# Nutrigenomics/Nutrigenetics

George Dedoussis
Associate Professor of Biology

*The FASEB Journal* • Review

# Nutrigenomics and nutrigenetics: the emerging faces of nutrition

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**Nutrigenomics** will unravel the optimal diet from within a series of nutritional alternatives, whereas

**Nutrigenetics** will yield critically important information that will assist clinicians in identifying the optimal diet for a given individual, i.e., personalized nutrition

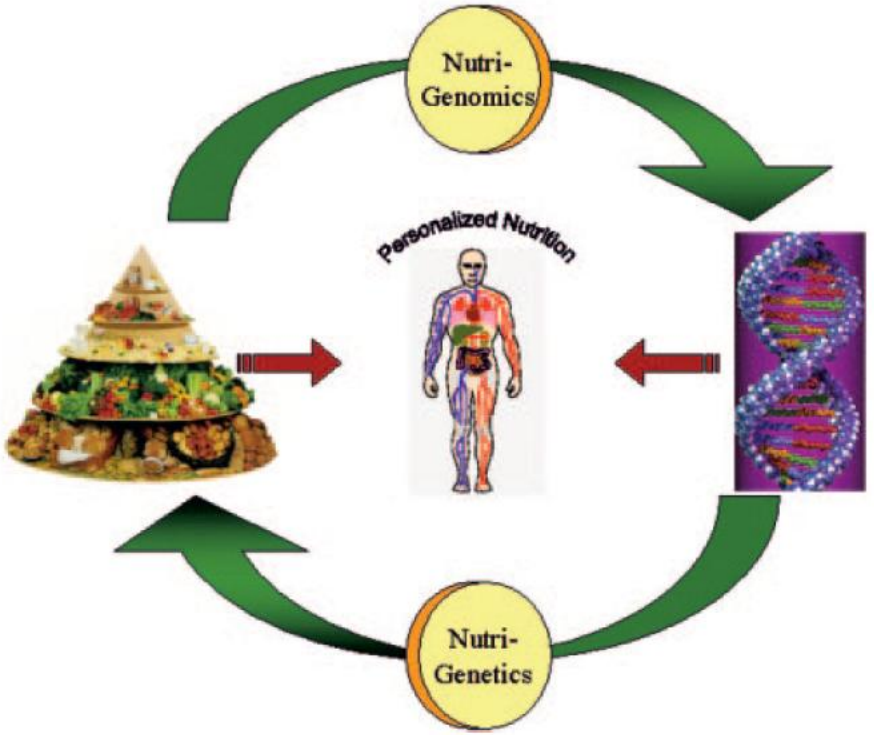



**Figure 1.** Nutrigenomics and nutrigenetics: two sides of a coin. For the target goal of personalized nutrition to be realized, the effects of diet on whole-body metabolism (i.e., genes, proteins, and metabolites) and the influence of genotype on nutritionally related disease must be considered. Food pyramid image obtained from: http://www.shb.ie/content454667358_1.cfm.

**Nutrigenomics aims** to determine the influence of common dietary ingredients on the genome, and attempts to relate the resulting different phenotypes to differences in the cellular and/or genetic response of the biological system.

More practically, nutrigenomics **describes** the use of functional genomic tools to probe a biological system following a nutritional stimulus that will permit an increased understanding of how nutritional molecules affect metabolic pathways and homeostatic control

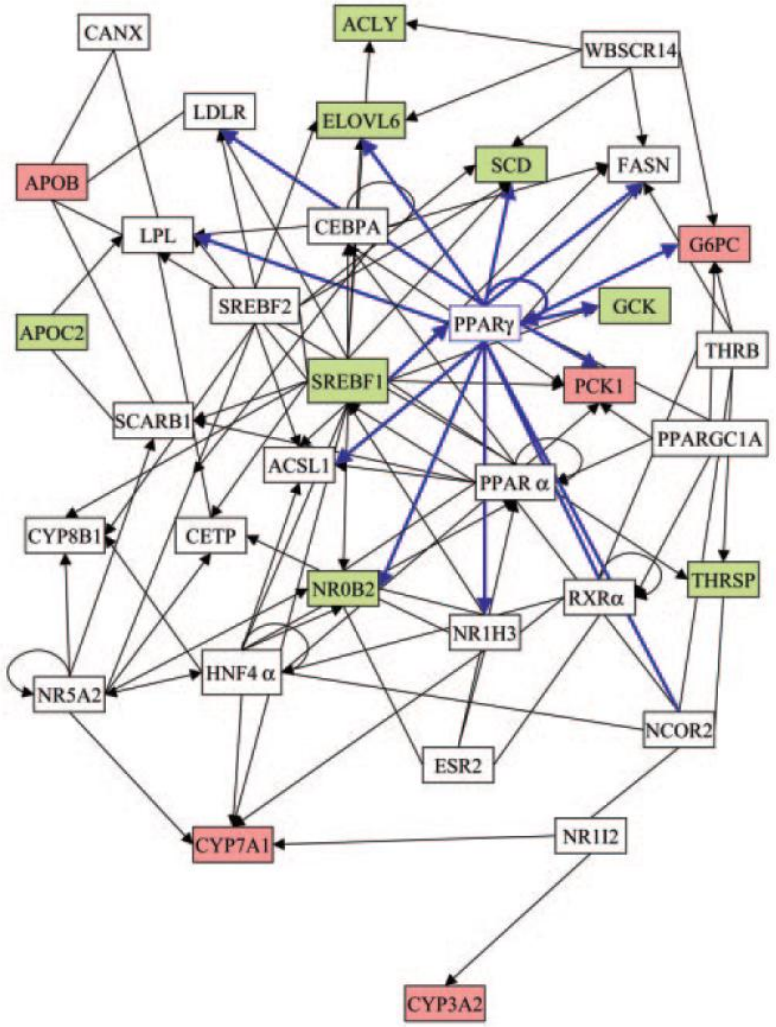



**Figure 2.** Biological network triggered after the consumption of LC-PUFA. As reported, LC-PUFA actions are mediated by transcription factors, such as PPAR and SREBP. These transcription factors may be both differentially expressed themselves and/or directly activated to instigate the functional consequences of consuming LC-PUFA. Highlighted in blue are known functional and/or physical interactions between PPAR-γ and other genes. Network created using Ingenuity Systems, Inc. software (www.ingenuity.com), where green is indicative of a down-regulation, red of an up-regulation and clear of no regulation for a given gene.

# Nutrients acts as dietary signals

Nutritional factors

↓

Transcription factors

↓

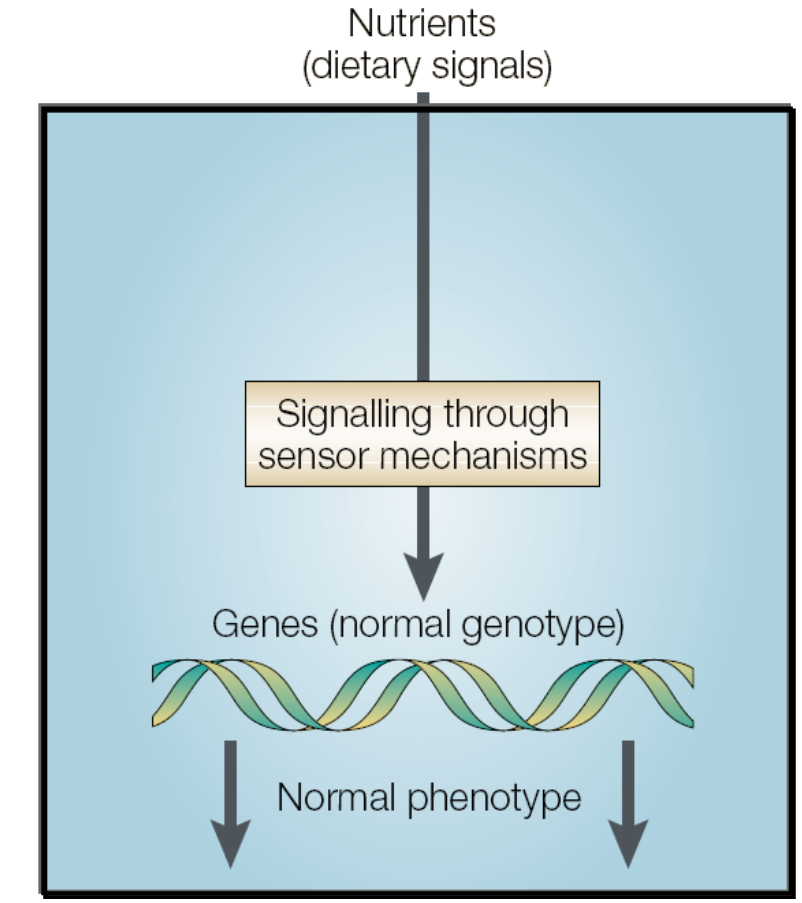
Gene transcription

↓

Energy homeostasis

Cell proliferation

Nutrient absorption



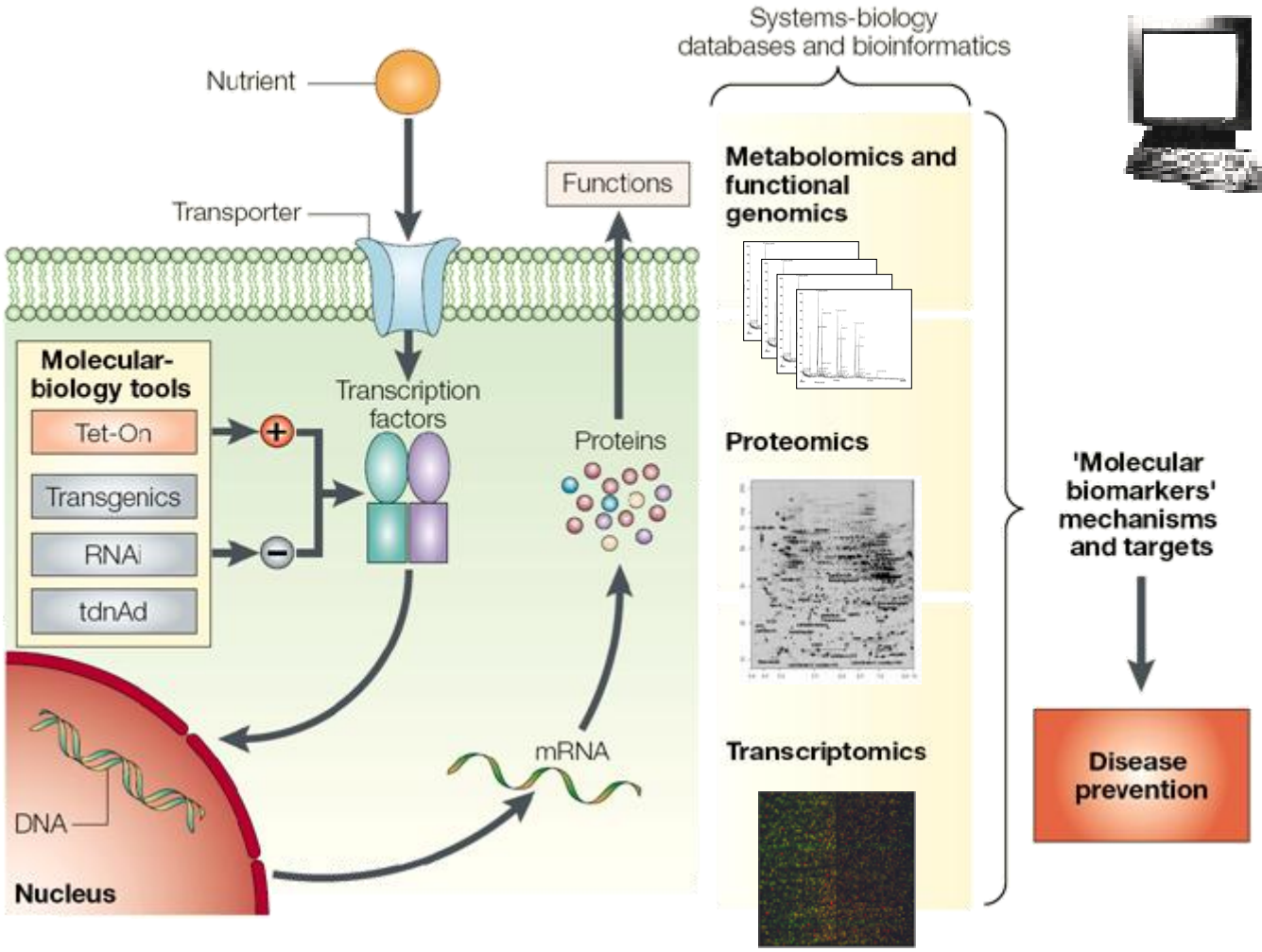
# “Molecular Nutrition & Genomics”
# The strategy of Nutrigenomics


50000 (?) metabolites

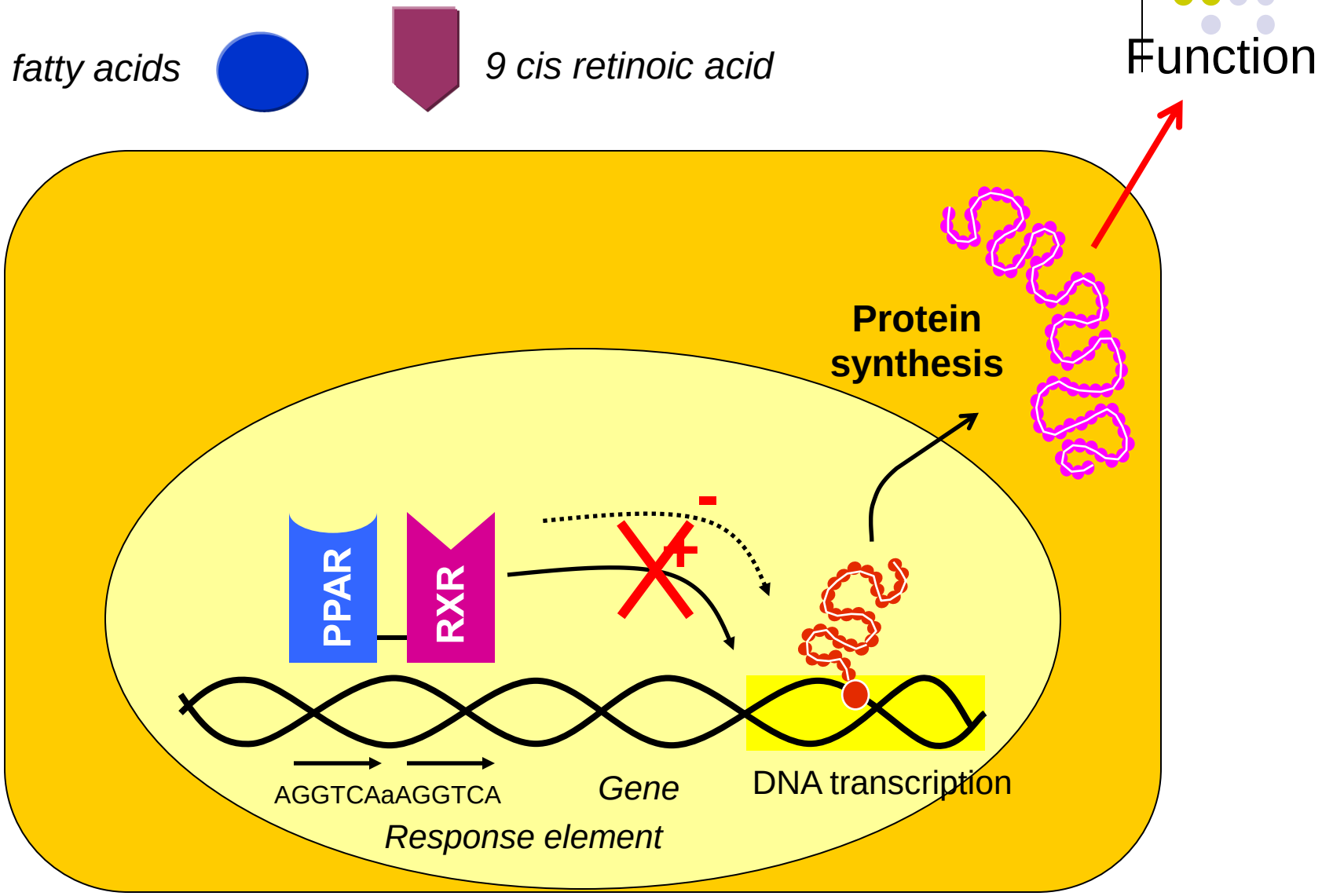
80-100000 proteins

100000 transcripts

20-25000 genes



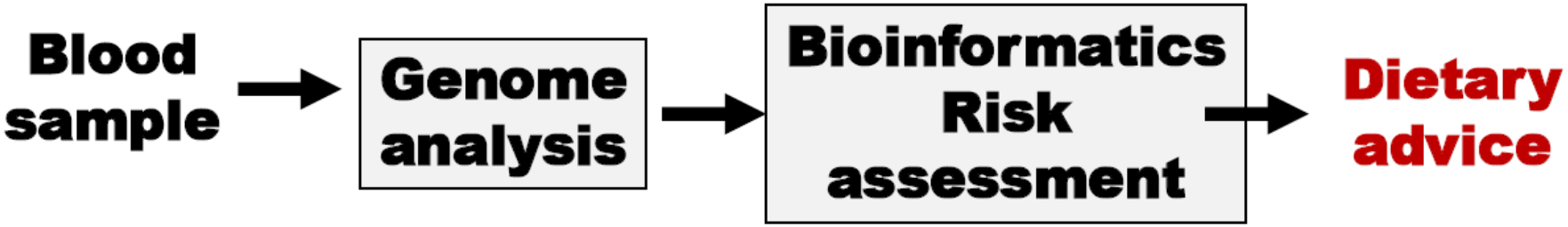
# PPARs are ligand activated transcription factors



