MEDICAL GENETICS CLINIC

HANDBOOK

VOLUME 2

CRAFTON AND GENEADVISE PUBL

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NUTRITIONAL GENETICS

L.Camurri PhD Editor

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GENETIC VARIANTS AND NUTRITION

Nutrigenetics: science that studies the effects of genetic variations on the response to nutrients, with the aim of identifying the foods most suitable for a particular person.
Nutrigenomics: science that studies the effects of nutrients on the expression of genes, i.e. how nutrients act directly at the DNA level and therefore at the level of the proteome and metabolome. Nutriepigenomics: science that studies specific nutritional interventions capable of favorably regressing epigenetic alterations.

Dietary lifestyle is a fundamental determinant of risk for the most widespread chronic diseases in the Western world: cardiovascular, obesity, diabetes and many cancers. There are many guidelines, based on large-scale epidemiological studies, aimed at the general population or homogeneous groups of patients who share the same condition of possible risk or pathology. It is also known that the individual response to the same type of diet is variable, both in terms of clinical outcomes and the modulation of the risk of disease due to psychosocial, cultural and economic causes, and for the expected, much less well-known, complex interactions, between genetic and environmental factors, certainly not easily qualified in a reliable way today.
The availability of new technologies and ever-increasing knowledge in the “omics” field have led to the hypothesis of a possible evolution towards personalized nutrition. The molecular analysis of the genome and the metabolome has in fact highlighted numerous variants differently associated with dietary factors, and in this sense potentially attributable to susceptibility to many chronic diseases.

The enormous potential of these developments does not currently correspond to results validated in the clinical field, despite being highly suggestive in terms of pathophysiological bases.
The examples of genetic variants involved in the risk of disease, through interaction with diet, are numerous and concern many highly prevalent conditions, for example hypercholesterolemia, hypertriglyceridemia, breast cancer, osteoporosis, metabolic syndrome, type 2 diabetes, obesity, non-alcoholic fatty liver disease. In the context of glucose metabolism, approximately 100 genetic variants have been identified for type 2 diabetes and over 40 for type 1, capable of interacting with the intake of both carbohydrates and fibers to weakly modulate the risk of the disease4.
We also note the polymorphisms of the vitamin D receptor (VDR) gene, associated with post-menopausal osteoporosis in women who consume little calcium6, and the variants of the genes that regulate homocysteine metabolism, for example MTHFR and MTR, associated with the risk of breast cancer in subjects with low intakes of folate, vitamin B6 and B127.
Genetic studies have also highlighted 97 loci relating to the accumulation of adipose tissue and another 49 relating to fat distribution. The variants of the first so-called “obesity gene” identified, FTO (fat mass and obesity associated), are closely associated with the increase in BMI (body mass index), especially in the presence of diets rich in

fats and proteins. A common polymorphism of the PLIN (perilipin) gene, involved in the regulation of fat accumulation in adipocytes, can reduce the risk of obesity in association with a diet rich in carbohydrates but increase it in case of reduced intake8.
These data help to explain the well-known, and expected, poor results of the usual generalized approach (one-size fits all) to reducing body weight. Important methodological-linguistic note: the use of the term association is not accidental: in epidemiology and statistics it indicates a substantially descriptive relationship between "causes" and "effects" but does not explain whether one phenomenon is the cause of the other: that is, it indicates a possible line of research.

Genetics and diet personalization Studies concerning the metabolome have identified markers which, modifiable by diet, can constitute a premise for studies on the stratification of dietary interventions in type 2 diabetes. For example, in a meta-analysis of 8 prospective studies, conducted on 8,000 individuals, of which 1,940 diabetics type 2, a positive association was found between the risk of diabetes and the plasma concentration of some branched-chain amino acids (leucine and valine) and aromatics (tyrosine and phenylalanine), while glycine and glutamine demonstrated an inverse correlation.
In a case-control study, on a cohort of approximately 30,000 subjects from the EPIC-InterAct study, while the importance of obesity as a universal risk factor for diabetes was confirmed, at any level of genetic risk, no correlation emerged significant between polygenic diabetic risk score and Mediterranean diet.

A prospective cohort study highlighted that better adherence to healthy dietary patterns reduced the effects of genetic variants associated with weight gain, especially in subjects at high risk of obesity, while a prospective case-control study on over 8,000 subjects of the INTERHEART study and almost 20,000 of the FINRISK, highlighted the favorable effect of a diet rich in fruit and vegetables on subjects at risk of myocardial infarction on a genetic basis. On the contrary, unhealthy diet, rich in simple sugars and saturated fats, have been found to be able to amplify the effects of genetic variants predisposing to obesity.
The type of diet can have a favorable or unfavorable impact through the direct influence on the expression of genes that regulate metabolic pathways14. For example, in a cross-sectional study on 220 healthy subjects, the Western diet resulted in an increased pro-inflammatory and carcinogenic gene expression profile compared to a Mediterranean diet. Similarly, a diet rich in red meat, associated with particular genetic variants, has determined metabolic patterns associated with increased risk of colon cancer.

WIDE PANEL OF GENETIC VARIANTS POTENTIALLY INVOLVED IN NUTRITION AND METHABOLISM

METABOLISMO DELL'O				
CBS C699T C-T rs234706:	TT+	CC-		OMOCIST
CBS T1080C T-C rs180118	TT-	CC+		OMOCIST
MTHFR C677T C-T rs180	CC-		PESO CARDI	OMOCIST
MTHFR A1298C A-C rs18	C-		PESO	OMOCIST
MTR A2756G A-G rs1805	G+		PESO	OMOCIST
MTRR A66G A-G rs18013	G+		PESO	OMOCIST
TCN2 776 C-G rs1801198:	GG+			OMOCIST
RISPOSTA INFIAMMAT				
AACT -51 G-T rs1884082:				
CRP 3872 G-A rs1205: AA				
IL-1B -511 C-T rs16944: C				
IL-1B c.81 C-T rs143634:				
IL-6 -572 G-C rs1800796:				
IL-6 -174 G-C rs1800795:				
IL-10 -1082 G-A rs180089				
IL1RN c.69 T-C rs419598:				
IL6R D358A A-C rs222814				
IFNG +874 A-T rs2430561				
TNFa -308 G-A rs1800629:				
SALUTE CARDIOVASC				
ACE Ins/Del rs4340: D/D	DD-		MET MUSC CARDIO	
ADIPOq -11391 G-A rs173				
ADRA2B Ins/Del cod.299:				
ADRB1 G389R G-C rs180				
ADRB2 G16R G-A rs1042				
ADRB2 Q27E C-G rs1042				
ADRB3 W64R T-C rs4994				
AGT M235T T-C rs699: T	C-		MET MUSC CIRC	
AGTR1 A1166C A-C rs518	C-		CARDIO	
Apo B R3500Q G-A rs574	A-		MET MUSC CIRC	
APO E: E3/E3	E1E1-	E2E2	GRASSI	PESO
APOA1 -75 G-A rs670: GA				
APOA2 -265 C-T rs5082: T				
APOC3 C3175G C-G rs512				
FGB C148T C-T rs180078	GG+		MET MUSC CIRC	
CETP G279A G-A rs70827				
CETP G1353A G-A rs180				
E-Selectin Ser128Arg A-C				
EDN1 Lys198Asn G-T rs5				
FABP2 A54T G-A rs17998	A-		MET MUSC CARDIO	
Factor V R506Q G-A rs602				
FTO T-A rs9939609: TA				
FTO C-A rs8050136: CA				
FTO C-T rs1121980: CT				
FTO T-C rs1421085: TC				
FTO T-G rs17817449: TG				
GHSR G477A G-A rs5721				
GJA4 (CX37) Pro319Ser C				
HMGCR -911 C-A rs37617				
Leptin -2548 G-A rs779903				
LIPC -514 C-T rs1800588:				
LPA A-G rs10455872: AA				
LPL C1595G C-G rs328: C				
MC4R g.60183864 T-C rs1				
MMP3 1171 5A-6A rs3506				
MTNR1B g.92975544 C-G				
NOS3 -786 T-C rs2070744	T-		MET MUSC CIRC	
NOS3 Glu298Asp G-T rs17				

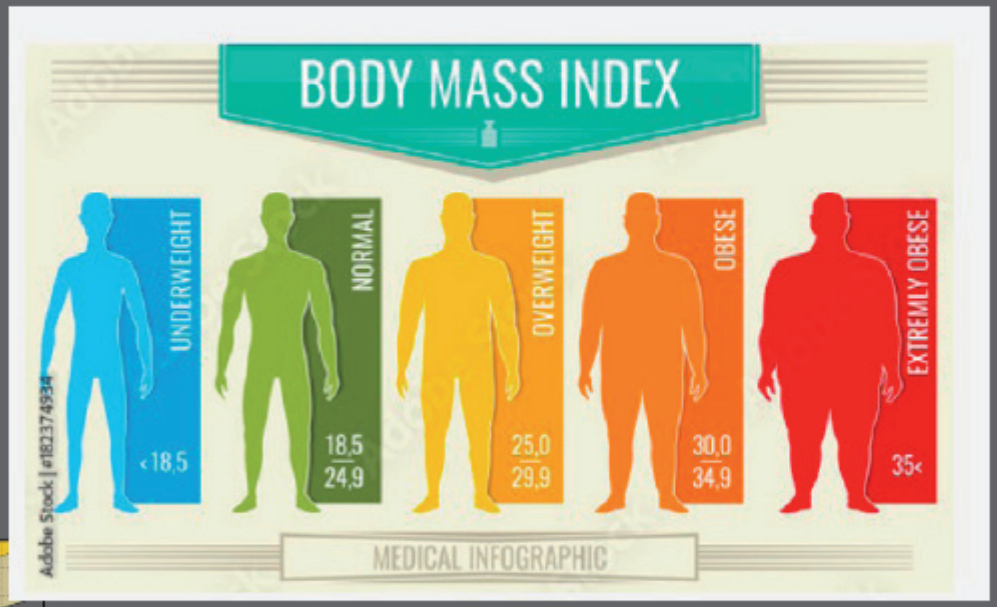
NOX p22 PHOX (CYBA) C		
NPY L7P T-C rs16139: TT		
PON1 Gln192Arg A-G rs66	AA-	CARDIO
PPARA L162V G-C rs4253		
PPARG P12A C-G rs18012		
PPARGC1A G482S G-A rs		
PROCR Ser219Gly A-G rs8		
SREBF2 Gly595Ala G-C rs		
TCF7L2 c.382-41435 C-T rs		
VEGF c.-1507 C-G rs20109		
VEGF -2578 C-A rs699947		
SALUTE DELLE OSSA		
COL12A1 Gly3058Ser G-A		
COL27A1 g.117049891 T-C		
COL5A1 c.267 C-T rs12722	T-	tendon
COL6A4P1 g.15216429 C-T	TT-	
COL1A1 c.104-441 G-T rs1	TT+	
CTR Pro463Leu C-T rs1801	TT-	
ESR1 PvuII (IVS1-397) C-T		
ESR1 XbaI (IVS1-351) A-G		
ESR2 39 A-G rs4986938: A		
GDF5 +104 C-T rs143383:	T-	
IGF2 G17200A G-A rs680:	A-	MET MUSC CIRC
IGF2 C18790G C-G rs3213		
IGF2As G11711T G-T rs79		
IGFBP-3 -C1592A C-A rs21		
LRP5 Ala1330Val C-T rs37	T-	
MBL2 g.797 C-A rs456025		
MCT1 A1470T A-T rs1049	TT-	
MMP1 -1607 G-2G rs1799		
MMP10 g.102779693 C-T r		
MMP12 g.102875061 A-G r		
MMP3 g.102842889 A-G rs		
MMP3 g.102840607 T-C rs		
MMP3 g.102838056 G-A rs		
TNC g.117813990 C-T rs13		
TNC g.117808785 T-A rs21		
VDR Fok1 (ATG-ACG cod	TT-	
VDR BsmI intr8 A-G rs154	GG+	
VDR TaqI es9 T-C rs731236	C-	
STRESS OSSIDATIVO - A		
5HTTPLR S/L rs25531: L/L		
CAT C262T C-T rs1001179		protrtt o atti
EPHX1 Y113H T-C rs10517		
EPHX1 R139H A-G rs2234	G-	
GPX1 P200L C-T rs105045		
GSTM1 delezione gene no d		
GSTP1 I105V A-G rs1695:		
GSTP1 A114V C-T rs11382		
GSTT1 delezione gene no d		
MnSOD (SOD2) A16V C-T		
MnSOD (SOD2) T175C T-C		
SOD3 C760G C-G rs17998		
SUOX Q364X C-T: CC		
SUOX S370S G-C rs773115		
SUOX S370Y C-A: CC		
SUOX cod.381 del TAGA:		
WEIGHT CONTROL		
ADIPOq -11391 G-A rs173	AA+	GG PESO
ADRB1 G389R G-C rs1801	C-	PESO

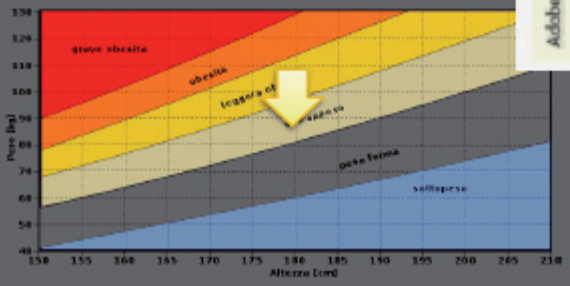
ADRB2 G16R G-A rs1	GG+	A-	GRASSI	E+ E-	ESERCIZIO
ADRB3 W64R T-C rs4	**TT+**	C-		E+ E-	LIPOLISI **>DIET IPOCAL**
APOA2 -265 C-T rs508	TT+	C-	GRASSI sens	AG= AG+	GRASSI SATURI INS RES
APOA5 -1131 T-C rs6	TT+		PESO		
FABP2 A54T G-A rs17	**GG+**	A-	GRASSI	E+ E-	ESERCIZIO
FTO T-A rs9939609: T	A-	T+	PESO	E+ E-	ESERCIZIO
FTO C-A rs8050136: C	A-		PESO		
FTO C-T rs1121980: C	T-		PESO		
FTO T-C rs1421085: T	C-		PESO		
FTO T-G rs17817449:	G-		PESO		
GHSR G477A G-A rs5					
Leptin -2548 G-A rs77	A-		PESO		
MC4R g.60183864 T-C	AA-		PESO		
NPY L7P T-C rs16139:	C-		PESO		
PPARG P12A C-G rs1	deleted				
VEGFA c.-1507 C-G rs	**G+**	CC-	GRASSI MUSC INS	E+ E-	ESERCIZIO
5HTTPLR S/L rs25531	deleted				
ADRA2B Ins/Del cod.2					

CARBO-LIPIDI	6
PESO	16
GRASSI	6
ESERCIZIO	4
OSTEO	10
MET MUSC CIRC	7
OMOCISTEINA	7
CARDIO	4

BUONO +
CATTIVO -
INTOLL SENS -

PERSONALIZED PHYSIOLOGY
FAT INTAKE AND BODY MASS INDEX





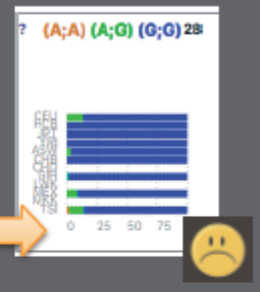
GeneAdvise

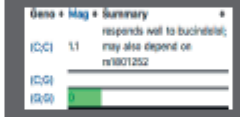
Geno	Mag	Summary
(-;-)		
(A;A)	2.5	short form of 5-HTTLPR. lower levels of serotonin, slightly less happy, benefits from more support
(G;G)	2.1	long form of 5-HTTLPR. less sensitive to pain

Discussion: In conclusion, our findings indicate that 5-HTTLPR polymorphism may be linked with BMI and also with obesity and/or overweight in adult male population, reinforcing the role of the serotonin transporter as a risk factor for the obesity phenotype and suggesting potential new

GENE	VARIANTI	RSnumber	Nucleotide		
SLC6A4/ 5HTTPLR	Ins/Del	rs25531	GWAS NO DATA FEW MARGINAL STUDIES		S/S=lento adattamento S/L=medio adattamento L/L=rapido adattamento
ADIPOq	-11391 G/A	rs17300539	G	A	Presenza allele A (AA o AG) = possibile aumento della probabilità di [illegible] obesità, insul[illegible]nza, diabete e [illegible]rome metabolica
ADRA2B	Ins/Del cod.299		NOT CONFIRMED		Del cod 299=possibile aumento rischio cardiovascolare e tendenza aumento di peso
ADRB1	G389R	rs1801253	G	C	Presenza allele C (CC o CG) = aumento della probabilità di sviluppare obesità
ADRB2	G16R	rs1042713	G	A	Presenza allele A (AA o AG) = aumento della probabilità di sviluppare obesità
ADRB3	W64R	rs4994	T	C	Presenza allele C (CT o CC) = possibile fattore di rischio cardiovascolare e tendenza all'obesità
APOA2	-265 C-T	rs5082	C	T	CC=possibile predisposizione all'aumento del peso
APOA5	-1131T> C	rs662799	T	C	Presenza allele C (TC o CC) = predisposizione all'aumento di peso
FABP2	A54T	rs1799883	G	A	Presenza allele A (AA o AG) = associato ad alto/moderato rischio cardiovascolare e alta/moderata sensibilità ai carboidrati raffinati
FTO	T-A	rs9939609	T	A	Presenza allele A (AA o AT) = associato a significativa tendenza all'aumento di peso
	C-A	rs8050136	C	A	Presenza allele A (AA o AC) = associato a significativa tendenza all'aumento di peso
	C-T	rs1121980	C	T	Presenza allele T (TT o TC) = associato a significativa tendenza all'obesità
	T-C	rs1421085	T	C	Presenza allele C (CC o CT) = associato a significativa tendenza all'obesità
	T-G	rs17817449	T	G	Presenza allele G (GG o GT) = associato a significativa tendenza all'obesità

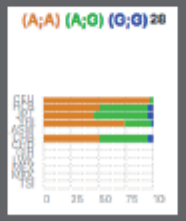
Geno	Mag	Summary
(A;A)	1	higher adiponectin levels
(A;G)		if obese, dieting more effective
(G;G)	1	increased risk of insulin resistance





Pharmacogenetics. GWAS NO DATA

C (G) higher trygliceride levels



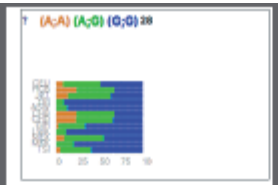
Geno	Mag	Summary
(A;A)	0	normal
(A;G)	2	1.4x higher early heart attack risk; less weight gain on high fat diets
(G;G)	2	2x higher early heart attack risk; less weight gain on high fat diets

GENOMA®

GeneAdvise

Not related to obesity

GHSR	G477A	rs572169	G		A	Presenza allele A (AA o AG) = possibile predisposizione all'assunzione di grandi quantità di cibo e tendenza all'obesità
Leptin	-2548 G-A	rs7799039	G		A	AA=possibile fattore di rischio cardiovascolare e tendenza all'obesità
MC4R	g.60183864T>C	rs17782313	T		C	Presenza allele C (CC o CT) = possibile presenza di disordini dell'appetito, tendenza all'obesità
NPY	L7P	rs16139	T		C	Presenza allele C (CC o CT) = possibile fattore di rischio cardiovascolare o predisposizione all'aumento di peso
PPARG	P12A	rs1801282	C		G	Presenza allele G (GG o CG) = possibile predisposizione all'aumento di peso
VEGF	c.-1507 C-G	rs2010963	C		G	Presenza G (GG o CG) = possibile fattore di rischio cardiovascolare o predisposizione all'aumento di peso



GWAS snp

PMID	[PMID 20081960]
Trait	Height
Title	Hundreds of variants clustered in genomic loci and biological pathways affect human height
Risk Allele	T
P-val	3E-18
Odds Ratio	0.03 [NR] unit increase

military conscripts. AA homozygotes of leptin promoter SNP-2548 showed higher body fat and BMI values than G allele carriers. Acute exercise decreased leptin levels in G allele carriers, but increased in AA homozygotes. Physical training significantly decreased BMI values and also a tendency for decreased plasma leptin levels was observed in all subjects. In G allele carriers, BMI loss was mainly due to decreased fat mass, whereas in AA homozygotes due to loss of fat-free mass. Training increased VO(2)peak in all subjects with most prominent effects in G allele carriers.

GHSR	G477A	rs572169	G		A	Presenza allele A (AA o AG) = possibile predisposizione all'assunzione di grandi quantità di cibo e tendenza all'obesità
Leptin	-2548 G-A	rs7799039	G		A	AA=possibile fattore di rischio cardiovascolare e tendenza all'obesità
MC4R	g.60183864T>C	rs17782313	T		C	Presenza allele C (CC o CT) = possibile presenza di disordini dell'appetito, tendenza all'obesità
NPY	L7P	rs16139	T		C	Presenza allele C (CC o CT) = possibile fattore di rischio cardiovascolare o predisposizione all'aumento di peso
PPARG	P12A	rs1801282	C		G	Presenza allele G (GG o CG) = possibile predisposizione all'aumento di peso
VEGF	c.-1507 C-G	rs2010963	C		G	Presenza G (GG o CG) = possibile fattore di rischio cardiovascolare o predisposizione all'aumento di peso

GWAS

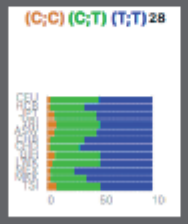
SNP	rs17782313
PubMedID	[PMID 19454149]
Condition	Body mass index
Gene	MC4R
Risk Allele	C
pValue	3.00E-016
OR	0.05
95% CI	0.04-0.06] unit increase in log(BMI

GWAS snp

PMID	[PMID 19151714]
Trait	Obesity
Title	Genome-wide association study for early-onset and morbid adult obesity identifies three new risk loci in European populations
Risk Allele	C
P-val	5E-15
Odds Ratio	1.22 [1.05-1.40]

GWAS snp

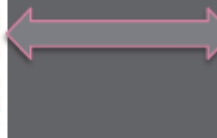
PMID	[PMID 19078963]
Trait	Body mass index
Title	Six new loci associated with body mass index highlight a neuronal influence on body weight regulation
Risk Allele	C
P-val	5E-18
Odds Ratio	0.25 [0.12-0.25] kg/m2 increase



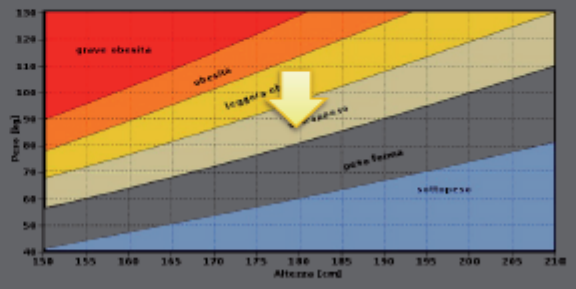
Geno	Mag	Summary
(C;C)	2.5	adults likely to be 0.44 BMI units higher
(C;T)	2	adults likely to be 0.22 BMI units higher
(T;T)	0	normal

GeneAdvise

GHSR	G477A	rs572169	G	A	Presenza allele A (AA o AG) = possibile predisposizione all'assunzione di grandi quantità di cibo e tendenza all'obesità
Leptin	-2548 G-A	rs7799039	G	A	AA-possibile fattore di rischio cardiovascolare e tendenza all'obesità
MC4R	g.60183864T>C	rs17782313	T	C	Presenza allele C (CC o CT) = possibile presenza di disordini dell'appetito, tendenza all'obesità
NPY	 Cholesterol, alcohol, depression G (C) rare NO GWAS	16139	T	C	Presenza allele C (CC o CT) = possibile fattore di rischio cardiovascolare o predisposizione all'aumento di peso
PPARG	P12A	rs1801282	C	G	Presenza allele G (GG o CG) = possibile predisposizione all'aumento di peso
VEGF	c.-1507 C-G	rs2010963	C	G 	Presenza G (GG o CG) = possibile fattore di rischio cardiovascolare o predisposizione all'aumento di peso



Meta-analysis
NO GWAS

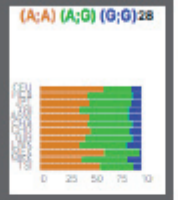


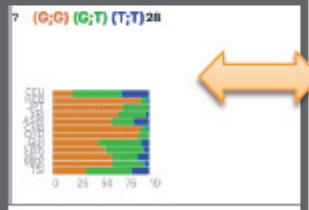
GeneAdvise

PERSONAL GENETICS
BONES-TENDONS PHYSIOLOGY AND INJURIES

GeneAdvise

PERSONAL GENETICS
BONES-TENDONS
PHYSIOLOGY
AND INJURIES

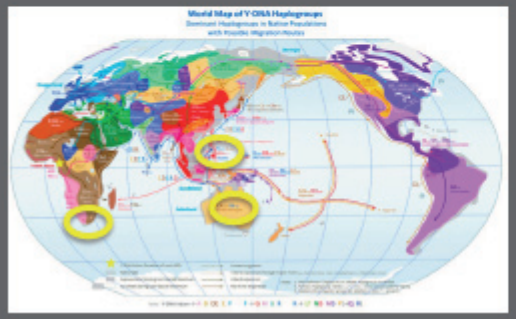




GWAS snp

PMID	[PMID 18391951]
Trait	Height
Title	Many sequence variants affecting diversity of adult human height
Risk Allele	T
P-val	1.8999999999999999E-7
Odds Ratio	4.40 [2.83–5.97] % SD taller

Collagen genes
LDL receptor genes
Vitamin D Receptor genes



Gene	Variante	RSnumber	Nucleotide	Variazione	Interpretazione
COL1ZA1	Gly3058Ser	rs970547	G	A	AA= tendenza alla lassità articolare, possibile predisposizione alla rottura del legamento crociato anteriore
COL27A1	g.117049891T>G	rs946053	T	G	Presenza allele G= possibile predisposizione alle tendinopatie croniche (Tendine d'Achille)
COL5A1	C / T	rs12722	C	T	Presenza allele T= marcatore di suscettibilità ai crampi muscolari; marcatore di debolezza tendinea
COL6A4P1	g.15216429C>T	rs7639618	C	T	TT=debolezza delle cartilagini articolari (prevalentemente ginocchio), possibile predisposizione all'osteoartrosi
COL1A1	c.104-441 G-T	rs1800012	G	T	Presenza allele T=possibile aumentato rischio per osteoporosi TT= fattore di protezione per rottura legamento crociato anteriore
CTR	Pro463Leu	rs1801197	C	T	TT= possibile tendenza alla riduzione della massa ossea
ESR1	PvuII IVS1- 397 T/C	rs2234693	C	T	TT= possibile fattore di rischio per osteoporosi
	XbaI (IVS1-351 A/G)	rs9340799	A	G	GG=possibile tendenza alla frattura ossea per riduzione BMD
ESR2	39 A-G	rs4986938	A	G	GG=possibile tendenza alla frattura

> Front Genet. 2021 Aug 10;12:695861. doi: 10.3389/fgene.2021.695861. eCollection 2021.

COL12A1 rs970547 Polymorphism Does Not Alter Susceptibility to Anterior Cruciate Ligament Rupture: A Meta-Analysis

All from Collins, indirect, flanking marker, Risk allele T. South Africa Pop.

