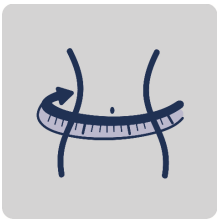
ObesChip

Code analysis:

Reference:

Date:

LABORATORIO DE ANÁLISIS ECHEVARNE



ObesChip

INTRODUCTION TO THE TEST

Weight is the result of many factors, including: the environment, family history, genetics, how metabolism converts food and oxygen into energy, etc. Being overweight or obese you are exposed to a higher risk of health problems.

The main cause of obesity is the imbalance in the energy balance, which implies a higher calorie intake versus energy expenditure that your body makes during the day.

This imbalance is corrected with a healthy lifestyle and a better understanding of the genetics of each.

The test ObesChip identifies genetic characteristics about obesity and may provide valuable information to the health professional to take the most appropriate measures for your particular situation: preventive and / or therapeutic.

ObesChip is a useful tool for the clinician to establish dietary guidelines and recommendations for lifestyle with greater probability of success in the treatment or prevention of obesity.

The "ObesChip" nutrigenomic test is performed from the DNA of a sample of saliva or blood and analyzes 30 SNPs in 12 genes associated with predisposition to overweight and obesity.

The information provided by this test is provided in several sections:

1. Genetic predisposition to obesity (based on GWAS studies)

2. Energy balance for the absorption, transport, storage and metabolism of fatty acids studies (based on studies of candidate genes)

3. The regulation of appetite, satiety and emotional intake (based on candidate gene studies)

4. Weight loss in response to exercise (based on candidate gene studies)

INTERPRETATION:

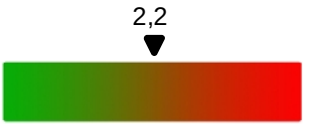
You should be aware that this test reflects Information from present state of scientific knowledge (especially in the area of genetics) and they, as part of the basic principle of biology, evolve. Therefore, you should not stop paying attention to new scientific and medical advances.

This test is based on two types of studies:

a) Association studies of complete genomes (GWAS, paragraph 1) (more info).

The risk is determined quantitatively based on the knowledge of GWAS studies. These studies are performed on the basis of case studies / control over hundreds of thousands of people for a very high probability value.

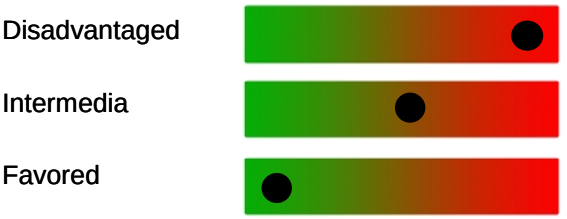
Example: The value 2.2 means it has more than twice the statistical probability of being overweight or obese than the rest of the population.



b) Studies of candidate genes (in paragraph 2, 3 and 4) (more info).

The test result in these sections is determined qualitatively. Successful candidates are widely characterized genes in both humans and many other animal species. It has been demonstrated that these genes contribute decisively in overweight and obesity character.

The test identifies three categories based on how favorable genetics is about the character:



It is essential that this test will be given by a health professional to provide you with the information needed to improve your health. You should not interpret the information in this test without the clinician considers it.

Summary of results

1. Genetic predisposition to obesity

Risk calculation based on data from GWAS association studies. **8 SNPs**

2,2

FTO and MC4R genes

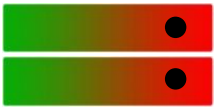
2. Energy Balance

Genes related to the absorption, transport, storage and metabolism of fatty acids. **12 SNPs**

2.1 Absorption

Total Fatty Acids and FABP2 gene

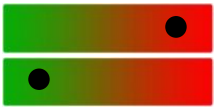
Polyunsaturated fatty acids and FADS gene



2.2 Transportation: genes related to high levels of blood triglycerides

APOA5 gene

LPL gene



2.3 Storage of fatty acids

Diet and PPAR genes

2.4 Metabolism

Gen ADIPOQ synthesizes adiponectin hormone

3. INPUT: appetite, satiety and binge eating

Genes involved in the regulation of appetite, satiety and emotional eating. **7 SNPs**