**Nutrigenetics**, on the other hand, aims to understand how the genetic makeup of an individual coordinates their response to diet, and thus considers underlying genetic polymorphisms. In other words, nutrigenetics embodies the science of identifying and characterizing gene variants associated with differential responses to nutrients, and relating this variation to disease states

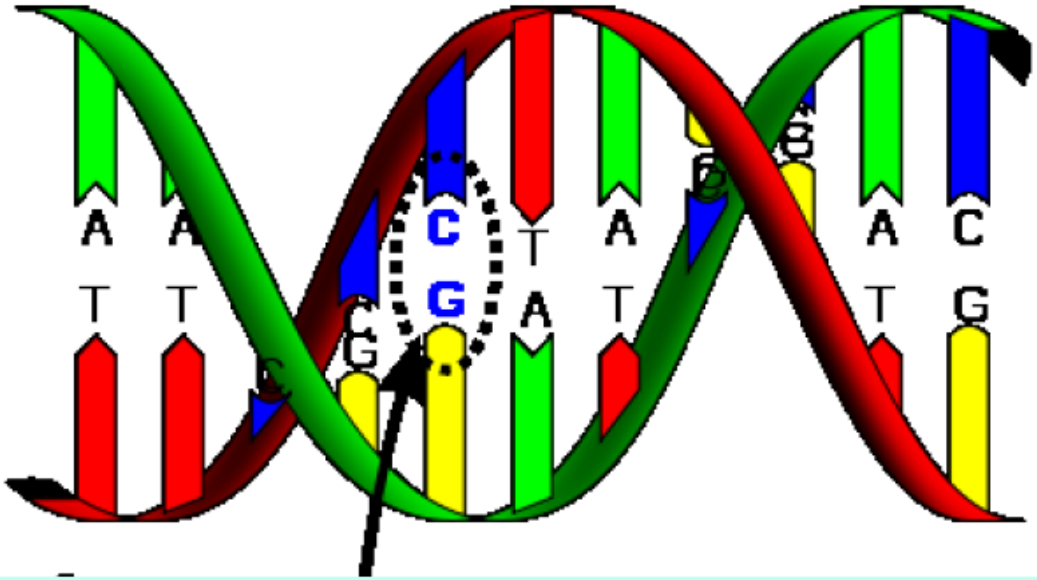
# Dietary advice based on genetics

## The "vision"




**Only 24.000 genes…However, 9.000.000 variants**

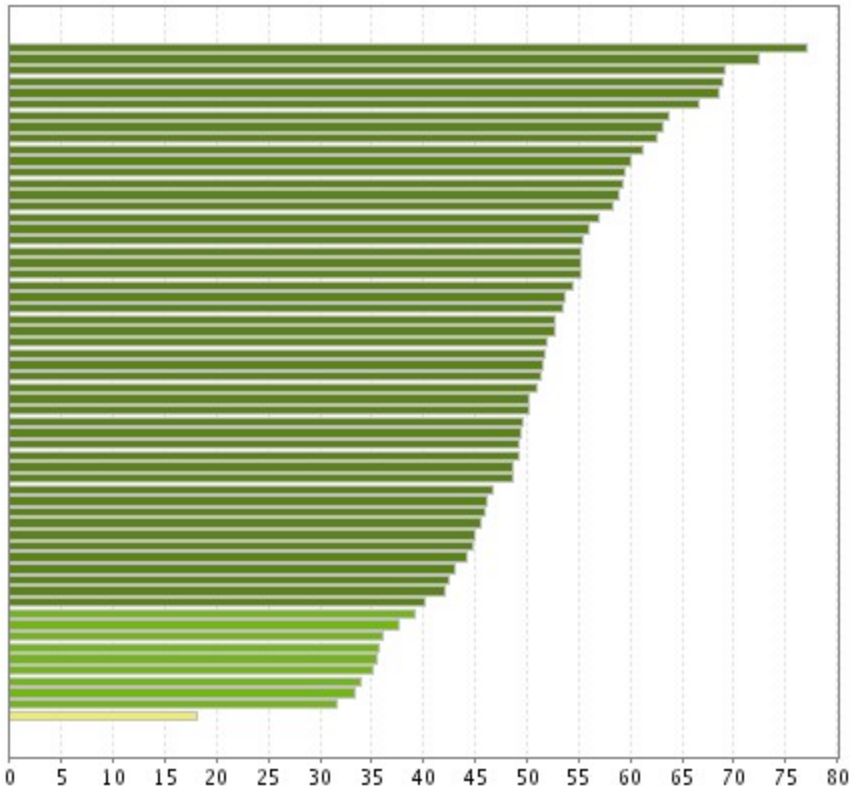
- ❑ Single Nucleotide Polymorphisms (SNP)
- ❑ Sequencing



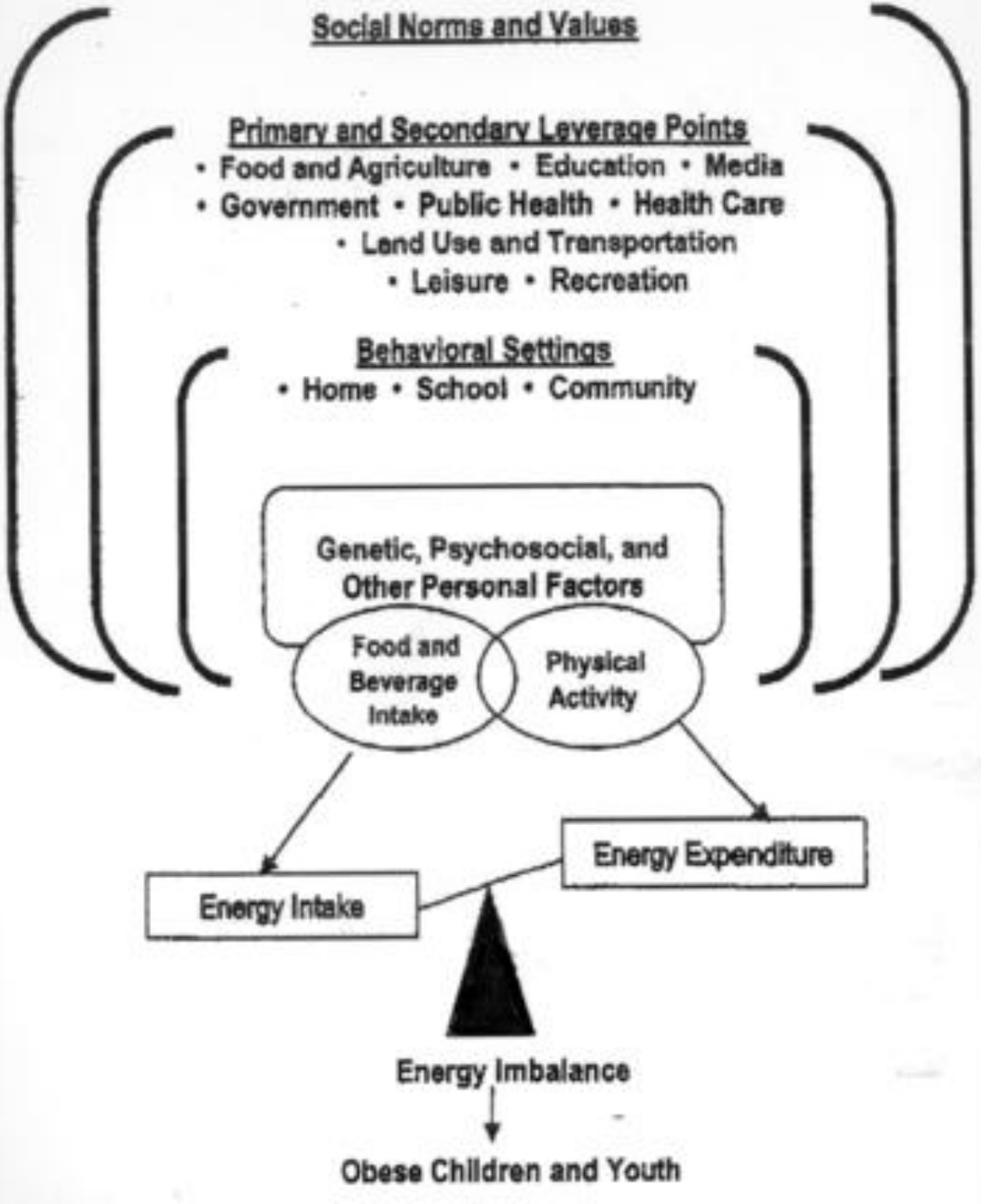

**Single Nucleotide Polymorphism SNP**

# % of adults normal-weight

77% adults from Laos Republic
72% from Ghana
69% from Madagascar
……
60% from Estonia
……
……
.....
42% from Ireland
35% from Croatia
35% from Malta
31% from Panama
18% from Kiribaldi



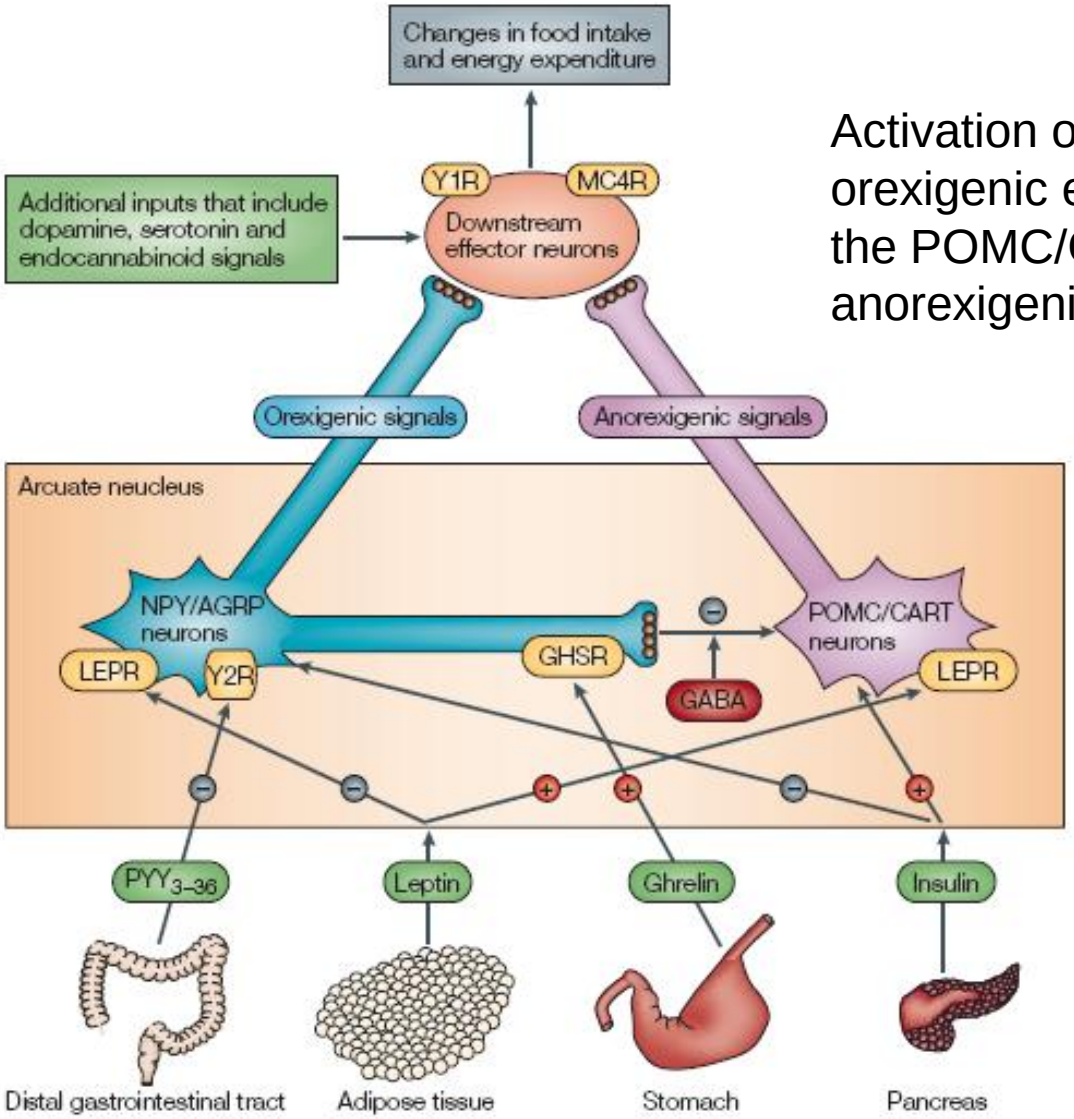

*WHO, 2011*




# Factors predisposing to an energy imbalance resulting in overweight.

*National Academy of Sciences,* **Preventing Childhood Obesity: Health in the Balance,** ***2005.***

# Physiological regulation of energy balance




Activation of the NPY/AGRP neurons has an orexigenic effect, promoting food intake,whereas the POMC/CART neurons have the opposite anorexigenic effect.

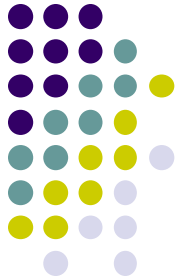
The NPY/AGRP neurons also have an inhibitory effect on the POMC/CART neurons through the release of γ-aminobutyric acid (GABA), which might be stimulated by the binding of ghrelin to GHSRs.

*Bell et al., Nature Reviews Genetics*

Table 1 | **Phenotypes that are commonly used in obesity genetics research**

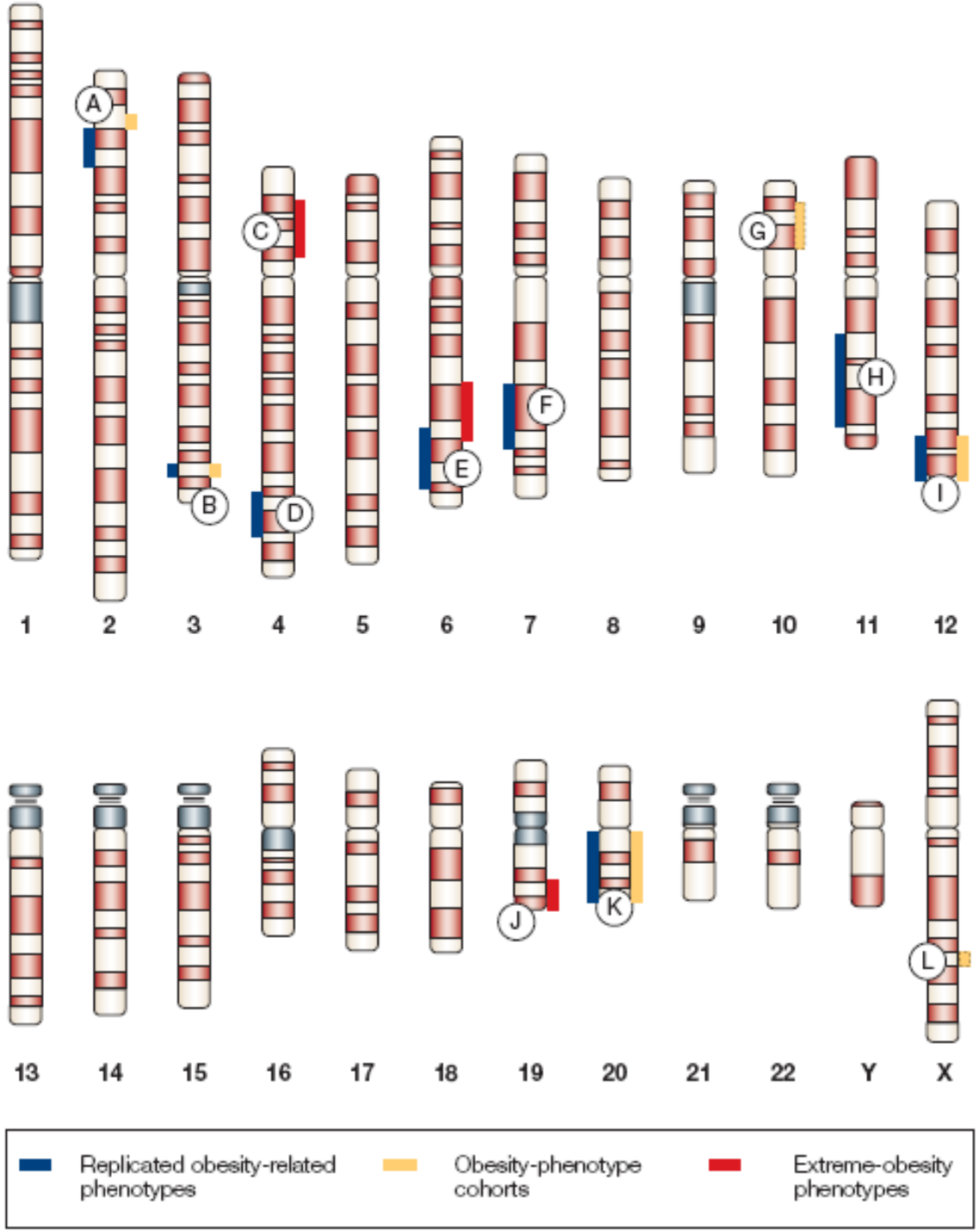
| Phenotypes | Measurement methods | Comments |
|---|---|---|
| ***Physical phenotypes*** | | |
| Weight | Scales | Quick, easy, cheap. Self-reported, so can be inaccurate. |
| Waist circumference<br>Waist–hip ratio | Tape measure | Quick, easy, cheap. Used to define central obesity. Correlates well with BMI, visceral fatness and total body fatness. |
| Body mass index (BMI) | Scales and tape measure | Quick, easy, cheap. Used to define clinical obesity that is due to high correlation with fatness. Often calculated retrospectively for study groups that have been recruited for other reasons. |
| Caloric intake | Questionnaire or subject recall observation | Cheap and relatively simple if it is questionnaire-based. Complex and time-consuming if observation is required in controlled conditions. |
| Feeding behaviour | Questionnaire or subject recall observation | Cheap and relatively simple if it is questionnaire-based. Complex and time-consuming if observation is required in controlled conditions. |
| Skinfold thickness | Skin callipers | A relatively simple measure of subcutaneous fat. Usually used as the sum of several measures or as a ratio of thicknesses. |
| Central fat mass (CFM)<br>Visceral fat mass (VFM)<br>CFM–VFM ratio | DEXA | Precise and accurate, but expensive, complex and time-consuming. Unsuitable for large-scale screening. |
| Body-fat distribution | CT<br>MRI | Precise and accurate, but expensive, complex and time-consuming. Unsuitable for large-scale screening. |
| ***Molecular phenotypes*** | | |
| Hormone levels | ELISA<br>RIA | Typically assessed in blood samples. Difficult to do *in vivo* for differentiated organs and tissues; for example, adipose tissue. Reflects the sum of all influences on a particular hormone. Expensive for large-scale studies. |
| Transcription levels | RT-PCR<br>Real-time PCR<br>Microarray | A wide range of tissues can be investigated; comparisons of different physiological states are possible. Only small numbers are used as it is currently expensive. Large datasets present analytical challenges. Measures relative RNA levels and not levels of biologically active proteins. |
| Metabolic profiling | HPLC<br>NMR | Typically assessed in body fluids. Sample acquisition is relatively easy, but generates a complex metabolic profile, is expensive and is not easily applicable to solid tissues. |