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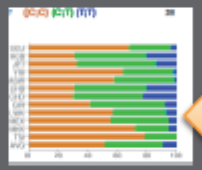
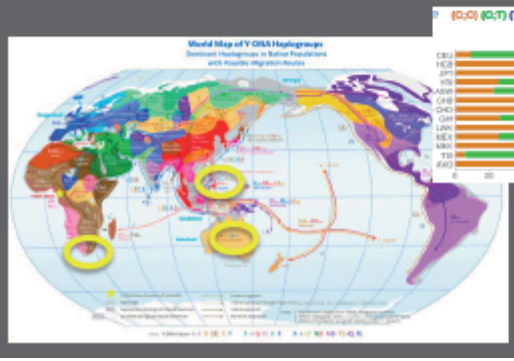
PERSONAL GENETICS BONES-TENDONS PHYSIOLOGY AND INJURIES

Only tendons JPN





Gene	Variante	RSnumber	Nucleotide	Variazione	Interpretazione
COL12A1	Gly3058Ser	rs970547	G	A	AA- tendenza alla lassità articolare, possibile predisposizione alla rottura del legamento crociato anteriore
					Presenza allele G= possibile predisposizione alle tendinopatie croniche (Tendine d'Achille)
COL5A1	C / T	rs12722	C	T	Presenza allele T- marcatore di suscettibilità ai crampi muscolari; marcatore di debolezza tendinea
COL6A4P1	g.15216429C>T	rs7639618	C	T	TT-debolezza delle cartilagini articolari (prevalentemente ginocchio), possibile predisposizione all'osteoartrosi
COL1A1	c.104-441 G-T	rs1800012	G	T	Presenza allele T-possibile aumentato rischio per osteoporosi
CTR	Pro463Leu	rs1801197	C	T	TT- fattore di protezione per rottura legamento crociato anteriore
					TT- possibile tendenza alla riduzione della massa ossea
ESR1	PvuII IVS1- 397 T/C	rs2234693	C	T	TT- possibile fattore di rischio per osteoporosi
	XbaI (IVS1-351	rs9340799	A	G	GG=possibile tendenza alla frattura ossea per riduzione BMD
ESR2	39 A-G	rs4986938	A	G	GG-possibile tendenza alla frattura

Oncotarget. 2018 Mar 16; 9(20): 15365–15374. PMCID: PMC5880610
Published online 2017 Dec 27. doi: 10.18632/oncotarget.23805 PMID: 29632650

Association between polymorphism rs12722 in COL5A1 and musculoskeletal soft tissue injuries: a systematic review and meta-analysis

Research article | Open Access | Published: 02 December 2019

***COL5A1* rs12722 polymorphism is not associated with passive muscle stiffness and sports-related muscle injury in Japanese athletes**

Metaanalisi/Japan/osteoartite

Metaanalisi/solo TT protettivo

Osteoporosis HS

Estrogen Receptor-women-patology-NS

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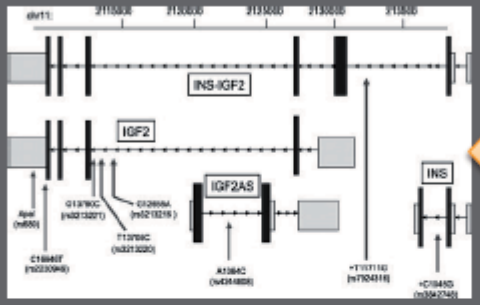

Manage ensamble – muscle performance weakness in men

GDF5 **Growth Differentiation Factor** **Metaanalisi/1,1CT 1,3TT/HS**	+ 104T/C	rs143383	C	T	☺	Presenza allele T=possibile fattore di rischio per osteoartrosi e frattura ossea
IGF2 **Insulin Growth Factor** **Muscle power/men/NS**	G17200A	rs680	G	A	☹	Presenza allele A-tendenza alla lesione muscolare, allungamento dei tempi di recupero
	C13790G	rs3213221	C	G	☹	Presenza allele G-tendenza alla lesione muscolare, allungamento dei tempi di recupero
IGF2As **1 studio 1985/men/NS**	G11711T	rs7924316	G	T	☹	Presenza allele T-tendenza alla lesione muscolare, allungamento dei tempi di recupero
IGFBP-3 **1 studio 1985/men/NS**	-C1592A	rs2132570	C	A	☹	Presenza allele A-tendenza alla lesione muscolare, allungamento dei
LRP5 **LDL Receptor Related Protein** **Metaanalisi HS**	A1330V-I	rs3736228	C	T	☺	Presenza allele T-possibile tendenza alla frattura ossea
MCT1 **Monocarboxilate Transporter Gene/trasporto acido lattico** **1 studio/football/HS**	T1470A	rs1049434	A	T	☺	TT- tendenza a rapida saturazione delle cellule muscolari (crampi)
MMP1 **Matrix Metalloproteinase G** **Eterogeneo/1 stud/osteoporosi/NS**	-1607 1G/2G	rs1799750			☹	2G/2G-tendenza alla lassità articolare, possibile predisposizione alla rottura del legamento crociato anteriore
MMP10 **1 studio mirato/??**	g.102779693C>T	rs486055	C	T	☹	Presenza Allele T-tendenza alla lassità articolare, possibile predisposizione alla rottura del legamento crociato anteriore

Sports Med Open. 2015 Dec; 1: 33. PMCID: PMC4600723
Published online 2015 Oct 11. doi: 10.1186/s40798-015-0033-9

Influence of the MCT1 rs1049434 on Indirect Muscle Disorders/Injuries in Elite Football Players

Myosotis Massidda,[✉1] Nir Eynon,[2] Valeria Bachis,[1] Laura Corrias,[1] Claudia Culigioni,[1] Francesco Piras,[3] Paolo Cugia,[3] Marco Scorcu,[3] and Carla M. Calò[1]

Breakdown of extracellular matrix in normal physiological processes, such tissue remodeling

This secreted protease breaks down fibronectin, laminin, elastin, proteoglycan core protein, gelatins, and several types of collagen

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PERSONAL GENETICS
BONES-TENDONS PHYSIOLOGY
AND INJURIES

3 studi indip HS

MMP12	g.102875061A> G	rs2276109	A	G		Presenza Allele G= tendenza alla lassità articolare, possibile predisposizione alla rottura del legamento crociato anteriore
1 studio mirato/??						
MMP3	g.102842889A>G	rs679620	A	G		GG= possibile predisposizione alle tendinopatie croniche (Tendine d'Achille)
Collins/Australia/COL5A1/100 paz						
	g.102840607T>C	rs591058	T	C	☹	CC= possibile predisposizione alle tendinopatie croniche (Tendine d'Achille)
Collins/Australia/COL5A1						
	g.102838056G>A	rs650108	G	A		AA= possibile predisposizione alle tendinopatie croniche (Tendine d'Achille)
Collins/Australia/COL5A1						
NRF2 (GABPB1)	c.16-8797 T-C **Nuclear Respiratory Factor**	rs7181866	T	C	☺	Presenza allele C= vantaggio per sport e performance di resistenza
TNC	g.117813990C>T	rs1330363	C	T	☹	TT= possibile predisposizione alle tendinopatie croniche (Tendine d'Achille)
2 studi/COL27A1/ LS						
	g.117808785T>A	rs2104772	T	A	☹	Presenza allele A= possibile predisposizione alle tendinopatie croniche (Tendine d'Achille)
2 studi/COL27A1/ LS						
VDR	Fok1 (ATG-ACG cod 1) **Vitamin D Receptor**	rs2228570	T	C		TT=possibile predisposizone alla diminuzione della densità ossea
HS						
	BsmI (A-G intr 8)	rs1544410	A	G	☺	GG=possibile ridotto assorbimento di calcio a livello intestinale
Uncorrect/GG protettivo						
	TaqI (T-C es 9)	rs731236	T	C		Presenza allele C=possibile fattore di rischio per osteoporosi
HS						

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PERFORMANCE

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PERSONAL GENETICS PERFORMANCE

Angiotensin vasopressor/aldosterone stimulating peptide that controls blood pressure and fluid-electrolyte balance
Associato ipertensione (DD) > aumento apporto sangue muscolare

Alfa actinina 3/ skeletal muscle-structural component of sarcomeric Z line
Studio ridotto, evidenza solo su femmine. Non confermati in replica

Nitric oxide synthetase 3/regulating vascular tone Uno studio su atleti. HS.

Vascular Endothelial Growth Factor/angiogenesi
1 studio russo

GENE	VARIANTI	RSnumber	Nucleotide	Variazione		Interpretazione
ACE	Ins/Del	rs4340				DD (Del/Del)–predisposizione agli sport di potenza II (Ins/Ins)= predisposizione agli sport di resistenza
ACTN3	R577X	rs1815739	C	T		TT–predisposizione per sport e performance di resistenza CT=profilo intermedio CC=vantaggio per sport e performance di velocità e potenza
CYP1A2	-163C>A	rs762551	C/*1A	A/*1F		AA=rapido metabolizzatore della caffeina-effetto ergogenico AC o CC= lento metabolizzatore della caffeina - nessun effetto ergogenico
LTC	-13910 T-C	rs4988235	T	C		CC= Intollerante al lattosio
	G/A(-22018)	rs182549	A	G		GG= Intollerante al lattosio
NOS3	-786 T / C	rs2070744	T	C		TT o TC= predisposizione agli sport di potenza
VEGF	G-634C	Rs2010963	G	C		Presenza di C (GC o CC) = migliore performance negli sport di resistenza

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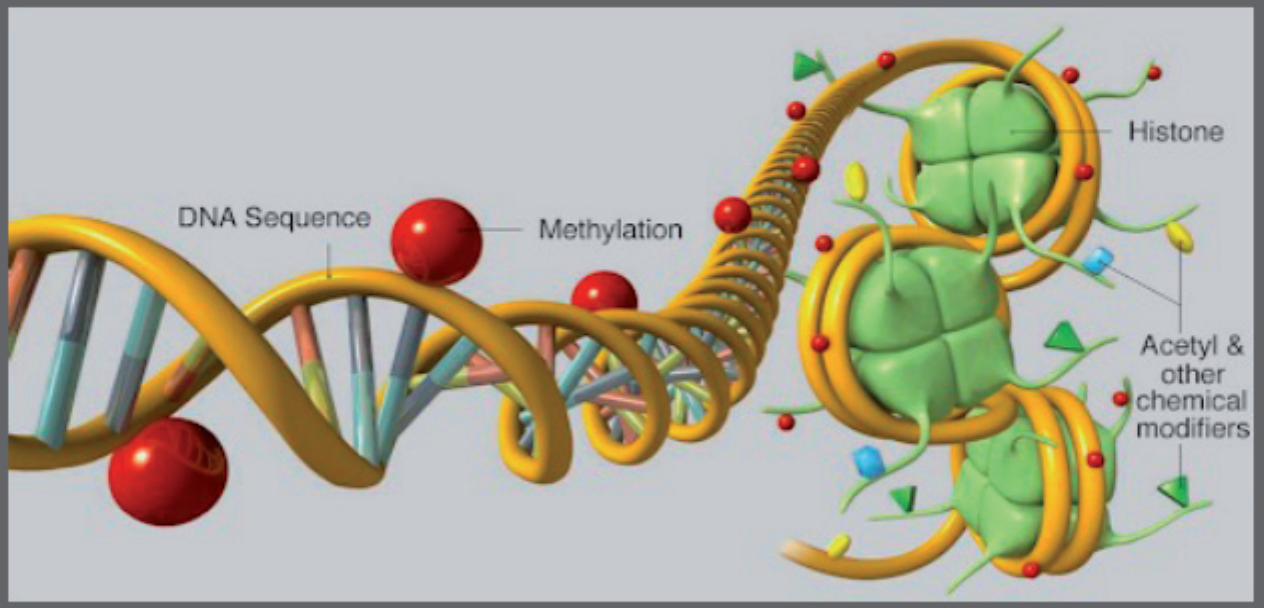
PERSONAL GENETICS
OMOCISTEIN - METHYLATION



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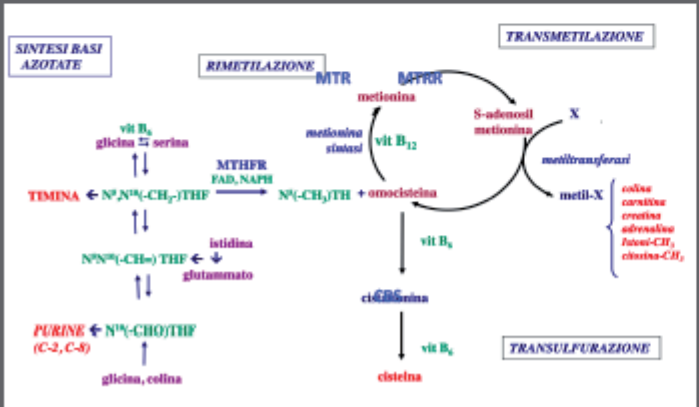
PERSONAL GENETICS
OMOCISTEIN - METHYLATION

Metabolismo dell'omocisteina, sintesi della metionina e metilazione.
Deficit di metilazione è coinvolto nel metaboismo lipidico.
Ipometilazione > BMI

Marker chimico: omocisteina ematica elevata necessita supplementazione vitamine gruppo B fino a omeostasi > controllo spessore carotideo



GENE	VARIANTI	RSnumber	Nucleotide	Variazione	Interpretazione
CBS	C699T	rs234706	C	T	TT= possibile fattore di prevenzione per eventi cardiovascolari-alta sensibilità all'attività dell'acido folico nell'abbassamento dei livelli di omocisteina CC-possibile fattore di rischio per eventi cardiovascolari
	T1080C	rs1801181	T	C	CC= possibile fattore di prevenzione per eventi cardiovascolari-alta sensibilità all'attività dell'acido folico nell'abbassamento dei livelli di omocisteina TT=possibile fattore di rischio per eventi cardiovascolari
MTHFR	C677T	rs1801133	C	T	Presenza allele T (CT o TT) – correlato a bassi livelli di B12 e folati, alti livelli di omocisteina
	A1298C	rs1801131	A	C	Presenza allele C (AC o CC) – correlato a riduzione di B12 e folati e aumento livelli di omocisteina
MTR	A2756G	rs1805087	A	G	Presenza allele G (AG o GG) = correlato a aumento omocisteina e riduzione di B12 e folati
MTRR	A66G	rs1801394	A	G	Presenza allele G (AG o GG) – possibile aumento del rischio cardiovascolare
TCN2	776C/G	rs1801198	C	G	GG-possibile aumento dell'omocisteinemia e riduzione della VitB12

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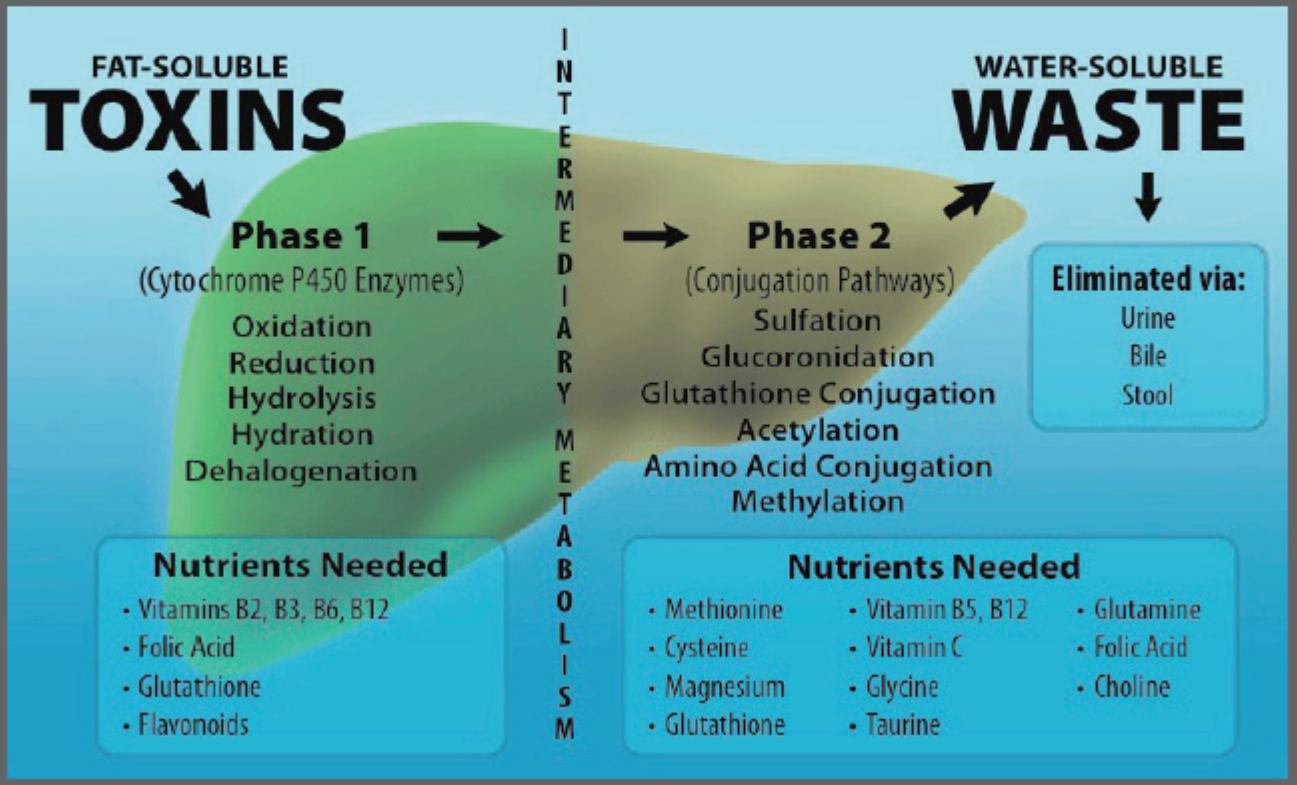
PERSONAL GENETICS
DETOXI



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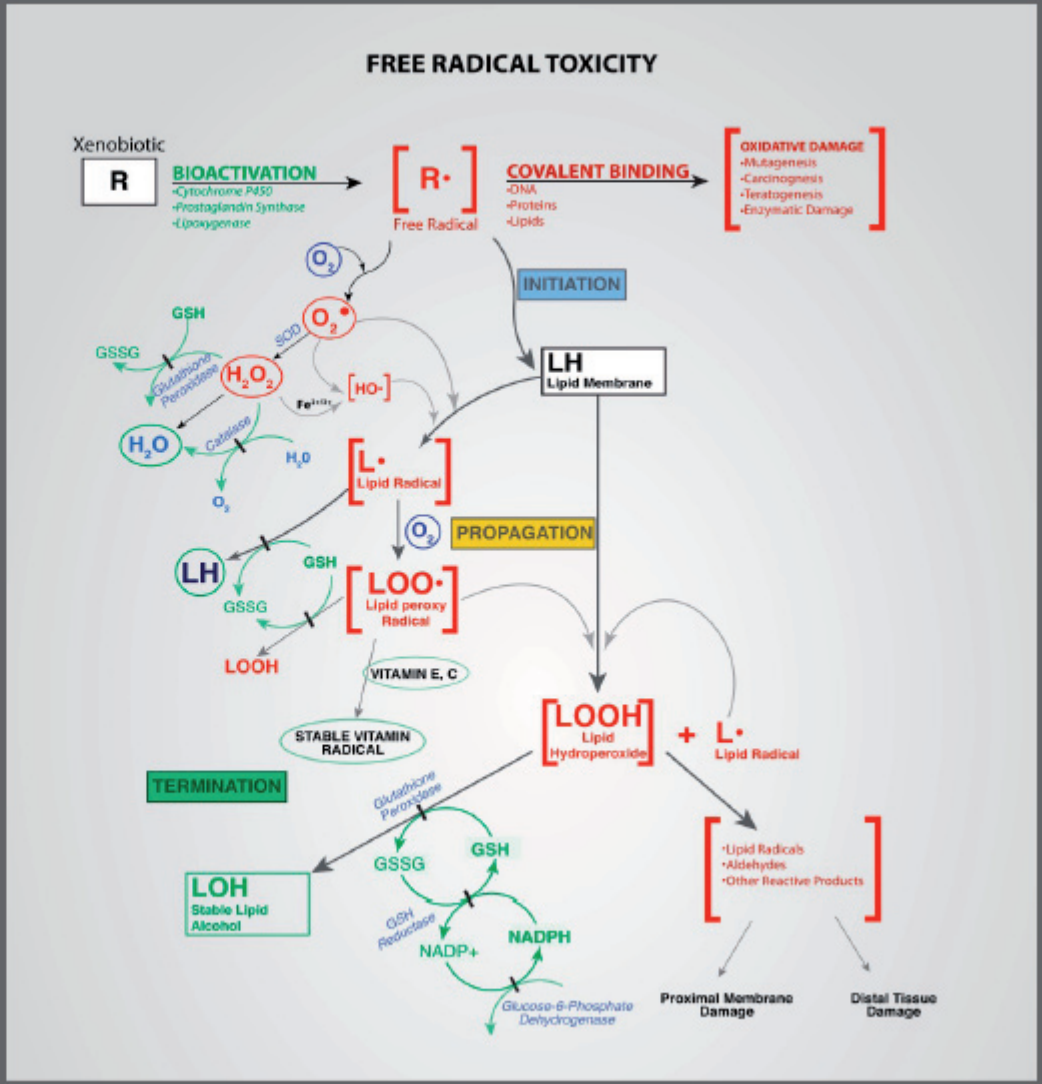
PERSONAL GENETICS DETOXI

The metabolism of xenobiotic agents is a complex pathway of various genes that can rise to stable products or to free radicals with increased cytotoxicity.

Breaking down the role of each gene is an improper action. The different efficiency of the polymorphisms / variants is not a discriminating element in the behavior of life, which envisages as a central point the control of xenobiotic agents before contact.

The polymorphic data show little selective pressure, ethnic dependent behavior, sometimes concomitant detrimental-protective action.



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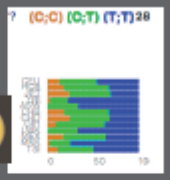
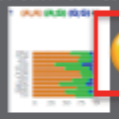
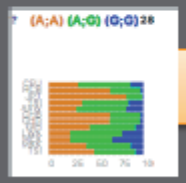
PERSONAL GENETICS
DETOXI

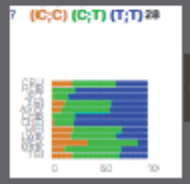


Retroattivo. Tested on carcinogen exposure and prognosis of diseases





(A;A) 0 /normal asthma risk in certain populations (A;G) ? (G;G) 2.1 3.5x /asthma risk in certain populations LS



SUOX

The **SUOX** gene codes the mitochondrial enzyme, sulfite oxidase. Sulfite oxidase is a metallo-enzyme that uses a molybdopterin cofactor and a heme group to oxidize sulfite to sulfate.

SLC6A4/ 5HTTPLR	Ins/Del	rs25531			S/S=lento adattamento S/L=medio adattamento L/L=rapido adattamento
CAT	C-262T	rs1001179	C	T	Presenza allele T (CT o TT) = possibile diminuzione della capacità detossificante
	Y113H	rs1051740	T	C	Presenza allele C (TC o CC) = possibile ridotta capacità detossificante e antiossidante
EPHX1	H139R	rs2234922	A	G	possibile ridotta capacità detossificante e antiossidante
GPX1	P200L	rs1050450	C	T	Presenza allele T (CT o TT) = possibile ridotta capacità
GSTM1	Del gene				Del gene: ridotta capacità di detossificazione
GSTP1	I105V	rs1695	A	G	Presenza allele G (AG o GG) = possibile ridotta capacità detossificante e antiossidante
	A114V	rs1138272	C	T	Presenza allele T (CT o TT) = possibile ridotta capacità detossificante e antiossidante
GSTT1	Del gene				Del gene: ridotta capacità di detossificazione
MnSOD	A16V	rs4880	C	T	Presenza allele T (CT o TT) = possibile aumento del rischio cardiovascolare
	T175C	rs1141718	T	C	Presenza allele C (TC o CC) = possibile fattore di rischio cardiovascolare e ridotta capacità antiossidante
SOD3	C760G	rs1799895	C	G	Presenza allele G (CG o GG) = possibile ridotta capacità detossificante e antiossidante, e possibile fattore di rischio cardiovascolare
SUOX	Q364X		C	T	Presenza allele T (CT o TT) = possibile aumento del rischio di accumulo di solfiti e neurotossicità
	S370S	rs773115		C	Presenza allele C (GC o CC) = possibile aumento del rischio di accumulo di solfiti e neurotossicità
	S370Y		C	A	Presenza allele A (CA o AA) = possibile aumento del rischio di accumulo di solfiti e neurotossicità

Retroattivo. Tested on carcinogen exposure and prognosis of diseases. No pressione selettiva.

HS. Dati uniformi da studi diversi. G selezionato a sfavore M1

No metaanalisi, pochi studi contraddittori
Tested on carcinogen exposure

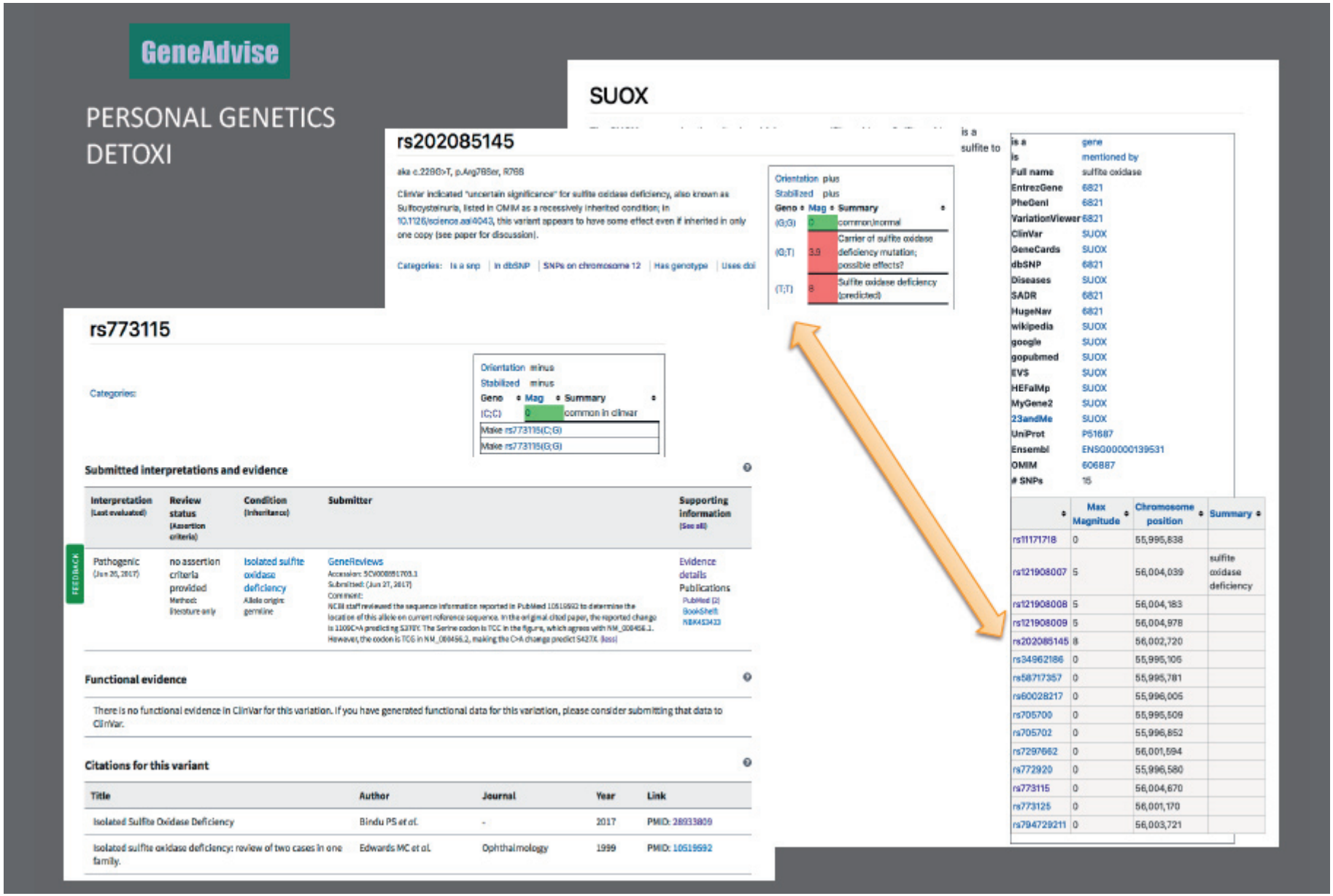
Contraddittorio. Protettivo/detrimente diversi tessuti

