
بسم الله الرحمن الرحیم

Genomics of Obesity

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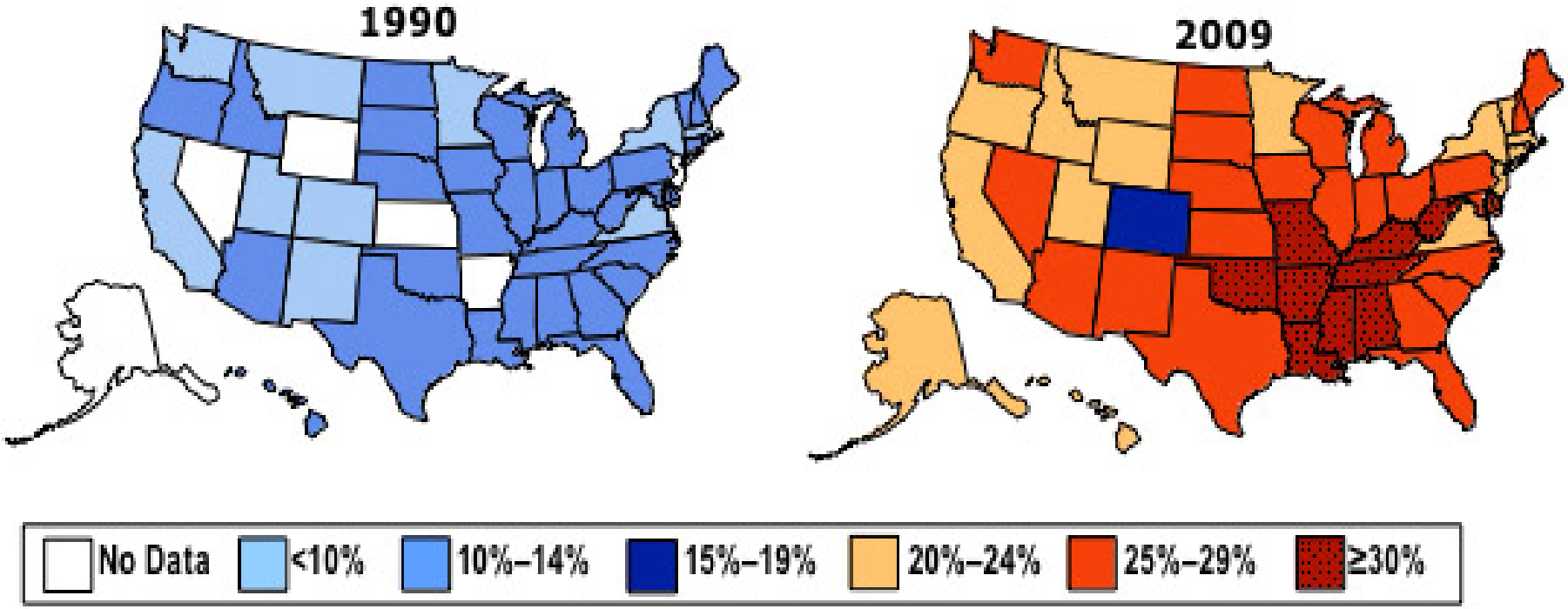
Obesity is one of the world's greatest public health challenges

Obesity Trends* Among U.S. Adults

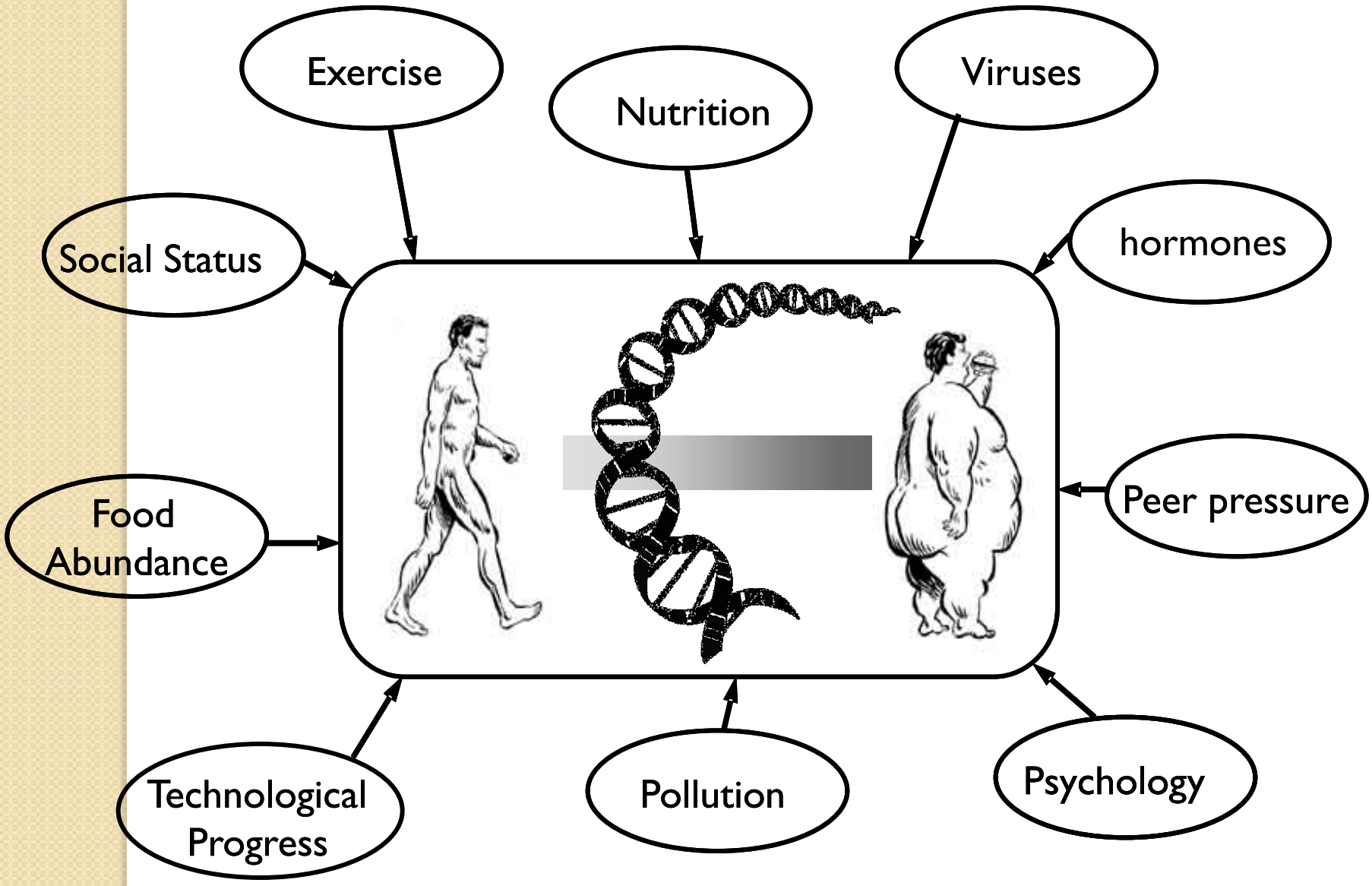
BRFSS, 1990, 1999, 2009

(*BMI ≥30, or about 30 lbs. overweight for 5'4" person)