# Heritability of obesity phenotypes

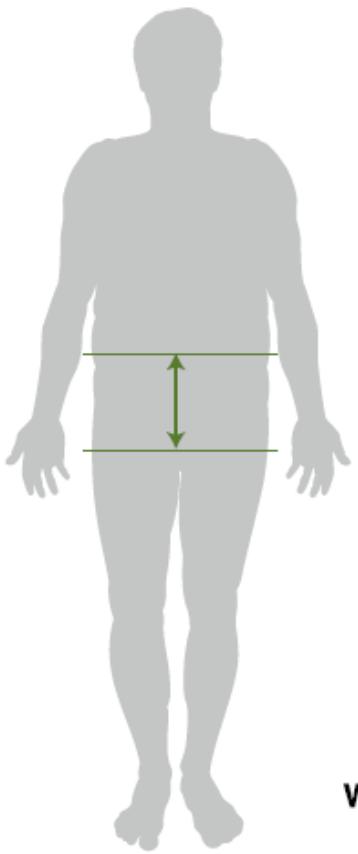


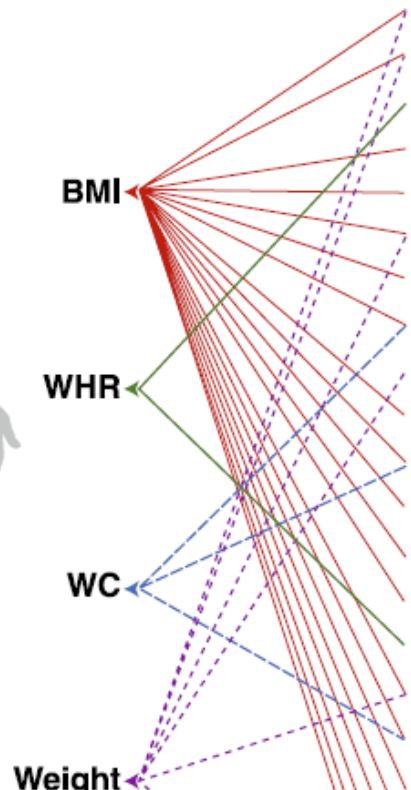
The high heritability (h2) for different measures of obesity—BMI (h2=0.4–0.7),

subscapular skinfold thickness (h2~0.77), WC (h2 ~0.76) and WHR (h2 ~ 0.45)—highlight the effect of genetics in increasing risk to obesity.




# Genetic-linkage map for obesity






| Gene name | Position | Study |
|---|---|---|
| *NEGR1* | 1p31 | [36**, 37**] |
| *SEC16B, RASAL2* | 1q25 | [37**] |
| *LYPLAL1, ZC3H11B* | 1q41 | [17**] |
| *SDCCAG8* | 1q43–q44 | [39] |
| *TMEM18* | 2p25 | [36**, 37**, 39] |
| *Near ETV5* | 3q27 | [37**] |
| *Near GNPDA2* | 4p13 | [36**] |
| *TFAP2B* | 6p12 | [17**] |
| *NCR3, AIF1, and BAT2* | 6p21 | [37**] |
| *PRL* | 6p22.2–p21.3 | [38**] |
| *MSRA* | 8p23.1 | [17, 39] |
| *PTER* | 10p12 | [38**] |
| *MTCH2* | 11p11.2 | [36**] |
| *BDNF region* | 11p14 | [37**] |
| *C12orf51/PTPN11* | 12q24 | [53**] |
| *FAIM2, BCDIN3D* | 12q13 | [37**] |
| *NRXN3* | 14q31 | [47] |
| *SH2B1 region* | 16p11.2 | [36**, 37**] |
| *MAF* | 16q22–q23 | [38**] |
| *FTO*[a] | 16q22.2 | [29**, 30, 35**–38**, 39] |
| *NPC1* | 18q11.2 | [38**] |
| *MC4R*[b] | 18q22 | [35**–38**, 39, 40**] |
| *KCTD15* | 19q13.11 | [36**, 37**] |

**Fig. 1** Genes associated with obesity-related anthropometric measures. *BMI* body mass index, *WC* waist circumference, *WHR* waist to hip ratio. [a]Indicates type 2 diabetes association. [b]Indicates association with monogenic obesity

nature genetics

# Variation in *FTO* contributes to childhood obesity and severe adult obesity

Christian Dina[1], David Meyre[1], Sophie Gallina[1], Emmanuelle Durand[1], Antje Körner[2], Peter Jacobson[3], Lena M S Carlsson[3], Wieland Kiess[2], Vincent Vatin[1], Cecile Lecoeur[1], Jérome Delplanque[1], Emmanuel Vaillant[1], François Pattou[4], Juan Ruiz[5], Jacques Weill[6], Claire Levy-Marchal[7], Fritz Horber[8], Natascha Potoczna[8], Serge Hercberg[9], Catherine Le Stunff[10], Pierre Bougnères[10], Peter Kovacs[11], Michel Marre[12], Beverley Balkau[13,14], Stéphane Cauchi[1], Jean-Claude Chèvre[1] & Philippe Froguel[1,15]



Science

# A Common Variant in the *FTO* Gene Is Associated with Body Mass Index and Predisposes to Childhood and Adult Obesity

Timothy M. Frayling,[1,2*] Nicholas J. Timpson,[3,4*] Michael N. Weedon,[1,2*] Eleftheria Zeggini,[3,5*] Rachel M. Freathy,[1,2] Cecilia M. Lindgren,[3,5] John R. B. Perry,[1,2] Katherine S. Elliott,[3] Hana Lango,[1,2] Nigel W. Rayner,[3,5] Beverley Shields,[2] Lorna W. Harries,[2] Jeffrey C. Barrett,[3] Sian Ellard,[2,6] Christopher J. Groves,[5] Bridget Knight,[2] Ann-Marie Patch,[2,6] Andrew R. Ness,[7] Shah Ebrahim,[8] Debbie A. Lawlor,[9] Susan M. Ring,[9] Yoav Ben-Shlomo,[9] Marjo-Riitta Jarvelin,[10,11] Ulla Sovio,[10,11] Amanda J. Bennett,[5] David Melzer,[1,12] Luigi Ferrucci,[13] Ruth J. F. Loos,[14] Inês Barroso,[15] Nicholas J. Wareham,[14] Fredrik Karpe,[5] Katharine R. Owen,[5] Lon R. Cardon,[3] Mark Walker,[16] Graham A. Hitman,[17] Colin N. A. Palmer,[18] Alex S. F. Doney,[19] Andrew D. Morris,[19] George Davey Smith,[4] The Wellcome Trust Case Control Consortium,† Andrew T. Hattersley,[1,2]‡§ Mark I. McCarthy[3,5]‡

Science

- An additive association of the variant with BMI was replicated in 13 cohorts with 38,759 participants.
- The 16% of adults who are homozygous for the risk allele weighed about **3** kilograms more and had **1.67**-fold increased odds of obesity when compared with those not inheriting a risk allele.
- This association was observed from **age 7** years and reflects a specific increase in fat mass.

**Table 2.** Association of BMI (corrected for sex) and birth weight (corrected for sex and gestational age) with rs9939609 genotypes in children. *P* values represent the change in log BMI per A allele. BMI presented as geometric means and back-transformed 95% confidence intervals.

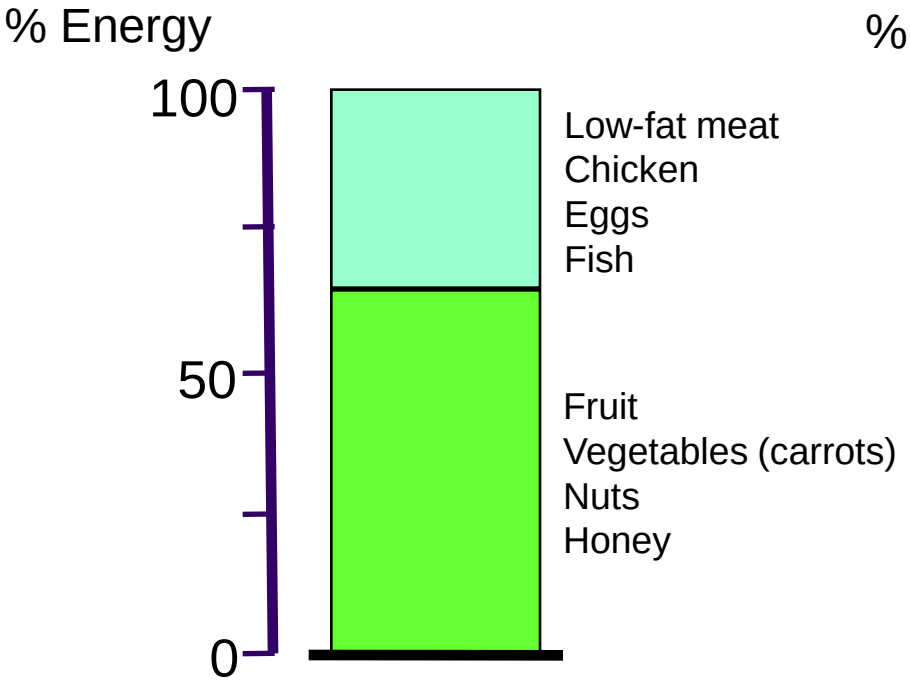
| Cohort | Age (years) | Males (%) | *N* | Mean trait value (95% CI) by genotype | | | *P* |
|---|---|---|---|---|---|---|---|
| | | | | TT | AT | AA | |
| | | | | Children* | | | |
| ALSPAC | 7 | 51 | 5969 | 16.00 (15.92, 16.07) | 16.11 (16.04, 16.18) | 16.31 (16.19, 16.43) | $3 \times 10^{-5}$ |
| | 8 | 50 | 4871 | 16.80 (16.70, 16.90) | 17.01 (16.92, 17.09) | 17.29 (17.14, 17.45) | $1 \times 10^{-7}$ |
| | 9 | 50 | 5459 | 17.20 (17.08, 17.31) | 17.53 (17.43, 17.63) | 17.86 (17.69, 18.04) | $5 \times 10^{-11}$ |
| | 10 | 50 | 5273 | 17.66 (17.54, 17.79) | 18.05 (17.94, 18.17) | 18.37 (18.18, 18.57) | $1 \times 10^{-10}$ |
| | 11 | 49 | 5010 | 18.46 (18.32, 18.61) | 18.82 (18.70, 18.94) | 19.20 (18.98, 19.42) | $7 \times 10^{-9}$ |
| NFBC1966 (age 14) | 14 | 47 | 4203 | 19.14 (19.02, 19.26) | 19.25 (19.14, 19.36) | 19.38 (19.19, 19.57) | 0.04 |
| | | | | Birth† | | | |
| ALSPAC | 0 | 51 | 7477 | 3438 (3422, 3455) | 3452 (3437, 3466) | 3454 (3429, 3480) | 0.21 |
| NFBC1966 | 0 | 47 | 4320 | 3523 (3501, 3546) | 3538 (3518, 3558) | 3536 (3501, 3571) | 0.42 |

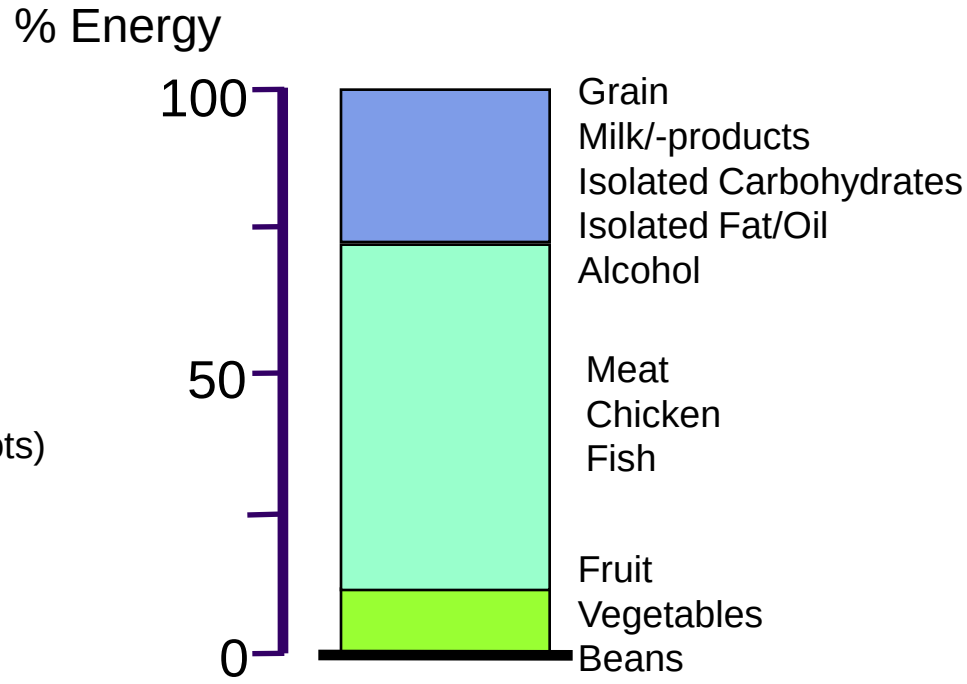
*ALSPAC children are offspring of the participants included in the adult study (Table 1), and data are shown at five available ages. NFBC1966 children are the same participants as those in the adult study (Table 1). †ALSPAC birth data are for the same participants as those in the children study. NFBC1966 birth data are for the same participants as those in the children and adult studies. Non-singleton births and individuals born at gestation <36 weeks were excluded from the birth-weight analysis.

# The same genes – The changed diet

Older times

Modern Times



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# An Obesity-Associated *FTO* Gene Variant and Increased Energy Intake in Children

Joanne E. Cecil, Ph.D., Roger Tavendale, Ph.D., Peter Watt, Ph.D., Marion M. Hetherington, Ph.D., and Colin N.A. Palmer, Ph.D.

**Table 1.** ***FTO*** **Genotype Frequencies and the Frequency of the A Allele in the Total Study Sample and the Subsample.***

| Polymorphism rs9939609 | Total Population (N = 2726) | | Subsample (N = 97) | |
|---|---|---|---|---|
| | No. of Participants | Genotype Frequency | No. of Participants | Genotype Frequency |
| | | % | | % |
| TT | 1016 | 37 | 36 | 37 |
| AT | 1322 | 49 | 48 | 50 |
| AA | 388 | 14 | 13 | 13 |
| Frequency of A allele | | 0.385 | | 0.381 |

* AA denotes homozygous carriers of the A allele, AT heterozygous carriers, and TT noncarriers.