Contraddittorio. Protettivo/detrimente

4

NUTRINEXT
NUTRIZIONE SU MISURA

	Cod TAGA	381del			Del cod 381= possibile aumento del rischio di accumulo di solfiti e neurotossicità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PERSONAL GENETICS
DETOXI
SUOX
is a
sulfite to
rs202085145
aka c.2290>T, p.Arg788Ser, R768
ClinVar indicated "uncertain significance" for sulfite oxidase deficiency, also known as Sulfocysteinuria, listed in OMIM as a recessively inherited condition; in 10.1126/science.aal4043, this variant appears to have some effect even if inherited in only one copy (see paper for discussion).
Categories: Is a snp | In dbSNP | SNPs on chromosome 12 | Has genotype | Uses dbi
Orientation plus
Stabilized plus
Geno Mag Summary
(G;G) 0 common/normal
(G;T) 3.9 Carrier of sulfite oxidase deficiency mutation; possible effects?
(T;T) 8 Sulfite oxidase deficiency (predicted)
is a gene
is mentioned by
Full name sulfite oxidase
EntrezGene 6821
PheGenI 6821
VariationViewer 6821
ClinVar SUOX
GeneCards SUOX
dbSNP 6821
Diseases SUOX
SADR 6821
HugeNav 6821
wikipedia SUOX
google SUOX
gopubmed SUOX
EVS SUOX
HEFalMp SUOX
MyGene2 SUOX
23andMe SUOX
UniProt P51687
Ensembl ENSG00000139531
OMIM 606887
SNPs 16
rs773115
Categories:
Orientation minus
Stabilized minus
Geno Mag Summary
(C;C) 0 common in clinvar
Make rs773115(C;G)
Make rs773115(G;G)
Submitted interpretations and evidence
Interpretation (Last evaluated)
Review status (Assertion criteria)
Condition (Inheritance)
Submitter
Supporting information (See all)
Pathogenic (Jun 20, 2017)
no assertion criteria provided
Method: literature only
Isolated sulfite oxidase deficiency
Allele origin: germline
GeneReviews
Accession: SCV000551703.1
Submitted: (Jun 27, 2017)
Comment:
NCBI staff reviewed the sequence information reported in PubMed 10519592 to determine the location of this allele on current reference sequence. In the original cited paper, the reported change is 1109C>A predicting S370Y. The Serine codon is TCC in the figure, which agrees with NM_000456.1. However, the codon is TCG in NM_000456.2, making the C>A change predict S427X. (less)
Evidence details
Publications
PubMed (2)
BookShelf
NBK453433
FEEDBACK
Functional evidence
There is no functional evidence in ClinVar for this variation. If you have generated functional data for this variation, please consider submitting that data to ClinVar.
Citations for this variant
Title
Author
Journal
Year
Link
Isolated Sulfite Oxidase Deficiency
Bindu PS et al.
-
2017
PMID: 28933809
Isolated sulfite oxidase deficiency: review of two cases in one family.
Edwards MC et al.
Ophthalmology
1999
PMID: 10519592
Max Magnitude
Chromosome position
Summary
rs11171718 0 55,995,838
rs121908007 5 56,004,039 sulfite oxidase deficiency
rs121908008 5 56,004,183
rs121908009 5 56,004,978
rs202085145 8 56,002,720
rs34962186 0 55,995,106
rs58717357 0 55,995,781
rs60028217 0 55,996,005
rs705700 0 55,995,509
rs705702 0 55,996,852
rs7297662 0 56,001,594
rs772920 0 55,996,580
rs773115 0 56,004,670
rs773125 0 56,001,170
rs794729211 0 56,003,721

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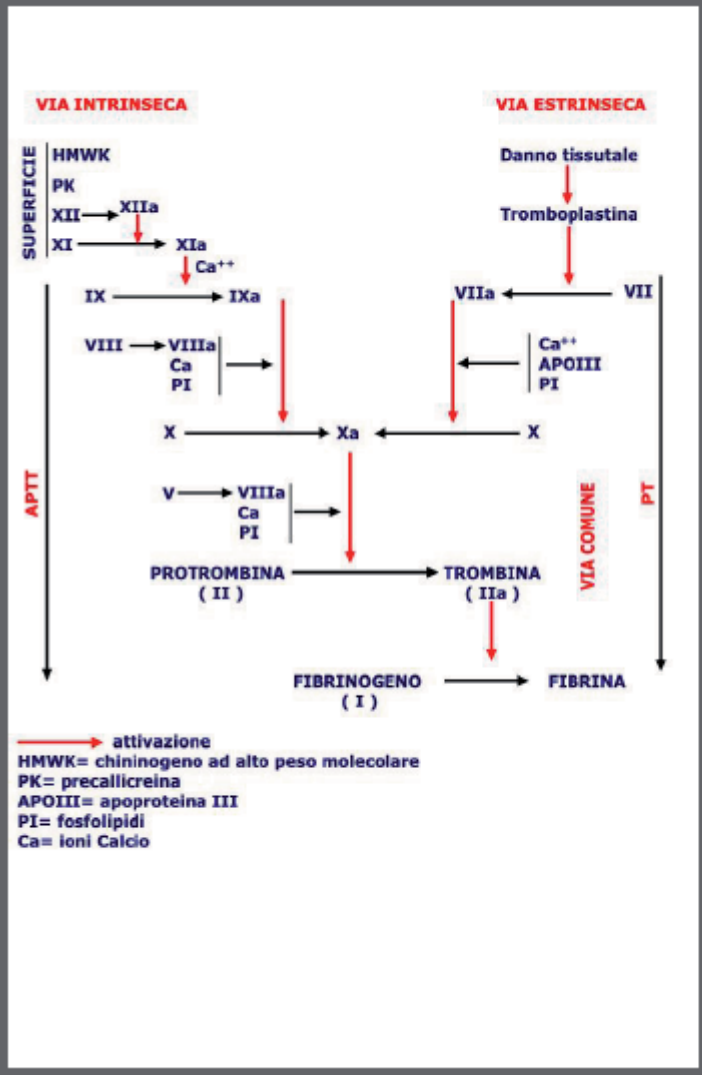
PERSONAL GENETICS
COAGULATION FACTORS

HYPERTENSIVE FACTORS
RENIN-ANGIOTENSIN
APOLIPOPROTEINS



With the completion of human genome sequencing and entering the-Omics area, the new term “Nutritional Genomics” tends to replace the former “nutrient-gene interactions”. It has been demonstrated that numerous genetic polymorphisms can influence protein structure function. The Nutritional genomic area includes two parts: first Nutrigenomics that is the study of interaction between dietary components and the genome, and the regulating changes in proteins and other metabolism; second Nutrigenetics that identify the response to dietary components with regard to genetic differences. Nutrients are as environmental factors can interact with genetic material. It has been clearly demonstrated that DNA metabolism and repair depend on a wide range of dietary factors that act as cofactors or substrates in metabolic pathway, but much less is known about the impact of cofactors and/or micronutrients deficiency or excess on the fidelity of DNA replication and repair. Although the nutrients can influence the development of a particular phenotype, the response to a specific nutrient that determined by the individual genotype has also to be considered. The central role of genetic code in determining genome stability and related health outcomes such as developmental defects, degenerative diseases, and cancer is well-established. The etiology of complex chronic diseases obviously relates to both environmental and genetic factors. Specifically, the “fetal basis of adult disease” or “early origins hypothesis” postulates that nutrition and other environmental factors during prenatal and early postnatal development influence gene expression and cellular plasticity, which can alter susceptibility to adult diseases (cardiovascular diseases, diabetes, obesity). The concept of nutrients effects on DNA stability, repair and on the different gene expression processes, recently became more prominent in nutritional science. Numerous dietary components can alter genetic and epigenetic events and therefore influence health. SNPs (single nucleotide polymorphisms) are the most common genetic variation, occur at about 500–2000 bp throughout the human genome, and normally found in at least 1% of the population. Many human studies have demonstrated the evidence for interaction between SNPs in various genes and the metabolic response to the diet. Moreover, SNPs analysis provides a potential molecular tool for investigating the role of nutrition in human health, diseases and identification of optimal diets. Nutrients and genome interact at two levels: 1) Nutrients can induce or repress gene expression thereby altering individual phenotype. 2) Conversely, single nucleotide polymorphisms can alter the bioactivity of important metabolic pathways and mediators and influence the ability of nutrients to interact with them.

NUTRIGENETICS

Nutrigenetics term was used first time by Dr R.O Brennan in 1975 in his book Nutrigenetics. Nutrigenetics points to understanding how the genetic background of an individual impact to the diet. The study of gene-nutrient interaction is a developing area of science. This idea that adverse diet/genome interaction can cause disease is not new and the unsuitable diet for any individual genotype could be a risk factor for monogenetic and polygenetic disease. Genetic polymorphisms can influence response to environmental elements,

such as enzymatic activities changes that affect circulating concentrations and ultimately the effectiveness of chemicals and their metabolites. Furthermore, metabolic disorders are other examples of influence of the genetic variations to diet such as PKU, defects associated with long chain fatty acid oxidation, iron absorption (haemochromatosis), which can be reasonably well managed with dietary restrictions. As mentioned earlier SNPs study can be categorized in the field of Nutrigenetics. Some specific examples of the association between SNPs and specific food components such as enzymes deficiency are reviewed in this article. For example, different mutations in galactose-1-phosphate uridyltransferase (GALT) gene, phenylalanine hydroxylase gene, and Glucose-6-phosphate dehydrogenize (G6PD) gene resulted in Galactosemia, Phenylketonuria (PKU), and Favism diseases, respectively. Other examples of enzyme polymorphisms include Lactase-phlorizin hydrolase gene (LPH) polymorphisms that show how SNPs alter gene expression. This polymorphism is in the upstream of the lactase-phlorizin hydrolase gene (LPH) associated with hypolactasia and changes tolerance to dietary lactose (milk sugar, LPH hydrolyzes lactose into glucose and galactose) and allows different expression of the LPH. Glutathione peroxide gene polymorphism is another example. The association between selenium supplementation and reduced incidence of liver, colon, prostate, and lung cancer in human has been shown. However, no individuals may respond equally. Glutathione peroxide is a selenium-dependent enzyme that acts as an antioxidant enzyme. Polymorphism at codon 198 of human glutathione peroxides results in a substitution of proline to leucine amino acid, and has been associated with an increased risk of lung cancer. Investigators shown that persons with (Pro/Lue) genotype were at 80% greater risk for lung cancer and (Lue/Lue) genotypes were at 130% greater risk compared risk those with the (Pro/Pro) genotype. The leucine-coding allele was less responsive to increased activity because of selenium supplementation as compared with the proline-containing allele. Manganese super oxide dismutase (MnSOD) is a mitochondrial enzyme that plays a key role in detoxification of reactive oxygen species. A polymorphism valine to alanine substitution in in this enzyme alters its transport into mitochondria, which has been associated with increased risk of breast cancer. Methylene tetrahydrofolate reductase (MTHFR) enzyme catalyzes the reaction that produces 5-methyl tetrahydrofolate. The one-carbon units are carried on N-5 or N10 of tetrahydrofolate. One-carbon metabolism is needed for the de novo synthesis of purine nucleotides and thymydilate and for the re methylation of homocysteine to methionine. With methionine adenylation S-adenosylmethionine (SAM) is formed, which is a cofactor for numerous methylation reactions such as DNA methylation that affect gene regulation. For the MTHFR gene tow important SNPs has been well recognized: C677T (cytosine-to-thymidine substitution resulting in the conversion of an alanine to valine) and A1298C (adenine-to-cytosine substitution resulting in the conversion of an alanine to glutamic acid). The C677T polymorphism is the most common variant that occurs as homozygous T/T in 5–10% of the and as heterozygous C/T genotypes up to 40% general population. The presence of C677T or A1298C mutations is associated with reduction in MTHFR enzyme activity and impairs

folate accumulation, which may cause increases homocysteine concentration in plasma, a risk factor for venous thromboembolic and ischemic arterial diseases. Another polymorphism of MTHFR gene is Ala222Val that affects folate metabolism. It increases the conversion of dUMP to dTMP and leads to more folate-dependent thymidine biosynthesis and folate deficiency. This polymorphism is a risk factor for spontaneous abortions and decreased fetal viability, thus maternal folate supplementation can be useful for individuals with this polymorphism. MTHFR is also involved in maintenance genomic CpG methylation patterns and prevention of DNA strand breaks, these mutations are associated with increased risk of neural tube defects and some types of cancer. Changes in the concentration of folate (the MTHFR substrate) and riboflavin (the MTHFR cofactor) can modulate the activity of MTHFR gene. Generally, folic acid supplementation can help the negative health effect of these SNPs with decrease in plasma homocysteine levels. Enzymes that utilize and metabolize vitamin B12 have been associated with NTDs, increased risk of Down syndrome and colon cancer. For example, a common polymorphism in the HFE gene (Cys282Tyr) is associated with iron storage disease hereditary haemochromatosis, leading to an iron accumulation in the liver, heart and endocrine glands. This protein is an important regulator of cellular iron homeostasis and has role in intestinal iron absorption by regulating the interaction of the transferrin receptor with transferrin. Cytochrome P450s (CYPs) enzymes play a central role in the oxidative biotransformation of steroids, prostaglandins, nutrients, drugs, chemicals and carcinogens. Several dietary factors can alter the expression of CYP isoforms. CYP1A2 plays an essential role in the metabolism of wide range of drug and chemical substances. For example, CYP1A2 activates dietary carcinogens such as aromatic amines, but also detoxifies compounds such as caffeine. Low-activity CYP1A2 genotype with an increased risk of myocardial infarction suggests that this enzyme detoxify a substance, which may be an important risk factor in the population. Indeed, individuals with a low-activity CYP1A2 genotype are at a greater risk of coffee-associated heart disease. As caffeine is the main substance in coffee and is detoxified by CYP1A2, it may be an important risk factor for heart disease in certain population. Glutathione S transferase (GST) enzyme is a superfamily of enzymes that play an important role in the detoxification of several dietary compounds. GSTM1, GSTT1 and GSTP1 are isoforms of this enzyme. The GSTM1 and GSTT1 null genotype have been associated with both an increased and a decreased risk of some types of cancers such as breast cancer. Some components such as dietary isothiocyanates that are found in cruciferous vegetables are eliminated with GSTs enzymes. Indeed, protective effect of the GSTM1 null genotype on colon and lung cancer has been related to lower urinary excretion of glutathione-conjugated phytochemicals indicating they are not rapidly excreted. GSTT1 plays a similar role to GSTM1 in eliminating beneficial phytochemicals found in cruciferous vegetables. Moreover, in vegetables rich in phytochemicals such as isothiocyanates the expression of GSTs is increased conjugating them to more water-soluble forms that are easily excreted.

Endothelial nitric oxide synthase (eNOS) is synthesized from the amino acid L-arginine by NO synthase (NOS). The eNOS is expressed in the endothelium and produces NO that diffuses to vascular smooth muscle cell, where it increases the concentration of cGMP, leading to vascular relaxation. NO has central role in the pathogenesis of coronary spasm and atherogenesis. Several polymorphisms of eNOS may be associated with specific phenotype. For example, a Glu298Asp polymorphism in the eNOS gene has been associated with ischemic heart disease, myocardial infarction, and coronary spasm. Genetic polymorphisms in catechol-O-methyltransferase, sulfotransferase, and UDP-glucuronosyltransferase result in differences in enzymatic activity. These enzymes metabolize some of dietary compounds. For example, green tea was associated with a lower risk of breast cancer only in women with the low-activity allele for catechol-O-methyltransferase. This enzyme catalyzes the methylation of catechins (a polyphenolic antioxidant plant secondary metabolite) in green tea making them more quickly eliminated (5). Apolipoprotein E (ApoE) gene has three different alleles (□2, □3, □4). Persons with □4 variant respond to a high-fat diet negatively with an increased risk for coronary heart disease (CHD). In these individuals, low-fat diet should be useful. Moreover, there is an important relationship between allelic variants in the ApoA1/C3/ A4/A5 genes and the effect of dietary fats on lipoprotein metabolism and CVD (cardio vascular diseases) risk. Linkage disequilibrium within Apo A1/C3/A4/A5 cluster has been represented to affect plasma lipid concentration and CVD risk. Apolipoprotein A-1 is and is a key component of high-density lipoprotein particles (HDL). The locus of gene encoding APOA-1 is on chromosome 11q and highly polymorph and has a specific SNP in its promoter region. An Adenine/Guanine substitution in the promoter region (–75bp) of the ApoA1 gene is common in different populations. The presence of A allele (A/A and A/G) has been associated with incresed HDL-cholesterol. Moreover, mild increase in APOA-1 concentrations in subjects with the G/G genotype was observed. APOA-5 gene is also an important regulator of triglyceride (TG)-rich lipoprotein (TRL) metabolism. One of the Vitamin D receptor (VDR) polymorphism is FokI. Individuals with F allele have three amino acids more than those without F allele in their VDR. The Ff or ff genotype is associated with 51% and 84% greater risk of colorectal cancer, respectively. Individuals that consumed low calcium and fat diet have more than double risk of colorectal cancer, specifically in persons with ff genotype rather than Ff genotype. VDR polymorphisms have been also associated with childhood and adult's asthma. Peroxisome proliferator-activated receptors (PPARs) are nuclear receptor supper family that plays an essential role in fatty acid oxidation, glucose, and extracellular lipid metabolism. PPARs are the best-known fatty-acid-regulated nuclear receptors. One of the three members of the PPARs family regulates many genes involved in fatty acid metabolism. PPR-□ (PPARA) plays a central role in lipid oxidation and inflammation, whereas PPAR-□ is involved in adipocytes differentiation, glucose and lipid storage, and inflammation. PPAR-□ (also known as PPAR-□), may has a crucial role in development, lipid metabolism, and inflammation. These receptors bind to fatty acid and regulate the expression of genes involved in fatty acid transport

and metabolism. PPARs family also involve in activation of about 300 genes. The PPAR-□ gene has a polymorphism at codon 162 (Lue162Val) that has been associated with changes in total cholesterol, LDL-associated cholesterol, and Apo B concentrations. The less common V162 allele is associated with significantly higher serum concentration of total cholesterol, LDL cholesterol, Apo B, and Apo C-III than in carriers of L162 allele, especially in men. For individuals with the common L162 allele, increased intake of polyunsaturated fatty acids (PUFAs) had little effect on fasting triacylglycerol concentrations. In those with the less common V162 allele, however, fasting triacylglycerol concentrations fell abundantly with increasing PUFA intake

GENES ASSOCIATED WITH SPORT

Caffeine, found naturally occurring in several plant species including coffee, tea, cocoa, and guarana, is widely used in sport as a performance enhancer or ergogenic aid often in the form of caffeinated tablets, gels or chews. In the field of nutrigenomics, caffeine is the most widely researched compound with several randomized controlled trials investigating the modifying effects of genetic variation on athletic performance. Numerous studies have investigated the effect of supplemental caffeine on exercise performance, but there is considerable inter-individual variability in the magnitude of these effects, or in the lack of an effect when compared to placebo. These inter individual difference appear to be partly due, to variation in genes such as CYP1A2 and possibly ADORA2, which are associated with caffeine metabolism, sensitivity and response. Over 95% of caffeine is metabolized by the CYP1A2 enzyme, which is encoded by the CYP1A2 gene. The–163A>C (rs762551) single nucleotide polymorphism (SNP) has been shown to alter CYP1A2 enzyme activity, and has been used to identify individuals as “fast” or “slow” metabolizers of caffeine. Individuals who are considered slow metabolizers, that is with the AC or CC genotype, have an elevated risk of myocardial infarction, hypertension and elevated blood pressure, and pre-diabetes, with increasing caffeinated coffee consumption, whereas those with the AA genotype (fast metabolizers) do not appear to carry these risks. The largest caffeine and exercise study to date, examined the effects of caffeine and CYP1A2 genotype, on 10-km cycling time trial performance in competitive male athletes after ingestion of caffeine at 0 mg, 2 mg (low dose) or 4 mg (moderate dose) per kg body mass. There was a 3% improvement in cycling time in the moderate dose in all subjects, which is consistent with previous cycling time trial studies using similar doses. However, there was a significant caffeine-gene interaction where improvements in performance were seen at both caffeine doses, but only in those with the AA genotype who are “fast metabolizers” of caffeine. In that group, a 6.8% improvement in cycling time was observed at 4 mg/kg, which is >2–4% mean improvement seen in several other cycling time trial studies, using similar doses. Among those with the CC genotype, 4 mg/kg caffeine impaired performance by 13.7%, and in those with the AC genotype there was no effect of either caffeine dose. The findings are consistent with a previous study, which observed a caffeine-gene interaction and improved time trial cycling performance with caffeine only in those with the AA genotype. Some previous endurance-type studies either did not observe

any impact of the CYP1A2 gene on caffeine-exercise studies, or reported benefits only in slow metabolizers. There are several reasons that may explain discrepancies in study outcomes including smaller sample sizes (<20 subjects) that cause very low numbers and/or no subjects with the CC genotype, and shorter distance or different type (power vs. endurance) of performance test , compared to those that reported improved endurance after caffeine ingestion in those with the AA genotype of CYP1A2. The effects of genotype on performance appear to be most prominent during exercise of longer duration or an accumulation of fatigue (aerobic or muscular endurance) (69, 70). Fast metabolizers may quickly metabolize caffeine and achieve the benefits of caffeine metabolites as exercise progresses, or override the short duration of negative impacts (the initial stages of exercise), whereas the adverse effects of restricted blood flow and/or other impacts of adenosine blockage in slow metabolizers are likely to remain for a longer duration. Indeed, in a study of basketball performance in elite players, caffeine improved repeated jumps (muscular endurance; an accumulation of fatigue), but only in those with the AA genotype, however, there was no genotype effect in the other two performance components of the basketball simulation. Similarly, a cross-over design of 30 resistance-trained men found that caffeine ingestion resulted in a higher number of repetitions in repeated sets of three different exercises, and for total repetitions in all resistance exercises combined, which resulted in a greater volume of work compared to placebo conditions, but only in those with the CYP1A2 AA genotype. Taken together, the weight of the evidence supports the role of CYP1A2 in modifying the effects of caffeine ingestion on aerobic or muscular endurance-type exercise. The ADORA2A gene is another potential genetic modifier of the effects of caffeine on performance. The adenosine A2A receptor, encoded by the ADORA2A gene, has been shown to regulate myocardial oxygen demand and increase coronary circulation by vasodilation. The A2A receptor is also expressed in the brain, where it regulates glutamate and dopamine release, with associated effects on insomnia and pain. The antagonism of adenosine receptors by caffeine could differ by ADORA2A genotype, resulting in altered dopamine signaling. Dopamine has been associated with motivation and effort in exercising individuals, and this may be a mechanism by which differences in response to caffeine are manifested. One small pilot study has examined the effect of ADORA2A genotype (rs5751876) on the ergogenic effects of caffeine under exercise conditions. Twelve female subjects underwent a double-blinded, crossover trial comprising two 10-min cycling time trials following caffeine ingestion or placebo. Caffeine benefitted all six subjects with the TT genotype but only one of the six C allele carriers. Further studies are needed to confirm these preliminary findings and include a larger sample to distinguish any effects between the different C allele carriers (i.e., CT vs. CC genotypes). Sleep is recognized as an essential component of physiological and psychological recovery from, and preparation for, high- intensity training in athletes. The ADORA2A rs5751876 genotype has also been implicated, by both objective and subjective measures, in various parameters of sleep quality after caffeine ingestion in several studies. Adenosine promotes sleep by binding to its receptors in the brain, mainly A1 and A2A receptors, and caffeine reverses these effects by blocking the adenosine

receptor, which promotes wakefulness. This action, as well as the potency of caffeine to restore performance (cognitive or physical) in ecological situations, such as highway-driving during the night, support the notion that the adenosine neuromodulator/ receptor systemplays a major role in sleep–wake regulation. This action of caffeine may also serve athletes well under conditions of jetlag, and irregular or early training or competition schedules. Psychomotor speed relies on the ability to respond, rapidly and reliably, to randomly occurring stimuli which is a critical component of most sports. Genetic variation in ADORA2A has been shown to be a relevant determinant of psychomotor vigilance in the rested and sleep-deprived state and modulates individual responses to caffeine after sleep deprivation. In support of this notion, individuals who had the TT genotype for ADORA2A rs5751876 consistently had faster response times (in seconds) than C allele carriers after ingesting 400 mg caffeine during a sustained vigilant attention task after sleep loss. Consistent with the "adenosine hypothesis" of sleep where the accumulation of adenosine in the brain promotes sleep, caffeine prolongs the time to fall asleep, decreases the deep stages of non-rapid-eye movement (not REM) sleep, reduces sleep efficiency, and alters the waking and sleep electroencephalogram (EEG) frequencies, which reliably reflect the need for sleep. Although additional research in this area is warranted, genetic variation appears to contribute to subjective and objective responses to caffeine on sleep. Carriers of the ADORA2A (rs5751876) C allele have greater sensitivity toward caffeine- induced sleep disturbance compared to those with the TT genotype. Taken together, it appears that individuals with the TT genotype for the rs5751876 SNP in the ADORA2A gene may have better performance outcomes, faster response times and less sleep disturbance following caffeine ingestion.

Vitamin A. No studies have examined the role of genetic modifiers of vitamin A status directly on athletic performance, however, there are several important functions of this micronutrient that are associated with optimal health, immunity and performance in athletes. Vitamin A is a fat-soluble vitamin, which plays a key role in both vision and immunity in its biologically active forms (retinal and retinoic acid). Vitamin A has diverse immune modulatory roles; hence, vitamin A deficiency has been associated with both immune dysfunctions in the gut, and several systemic immune disorders. Vitamin A is also a powerful antioxidant, protecting eyes from ocular diseases and helping to maintain vision. High-performance athletes appear to have superior visual abilities based on their capacity to access distinct visual skills, such as contrast sensitivity, dynamic acuity, stereoacuity, and ocular judgment, needed to accomplish interceptive actions (e.g., hand-eye coordination) and resolve fine spatial detail, which is required by many sports. In addition, slow visuomotor reaction time (VMRT) has been associated with musculoskeletal injury risk in sporting situations where there are greater challenges to visual stimulus detection and motor response execution. These visuomotor skills are key contributors to enhanced sport performance, and accordingly, require exceptional eye health. Deficiencies of certain micronutrients such as vitamin A decrease immune defense against invading pathogens and can cause the athlete to be more susceptible to infection. Low energy availability (dieting), poor

food choices, jetlag, physical and psychological stress, and exposure to pollution and foreign pathogens in air, food and water while traveling can result in a deterioration in immune function and increased susceptibility to illness. Athletes following high volume, high intensity training and competition schedules are also known to have more frequent upper respiratory tract infections (URTI) compared to both sedentary and moderately exercising populations. Upon absorption, provitamin A carotenoids are readily converted to vitamin A by the BCMO1 enzyme expressed in enterocytes of the intestinal mucosa. β-Carotene is the most abundant provitamin A carotenoid in the diet and the conversion of beta-carotene to retinal or retinoic acid is necessary for vitamin A to exert its biological functions. The rs11645428 variant in the BCMO1 gene affects circulating plasma carotenoid levels by impacting the conversion of dietary provitamin A carotenoids to active forms of vitamin A in the small intestine. Individuals with the GG genotype are inefficient at this conversion, and may be at higher risk for vitamin A deficiency. These individuals are considered low responders to dietary β-carotene so consuming enough dietary pre-formed vitamin A (or supplements for vegans), can help to ensure that circulating levels of active vitamin A are adequate to support vision, immunity and normal growth and development. Anemia-Related Micronutrients: Iron, Folate, and Vitamin B12 There is an abundance of research demonstrating the adverse effects of low iron storage and anemia on athletic performance. The estimated prevalence of anemias and low levels of iron, folate, and vitamin B12 appear to be higher in elite-level athletes than in the general population, and these deficiencies can have significant negative impacts on performance. The most common symptoms of this disorder are fatigue, weakness and, in extreme cases, shortness of breath or palpitations. The importance of iron to athletes is established through its biological role in supporting the function of proteins and enzymes essential for maintaining physical and cognitive performance. Iron is incorporated into hemoglobin and myoglobin, proteins responsible for the transport and storage of oxygen. Iron-deficiency anemia is the most common type of anemia among athletes, who have higher iron requirements due to increased erythropoietic drive through higher intensities and volumes of training. The female athlete is at particular risk of iron deficiency due to menstruation and generally, a lower total energy or food intake compared to males. Along with dietary intake, foot strike hemolysis, gastrointestinal bleeding, exercise-induced inflammation, non-steroidal autoinflammatory drug (NSAID) use and environmental factors such as hypoxia (altitude), may influence iron metabolism in athletes of both sexes. Macrocytic anemias, which occur when erythrocytes are larger than normal, are generally classified into megaloblastic or not megaloblastic anemia. Megaloblastic anemia is caused by deficiency or impaired utilization of vitamin B12 and/or folate, whereas non-megaloblastic macrocytic anemia is caused by various diseases, and will not be discussed here. Other factors that are associated with anemia risk include genetic variation, which can alter micronutrient metabolism, transport or absorption, and can be used to identify individuals at risk of inadequate levels of vitamin B12, folate and iron stores. Performance improvements are usually seen with the treatment of anemia, which is related to improvements in symptoms such as general feelings of

fatigue and weakness, difficulty exercising, and in more severe cases, dyspnea and palpitations. Hyperhomocysteinemia, which can result from low folate and/or vitamin B12 intake, may also increase the risk of skeletal muscle malfunction, including muscle weakness and muscle regeneration, and will be discussed further below

