Genômica Nutricional

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Faculdade de Saúde Pública – USP
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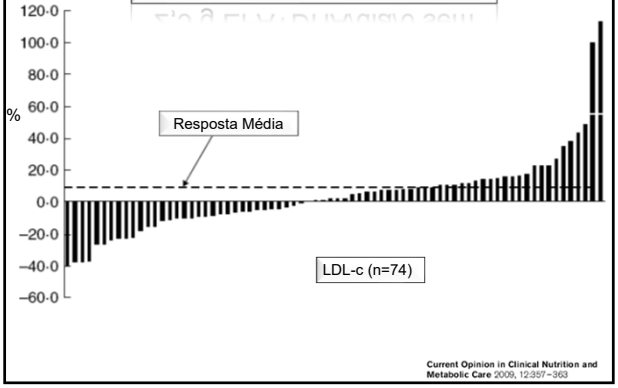
1

Por que estudar Genômica Nutricional?

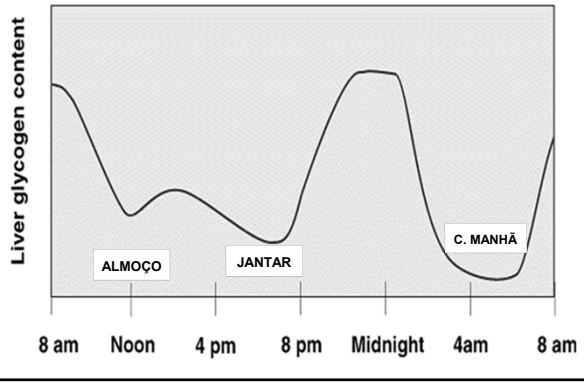
2

LDL-colesterol e ingestão de 2,5 g EPA+DHA/dia/6 sem



3

Glicogênio Hepático



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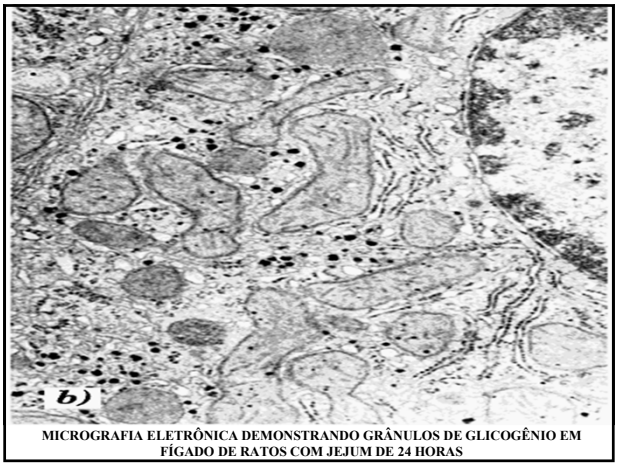
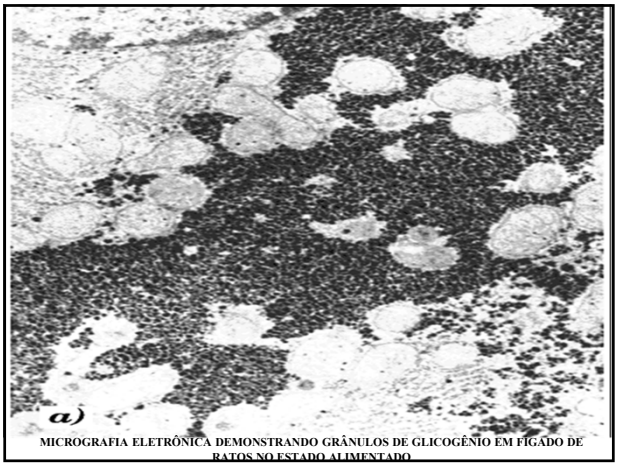


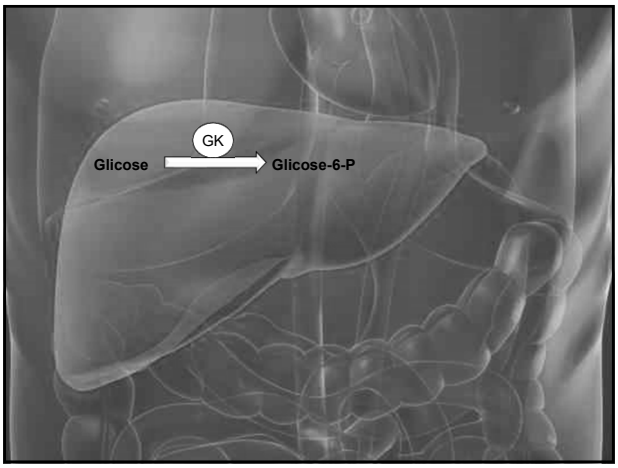
MICROGRAFIA ELETRÔNICA DEMONSTRANDO GRÂNULOS DE GLICOGÊNIO EM FÍGADO DE RATOS COM JEJUM DE 24 HORAS

5

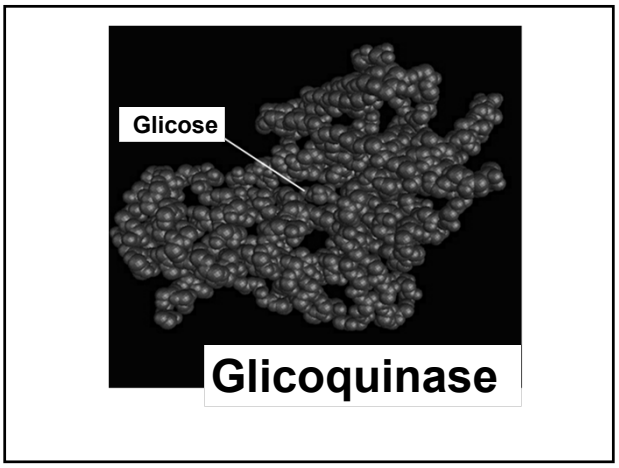


MICROGRAFIA ELETRÔNICA DEMONSTRANDO GRÂNULOS DE GLICOGÊNIO EM FÍGADO DE RATOS NO ESTADO ALIMENTADO

6



7



8

Genômica Nutricional

9

Nascimento da Biologia Molecular Moderna

25-04-1953

Watson JD. Crick FH. Molecular structure of nucleic acids. Nature 171:737-738, 1953

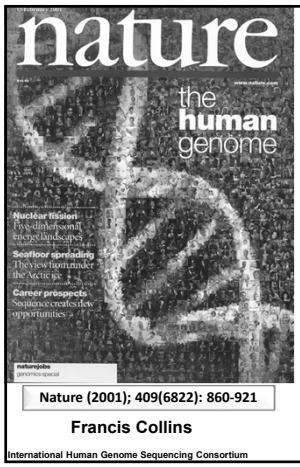
1962 Nobel Prize for Physiology or Medicine

