



PATIENT

PFirst PLast
DOB: 01/01/54

ORDERING PROVIDER

Example Organization

LABORATORY INFORMATION

Lab ID: N8C9841
Collection Date: 01/11/10
Test Date: 01/21/10
Report Date: 01/22/10

GENE MARKER	NORMAL	TEST RESULT	RISK ALLELE	ASSOCIATION
FTO	T/T	A/T	●	Appetite regulation and craving frequency
MC4R	T/T	C/T	●	Satiety and metabolism regulation
FABP2	G/G	A/G	●	Dietary fat sources and fat utilization
ADRB2	C/C	C/G	●	Carbohydrate digestion and physical activity
SH2B1	A/A	A/G	●	Regulation of leptin and insulin

RISK ALLELE KEY: ○ No Risk ● Risk Allele Heterozygous ● Risk Allele Homozygous

COMMENTS: KEY ASPECTS FOR CONSIDERATION

FTO	A/T	Weight gain likely around midsection and a greater increase in body mass. Increased risk of developing obesity in adulthood. Cravings for calorie-dense and high-fat foods. Reduced feelings of fullness after meals.
MC4R	C/T	Reduced sense of fullness after meals. Frequently craving calorie dense and high fat foods. Increased perception of hunger leading to weight gain. Excessive snacking behavior. Increased risk for weight gain for sedentary individuals.
FABP2	A/G	Increased ability for the body to produce and store fat. Higher fasting plasma glucose and lipid concentrations. Greater possible risk of developing cardiovascular disease and diabetes. Resistance to weight loss by traditional aerobic exercise from compromised resting metabolic rate.
ADRB2	C/G	Weight gain when consuming a high carbohydrate diet. Larger fat cells and higher amounts of fat mass. Longer timeframe to achieve weight loss results due to a lower level of fat burn after exercise. Increased insulin levels and higher BMI. Greater risk of developing obesity.
SH2B1	A/G	An increase in hunger due to leptin resistance. Overeating calorie dense food groups. Weight gain from diets high in fats, particularly saturated fats. Eating larger than normal portions likely. Increased chance for insulin and leptin resistance.

DIET RECOMMENDATIONS

Eat five or more small meals a day which will help minimize hunger spikes, reduce inadvertent overeating, support an increased metabolism, and regulate insulin demand. Eat a higher amount of calories from protein which digests slowly, and a lower amount of calories from fat, thus encouraging use of existing fat stores. Substitute saturated fat with polyunsaturated and monounsaturated fat choices such as olive oil, almonds, cashews and avocados. Excess fat in the liver leads to high levels of insulin and glucose in the bloodstream which can lead to weight gain, insulin resistance, metabolic syndrome, and eventually diabetes. Eat foods that are low in calorie density like vegetables and fruits. Green leafy salads with a light dressing are a good choice, such that if portions are too large, the excess calories are from lower calorie-dense foods. Fatty foods have a higher calorie density and should be minimized. Choose complex carbohydrates like whole grains, low starch vegetables, and fruits with skin to increase fiber. This helps to control food cravings, blood sugar levels, leptin levels, insulin levels, and fat in the bloodstream. Ideally eat carbohydrates with a high fiber content that have a glycemic index of 55 or less.

Follow this link to a more detailed meal plan for your genotype: <https://ref.kashilab.com/fp-sh2b1>



WEIGHT MANAGEMENT PANEL

Genetic Analysis Report

EXERCISE RECOMMENDATIONS

Regular exercise is important for how your body uses carbohydrates. **You can benefit from daily exercise at a lower intensity (50 to 70% of maximum heart rate, or HR Max%), such as brisk walking.** Starting a new exercise program may take time. Start at 20 minutes of exercise daily and work your way up to 60 minutes daily most days of the week. The more exercise you engage in the better results. As you improve your eating habits and increase your physical activity, know that results may take a little longer to achieve because of your reduced response to physical activity. High-impact aerobic exercise programs may not provide benefit for sustained weight loss with your variant alleles, however resistance training may improve fat-muscle ratios.

Please remember to buffer some time around your workout for warming up and cooling down with stretches to prevent injury and maximize exercise benefits. Consult your doctor before starting any new exercise regimen.