Folate. Methylene tetrahydrofolate reductase (MTHFR) is the rate- limiting enzyme in the methyl cycle, and is encoded by the MTHFR gene (112). The C677T (rs1801133) polymorphism in the MTHFR gene has been associated with low serum and red blood cell folate as well as elevated plasma homocysteine levels, which is an independent risk factor for cardiovascular disease (CVD). Several studies in athletic and non-athletic populations have shown that individuals with the CT or TT genotype are at an increased risk of low circulating folate levels when their diet is low in folate. Although there are no studies examining performance outcomes related to MTHFR genotypes or dietary folate intake, hyperhomocysteinemia has been shown to be associated with diminished muscle function. Several studies conducted in older adults have found a significant association between elevated plasma homocysteine concentrations and declined physical function, which may be mediated by a reduction in strength. Compared to those with the rs1801133 CC genotype, individuals with TT genotype and possibly the CT genotype may be at a greater risk for hyperhomocysteinemia, although this may not be causative for lower physical performance. However, soccer players and sedentary individuals with the CC genotype have been shown to have more favorable body composition and performance measures such as aerobic and anaerobic threshold rates, compared to carriers of the T allele. Vitamin B12. Vitamin B12 is also associated with RBC formation and aerobic capacity. Megaloblastic anemia results from vitamin B12 deficiency and is associated with elevated homocysteine, and results in general feelings of fatigue and weakness. Megaloblastic anemia limits the blood's oxygen carrying capacity, thus reducing its availability to cells. Variation in the FUT2 gene (rs602662) has a significant impact on serum B12 levels where individuals with GG or GA genotypes possess the greatest risk for low serum vitamin B12 levels, but only when the diet is low in bioavailable sources of vitamin B12. This is consistent with previous genome-wide association studies, which found that individuals with the AA genotype had significantly higher concentrations of serum vitamin B12 compared to carriers of the G allele. Vitamin C. Vitamin C is a water-soluble antioxidant that aids in the reduction of exercise-induced free-radical production. The production of potentially harmful ROS in athletes is greater than in non-athletes due to the massive increases (up to 200-fold at the level of skeletal muscle) in oxygen consumption during strenuous exercise. Vitamin C supplementation was once thought to mitigate this risk; however, studies have shown that excess vitamin C supplementation during endurance training can blunt beneficial training-induced physiological adaptations, such as muscle oxidative capacity and mitochondrial biogenesis and may actually diminish performance. Dietary consumption of vitamin C, up to 250 mg daily from fruits and vegetables, is likely sufficient to reduce oxidative stress without having a negative effect on performance. Additionally, collagen is a key constituent of connective tissue such as tendons and ligaments, and vitamin

C is necessary for collagen production. This suggests that vitamin C may play a role in muscle growth and repair. Indeed, a recent landmark study examining collagen synthesis in athletes, reported that adding a gelatin and vitamin C supplement to an intermittent exercise protocol improves collagen synthesis and could play a beneficial role in injury prevention and accelerate musculoskeletal, ligament, and/or tendon tissue repair. The relationship between dietary vitamin C and circulating levels of ascorbic acid depend on an individual's GSTT1 genotype. Individuals who do not meet the Recommended Dietary Allowance (RDA) for vitamin C are significantly more likely to be vitamin C deficient (as assessed by serum ascorbic acid levels) than those who meet the RDA, but this effect is much greater in individuals with the GSTT1 Del/Del genotype than those with the Ins allele. Genetic testing can help to identify athletes who may be at the greatest risk of low circulating vitamin C (ascorbic acid) levels in response to intake. These low circulating ascorbic acid levels may, in turn, diminish performance through an increased risk of high ROS and diminished muscle or connective tissue repair. Although studies have identified associations between circulating ascorbic acid concentrations and vitamin C transporters, SVCT1 and SVCT2, which are encoded by SLC23A1 and SLC23A2, there is no evidence that response to vitamin C intake differs by genotype. As such, the use of variants in SLC23A1 and SLC23A2 to make personalized dietary recommendations is not supported by the studies to date. Vitamin D. There are no studies that link genetic modifiers of vitamin D status on athletic performance outcomes; however, there are several functions of this vitamin that are associated with bone health, immunity, recovery from training and various performance variables. Genetic determinants of circulating 25- hydroxyvitamin D (25(OH)D) can influence each of these factors thereby influencing performance. Vitamin D is essential to calcium metabolism, increasing calcium absorption for optimal bone health (1), which is relevant to all athletes, but particularly those participating in sports with a high risk of stress fracture. Research comparing individuals with sufficient levels to insufficient or deficient levels of 25(OH)D has shown that it helps to prevent injury, promote larger type II muscle fiber size, reduce inflammation, reduce risk of acute respiratory illness enhance functional rehabilitation, thereby optimizing recovery and acute adaptive responses to intense training through reduced inflammation and increased blood flow. Two genes that have been shown to impact vitamin D status are the GC gene and the CYP2R1 gene. Variations in the GC and CYP2R1 genes are associated with a greater risk for low serum 25(OH)D. In one study, where 50% of participants took vitamin D supplements, only 22% of the participants had sufficient serum 25(OH) D levels. In the remaining 78% who had insufficient levels, also only about half (47%) took vitamin D supplements. Within this population, vitamin D supplementation only explained 18% of the variation, compared to 30% from genetics, suggesting that genetics may play a greater role than supplementation in determining risk for low 25(OH)D levels. Out of the four genotypes analyzed, only CYP2R1 (rs10741657) and GC (rs2282679) were significantly associated with vitamin D status. Specifically, participants with the GG or GA genotype of CYP2R1 (rs10741657) were nearly four times more likely to have insufficient vitamin D levels. Those with the GG genotype of the GC gene (rs2282679)

were significantly more likely to have low vitamin D levels compared to those with the TT genotype. These results were consistent with findings from previous studies, including the Study of Underlying Genetic Determinants of Vitamin D and Highly Related Traits (SUNLIGHT), which found significance on a genome-wide basis in 15 cohorts with over 30,000 participants between three genetic variants including CYP2R1 (rs10741657) and GC (rs2282679) on vitamin D status. Not surprisingly, the number of risk variants that the participants possessed was directly related to their risk for vitamin D insufficiency. These findings demonstrate that genetic variation may be more impactful than supplementation intakes and behaviors on determining risk for vitamin D insufficiency.

Calcium. Although studies linking calcium intake, genetics and bone fracture has not been conducted in athletes specifically, genetic variation as it relates to risk of calcium deficiency and fracture risk have been studied in a large cohort of individuals, described below (167). Calcium is necessary for growth, maintenance and repair of bone tissue and impacts maintenance of blood calcium levels, regulation of muscle contraction, nerve conduction, and normal blood clotting. In order to absorb calcium, adequate vitamin D intake is also necessary. Inadequate dietary calcium and vitamin D increases the risk of low bone mineral density (BMD) and stress fractures. Low energy intakes, and menstrual dysfunction in female athletes, along with low vitamin D and calcium intakes further increase the risk of stress fractures in both males and females, and stress fractures are common and serious injuries in athletes. Some individuals do not utilize dietary calcium as efficiently as others and this may depend on variations in the GC gene. In one study, subjects (n = 6,181) were genotyped for two SNPs in the GC gene, rs7041 (VDBP gene, encodes an aspartic acid (Asp) at position 432 in the vitamin D binding protein (VDBP)) and rs4588 (encodes a threonine (Thr) at position 436 in the vitamin D binding protein (VDBP), and calcium intake was assessed in relation to the participants' risk for bone fracture (167). In the entire sample of participants, only a small increased risk of bone fracture was observed for individuals homozygous for the G allele of GC (rs7041) and the C allele of GC (rs4588). However, in participants with low dietary calcium intake (<1.09 g/day) and who were homozygous for the G allele of rs7041 and the C allele of rs4588, there was a 42% increased risk of fracture compared to other genotypes. No differences between genotypes were found in participants with high dietary calcium intakes. These findings suggest that calcium intake recommendations could be based on GC genotype in athletes to help prevent stress fracture.

Protein. The FTO gene is also known as the 'fat mass and obesity- associated gene' since it has been shown to impact weight management and body composition. Dietary interventions may mitigate genetic predispositions associated with a higher body mass index (BMI) and body fat percentage, as determined by genetic variation in the FTO gene. Specifically, the Preventing Overweight Using Novel Dietary Strategies (POUNDS Lost) multicenter trial found that carrying an A allele of the FTO gene (rs1558902–a surrogate marker for rs9939609) and consuming a high protein diet was associated with a significantly lower fat mass at the 2-year follow up period compared to carrying

two T alleles. Importantly, participants with the AA genotype (lesser effects in those with AT genotype) who were following the high protein diet protocol had significantly greater losses of total fat mass, total adipose tissue, visceral adipose tissue, lower total percent fat mass and percent trunk fat, compared to those following a lower protein diet protocol. Other studies have shown similar results where dietary protein intake was shown to be protective against the effect of the FTO risk variants on BMI and waist circumference. A randomized controlled trial (RCT) in 195 individuals showed that a hypocaloric diet resulted in greater weight loss in rs9939609 A allele carriers than noncarriers in both higher and lower protein diets, although metabolic improvements improved in all genotypes in the higher protein diets. Athletes who possess the AA genotype of the FTO gene at rs1558902 would benefit the most in terms of consuming a moderate-to-high protein diet (at least 25% of energy from protein) to optimize body composition. Greater lean mass in athletes has been associated with improved performance in strength and power sports, as well as some endurance events, and a decreased risk for injuries. For those athletes who do not possess the response variant (i.e., greater fat loss with higher protein intakes), following a diet with moderate protein intake (15–20% energy), to achieve and maintain an ideal body composition is important to note, as excess protein calories may be counterproductive toward this goal. In this instance, dietary goals for optimal performance may be better met by substituting protein energy for other macronutrients such as carbohydrates for fuel, fiber, prebiotics and other micronutrients, or by increasing intakes of essential fats.

Dietary Fat. Dietary fat, an essential component of the human diet, provides energy for aerobic endurance exercise and is necessary for the absorption of the fat-soluble vitamins A, D, E, and K. Independent of total energy intake, the percentage of energy derived from fat in an athlete's diet can impact body composition, based on genetic variation. Individuals possessing the TT genotype of TCF7L2, transcription factor 7 like 2, at rs7903146 appear to benefit from consuming a lower percent of total energy from fat (20–25% of energy) to optimize body composition. Specifically, participants with the TT genotype lost more fat mass when they were consuming a low-fat diet, compared to a high-fat diet (40–45% of energy). Moreover, individuals with the CC genotype in rs7903146 who consumed lower-fat diets actually lost significantly more lean mass, suggesting that these individuals should avoid low-fat nutrition interventions in order to optimize body composition for athletic performance. Body composition can, therefore, be optimized by targeting fat intake based on genetic variation in the TCF7L2 gene.

MonoUnsaturated Fat. Recommendations for fat intake can be further targeted to the different types of fats comprising total dietary fat. Athletes with the GG or GC genotype of the PPAR 2 gene at rs1801282 would benefit from a weight loss intervention that specifically targets body fat, while preserving lean body mass. Such individuals have been shown to demonstrate an enhanced weight loss response when consuming > 56% of total fat from monounsaturated fatty acids (MUFAs) compared to those with the GG or GC genotype who consume < 56% of total fat from MUFAs. These results

have not been found in those with the CC genotype of PPAR 2 at rs1801282 (208). MUFAs can be targeted in athletes who are aiming to decrease their body fat. It is well-known that a lower body fat percentage is associated with enhanced performance in most sports (191, 207), however, sport clinicians must be cautious about nutrition recommendations aimed at reducing body fat. Striving for very low levels of body fat is highly correlated with the Relative Energy Deficiency in Sport (RED-S) syndrome in both females and males, which refers to 'impaired physiological functioning caused by relative energy deficiency and includes impairments of metabolic rate, menstrual function, bone health, immunity, protein synthesis and cardiovascular health (209).

Saturated Fat and Polyunsaturated Fat. A nested case-control study found that the ratio of dietary saturated fatty acids (SFA) to polyunsaturated fatty acids (PUFA) influenced the risk of obesity associated with the TA and AA variants of the FTO gene at rs9939609 (210). Specifically, participants possessing the A allele had a significantly higher BMI and waist circumference (WC) compared to TT homozygotes, but only when intakes of SFA were high and PUFAs were low. When participants with the A allele consumed < 15% of energy from SFA and had a higher dietary PUFA:SFA ratio, there were no significant differences in WC and BMI between this group and participants with the TT genotype of rs9939609. These findings have implications for nutrition counseling impacting body composition (abdominal fat specifically) and BMI. Athletes with the TA or AA genotype may have a greater risk for accumulating excessive abdominal fat. An athlete can mitigate this risk by aiming to consume <10% of energy from SFA (to also account for heart health) and > 4% of energy from PUFAs, resulting in a PUFA:SFA ratio of at least 0.4 (210).
.

Many variants are improperly used in predictive panels of toxicity, bone metabolism, sports performance due to defects in data collection, selection of reference population, frequency in the general population and selective effects.
A drastic reduction in variants allows to create two types of panels.

1. Genetics, nutrition, physical exercise with 28 genes involved centered on lipoglycidic balance

2. Genetics, bones and muscles, sports with 11 genes involve

GeneAdvise

Advisor in Human Genetics

GENE-PERSONA

Lamberto Camurri, PhD, PM

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Mendel Genetica Medica Modena
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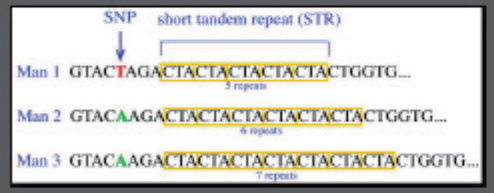
Istituto Genetica Medica

Centro Cuore Salute Reggio Emilia
FASI Fed.Arrampicata Sportiva Italiana

Crew
Francesca Camurri, BS, PA
Angela Godi Palmi, AA, EA



GENETICS AND PERSONALIZED MEDICINE
PREDICTIVE AND FUNCTIONAL MARKERS

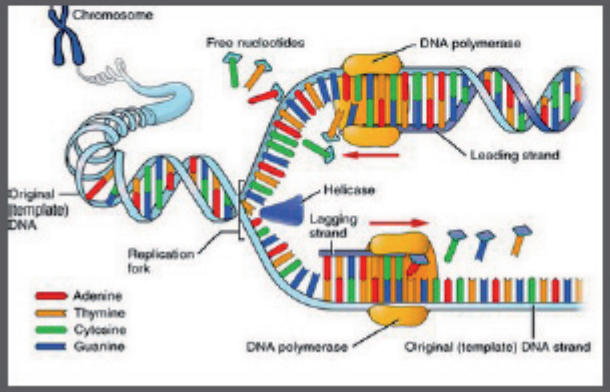
POLYMORPHIC GENES
GENETICS AND BODY EFFICIENCY

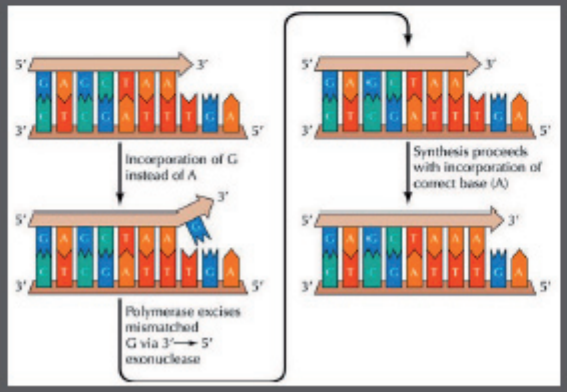
METHABOLISM, CARBO-LIPIDIC BALANCE,SPORT AND DIET

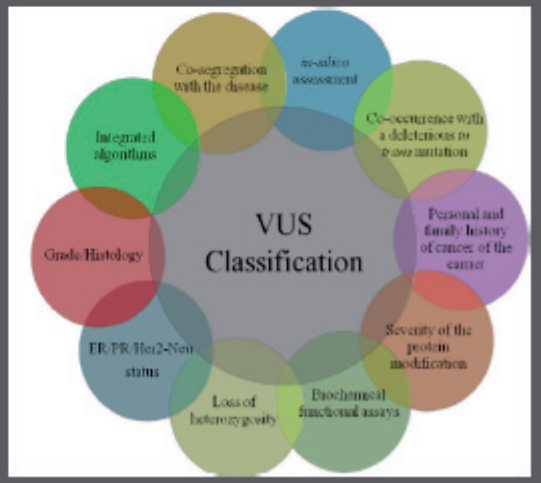
GeneAdvise

Some technical / scientific information.

Each gene is present in the cells of the body in two copies (alleles). The same gene can differ from one person to another even for just one base, one letter of its code: SNP (Single Nucleotide Polymorphism) Variations in the sequence of genes can give rise to Variants. Pathogenetic variants have harmful effects on the functioning of the gene, even blocking it. Non-pathogenic variants have different frequency in the general population and are associated with differences that modify the function of the gene without compromising it.







GeneAdvise

Chrom

-osome

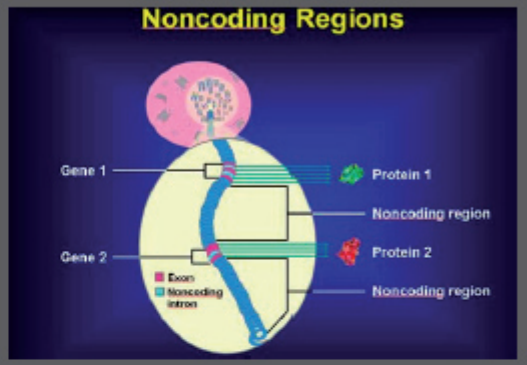
A threadlike structure of nucleic acids and proteins found in the nucleus of most living cells, carrying genetic information in the form of genes.

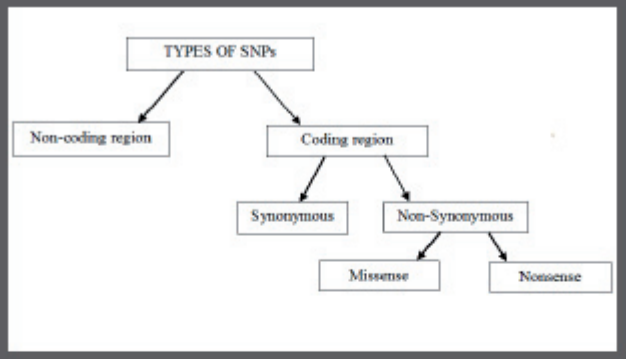
-atid

Each of the two threads or strands into which a chromosome divides longitudinally during cell division. Each contains a double-helix of DNA.

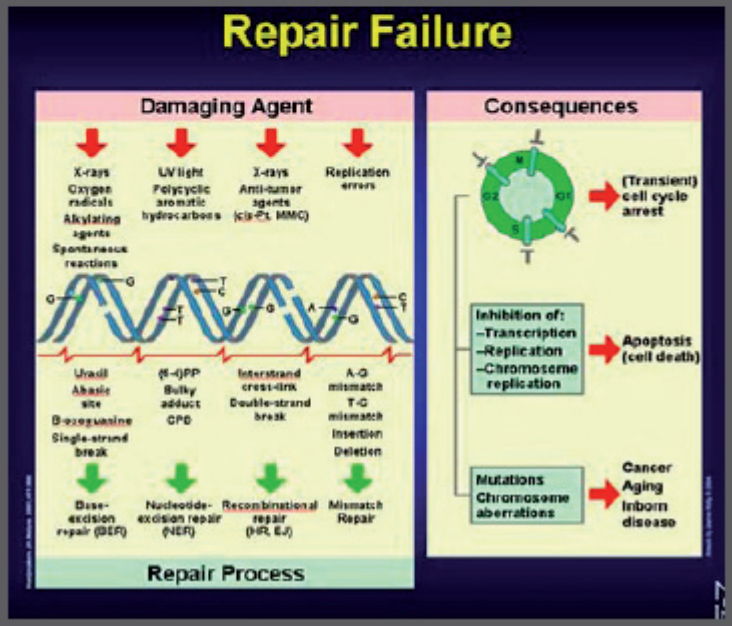
-atin

The material of which the chromosomes of organisms other than bacteria (i.e. eukaryotes) are composed, consisting of proteins, RNA and DNA.





	U	C	A	G
U	UUU Phe, UUC Phe, UUA Leu, UUG Leu	UCU, UCC, UCA, UCG Ser	UAU Tyr, UAC Tyr, UAA Stop, UAG Stop	UGU Cys, UGC Cys, UGA Stop, UGG Trp
C	CUU, CUC, CUA, CUG Leu	CCU, CCC, CCA, CCG Pro	CAU His, CAC His, CAA Gln, CAG Gln	CGU, CGC, CGA, CGG Arg
A	AUU, AUC, AUA Ile, AUG Met	ACU, ACC, ACA, ACG Thr	AAU Asn, AAC Asn, AAA Lys, AAG Lys	AGU Ser, AGC Ser, AGA Arg, AGG Arg
G	GUU, GUC, GUA, GUG Val	GCU, GCC, GCA, GCG Ala	GAU Asp, GAC Asp, GAA Glu, GAG Glu	GGU, GGC, GGA, GGG Gly



		Silent	Nonsense	Missense	
				Conservative	Non-conservative
DNA	TTC	TTT	ATC	TCC	TGC
mRNA	AAG	AAA	UAG	AGG	ACG
Protein	Lys	Lys	STOP	Arg	Thr

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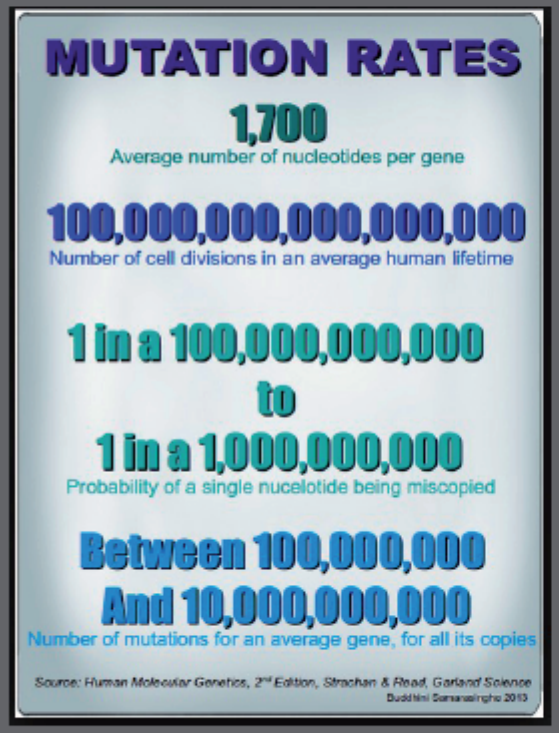
SNP amount, mutation, frequency (rate)



Chromosome	Length(bp)	All SNPs		TSC SNPs	
		Total SNPs	kb per SNP	Total SNPs	kb per SNP
1	214,066,000	129,931	1.65	75,166	2.85
2	222,889,000	103,664	2.15	76,985	2.90
3	186,938,000	93,140	2.01	63,669	2.94
4	169,035,000	84,426	2.00	65,719	2.57
5	170,954,000	117,882	1.45	63,545	2.69
6	165,022,000	96,317	1.71	53,797	3.07
7	149,414,000	71,752	2.08	42,327	3.53
8	125,148,000	57,834	2.16	42,653	2.93
9	107,440,000	62,013	1.73	43,020	2.50
10	127,894,000	61,298	2.09	42,466	3.01
11	129,193,000	84,663	1.53	47,621	2.71
12	125,198,000	59,245	2.11	38,136	3.28
13	93,711,000	53,093	1.77	35,745	2.62
14	89,344,000	44,112	2.03	29,746	3.00
15	73,467,000	37,814	1.94	26,524	2.77
16	74,037,000	38,735	1.91	23,328	3.17
17	73,367,000	34,621	2.12	19,396	3.78
18	73,078,000	45,135	1.62	27,028	2.70
19	56,044,000	25,676	2.18	11,185	5.01
20	63,317,000	29,478	2.15	17,051	3.71
21	33,824,000	20,916	1.62	9,103	3.72
22	33,786,000	28,410	1.19	11,056	3.06
X	131,245,000	34,842	3.77	20,400	6.43
Y	21,753,000	4,193	5.19	1,784	12.19
RefSeq	15,696,674	14,534	1.08		
Totals	2,710,164,000	1,419,190	1.91	887,450	3.05

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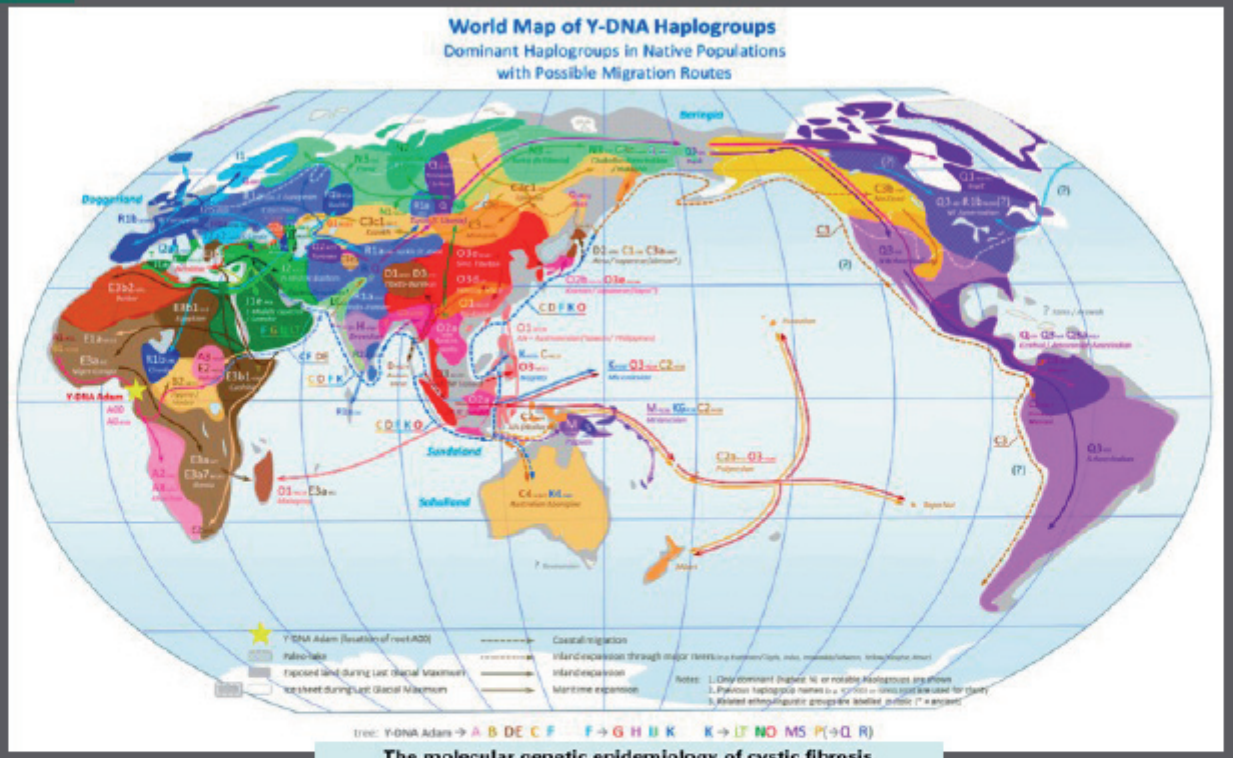
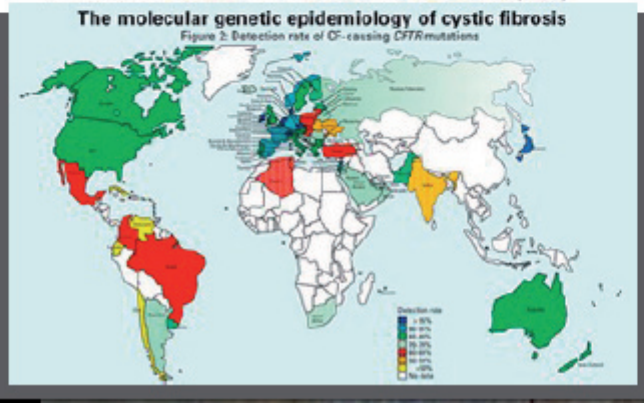




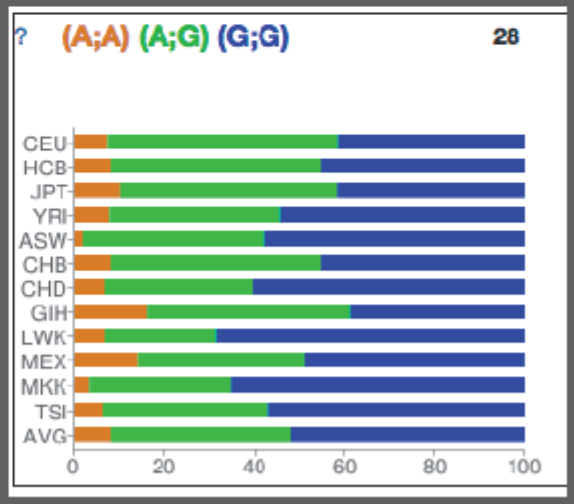
SNP Geographic distribution, drift

GeneAdvise

General population variants studies

The **International HapMap Project** was an organization that aimed to develop a haplotype map (**HapMap**) of the human genome, to describe the common patterns of human genetic variation. HapMap is used to find genetic variants affecting health, disease and responses to drugs and environmental factors. The information produced by the project is made freely available for research.