10

The Human Genome Project

1990 - 2003

11



Craig Venter

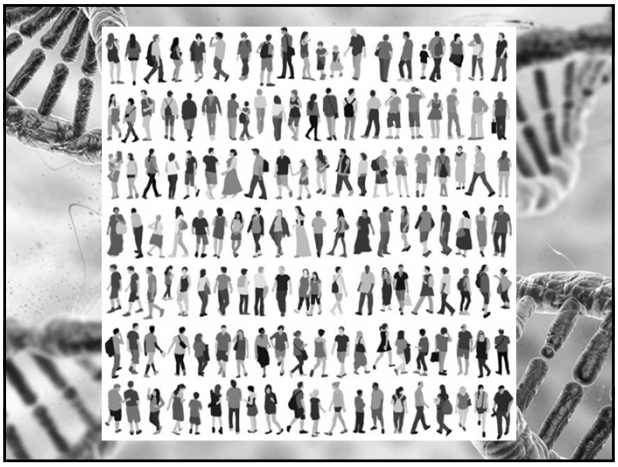
Science (2001); 291(5507): 1304-1351

Nature (2001); 409(6822): 860-921

Francis Collins

International Human Genome Sequencing Consortium

12



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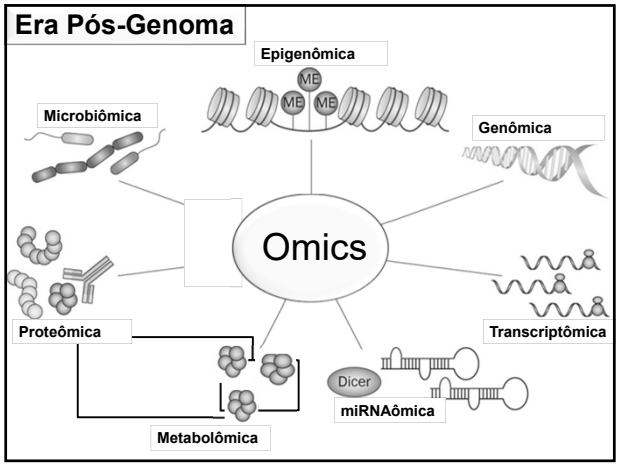
Era Pós-Genoma
Epigenômica
ME
ME
ME
Microbiômica
Genômica
Omics
Proteômica
Transcriptômica
Dicer
miRNAômica
Metabolômica

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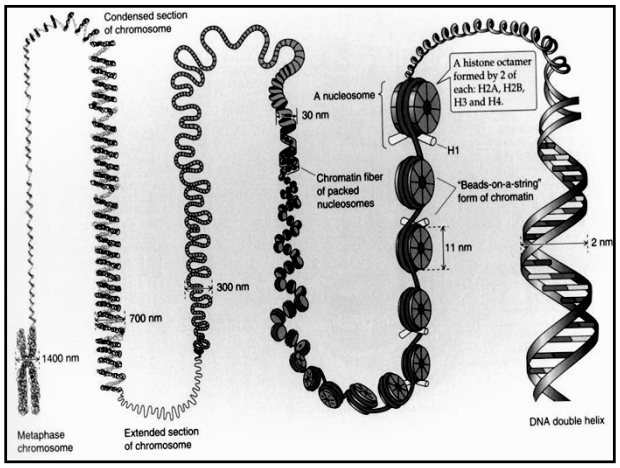
DNA

15


Condensed section of chromosome
A histone octamer formed by 2 of each: H2A, H2B, H3 and H4.
A nucleosome
30 nm
H1
Chromatin fiber of packed nucleosomes
"Beads-on-a-string" form of chromatin
11 nm
2 nm
300 nm
700 nm
1400 nm
Metaphase chromosome
Extended section of chromosome
DNA double helix

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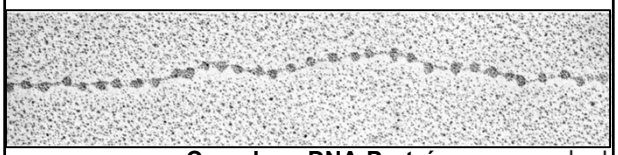
Nucleossomos

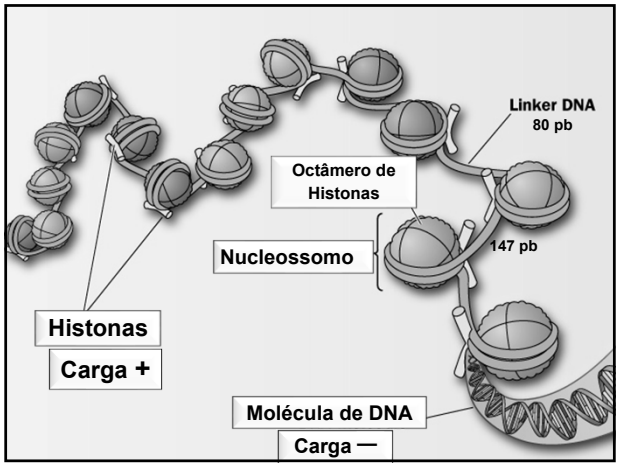


Complexo DNA-Proteína

50 nm

Unidade básica da estrutura do cromossomo eucariótico

17



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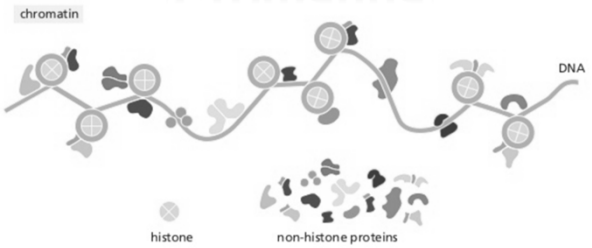
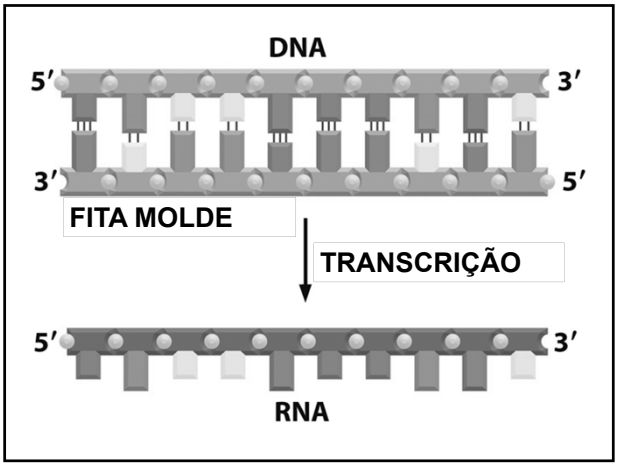
Cromatina