3.1 Regulation of hypothalamic appetite control

Genes FTO and MC4R

3.2 Emotional intake

Genes DRD2 and OPRM1

4. OUTPUT: Weight loss in response to exercise

Genes involved in the metabolism of fat in response to exercise. **3 SNPs**

Regulation of lipolysis and thermogenesis

ADRB2 gene and ADRB3

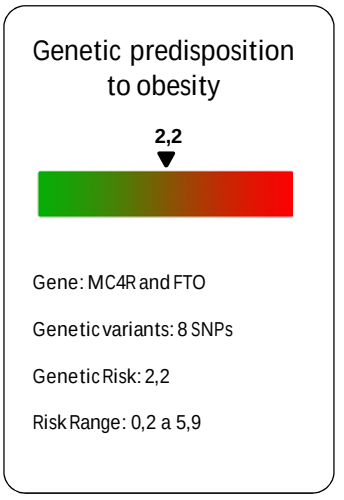
1. GENETIC PREDISPOSITION TO OBESITY

Obesity and FTO and MC4R genes

Numerous scientific studies of genome wide association (GWAS) have identified several genes responsible for the risk of overweight and obesity.

Among them, the genes MC4R (melanocortin 4 receptor) and FTO (Fat mass and Obesity) are known to be the major genetic factors predisposing to obesity and overweight. They are involved in the regulation of body weight and energy intake.

In these genes, they have been discovered certain genetic variants associated with significant risk of overweight and obesity. Some genetic variants reduce or cancel out the role of genes. Although these mutations are the cause of most of the symptoms of obesity heritable, its frequency is relatively low in the general population (approximately 6-8% of the severe symptoms).



Several SNPs (Single Nucleotide Polymorphisms) of FTO and MC4R genes have been shown to be associated with overweight and obesity. Analysis of genetic data from more than 100.000 European adults concluded that certain alleles of these genes are correlated with increased body mass index and risk of overweight.
These genetic variants and the results of sample analysis are summarized in the following table:

Locus	Chrom.	Gene variant	Normal Genotype	Patient Genotype	Genotype frequency	Relative Risk
FTO	16	rs1421085	TT	CC	19,5%	1,44
FTO	16	rs7185735	AA	AG	65,0%	1,02
FTO	16	rs8043757	AA	TT	11,7%	1,24
FTO	16	rs1558902	TT	AT	63,0%	1,01
MC4R	18	rs17782313	TT	TT	49,2%	0,88
MC4R	18	rs11152213	AA	CC	5,0%	1,27
MC4R	18	rs538656	CC	AC	46,7%	0,93
MC4R	18	rs10871777	AA	GG	3,5%	1,14
					Total risk	**2,2**

The study of the analyzed sample reveals that this person has a genotype associated with an increased risk of obesity of 2.2 with respect to the risk of the Caucasians.

2. ENERGY BALANCE

Knowing the concept of energy balance and apply it to our lives is perhaps the most important factor for maintaining a good health and a good shape.

The energy balance refers to the balance between the energy we consume through food and drink and the energy expended during daily activity.

$$\textit{Energy balance} = \frac{\textit{Energy intake}}{\textit{Energy consumption}}$$

But what happens to that energy in our body?

Briefly, we can say that the energy consumed through the diet goes through 4 phases: absorption, transport, storage and metabolism of energy molecules.

Absorption: is the process by which food nutrients pass into the bloodstream to be distributed throughout the body.

Transport: The circulatory system is responsible for transporting nutrients absorbed in the digestive system to each of our cells.

Storage: When energy intake is greater than expenditure derived from our activity, this extra energy is stored in the body, mainly in the form of fat in adipocytes.

Metabolism: When it comes to metabolism, in this paper we refer to the destruction of energetic molecules (especially fatty acids) for energy release, ie, we refer mainly to catabolism.

In these 4 phases or steps of the process, the conditioning factors are many: Some come from environmental factors and others from genetic factors. This is the reason why the same diet affects differently in some individuals and others.