**Table 2. Association of the rs9939609 Variant of the *FTO* Gene with Height, Weight, and Body-Mass Index in the Total Study Group.***

| Characteristic | No. of Participants | TT | AT | AA | P Value |
|---|---|---|---|---|---|
| Height | 2423 | 1.25±0.002 | 1.25±0.002 | 1.26±0.003 | 0.17 |
| Weight | 2422 | 26.99±0.168 | 27.16±0.148 | 28.07±0.270 | 0.003 |
| BMI† | 2422 | 17.09±0.075 | 17.17±0.066 | 17.58±0.121 | 0.003 |

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**Table 3.** Association of the rs9939609 Variant of the *FTO* Gene with Anthropometric Measures in the Subsample.*

| Anthropometric Measure | No. of Participants | TT | AT or AA | P Value |
|---|---|---|---|---|
| Height (m) | 97 | 1.25±0.01 | 1.26±0.01 | 0.42 |
| Weight (kg) | 97 | 25.80±0.76 | 27.73±0.58 | 0.05 |
| BMI† | 97 | 16.36±0.33 | 17.26±0.25 | 0.03 |
| Waist circumference (cm) | 97 | 57.75±0.98 | 59.29±0.75 | 0.22 |
| Hip circumference (cm) | 97 | 65.39±0.86 | 67.47±0.66 | 0.06 |
| Sum of skinfold values (cm) | 95 | 30.58±2.97 | 39.15±2.29 | 0.03 |
| Fat mass (kg) | | | | |
| By Lohman's equations | 95 | 6.26±0.55 | 8.04±0.43 | 0.01 |
| By isotope dilution | 71 | 8.21±0.58 | 9.49±0.46 | 0.10 |
| Lean mass (kg) | | | | |
| By Lohman's equations | 95 | 19.50±0.39 | 19.88±0.30 | 0.45 |
| By isotope dilution | 71 | 17.79±0.57 | 18.21±0.46 | 0.58 |

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| Anthropometric Measure | No. of Participants | TT | AT or AA | P Value |
|---|---|---|---|---|
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| Weight (kg) | 97 | 25.80±0.76 | 27.73±0.58 | 0.05 |
| BMI† | 97 | 16.36±0.33 | 17.26±0.25 | 0.03 |
| Waist circumference (cm) | 97 | 57.75±0.98 | 59.29±0.75 | 0.22 |
| Hip circumference (cm) | 97 | 65.39±0.86 | 67.47±0.66 | 0.06 |
| Sum of skinfold values (cm) | 95 | 30.58±2.97 | 39.15±2.29 | 0.03 |
| Fat mass (kg) | | | | |
| By Lohman's equations | 95 | 6.26±0.55 | 8.04±0.43 | 0.01 |
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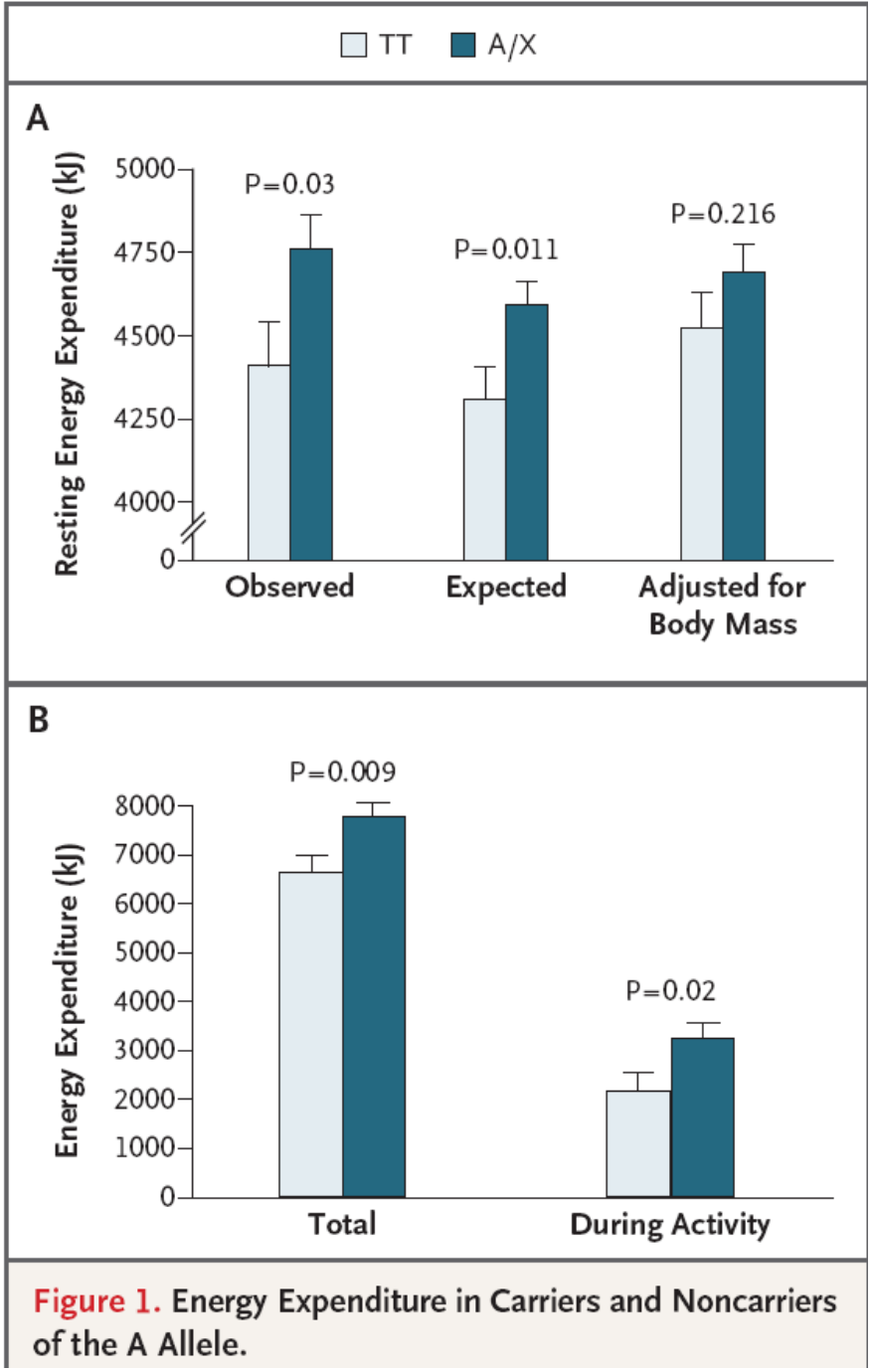


Figure 1. Energy Expenditure in Carriers and Noncarriers of the A Allele.

1.5 hours before a test-meal lunch, children ingested a beverage or combination of food and beverage that varied in energy density:

a no-energy control consisting of 250 ml of water (0 kJ)

a low-energy combination of a 250-ml orange drink and 56-g muffin (783 kJ)

a high-energy combination of a 250-ml orange drink and 56-g muffin (1628 kJ)

The amount of food subsequently consumed at the test meal was assessed by weighing the food items before and after eating.

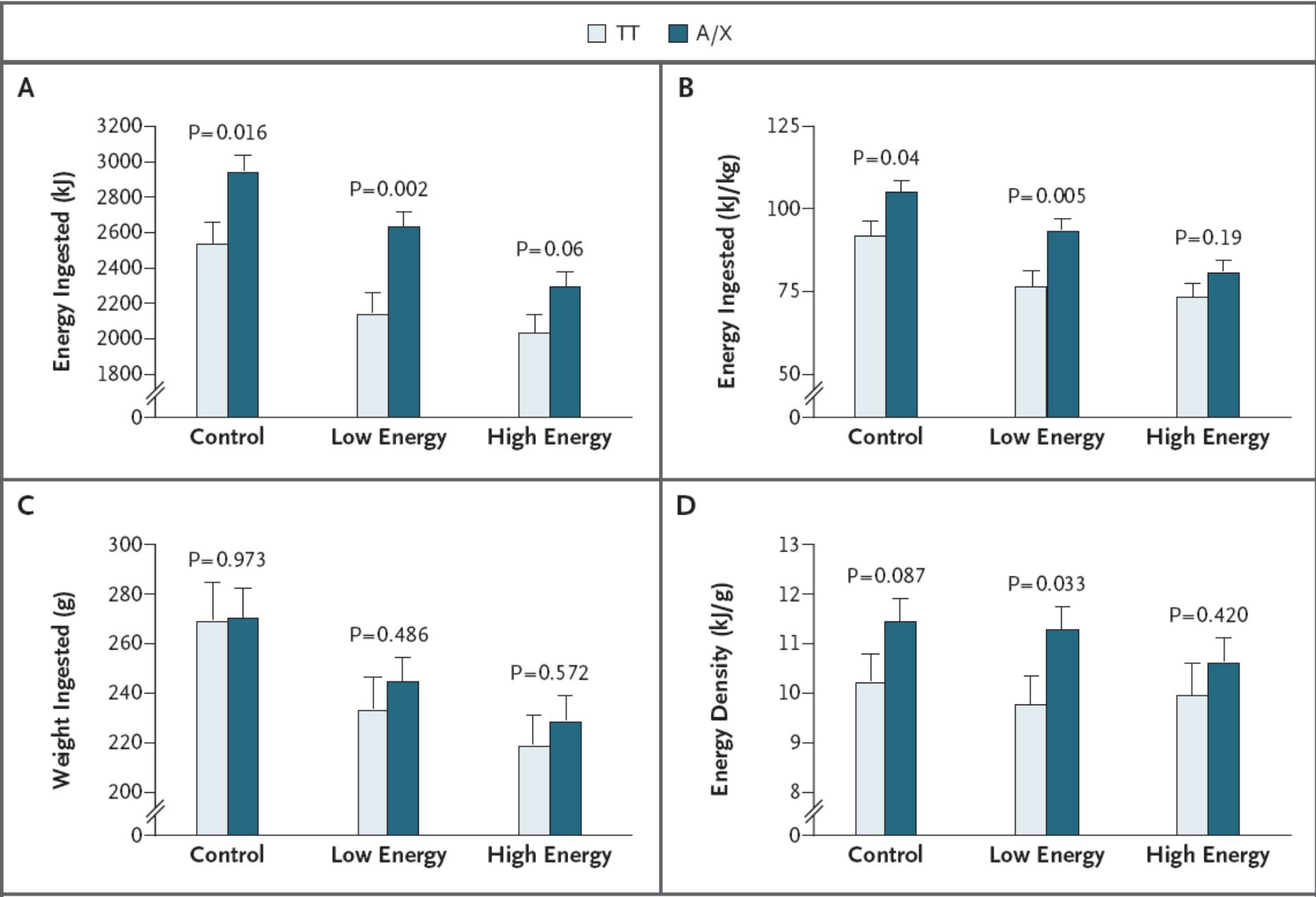


**Figure 2.** Energy Intake and Weight of Ingested Food at the Test Meal in Carriers and Noncarriers of the A Allele.

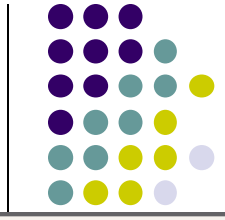

**Table 4.** Association of the rs9939609 Variant of the *FTO* Gene with Macronutrient Intake in the Subsample.*

| Macronutrient Intake and Premeal Energy Load | No. of Participants | TT | AT or AA | P Value | | |
|---|---|---|---|---|---|---|
| | | | | Adjusted for Age | Adjusted for Age and Body Weight | Adjusted for Age, Body Weight, and Total Energy Intake |
| Fat (g) | 76 | | | | | |
| Control | | 28.10±1.85 | 33.98±1.42 | 0.01 | 0.02 | 0.64 |
| Low energy | | 23.19±1.80 | 30.14±1.41 | 0.003 | 0.004 | 0.71 |
| High energy | | 21.55±1.46 | 25.47±1.14 | 0.04 | 0.04 | 0.34 |
| Carbohydrate (g) | 76 | | | | | |
| Control | | 70.01±4.13 | 77.11±3.17 | 0.18 | 0.28 | 0.36 |
| Low energy | | 60.09±3.81 | 69.84±2.99 | 0.05 | 0.10 | 0.53 |
| High energy | | 58.76±3.88 | 62.01±3.04 | 0.51 | 0.75 | 0.10 |
| Protein (g) | 76 | | | | | |
| Control | | 21.23±1.72 | 25.36±1.32 | 0.06 | 0.10 | 0.83 |
| Low energy | | 18.57±1.53 | 22.55±1.20 | 0.04 | 0.08 | 0.71 |
| High energy | | 16.60±1.34 | 20.57±1.05 | 0.02 | 0.04 | 0.24 |

* Plus–minus values are means ±SE, with adjustment, as shown, after univariate analysis of variance. AA denotes homozygous carriers of the A allele, AT heterozygous carriers, and TT noncarriers.

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| | | | | Adjusted for Age | Adjusted for Age and Body Weight | Adjusted for Age, Body Weight, and Total Energy Intake |
| Fat (g) | 76 | | | | | |
| Control | | 28.10±1.85 | 33.98±1.42 | 0.01 | 0.02 | 0.64 |
| Low energy | | 23.19±1.80 | 30.14±1.41 | 0.003 | 0.004 | 0.71 |
| High energy | | 21.55±1.46 | 25.47±1.14 | 0.04 | 0.04 | 0.34 |
| Carbohydrate (g) | 76 | | | | | |
| Control | | 70.01±4.13 | 77.11±3.17 | 0.18 | 0.28 | 0.36 |
| Low energy | | 60.09±3.81 | 69.84±2.99 | 0.05 | 0.10 | 0.53 |
| High energy | | 58.76±3.88 | 62.01±3.04 | 0.51 | 0.75 | 0.10 |
| Protein (g) | 76 | | | | | |
| Control | | 21.23±1.72 | 25.36±1.32 | 0.06 | 0.10 | 0.83 |
| Low energy | | 18.57±1.53 | 22.55±1.20 | 0.04 | 0.08 | 0.71 |
| High energy | | 16.60±1.34 | 20.57±1.05 | 0.02 | 0.04 | 0.24 |

* Plus–minus values are means ±SE, with adjustment, as shown, after univariate analysis of variance. AA denotes homozygous carriers of the A allele, AT heterozygous carriers, and TT noncarriers.

# Does a short breastfeeding period protect from *FTO*-induced adiposity in children?

Table I. Anthropometric variables and *FTO* genotyping in all children cohorts.

| | GENDAI | ALSPAC | GENESIS | |
|---|---|---|---|---|
| *FTO* variant | rs9939609 (T>A) | | rs17817449 (T>G) | |
| n | 922 | 6131 | 394 | 775 |
| Age (years) | 11.2 ± 0.6 | 11.7 ± 0.22 | 2–3 | 3–4 |
| Sex (m/f) (%) | 46.9/53.1 | 51.5/48.5 | 54.8/45.2 | 52.9/47.1 |
| BMI (kg/m$^2$) | 20.0 ± 3.4 | 19.05 ± 3.4 | 16.4 ± 1.5 | 16.2 ± 1.6 |
| Waist (cm) | 68.7 ± 9.6 | 68.3 ± 9.4 | 49.5 ± 3.3 | 51.4 ± 3.9 |
| WHR | 0.8 ± 0.1 | 0.84 ± 0.06 | 0.9 ± 0.0 | 0.9 ± 0.0 |
| Tricept Skinfolds (mm) | 19.4 ± 7.5 | NA | 9.6 ± 2.5 | 9.5 ± 2.7 |
| Subscapular | 11.4 ± 5.3 | NA | 6.7 ± 2.1 | 6.7 ± 2.1 |
| Genotype (%) | AA (16.1) | AA (15.50) | GG (20.7) | GG (22.1) |
| | TA (52.0) | TA (47.17) | TG (32.6) | TG (33.5) |
| | TT (32.0) | TT (37.33) | TT (46.7) | TT (44.4) |
| MAF | A(0.421) | A(0.39) | G(0.370) | G(0.388) |

Table II. Obesity indices depending on the breastfeeding practices (mean, 95% CI).

| | GENDAI | | | ALSPAC | | | GENESIS | | |
|---|---|---|---|---|---|---|---|---|---|
| | Breastfeeders | Non-breastfeeders | P value | Breastfeeders | Non-breastfeeders | P value | Breastfeeders | Non-breastfeeders | P value |
| Weight (kg) | 44.3 (43.6, 45.1) | 44.5 (43.6, 45.4) | 0.8 | 43.3 (42.9, 43.6) | 44.2 (43.8, 44.7) | **0.0007** | 17.0 (16.8, 17.2) | 16.9 (16.6, 17.3) | 0.740 |
| BMI ($kg/m^2$) | 20 (19.7, 20.3) | 20 (19.7, 20.3) | 0.9 | 18.9 (18.8, 18.9) | 19.4 (19.3, 19.6) | **<0.0001** | 16.3 (16.2, 16.4) | 16.2 (16.0, 16.3) | 0.160 |
| Waist Circumference (cm) | 68.4 (67.7, 69.2) | 69.1 (68.3, 70.1) | 0.2 | 67.7(67. 5, 68) | 69.2 (68.8, 69.7) | **<0.0001** | 51.2 (50.9, 51.4) | 51.2 (50.7, 51.6) | 0.992 |
| WHR | 0.8 (0.8, 0.81) | 0.8 (0.8. 0.81) | 0.4 | 0.83 (0.83, 0.84) | 0.8 (0.84, 0.85) | **<0.0001** | 0.93 (0.92, 0.94) | 0.93 (0.92, 0.94) | 0.229 |
| Skinfolds (mm) Triceps | 19.2 (18.6, 19.8) | 19.1 (17.7, 20.5) | 0.7 | NA | NA | – | 9.6 (9.4, 9.7) | 9.4 (9.1, 9.6) | 0.233 |
| Subscapular | 11.2 (10.8, 11.6) | 11.3 (10.3, 12.3) | 0.9 | NA | NA | – | 6.6 (6.5, 6.7) | 7.0 (6.9, 7.2) | **0.024** |