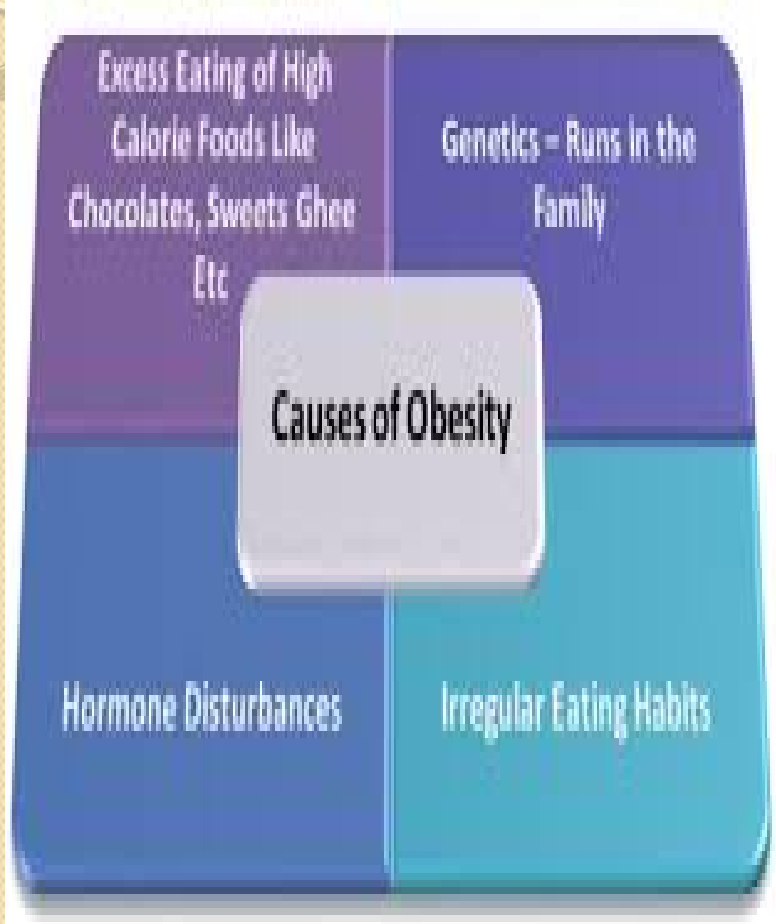
Source: Behavioral Risk Factor Surveillance System, CDC.

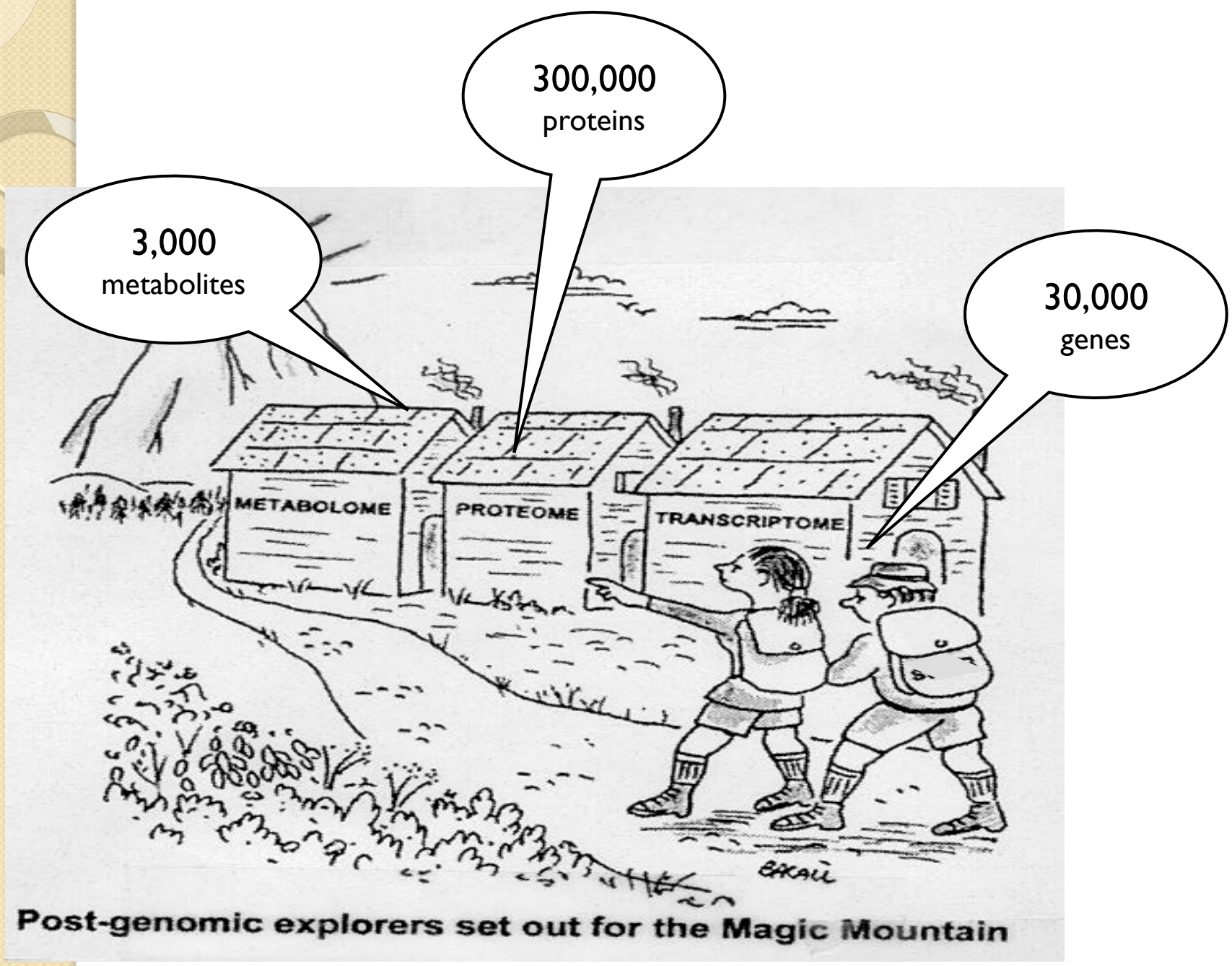
WHO was predicted that respectedly 75 and 41 percenter of the adult population will be over weight and obese by 2015



