NUTRITIONAL GENOMICS;
NUTRIGENETICS & NUTRIGENOMICS

Presented by Samaneh Palizban
Supervised by Dr. A. Dastgheyb

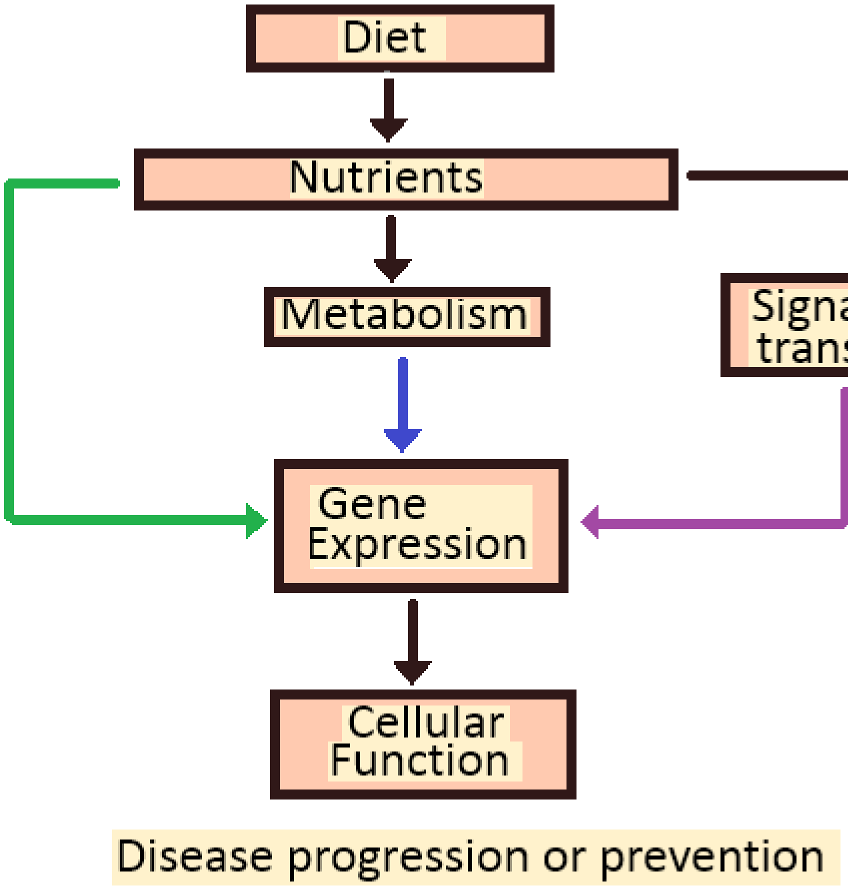
Outline:

- Our idea about the topic
  - Categorizing Foods
    - Mechanisms of interactions
      - Definition of Nutrigenomics and Nutrigenetics
        - Future prospective
- Conclusion

Nutritional Genomics:
Nutrigenetics & Nutrigenomics

Nutrient-gene interactions:

- Directly effects
- Indirectly effects



Bioactive Food Components

- Micronutrients
  - Vitamins
    - Vitamin A
    - Vitamin D
    - Vitamin E
    - Vitamin C
    - Biotin
  - Minerals
    - Calcium
    - Iron
    - Zinc
    - Selenium
- Macronutients:
  - Fats
    - Fatty acids
    - Cholestrol
  - Carbohydrates
    - Glucose
  - Proteins
    - Amino acids
- Other food components:
  - Flavonoids
  - Polyphenols
  - Xenobiotics

Minerals & Nutrigenomics

- Minerals
  - **Iron**
  - **Calcium**
  - **Zinc**
  - **Iodine**
  - **Selenium**
  - **Magnesium**
  - **Potassium**

- Participating in proteins and enzyme structures
- Cofactor functioning
- Interacting with transcription factors → altering gene expression
- As a signal in a cellular pathway

