, 157-9 (2009).
- 62. Cho YS et al. A Large-scale Genome-wide Association Study Of Asian Populations Uncovers Genetic Factors Influencing Eight Quantitative Traits. *Nature Genetics* **41**, 527-34 (2009).
- 63. Leskinen T et al. Leisure-time Physical Activity And High-risk Fat: A Longitudinal Population-based Twin Study. *International Journal Of Obesity (2005)* **33**, 1211-8 (2009).
- 64. Swinburn BA et al. Diet, Nutrition And The Prevention Of Excess Weight Gain And Obesity. *Public Health Nutrition* **7**, 123-46 (2004).
- 65. Goyenechea E et al. The 11391 G/A Polymorphism Of The Adiponectin Gene Promoter Is Associated With Metabolic Syndrome Traits And The Outcome Of An Energy-restricted Diet In Obese Subjects. *Hormone And Metabolic Research = Hormon- Und Stoffwechselforschung = Hormones Et Metabolisme* **41**, 55-61 (2009).
- 66. Loos RJ et al. Polymorphisms In The Leptin And Leptin Receptor Genes In Relation To Resting Metabolic Rate And Respiratory Quotient In The Québec Family Study. *International Journal Of Obesity (2005)* **30**, 183-90 (2006).
- 67. Puglisi MJ et al. Modulation Of C-reactive Protein, Tumor Necrosis Factor-alpha, And Adiponectin By Diet, Exercise, And Weight Loss. *The Journal Of Nutrition* **138**, 2293-6 (2008).
- 68. Qi Y et al. Adiponectin Acts In The Brain To Decrease Body Weight. Nature Medicine 10, 524-9 (2004).
- 69. Heid IM et al. Clear Detection Of ADIPOQ Locus As The Major Gene For Plasma Adiponectin: Results Of Genome-wide Association Analyses Including 4659 European Individuals. *Atherosclerosis* **208**, 412-20 (2010).
- 70. Natarajan P et al. High-density Lipoprotein And Coronary Heart Disease: Current And Future Therapies. *Journal Of The American College Of Cardiology* **55**, 1283-99 (2010).
- 71. Alwaili K et al. High-density Lipoproteins And Cardiovascular Disease: 2010 Update. *Expert Review Of Cardiovascular Therapy* **8**, 413-23 (2010).
- 72. American Diabetes Association. Standards Of Medical Care In Diabetes--2009. *Diabetes Care* **32 Suppl 1**, S13-61 (2009).
- 73. Davis N et al. Role Of Obesity And Lifestyle Interventions In The Prevention And Management Of Type 2 Diabetes. *Minerva Medica* **100**, 221-8 (2009).
- 74. Lindström J et al. Sustained Reduction In The Incidence Of Type 2 Diabetes By Lifestyle Intervention: Follow-up Of The Finnish Diabetes Prevention Study. *Lancet (London, England)* **368**, 1673-9 (2006).
- 75. Li G et al. The Long-term Effect Of Lifestyle Interventions To Prevent Diabetes In The China Da Qing Diabetes Prevention Study: A 20-year Follow-up Study. *Lancet (London, England)* **371**, 1783-9 (2008).
- 76. Chitnavis J et al. Genetic Influences In End-stage Osteoarthritis. Sibling Risks Of Hip And Knee Replacement For Idiopathic Osteoarthritis. *The Journal Of Bone And Joint Surgery. British Volume* **79**, 660-4 (1997).
- 77. Ingvarsson T et al. The Inheritance Of Hip Osteoarthritis In Iceland. Arthritis And Rheumatism 43, 2785-92 (2000).
- 78. Bliddal H et al. The Treatment And Prevention Of Knee Osteoarthritis: A Tool For Clinical Decision-making. *Expert Opinion On Pharmacotherapy* **10**, 1793-804 (2009).
- 79. Weisburger JH. Lifestyle, Health And Disease Prevention: The Underlying Mechanisms. *European Journal Of Cancer Prevention: The Official Journal Of The European Cancer Prevention Organisation (ECP)* **11 Suppl 2**, S1-7 (2002).