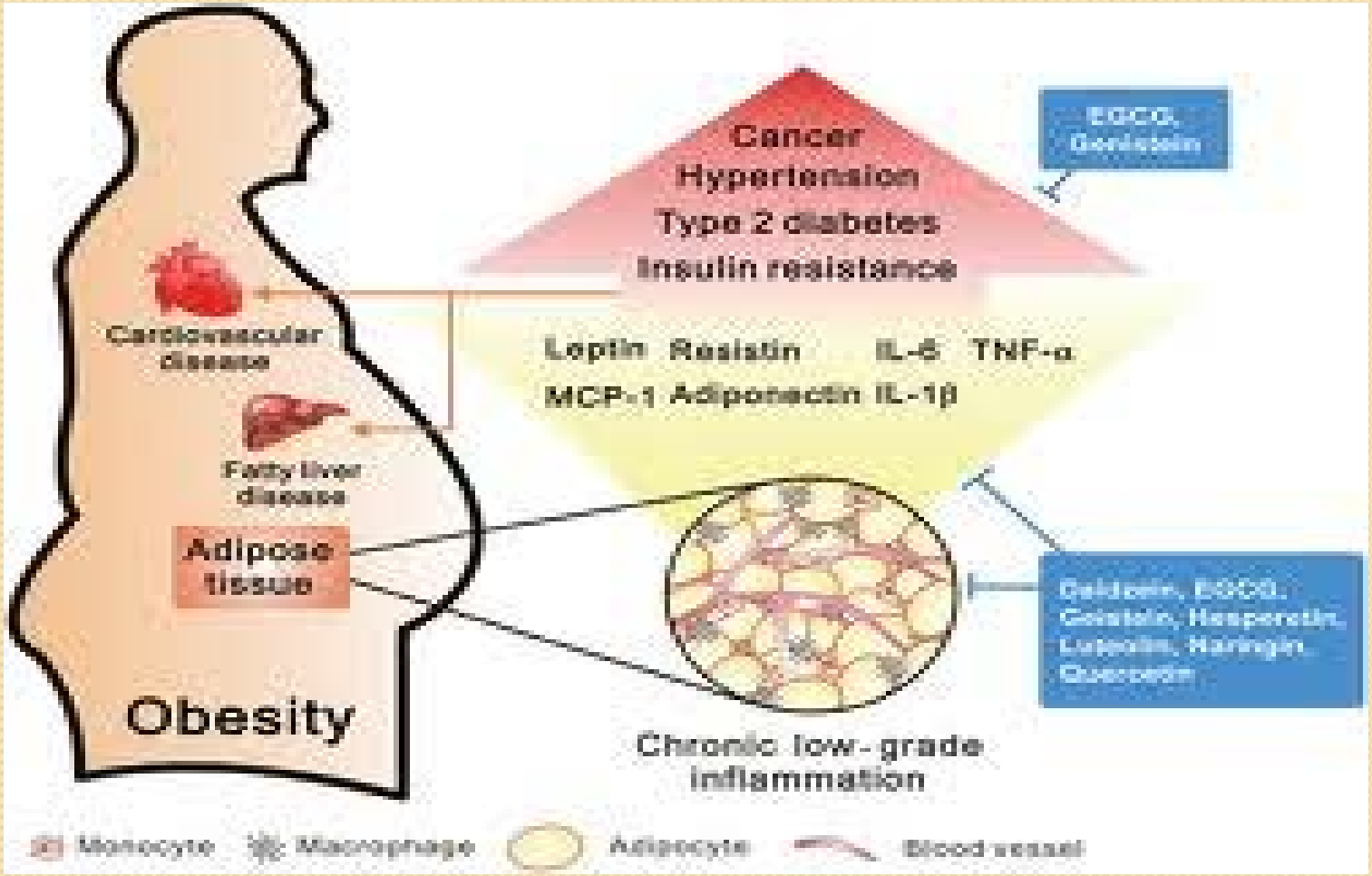
Mutch D & Clement K, Plos Genetics 2006

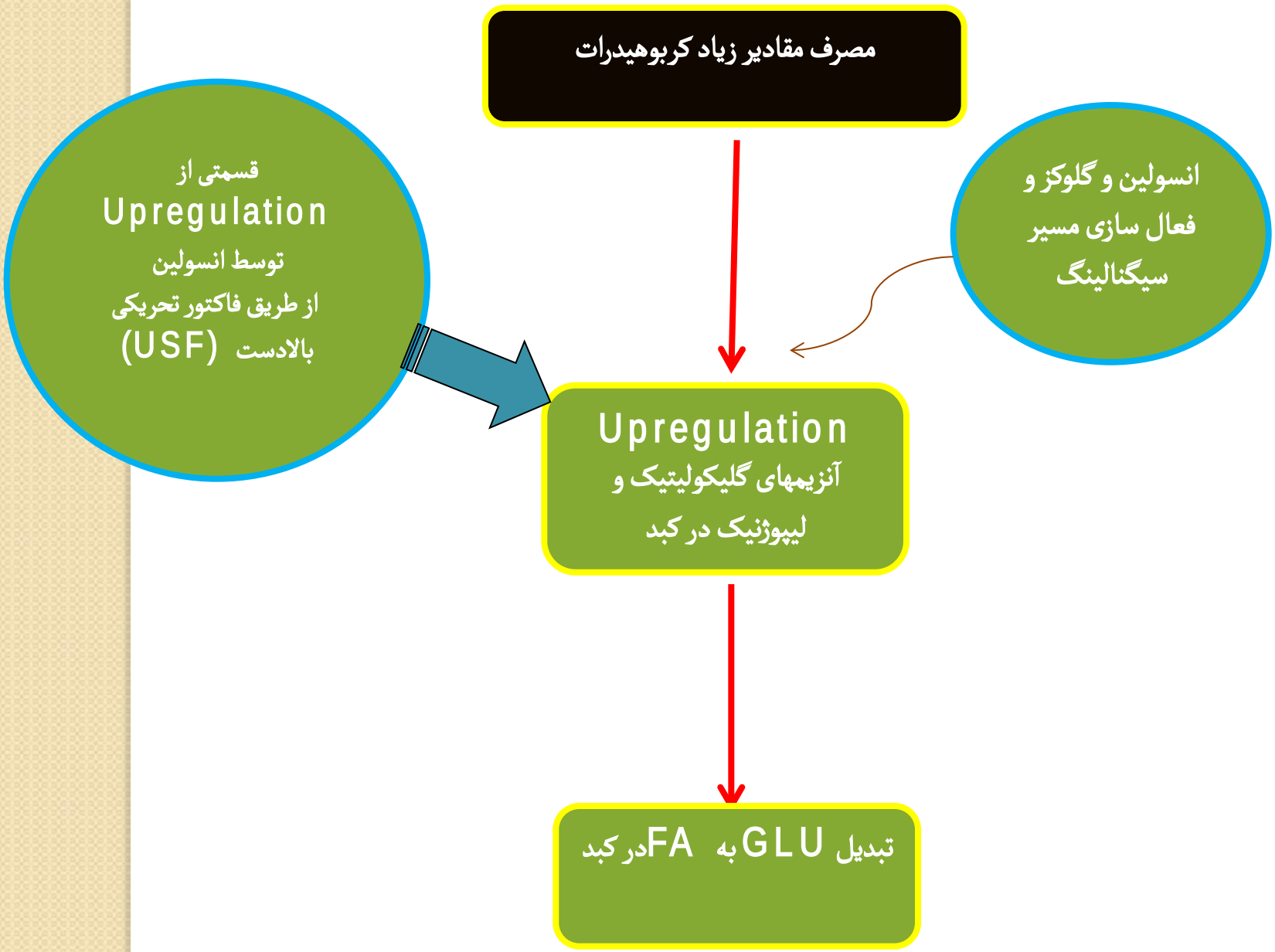
Obesity: a multifactorial disorder



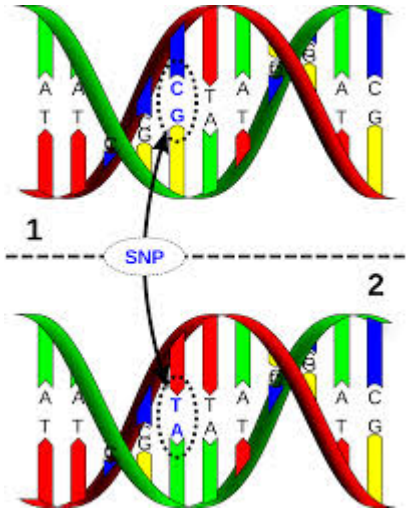

300,000
proteins
3,000
metabolites
30,000
genes
METABOLOME
PROTEOME
TRANSCRIPTOME
Post-genomic explorers set out for the Magic Mountain

Obesity, a chronic low-grade inflammatory condition is associated with the development of many comorbidities including dyslipidemia.




مصرف مقادیر زیاد کربوهیدرات
قسمتی از
Upregulation
توسط انسولین
از طریق فاکتور تحریکی
بالادست (USF)
انسولین و گلوکز و
فعال سازی مسیر
سیگنالینگ
Upregulation
آنزیمهای گلیکولیتیک و
لیپوژنیک در کبد
تبدیل GLU به FA در کبد