Iron

- Nutritional sources
- Related Disease
- Participating in biomolecules

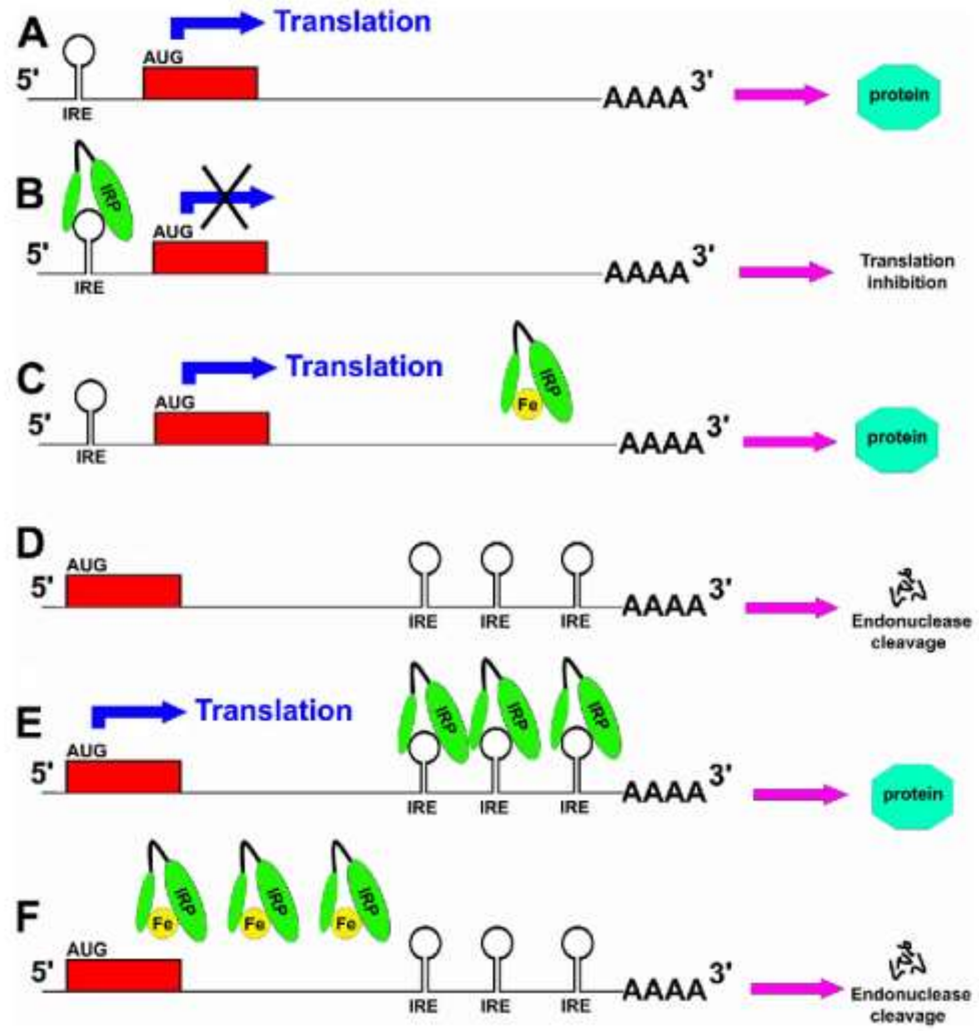
Iron interacting with genome

- IRE–IRP regulatory system:
  - IRP1 , IRP2

- BMP/SMAD pathway signaling :
  - SMAD1/5/8
  - STAT3

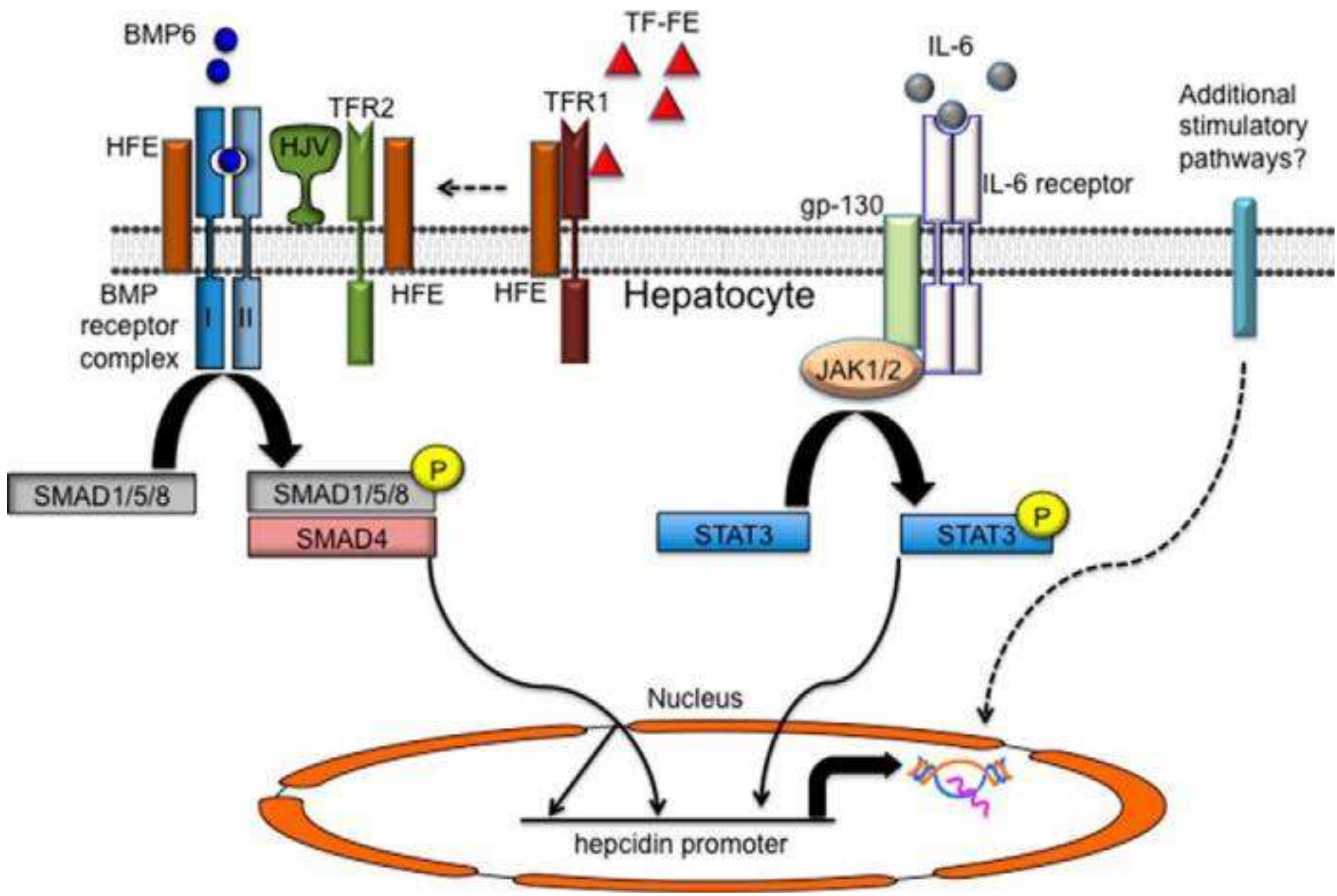
IRE–IRP regulatory system ;
An example of direct effect on gene expression