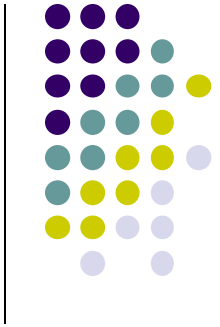
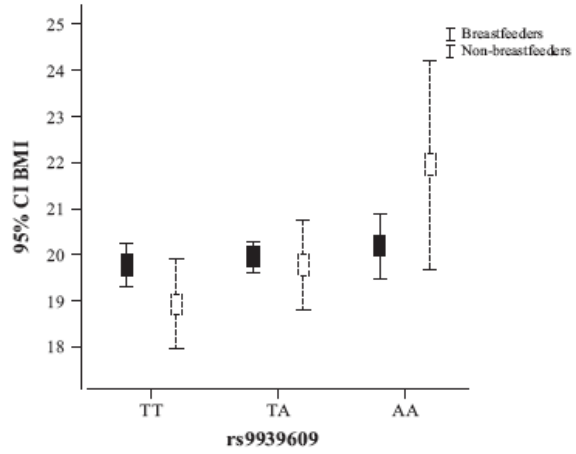
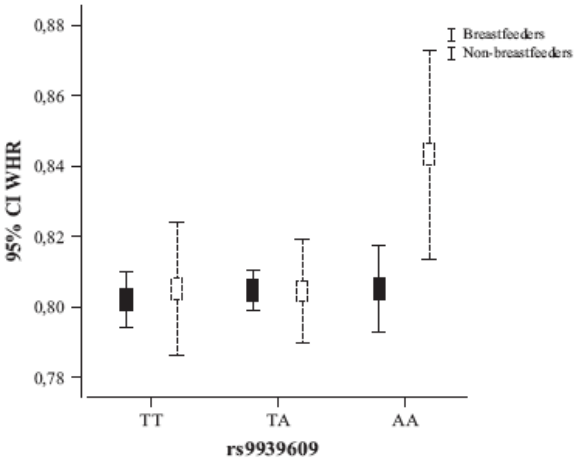


Table IV. Multiple linear regression models for the *FTO* polymorphisms *rs9939609* and *rs17817449*.

| | GENDAI | | ALSPAC | | GENESIS | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | 2–3 years | | 3–4 years | |
| Dependent variable | Beta (SE) | *P* | Beta (SE) | *P* | Beta (SE) | *P* | Beta (SE) | *P* |
| BMI (kg/m$^2$) | 0.430 (0.166) | **0.009** | **0.542 (0.096)** | **1.961e-08** | –0.046 (0.095) | 0.621 | 0.093 (0.073) | 0.203 |
| Waist circumference (cm) | 1.067 (0.456) | **0.019** | **1.468 (0.263)** | **2.803e-08** | 0.033 (0.213) | 0.876 | 0.473 (0.181) | **0.008** |
| WHR | 0.004 (0.003) | 0.061* | **0.005 (0.002)** | **0.004** | –0.001 (0.003) | 0.625 | 0.000 (0.002) | 0.989 |
| Triceps skinfold (mm) | 0.972 (0.367) | **0.003*** | NA | NA | –0.018 (0.163) | 0.929 | 0.221 (0.122) | 0.068 |
| Subscapular skinfold (mm) | 0.593 (0.261) | **0.023** | NA | NA | –0.099 (0.134) | 0.454 | 0.227 (0.095) | **0.014** |

The models in GENDAI and GENESIS were adjusted for the following confounders: age, sex, physical inactivity, Tanner stage. For the same confounders except age all models were adjusted in ALSPAC. Beta coefficients represent the effect of each extra minor allele. P* values are from log transformed variables.


95% CI BMI
25
24
23
22
21
20
19
18
TT
TA
AA
rs9939609
Breastfeeders
Non-breastfeeders


95% CI WHR
0,88
0,86
0,84
0,82
0,80
0,78
TT
TA
AA
rs9939609
Breastfeeders
Non-breastfeeders

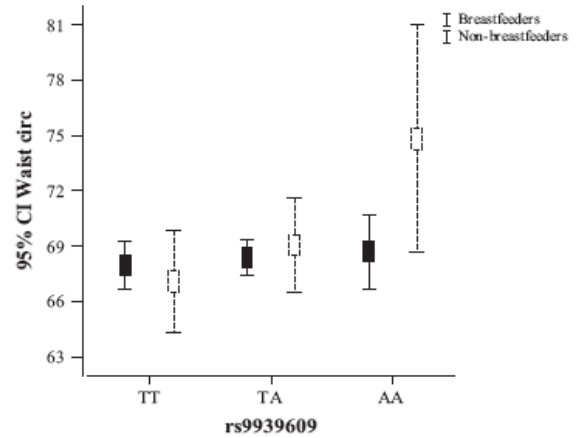

95% CI Waist circ
81
78
75
72
69
66
63
TT
TA
AA
rs9939609
Breastfeeders
Non-breastfeeders

Table V. Multivariate linear regression models for the interaction between breastfeeding (breastfeeders vs. non-breastfeeders) and *FTO* polymorphism *rs9939609*.

| | GENDAI | | ALSPAC | | GENESIS | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | 2–3 years | | 3–4 years | |
| Dependent variable | Beta (SE) | *P* | Beta | *P* | Beta (SE) | *P* | Beta (SE) | *P* |
| BMI (kg/m$^2$) | –0.025 (0.040) | 0.528 | 0.010 | 0.957 | –0.076 (0.028) | **0.007** | –0.005 (0.021) | 0.78 |
| Waist circumference (cm) | –0.144 (0.110) | 0.190 | NA | NA | –0.040 (0.064) | 0.51 | 0.03 (0.051) | 0.59 |
| WHR | –0.001 (0.001) | **0.009*** | –0.004 | 0.138 | 0.001 (0.001) | 0.055 | 0.0003 (0.001) | 0.53 |
| Triceps skinfold (mm) | –0.030 (0.089) | 0.922* | NA | NA | –0.04 (0.049) | 0.42 | –0.083 (0.035) | **0.015** |
| Subscapular skinfold (mm) | –0.076 (0.063) | 0.228 | NA | NA | 0.007 (0.041) | 0.85 | –0.025 (0.027) | 0.35 |

The models were adjusted for potential confounders: In all cohorts we adjusted for sex, physical inactivity and breastfeeding. ALSPAC and GENDAI were additionally adjusted for Tanner stage while GENDAI peri-adolescents were further adjusted for age. Beta coefficients represent the effect of each extra minor allele. P* values are from log transformed variables. NA: Not available.

In summary, our findings indicate that breastfeeding may exert a modifying effect on the relationship between *FTO* variants and adiposity indices in Greek children from the ages of three upwards. Longitudinal data are needed in order to evaluate whether the breastfeeding protection on the FTO-influenced phenotype is maintained beyond adolescence and whether the breastfeeding protection is also associated with other metabolic and inflammatory markers.

# PPAR gamma

**P**eroxisome proliferator activated receptor-(PPAR) is a member of the nuclear hormone receptor super-family of ligand-dependent **transcription factors.**

This particular subtype is mainly **expressed in adipose tissue**, where it acts as a major regulator of adipocyte differentiation and plays a central role in **lipid and glucose homeostasis**.

In vitro studies have shown that the Ala12 isoform of PPAR2 has a reduced ability in activating transcription and inducing adipogenesis. Subjects carrying the Ala12 allele have been reported to exhibit higher plasma concentrations of total and low-density lipoprotein (LDL) cholesterol

*Brief Genetics Report*

# Evidence for Gene-Nutrient Interaction at the *PPARγ* Locus

Jian'an Luan,[1] Paul O. Browne,[2] Anne-Helen Harding,[1] David J. Halsall,[2] Stephen O'Rahilly,[2] V.K. Krishna Chatterjee,[2] and Nicholas J. Wareham[1]

TABLE 1
Adjusted means of BMI, fasting insulin, and P:S ratio (adjusted for age)

| | Pro homozygotes | Ala allele carriers | *P* |
|---|---|---|---|
| Men | | | |
| *n* | 203 | 56 | |
| BMI (kg/m$^2$) | 26.54 (26.20–26.88) | 26.77 (26.10–27.43) | 0.554 |
| Fasting insulin (pmol/l)* | 39.50 (37.11–42.04) | 39.56 (35.03–44.69) | 0.981 |
| P:S ratio | 0.55 (0.52–0.58) | 0.56 (0.52–0.59) | 0.986 |
| Women | | | |
| *n* | 265 | 68 | |
| BMI (kg/m$^2$) | 25.93 (25.50–26.33) | 25.72 (24.88–26.57) | 0.678 |
| Fasting insulin (pmol/l)* | 38.04 (36.16–40.01) | 38.28 (34.59–42.36) | 0.914 |
| P:S ratio | 0.55 (0.52–0.57) | 0.56 (0.50–0.61) | 0.823 |

Data are arithmetic means (95% CI) and *geometric means (95% CI).

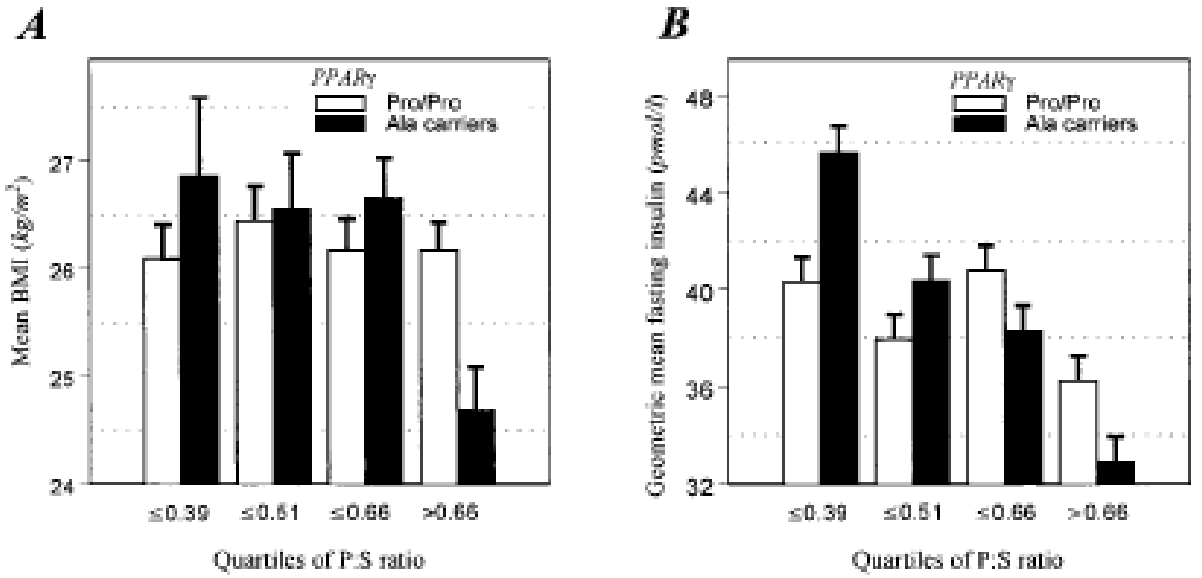
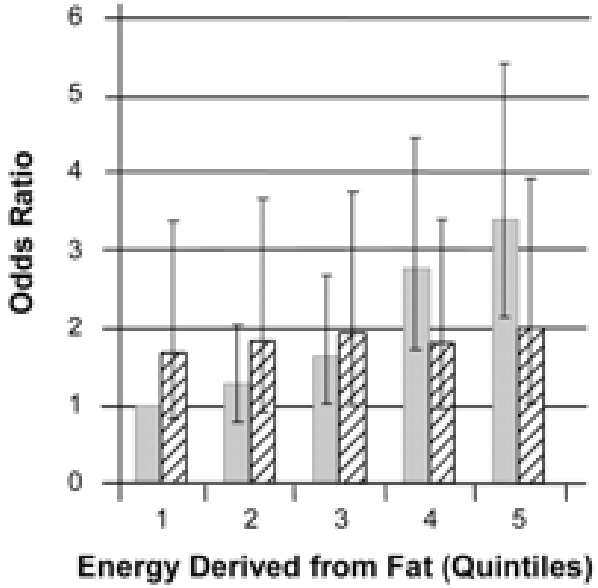



FIG. 1. Mean BMI (± SE) (kg/m$^2$) (*A*) and geometric mean (± SE) fasting insulin (pmol/l) (*B*) by P:S ratio and *PPARγ*.

# Pro12Ala and fat intake

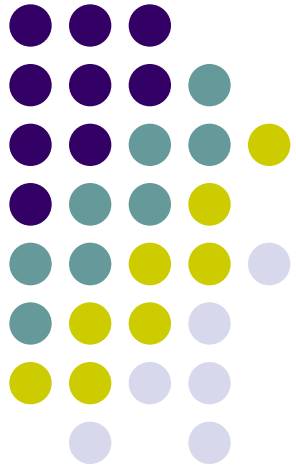



Healthy subjects (n=2141) within the **Nurses' Health Study**. Among homozygous wild-type **Pro/Pro** individuals(shaded bars) , those in the highest quintile of total fat intake, had significantly higher mean body mass index (BMI) compared with those in the lowest quintile whereas among 12Ala variant allele-carriers (hatched bars) there was no significant trend observed between dietary fat intake and BMI.

*(Memisoglou et al., 2003)*

# An age-dependent diet-modified effect of the *PPARγ* Pro12Ala polymorphism in children

George V. Dedoussis[a,*], Yannis Manios[a], Georgia Kourlaba[a], Stavroula Kanoni[a], Vasiliki Lagou[b], Johannah Butler[c,d], Constantina Papoutsakis[a], Robert A. Scott[b], Mary Yannakoulia[a], Yannis P. Pitsiladis[b], Joel N. Hirschhorn[c,d,e,f], Helen N. Lyon[c,d,g]



*Metabolism 2011*

Table 1
Anthropometric and adiposity outcomes stratified by the Pro12Ala genotype (data are presented as means ± SD)

| | Periadolescents | | | Young children | | |
|---|---|---|---|---|---|---|
| | Pro/Pro (n = 669) | Pro/Ala and Ala/Ala (n = 125) | *P* value | Pro/Pro (n = 1648) | Pro/Ala and Ala/Ala (n = 265) | *P* value |
| Girls | (n = 356) | (n = 64) | | (n = 792) | (n = 120) | |
| Weight (kg) | 44.2 ± 9.4 | 43.6 ± 10.3 | .57 | 16.8 ± 3.5 | 17.4 ± 3.2 | .13 |
| BMI (kg/m$^2$) | 19.9 ± 3.4 | 19.7 ± 3.9 | .55 | 16.2 ± 1.6 | 16.3 ± 1.6 | .38 |
| Obesity (%) | 7.8 | 6.7 | 1.00 | 4.4[a] | 5.6[a] | .58 |
| Skinfolds | | | | | | |
| Triceps (mm) | 19.8 ± 7.2 | 20 ± 8.0 | .92 | 9.9 ± 2.8 | 10.5 ± 3.0 | **.04** |
| Subscapular (mm) | 11.7 ± 5.3 | 12.3 ± 6.1 | .94 | 6.9 ± 2.2 | 7.4 ± 2.7 | **.05** |
| Waist circumference (cm) | 67.3 ± 9.1 | 68.9 ± 9.6 | .67 | 51.3 ± 4.7 | 52.1 ± 4.6 | .08 |
| TF (% of total energy) | 40 ± 6.5 | 38.5 ± 5.8 | **.05** | 40.0 ± 5.6 | 39.8 ± 5.6 | .71 |
| SFA (% of total energy) | 14.8 ± 3 | 13.5 ± 2.9 | **.002** | 16.5 ± 3.6 | 16.4 ± 3.7 | .86 |
| MUFA (% of total energy) | 16.2 ± 4.3 | 16.2 ± 4.2 | .99 | 16.4 ± 3.3 | 16.3 ± 3.4 | .60 |
| PUFA (% of total energy) | 4.7 ± 1.5 | 4.7 ± 1.6 | .73 | 4.2 ± 1.3 | 4.3 ± 1.3 | .49 |
| Boys | (n = 313) | (n = 61) | | (n = 842) | (n = 142) | |
| Weight (kg) | 44.8 ± 9.4 | 42.9 ± 9.3 | .13 | 17.1 ± 3.2 | 17.3 ± 3.2 | .55 |
| BMI (kg/m$^2$) | 20.4 ± 3.4 | 19.7 ± 3.4 | .11 | 16.3 ± 1.6 | 16.3 ± 1.5 | .72 |
| Obesity (%) | 8.8 | 7.0 | .80 | 3.5[a] | 3.7[a] | .90 |
| Skinfolds | | | | | | |
| Triceps (mm) | 19.4 ± 7.9 | 16.9 ± 6.9 | **.01** | 9.2 ± 2.6 | 9.0 ± 2.2 | .57 |
| Subscapular (mm) | 11.2 ± 5.4 | 9.6 ± 4.5 | **.02** | 6.3 ± 1.9 | 6.3 ± 1.9 | .06 |
| Waist circumference (cm) | 70.7 ± 9.6 | 68.7 ± 9.5 | .10 | 51.2 ± 4.3 | 51.2 ± 3.6 | .96 |
| TF (% of total energy) | 40.2 ± 7 | 41 ± 7 | .41 | 39.9 ± 5.5 | 40.8 ± 5.0 | .11 |
| SFA (% of total energy) | 14.7 ± 3.6 | 15 ± 3.7 | .52 | 16.4 ± 3.7 | 16.6 ± 3.0 | .57 |
| MUFA (% of total energy) | 16.4 ± 4.2 | 16.8 ± 4.4 | .53 | 16.5 ± 3.2 | 17.1 ± 3.6 | .08 |
| PUFA (% of total energy) | 4.9 ± 1.5 | 4.6 ± 1.4 | .23 | 4.3 ± 1.1 | 4.2 ± 1.1 | .80 |

[a] Only for children ≥2 years old, as there are no International Obesity Task Force obesity cutoff points for younger ages.