Certain genetic variants cause that proteins or enzymes responsible for these processes slow down or speed up their activity, causing an imbalance in some of these processes, which leads to increased risk of overweight, obesity and cardiovascular disease.

Throughout this nutrigenetic report we will address some key points of these processes from a genetic point of view to make simple recommendations that allow us to reduce or maintain our weight.

2.1 ABSORPTION OF FATTY ACIDS

2.1.1 Total Fatty Acids and FABP2 gene

Genetic predisposition to the absortion of total fatty acids

Gene: FABP2

Genetic variant: Ala54Trp

Risk allele frequency in the population: 0,31

Patient genotype: Trp/Trp

Introduction: The absorption of fats or lipids is mainly in the small intestine. The binding protein of intestinal fatty acid 2 (FABP2) participates in the absorption of fats in the intestine. This protein is synthesized from the FABP2 gene that is expressed only in cells of the simple absorptive columnar epithelium of the small intestine, where the fatty acids are transported from the luminal plasma membrane to the rough endoplasmic reticulum. Once there, the fatty acids are processed to form chylomicron triglycerides and subsequently be transported through the plasma. Scientific studies show that certain genetic variants in the FABP2 gene are associated with a higher rate of absorption of fatty acids and thus to a greater risk of overweight and obesity.

Result: The study of the sample analyzed reveals that this person has a genotype (Thr / Thr), associated with a higher rate of fatty acids uptake and, therefore, with a greater risk of overweight, obesity and a lower ability to reduce weight.

Recommendation: Clinical studies indicate that subjects with this genotype should reduce saturated fats and trans fats, and increase monounsaturated fats, and have a moderate carbohydrate diet.

Reference: PMID: 11487582, PMID: 17209184, PMID: 24640155

2.1.2 Absorption of polyunsaturated fatty acids and gene FADS1

Absortion of essential fattid acids

Gene: FADS1

Genetic Variant: rs174547

Risk allele frequency in the population: 0,33

Patient Genotype: CC

Introduction: Polyunsaturated fatty acids are a type of fatty acids that should be consumed in the diet because they are not synthesized in sufficient quantities by the body . Therefore, they are called "essential " . They are involved not only in the maturation of the brain and retinal growth of the child , but they are involved in the processes of inflammation , coagulation , blood pressure, reproductive organs and fat metabolism, decreasing total cholesterol. Within this group, we find the linolenic acid (omega 3) and linoleic (omega 6) that are essential for humans. Several scientific articles have described a strong association between certain variant in the gene for fatty acid desaturase 1 (FADS1 , encoding Δ -5 desaturase) and decreased blood levels of omega 3 and 6 fatty acids.

Result: The study of the sample analyzed reveals that this person has a CC genotype associated with lower processing polyunsaturated fatty acids considered essential (omega 3 and omega 6) . Genotypes CC and CT for this variant are associated with lower blood levels of EPA and ARA .

Recommendation: Increase intake of these polyunsaturated fats in your diet . They can be obtained especially for marine fish, including blue, and vegetables, such as corn, soybean, sunflower , pumpkin, walnut .

Reference *: PMID: 19148276 , PMID: 21829377 , PMID: 20045144 , PMID: 22503634*

2.2 FATTY ACID TRANSPORT

2.2.1 The APOA5 gene and lipids transport

High levels of Triglycerides

Gene: APOA5

Genetic Variant: haplotypes APOA5*2 y APOA5*3

Risk haplotype frequency in the population: 0,16 y 0,12

Patient Genotype: APOA5*2/ APOA5*2

Introduction: The apolipoproteins are fundamental components of lipoproteins that act as vehicles of the fat and cholesterol in the blood circulation. Apolipoproteins are a component of various lipoprotein fractions including VLDL, HDL, chylomicrons. The APOA5 gene is one of the key genetic factors in the regulation of triglyceride levels in the blood and, therefore, a major risk factor for cardiovascular disease. Some variants of APOA5 gene, arranged in haplotypes APOA5 * 2 and APOA5 * 3 make their carriers more likely to have high levels of triglycerides in the blood, a risk factor for cardiovascular disease.