- Iron Response Proteins:
  - Transcription factors
  - controllers of vertebrate iron metabolism
  - major iron homeostasis genes



Regulation of Iron Metabolism by Hepcidin
An example of indirect effect through signal transduction

- TF-FE & TFR1
- BMP/SMAD pathway:
  - SMAD1/5/8
  - STAT3
- regulating body iron homeostasis

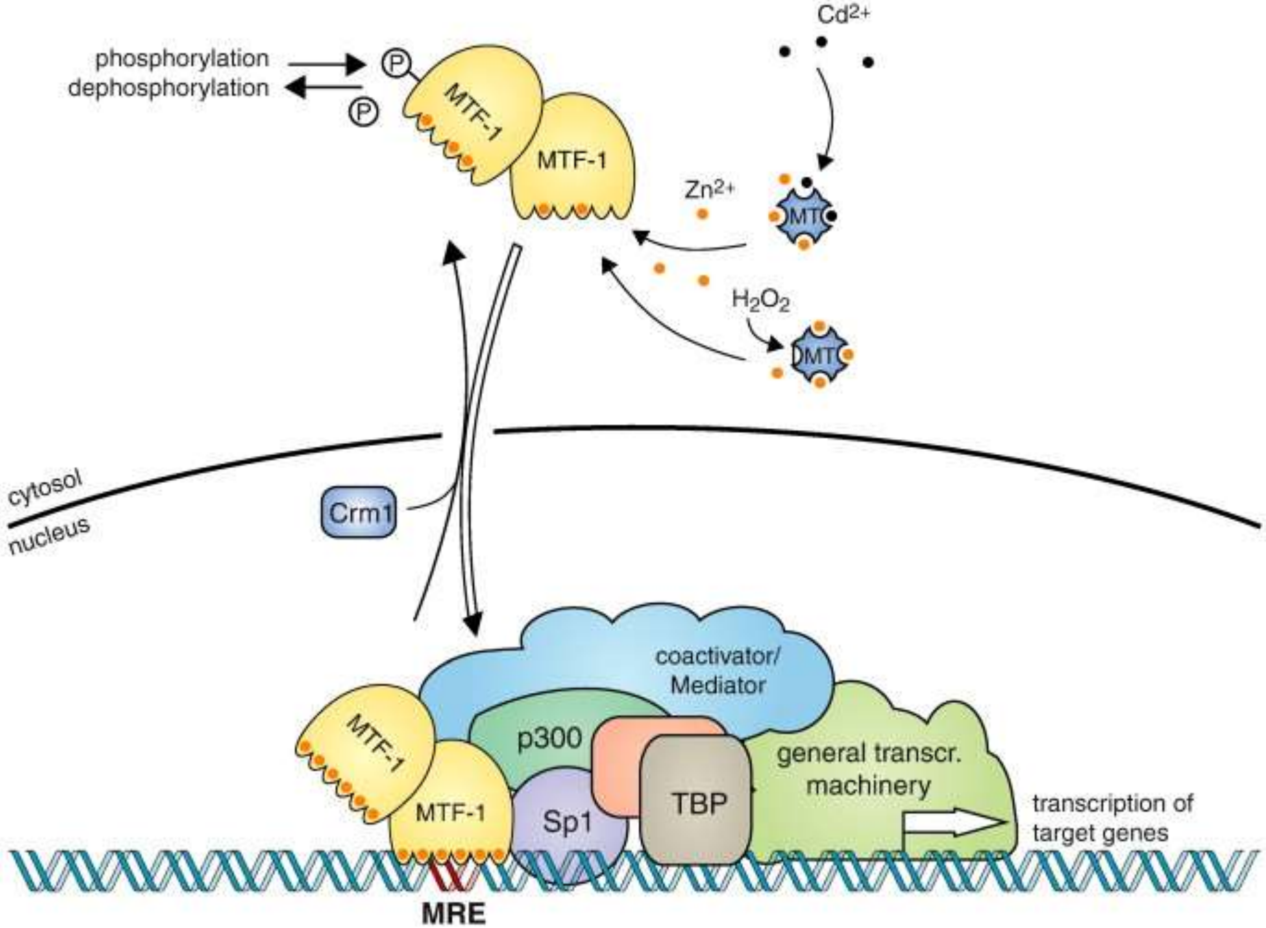


Zinc

- Nutritional sources
- Related function in our body
- cofactor function

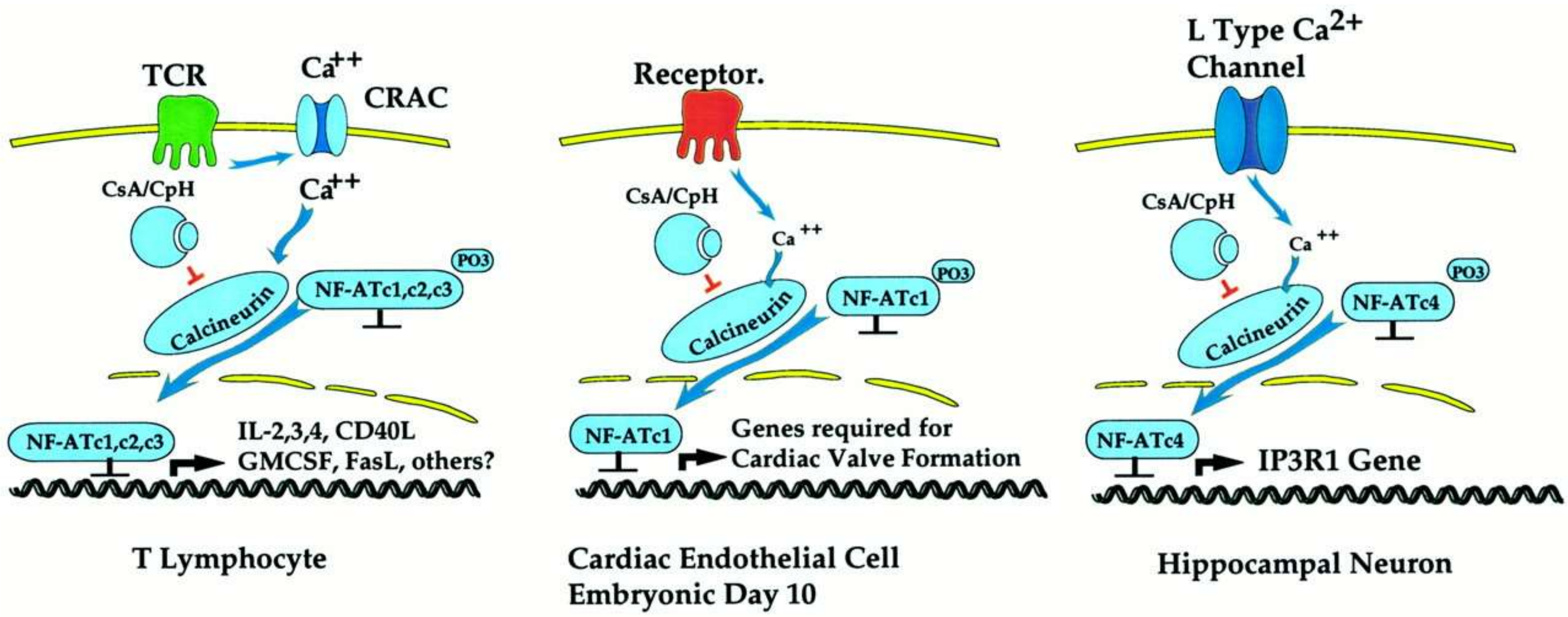
Zinc & gene expression

- metal-responsive transcription factor 1 (MTF1)