Table 2
Obesity-related outcomes in girls adjusted for dietary fat intake (in grams) stratified by *Pro12Ala* polymorphism

| Outcome | Predictor | Periadolescents | | | | Young children | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Pro/Pro | | Pro/Ala and Ala/Ala | | Pro/Pro | | Pro/Ala and Ala/Ala | |
| | | Standardized $\beta$ | *P* value | Standardized $\beta$ | *P* value | Standardized $\beta$ | *P* value | Standardized $\beta$ | *P* value |
| BMI (kg/m$^2$) | TF | 0.010 | .83 | 0.096 | .47 | 0.049 | .21 | −0.008 | .94 |
| | SFA | −0.089 | .11 | 0.188 | .16 | 0.096 | **.01** | −0.019 | .85 |
| | MUFA | 0.040 | .42 | 0.021 | .88 | −0.002 | .95 | −0.033 | .76 |
| | PUFA | −0.069 | .26 | 0.053 | .70 | −0.082 | **.04** | 0.056 | .60 |
| Triceps skinfold thickness (mm) | TF | 0.013 | .96 | 0.071 | .60 | 0.159 | $\mathbf{10^{-5}}$ | 0.115 | .26 |
| | SFA | −0.029 | .69 | 0.192 | .18 | 0.223 | $\mathbf{10^{-9}}$ | 0.098 | .34 |
| | MUFA | 0.020 | .63 | −0.019 | .89 | 0.028 | .47 | 0.081 | .44 |
| | PUFA | −0.079 | .09 | −0.102 | .47 | −0.037 | .35 | 0.136 | .20 |
| Subscapular skinfold thickness (mm) | TF | 0.023 | .51 | 0.062 | .65 | 0.150 | $\mathbf{10^{-4}}$ | 0.134 | .20 |
| | SFA | −0.038 | .59 | 0.278 | .06 | 0.186 | $\mathbf{10^{-6}}$ | 0.190 | .07 |
| | MUFA | 0.043 | .45 | −0.034 | .80 | 0.038 | .34 | 0.062 | .56 |
| | PUFA | −0.068 | .52 | −0.078 | .61 | −0.002 | .95 | 0.001 | .99 |
| Waist circumference (cm) | TF | 0.047 | .39 | 0.042 | .75 | 0.033 | .33 | −0.006 | .99 |
| | SFA | −0.078 | .15 | 0.203 | .13 | 0.079 | **.02** | −0.016 | .86 |
| | MUFA | −0.096 | .07 | −0.044 | .75 | −0.014 | .69 | 0.001 | .99 |
| | PUFA | −0.058 | .56 | −0.100 | .60 | −0.051 | .14 | 0.082 | .39 |

Multivariate linear regression models were adjusted for potential confounders: age and minutes of sedentary activities.

Table 3
Obesity-related outcomes for boys adjusted for dietary fat intake (in grams) stratified by *Pro12Ala* polymorphism

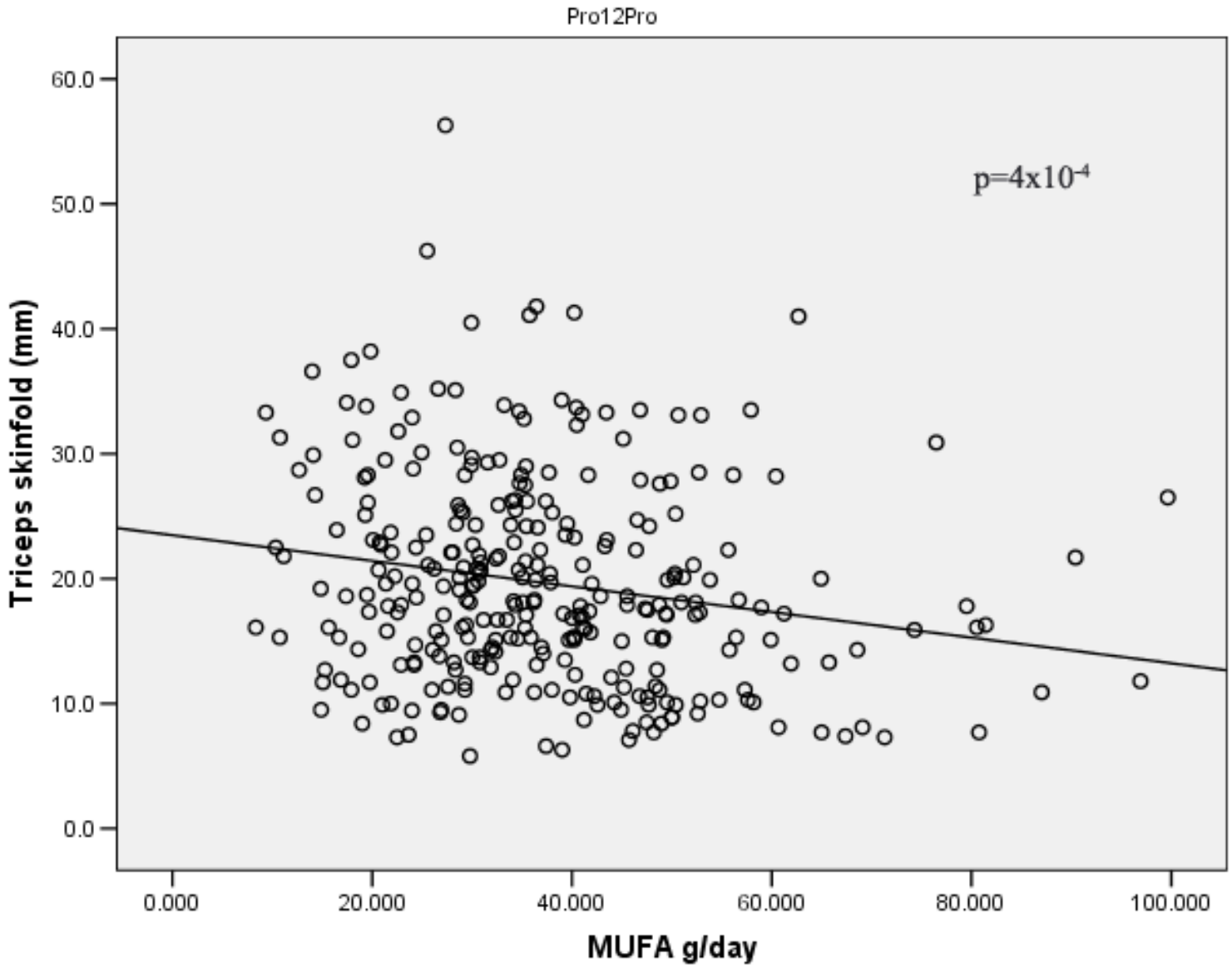
| Outcome | Predictor | Periadolescents | | | | Young children | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Pro/Pro | | Pro/Ala and Ala/Ala | | Pro/Pro | | Pro/Ala and Ala/Ala | |
| | | Standardized $\beta$ | $P$ value | Standardized $\beta$ | $P$ value | Standardized $\beta$ | $P$ value | Standardized $\beta$ | $P$ value |
| BMI (kg/m$^2$) | TF | −0.081 | .17 | −0.024 | .87 | 0.090 | **.02** | 0.006 | .95 |
| | SFA | 0.03 | .62 | 0.110 | .45 | 0.062 | .09 | 0.003 | .97 |
| | MUFA | −0.128 | **.03** | −0.048 | .75 | 0.036 | .07 | 0.018 | .85 |
| | PUFA | −0.095 | .08 | −0.128 | .37 | 0.034 | .36 | 0.033 | .73 |
| Triceps skinfold thickness (mm) | TF | −0.078 | .19 | 0.095 | .51 | 0.080 | **.04** | 0.100 | .31 |
| | SFA | 0.017 | .54 | 0.287 | **.05** | 0.093 | **.01** | 0.215 | **.02** |
| | MUFA | −0.135 | **.02** | 0.002 | .99 | 0.036 | .34 | −0.021 | .83 |
| | PUFA | −0.048 | .40 | −0.176 | .22 | −0.009 | .80 | 0.029 | .76 |
| Subscapular skinfold thickness (mm) | TF | 0.025 | .67 | 0.072 | .67 | 0.051 | .18 | 0.101 | .29 |
| | SFA | 0.119 | **.04** | 0.125 | .40 | 0.067 | .07 | 0.189 | **.04** |
| | MUFA | −0.044 | .41 | 0.075 | .62 | 0.012 | .76 | −0.023 | .81 |
| | PUFA | −0.059 | .30 | −0.126 | .13 | −0.010 | .79 | 0.026 | .78 |
| Waist circumference (cm) | TF | −0.070 | .23 | 0.057 | .69 | 0.040 | .24 | −0.074 | .40 |
| | SFA | 0.027 | .64 | 0.106 | .46 | 0.032 | .34 | −0.021 | .81 |
| | MUFA | −0.125 | **.03** | 0.094 | .53 | 0.052 | .12 | −0.049 | .58 |
| | PUFA | −0.022 | .62 | −0.072 | .62 | 0.034 | .32 | −0.069 | .43 |

The multivariate linear regression models were adjusted for potential confounders: age and minutes of sedentary activities.

Table 4
Gene-diet modification in Pro/Pro homozygotes by age group in young children from the GENESIS cohort

| Outcome | Age groups (mo) | Girls | | | | Age groups (mo) | Boys | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | TF | | SFA | | | TF | | SFA | |
| | | Standardized $\beta$ | $P$ value | Standardized $\beta$ | $P$ value | | Standardized $\beta$ | $P$ value | Standardized $\beta$ | $P$ value |
| Triceps skinfold thickness (mm) | 12-24 (n = 59) | 0.306 | **.03** | 0.416 | **.003** | 12-24 (n = 69) | −0.170 | .19 | −0.076 | .57 |
| | 24-36 (n = 150) | 0.271 | **.001** | 0.297 | **$10^{-4}$** | 24-36 (n = 173) | 0.113 | .16 | 0.224 | **.005** |
| | 36-48 (n = 297) | 0.153 | **.01** | 0.249 | **$10^{-4}$** | 36-48 (n = 334) | 0.059 | .31 | 0.104 | .08 |
| | 48-60 (n = 254) | 0.078 | .250 | 0.127 | .06 | 48-60 (n = 234) | 0.168 | **.02** | 0.033 | .63 |
| Subscapular skinfold thickness (mm) | 12-24 (n = 59) | 0.291 | **.05** | 0.340 | **.02** | 12-24 (n = 69) | −0.186 | .15 | −0.105 | .43 |
| | 24-36 (n = 150) | 0.248 | **.004** | 0.270 | **.001** | 24-36 (n = 173) | 0.013 | .87 | 0.179 | **.03** |
| | 36-48 (n = 297) | 0.162 | **.009** | 0.186 | **.003** | 36-48 (n = 334) | 0.049 | .40 | 0.092 | .12 |
| | 48-60 (n = 254) | 0.059 | .39 | 0.116 | .09 | 48-60 (n=234) | 0.168 | **.02** | 0.013 | .85 |

All models were adjusted for minutes of sedentary activities.


Pro12Pro
p=4x10-4
Triceps skinfold (mm)
60.0
50.0
40.0
30.0
20.0
10.0
0.0
0.000
20.000
40.000
60.000
80.000
100.000
MUFA g/day

# *ADIPOQ* gene polymorphism rs1501299 interacts with fibre intake to affect adiponectin concentration in children: the GENe–Diet Attica Investigation on childhood obesity

Table 1 Effect of rs1501299 genotype × fibre intake interaction on adiponectin concentration (μg/mL)

| | Core model | | Core model + rs1501299 × fibre interaction | |
|---|---|---|---|---|
| | Beta ± SD | *P* | Beta ± SD | *P* |
| Gender | 0.004 ± 0.221 | 0.906 | 0.023 ± 0.221 | 0.828 |
| Pubertal status (pre-pubertal vs pubertal) | −0.550 ± 0.392 | 0.126 | −0.567 ± 0.391 | 0.117 |
| BMI (kg/m$^2$) | −0.093 ± 0.032 | 0.005 | −0.096 ± 0.032 | 0.004 |
| MET score | 0.000 ± 0.000 | 0.053 | 0.000 ± 0.000 | 0.067 |
| Total energy intake (kcal/day) | 0.000 ± 0.000 | 0.188 | 0.000 ± 0.000 | 0.154 |
| Underreporting (no vs yes) | 0.282 ± 0.349 | 0.545 | 0.305 ± 0.348 | 0.471 |
| Fibre intake (g/day) | −0.009 ± 0.015 | 0.381 | 0.015 ± 0.019 | 0.502 |
| rs1501299 (GG vs GT + TT) | 0.325 ± 0.213 | 0.140 | 1.100 ± 0.450 | 0.014 |
| Interaction [rs1501299 (GG vs GT + TT) × fibre] | | | −0.049 ± 0.025 | 0.028 |
| Adjusted $R^2$ of the model | 0.019 | 0.020 | 0.026 | 0.006 |

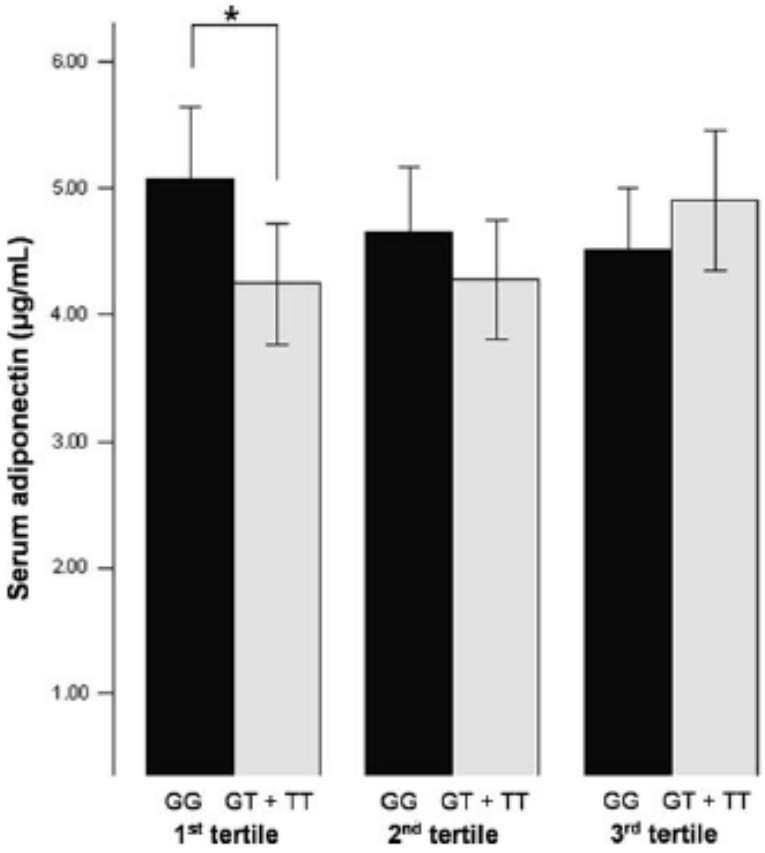



Fig. 1 Serum adiponectin concentration by rs1501299 genotype and fibre intake tertile. * Statistically significant difference between GG and GT + TT ($P = 0.017$) even after adjustment for confounders (gender, pubertal status, BMI, MET score, energy intake, low energy reporting) ($P = 0.020$)

The results show that with lower fiber intake (1st quartile), children with the minor allele have lower adiponectin levels, while those with the common allele are protected

# Dairy intake associates with the IGF2 rs680 polymorphism to height variation in periadolescent children

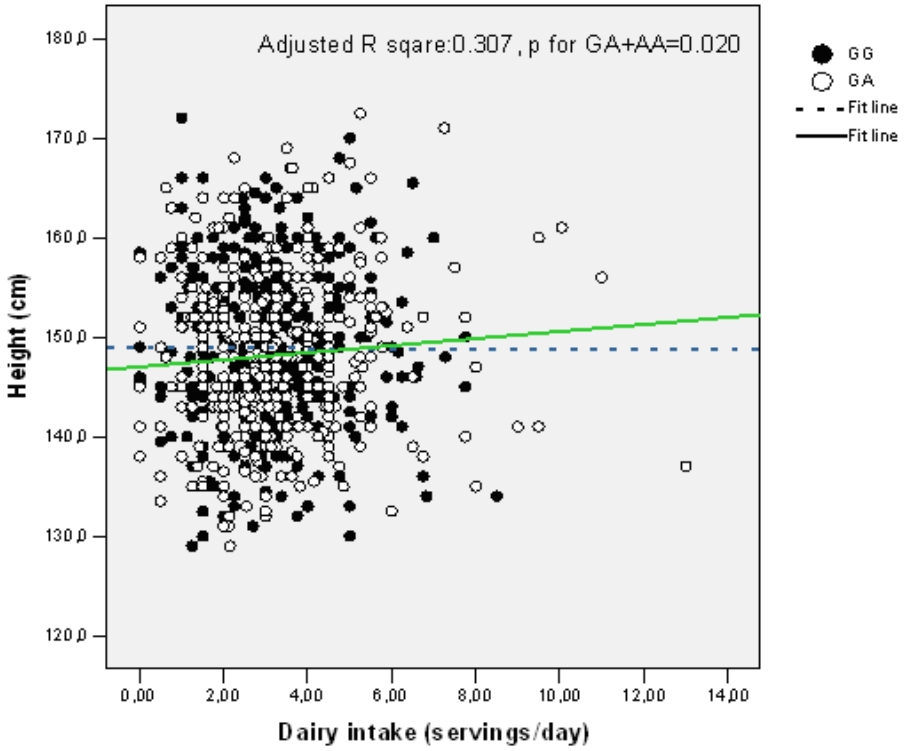
GV Dedoussis, E Louizou, C Papoutsakis, KP Skenderi and M Yannakoulia