- 80. Dixon JB. The Effect Of Obesity On Health Outcomes. Molecular And Cellular Endocrinology 316, 104-8 (2010).

- 81. Varga EA et al. Management Of Inherited Thrombophilia: Guide For Genetics Professionals. *Clinical Genetics* **81**, 7-17 (2012).
- 82. White RH et al. Effects Of Race And Ethnicity On The Incidence Of Venous Thromboembolism. *Thrombosis Research* **123 Suppl 4**, S11-7 (2009).
- 83. Rosendaal FR. Venous Thrombosis: The Role Of Genes, Environment, And Behavior. *Hematology / The Education Program Of The American Society Of Hematology. American Society Of Hematology. Education Program*, 1-12 (2005).
- 84. Grody WW et al. American College Of Medical Genetics Consensus Statement On Factor V Leiden Mutation Testing. *Genetics In Medicine : Official Journal Of The American College Of Medical Genetics* **3**, 139-48 (2001).
- 85. Jang MJ et al. The 677C>T Mutation Of The MTHFR Gene Increases The Risk Of Venous Thromboembolism In Koreans And A Meta-analysis From Asian Population. *Clinical And Applied Thrombosis/hemostasis: Official Journal Of The International Academy Of Clinical And Applied Thrombosis/Hemostasis* **19**, 309-14 (2013).
- 86. Mega JL et al. Reduced-function CYP2C19 Genotype And Risk Of Adverse Clinical Outcomes Among Patients Treated With Clopidogrel Predominantly For PCI: A Meta-analysis. *JAMA* **304**, 1821-30 (2010).
- 87. Holmes MV et al. CYP2C19 Genotype, Clopidogrel Metabolism, Platelet Function, And Cardiovascular Events: A Systematic Review And Meta-analysis. *JAMA* **306**, 2704-14 (2011).
- 88. Zabalza M et al. Meta-analyses Of The Association Between Cytochrome CYP2C19 Loss- And Gain-of-function Polymorphisms And Cardiovascular Outcomes In Patients With Coronary Artery Disease Treated With Clopidogrel. *Heart (British Cardiac Society)* **98**, 100-8 (2012).
- 89. Joy TR et al. Narrative Review: Statin-related Myopathy. Annals Of Internal Medicine 150, 858-68 (2009).
- 90. Thompson PD et al. Statin-associated Myopathy. JAMA 289, 1681-90 (2003).
- 91. Wilke RA et al. The Clinical Pharmacogenomics Implementation Consortium: CPIC Guideline For SLCO1B1 And Simvastatin-induced Myopathy. *Clinical Pharmacology And Therapeutics* **92**, 112-7 (2012).
- 92. Budnitz DS et al. National Surveillance Of Emergency Department Visits For Outpatient Adverse Drug Events. *JAMA* **296**, 1858-66 (2006).
- 93. Wysowski DK et al. Bleeding Complications With Warfarin Use: A Prevalent Adverse Effect Resulting In Regulatory Action. *Archives Of Internal Medicine* **167**, 1414-9 (2007).
- 94. Gage BF et al. Pharmacogenetics Of Warfarin: Regulatory, Scientific, And Clinical Issues. *Journal Of Thrombosis And Thrombolysis* **25**, 45-51 (2008).
- 95. Sanderson S et al. CYP2C9 Gene Variants, Drug Dose, And Bleeding Risk In Warfarin-treated Patients: A HuGEnet Systematic Review And Meta-analysis. *Genetics In Medicine : Official Journal Of The American College Of Medical Genetics* **7**, 97-104 (2005).
- 96. Limdi NA et al. Influence Of CYP2C9 And VKORC1 1173C/T Genotype On The Risk Of Hemorrhagic Complications In African-American And European-American Patients On Warfarin. *Clinical Pharmacology And Therapeutics* **83**, 312-21 (2008).