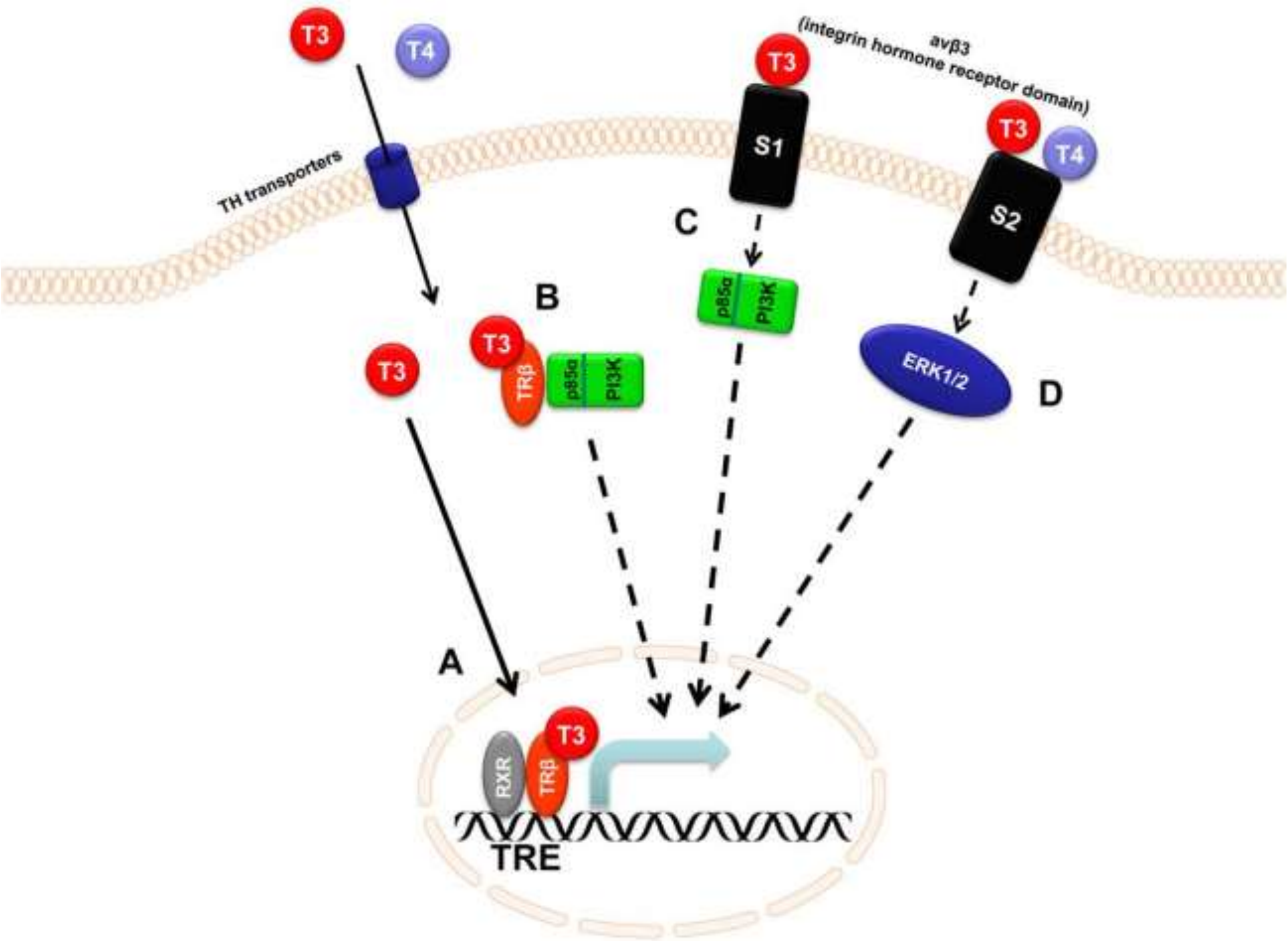


Calcium

- Transcription factors
  - calcineurin
  - NF-AT



Iodine


T3
T4
TH transporters
A
T3
RXR
TRβ
TRE
B
T3
TRβ
p85α
PI3K
C
T3
S1
p85α
PI3K
αvβ3
(integrin hormone receptor domain)
T3
T4
S2
ERK1/2
D

End of Part 1

Any Question Please?!

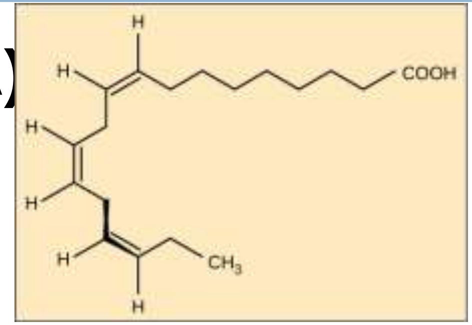
First Section

Part 2:

Fatty Acids category
Fat soluble vitamins category

Omega-3

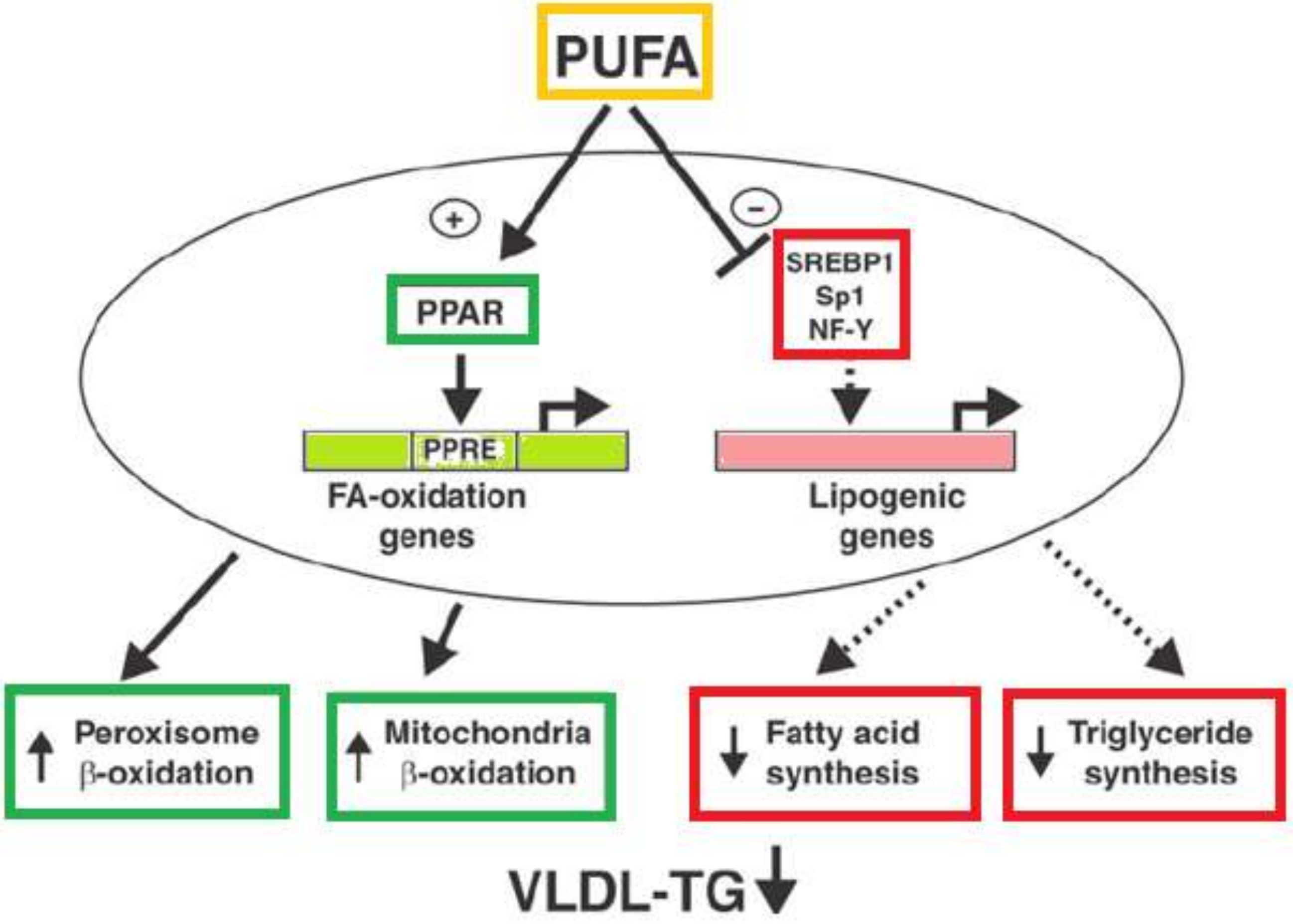
- **A polyunsaturated fatty acids (PUFA)**



- Neuroprotective (Alzheimer's disease)
- cardiovascular heart disease
- immune function
- bone health
- muscle tonus
- Cancer
- general quality of life in aging