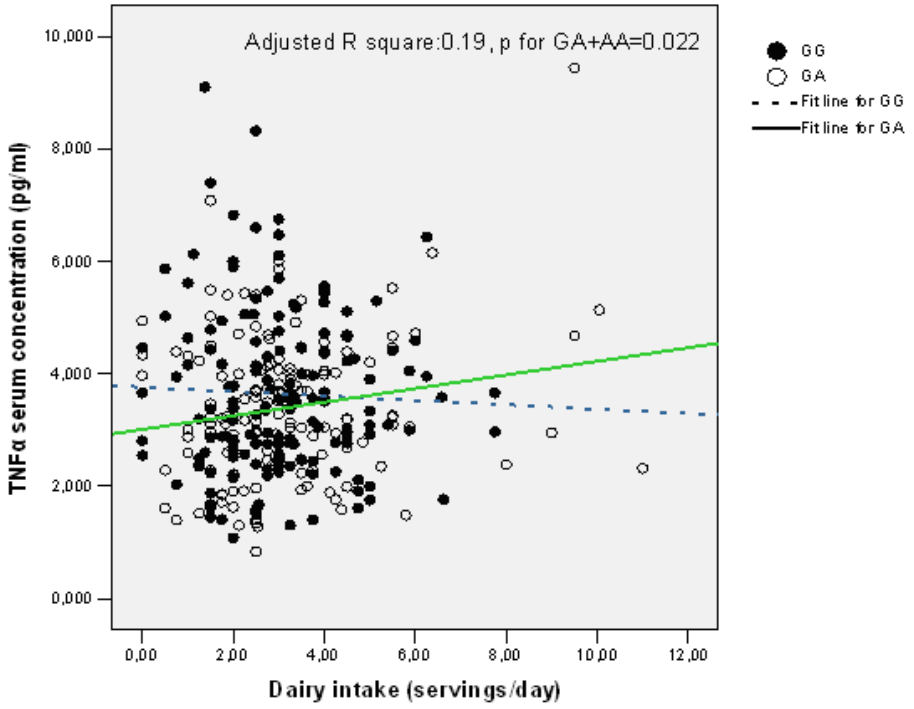
*Department of Dietetics – Nutrition, Harokopio University, Athens, Greece*

**Table 2.** Results of the multiple linear regression analyses using height as a dependent variable.

| Independent Variables | β ± SE | *P* |
|---|---|---|
| Age (yrs) | 5.7 ± 0.38 | 0.0004 |
| Sex | -1.0 ± 0.50 | 0.041 |
| Dairy products intake (servings/day) | 0.45± 0.18 | 0.013 |
| IGF2 rs680 (GG vs GA+AA) | 2.1± 0.95 | 0.026 |
| IGF2 rs680 (GG x Dairy products intake) vs (GA+AA x Dairy products intake) | -0.442 ± 0.26 | 0.09 |
| Adjusted R Squared | 0.23 | 0.0003 |

*Dedoussis et al., 2010 EJCN*




Grouping dairy intake, into **low** (1.9 ± 0.7 servings/day) and **high** dairy products eaters (4.4 ± 1.5 servings/day), children with the A allele being high dairy products eaters were taller compared with low dairy products eaters (**148.8 ± 0.5** cm vs. **147.4 ± 0.5** cm respectively, p=0.05)

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# Physical Activity Attenuates the Influence of *FTO* Variants on Obesity Risk: A Meta-Analysis of 218,166 Adults and 19,268 Children

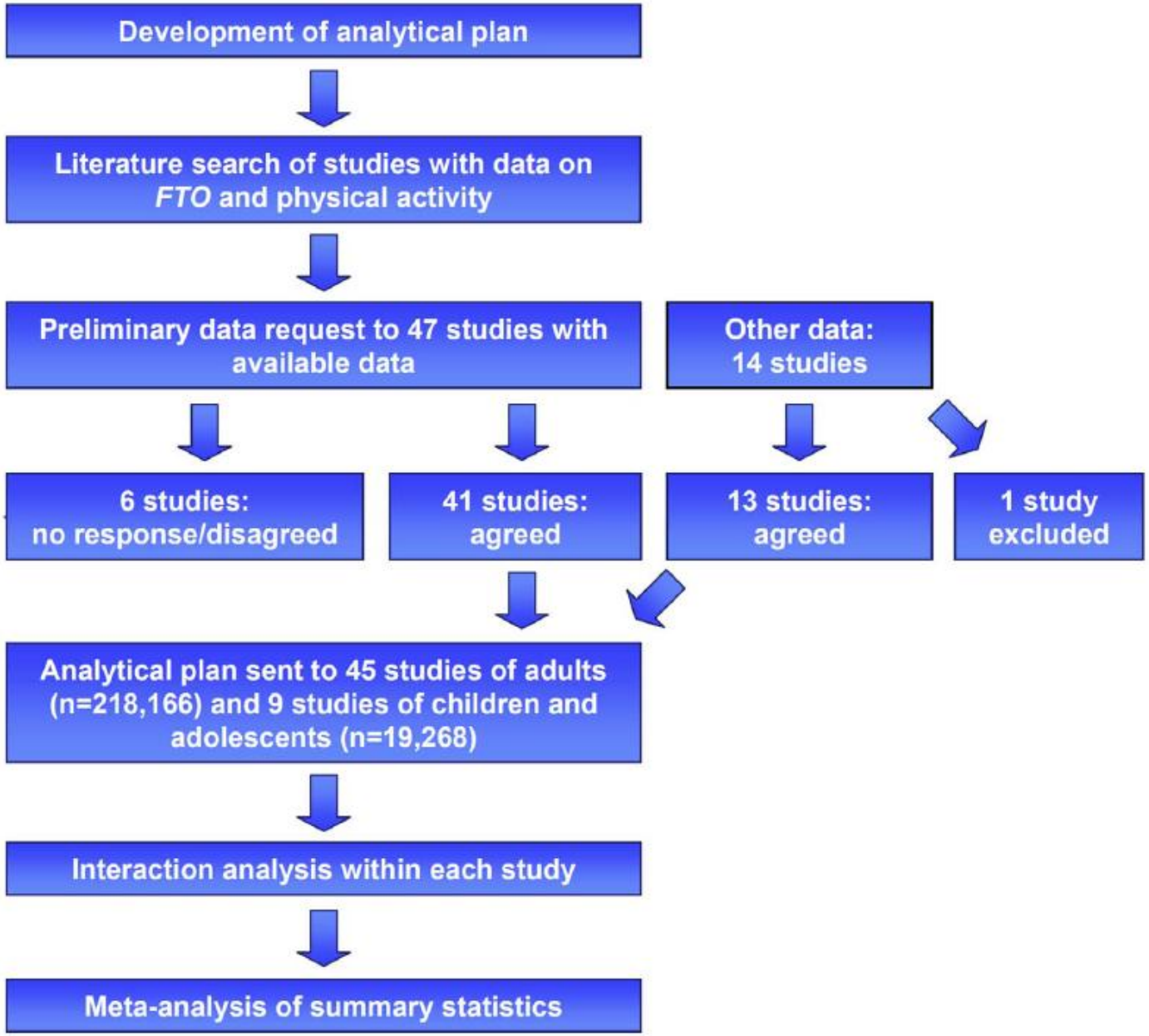
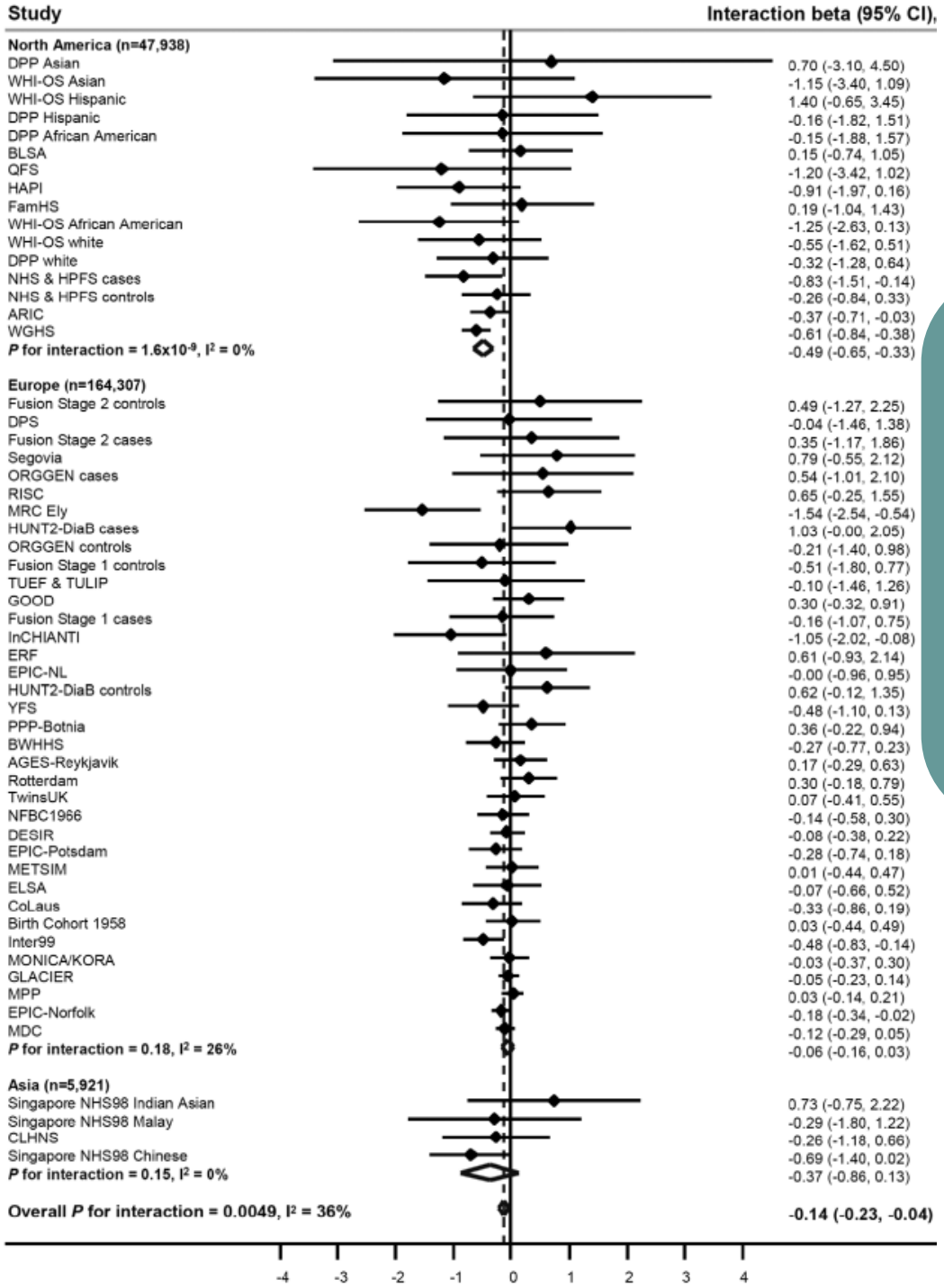
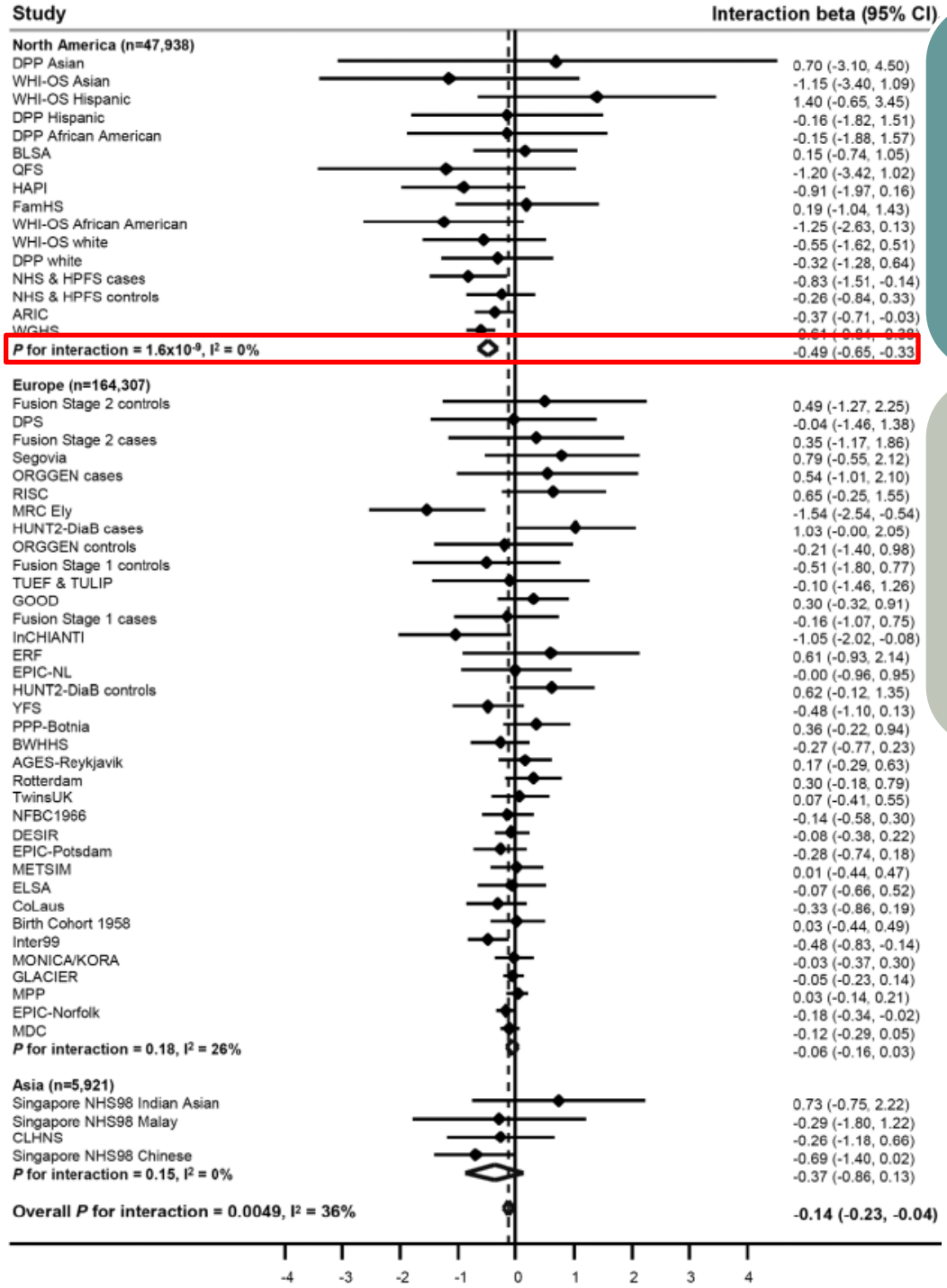



**Figure 1. Study design of the *FTO*×PA interaction meta-analysis.** Eligible studies were identified by a literature search, as well as through personal contacts (indicated in the figure as "other data"). Of all studies that were invited, 45 studies of adults ($n = 218,166$) and nine studies of children and adolescents ($n = 19,268$) joined the meta-analysis. A standardized analytical plan was sent to each of the studies. Summary statistics were subsequently meta-analyzed.
doi:10.1371/journal.pmed.1001116.g001




**Forest plot of the effect of the interaction between the FTO rs9939609 SNP and physical activity on BMI in a random effects meta-analysis of 218,166 adults.** The studies are sorted by sample size (largest sample size lowest).




Interestingly, we found a geographic difference in the interaction of FTO with PA, which was consistent across the studied phenotypes.

In particular, the interaction was stronger in North American populations than in populations from Europe.