Result: The study of the sample analyzed reveals that this person has a haplotype APOA5*2/ APOA5*2 associated with an increased risk of elevated triglycerides.

Recommendation: Carriers of these variants should consider a low calorie diet to prevent that triglycerides are maintained high in the blood Low calorie diets, rich in omega-3, can help preventing the development of obesity and cardiovascular disease.

Reference: PMID: 24387992, PMID: 17211608, ETC.

2.2.2 El gen LPL y el reparto de las grasas por el organismo

2.2.2 The LPL gene and the distribution of fat in the body

Regulation of plasma tryglicerides

Gene: LPL

Genetic Variant: rs328, rs320 and rs285

Risk allele frequency in the population: 0,1, 0,29 and 0,46

Patient genotype: CG, GG, CT

Introduction: Lipoprotein lipase (LPL) is an enzyme that hydrolyzes triglycerides of chylomicrons and very low density lipoproteins which travel through the blood and broken down into free fatty acids and glycerol, releasing them into muscle and adipose tissue. The LPL gene is a key gene in the regulation of triglyceride levels in blood. Triglycerides cannot cross cell membranes, so that , in order to reach the target cells must be packaged in specialized complexes called lipoproteins, which travel through the blood . Once they reach the target tissues, these lipoproteins are hydrolyzed by the enzyme LPL, localized on the surface of blood vessels, which allow that fatty acids are free and can be absorbed by the target cells. Certain variants of the LPL gene (Rs328, Rs320 and Rs285) increase LPL activity and are associated with lower triglyceride levels and higher HDL in the blood, which confer a protective effect.

Result: The study of the sample analyzed reveals that this person has a genotype associated with a protective effect with lower triglyceride levels and higher HDL in the blood.

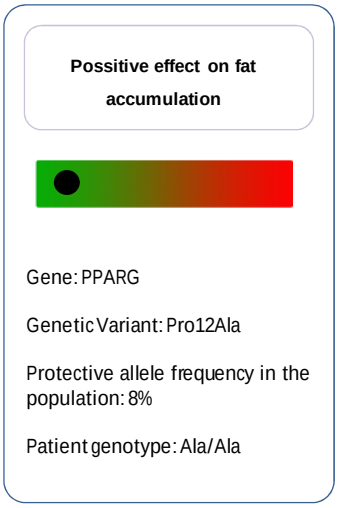
Recommendation: Despite the protective effect, you should continue caring triglyceride levels in the blood, following a balanced diet and daily exercise.

References: (PMID: 16574898, PMID: 20429872, PMC2730542, PMID: 18922999).

2.3 STORAGE

Diet and PPAR genes

Introduction: Most of the excess energy is stored as fat in adipose tissue. The receptor, activated by the peroxisome proliferator (PPARG) is highly expressed in these fat cells and plays a key role in the formation of adipocytes and is crucial in the lipid metabolism . The PPARG gene is responsible for the synthesis of PPARy protein and is one of the key genes in energy storage . In the presence of excess energy storage PPARy starts by empowering fat synthesis. Certain genetic variants in the PPARG gene were associated with less susceptibility to weight gain. However, this protective effect is lost when individuals ingest diets rich in fatty acids.



Results: The study of the sample analyzed reveals that this person has a genotype associated with a lower risk of obesity.

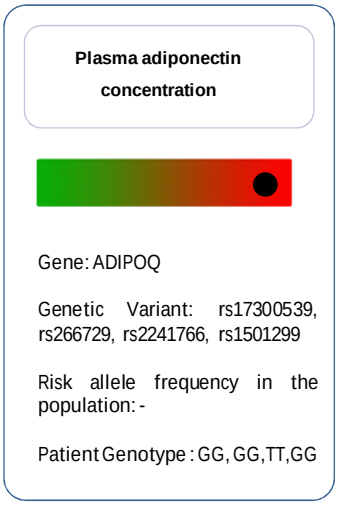
Recommendation: Clinical studies indicate that subjects with this genotype should maintain a diet low in fatty acids to retain the protective effect of this genetic variant.