PUFA and modifying gene expression

- PPARs, SREBPs, LXR, HNF4, ChREBP



Carotenoids

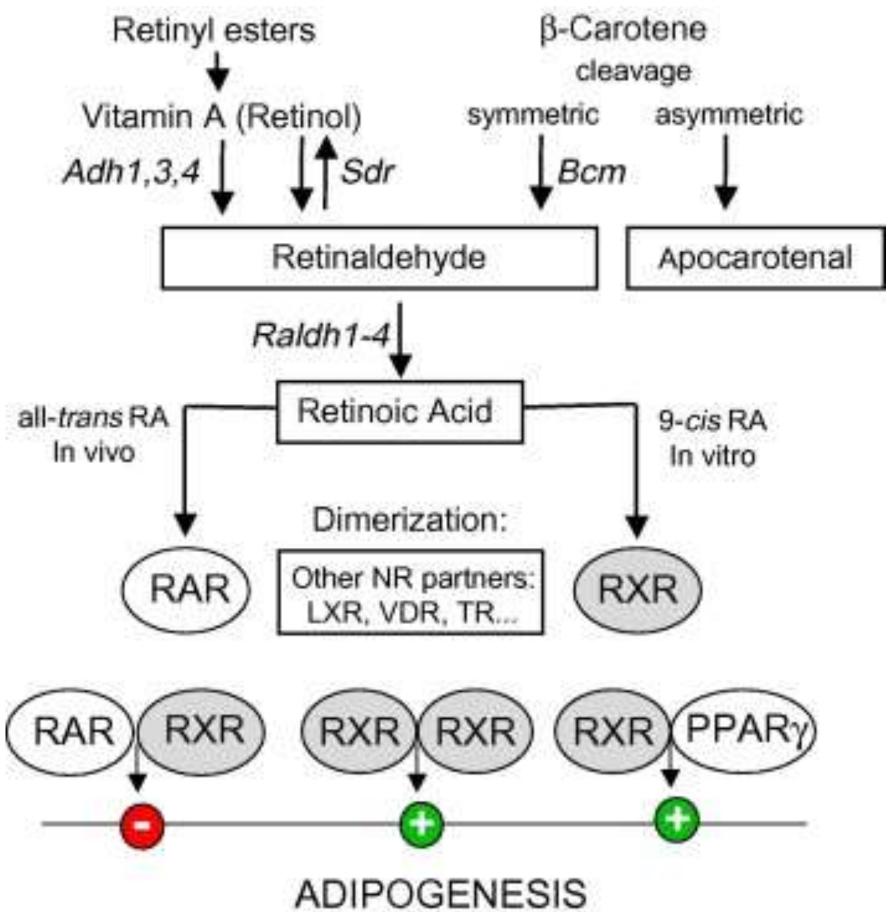
- **Carotenoids (**most notably beta-carotene**)**
  - no role in the formation of vitamin A

  antioxidants and anti-inflammatory agents
  - provitamin A , **Vitamin A** group (retinol, retinal, retinoic acid)

- promoting good vision (the retina of the eye), early atherosclerosis, cardiovascular disease ,skin aging and cancer development, immune system

Vitamin A and Gene Expression

- a ligand for nuclear receptors (RAR, RXR)
- Esp. in the retinoic acid form

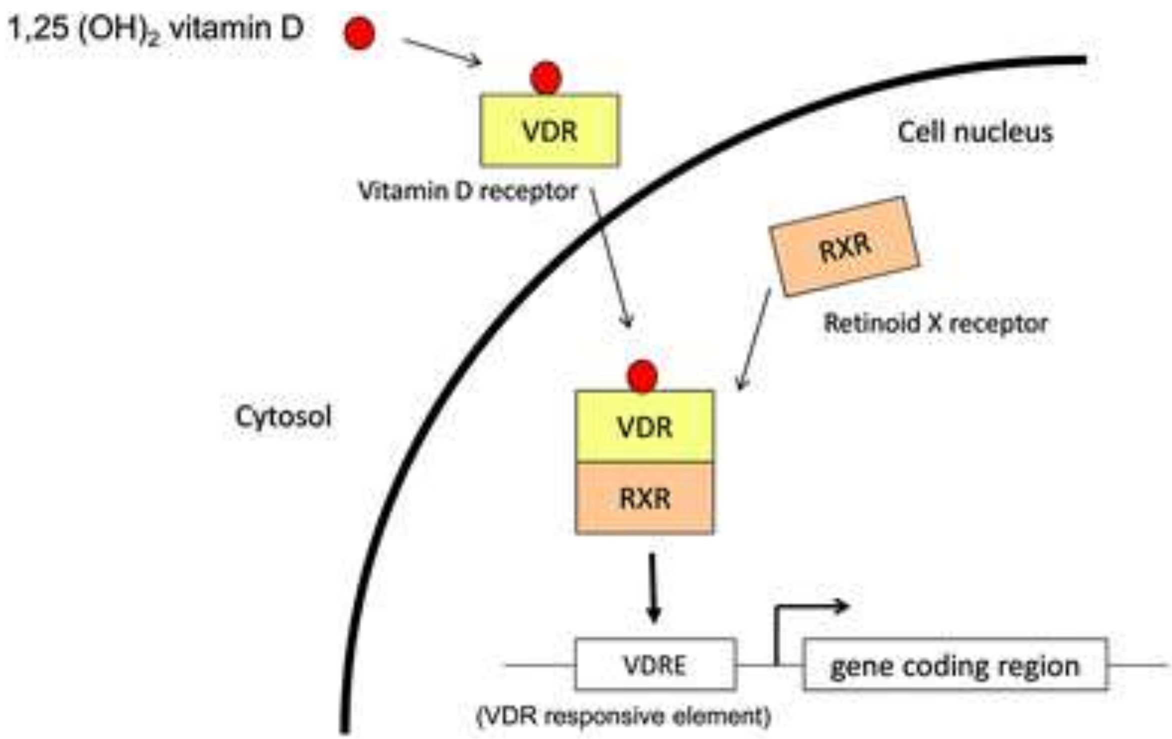


Vitamin D

- Regulating genes in:
  - promoting intestinal calcium and phosphate absorption
  - bone remodeling
  - neuroprotective actions as Serotonin Production
  - controlling cell growth and differentiation in a variety of tissues