19

Transcrição

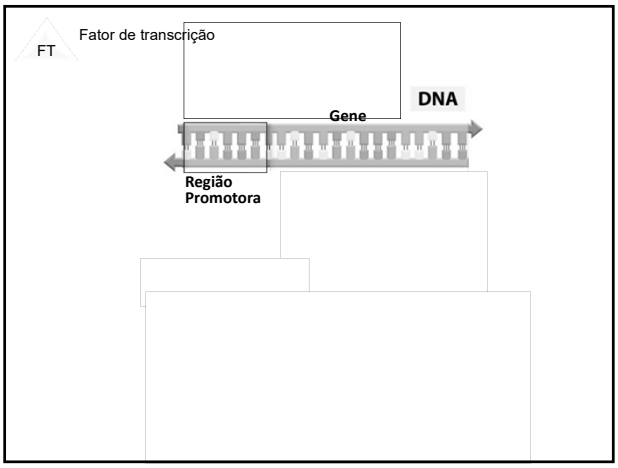
20



21

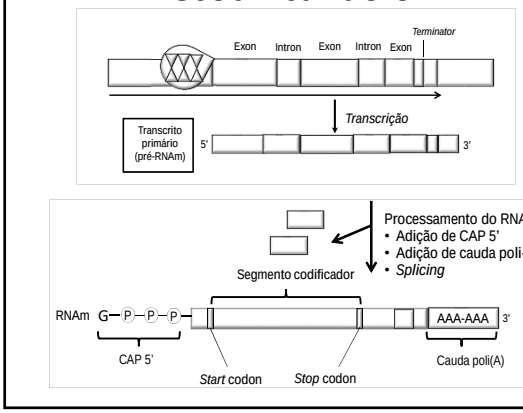
Fatores de Transcrição

22



23

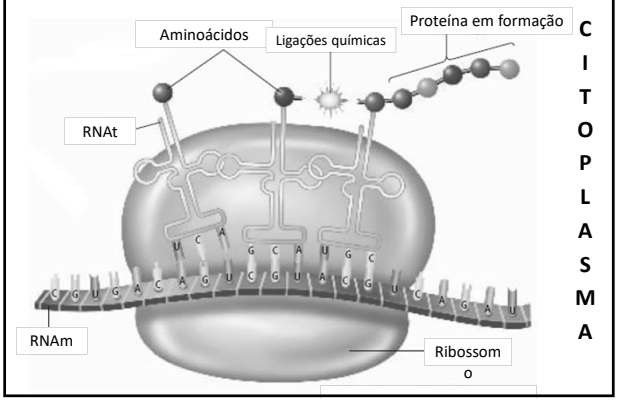
Decodificando o DNA



NÚCLEO CELULAR

24

Tradução em Proteína



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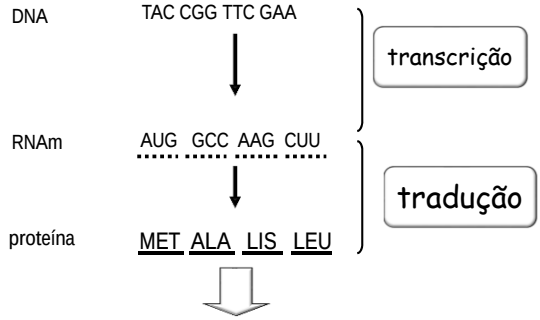
Expressão Gênica



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Degeneração no Código Genético

GCA GCC GCG GCU	AGA AGG CGA CGC CGG CGU	GAC GAU	AAC AAU	UGC UGU	GAA GAG	CAA CAG	GGA GGC GGG GGU	CAC CAU	AUA AUC AUU	UUA UUG CUA CUC CUG CUU
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu
A	R	D	N	C	E	Q	G	H	I	L

AAA AAG	AUG	UUC UUU	CCA CCC CCG CCU	AGC AGU UCA UCC UCG UCU	ACA ACC ACG ACU	UGG	UAC UAU	GUA GUC GUG GUU	UAA UAG UGA
Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	stop
K	M	F	P	S	T	W	Y	V	

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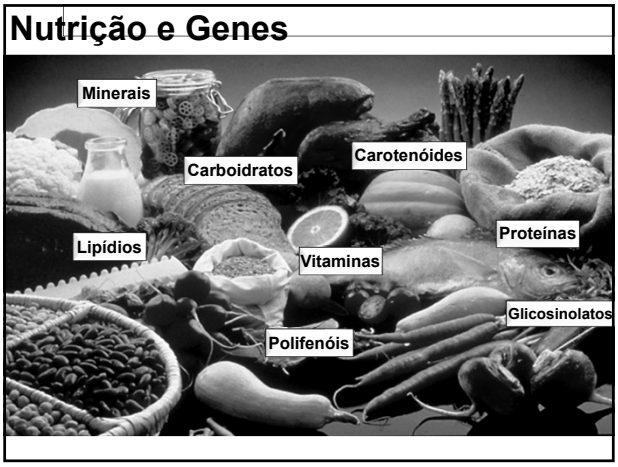
Nutrição e Genes
Minerais
Carboidratos
Carotenóides
Lipídios
Proteínas
Vitaminas
Glicosinolatos
Polifenóis

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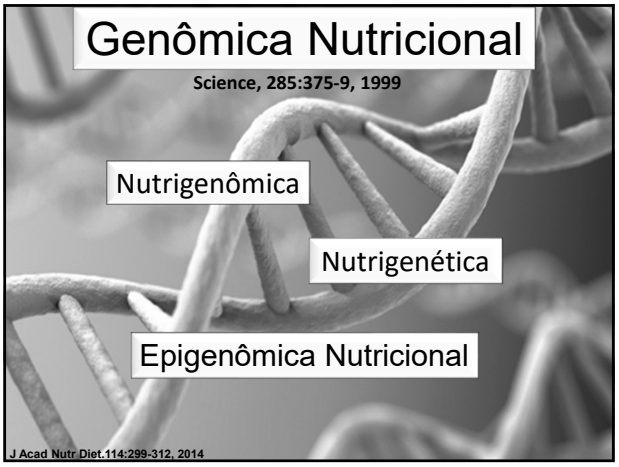
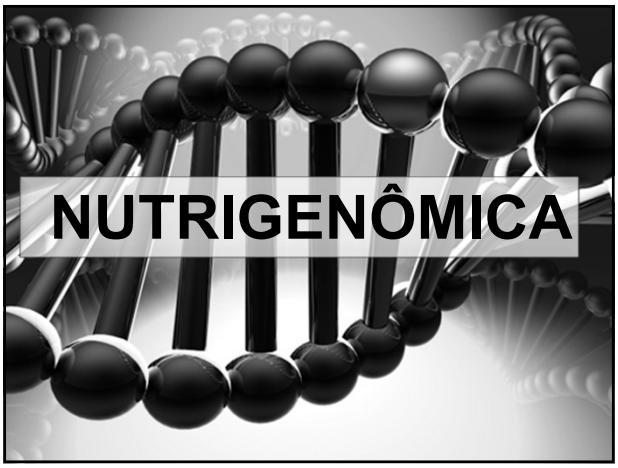

Genômica Nutricional
Science, 285:375-9, 1999
Nutrigenômica
Nutrigenética
Epigenômica Nutricional
J Acad Nutr Diet.114:299-312, 2014

30


NUTRIGENÔMICA

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MODO
INDIRETO

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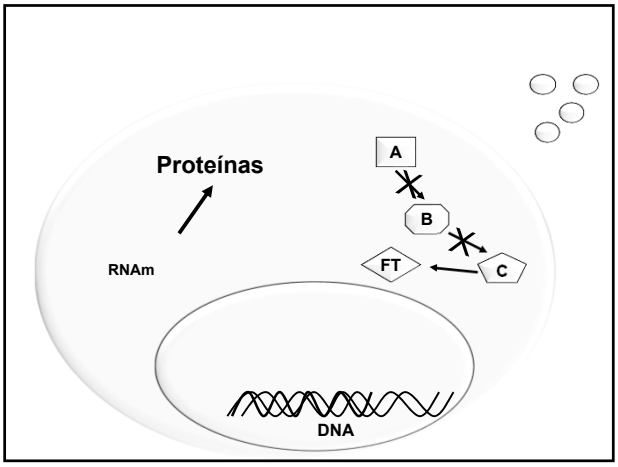
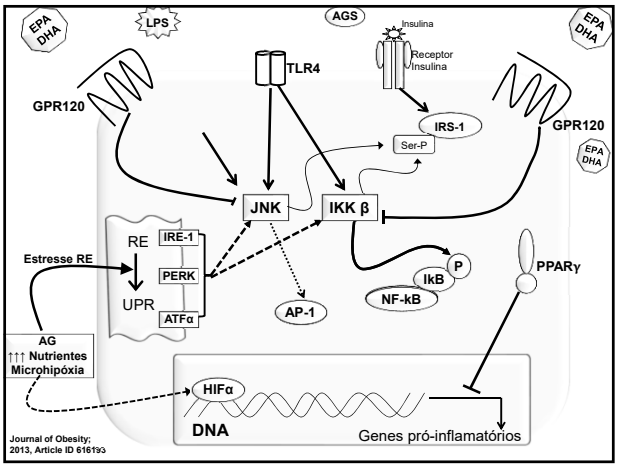