Phase	ID	Place	Population
I/II	CEU		Utah residents with Northern and Western European ancestry from the CEPH collection
I/II	CHB		Han Chinese in Beijing, China
I/II	JPT		Japanese in Tokyo, Japan
I/II	YRI		Yoruba in Ibadan, Nigeria
III	ASW		African ancestry in the Southwest USA
III	CHD		Chinese in metropolitan Denver, CO, United States
III	GIH		Gujarati Indians in Houston, TX, United States
III	LWK		Luhya in Webuye, Kenya
III	MKK		Maasai in Kinyawa, Kenya
III	MXL		Mexican ancestry in Los Angeles, CA, United States
III	TSI		Toscani in Italia



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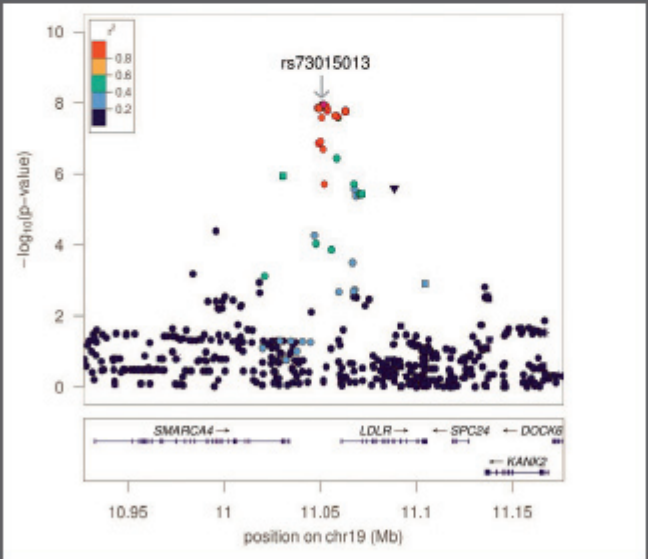
In genomics, a **genome-wide association study** (**GWA study**, or **GWAS**), also known as **whole genome association study** (**WGA study**, or **WGAS**), is an observational study of a genome-wide set of genetic variants in different individuals to see if any variant is associated with a trait. GWA studies typically focus on associations between single nucleotide polymorphisms (SNPs) and traits like major human diseases, but can equally be applied to any other genetic variants and any other organism.
This approach is known as phenotype-first, in which the participants are classified first by their clinical manifestation(s), as opposed to genotype-first. Each person gives a sample of DNA, from which millions of genetic variants are read using SNP ARRAYS.



GWAS snp	
PMID	[PMID 17463246]
Trait	Type 2 diabetes
Title	Genome-wide association analysis identifies loci for type 2 diabetes and triglyceride levels
Risk Allele	C
P-val	0.00000199999999999999999
Odds Ratio	1.14 [1.08-1.20]

GWAS snp	
PMID	[PMID 17463248]
Trait	Type 2 diabetes
Title	A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants
Risk Allele	C
P-val	0.00000199999999999999999
Odds Ratio	1.14 [1.08-1.20]

GWAS snp	
PMID	[PMID 17463249]
Trait	Type 2 diabetes
Title	Replication of genome-wide association signals in UK samples reveals risk loci for type 2 diabetes
Risk Allele	C
P-val	0.00000199999999999999999
Odds Ratio	1.14 [1.08-1.20]

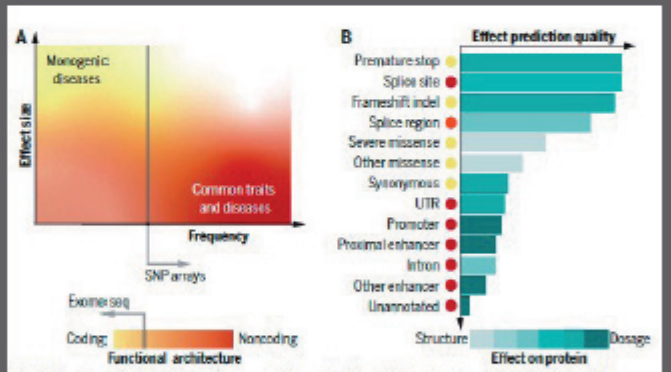


Fig. 1. Genetic variant effects on disease and gene function. (**A**) Functional genetic architecture of human disease ranging from a spectrum of monogenic diseases driven by rare predominantly coding variants with a strong effect on disease to common diseases and traits whose heritability is dominated by noncoding common variants with small effect sizes. However, these classifications are not exclusive: Noncoding causal variants in Mendelian disease exist, as do rare variants affecting common traits and diseases. (**B**) Quality of variant effect predictions by functional annotation class. The color of the bars indicates whether the variant classes tend to affect protein structure or dosage or whether a given class of variants can affect both—for example, via nonsense-mediated decay and splicing. The color of the labels indicates coding and noncoding annotation.

GeneAdvise

HUMAN GENOMICS

Protein-coding repeat polymorphisms strongly shape diverse human phenotypes

Ronen E. Mukamel[1,2*†], Robert E. Handsaker[2,3,4*†], Maxwell A. Sherman[1,2,5], Alison R. Barton[1,2,6], Yiming Zheng[2,3], Steven A. McCarroll[2,3,4*‡], Po-Ru Loh[1,2*‡]

Many human proteins contain domains that vary in size or copy number because of variable numbers of tandem repeats (VNTRs) in protein-coding exons. However, the relationships of VNTRs to most phenotypes are unknown because of difficulties in measuring such repetitive elements. We developed methods to estimate VNTR lengths from whole-exome sequencing data and impute VNTR alleles into single-nucleotide polymorphism haplotypes. Analyzing 118 protein-altering VNTRs in 415,280 UK Biobank participants for association with 786 phenotypes identified some of the strongest associations of common variants with human phenotypes, including height, hair morphology, and biomarkers of health. Accounting for large-effect VNTRs further enabled fine-mapping of associations to many more protein-coding mutations in the same genes. These results point to cryptic effects of highly polymorphic common structural variants that have eluded molecular analyses to date.

Table 1. VNTRs within protein-coding sequences affect diverse human phenotypes. For each of five protein-altering VNTRs involved in phenotype associations that passed stringent fine-mapping criteria, *P* values [in linear mixed-model analyses of $N = 415{,}280$ unrelated UKB participants of European (EUR) ancestry] and estimated effect size ranges (across the longest and shortest alleles sufficiently common to be amenable to our computational analysis) are listed for the most strongly associated phenotype.

Gene	Cytoband	Repeat unit size	Repeat count (EUR)	Protein domain (effect)	Phenotype	Effect range ± SE	*P* value
LPA	6q25.3-q26	~5.6 kb (114 aa, two exons)	2–40	KIV (number)	Lipoprotein(a) concentration	5.1 ± 0.5 SD (= 233 ± 23 nmol/liter)	4.4×10^{-325}
ACAN	15q26.1	57 bp (19 aa)	13–44	Chondroitin sulfate (size)	Height	0.49 ± 0.04 SD (= 3.2 ± 0.3 cm)	1.7×10^{-234}
TENT5A	6q14.1	15 bp (5 aa)	2–7	Unknown (size)	Height	0.09 ± 0.01 SD (= 0.6 ± 0.1 cm)	2.5×10^{-63}
MUC1	1q22	60 bp (20 aa)	20–125	Extracellular (size)	Serum urea	0.16 ± 0.01 SD (= 0.22 ± 0.01 mmol/liter)	2.7×10^{-183}
TCHH	1q21.3	18 bp (6 aa)	5–15	α-Helix rod (size)	Male pattern baldness score	−0.063 ± 0.006 SD	1.6×10^{-25}

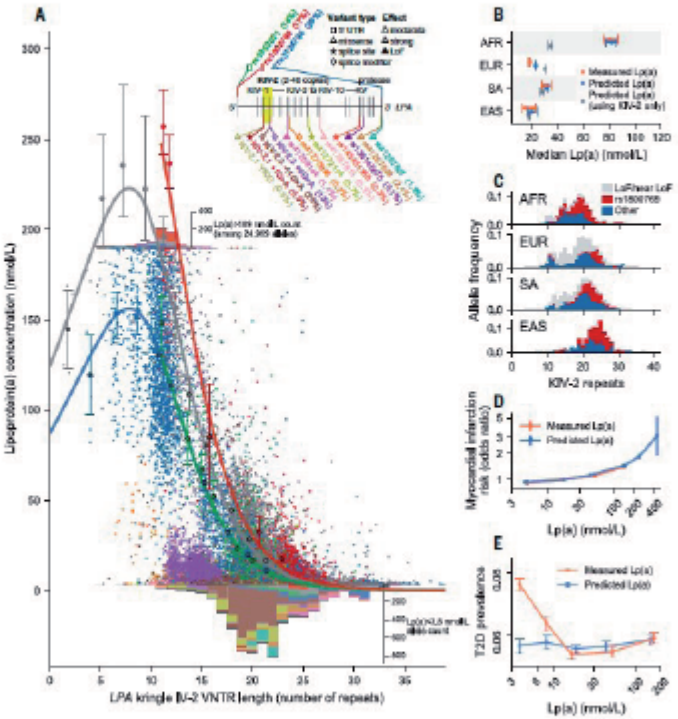


Fig. 1. Kringle IV-2 repeat length variation and 23 *LPA* SNPs together explain ~90% of lipoprotein(a) heritability. (**A**) Serum Lp(a) versus KIV-2 VNTR length in an effective-haploid model of Lp(a) involving 24,969 *LPA* alleles (in exome-sequenced UKB participants of European ancestry) for which the allele on the homologous chromosome was predicted to produce negligible Lp(a) (<4 nmol/liter). Colors indicate the 15 most common Lp(a)–modifying SNPs identified by fine-mapping analysis (full list in table S4). Curves indicate parametric fits of Lp(a) to KIV-2 length. Gray indicates alleles not carrying any Lp(a)–modifying SNPs; red, blue, and green are carriers of a single common Lp(a)–modifying SNP; large points are mean Lp(a) among such alleles in KIV-2 length bins. Error bars indicate 95% CIs. Histograms (top and bottom) show counts of Lp(a) measurements outside of the reportable range (<3.8 or >189 nmol/liter) colored by Lp(a)–modifying SNPs (*7*). (**B**) Observed and predicted median Lp(a) among individuals of African (AFR; $N = 893$), European (EUR; $N = 42{,}362$), South Asian (SA; $N = 954$), and East Asian (EAS; $N = 156$) ancestry. (**C**) *LPA* allele frequencies by ancestry. VNTR alleles in cis with a large-effect Lp(a)–reducing variant (respectively, the Lp(a)–increasing 5′ UTR variant rs3800769) are indicated in gray (respectively, red). (**D** and **E**) Myocardial infarction risk (D) and T2D prevalence (E) versus measured or genetically predicted Lp(a). Error bars indicate 95% CIs.

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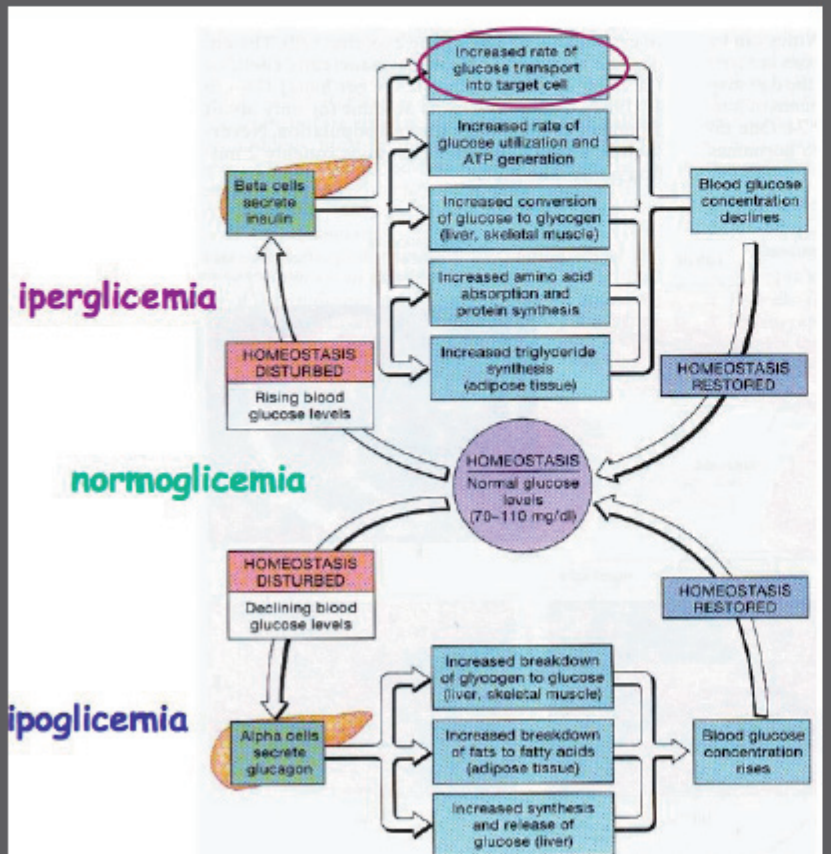
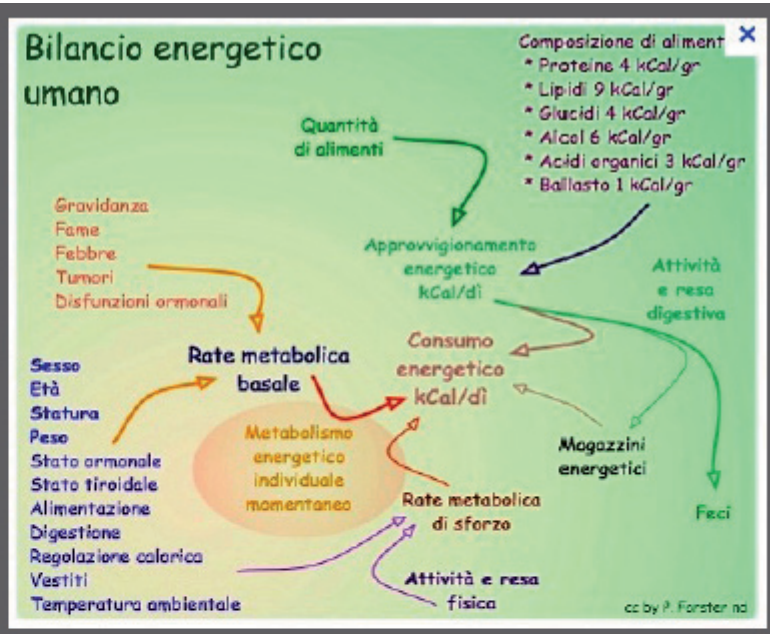
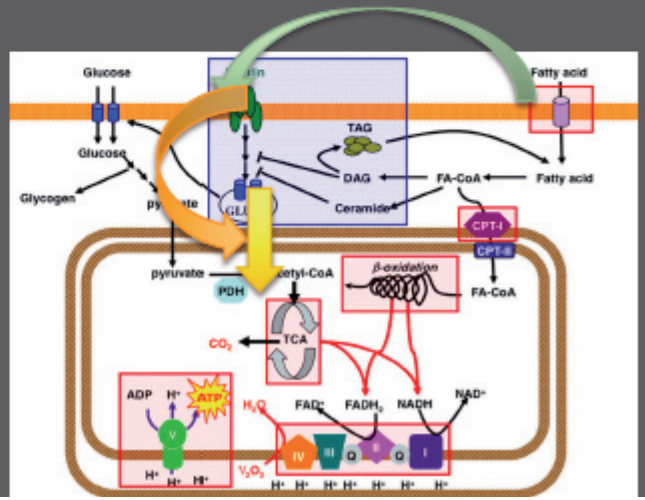
PERSONALIZED PHYSIOLOGY

FOOD AND ENERGETIC CONSUMPTION

CARBO-LIPO COMPLEX







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PERSONALIZED PHYSIOLOGY

FOOD AND ENERGETIC CONSUMPTION

CARBO-LIPO COMPLEX

Fatty acid-binding protein-2 **FABP2**
absorption of fatty acids, abdominal fat deposits, leptin levels (appetite and satiety, calorie expenditure)

Melanocortin-4 receptor **MC4R**
action of anorectic hormones

Peroxisome proliferator-activated receptor **PPARg**
Differentiation of fat cells, regulation of glucose-lipid balances, diet-sport combination

Adrenergic-beta-2-receptor **ADRB2**
use of cell fat for energy is strongly involved in the combined diet-sport action

Adrenergic-beta-3-receptor **ADRB3**
consumption of fat for thermoregulation purposes and is conditioned by physical activity

Fat Mass and Obesity Associated Gene **FTO**
risk of obesity, is modulated by physical activity

Apolipoproteina A-2 **APOA2**
weight gain and insulin resistance in saturated fat intake, and related dietary response

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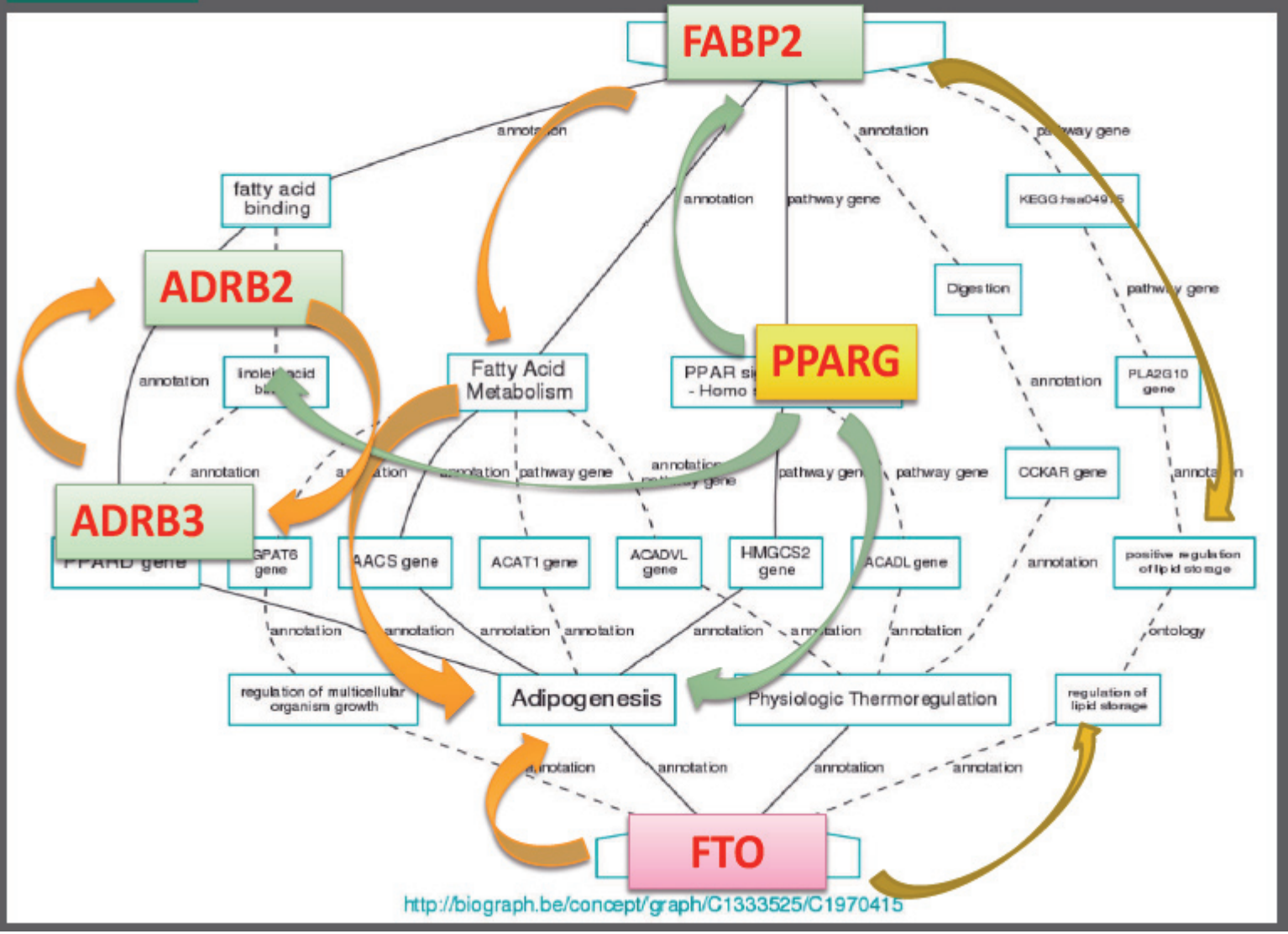
GENE	VARIANTI	RSnumber	Nucleotide	Variazione	Interpretazione
SLC6A4/ 5HTTPLR	Ins/Del	rs25531			S/S=lento adattamento S/L=medio adattamento L/L=rapido adattamento
ADIPOq	-11391 G/A	rs17300539	G	A	Presenza allele A (AA o AG) = possibile aumento della probabilità di sviluppare obesità, insulino-resistenza, diabete e sindrome metabolica
ADRA2B	Ins/Del cod.299				Del cod 299=possibile aumento rischio cardiovascolare e tendenza aumento di peso
ADRB1	G389R	rs1801253	G	C	Presenza allele C (CC o CG) = aumento della probabilità di sviluppare obesità
ADRB2	G16R	rs1042713	G	A	Presenza allele A (AA o AG) = aumento della probabilità di svilupparo obesità
ADRB3	W64R	rs4994	T	C	Presenza allele C (CT o CC) = possibile fattore di rischio cardiovascolare e tendenza all'obesità
APOA2	-265 C-T	rs5082	C	T	CC=possibile predisposizione all'aumento del peso
APOA5	-1131T> C	rs662799	T	C	Presenza allele C (TC o CC) = predisposizione all'aumento di peso
FABP2	A54T	rs1799883	G	A	Presenza allele A (AA o AG) = associato ad alto/moderato rischio cardiovascolare e alta/moderata sensibilità ai carboidrati raffinati
FTO	T-A	rs9939609	T	A	Presenza allele A (AA o AT) = associato a significativa tendenza all'aumento di peso
	C-A	rs8050136	C	A	Presenza allele A (AA o AC) = associato a significativa tendenza all'aumento di peso
	C-T	rs1121980	C	T	Presenza allele T (TT o TC) = associato a significativa tendenza all'obesità
	T-C	rs1421085	T	C	Presenza allele C (CC o CT) = associato a significativa tendenza all'obesità
	T-G	rs17817449	T	G	Presenza allele G (GG o GT) = associato a significativa tendenza all'obesità
GHSR	G477A	rs572169	G	A	Presenza allele A (AA o AG) = possibile predisposizione all'assunzione di grandi quantità di cibo e tendenza all'obesità
Leptin	-2548 G-A	rs7799039	G	A	AA=possibile fattore di rischio cardiovascolare e tendenza all'obesità
MC4R	g.60183864T>C	rs17782313	T	C	Presenza allele C (CC o CT) = possibile presenza di disordini dell'appetito, tendenza all'obesità
NPY	L7P	rs16139	T	C	Presenza allele C (CC o CT) = possibile fattore di rischio cardiovascolare e predisposizione all'aumento di peso
PPARG	P12A	rs1801282	C	G	Presenza allele G (GG o CG) = possibile predisposizione all'aumento di peso
VEGF	c.-1507 C-G	rs2010963	C	G	Presenza G (GG o CG) = possibile fattore di rischio cardiovascolare e predisposizione all'aumento di peso

AVAGENOMA®

GeneAdvise


FABP2
ADRB2
ADRB3
PPARG
fatty acid binding
Fatty Acid Metabolism
Digestion
PLA2G10 gene
CCKAR gene
GPAT6 gene
AACS gene
ACAT1 gene
ACADVL gene
HMGCS2 gene
ACADL gene
positive regulation of lipid storage
regulation of multicellular organism growth
Adipogenesis
Physiologic Thermoregulation
regulation of lipid storage
FTO
annotation
pathway gene
ontology
http://biograph.be/concept/graph/C1333525/C1970415

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Gene FABP2
Fatty acid-binding protein-2

Localizzazione: cromosoma 4 (locus 4q28-q31)
Dimensioni e struttura: 11.912 paia di basi, contiene 4 esoni
Prodotto proteico corrispondente: proteina intracellulare, denominata ***fatty acid-binding protein-2*** (FABP2), composta da 132 aminoacidi.

FABP2 encodes the proteins involved in the uptake, transport and intracellular metabolism of long-chain fatty acids.

FABP2 is also able to bind unsaturated fatty acids, always with a long chain. It probably participates in the maintenance of energy homeostasis by functioning as a "lipid sensor".

Polimorfismo A54T
Genotipo AA-AG

The presence of the AA-AG genotype is correlated with:
increased absorption of fatty acids in the intestine
high body mass index and increased abdominal fat deposits

high level of leptin, a hormone in adipose tissue that limits satiety and the mechanisms of calorie expenditure

less efficacy of low caloric diets and exercise as weight loss strategies

postprandial increase in triglycerid levels if homozygous

NO DATA IN GWAS

Geno	Mag	Summary
(A;A)	0	Two copies of the Thr allele in the FABP2 is associated with significantly increased sensitivity to saturated fats. Also contributes to increased refined carb sensitivity.
(A;G)		A single copy of the Thr allele associated with a moderately increased sensitivity to saturated fats. Also contributes to increased refined carb sensitivity.
(G;G)		This genotype is not associated with increased sensitivity to saturated fats or refined carbohydrates.

GeneAdvise

Gene FABP2
Fatty acid-binding protein-2

Localizzazione: cromosoma 4 (locus 4q28-q31)
Dimensioni e struttura: 11.912 paia di basi, contiene 4 esoni
Prodotto proteico corrispondente: proteina intracellulare, denominata ***fatty acid-binding protein-2*** (FABP2), composta da 132 aminoacidi.

FABP2 encodes the proteins involved in the uptake, transport and intracellular metabolism of long-chain fatty acids.

FABP2 is also able to bind unsaturated fatty acids, always with a long chain. It probably participates in the maintenance of energy homeostasis by functioning as a "lipid sensor".

Polimorfismo A54T
Genotipo GG

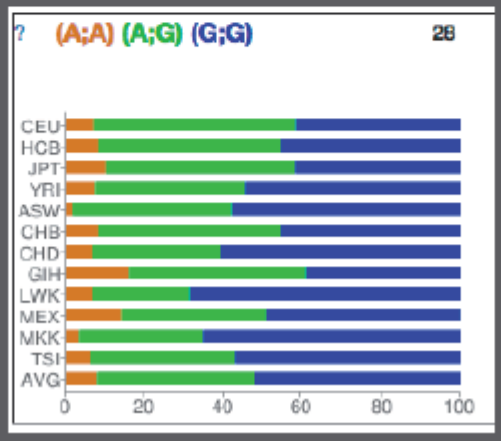
The presence of the GG genotype is correlated with:

normal absorption of fatty acids

a normal postprandial level of triglycerides

greater responsiveness to low-calorie diets and exercise as strategies aimed at increasing weight loss.

Allelic prevalence



GeneAdvise

Gene PPAR
Peroxisome proliferator-activated receptor

Localizzazione: cromosoma 3 (locus 3p25)
Dimensioni e struttura: 3302 paia di basi, contiene 6 esoni
Prodotto proteico: ***peroxisome proliferator-activated receptor-gamma*** (PPARg), composta da 477 aminoacidi.

PPARg regulates inflammatory processes, cell differentiation, glucose and lipid homeostasis,

PPARg is a determining factor for the transformation and maturation of adipocytes.
Alterations in PPARg function are related to diabetes-2. It is a candidate as a critical factor in obesity.

