Genetic profile

Obesity

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Obesity Genetic Profile
Lipid metabolism

Object
To analyse the genetic variants located in 5 genes involved in the modification of cholesterol levels in its different forms and their contribution to the atherogenic process as a risk factor for obesity.

Method
Obtaining DNA by purification with QIAamp DNA Blood Mini kit columns (QIAGEN). DNA quantification by spectrophotometry, in a Biophotometer, through the measurement of absorbance at a wavelength of 260nm. Amplification by RT-PCR using TaqMan probes in OpenArray 12K Flex (Thermo Fisher Scientific) in 5 genes related to vascular risk.

Result

		dbSNP	Risk	Polymorphism	Fequency	Result
APOE	**apolipoprotein E**					
Low risk	***Absence of risk variants***	rs429358	0,15 (C)	T>C	73.96 %	*3/*3
		rs7412	0,08 (T)	C>T		

APOE*E4 is linked to high cholesterol and beta-lipoprotein levels, as well as a propensity for cardiovascular disease. APOE*E2 is linked to increased risk of type III hyperlipoproteinaemia, high levels of cholesterol, triglycerides and beta-VLDL, as well as to the development of atherosclerosis and increased vascular risk.

APOC3	**apolipoprotein C-III**					
Medium risk	***Variant in heterocygosis (1 copy)***	rs5128	0,23 (G)	C>G	53.42 %	CG

APOC3*3175G is associated with increased risk of vascular disease due to its involvement in triglyceride metabolism.

APOB	**apolipoprotein B**					
Medium risk	***Variant in heterocygosis (1 copy)***	rs693	0,25 (T)	C>T	37.5 %	CT

APOB*2488C is associated with lower triglyceride, cholesterol, and LDL-cholesterol levels. Carriers of the APOB*2488T allele respond better to a low-fat, low-cholesterol diet, with a significantly greater decrease in their LDL and ApoB levels.

CETP	**cholesteryl ester transfer protein**					
Medium risk	***Variant in heterocygosis (1 copy)***	rs708272	0,38 (G)	G>A	47.12 %	GA

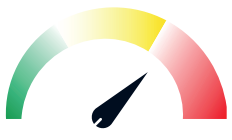
CETP*+279G is associated with low levels of HDL cholesterol and high levels of plasma CETP activity, which contribute to an increased risk of cardiovascular disease.

LPL	**lipoprotein lipase**					
Low risk	***Absence of risk variants***	rs328	0,81 (G)	C>G	65.61 %	CC

The LPL*1421C>G polymorphism is associated with a lower risk of CAD, due to its association with increased HDL and decreased triglycerides. The LPL*1421G variant has higher enzyme activity and is attributed with a protective effect against the development of atherosclerosis and subsequent CAD.

Conclusion - *Obesity with lipid metabolism component*

The genetic profile of the patient shows alterations in 3 of the 5 genes analyzed, representing a relative risk of obesity with lipid metabolism component of 60% (HIGH RISK).



Obesity Genetic Profile
Energy efficiency

Object
Energy is obtained by the breakdown of nutrients in the cell (carbohydrates, proteins, and fats) in the presence of oxygen. This process is known as cellular respiration or metabolism. Basal metabolism is the minimum amount of energy required to maintain the body's vital processes during rest. Basal metabolism can vary between individuals. This panel looks at potential causes of obesity through alterations in genes that are expressed in adipose tissue. These genes regulate: i) Adipocyte growth and differentiation; ii) Energy expenditure. The genetic polymorphisms chosen for this panel analyse an individual's genetic predisposition to obesity and/or additional obesity-related risks.

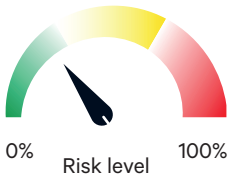
Method
Obtaining DNA by purification with QIAamp DNA Blood Mini kit columns (QIAGEN). DNA quantification by spectrophotometry, in a Biophotometer, through the measurement of absorbance at a wavelength of 260nm. Amplification by RT-PCR using TaqMan probes in OpenArray 12K Flex (Thermo Fisher Scientific) in 3 genes related to obesity risk.