Associations between single nucleotide polymorphisms and phenotype



Obesity is related to gene–environment interactions

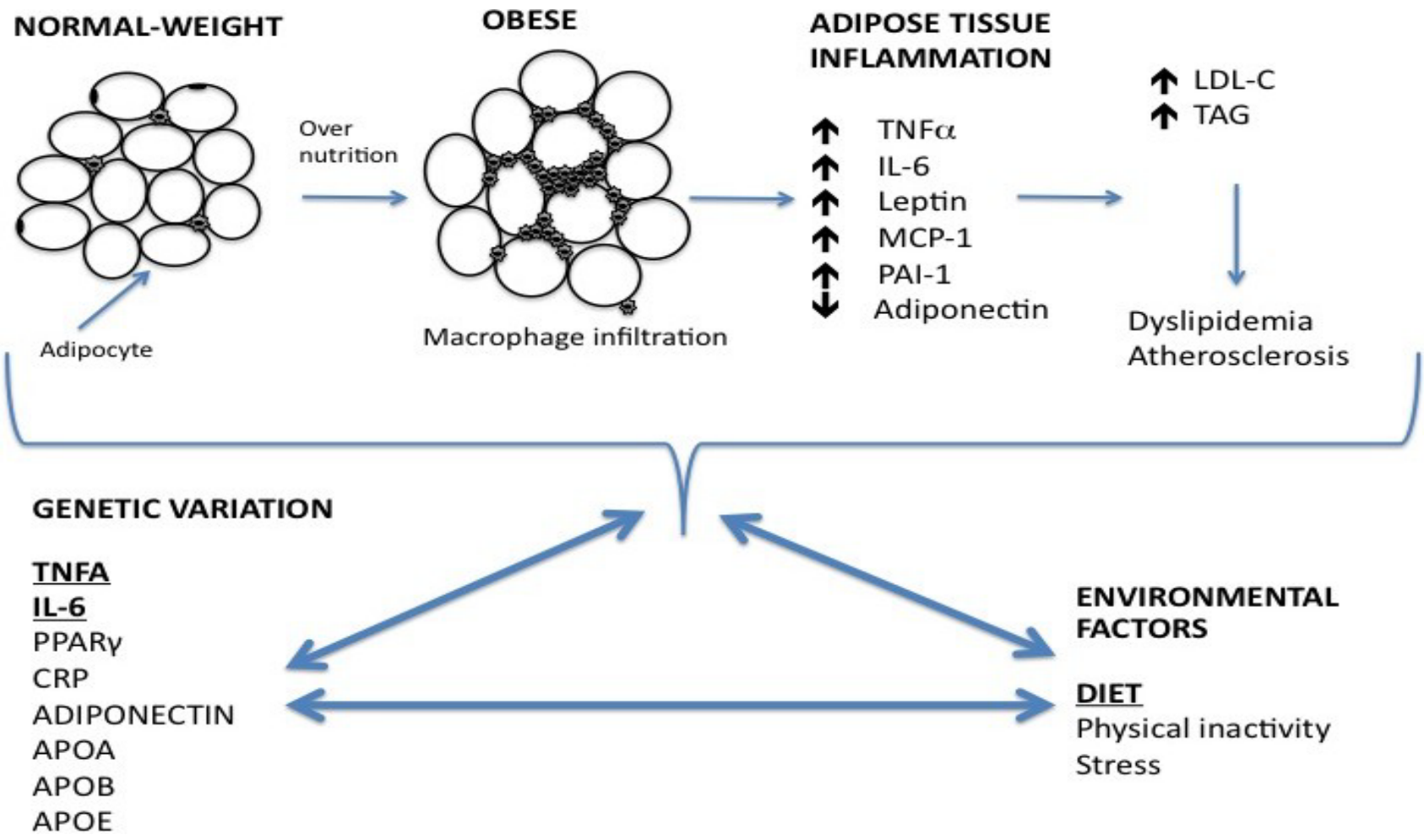
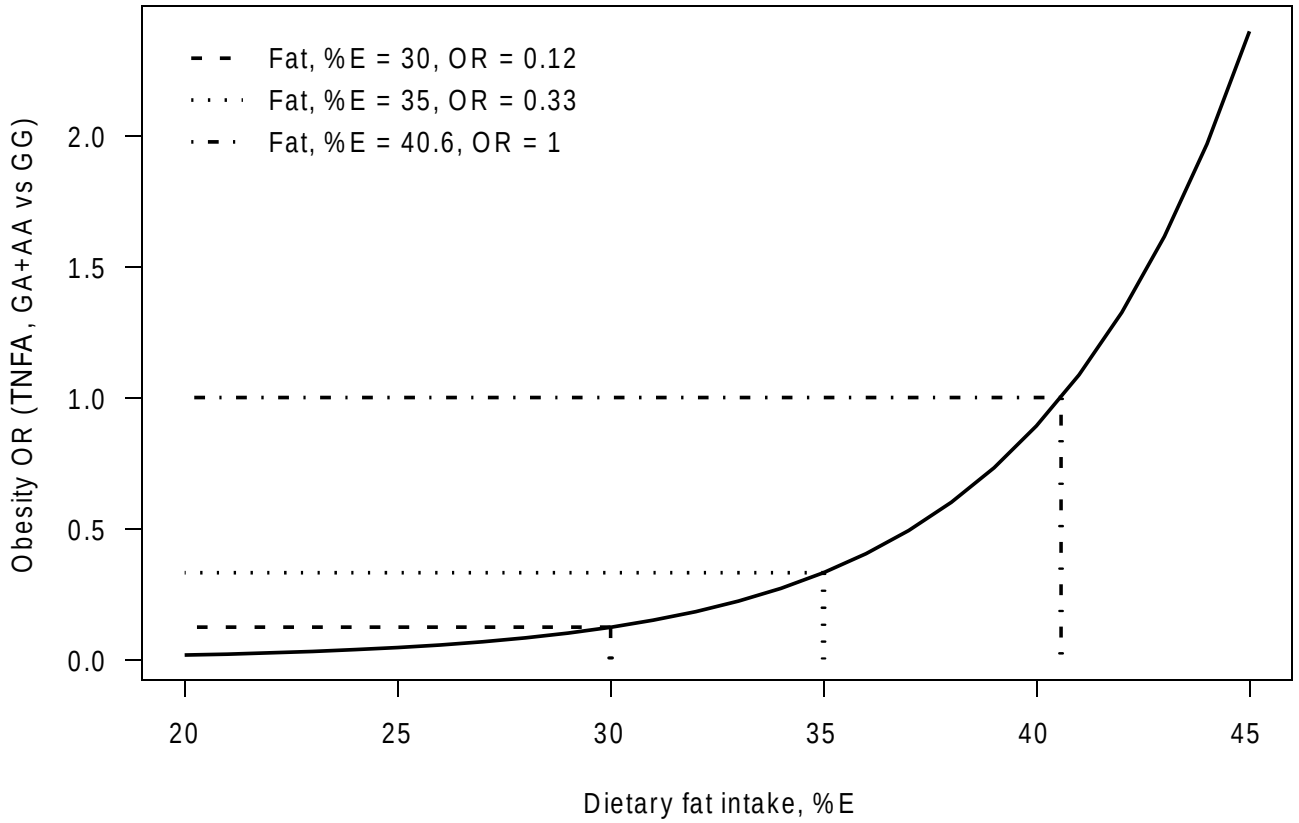


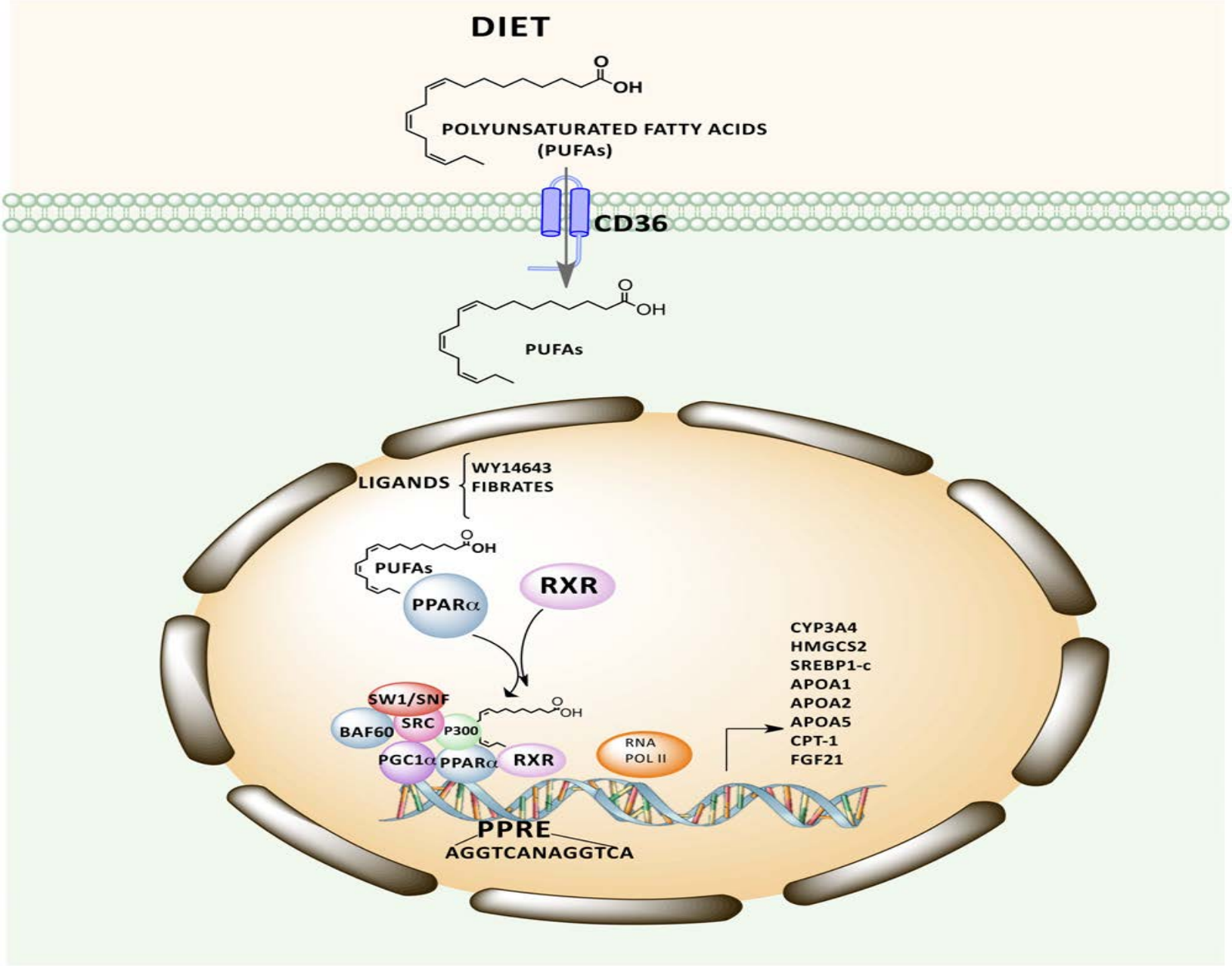
Figure 2. *The modeled relationship between the odds of being obese (odds of being obese vs. being normal weight), TNFA –308 genotype and dietary fat intake (%E) for black SA women. The curve gives the modeled obesity OR for genotype GA + AA versus genotype GG, at each fat intake (%E). Lines show the total dietary fat intake (%E) of equal odds (OR = 1, for the genotype groups), namely 40.6 (%E), the OR for fat intake = 30 (%E) namely 0.12 and the OR for fat intake = 35 (%E), namely 0.33 [3].*