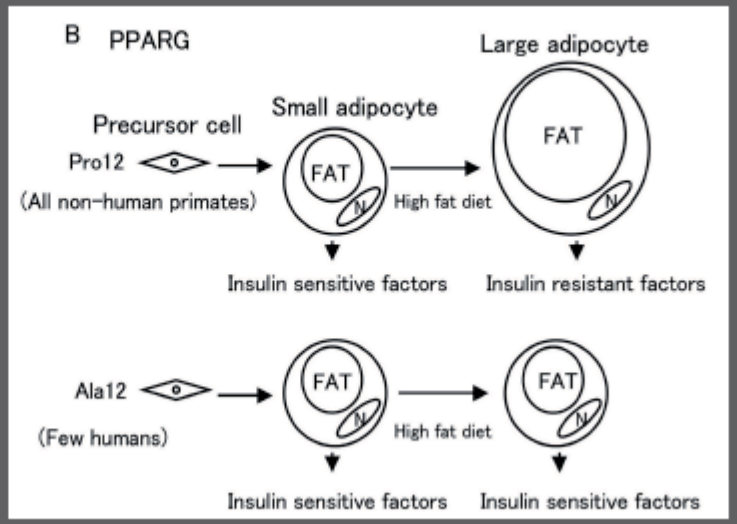
PPARCC polymorphism is related to decreased activity of the protein.

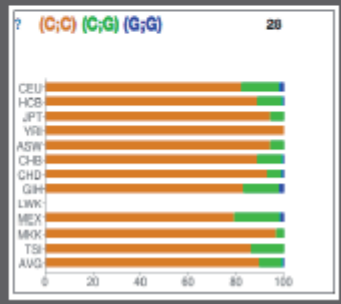
Polimorfismo 12Pro/Ala
Genotipo GG/CG

The presence of the GG / GC genotype is correlated with:

a lower susceptibility to body weight gain in relation to the amount of fat consumed in the diet

High response to weight loss following constant exercise and a controlled diet.





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Alterations in PPARg function are related to diabetes-2. It is a candidate as a critical factor in obesity.

PPARCC polymorphism is related to decreased activity of the protein.

Polimorfismo 12Pro/Ala
Genotipo CC

The presence of the CC genotype is correlated with:

greater sensitivity of the Body Mass Index to the amount of fat consumed in the diet

ability to lose weight poorly conditioned by exercise

GWAS snp	
PMID	[PMID 17463246]
Trait	Type 2 diabetes
Title	Genome-wide association analysis identifies loci for type 2 diabetes and triglyceride levels
Risk Allele	C
P-val	0.00000199999999999999999
Odds Ratio	1.14 [1.08-1.20]

GWAS snp	
PMID	[PMID 17463248]
Trait	Type 2 diabetes
Title	A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants
Risk Allele	C
P-val	0.00000199999999999999999
Odds Ratio	1.14 [1.08-1.20]

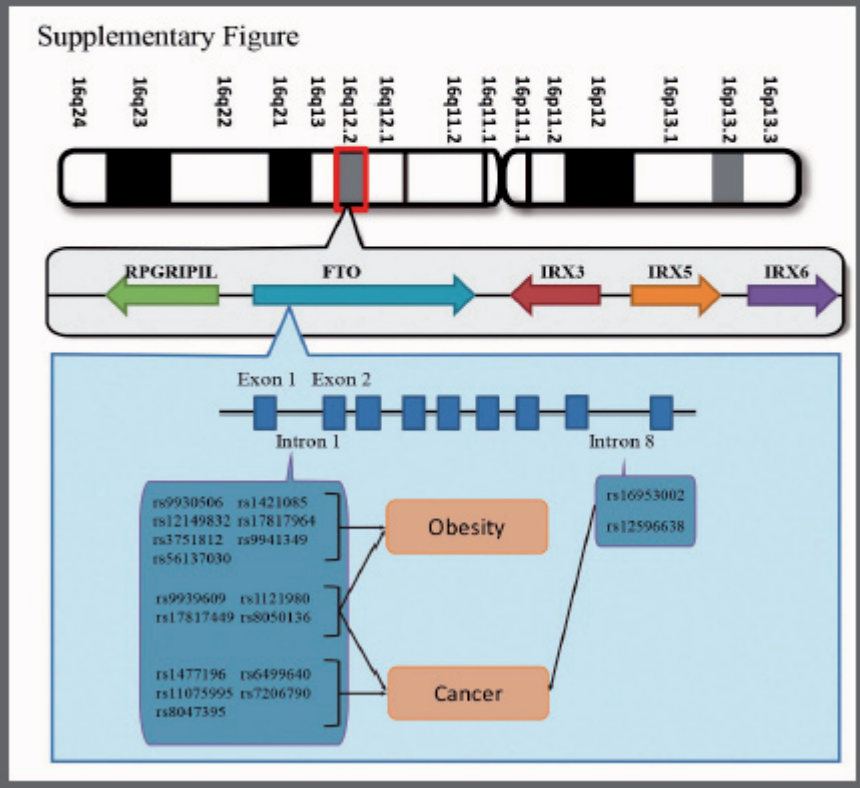
GWAS snp	
PMID	[PMID 17463249]
Trait	Type 2 diabetes
Title	Replication of genome-wide association signals in UK samples reveals risk loci for type 2 diabetes
Risk Allele	C
P-val	0.00000199999999999999999
Odds Ratio	1.14 [1.08-1.20]

GeneAdvise

Gene FTO “FAT GENE”

Localizzazione: cromosoma 16
Dimensioni e struttura: 410505 paia di basi, contiene 9 esoni
Prodotto : proteina diossigenase alfa-chetoglutarato-dipendente, composta da 505 aminoacidi.

FTO (Fat Mass and Obesity Associated Gene) has unknown function.
It appears to be a role of FTO in DNA demethylation. Its level of expression is regulated by the nutritional behaviour.
FTO has particular importance in regulating body weight due to the relationship between its polymorphisms and the impact of physical exercise on anthropometric parameters.



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Rs9939609 Genotipo AA/AT

increase in anthropometric indices,
risk of obesity
good responsiveness of the subject to physical exercise

Rs1421085 Genotype CC / CT

The presence of the CC / CT genotype:
increase in anthropometric indices, risk of obesity

Rs17817449 GG / GT Genotype

The presence of the GG / GT genotype:
increase in anthropometric indices (1.3-1.7), obesity risk

GWAS	
SNP	rs9939609
PubMedID	[PMID 17434869]
Condition	Body mass index
Gene	FTO
Risk Allele	A
pValue	2.00E-020
OR	0.36
95% CI	NR) kg/m2 per copy in adult

GWAS snp	
PMID	[PMID 19079261]
Trait	Body mass index
Title	Six new loci associated with body mass index highlight a neuronal influence on body weight regulation
Risk Allele	A
P-val	4E-51
Odds Ratio	0.33 [0.27-0.39] kg/m2 increase

GWAS snp	
PMID	[PMID 19396169]
Trait	Biomedical quantitative traits
Title	A large-scale genome-wide association study of Asian populations uncovers genetic factors influencing eight quantitative traits
Risk Allele	A
P-val	2E-7
Odds Ratio	0.24 [0.14-0.32] kg/m2 increase

GWAS snp	
PMID	[PMID 19151714]
Trait	Obesity
Title	Genome-wide association study for early-onset and morbid adult obesity identifies three new risk loci in European populations
Risk Allele	C
P-val	1E-28
Odds Ratio	1.39 [1.27-1.51]

GWAS snp	
PMID	[PMID 21552555]
Trait	
Title	A genome-wide association study on obesity and obesity-related traits.
Risk Allele	
P-val	2E-12
Odds Ratio	None None

Geno	Mag	Summary
(A;A)	3	obesity risk and 1.6x risk for T2D
(A;T)	2.4	1.3x risk for T2D; obesity risk
(T;T)	1.5	lower risk of obesity and Type-2 diabetes

Geno	Mag	Summary
(C;C)	3.1	~1.7x increased obesity risk
(C;T)	2.5	~1.3x increased obesity risk
(T;T)	0.1	normal obesity risk

Geno	Mag	Summary
(G;G)		~1.7x increased obesity risk
(G;T)		~1.3x increased obesity risk
(T;T)	0	normal

GeneAdvise

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It appears to be a role of FTO in DNA demethylation. Its level of expression is regulated by the nutritional behaviour.

FTO has particular importance in regulating body weight due to the relationship between its polymorphisms and the impact of physical exercise on anthropometric parameters.

Rs9939609 Genotipo TT

La presenza del genotipo TT

normal increase in anthropometric parameters, low risk of obesity.

poor sensitivity of the body mass index to physical exercise as a strategy for weight loss

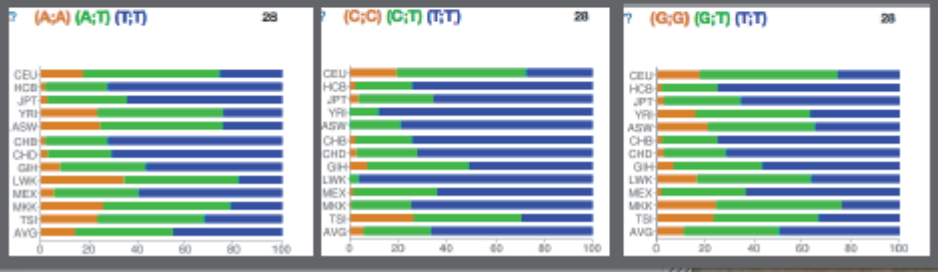
Rs1421085 TT genotype

The presence of the TT genotype Normal risk of obesity

Rs17817449 TT genotype
The presence of the TT genotype

Normal risk of obesity

Allelic prevalence



GeneAdvise

Gene MC4R

Localizzazione: Cromosoma 18 (locus 18q22)
Dimensioni e struttura: 8448 paia di basi, contiene 1 esone
Prodotto : proteina recettoriale, denominata *melanocortin-4 receptor* (MC4R), composta da 332 aminoacidi.

MC4R.
In the hypothalamus, α-MSH (alpha-melanocyte stimulating hormone) exerts an anorectic action by binding to the MC4R receptor.

Inactivation of MC4R shows a tendency to obesity.

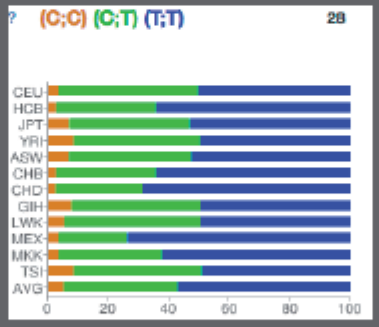
MC4R * polymorphism is associated with low disposition to obesity.

Polimorfismo g.60183864T>G

The absence of the TT genotype is correlated with:

predisposition to normal BMI (Body Mass Index)

The presence of CC / CT polymorphism correlates with: predisposition to high BMI (Body Mass Index)



Prevalence of genotype CC/CT in Northern Italian population

			pres		pres		pres		ass		ass		pres		pres		pres
			>ass lip														<lipolisi
Indicazione			ac grass				sens fat		ob		sens fat				>obes		
			ex poor		ob						ex poor		ex good		*ex poor		ex poor
POLIMORFISMO			APOA2*		FTO*		FABP2*		MC4R*		PPARg*		FTO**		ADRB2*		ADRB3*
Assente			301		120		360		370		310		131		111		592
Presente eterozigosi			290		381		231				71		381		290		51
Presente omozigosi			51		132		42				11		120		231		

GeneAdvise

Gene ADRB2

Localizzazione: cromosoma 5 (locus 5q31-q32)
Dimensioni e struttura: 2033 paia di basi, contiene 4 esoni
Prodotto : proteina intracellulare, **adrenergic- beta-2- receptor** (ADRB2), composta da 413 aminoacidi.

ADRB2 encodes the type 2 beta adrenergic receptor which inserts into the cell membrane where it interacts with mediators (adrenaline / noradrenaline).

The ADRB2 receptor is directly associated with its final effector, an L-type calcium channel (Ca (V) 1.2). This receptor / channel complex binds to a cAMP-dependent G protein that allows for the rapid transmission of specific biochemical signals.

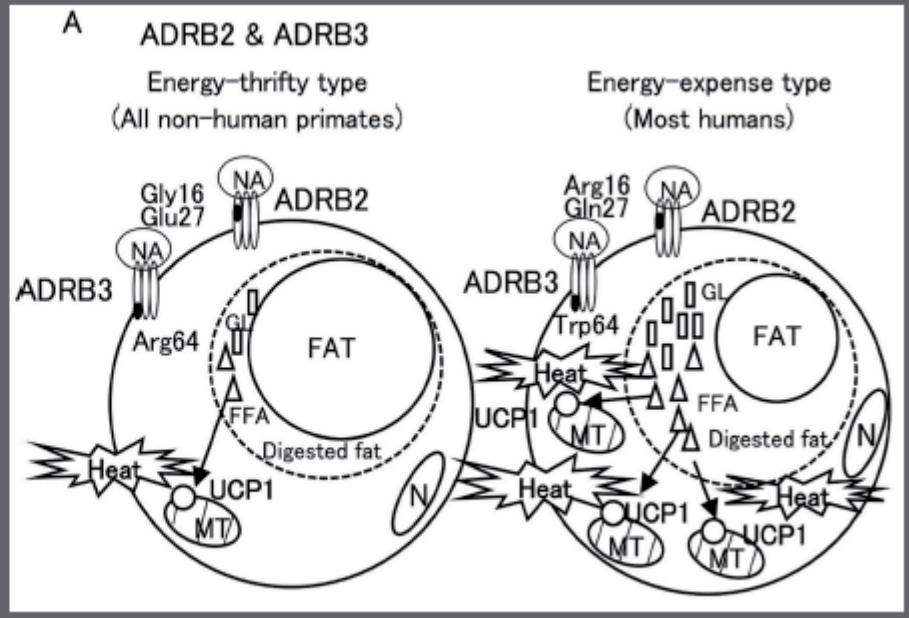
ADRB2 is preferentially expressed in adipose tissue and is responsible for the processes of mobilization of fat for energy purposes.

Polimorfismo 16Gly/Arg

Genotipo AA/AG

The presence of the AA / AG genotype:

Increase in pathology in asthmatic patients greater weight gain a low attitude to lose weight following physical exercise



GeneAdvise

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ADRB2 is preferentially expressed in adipose tissue and is responsible for the processes of mobilization of fat for energy purposes.

Polimorfismo 16Gly/Arg

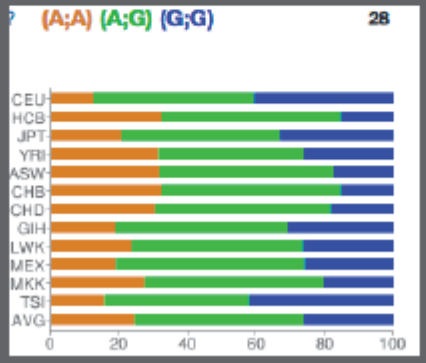
Genotipo GG

The presence of the GG genotype:

low susceptibility to weight gain with increasing age

good predisposition to lose weight following exercise good aerobic sports performance

Allelic prevalence



GeneAdvise

Gene ADRB3

Localizzazione: cromosoma 8 (locus 8p12-p11.2)
Dimensioni e struttura: 10672 paia di basi, non contiene introni
Prodotto: proteina intracellulare, **adrenergic- beta- 3- receptor** (ADRB3), composta da 408 aminoacidi.

ADRB3 encodes the type 3 beta adrenergic receptor, which regulates cellular or tissue functions by acting with transmitters such as adrenaline or noradrenaline.

ADRB3 is expressed in visceral adipose tissue and is present in fat deposits, where it is involved in lipolysis processes and thermal regulation.

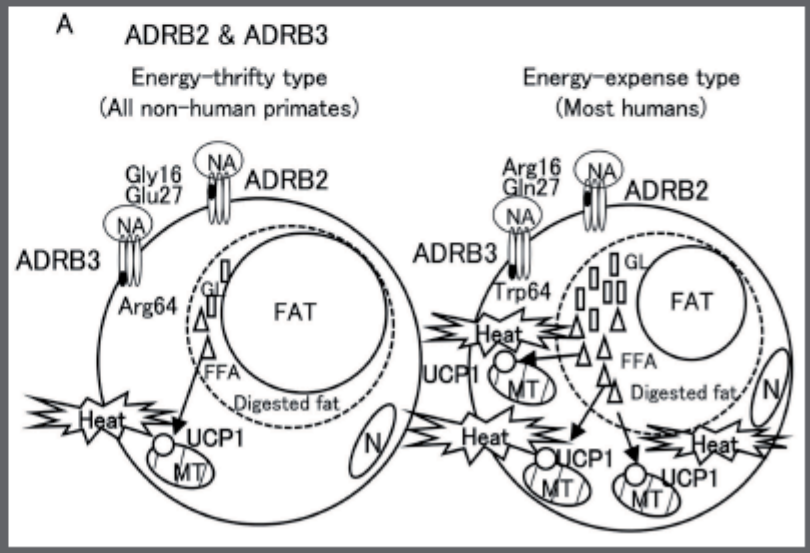
Polimorfismo 64Arg/Trp

Genotipo CC/CT

The presence of the CC / CT genotype:

reduced lipolysis in response to catecholamines and consequent lower response to physical activity as a strategy aimed at weight loss

increase in body mass index and greater risk of obesity poor responsiveness to low-calorie diets



GeneAdvise

Gene ADRB3

Localizzazione: cromosoma 8 (locus 8p12-p11.2)
Dimensioni e struttura: 10672 paia di basi, non contiene introni
Prodotto: proteina intracellulare, **adrenergic- beta- 3- receptor** (ADRB3), composta da 408 aminoacidi.

ADRB3 encodes the type 3 beta adrenergic receptor, which regulates cellular or tissue functions by acting with transmitters such as adrenaline or noradrenaline.

ADRB3 is expressed in visceral adipose tissue and is present in fat deposits, where it is involved in lipolysis processes and thermal regulation.

Polimorfismo 64Arg/Trp

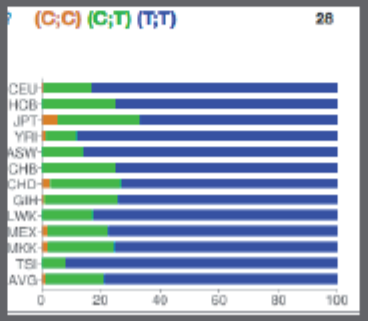
Genotipo TT

The presence of the TT genotype:

good response to low-caloric diets

good predisposition to lose weight following exercise

Allelic prevalence



NO DATA GWAS

Geno	Mag	Summary
(A;A)	1.7	1.7x increased risk that pediatric inhaler use may make asthma worse
(A;G)	1.3	1.3x increased risk that pediatric inhaler use may make asthma worse
(G;G)		normal

GeneAdvise

Gene APOA2

Localizzazione: cromosoma 1 (locus 1q21-q23)
Dimensioni e struttura: 2586 paia di basi, contiene 3 esoni
Prodotto: Apolipoproteina A-II, composta da 100 aminoacidi.

APOA2 is a high density lipoprotein (HDL).

It plays a crucial role in the functioning of the arterial system, probably through the metabolism of very-low-density lipoprotein particles and has a protective function against cardiovascular events.

Polymorphisms respond a lot to the fat diet

Polimorfismo ...82 T/C

Genotipo CC

The presence of the CC genotype:

increased risk of obesity and diabetes in people who eat high levels of saturated fat

good responsiveness of anthropometric indices to reduced levels of saturated fats

GWAS NO DATA

Geno	Mag	Summary
(C;C)	2.5	saturated fat contributes to obesity, but 0.57 % lower risk for coronary artery disease
(C;T)	0	normal risk
(T;T)	0	normal risk

GeneAdvise

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Polymorphisms respond a lot to the fat diet

Polimorfismo ...82 T/C

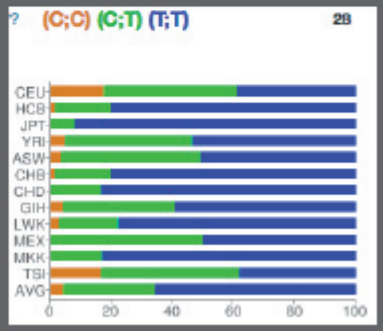
Genotipo TT

The presence of the TT genotype:

low susceptibility to obesity

low susceptibility to weight gain following the intake of saturated fatty acids

La prevalenza allelica del gene



		< unfavor				<EXP >RES
	ASSOR AC GRA/GRA BMI		DIETE IPOCALORICHE		ESERCIZIO FISICO		METAB MUSC CIRC
FABP2	A <	GG =	A <	GG >	A <	GG >	
PPAR-G	CC <	G >	CC <	G >	CC <	G >	
FTO RS -609	A < (OB)	TT =			TT <	A >	
MC4R	C < (>BMI)	TT =					
ADRB2	A <	GG >			A <	GG >	A = GG >
ADRB3	C < (BMI)	TT=	C <	TT >	C <	TT >	
APOA2 AC.GRASSI	CC <	T >		CC >			

		ADBR2	ADBR2	If ADRB3 is TT:		If ADRB3 is CC or CT:	
FABP2	PPRAG	codon 16	codon 27	ADRB3	Diet#	ADRB3	Diet#
AA	CC	GG	GG	TT	1	CC or CT	1
AA	CC	GG	GC	TT	2	CC or CT	2
AA	CC or GC	GG	CC	TT	3	CC or CT	3
GA	CC	GG or GA	GG	TT	4	CC or CT	1
GA	CC	GG or GA	GC	TT	5	CC or CT	2
GA	CC or GC	GG or GA	CC	TT	6	CC or CT	3
GG	CC	GA or AA	GG	TT	7	CC or CT	4
GG	CC or GC	GG or GA or AA	GC	TT	8	CC or CT	5
GG	CC or GC	GG or GA or AA	CC	TT	9	CC or CT	6
GG	GG or GC	GA or AA	GG	TT	10	CC or CT	7
GG	GC	GA or AA	GC	TT	11	CC or CT	8
GG	GG	GA or AA	CC	TT	12	CC or CT	9

TABLE 3

	Diet #	Fat (%)	Carbohydrate (%)	Protein (%)	Fiber (g)
Very Sensitive to Fat/Very Sensitive to Carbohydrate	1	20	25	55	35
Very Sensitive to Fat/Sensitive to Carbohydrate	2	20	35	45	35
Very Sensitive to Fat/Moderate to Carbohydrate	3	20	45	35	30
Sensitive to Fat/Very Sensitive to Carbohydrate	4	25	25	50	35
Sensitive to Fat/Sensitive to Carbohydrate	5	25	35	40	30
Sensitive to Fat/Moderate to Carbohydrate	6	25	45	30	25
Moderate to Fat/Very Sensitive to Carbohydrate	7	30	25	45	35
Moderate to Fat/Sensitive to Carbohydrate	8	30	35	35	30
Moderate to Fat/Moderate to Carbohydrate	9	30	45	25	25
Higher Tolerance to Fat/Very Sensitive to Carbohydrate	L0	35	25	40	30
Higher Tolerance to Fat/Sensitive to Carbohydrate	L1	35	35	30	25
Higher Tolerance to Fat/Moderate to Carbohydrate	L2	35	45	20	25

PERDITA DI PESO	ALTA	MEDIA	BASSA	
FUNZIONE	ASSORBIMENTO ACIDI GRASSI		TRASFORMAZIONE ADIPOCITI	
	NORMALE	AUMENTATO	STANDARD	AUMENTATA
GENE	FABP2	FABP2*	PPARγ	PPARγ*
DIETA IPOCALORICA	GG	A	CC	G/GG
ESERCIZIO FISICO	GG	A	CC	G/GG
FUNZIONE	USO GRASSI PER ENERGIA		LIPOLISI/REGOLAZ.TERMICA	
	NORMALE	BASSO	ALTA	BASSA
GENE	ADBR2	ADBR2*	ADRB3	ADRB3*
DIETA IPOCALORICA	GG	A	TT	C
ESERCIZIO FISICO	GG	A	TT	C
FUNZIONE	GRASSI/ESERCIZIO FISICO		GRASSI SATURI/DIETA	
GENE	FTO	FTO* FTO**	APOA2	APOA2* APOA2*/APOA2*
DIETA IPOCALORICA	TT	A/AA		CC MOLTO ALTA
ESERCIZIO FISICO	TT	A/AA MOLTO ALTA		

FABP2 *_**	PPRAG *_**	ADRB2 *	ADRB3 *_**	DIET	ADRB3 *_**	DIET	EXER*/DIET** >5/>4 add fto-apoa2	FTO* A /TT	APOA2** CC/T
A	CC	GG	TT	4	CC/CT	1			
A	GC	GG		3		3			
A	CC	A		1		1			
GG	CC	A		7		4			
GG	GC	A		8		5			
GG	GC	GG		9		6			
GG	GG	A		10		7			
GG	GG	GG		12		8			
		16						A OB TT =	CC assorb ac.grasssi >

DIET	SENSITIVITY FAT	SENSITIVITY CARBOHYDRATES	FAT %	CARBO %	PROTEIN %	FIBER g
1	VERY 4	VERY 4	20	25	55	35
2	VERY 4	SENS 3	20	35	45	35
3	VERY 4	MODERATE 2	20	45	35	30
4	SENS 3	VERY 4	25	25	50	35
5	SENS 3	SENS 3	25	35	40	30
6	SENS 3	MODERATE 2	25	45	30	25
7	MODERATE 2	VERY 4	30	25	45	35
8	MODERATE 2	SENS 3	30	35	35	30
9	MODERATE 2	MODERATE 2	30	45	25	25
10	TOLERANT 1	VERY 4	35	25	40	30
11	TOLERANT 1	SENS 3	35	35	30	25
12	TOLERANT 1	MODERATE 2	35	45	20	25

A drastic reduction in variants allows to create two types of panels.

1. Genetics, nutrition, physical exercise with 28 genes involved centered on lipoglycidic balance

2. Genetics, bones and muscles, sports with 11 genes involve

GeneAdvis

METABOLISMO LIPIDI-CARBOIDRATI

Gene ADRB2

ADRB2 è espresso preferenzialmente nel tessuto adiposo ed è deputato ai processi di mobilizzazione del grasso a scopo energetico.

Gene ADRB3

ADRB3 è espresso nel tessuto adiposo viscerale ed è presente nei depositi di grasso, in cui è coinvolto nei processi di lipolisi e nella regolazione termica.

Gene FABP2

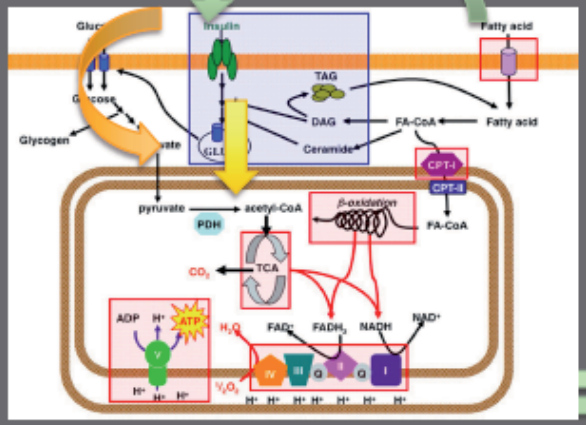
Fatty acid-binding protein-2

FABP2 codifica per proteine coinvolte nella captazione, nel trasporto e nel metabolismo intracellulare di acidi grassi a lunga catena.

Gene PPAR

Peroxisome proliferator-activated receptor

PPARg regola processi infiammatori, differenziamento cellulare, omeostasi del glucosio e dei lipidi. PPARg è un fattore determinante per la trasformazione e maturazione degli adipociti.



basso	no	si	8/14		3/1	1/5
basso	si	si	4/14		2,5/1,5	1/5
bilanciato	si	si	9/14		2,5/1,5	0/5
basso	si	si	8/14		3/1	1/5
bilanciato	no	si	3/14		3,5/0,5	1/5
bilanciato	si	si	8/14		2/2	0/5
bilanciato	si	no	4/14		2/2	0/5
bilanciato	no	si	7/14		3,5/0,5	1/5
basso	no	no	6/14		3,5/0,5	2/5
bilanciato	si	si	5/14		1,5/2,5	0/5
basso	no	no	8/14		2/2	0/5
alto	si	no	7/14		2/2	2/5
bilanciato	si	no	3/14		3/1	0/5
basso	no	no	5/14		2,5/1,5	0/5
bilanciato	no	no	8/14		2,5/1,5	2/5
alto	si	no	7/14		3,5/0,5	0/5
basso	no	no	9/14		3,5/0,5	0/5
bilanciato	si	si	5/14		2/2	0/5
bilanciato	no	si	9/14		1,5/2,5	1/5
bilanciato	si	si	2/14		3/1	0/5
bilanciato	si	si	5/14		2/2	1/5
bilanciato	si	no	4/14		1,5/2,5	1/5
bilanciato	no	no	8/14		2/2	0/5
alto	si	si	2/14		2,5/1,5	0/5
bilanciato	si	si	2/14		2,5/1,5	1/5
basso	no	si	9/14		2,5/1,5	2/5
bilanciato	no	no	8/14		3,5/0,5	0/5
basso	no	no	8/14		3,5/0,5	2/5
bilanciato	si	no	3/14		2/2	0/5
bilanciato	si	si	3/14		2/2	1/5
Carbo/lipidi	Esercizio fisico	Acidi grassi	> BMI		Forza espl/resist	Osteo injuries

ADIPOA/A	ADRB1/C	APOA5/C	GHSR/A	LEPTIN/AA	NPY/C	VEGF/G	FTO /136A	FTO /980T	FTO /085C	FTO /449G

GeneAdvise

Gene ADRB2

ADRB2 è espresso preferenzialmente nel tessuto adiposo ed è deputato ai processi di mobilizzazione del grasso a scopo energetico.