Result

PPARG	**peroxisome proliferator-activated receptor gamma**	**dbSNP**	**Risk**	**Polymorphism**	**Fequency**	**Result**	
Medium risk	***Variant in heterocygosis (1 copy)***	rs1801282	0,11 (G)	C>G	19,71%	CC	
rs1801282*C (12Ala) plays a protective role against obesity, provided that the intake of saturated fatty acids is low.							
UCP2	**uncoupling protein 2**						
Low risk	***Absence of risk variants***	rs659366	0,36 (T)	C>T	40,96%	CC	
rs659366*T is associated with increased energy intake and reduced risk of obesity.							
ADRB3	**beta-3 adrenergic receptor**						
Low risk	***Absence of risk variants***	rs4994	0,08 (G)	A>G	84,64%	AA	
rs4994*G is associated with obesity, metabolic syndrome, and insulin resistance.							

Conclusion - *Obesity with energy efficiency component*

The genetic profile of the patient shows alterations in 1 of the 3 genes analyzed, representing a relative risk of obesity with energy efficiency component of 33% (LOW RISK).



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Obesity Genetic Profile
Appetite control

Object
The control of intake can be explained on the basis of two different regulatory systems (a) Short-term control: thanks to satiety signals, such as gastric distension or peptides and (b) Long-term control: thanks to adiposity signals that modulate satiety. In the obesity gene panel, we study genes involved in the modulation of long-term satiety signals.

Method
Obtaining DNA by purification with QIAamp DNA Blood Mini kit (QIAGEN). Quantification of DNA by spectrophotometry, in a biophotometer, by measuring the absorbance at a wavelength of 260 nm. Amplification by RT-PCR using TaqMan probes in OpenArray 12K Flex (Thermo Fisher Scientific) in 3 genes related to appetite control and obesity risk.

Result

LEP	**leptin**	**dbSNP**	**Risk**	**Polymorphism**	**Fequency**	**Result**
Medium risk	***Carrier of the risk variant in heterozygosis (1 copy)***	rs2167270	0,63 (G)	A>G	46,62%	AG

It acts as a satiety factor and individuals homozygous for the rs2167270 * G allele have lower levels of leptin, which increases the risk of obesity.

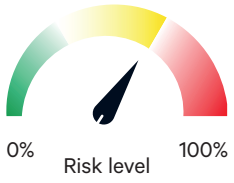
LEPR	**leptin receptor**					
Medium risk	***Carrier of the risk variant in heterozygosis (1 copy)***	rs1137101	0,48 (G)	A>G	49,92%	AG

rs1137101*G is associated with obesity and predicts a small percentage of body weight.

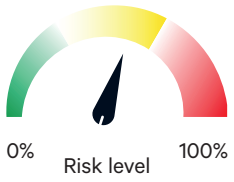
NPY	**neuropeptide Y**					
Low risk	***Absence of risk variants***	rs16139	0,04 (C)	T>C	92,16%	TT

rs16139*C (7Pro) is associated with obesity associated with high levels of triglycerides, total and LDL cholesterol.

Conclusion - *Obesity with appetite control component*
The genetic profile of the patient shows alterations in 2 of the 3 genes analyzed, representing a relative risk of obesity with appetite control component of 67% (HIGH RISK).



Conclusion - *Obesity risk*
The obesity risk in our protocol includes lipid metabolism, energy efficiency and appetite control. The overall count of genes affected is 6 out of 11 (relative risk of 54,54%, MEDIUM-HIGH RISK), with a prominent risk component associated with LIPID METABOLISM AND APPETITE CONTROL.



Genetic counseling
In asymptomatic patients with a relative risk greater than 50%, medical review and implementation of a preventive plan is recommended.

In symptomatic patients with a relative risk greater than 50%, medical review and implementation of a personalized therapeutic plan is recommended.