Nutrients ***2013****, 5, 1672-1705;*
doi:10.3390/nu5051672

The Role of Ethnicity and Gender as Confounders

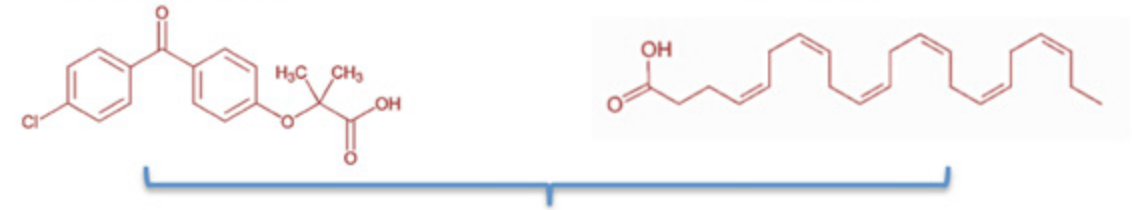
- **Prevalence of obesity-associated comorbidities differ between ethnic groups** by:
  - Genotype and allele frequencies of SNPs
  - Diet and lifestyle, (dietary intake, physical activity level)
  - Body fat distribution (VAT *vs.* SAT) , …….
  - Cultural, behavioral and socio-demographic conditions
- **Gender (sex) of study participants may impact genotype-phenotype interactions**

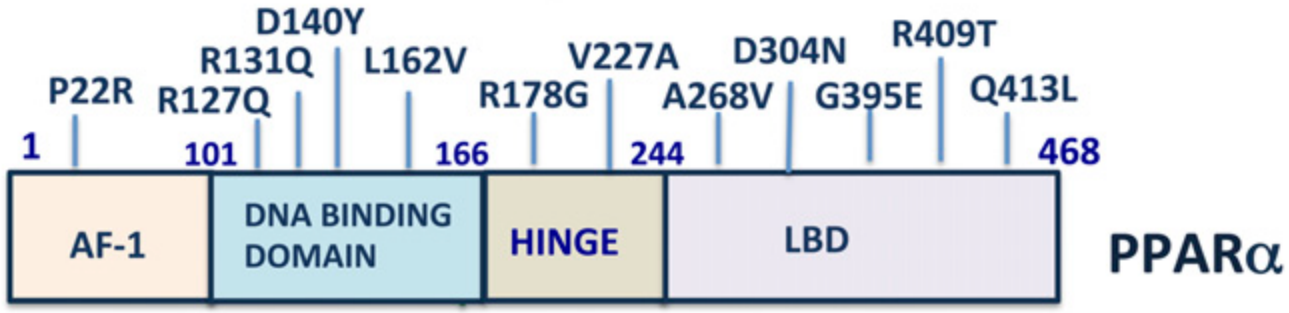


Adv. Nutr. 4: 439–452, 2013;
doi:10.3945/an.113.003798

Pharmacologica factors
(Fenofibrate)

Dietary factors
(PUFAs)