Gene ADRB3

ADRB3 è espresso nel tessuto adiposo viscerale ed è presente nei depositi di grasso, in cui è coinvolto nei processi di lipolisi e nella regolazione termica.

Gene FABP2
Fatty acid-binding protein-2
FABP2 codifica per proteine coinvolte nella captazione, nel trasporto e nel metabolismo intracellulare di acidi grassi a lunga catena.

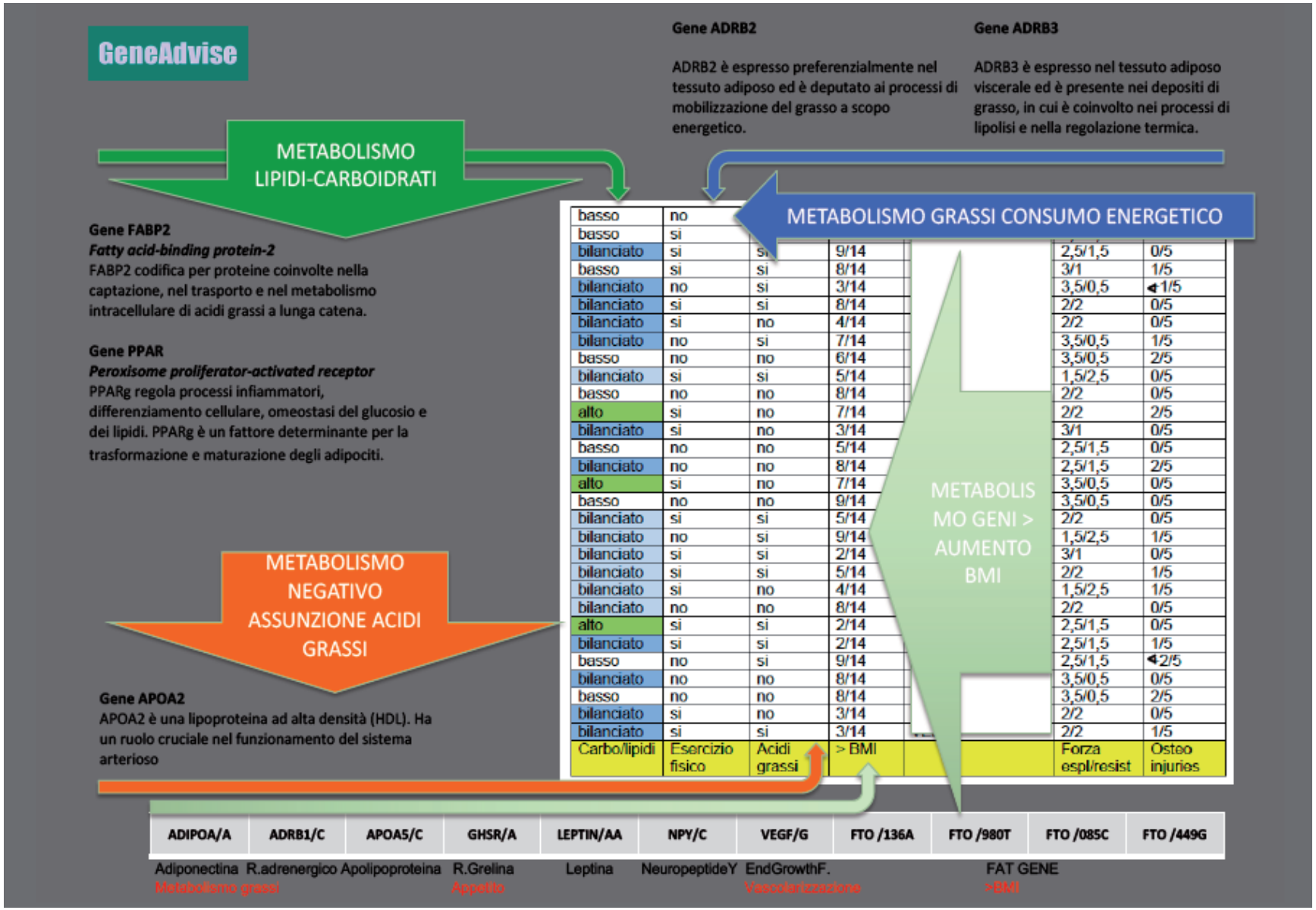
Gene PPAR
Peroxisome proliferator-activated receptor
PPARg regola processi infiammatori, differenziamento cellulare, omeostasi del glucosio e dei lipidi. PPARg è un fattore determinante per la trasformazione e maturazione degli adipociti.

Gene APOA2
APOA2 è una lipoproteina ad alta densità (HDL). Ha un ruolo cruciale nel funzionamento del sistema arterioso

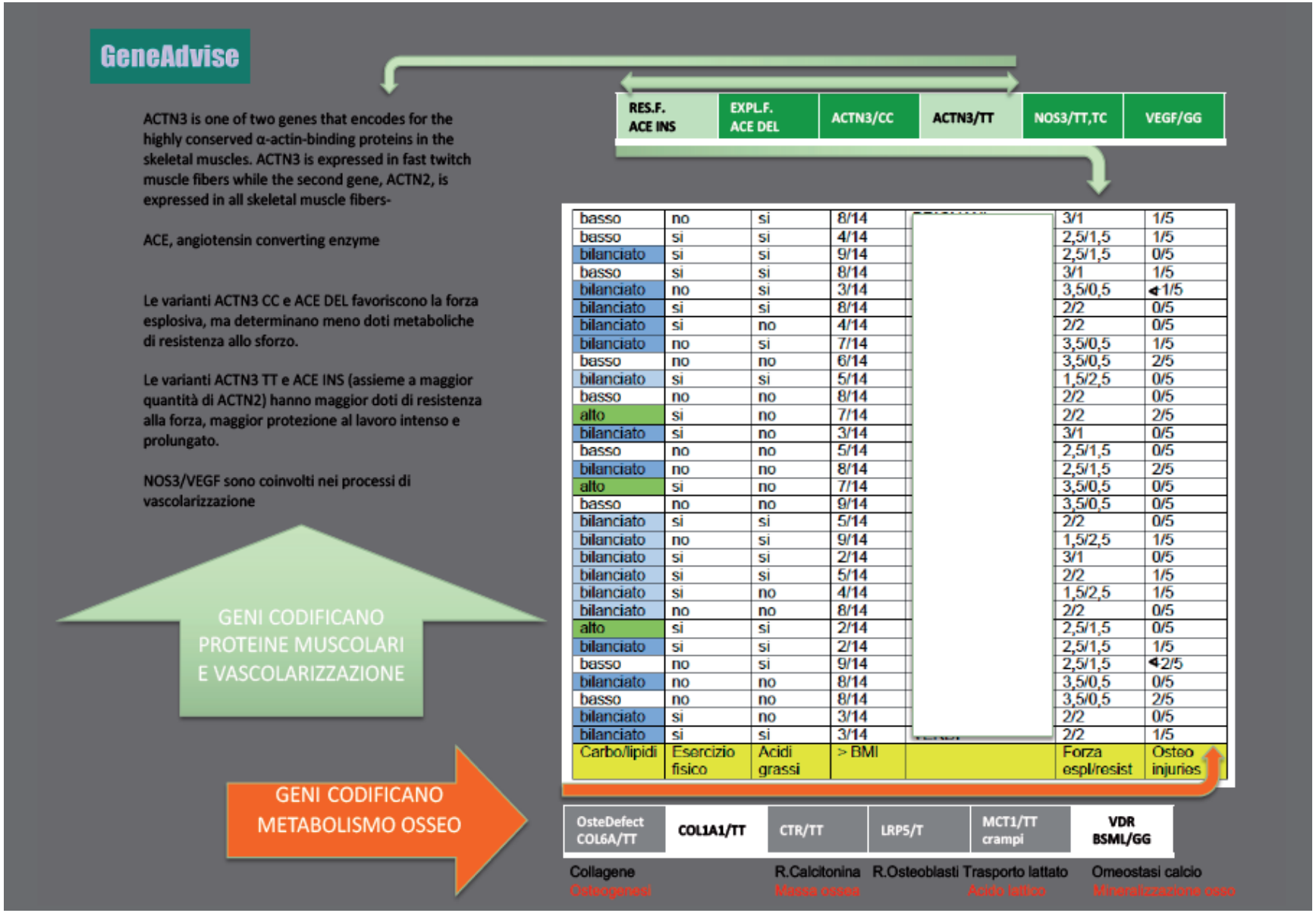
basso	no	si	8/14		3/1	1/5
basso	si	si	4/14		2,5/1,5	1/5
bilanciato	si	si	9/14		2,5/1,5	0/5
basso	si	si	8/14		3/1	1/5
bilanciato	no	si	3/14		3,5/0,5	◄1/5
bilanciato	si	si	8/14		2/2	0/5
bilanciato	si	no	4/14		2/2	0/5
bilanciato	no	si	7/14		3,5/0,5	1/5
basso	no	no	6/14		3,5/0,5	2/5
bilanciato	si	si	5/14		1,5/2,5	0/5
basso	no	no	8/14			
alto	si	no	7			
bilanciato	si	no				
basso	no	no				
bilanciato	no	no				
alto	si	no				
basso	no	no				
bilanciato	si	si	5/1			
bilanciato	no	si	9/14		1,5/2,5	1/5
bilanciato	si	si	2/14		3/1	0/5
bilanciato	si	si	5/14		2/2	1/5
bilanciato	si	no	4/14		1,5/2,5	1/5
bilanciato	no	no	8/14		2/2	0/5
alto	si	si	2/14		2,5/1,5	0/5
bilanciato	si	si	2/14		2,5/1,5	1/5
basso	no	si	9/14		2,5/1,5	◄2/5
bilanciato	no	no	8/14		3,5/0,5	0/5
basso	no	no	8/14		3,5/0,5	2/5
bilanciato	si	no	3/14		2/2	0/5
bilanciato	si	si	3/14		2/2	1/5
Carbo/lipidi	Esercizio fisico	Acidi grassi	> BMI		Forza espl/resist	Osteo injuries

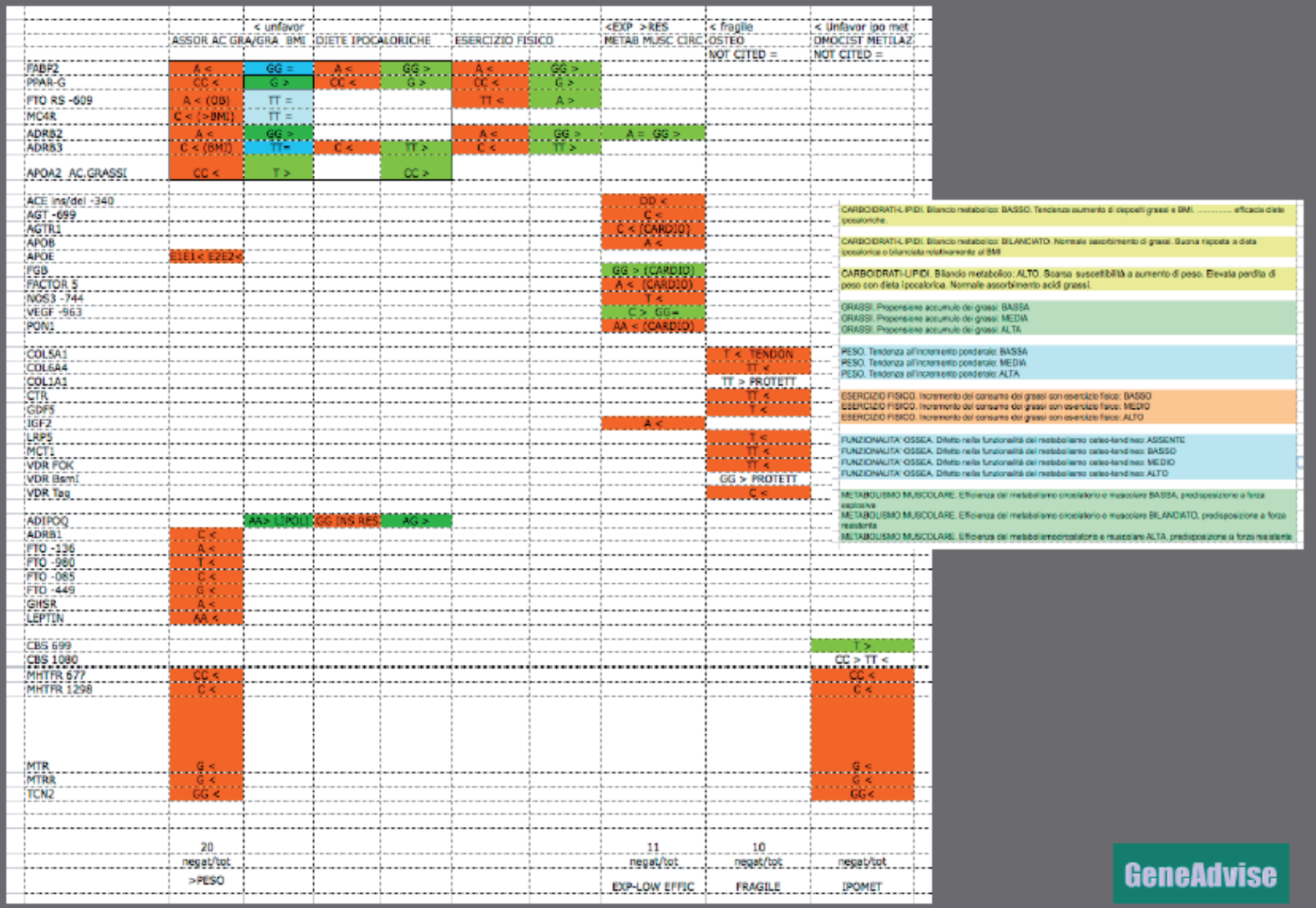
METABOLISMO
MOBILIZZAZIONE GRASSI
PER ENERGIA

ADIPOA/A	ADRB1/C	APOA5/C	GHSR/A	LEPTIN/AA	NPY/C	VEGF/G	FTO /136A	FTO /980T	FTO /085C	FTO /449G



basso	no						
basso	si						
bilanciato	si	si	9/14			2,5/1,5	0/5
basso	si	si	8/14			3/1	1/5
bilanciato	no	si	3/14			3,5/0,5	◀1/5
bilanciato	si	si	8/14			2/2	0/5
bilanciato	si	no	4/14			2/2	0/5
bilanciato	no	si	7/14			3,5/0,5	1/5
basso	no	no	6/14			3,5/0,5	2/5
bilanciato	si	si	5/14			1,5/2,5	0/5
basso	no	no	8/14			2/2	0/5
alto	si	no	7/14			2/2	2/5
bilanciato	si	no	3/14			3/1	0/5
basso	no	no	5/14			2,5/1,5	0/5
bilanciato	no	no	8/14			2,5/1,5	2/5
alto	si	no	7/14			3,5/0,5	0/5
basso	no	no	9/14			3,5/0,5	0/5
bilanciato	si	si	5/14			2/2	0/5
bilanciato	no	si	9/14			1,5/2,5	1/5
bilanciato	si	si	2/14			3/1	0/5
bilanciato	si	si	5/14			2/2	1/5
bilanciato	si	no	4/14			1,5/2,5	1/5
bilanciato	no	no	8/14			2/2	0/5
alto	si	si	2/14			2,5/1,5	0/5
bilanciato	si	si	2/14			2,5/1,5	1/5
basso	no	si	9/14			2,5/1,5	◀2/5
bilanciato	no	no	8/14			3,5/0,5	0/5
basso	no	no	8/14			3,5/0,5	2/5
bilanciato	si	no	3/14			2/2	0/5
bilanciato	si	si	3/14			2/2	1/5


GeneAdvise
ACTN3 is one of two genes that encodes for the highly conserved α-actin-binding proteins in the skeletal muscles. ACTN3 is expressed in fast twitch muscle fibers while the second gene, ACTN2, is expressed in all skeletal muscle fibers-
ACE, angiotensin converting enzyme
Le varianti ACTN3 CC e ACE DEL favoriscono la forza esplosiva, ma determinano meno doti metaboliche di resistenza allo sforzo.
Le varianti ACTN3 TT e ACE INS (assieme a maggior quantità di ACTN2) hanno maggior doti di resistenza alla forza, maggior protezione al lavoro intenso e prolungato.
NOS3/VEGF sono coinvolti nei processi di vascolarizzazione
GENI CODIFICANO PROTEINE MUSCOLARI E VASCOLARIZZAZIONE
GENI CODIFICANO METABOLISMO OSSEO
RES.F. ACE INS
EXPL.F. ACE DEL
ACTN3/CC
ACTN3/TT
NOS3/TT,TC
VEGF/GG
basso no si 8/14 3/1 1/5
basso si si 4/14 2,5/1,5 1/5
bilanciato si si 9/14 2,5/1,5 0/5
basso si si 8/14 3/1 1/5
bilanciato no si 3/14 3,5/0,5 1/5
bilanciato si si 8/14 2/2 0/5
bilanciato si no 4/14 2/2 0/5
bilanciato no si 7/14 3,5/0,5 1/5
basso no no 6/14 3,5/0,5 2/5
bilanciato si si 5/14 1,5/2,5 0/5
basso no no 8/14 2/2 0/5
alto si no 7/14 2/2 2/5
bilanciato si no 3/14 3/1 0/5
basso no no 5/14 2,5/1,5 0/5
bilanciato no no 8/14 2,5/1,5 2/5
alto si no 7/14 3,5/0,5 0/5
basso no no 9/14 3,5/0,5 0/5
bilanciato si si 5/14 2/2 0/5
bilanciato no si 9/14 1,5/2,5 1/5
bilanciato si si 2/14 3/1 0/5
bilanciato si si 5/14 2/2 1/5
bilanciato si no 4/14 1,5/2,5 1/5
bilanciato no no 8/14 2/2 0/5
alto si si 2/14 2,5/1,5 0/5
bilanciato si si 2/14 2,5/1,5 1/5
basso no si 9/14 2,5/1,5 2/5
bilanciato no no 8/14 3,5/0,5 0/5
basso no no 8/14 3,5/0,5 2/5
bilanciato si no 3/14 2/2 0/5
bilanciato si si 3/14 2/2 1/5
Carbo/lipidi
Esercizio fisico
Acidi grassi
> BMI
Forza espl/resist
Osteo injuries
OsteDefect COL6A/TT
COL1A1/TT
CTR/TT
LRP5/T
MCT1/TT crampi
VDR BSML/GG
Collagene
Osteogenesi
R.Calcitonina
Massa ossea
R.Osteoblasti
Trasporto lattato
Acido lattico
Omeostasi calcio
Mineralizzazione osso


< unfavor
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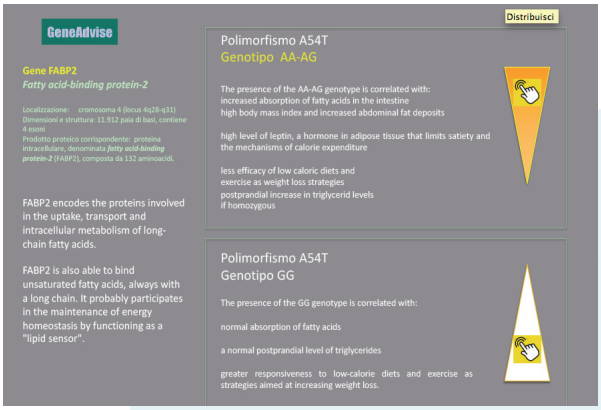
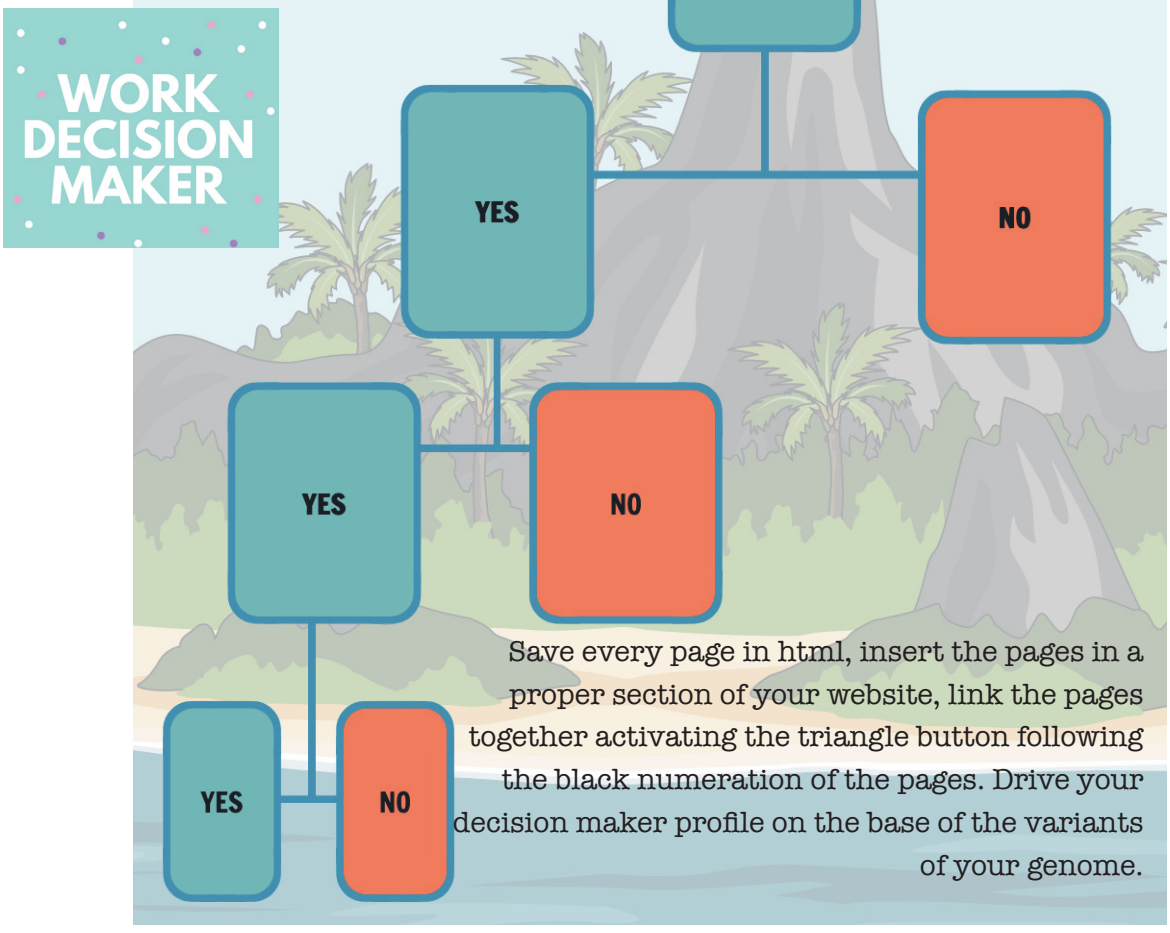
ASSOR AC GRA/GRA BMI
DIETE IPOCALORICHE
ESERCIZIO FISICO
METAB MUSC CIRC
OSTEO
OMOCIST METILAZ
NOT CITED =
NOT CITED =
FABP2
PPAR-G
FTO RS -609
MC4R
ADRB2
ADRB3
APOA2 AC.GRASSI
ACE ins/del -340
AGT -699
AGTR1
APOB
APOE
FGB
FACTOR 5
NOS3 -744
VEGF -963
PON1
COL5A1
COL6A4
COL1A1
CTR
GDF5
IGF2
LRP5
MCT1
VDR FOK
VDR BsmI
VDR Taq
ADIPOQ
ADRB1
FTO -136
FTO -960
FTO -085
FTO -449
GHSR
LEPTIN
CBS 699
CBS 1080
MHTFR 677
MHTFR 1298
MTR
MTRR
TCN2
AA> LIPOLI
GG INS RES
AG >
20
negat/tot
>PESO
11
negat/tot
EXP-LOW EFFIC
10
negat/tot
FRAGILE
negat/tot
[POMET
CARBOIDRATI-LIPIDI. Bilancio metabolico: BASSO. Tendenza aumento di depositi grassi e BMI. ..... efficacia diete ipocaloriche.
CARBOIDRATI-LIPIDI. Bilancio metabolico: BILANCIATO. Normale assorbimento di grassi. Buona risposta a dieta ipocalorica o bilanciata relativamente al BMI
CARBOIDRATI-LIPIDI. Bilancio metabolico: ALTO. Scarsa suscettibilità a aumento di peso. Elevata perdita di peso con dieta ipocalorica. Normale assorbimento acidi grassi.
GRASSI. Propensione accumulo dei grassi: BASSA
GRASSI. Propensione accumulo dei grassi: MEDIA
GRASSI. Propensione accumulo dei grassi: ALTA
PESO. Tendenza all'incremento ponderale: BASSA
PESO. Tendenza all'incremento ponderale: MEDIA
PESO. Tendenza all'incremento ponderale: ALTA
ESERCIZIO FISICO. Incremento del consumo dei grassi con esercizio fisico: BASSO
ESERCIZIO FISICO. Incremento del consumo dei grassi con esercizio fisico: MEDIO
ESERCIZIO FISICO. Incremento del consumo dei grassi con esercizio fisico: ALTO
FUNZIONALITA' OSSEA. Difetto nella funzionalità del metabolismo osteo-tendineo: ASSENTE
FUNZIONALITA' OSSEA. Difetto nella funzionalità del metabolismo osteo-tendineo: BASSO
FUNZIONALITA' OSSEA. Difetto nella funzionalità del metabolismo osteo-tendineo: MEDIO
FUNZIONALITA' OSSEA. Difetto nella funzionalità del metabolismo osteo-tendineo: ALTO
METABOLISMO MUSCOLARE. Efficienza del metabolismo circolatorio e muscolare BASSA, predisposizione a forza esplosiva
METABOLISMO MUSCOLARE. Efficienza del metabolismo circolatorio e muscolare BILANCIATO, predisposizione a forza resistente
METABOLISMO MUSCOLARE. Efficienza del metabolismo circolatorio e muscolare ALTA, predisposizione a forza resistente

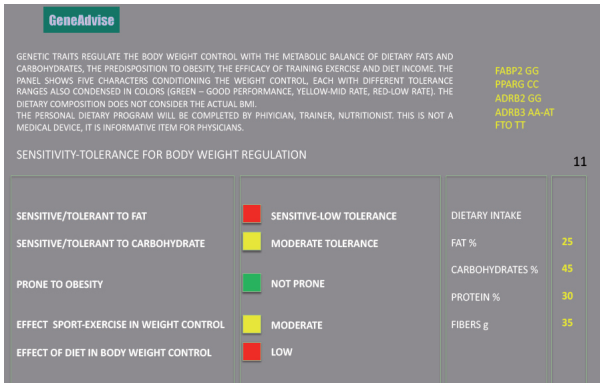
GeneAdvise

TOOLS FOR AN INTERACTIVE APPROACH TO A GENETIC NUTRITION PROFILE





Save every page in html, insert the pages in a proper section of your website, link the pages together activating the triangle button following the black numeration of the pages. Drive your decision maker profile on the base of the variants of your genome.