Referring Physician:

Performed by:

Date:

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Analysed genes

APOE apolipoprotein E

GENE ID: 348 OMIM: 107741 LOCUS: 19q13.32 dbSNP: rs429358 rs7412 POLYMORPHISM: *4, c.3932T>C, C112R *2, c.4070C>T, C158R

It codes for apolipoprotein E, which participates in catabolism of triglyceride-rich proteins and cholesterol homeostasis. The presence of the APOE*E4 allele of the APOE gene is linked to high cholesterol and beta-lipoprotein levels, as well as a propensity for cardiovascular disease. The presence of the APOE*E2 allele is linked to increased risk of type III hyperlipoproteinaemia, high levels of cholesterol, triglycerides and beta-VLDL, as well as to the development of atherosclerosis and increased vascular risk.

APOC3 apolipoprotein C-III

GENE ID: 345 OMIM: 107720 LOCUS: 11q23.3 dbSNP: rs5128 POLYMORPHISM: c.3175C>G,S1/S2

The APOC3 gene, located on chromosomal region 11q23.3, codes for a glycoprotein synthesized in liver and intestine that plays a key role in lipoprotein metabolism. The C3175G (rs5128) polymorphism, also known as Sst I, is located in the 3'UTR region of the APOC3 mRNA. The APOC3*3175G (S2) variant is associated with increased stability and higher expression levels of APOCIII and is therefore associated with increased risk of vascular disease due to its involvement in triglyceride metabolism.

APOB apolipoprotein B

GENE ID: 338 OMIM: 107730 LOCUS: 2p24.1 dbSNP: rs693 POLYMORPHISM: c.2488C>T

It codes for apolipoprotein B present in all lipoproteins except HDL. Increased ApoB levels are directly associated with atherogenic lipoproteins, VLDL, IDL and LDL. It is synthesised in liver and intestine. The APOB*2488C allele is associated with lower levels of triglycerides, cholesterol, and LDL-cholesterol. However, individuals carrying the APOB*2488T allele respond better to a low-fat, low-cholesterol diet, with a significantly greater decrease in their LDL and ApoB levels.

CETP cholesteryl ester transfer protein

GENE ID: 1071 OMIM: 118470 LOCUS: 16q13 dbSNP: rs708272 POLYMORPHISM: c.+279G>A

It codes for the cholesteryl ester transfer protein (CETP) that facilitates the exchange of triglycerides and cholesteryl esters by stimulating cholesterol retrieval. The G+279A polymorphism (rs708272) of the CETP gene (also called Taq IB) is associated with low levels of HDL cholesterol and high levels of plasma CETP activity (presence of the CETP*+279G or B1 allele), which contribute to an increased risk of cardiovascular disease.

LPL lipoprotein lipase

GENE ID: 4023 OMIM: 609708 LOCUS: 8p21.3 dbSNP: rs328 POLYMORPHISM: c.1421C>G,p.Ser447Ter

It plays a key role in lipoprotein metabolism by hydrolyzing triglycerides that are part of VLDL and chylomicrons, as well as by removing lipoproteins from the circulation. LPL influences the interaction of atherogenic lipoproteins with cell surface and vascular wall receptors. Recent studies link the C1421G (rs328) [S447X] polymorphism to a lower risk of CAD, due to its association with increased HDL and decreased triglycerides. Therefore, the 447X variant has a higher enzyme activity and is therefore attributed with a protective effect against the development of atherosclerosis and subsequent CAD.

PPARG peroxisome proliferator-activated receptor gamma

GENE ID: 5468 OMIM: 601487 LOCUS: 3p25.2 dbSNP: rs1801282 POLYMORPHISM: c.-2-28078C>G; p.Pro12Ala

Encodes for the peroxisome proliferator-activated receptor gamma. This receptor is a regulator of adipocyte differentiation and a modulator of insulin sensitivity, as well as being involved in energy homeostasis. The presence of the Ala12 allele decreases the risk of type II diabetes by 25%, promotes a higher BMI (Body Mass Index) when the diet contains more saturated fatty acids. The presence of the Ala12 allele promotes low insulin levels, protects against insulin resistance, and promotes increased plasma levels of HDL cholesterol. The Ala12 allele has a protective role against obesity as long as the intake of saturated fatty acids is low.