Gene	Intensity	HR Max% / Exertion	Duration / Frequency	Examples
MC4R	High 	80-90% Feels like: out of breath with muscular fatigue and heavy sweating	Duration: short bursts for seconds to minutes, depending on the activity Frequency: depends on level of fitness and time needed for rest and recovery	sprinting, running, bicycle riding on hilly terrain, climbing stairs, jump roping, cross-country skiing, snowshoeing on an incline, racquet sports
FTO SH2B1	Moderate 	70-80% Feels like: slightly out of breath with some muscle fatigue and sweating	Duration: 40-60 minutes Frequency: 5- 7 days a week	jogging, brisk walking, bicycle riding on level ground, hiking, water aerobics, swimming, snowshoeing on level ground
ADRB2 FABP2	Low 	60-70% Feels like: easy breathing and effort with light sweating	Duration: 40-60 minutes Frequency: daily; especially before meals and the day after high, maximum and HIIT exercises	walking, yoga, kayaking, casual bicycle riding, casual swimming, rollerblading, roller skating, golf, bowling, low-impact yoga

HELPFUL DIET RECOMMENDATIONS AND TIPS

- ❖ Reduce fructose and added sugars. Become an expert in hidden sugars in foods; read labels to see how much sugar is in packaged food.
- ❖ Green Tea – find the flavor of green tea that you like and drink 3-5 cups a day. Green tea has been shown to influence the regulation of weight and can help with mood.
- ❖ Flavonoids are a nutrient group known for antioxidant and anti-inflammatory benefits. Eat 8 helpings a day of flavonoids e.g. blueberries, onions, apples, kale, nuts, seeds.
- ❖ Curcumin (turmeric) can improve leptin resistance, try making curries or taking a daily supplement.
- ❖ The right fats: Avoid trans fats, choose polyunsaturated fats which may help insulin secretion and support healthy glucose levels.

LIFESTYLE RECOMMENDATIONS

- ❖ Mindful eating. Chew food slowly, mixing saliva with the food to help prepare it for digestion. The more chewed and wet the food is by the time you swallow, the easier it is digested and absorbed through the intestine wall. Chewing also helps stimulate release of enzymes that break down free fatty acids.
- ❖ Stress Management. Research shows a distinct and strong relationship between obesity and levels of the stress hormone cortisol. Managing stress is a critical part of weight management.
- ❖ Meditation has been shown to modulate the stress hormones and neurotransmitters in the brain. With balanced levels of stress chemicals there is less likely to be binge or emotional comforting eating. Meditation can last from 5-20 minutes as many times a day as you need to take a big deep breath and relax.
- ❖ Sleep. Humans need sleep for rebuilding and repair of normal daily damage as well as to cement learning. Sleep also regulates hormones such as leptin. At least 7-8 hours of sleep a night will reduce leptin levels and therefore reduce night time eating. The risk of obesity significantly increases at less than 6 hours sleep per night.



SCIENTIFIC DETAILS

❖FTO

FTO, also known as the human fat-mass and obesity-associated gene, is found on chromosome 16. Discovered in 2007 it is one of the strongest genetic risk factors for obesity. Frayling et al, found a significant association between weight, Body Mass Index and the FTO risk allele in over 38,000 participants. It was determined that adults who have two copies of the risk allele weighed an average of 6.6 pounds more and had a 1.7-fold increased risk of developing obesity when compared with those not carrying a risk allele. The association has been confirmed in multiple populations of differing ethnicities. FTO carriers appear to have a higher amount of FTO expression in the brain and body which has been shown to result in an imbalance that increases the risk of becoming overweight. This risk may result in a preference for high-calorie foods or decreased feelings of satiety. It has been recently shown that individuals with this variant do respond well to dietary, physical activity, or drug based weight loss interventions.

❖MC4R

Melanocortin 4 Receptor refers to a gene found on chromosome 18 and the receptor that this gene creates. The MC4R is located in the hypothalamus, a region of the brain responsible for appetite (among many other functions). Mutations in and near the MC4R gene account for up to 6% of severe early-onset obesity cases, suggesting an important role for the central melanocortin system in the maintenance of normal body weight. The MC4R risk allele has been linked to obesity, diminished insulin response in the brain, altered eating behaviors, and is believed to impair MC4R function. There is a tendency for increased appetite and a preference for calorie-dense foods. However, studies in children and teens show that even though carriers of the high risk allele near MC4R are more prone to weight gain, homozygous variant carriers may be even more responsive to lifestyle modifications than non-carriers or heterozygotes.

❖FABP2

Fatty Acid Binding Protein 2 is the intracellular protein product of a gene found on chromosome 4. The FABP2 protein helps in fat transportation and absorption, specifically in mobilizing fat from the small intestine into circulation for downstream deposit and storage in fat cells and the liver. FABP2 variants result in increased absorption and transportation of fats in the body. This variant has also been linked to type 2 diabetes mellitus risk in certain ethnic populations. Controlling the amount and types of fat in your diet, particularly saturated fat, is important for weight management in individuals with this variant allele.