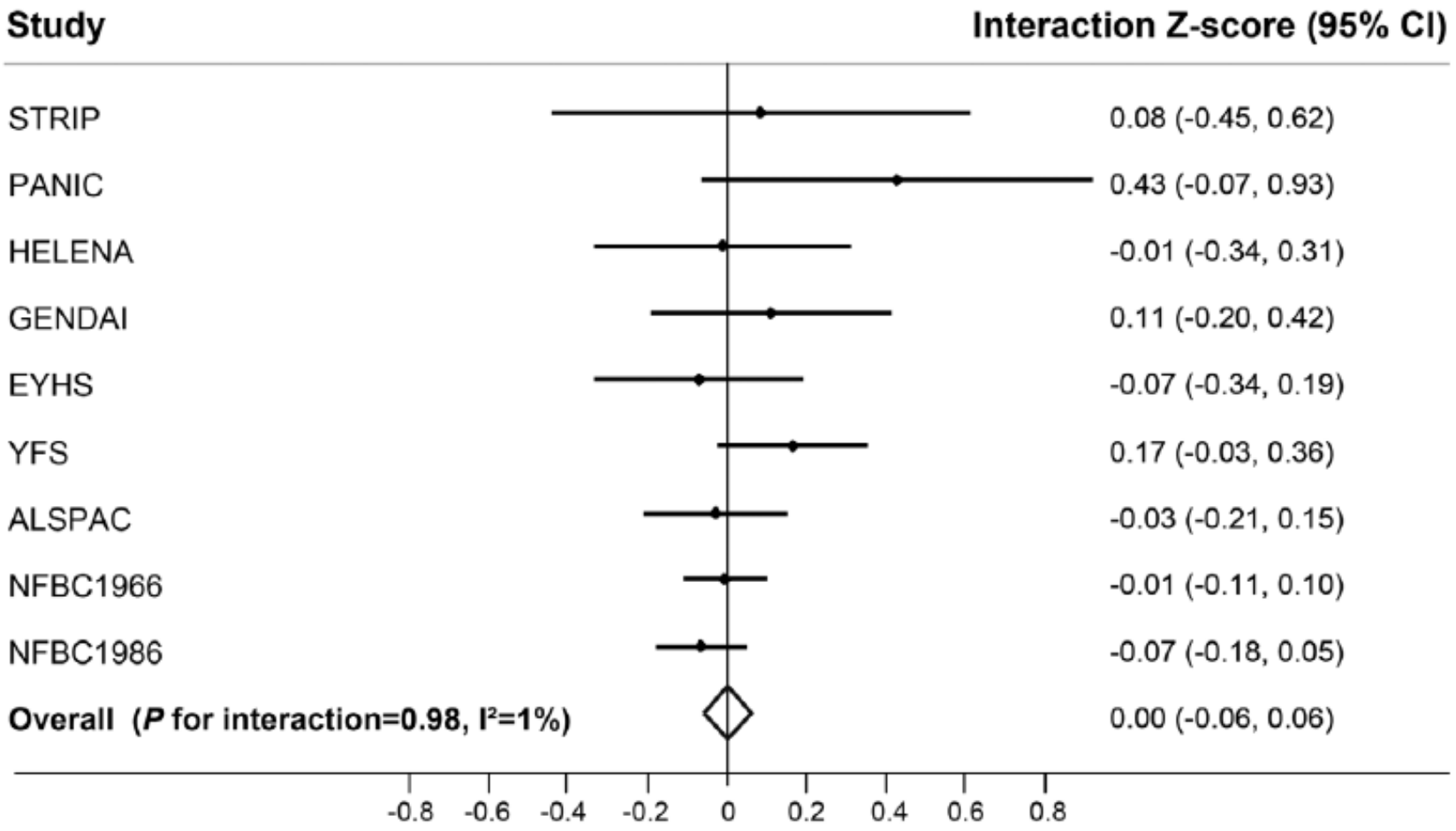
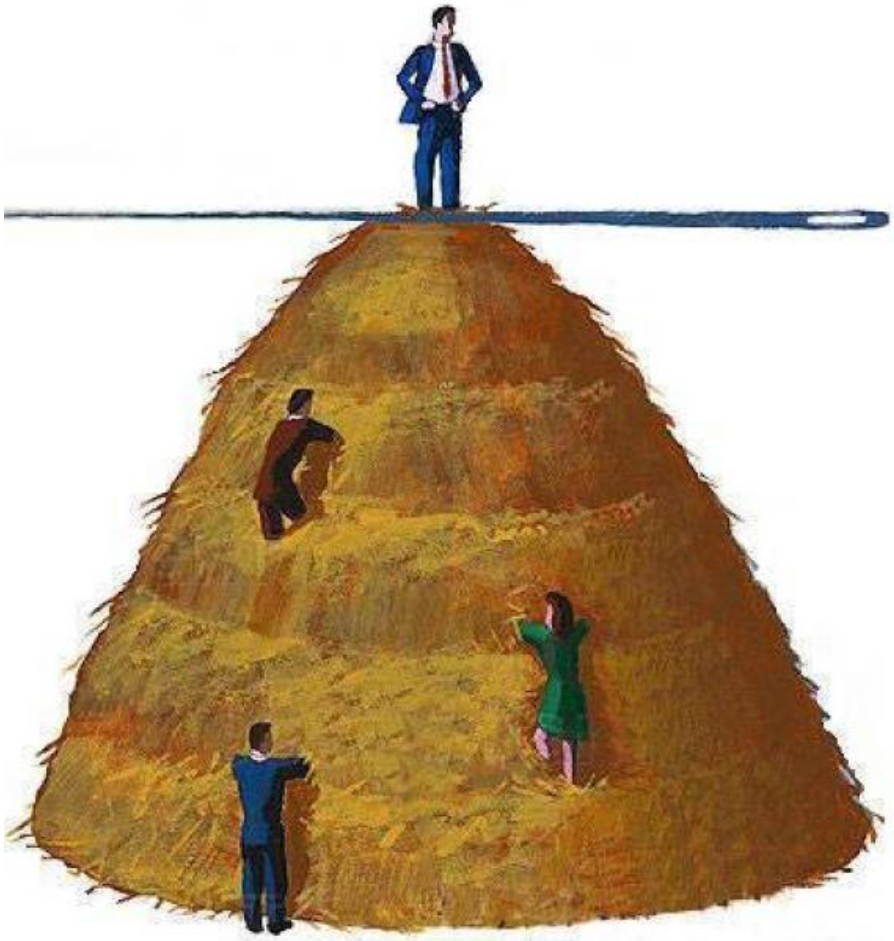



**Figure 3. Forest plot of the effect of the interaction between the *FTO* rs9939609 SNP and physical activity on BMI in a random effects meta-analysis of 19,268 children and adolescents.** The studies are sorted by sample size (largest sample size lowest). Details of the studies are given in Text S1. The interaction *Z*-score represents the difference in age- and sex-standardized BMI per minor (A−) allele of rs9939609 comparing physically active children to inactive children. For example, a $beta_{interaction}$ of −0.1 represents a 0.1 unit attenuation in the BMI *Z*-score-increasing effect of the rs9939609 minor allele in physically active children compared to inactive children.

doi:10.1371/journal.pmed.1001116.g003

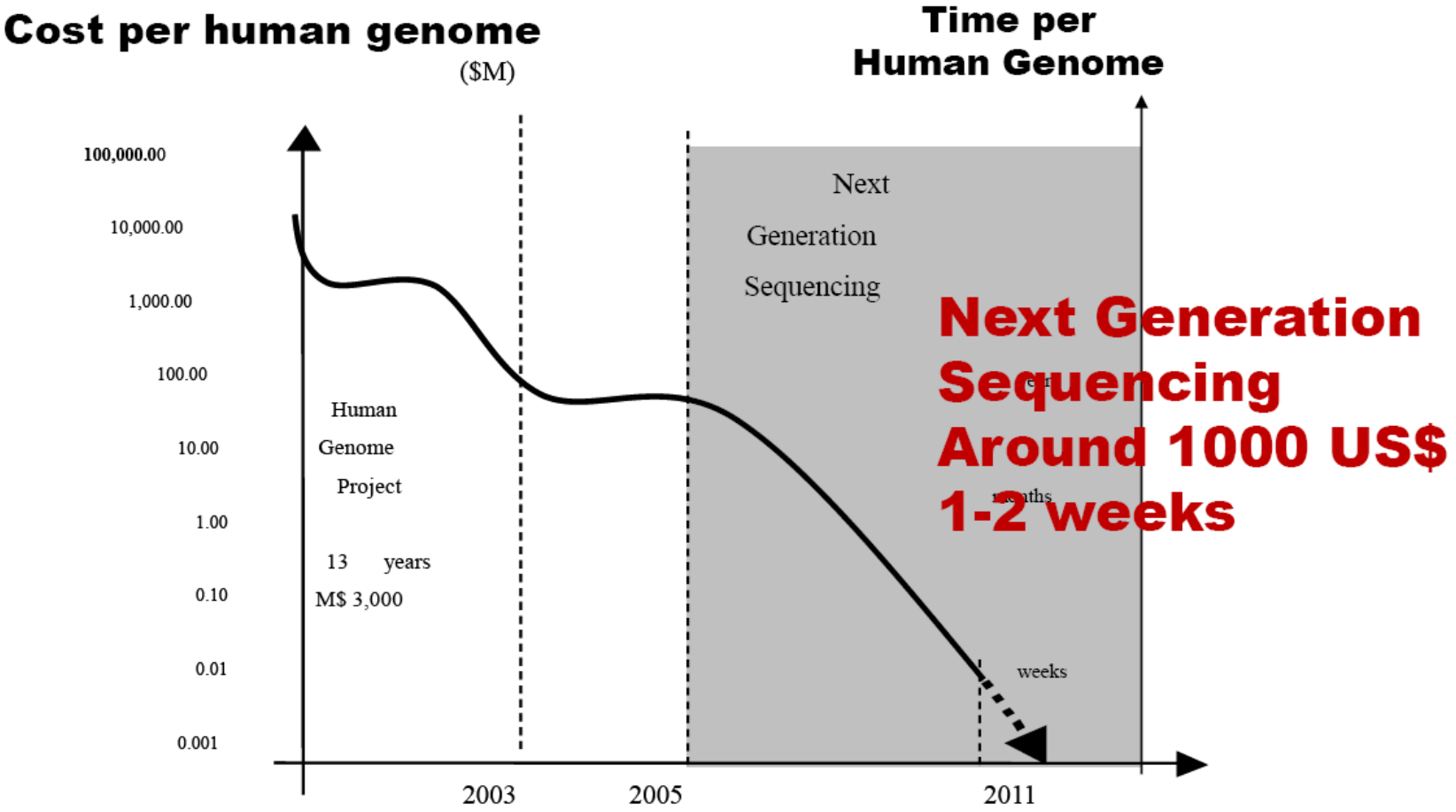


**10-30 million SNPs believed to exist (4 million known)**

**How useful is data on 1 SNP?**

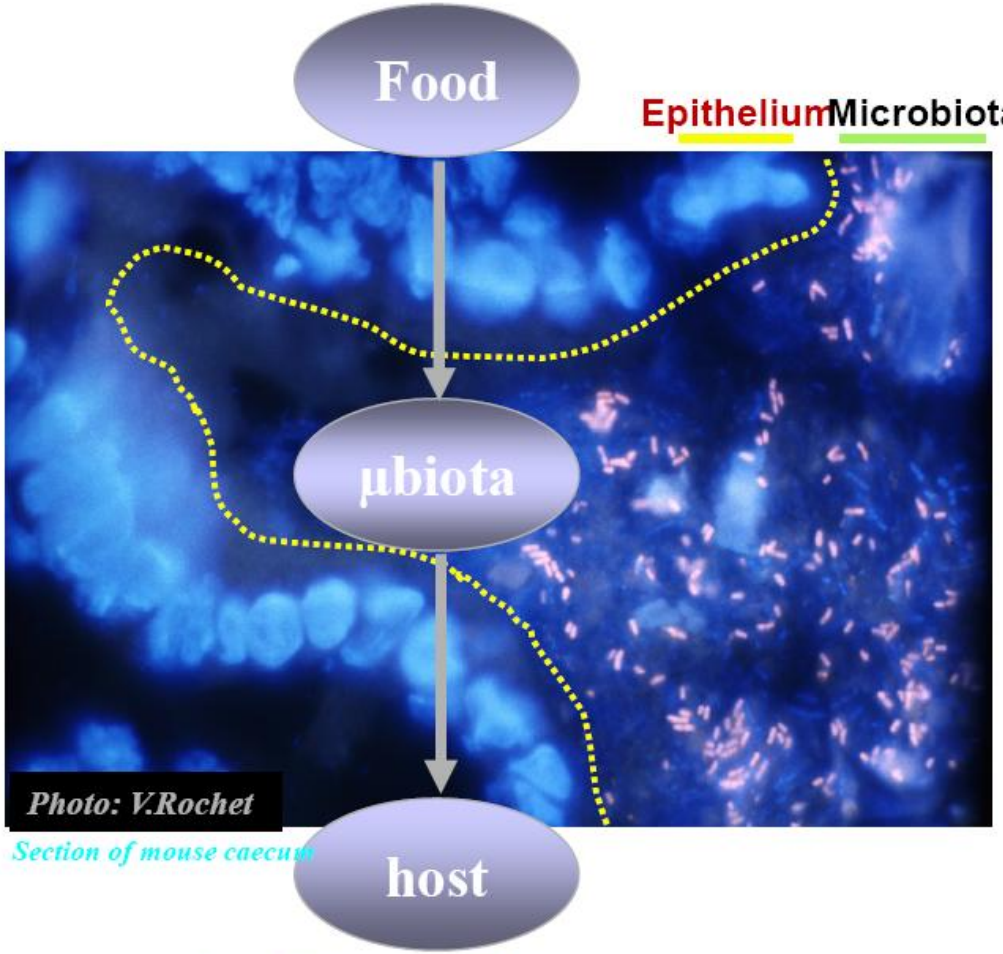
**The future relies on Genome Wide Association Studies (GWAS) (+100,000 SNPs)**

# DNA sequencing is now amenable to a diagnostic test context




**Key issue: Integration of data, bioinformatics**

# The human intestinal microbiota : dense, structurally and functionally diverse




Health <-> Disease

- faecal microbiota : 100 trillions microorganisms
- hundreds of species ...
- normal consortium adapted and functionally stable

- nutrition, physiology, immunity & protection

Vol 444 | 21/28 December 2006 | doi:10.1038/nature05414 nature

ARTICLES

# An obesity-associated gut microbiome with increased capacity for energy harvest

Peter J. Turnbaugh[1], Ruth E. Ley[1], Michael A. Mahowald[1], Vincent Magrini[2], Elaine R. Mardis[1,2] & Jeffrey I. Gordon[1]

**BRIEF COMMUNICATIONS**

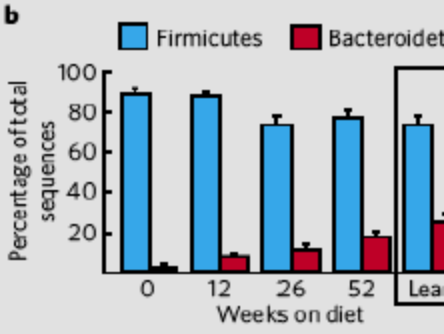


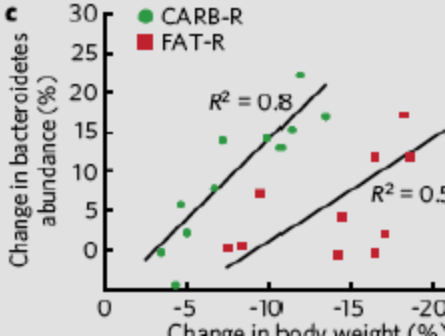
**MICROBIAL ECOLOGY**

# Human gut microbes associated with obesity

**Ruth E. Ley, Peter J. Turnbaugh, Samuel Klein, Jeffrey I. Gordon**
Washington University School of Medicine, St Louis, Missouri 63108, USA

**Suggested that Obese Individuals may have a lower Bacteroidetes: Firmicutes ratio than Lean Individuals – and this can be modulated by diet.**

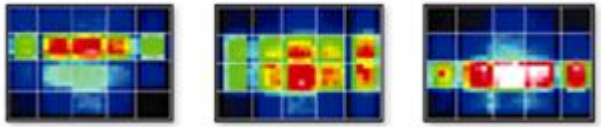


# Our “gene passports” and nutrition


Individual genotype
Functional phenotype

AA AB BB



Optimal Nutrition


Lifestyle

Improvement
Maintenance
of Health

“Eat right for your genotype??”

# Personalized diets?

genelex
*Science that benefits humanity*

## Nutritional Genetic Profile Request Form

### Client Information

To order testing, either contact Genelex directly or complete this form and return it either by fax at (425) 825-1870 or mail to Genelex Corporation, 12277 134th Ct NE, Ste. 130 Redmond, WA 98052.

Name: _____ Phone: _____ E-mail: _____

Address: _____

City: _____ State: _____ Zip: _____

### Nutritional Genetic Profile Requested

| Item | Number ordered | Cost (per item) | Total |
|---|---|---|---|
| Nutritional Genetic Panel | | $445.00 | |
| Nutritional Genetic Collection Kit (Additional $410 due with samples) | | $35.00 | |
| International Shipping | | $50.00 | |
| Amount Due | | | |

**Payment:** Prepayment is required. Send Cash, Check, or Money Order to the address shown above.

Cash ☐ Check or Money Order ☐ Credit Card (all major cards) ☐

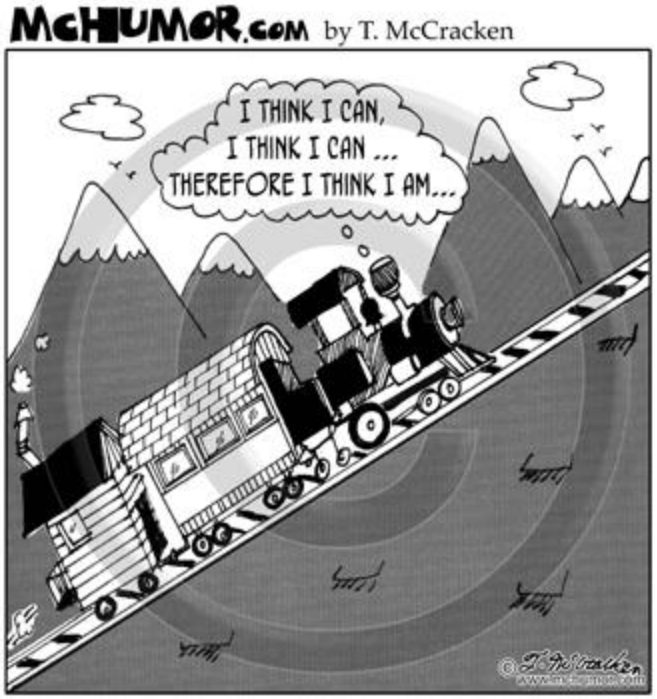
Type of credit card: _____

Print cardholder's name: _____

Card number: _____ Expiration date: _____

For immediate consultation Call 800-TEST-DNA (800-837-8362)
Hours 7:00 AM to 6:00 PM PST, 10:00 AM to 9:00 PM EST, fax
e-mail: info@genelex.com
www.genelex.com


NATURE | VOL 426 | 13 NOVEMBER 2003




**We are on the right track but still, there is a lot of work to do……..**

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