UCP2 uncoupling protein 2

GENE ID: 7351 OMIM: 601693 LOCUS: 11q13.4 dbSNP: rs659366 POLYMORPHISM: c.-1245G>A

This gene is primarily expressed in adipose tissue and muscle. Uncoupling proteins promote the release of energy in the form of heat, preventing the formation of ATP. Activation of UCPs regulates body weight and body temperature in states of overfeeding or cold exposure. The -866A allele is associated with increased transcriptional activity, contributing to increased energy expenditure, and decreasing the risk of obesity. The presence of the -866G allele and the 866GG genotype is interpreted as an enhancer of obesity. Although the effect of the -866G allele is more modest than the effect of the -866A allele.

ADRB3 beta-3 adrenergic receptor

GENE ID: 155 OMIM: 109691 LOCUS: 8p11.23 dbSNP: rs4994 POLYMORPHISM: c.190T>C; p.Trp64Arg

The product of this gene is the beta-adrenergic receptor 3, located mainly in adipose tissue. It is related to lipolysis and thermogenesis. The presence of the Arg64 allele contributes to increased abdominal adiposity, decreased basal energy expenditure, increased resistance to weight loss and early development of type 2 diabetes. The Arg64 allele is associated with obesity, metabolic syndrome and insulin resistance.

LEP leptin

GENE ID: 3952 OMIM: 147720 LOCUS: 7q32.1 dbSNP: rs2167270 POLYMORPHISM: c.+19A>G

Encodes for the protein leptin. It is mainly expressed in adipose tissue, and its levels are proportional to the individual's energy reserve levels. It acts as a satiety factor preventing the development of obesity. Subjects homozygous for the G allele have lower levels of leptin, but there is no significant evidence associating it with BMI.

LEPR leptin receptor

GENE ID: 3953 OMIM: 601007 LOCUS: 1p31.3 dbSNP: rs1137101 POLYMORPHISM: c.668A>G; p.Gln223Arg

It codes for the leptin receptor. Leptin acts by binding and activating the leptin receptor in the hypothalamus, leading to reduced intake and increased energy expenditure. The Gln223Arg polymorphism is associated with altered receptor function. The 223Arg allele is associated with obesity and predicts a small percentage of body weight.

NPY neuropeptide Y

GENE ID: 4852 OMIM: 162640 LOCUS: 7p15.3 dbSNP: rs16139 POLYMORPHISM: c.1128T>C; Leu7Pro

Encodes for neuropeptide Y, a neurotransmitter located in the hypothalamus. It stimulates intake, insulin secretion and lipoprotein lipase activity in adipose tissue, thus facilitating the anabolism of energy stores. The 7Pro allele is related to obesity associated with high levels of triglycerides, total and LDL cholesterol.

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Relevance of genetic testing

- Genetic susceptibility is the probability of an individual to develop a certain disease as a result of his or her genetic profile and external conditioning factors.
- Genetic testing for complex diseases determines an individual's susceptibility to a disease. Therefore, the test result only indicates that a person may be more likely than most people to suffer from a particular disease, but it does not mean that he or she will suffer from it, since that risk is conditioned by other variables.
- The design of a personalized medical strategy based on a specific genetic profile that will adjust external conditioning factors such as diet and lifestyle (exercise, alcohol consumption, tobacco consumption, etc.) In addition to pharmacological treatment and the use of nutraceuticals or functional foods, in order to intervene in an individual's susceptibility to the development of a given disease.

Obesity

Obesity is a complex disease caused by hereditary predisposition, imbalance in diet, metabolism and lack of physical exercise. Obesity is one of the main risk factors for cardiovascular diseases and many other important diseases. The objective of this genetic panel is to determine the susceptibility or predisposition of an individual to obesity. To do this, we analyze genes that intervene in three physiological mechanisms that regulate body weight: ENERGY EFFICIENCY, APPETITE CONTROL and LIPID METABOLISM.

Energy is obtained through the degradation of nutrients in the cell (carbohydrates, proteins and fats) in the presence of oxygen. This process is known as cellular respiration or metabolism. Basal metabolism is the minimum amount of energy required to maintain the body's vital processes during rest. Basal metabolism can vary between different individuals.

The control of intake can be explained on the basis of two different regulatory systems: (a) Short-term control: thanks to satiety signals, such as gastric distension or peptides and (b) Long-term control: thanks to adiposity signals that modulate satiety. In the obesity genetic panel we study genes involved in the modulation of long-term satiety signals.