Proteínas
A
B
FT
C
RNAm
DNA

33


AGPI ω-3

34


EPA
DHA
LPS
AGS
Insulina
Receptor
Insulina
TLR4
GPR120
IRS-1
Ser-P
GPR120
EPA
DHA
JNK
IKK β
RE
IRE-1
Estresse RE
PERK
UPR
ATFα
P
IkB
NF-kB
AP-1
PPARγ
AG
↑↑↑ Nutrientes
Microhipóxia
HIFα
DNA
Genes pró-inflamatórios
Journal of Obesity;
2013, Article ID 616193

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MODO
DIRETO

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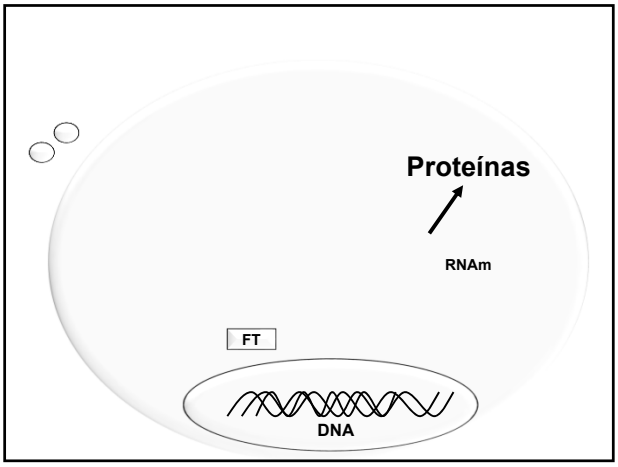
Proteínas
RNAm
FT
DNA

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VDR:
Regulação da Expressão Gênica pela Vitamina D em Enterócitos

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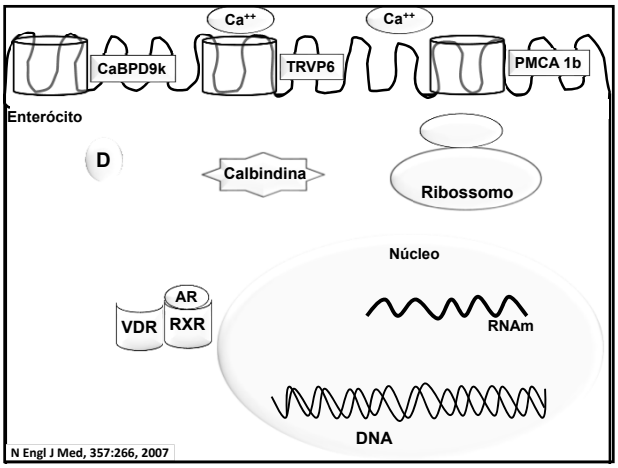
Ca++
Ca++
CaBPD9k
TRVP6
PMCA 1b
Enterócito
D
Calbindina
Ribossomo
Núcleo
AR
VDR
RXR
RNAm
DNA
N Engl J Med, 357:266, 2007

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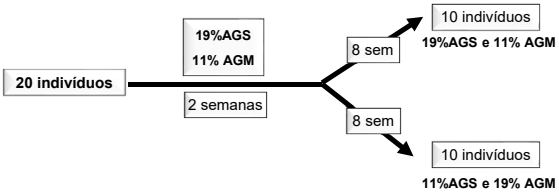
Azeite de Oliva Extra Virgem
Ácido Oleico (ω-9)
Tirosol
Hidroxitirosol
Ácido Cafeico
Ácido Cumárico

40

A saturated fatty acid–rich diet induces an obesity-linked proinflammatory gene expression profile in adipose tissue of subjects at risk of metabolic syndrome[1–3]

Susan J van Dijk, Edith JM Feskens, Marieke B Bos, Dianne WM Hoelen, Rik Heijligenberg, Mechteld Grootte Bromhaar, Lisette CPGM de Groot, Jeanne HM de Vries, Michael Müller, and Lydia A Afman

Am J Clin Nutr 2009;90:1656–64. Printed in USA. © 2009 American Society for Nutrition



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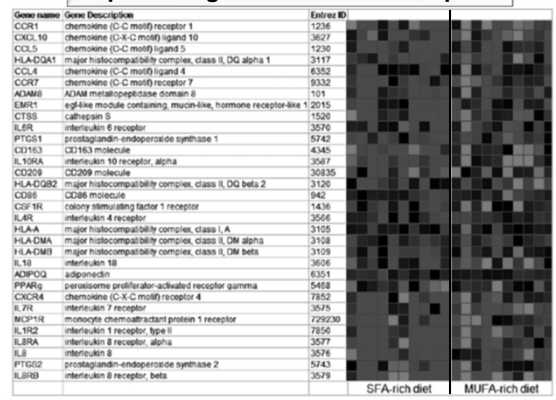
Expressão gênica no Tecido Adiposo

Gene name	Gene Description	Entrez ID
CCR1	chemokine (C-C motif) receptor 1	1236
CXCL10	chemokine (C-X-C motif) ligand 10	3627
CCL5	chemokine (C-C motif) ligand 5	1230
HLA-DQA1	major histocompatibility complex, class II, DQ alpha 1	3117
CCL4	chemokine (C-C motif) ligand 4	6352
CCR7	chemokine (C-C motif) receptor 7	9332
ADAM8	ADAM metallopeptidase domain 8	101
EMR1	egf-like module containing, mucin-like, hormone receptor-like 1	2015
CTSS	cathepsin S	1520
IL6R	interleukin 6 receptor	3570
PTGS1	prostaglandin-endoperoxide synthase 1	5742
CD163	CD163 molecule	4345
IL10RA	interleukin 10 receptor, alpha	3587
CD209	CD209 molecule	30835
HLA-DQB2	major histocompatibility complex, class II, DQ beta 2	3126
CD86	CD86 molecule	942
CSF1R	colony stimulating factor 1 receptor	1436
IL4R	interleukin 4 receptor	3566
HLA-A	major histocompatibility complex, class I, A	3105
HLA-DMA	major histocompatibility complex, class II, DM alpha	3108
HLA-DMB	major histocompatibility complex, class II, DM beta	3109
IL18	interleukin 18	3606
ADIPOQ	adiponectin	9351
PPARG	peroxisome proliferator-activated receptor gamma	5468
CXCR4	chemokine (C-X-C motif) receptor 4	7852
IL7R	interleukin 7 receptor	3575
MCP1R	monocyte chemoattractant protein 1 receptor	729230
IL1R2	interleukin 1 receptor, type II	7850
IL8RA	interleukin 8 receptor, alpha	3577
IL8	interleukin 8	3576
PTGS2	prostaglandin-endoperoxide synthase 2	5743
IL8RB	interleukin 8 receptor, beta	3579