Reference: PMID: 14506127, PMID: 9806549, PMID: 9425261, PMID: 9792554

2.4.- METABOLISM

Metabolism of fatty acids and the ADIPOQ gene

Introduction: One of the genes that contribute significantly to the metabolism of fatty acids is the ADIPOQ gene. This gene contains the instructions for the synthesis of hormone adiponectin. This hormone is synthesized almost exclusively by adipocytes (fat cells) and travels through the blood to reach the muscle cells and the liver, where it is responsible for glucose utilization, reduce fat and improvement in sensitivity to insulin. In general, a lower concentration of adiponectin in blood correlates with a higher body mass index (BMI) and insulin resistance, which increases the risk of type 2 diabetes mellitus. People who carry ADIPOQ certain gene variants have decreased blood adiponectin levels, and thus, an increased risk of obesity and type 2 diabetes mellitus.



Results: The study of the analyzed sample shows that this person has a genotype associated with decreased blood adiponectin levels and, consequently, an increased risk of obesity associated and type 2 diabetes.

Recommendation: This risk can be reduced by restricting calories and a low fat diet.

References: (PMID: 19238139, PMID: 18949681, PMID: 20576642, PMID: 22443353)

3. - INPUT: APPETITE, SATIETY AND EMOTIONAL EATING

3.1 Regulation of hypothalamic appetite control

Introduction: The appetite is the desire to eat food, felt as hunger. Satiety can be described as the feeling of having no immediate need for food intake and feel full after eating. There are people who do not feel such a sense and tend to eat more without feeling satisfied. For those people, calorie restriction through the control of food intake and choice of smart foods are the best strategies to lose weight. In such cases, the person can increase the amount of fiber in his diet, eating whole wheat bread, oats, barley, lentils, artichokes and peas. Studies show that certain genetic variants in FTO and MC4R genes are associated with greater or lesser ability to satisfy the appetite. Another study of 38.759 Europeans found that people with two copies of a variant of the FTO gene are 1.67 times more likely to be obese (70 % increased risk) than those who do not have these variants.

Regulation of hypothalamic appetite control

Gen: MC4R y FTO

Genetic Variant:

Risk haplotype frequency in the population : -

Patient Genotype:

Results: The study of the sample analyzed reveals that this person has a genotype associated with regulation of appetite and satiety correct and therefore a lower risk of overweight.

Recommendation: Although, it is recommended to pay attention to a moderate intake with low calorie diets and adequate daily physical activity.

Reference: PMID: 18583465, PMID: 19793853, PMID: 19880856, PMID: 24458996.

3.2 Emotional intake

Introduction: Some people eat more than usual when they are bored, angry, stressed, or feel depression, anxiety, sadness or boredom rather than hunger. By eating emotionally, unconsciously they seek in the food comfort or pleasure. Over time, overeating will lead to weight gain and may cause overweight or obesity. The DRD2 gene is a key gene in the neuronal circuits of dopamine. Dopamine is the neurotransmitter that causes the person to feel pleasure. Furthermore, the OPRM1 gene is a key gene in opioid neuronal circuits that leads to the production of dopamine, and determining the level of pleasure. An unbalanced neuronal activity between different circuits often leads to eat emotionally. The DRD2 and OPRM1 genes work in the brain's reward system. Variations in these genes are associated with emotional eating and weight gain. About 11 % of Caucasians and 14% of Asians carry a combination of these two genes that increase the risk of obesity.

Emotional intake

Gene: DRD2 and OPRM1

Genetic Variant: rsxxxxx

Risk allele frequency in the population : 0,31

Patient genotype:

Result: The study of the sample analyzed reveals that this person has a genotype associated with a lower predisposition to emotional eating, which implies a lower risk of overweight and obesity.

Recommendation: Keep this attribute and continue taking a regular habit in their periods of breakfast, afternoon tea and dinner. References: PMID: 19282821, PMID: 18262320, PMID: 23670889.