GeneAdvise
Advisor in Human Genetics

GENE-PERSONA

Lamberto Camurri, PhD, PM

Medi Saluser Parma
Mendel Genetica Medica Modena
Fellow Università Tor Vergata Roma-
Istituto Genetica Medica

Centro Cuore Salute Reggio Emilia
FASI Fed Arrampicata Sportiva Italiana

Francesca Camurri, BS, PA
Angela Godi Palmi, AA, EA

GENETICS AND PERSONALIZED MEDICINE
PREDICTIVE AND FUNCTIONAL MARKERS

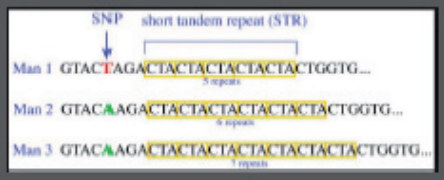
MODEL FOR INTERACTIVE EVALUATION OF GENETIC PROFILES

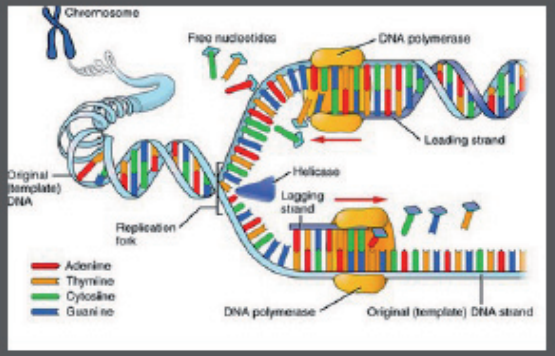
METHABOLISM, CARBO-LIPIDIC BALANCE, SPORT AND DIET

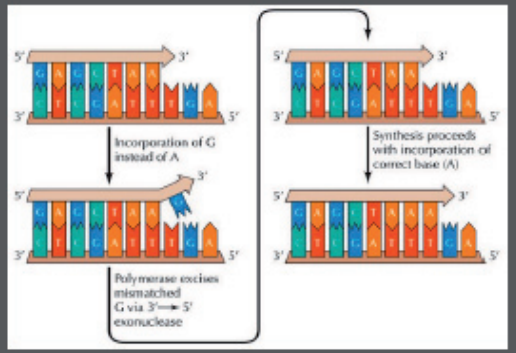
GeneAdvise

Some technical / scientific information.

Each gene is present in the cells of the body in two copies (alleles). The same gene can differ from one person to another even for just one base, one letter of its code: SNP (Single Nucleotide Polymorphism) Variations in the sequence of genes can give rise to Variants. Pathogenetic variants have harmful effects on the functioning of the gene, even blocking it. Non-pathogenic variants have different frequency in the general population and are associated with differences that modify the function of the gene without compromising it.

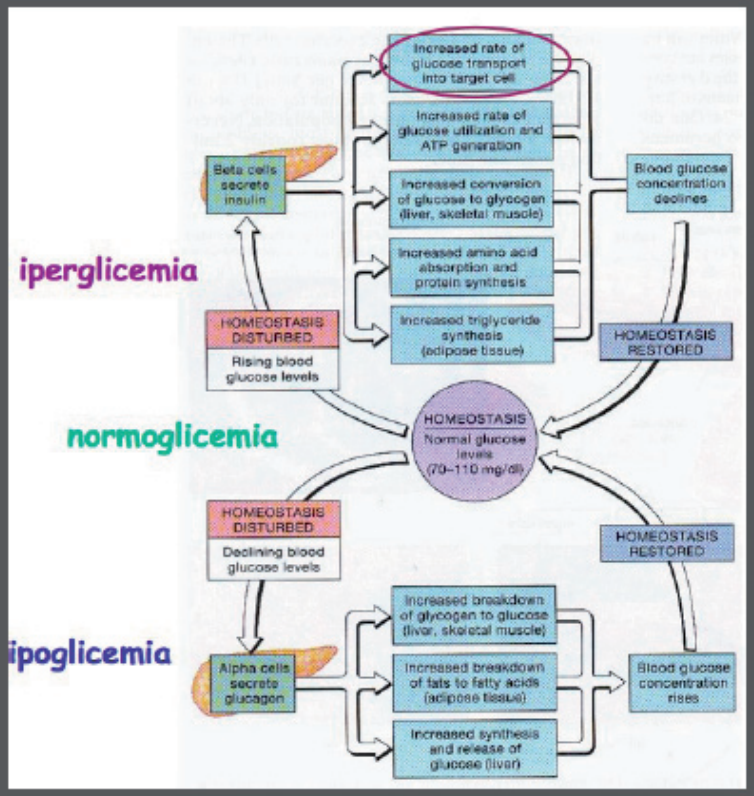


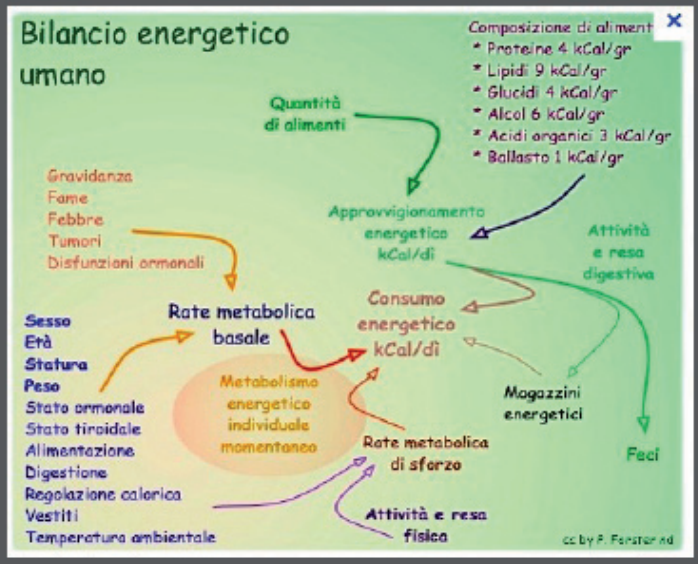


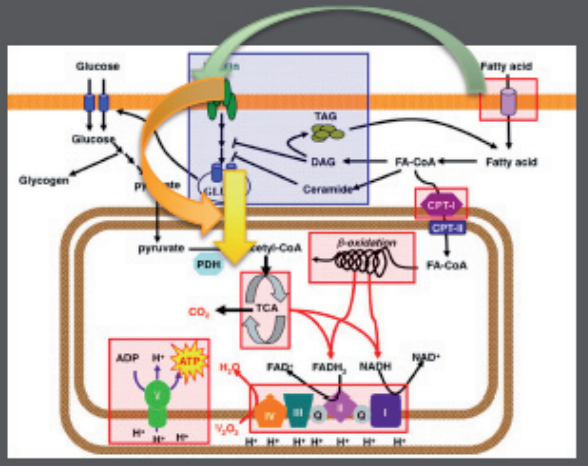


GeneAdvise

PERSONALIZED PHYSIOLOGY
FOOD AND ENERGETIC CONSUMPTION
CARBO-LIPO COMPLEX







GeneAdvise

PERSONALIZED PHYSIOLOGY
FOOD AND ENERGETIC CONSUMPTION
CARBO-LIPO COMPLEX

Fatty acid-binding protein-2 **FABP2 (A54T G-A rs1799883)**
absorption of fatty acids, abdominal fat deposits, leptin levels (appetite and satiety, calorie expenditure)

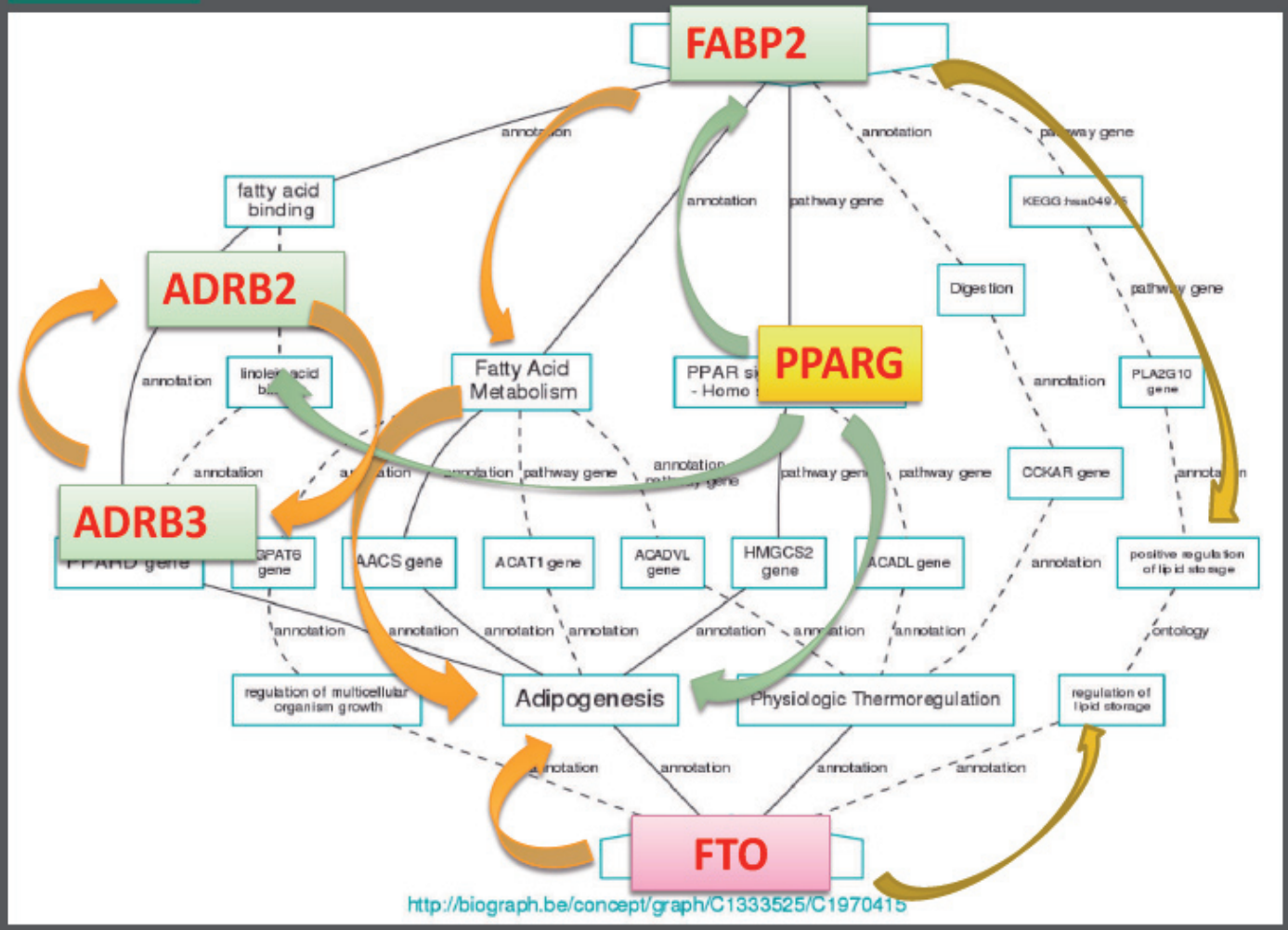
Peroxisome proliferator-activated receptor **PPARg (P12A C-G rs1801282)**
Differentiation of fat cells, regulation of glucose-lipid balances, diet-sport combination

Adrenergic-beta-2-receptor **ADRB2 (G16R G-A rs1042713)**
use of cell fat for energy is strongly involved in the combined diet-sport action

Adrenergic-beta-3-receptor **ADRB3 (W64R T-C rs4994)**
consumption of fat for thermoregulation purposes and is conditioned by physical activity

Fat Mass and Obesity Associated Gene **FTO (T-A rs9939609)**
risk of obesity, is modulated by physical activity

GeneAdvise


FABP2
ADRB2
ADRB3
PPARG
FTO
fatty acid binding
Fatty Acid Metabolism
Digestion
CCKAR gene
PLA2G10 gene
positive regulation of lipid storage
GPAT6 gene
AACS gene
ACAT1 gene
ACADVL gene
HMGCS2 gene
ACADL gene
regulation of multicellular organism growth
Adipogenesis
Physiologic Thermoregulation
regulation of lipid storage
annotation
pathway gene
ontology
http://biograph.be/concept/graph/C1333525/C1970415

GeneAdvise

Gene FABP2

Fatty acid-binding protein-2

Localizzazione: cromosoma 4 (locus 4q28-q31)
Dimensioni e struttura: 11.912 paia di basi, contiene 4 esoni
Prodotto proteico corrispondente: proteina intracellulare, denominata ***fatty acid-binding protein-2*** (FABP2), composta da 132 aminoacidi.

FABP2 encodes the proteins involved in the uptake, transport and intracellular metabolism of long-chain fatty acids.

FABP2 is also able to bind unsaturated fatty acids, always with a long chain. It probably participates in the maintenance of energy homeostasis by functioning as a "lipid sensor".

Polimorfismo A54T
Genotipo AA-AG

The presence of the AA-AG genotype is correlated with:
increased absorption of fatty acids in the intestine
high body mass index and increased abdominal fat deposits

high level of leptin, a hormone in adipose tissue that limits satiety and the mechanisms of calorie expenditure

less efficacy of low caloric diets and exercise as weight loss strategies
postprandial increase in triglycerid levels if homozygous

Polimorfismo A54T
Genotipo GG

The presence of the GG genotype is correlated with:

normal absorption of fatty acids

a normal postprandial level of triglycerides

greater responsiveness to low-calorie diets and exercise as strategies aimed at increasing weight loss.

GeneAdvise

Gene PPAR
Peroxisome proliferator-activated receptor

Localizzazione: cromosoma 3 (locus 3p25)
Dimensioni e struttura: 3302 paia di basi, contiene 6 esoni
Prodotto proteico: ***peroxisome proliferator-activated receptor-gamma*** (PPARg), composta da 477 aminoacidi.

PPARg regulates inflammatory processes, cell differentiation, glucose and lipid homeostasis,

PPARg is a determining factor for the transformation and maturation of adipocytes.
Alterations in PPARg function are related to diabetes-2. It is a candidate as a critical factor in obesity.

PPARCC polymorphism is related to decreased activity of the protein.

Polimorfismo 12Pro/Ala
Genotipo GG/CG

The presence of the GG / GC genotype is correlated with:

A lower susceptibility to body weight gain in relation to the amount of fat consumed in the diet

High response to weight loss following constant exercise and a controlled diet.

FABP2 AA-AG

Polimorfismo 12Pro/Ala
Genotipo CC

The presence of the CC genotype is correlated with:

greater sensitivity of the Body Mass Index to the amount of fat consumed in the diet

ability to lose weight poorly conditioned by exercise

GeneAdvise

Gene PPAR

Peroxisome proliferator-activated receptor

Localizzazione: cromosoma 3 (locus 3p25)
Dimensioni e struttura: 3302 paia di basi, contiene 6 esoni
Prodotto proteico: ***peroxisome proliferator-activated receptor-gamma*** (PPARg), composta da 477 aminoacidi.

PPARg regulates inflammatory processes, cell differentiation, glucose and lipid homeostasis,

PPARg is a determining factor for the transformation and maturation of adipocytes.
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Genotipo GG/CG

The presence of the GG / GC genotype is correlated with:

A lower susceptibility to body weight gain in relation to the amount of fat consumed in the diet

High response to weight loss following constant exercise and a controlled diet.

FABP2 GG

Polimorfismo 12Pro/Ala
Genotipo CC

The presence of the CC genotype is correlated with:

greater sensitivity of the Body Mass Index to the amount of fat consumed in the diet

ability to lose weight poorly conditioned by exercise

GeneAdvise

Gene ADRB2

Localizzazione: cromosoma 5 (locus 5q31-q32)
Dimensioni e struttura: 2033 paia di basi, contiene 4 esoni
Prodotto : proteina intracellulare, **adrenergic- beta-2- receptor** (ADRB2), composta da 413 aminoacidi.

ADRB2 encodes the type 2 beta adrenergic receptor which inserts into the cell membrane where it interacts with mediators (adrenaline / noradrenaline).

The ADRB2 receptor is directly associated with its final effector, an L-type calcium channel (Ca (V) 1.2). This receptor / channel complex binds to a cAMP-dependent G protein that allows for the rapid transmission of specific biochemical signals.

ADRB2 is preferentially expressed in adipose tissue and is responsible for the processes of mobilization of fat for energy purposes.

Polimorfismo 16Gly/Arg
Genotipo AA/AG

The presence of the AA / AG genotype:

Increase in pathology in asthmatic patients
greater weight gain a low attitude to lose weight
following physical exercise

Polimorfismo 16Gly/Arg
Genotipo GG

The presence of the GG genotype:

low susceptibility to weight gain with increasing age

good predisposition to lose weight following
exercise good aerobic sports performance

FABP2 GG
PPARG GG-CG

GeneAdvise

Gene ADRB2

Localizzazione: cromosoma 5 (locus 5q31-q32)
Dimensioni e struttura: 2033 paia di basi, contiene 4 esoni
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Genotipo GG

The presence of the GG genotype:

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good predisposition to lose weight following
exercise good aerobic sports performance

FABP2 AA-AG
PPARG CC

GeneAdvise

Gene ADRB3

Localizzazione: cromosoma 8 (locus 8p12-p11.2)
Dimensioni e struttura: 10672 paia di basi, non contiene introni
Prodotto: proteina intracellulare, **adrenergic- beta- 3- receptor** (ADRB3), composta da 408 aminoacidi.

ADRB3 encodes the type 3 beta adrenergic receptor, which regulates cellular or tissue functions by acting with transmitters such as adrenaline or noradrenaline.

ADRB3 is expressed in visceral adipose tissue and is present in fat deposits, where it is involved in lipolysis processes and thermal regulation.

Polimorfismo 64Arg/Trp
Genotipo CC/CT

The presence of the CC / CT genotype:

reduced lipolysis in response to catecholamines and consequent lower response to physical activity as a strategy aimed at weight loss
Increase in body mass index and greater risk of obesity poor responsiveness to low-calorie diets

Polimorfismo 64Arg/Trp
Genotipo TT

The presence of the TT genotype:

good response to low-caloric diets

good predisposition to loose weight following exercise

FABP2 GG
PPARG GG-CG
ADRB2 AA-AG

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Gene ADRB3

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good predisposition to loose weight following exercise

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Genotipo TT

The presence of the TT genotype:

good response to low-caloric diets

good predisposition to loose weight following exercise

FABP2 AA-AG
PPARG CC
ADRB2 GG

GeneAdvise

Gene FTO "FAT GENE"

Localizzazione: cromosoma 16
Dimensioni e struttura: 410505 paia di basi, contiene 9 esoni
Prodotto : proteina diossigenase alfa-chetoglutarato-dipendente, composta da 505 aminoacidi.

FTO (Fat Mass and Obesity Associated Gene) has unknown function.
It appears to be a role of FTO in DNA demethylation. Its level of expression is regulated by the nutritional behaviour.
FTO has particular importance in regulating body weight due to the relationship between its polymorphisms and the impact of physical exercise on anthropometric parameters.

Rs9939609 Genotipo AA/AT
Presence of genotype AA/AT

increase in anthropometric indices, risk of obesity

good responsiveness of the subject to physical exercise

Rs9939609 Genotipo TT
Presence of genotype TT

normal increase in anthropometric parameters, low risk of obesity.

poor sensitivity of the body mass index to physical exercise as a strategy for weight loss

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PPARG GG-CG
ADRB2 AA-AG
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PPARG CC
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FABP2 AA-AG
PPARG CC
ADRB2 AA-AG
ADRB3 TAA-AT

GeneAdvise

GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 CC-CT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

1

SENSITIVE/TOLERANT TO FAT	**MODERATE TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**VERY SENSITIVE-LOW TOLERANCE**	FAT %	30
		CARBOHYDRATES %	25
PRONE TO OBESITY	**PRONE**	PROTEIN %	45
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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FABP2 GG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 CC-CT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

1

SENSITIVE/TOLERANT TO FAT	**MODERATE TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**VERY SENSITIVE-LOW TOLERANCE**	FAT %	30
		CARBOHYDRATES %	25
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	45
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**LOW**	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

GeneAdvise

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FABP2 GG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

2

SENSITIVE/TOLERANT TO FAT	**HIGHER TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE**	FAT %	30
PRONE TO OBESITY	**PRONE**	CARBOHYDRATES %	45
		PROTEIN %	20
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**VERY HIGH**	FIBERS g	25
EFFECT OF DIET IN BODY WEIGHT CONTROL	**HIGH**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

2

SENSITIVE/TOLERANT TO FAT	**HIGHER TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**30**
		CARBOHYDRATES %	**45**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**20**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**HIGH**	FIBERS g	**25**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**HIGH**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG GG-CG
ADRB2 GG
ADRB3 AA-AT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

3

SENSITIVE/TOLERANT TO FAT	SENSITIVE-LOW TOLERANCE	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	MODERATE TOLERANCE	FAT %	30
PRONE TO OBESITY	PRONE	CARBOHYDRATES %	25
		PROTEIN %	45
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	HIGH	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	MODERATE		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG GG-CG
ADRB2 GG
ADRB3 AA-AT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

3

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**30**
		CARBOHYDRATES %	**25**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**45**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG GG-CG
ADRB2 GG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	**HIGHER TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**35**
		CARBOHYDRATES %	**40**
PRONE TO OBESITY	**PRONE**	PROTEIN %	**25**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**VERY HIGH**	FIBERS g	**25**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**HIGH**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG GG-CG
ADRB2 GG
ADRB3 TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

4

SENSITIVE/TOLERANT TO FAT	**HIGHER TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	35
		CARBOHYDRATES %	40
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	25
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**HIGH**	FIBERS g	25
EFFECT OF DIET IN BODY WEIGHT CONTROL	**HIGH**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 AA-AG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 AA-AT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

5

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**20**
		CARBOHYDRATES %	**45**
PRONE TO OBESITY	**PRONE**	PROTEIN %	**35**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**LOW**	FIBERS g	**30**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

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FABP2 AA-AG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 AA-AT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

5

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**20**
		CARBOHYDRATES %	**45**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**35**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**LOW**	FIBERS g	**30**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

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FABP2 AA-AG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

6

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**25**
		CARBOHYDRATES %	**45**
PRONE TO OBESITY	**PRONE**	PROTEIN %	**30**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**25**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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FABP2 AA-AG
PPARG GG-CG
ADRB2 AA-AG
ADRB3 TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

6

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**25**
		CARBOHYDRATES %	**45**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**30**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**25**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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FABP2 AA-AG
PPARG GG-CG
ADRB2 GG
ADRB3 AT-TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

7

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	20
		CARBOHYDRATES %	45
PRONE TO OBESITY	**PRONE**	PROTEIN %	35
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	30
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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FABP2 AA-AG
PPARG GG-CG
ADRB2 GG
ADRB3 AT-TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	20
		CARBOHYDRATES %	45
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	35
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	30
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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FABP2 AA-AG
PPARG GG-CG
ADRB2 GG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

8

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	20
		CARBOHYDRATES %	45
PRONE TO OBESITY	**PRONE**	PROTEIN %	35
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	30
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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FABP2 AA-AG
PPARG GG-CG
ADRB2 GG
ADRB3 TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	**20**
		CARBOHYDRATES %	**45**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**35**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**30**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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FABP2 GG
PPARG CC
ADRB2 AA-AG
ADRB3 AA-AT
FTO AA.AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	SENSITIVE-LOW TOLERANCE	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	VERY SENSITIVE-LOW TOLERANCE	FAT %	25
		CARBOHYDRATES %	25
PRONE TO OBESITY	PRONE	PROTEIN %	50
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	LOW	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	LOW		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG CC
ADRB2 AA-AG
ADRB3 AA-AT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**VERY SENSITIVE-LOW TOLERANCE**	FAT %	25
		CARBOHYDRATES %	25
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	50
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG CC
ADRB2 AA-AG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

10

SENSITIVE/TOLERANT TO FAT	**MODERATE TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**VERY SENSITIVE-LOW TOLERANCE**	FAT %	**30**
		CARBOHYDRATES %	**25**
PRONE TO OBESITY	**PRONE**	PROTEIN %	**45**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

GeneAdvise

GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG CC
ADRB2 AA-AG
ADRB3 TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

10

SENSITIVE/TOLERANT TO FAT	**MODERATE TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**VERY SENSITIVE-LOW TOLERANCE**	FAT %	**30**
		CARBOHYDRATES %	**25**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**45**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

GeneAdvise

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FABP2 GG
PPARG CC
ADRB2 GG
ADRB3 AA-AT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**MODERATE TOLERANCE**	FAT %	25
PRONE TO OBESITY	**PRONE**	CARBOHYDRATES %	45
		PROTEIN %	30
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

GeneAdvise

GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG CC
ADRB2 GG
ADRB3 AA-AT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

11

SENSITIVE/TOLERANT TO FAT	SENSITIVE-LOW TOLERANCE	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	MODERATE TOLERANCE	FAT %	25
		CARBOHYDRATES %	45
PRONE TO OBESITY	NOT PRONE	PROTEIN %	30
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	MODERATE	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	LOW		

GeneAdvise

GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 GG
PPARG CC
ADRB2 GG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

12

SENSITIVE/TOLERANT TO FAT	**MODERATE TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**SENSITIVE-LOW TOLERANCE**	FAT %	30
PRONE TO OBESITY	**PRONE**	CARBOHYDRATES %	25
		PROTEIN %	45
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**HIGH**	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

GeneAdvise

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FABP2 GG
PPARG CC
ADRB2 GG
ADRB3 TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

12

SENSITIVE/TOLERANT TO FAT	MODERATE TOLERANCE	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	SENSITIVE-LOW TOLERANCE	FAT %	30
PRONE TO OBESITY	NOT PRONE	CARBOHYDRATES %	25
		PROTEIN %	45
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	MODERATE	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	MODERATE		

GeneAdvise

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FABP2 AA-AG
PPARG CC
ADRB2 GG
ADRB3 AA-AT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**SENSITIVE-LOW TOLERANCE**	FAT %	20
		CARBOHYDRATES %	35
PRONE TO OBESITY	**PRONE**	PROTEIN %	45
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 AA-AG
PPARG CC
ADRB2 GG
ADRB3 AA-AT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

13

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**SENSITIVE-LOW TOLERANCE**	FAT %	**20**
		CARBOHYDRATES %	**35**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**45**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**LOW**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

GeneAdvise

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FABP2 AA-AG
PPARG CC
ADRB2 GG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

14

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**SENSITIVE-LOW TOLERANCE**	FAT %	**25**
		CARBOHYDRATES %	**30**
PRONE TO OBESITY	**PRONE**	PROTEIN %	**45**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 AA-AG
PPARG CC
ADRB2 AA-AG
ADRB3 TT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

15

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**SENSITIVE-LOW TOLERANCE**	FAT %	**25**
		CARBOHYDRATES %	**30**
PRONE TO OBESITY	**PRONE**	PROTEIN %	**45**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**MODERATE**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 AA-AG
PPARG CC
ADRB2 AA-AG
ADRB3 TT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

15

SENSITIVE/TOLERANT TO FAT	**SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**SENSITIVE-LOW TOLERANCE**	FAT %	**25**
		CARBOHYDRATES %	**30**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**45**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**LOW**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**MODERATE**		

GeneAdvise

GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 AA-AG
PPARG CC
ADRB2 AA-AG
ADRB3 AA-AT
FTO AA-AT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**VERY SENSITIVE-LOW TOLERANCE**	FAT %	20
		CARBOHYDRATES %	25
PRONE TO OBESITY	**PRONE**	PROTEIN %	55
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**LOW**	FIBERS g	35
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

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GENETIC TRAITS REGULATE THE BODY WEIGHT CONTROL WITH THE METABOLIC BALANCE OF DIETARY FATS AND CARBOHYDRATES, THE PREDISPOSITION TO OBESITY, THE EFFICACY OF TRAINING EXERCISE AND DIET INCOME. THE PANEL SHOWS FIVE CHARACTERS CONDITIONING THE WEIGHT CONTROL, EACH WITH DIFFERENT TOLERANCE RANGES ALSO CONDENSED IN COLORS (GREEN – GOOD PERFORMANCE, YELLOW-MID RATE, RED-LOW RATE). THE DIETARY COMPOSITION DOES NOT CONSIDER THE ACTUAL BMI.
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FABP2 AA-AG
PPARG CC
ADRB2 AA-AG
ADRB3 AA-AT
FTO TT

SENSITIVITY-TOLERANCE FOR BODY WEIGHT REGULATION

16

SENSITIVE/TOLERANT TO FAT	**VERY SENSITIVE-LOW TOLERANCE**	DIETARY INTAKE	
SENSITIVE/TOLERANT TO CARBOHYDRATE	**VERY SENSITIVE-LOW TOLERANCE**	FAT %	**20**
		CARBOHYDRATES %	**25**
PRONE TO OBESITY	**NOT PRONE**	PROTEIN %	**55**
EFFECT SPORT-EXERCISE IN WEIGHT CONTROL	**LOW**	FIBERS g	**35**
EFFECT OF DIET IN BODY WEIGHT CONTROL	**LOW**		

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PRENATAL DIAGNOSIS

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