Am J Clin Nutr., 90:1656–64, 2009

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A Dieta Mediterrânea na era da Nutrigenômica

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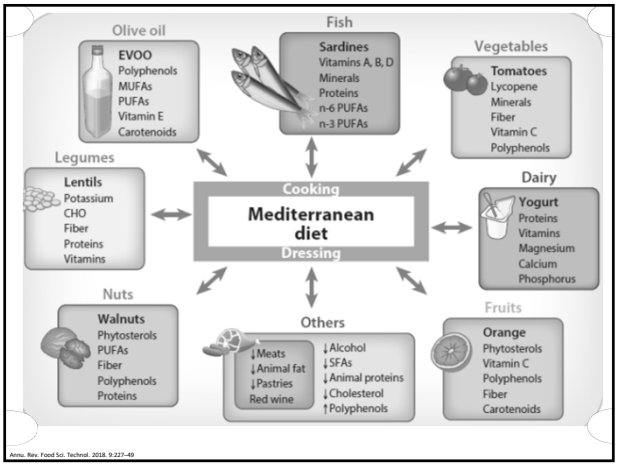
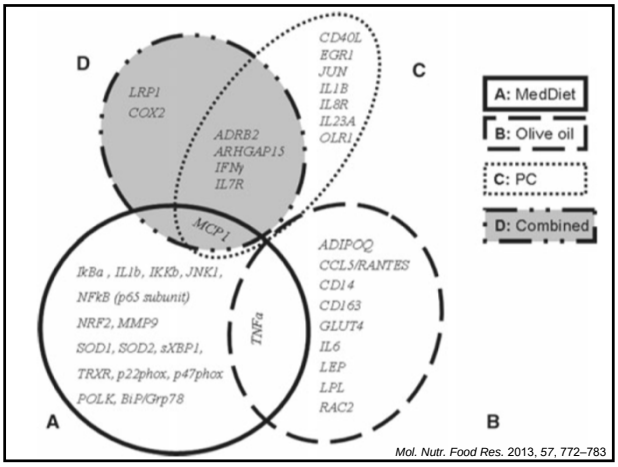


Annu. Rev. Food Sci. Technol. 2018. 9:227–49

44



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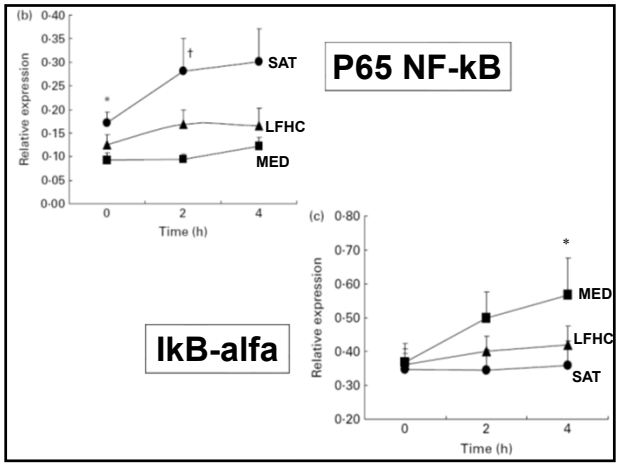
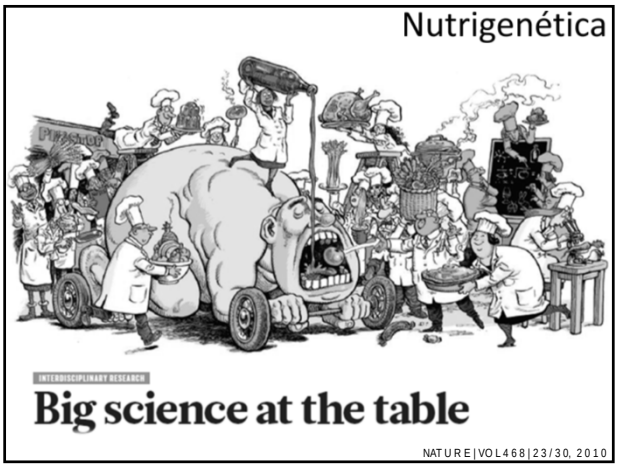


46



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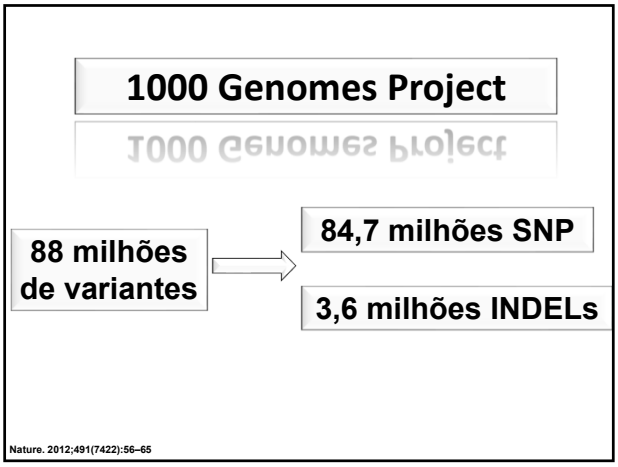
Nutrigenética

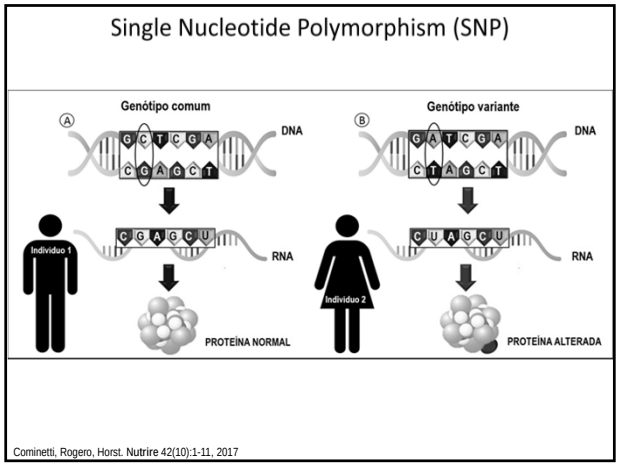
Influência da variabilidade genética na resposta à alimentação e no risco do desenvolvimento de doenças

German JB. *JADA*, 103: 530-531, 2005

48


1000 Genomes Project
88 milhões de variantes
84,7 milhões SNP
3,6 milhões INDELs
Nature. 2012;491(7422):56–65

49


Single Nucleotide Polymorphism (SNP)
Genótipo comum
Genótipo variante
DNA
RNA
Indivíduo 1
Indivíduo 2
PROTEÍNA NORMAL
PROTEÍNA ALTERADA
Cominetti, Rogero, Horst. Nutrire 42(10):1-11, 2017