❖ADRB2

The Beta-2 adrenergic receptor is a gene found on chromosome 5 that codes for a receptor located on cells of various tissues including liver and fat cells. Research suggests that mutations in the ADRB2 gene may be important risk factors for the development of obesity and may affect how an individual's weight changes in response to exercise or a carbohydrate rich diet. Women in particular who have this risk allele could benefit from lower carbohydrate intake. Some studies suggest that the ADRB2 variant may lower the rate of fat metabolism during the workout recovery phase although this is currently not conclusive.

❖SH2B1

The Sarcoma homology 2B adaptor protein 1 refers to a gene found on chromosome 16 and the protein that the gene produces. This protein is critical in maintaining the balance of insulin and leptin in the body. Insulin helps control blood sugar (glucose) and is strongly influenced by dietary fat and carbohydrate. Insulin is well known as a factor in diabetes. The hormone leptin is important in regulating appetite and the *feeling* of hunger through its impact on ghrelin, the hormone associated with initiating hunger. The body can become leptin resistant in the same way it can become insulin resistant, reducing leptin's ability to impact ghrelin production. The SH2B1 risk allele results in an altered form of the adapter protein that impairs insulin and leptin signaling resulting in increased appetite and associated weight gain. Controlling intake of fat and carbohydrate is important along with regular exercise to improve leptin signaling.

This test detects only specific targeted genetic variations and there is a possibility that other genetic variants not detected by this test may be present. The DNA variants tested for in this report have been scientifically determined to be possible risk factors for the reported condition. The content of this report is provided for informational purposes only, not as a diagnostic tool. The report does not supersede the judgment of a qualified medical provider. This test is not a substitute for a comprehensive consideration of all factors that influence the maintenance of a healthy body. Genetic risk factors are not guarantees that you will develop a condition, and in many cases, the presence of a particular DNA variant may only play a minor role in your risk for disease, compared with environmental and lifestyle factors. This test is not FDA approved. The test's performance characteristics have been established and maintained by Kashi Clinical Laboratories under CLIA and CAP compliance.

Reported and Reviewed By:

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MORE ON GENETIC TESTING



Each body has its own genetic code called DNA. The code has an alphabet with only four letters: A, G, T and C, which are the four nucleotide bases which make up the DNA: Adenine (A), Guanine (G), Thymine (T) and Cytosine (C). Unlike a book or computer screen, DNA isn't flat; it is a curved ladder shape called a double helix. The letters of the DNA alphabet make up the rungs, while special sugars and other atoms make up the handrail. A and T are usually paired together to make a rung, and C and G are usually paired together to make a rung.

Every person has two copies of each double helix, one which comes from the father and one which comes from the mother. Therefore, each person has two copies of each rung of the ladder. This can give three possible combinations or variants, for example: AA, TT, or AT. For many genes the actual variation doesn't particularly matter. However, as researchers learn about what each gene codes for, there is now more and more information available about which gene pair variants do make a difference to health.

For example: FTO is a gene that controls appetite and cravings. Everybody inherits two versions (alleles) of the FTO gene, one from each parent. Therefore, it is possible to have two alleles coding for the more active variant (called TT), two alleles resulting in the less active variant (called AA) or one of each (called AT). Each combination is called a genotype. The properly functioning genotype is TT.

For someone with the less active "AA" version of the gene, it may mean that the gene may not properly process the information needed to create a well-functioning FTO protein, thus this inefficient protein may lead to excess body weight gain. Research on the FTO gene is still in the very early stages, but some studies suggest that people with the AA version of FTO weigh an average of 6.6 pounds more and have an increased risk of obesity compared to people with the TT version. Individuals with the combination gene (AT) weigh on average 2.5 pounds more compared with people with the TT version.

These genetic variants that are inherited from your parents are known as Single Nucleotide Polymorphisms, or SNPs (pronounced "snips"). SNPs can act as biological markers, helping scientists locate gene alleles that are associated with disease. Some of these genetic differences, have proven to be very important in the study of human health.

Researchers have found SNPs that may help predict an individual's response to certain drugs, susceptibility to environmental factors such as toxins, and the risk of developing particular diseases. SNPs can also be used to track the inheritance of disease-related genes within families. Future studies will work to identify SNPs associated with complex diseases such as heart disease, diabetes, and cancer.

A person's genotype is the special allele combination that is in his or her genetic make-up. A person's phenotype refers to all the final observable physical features. These features are the result of the interaction between the person's genotype and the environment (including nutrition, exercise, stress) while he or she was growing up or developing. Weight is an example of a phenotype.

❖Glossary:

Genotype — the genetic make-up of a particular gene

Allele — any of the alternative forms of a gene that may occur at a given locus

Risk Allele — a significant gene variant that can have an influence on health

Phenotype — the observable properties of an organism that are produced by the interaction of the genotype and the environment

Receptor — a structure on the surface of a cell (or inside a cell) that selectively receives and binds a specific substance

Mutation — a permanent change in the nucleotide sequence of a gene