4. OUTPUT: WEIGHT LOSS IN RESPONSE TO EXERCISE

Regulation of lipolysis and thermogenesis

Introduction: Exercise is important for everyone and especially important if it comes to losing weight. To lose weight, you must burn more calories than you consume and, therefore, the exercise along with the low calorie diet is the best way to get it. The extent to which those calories are burned will be determined by the kind of exercises, their intensity and the time during which they are made. Beta2 -adrenoceptor (ADRB2) and beta3 (ADRB3) are obesity genes, which play a key role in the regulation of energy balance by increasing lipolysis and thermogenesis, two processes that involve the breakdown of stored fats in the body.

Scientific studies have shown that certain genetic variants in these genes ADRB2 and ADRB3 are associated with individuals with increased susceptibility to weight loss in response to exercise.

Weight loss in response to exercise

Gene: ADRB2 and ADRB3

Genetic Variant: rsxxxxx

Risk allele frequency in the population :

Patient genotype:

Result: The study of the sample analyzed reveals that this person has a genotype associated with increased susceptibility to weight loss because of exercise. This means that this person can benefit greatly from exercise when trying to lose weight.

Recommendation: An exercise program according to your individual characteristics, age, gender, physiology, in the hands of a professional, can help considerably to maintain or reduce your weight.

References: (PMID 20523301, PMID 19553224)

GLOSSARY OF TERMS

DNA

DNA or deoxyribonucleic acid is a biochemical component present in the nuclei of cells, which contains the genetic information necessary for the development and functioning of living organisms.

Nucleotide

Basic unit of DNA. It is the union of a sugar (pentose), a phosphoric acid and a nitrogenous base. In DNA exist four different nucleotides: adenine (A), cytosine (C), thymine (T) and guanine (G). To the particular sequence of these nucleotides we call gene.

Protein

A molecule composed of one or more chains of amino acids. The specific sequence of amino acids in the chain depends on the DNA nucleotide sequence. Proteins are responsible for a wide range of vital activities in the cell.

Gen

The gene is the physical and functional unit of heredity that is passed from parents to children. Genes are composed of specific nucleotide sequences and most of them contain the information necessary to produce a specific protein.

Genetic polymorphism

It is a variation or change in existing DNA sequence among individuals in a population.

Allele

It is each of the possible variants that may have a DNA sequence, due to changes or polymorphisms existing among individuals of a population.

Genotype

It is the genetic information provided by an individual.

Genetic marker

It is any DNA sequence, whether be or not a gen, which can be used to characterize an individual in a population.

Heterozygous

Individual whose genotype for a gene or genetic marker is characterized by the fact that its two alleles are different.

Homozygous

Individual whose genotype for a gene or genetic marker is characterized by the fact that its two alleles are equal.

Locus (singular) / loci (plural)

Place of a gene or marker on a chromosome.

SNP

A SNP is a variation in the DNA sequence that affects a single nucleotide (Single Nucleotide Polymorphism) , that is, a single " point " of the genetic code : adenine (A) , thymine (T), cytosine (C) or guanine (G) . The SNP's are up to 90% of all human genomic variations. These variations in DNA sequence can affect the response of individuals to diseases, bacteria, viruses, chemicals, drugs, etc.

Phenotype

It is the set of observable traits or characteristics of an organism. For example, its hair color, weight, or the presence or absence of disease. The phenotype is always something we can observe. It can be seen in the clinic, in the laboratory or in social interactions. A phenotype is the genetic constitution of an organism. It is some expression or the result of the genetic constitution of the organism and is thus determined by genes and the environment in which the person grows and develops.

Genetic Relative Risk

It is the risk presented by a person, with a given genotype, to suffer illness, compared with the average risk of the general population (In which all possible genotypes are present). This risk refers to a single polymorphism.

Total relative genetic risk

It is the risk presented by a person, with a given genotype, of suffering illness, compared with the average risk of the general population, in which all possible genotypes are present. This risk refers to the set of two or more polymorphisms and it is calculated by multiplying the relative risk of each of the polymorphisms analyzed.

Increased risk

The risk presented by an individual with a particular genotype compared to the risk of those who have the lowest risk genotype. It is obtained by dividing the relative risk of the patient between the relative risks of those people whose genotype have the lowest risk.

PMID

Stands for "Pub med Identity" and corresponds to a code assigned to a published scientific article.