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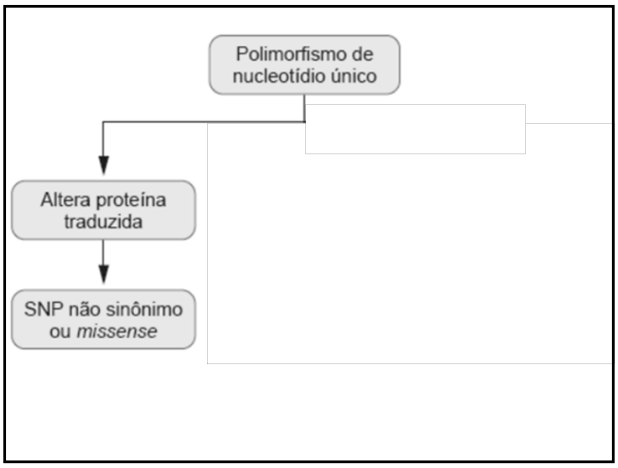
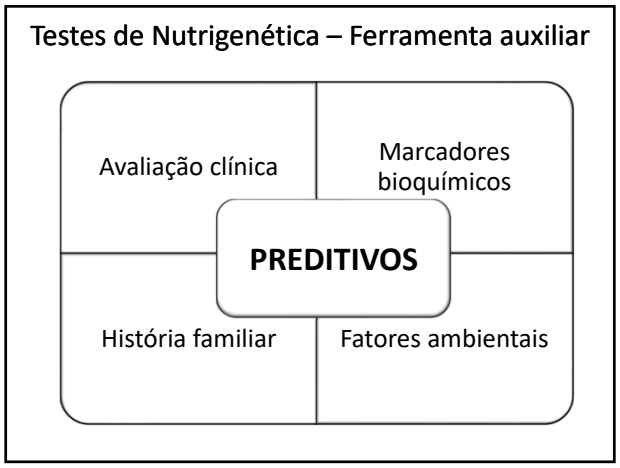

Polimorfismo de nucleotídio único
Altera proteína traduzida
SNP não sinônimo ou missense

51


Testes de Nutrigenética – Ferramenta auxiliar
Avaliação clínica
Marcadores bioquímicos
PREDITIVOS
História familiar
Fatores ambientais

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APO A1

rs 670

-75 G>A

53

AGPI,

Polimorfismo da Apo A1

e

HDL-colesterol

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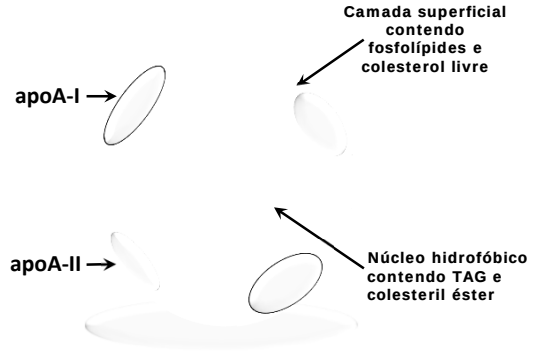
Estrutura da HDL



Rye KA et al. *Atherosclerosis* 1999;145:227-238

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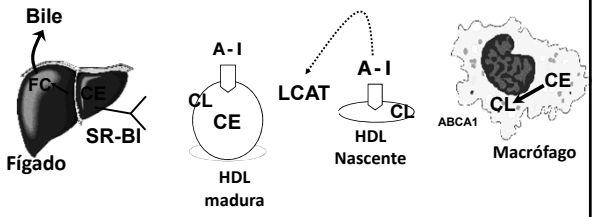
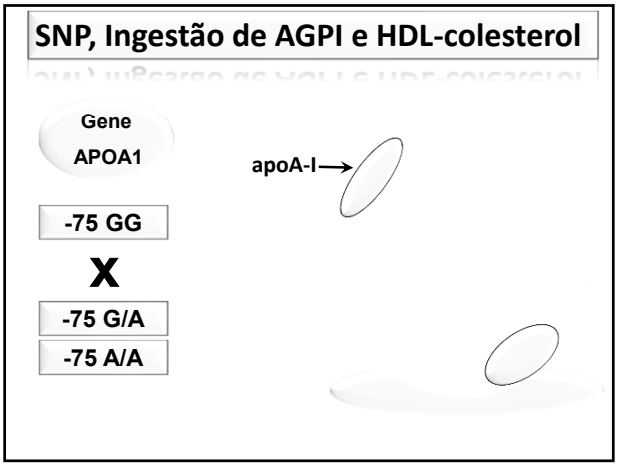
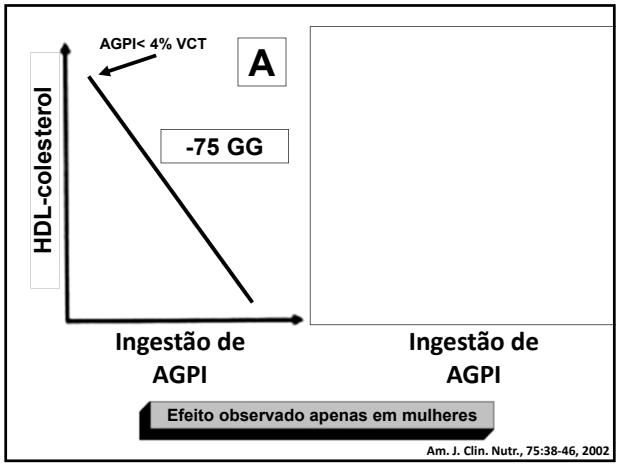
HDL e Transporte Reverso do Colesterol



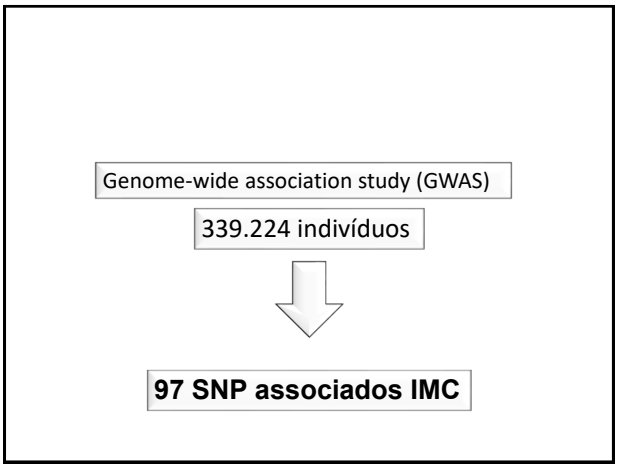
56


SNP, Ingestão de AGPI e HDL-colesterol
Gene
APOA1
apoA-I
-75 GG
X
-75 G/A
-75 A/A

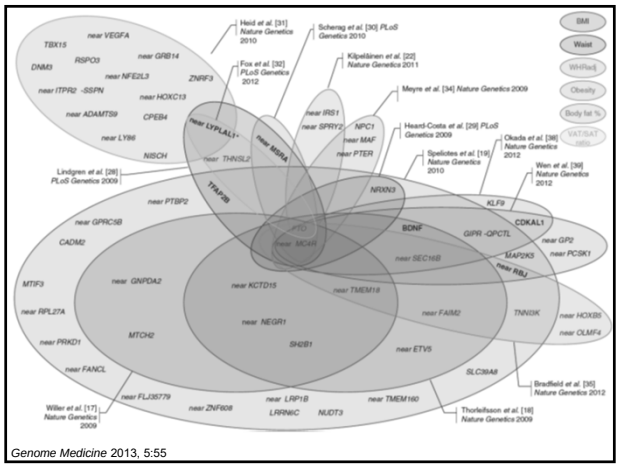
57


AGPI< 4% VCT
A
-75 GG
HDL-colesterol
Ingestão de AGPI
Ingestão de AGPI
Efeito observado apenas em mulheres
Am. J. Clin. Nutr., 75:38-46, 2002

58


Genome-wide association study (GWAS)
339.224 indivíduos
97 SNP associados IMC

59


Genome Medicine 2013, 5:55

60

GRS e Obesidade

J Acad Nutr Diet. 2014 December ; 114(12): 1954–1966. doi:10.1016/j.jand.2014.03.014.