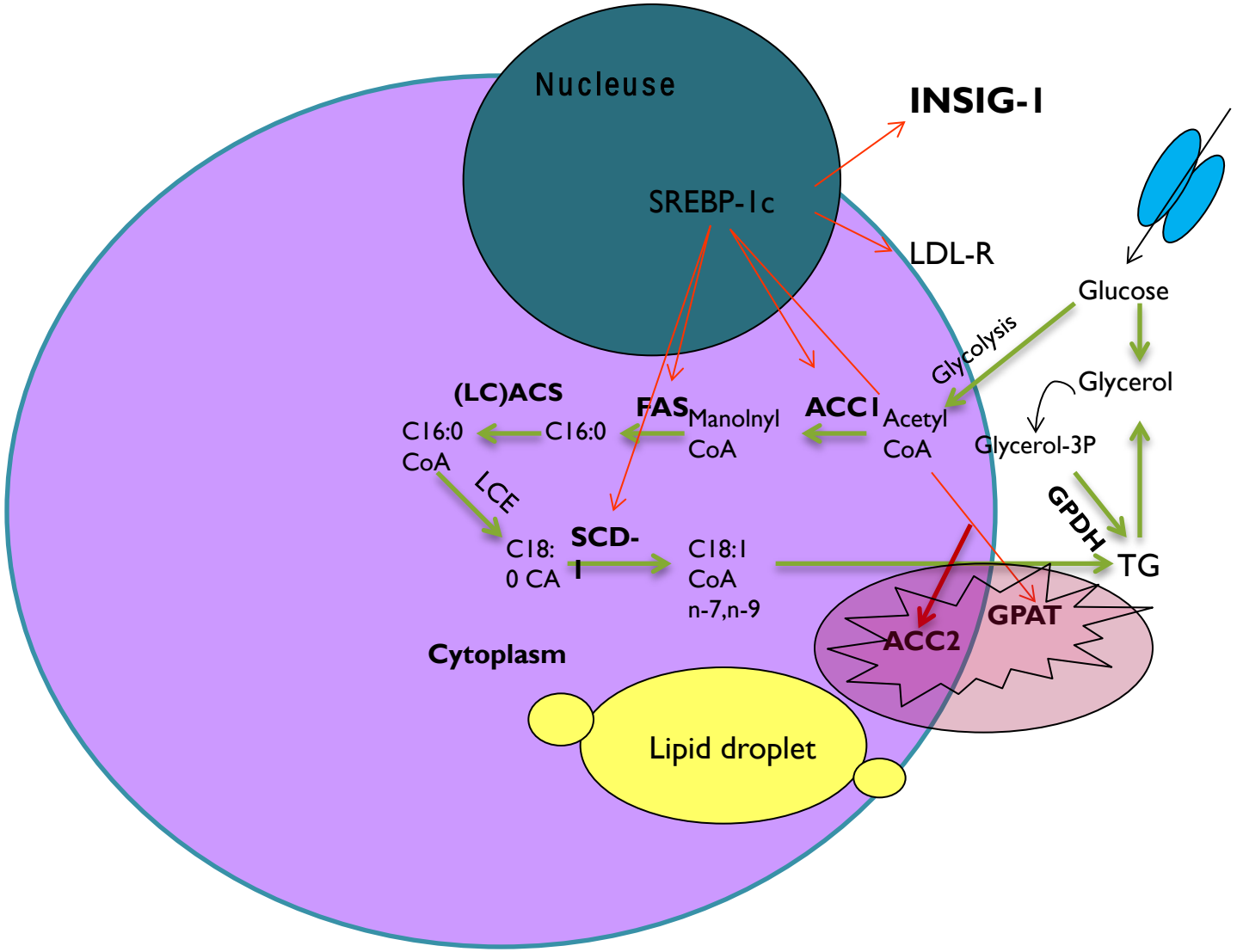


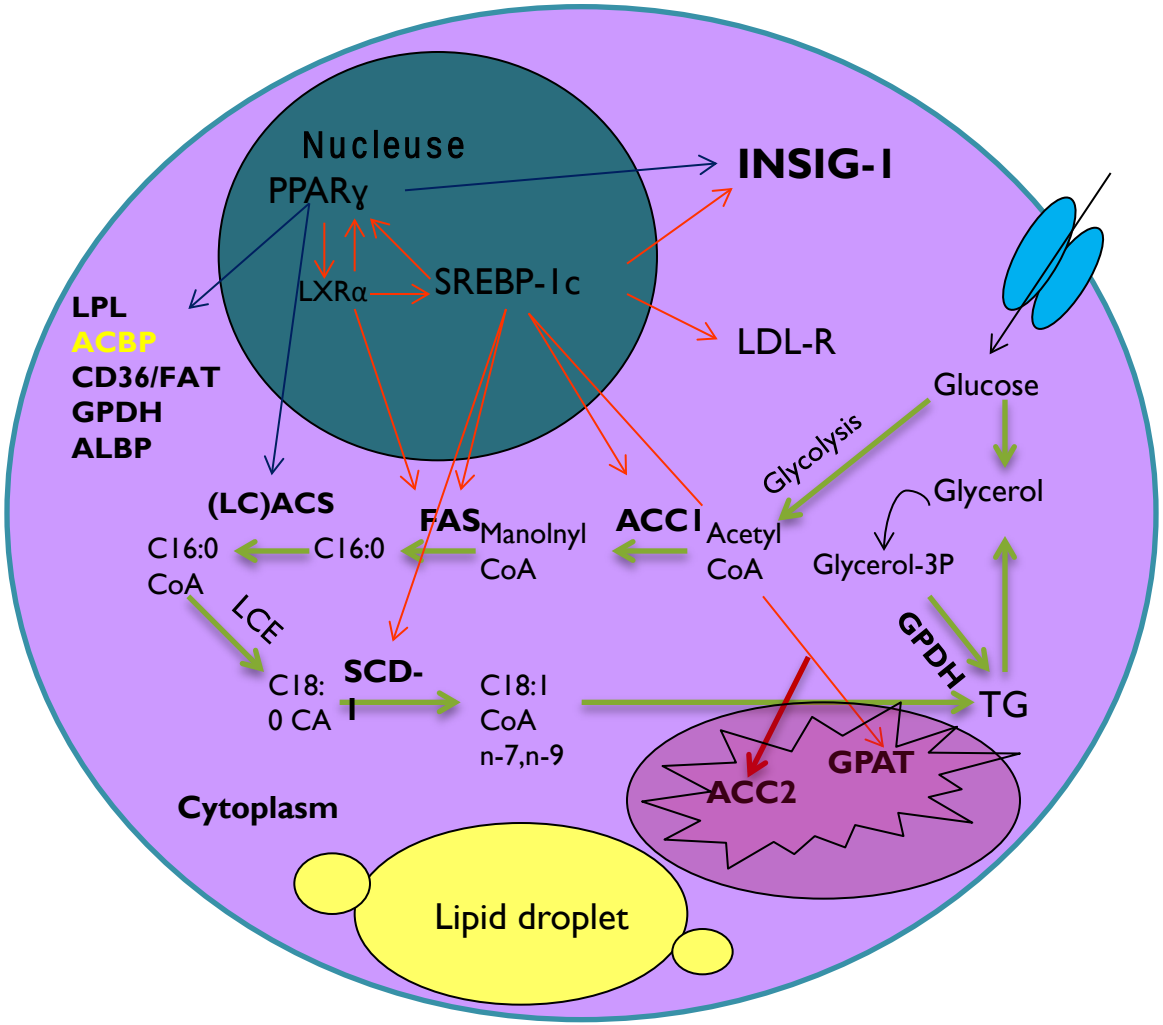
PPARα

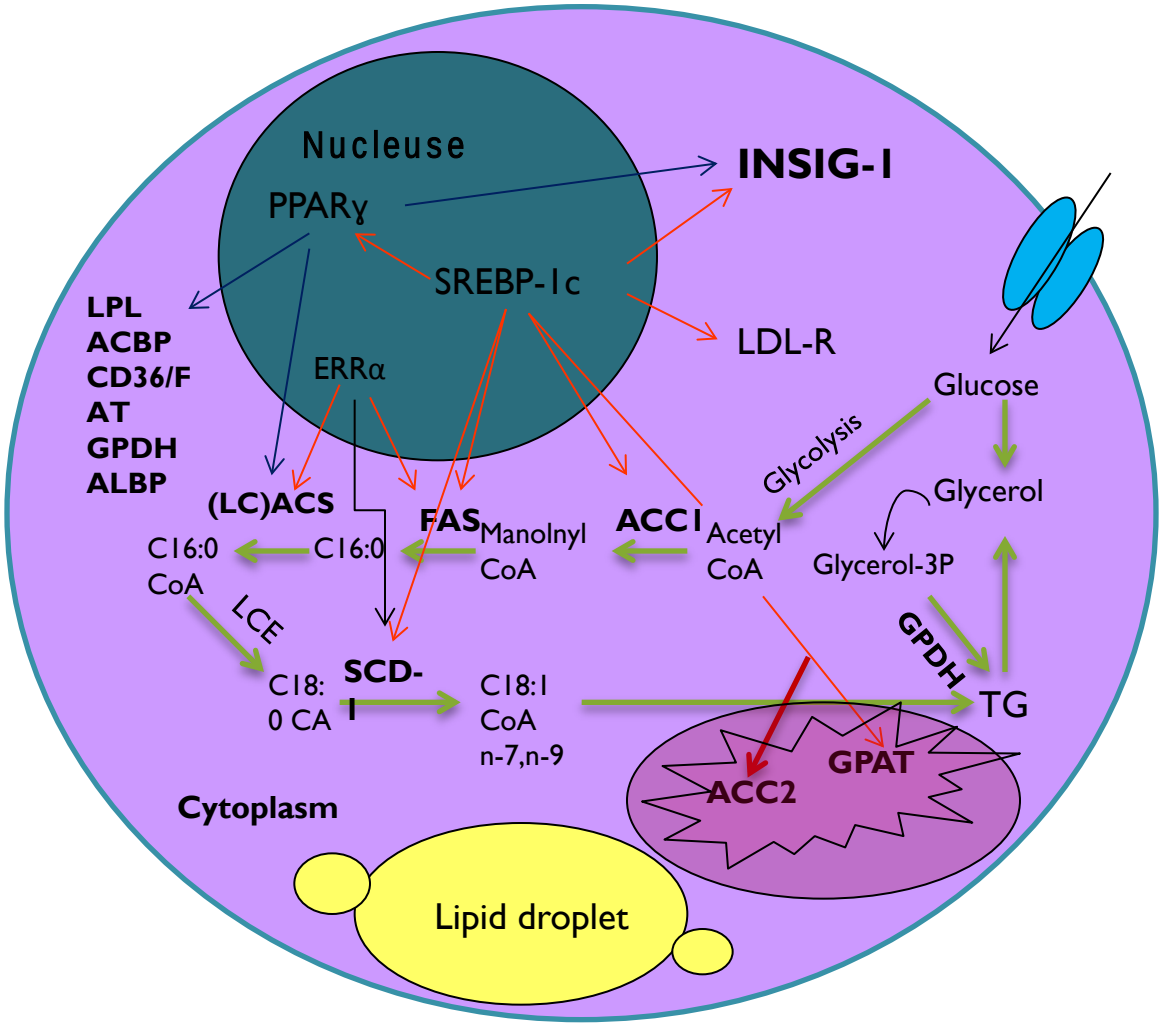
	L162V	V227A	Intron 7 G>C
Characteristics associated with the SNP	↑TG[80-82] ↑TC [69,73,79] ↑LDL-C[73,79] ↑ApoB[73,79] ↑ApoCIII[82] ↑Risk for T2D[74] ↓HDL[80]	↓TC[86] ↓TG[86]	↑ Dyslipidemia[85,94] ↑ Risk of non fatal myocardial infarction[83]
Dietary interactions with PUFAs	↓ApoA1[104] ↓TG[102] ↓ApoCIII[102]	↓HDL[88]	
Pharmacological interactions with fenofibrate			↓TG[119]

Ref: 2013 American Society for Nutrition. Adv. Nutr. 4: 439–452, 2013; doi:10.3945/an.113.003798

ژنهای لیپوژنیک به عنوان ژنهای هدف SREBP-1c در آدیپوسیت بالغ




Nucleuse
PPARγ
LXRα
SREBP-1c
INSIG-1
LDL-R
LPL
ACBP
CD36/FAT
GPDH
ALBP
Glucose
Glycolysis
Glycerol
(LC)ACS
FAS
ACC1
C16:0
CoA
C16:0
Manolnyl
CoA
Acetyl
CoA
Glycerol-3P
LCE
GPDH
C18:
0 CA
SCD-
1
C18:1
CoA
n-7,n-9
TG
GPAT
ACC2
Cytoplasm
Lipid droplet


Nucleuse
PPARγ
SREBP-1c
INSIG-1
LDL-R
ERRα
LPL
ACBP
CD36/F
AT
GPDH
ALBP
(LC)ACS
FAS
ACC1
Glucose
Glycolysis
Glycerol
Glycerol-3P
C16:0
CoA
C16:0
Manolnyl
CoA
Acetyl
CoA
LCE
SCD-
1
C18:
0 CA
C18:1
CoA
n-7,n-9
GPDH
TG
GPAT
ACC2
Cytoplasm
Lipid droplet

Conclusions

- These studies elucidate the reasons for inconsistencies of prior genetic association studies
- Support mechanistic relationships between genetic and nutritional factors,
- Provide a framework on which rational preventive nutritional strategies may eventually be based

Curr Opin Clin Nutr Metab Care. 2010 March ; 13(2): 139–144. doi:10.1097/MCO.0b013e3283357287.

Association Studies

- A widely used approach to find genes involved in "common" obesity are association studies.
- A vast number of such studies have been performed for obesity related traits (Human Obesity Gene Map; http://www.obesity.chair.ulaval.ca/genes.html).

- The coordinating scientific body of the HGP was provided by the Human Genome Organization (HUGO, www.hugointernational. org).
- Another international project aimed at better understanding disease state is the **Human Epigenome Project** (www.epigenome.org) in which genome-wide DNA methylation patterns are studied.