Saturated fat intake modulates the association between a genetic risk score of obesity and BMI in two US populations

Nearest Gene	Chr	SNP	Allele major/minor	Risk allele
CPEB4	5	rs6861681	G/A	G
PCSK1	5	rs6234	C/G	C
ZNF608	5	rs4836133	A/C	A
FLJ35779	5	rs2112347	T/G	T
PCSK1	5	rs6232	A/G	G
A1F1	6	rs2844479	T/G	T
VEGFA	6	rs6905288	A/G	A
RSPO3	6	rs9491696	G/C	C
HMGA1	6	rs206936	A/G	G
PRL	6	rs4712652	A/G	G
LIN28	6	rs11294421	G/T	G
TFAP2B	6	rs987237	A/G	G
NFE2L3	7	rs1055144	G/A	A
TNKS	8	rs17150703	G/A	G
LRRN6C	9	rs10968576	A/G	G
PTER	10	rs10508503	C/T	C
BDNF	11	rs6265	G/A	G
MTCH2	11	rs10838738	A/G	A
BDNF	11	rs925946	G/T	T
TUB	11	rs4929949	C/T	C
HOXC13	12	rs1443512	C/A	C
FA1M2	12	rs7138803	G/A	G
ITPR2/SSPN	12	rs718314	T/C	T

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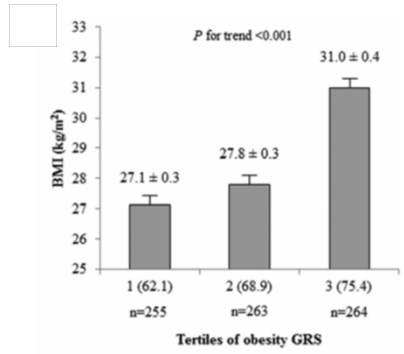

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FTO

(fat mass and obesity associated) gene

Science **2007**, *316*, 889–894.
PLoS Genet. **2007**, *3*, e115.

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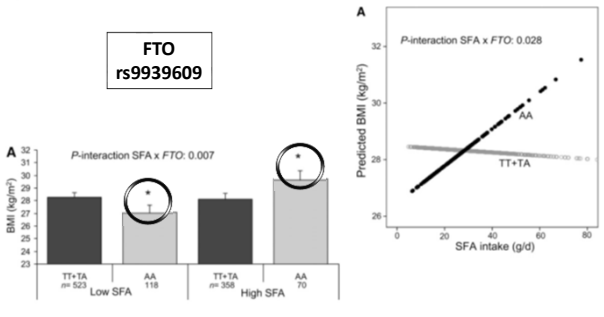
J. Nutr. 141: 2219–2225, 2011

The Journal of Nutrition Nutritional Epidemiology

A High Intake of Saturated Fatty Acids Strengthens the Association between the Fat Mass and Obesity-Associated Gene and BMI[1–3]

Dolores Corella,[4–6]* Donna K. Arnett,[7,14] Katherine L. Tucker,[8,14] Edmond K. Kabagambe,[7] Michael Tsai,[9] Laurence D. Parnell,[4] Chao-Qiang Lai,[4] Yu-Chi Lee,[4] Daruneewan Warodomwichit,[10] Paul N. Hopkins,[11] and Jose M. Ordovas[4,12,13]

FTO rs9939609



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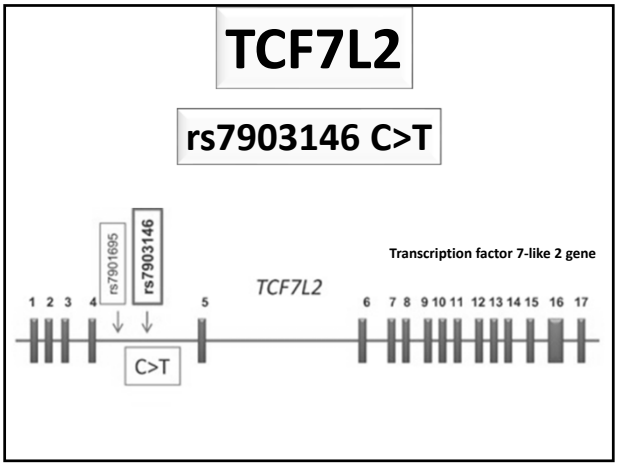
TCF7L2
rs7903146 C>T
rs7901695
rs7903146
Transcription factor 7-like 2 gene
TCF7L2
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
C>T

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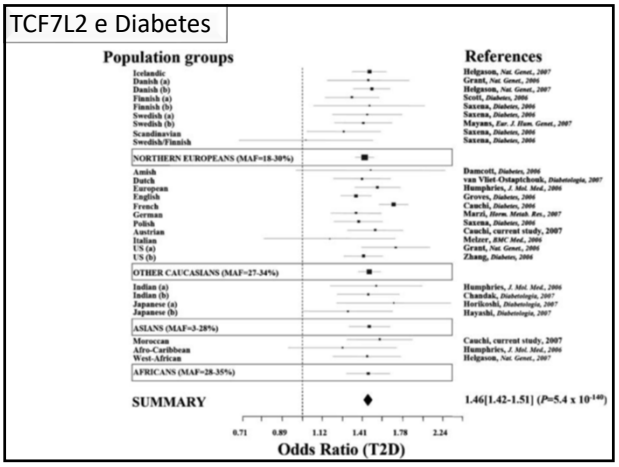
TCF7L2 e Diabetes
Population groups
References
NORTHERN EUROPEANS (MAF=18-30%)
OTHER CAUCASIANS (MAF=27-34%)
ASIANS (MAF=3-28%)
AFRICANS (MAF=28-35%)
SUMMARY
1.46[1.42-1.51] (P=5.4 x 10-140)
0.71 0.89 1.12 1.41 1.78 2.24
Odds Ratio (T2D)

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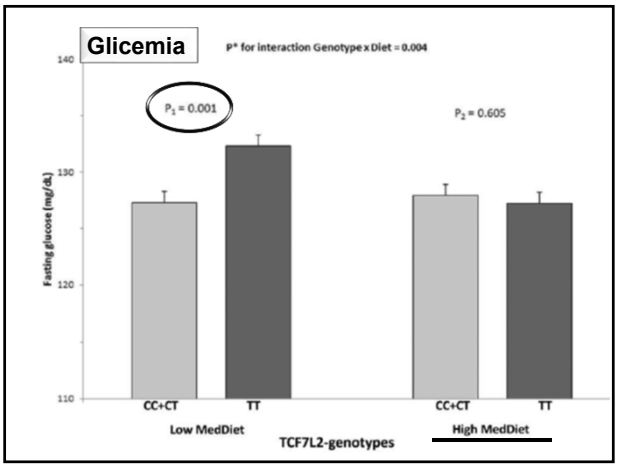
Glicemia
P* for interaction Genotype x Diet = 0.004
P1 = 0.001
P2 = 0.605
Fasting glucose (mg/dL)
140
130
120
110
CC+CT
TT
CC+CT
TT
Low MedDiet
High MedDiet
TCF7L2-genotypes

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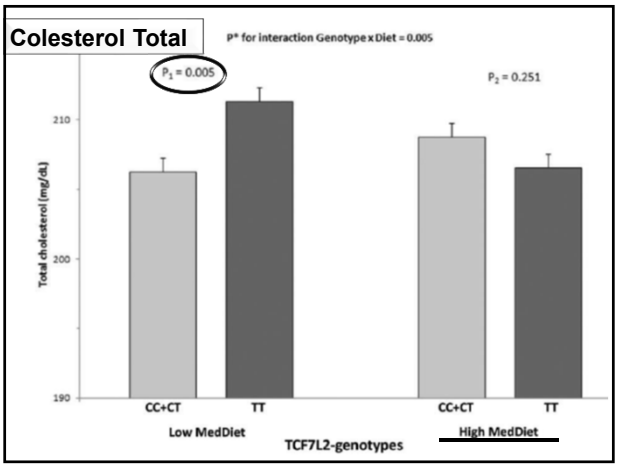
Colesterol Total
P* for interaction Genotype x Diet = 0.005
P1 = 0.005
P2 = 0.251
Total cholesterol (mg/dL)
210
200
190
CC+CT
TT
CC+CT
TT
Low MedDiet
High MedDiet
TCF7L2-genotypes

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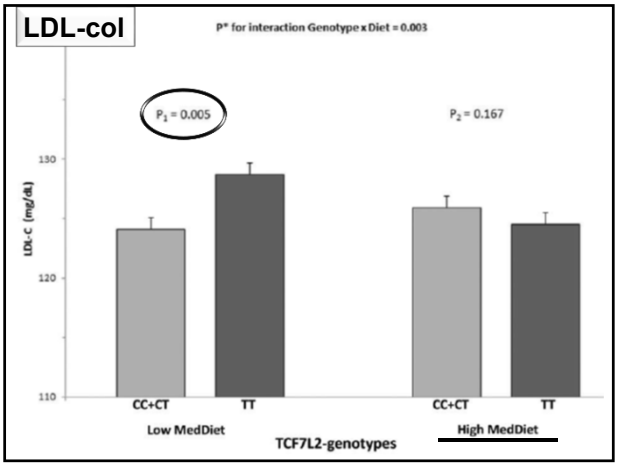

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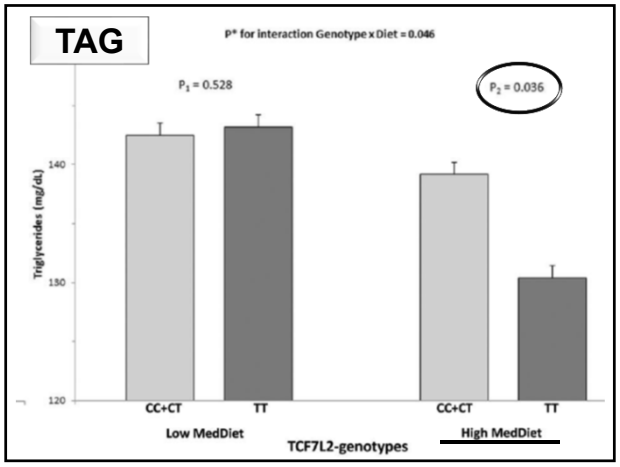

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Testes de Nutrigenética

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Perfil predisposição à obesidade

Gene	NCBI dbSNP	Risco	Resultado	Análise
FTO (T>A)	rs9939609	A	AA	
FTO (C>A)	rs8050136	A	AA	
ADRB2 (A>G)	rs1042713	A	GG	
ADRB2 (C>G)	rs1042714	G	CG	
LEP (G>A)	rs7799039	A	AA	
LEPR (G>C)	rs8179183	G	CG	
MC4R (T>C)	rs17782313	C	TT	
MC4R (G>A)	rs12970134	A	GG	
MC4R (G>A)	rs2229616	G	GG	
MC4R (A>G)	rs10871777	G	AA	
PPARG (C>G)	rs1801282	G	CC	

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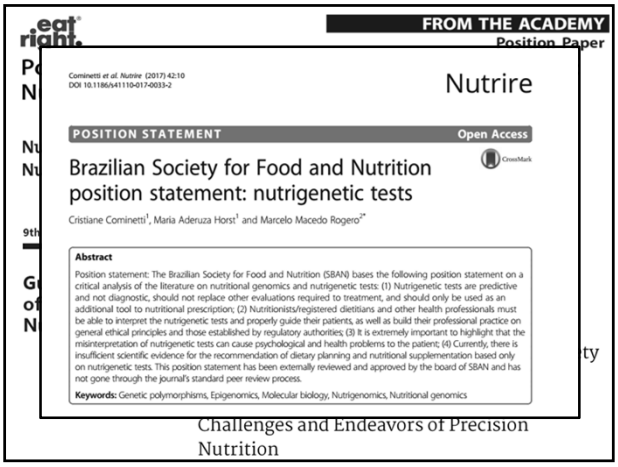

FROM THE ACADEMY
Position Paper

Cominetti et al. Nutrire (2017) 42:10
DOI 10.1186/s41110-017-0033-2

Nutrire

POSITION STATEMENT — Open Access

Brazilian Society for Food and Nutrition position statement: nutrigenetic tests

Cristiane Cominetti[1], Maria Aderuza Horst[1] and Marcelo Macedo Rogero[2*]

Abstract

Position statement: The Brazilian Society for Food and Nutrition (SBAN) bases the following position statement on a critical analysis of the literature on nutritional genomics and nutrigenetic tests: (1) Nutrigenetic tests are predictive and not diagnostic, should not replace other evaluations required to treatment, and should only be used as an additional tool to nutritional prescription; (2) Nutritionists/registered dietitians and other health professionals must be able to interpret the nutrigenetic tests and properly guide their patients, as well as build their professional practice on general ethical principles and those established by regulatory authorities; (3) It is extremely important to highlight that the misinterpretation of nutrigenetic tests can cause psychological and health problems to the patient; (4) Currently, there is insufficient scientific evidence for the recommendation of dietary planning and nutritional supplementation based only on nutrigenetic tests. This position statement has been externally reviewed and approved by the board of SBAN and has not gone through the journal's standard peer review process.

Keywords: Genetic polymorphisms, Epigenomics, Molecular biology, Nutrigenomics, Nutritional genomics

Challenges and Endeavors of Precision Nutrition

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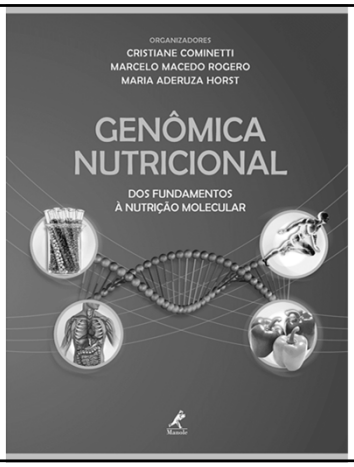

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