1,25D/VDR signaling

- 1,25-Dihydroxyvitamin D_3 (1,25D)
  - The endocrine metabolite of vitamin D
  - Vitamin D receptor (VDR)



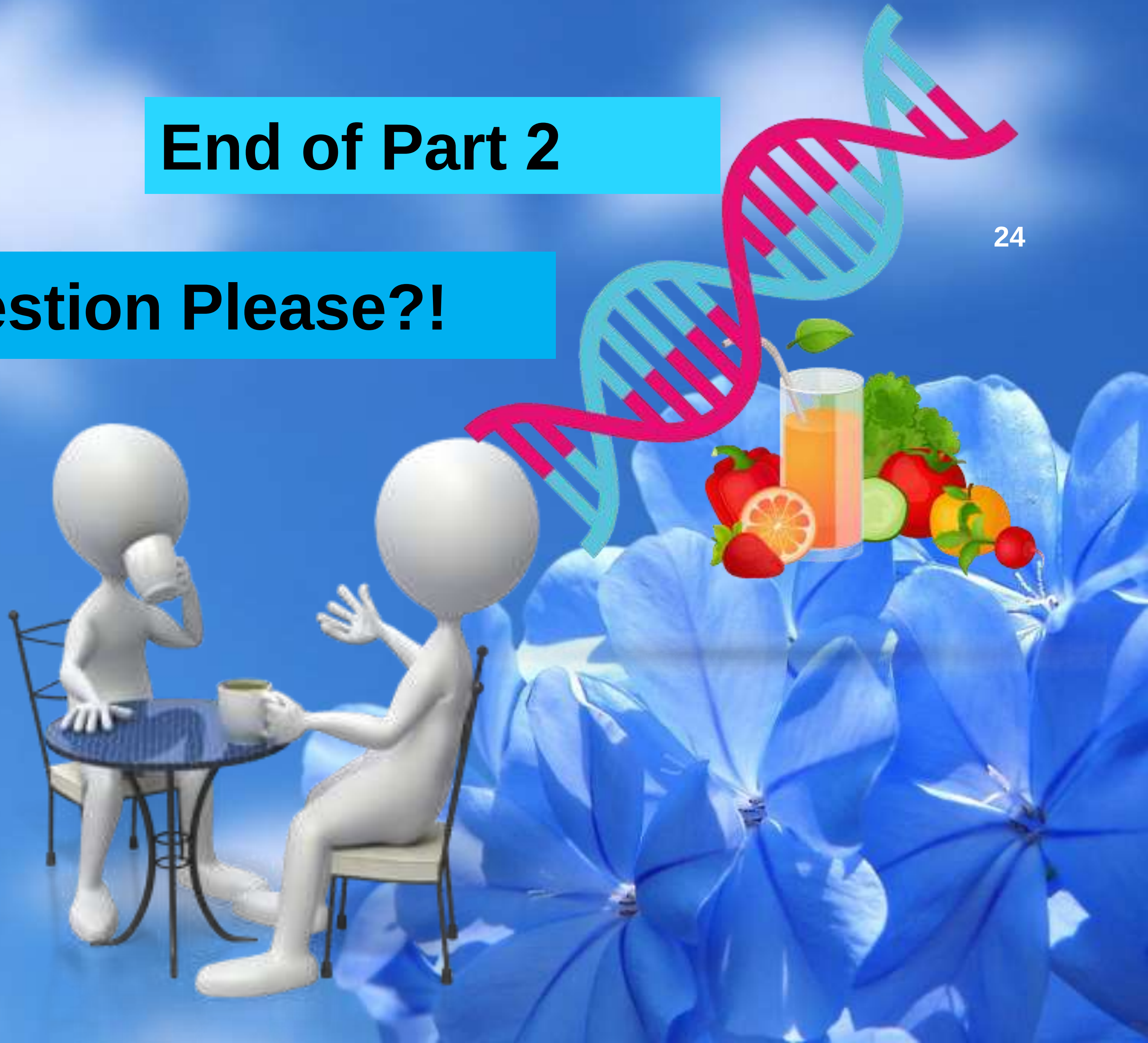
Vitamin E

- vitamin E family (α, β, γ, δ) tocopherols and the corresponding tocotrienols
- Inflammatory/Immune Response

- pregnane X receptor (PXR), a nuclear receptor regulating a variety of drug metabolizing enzymes

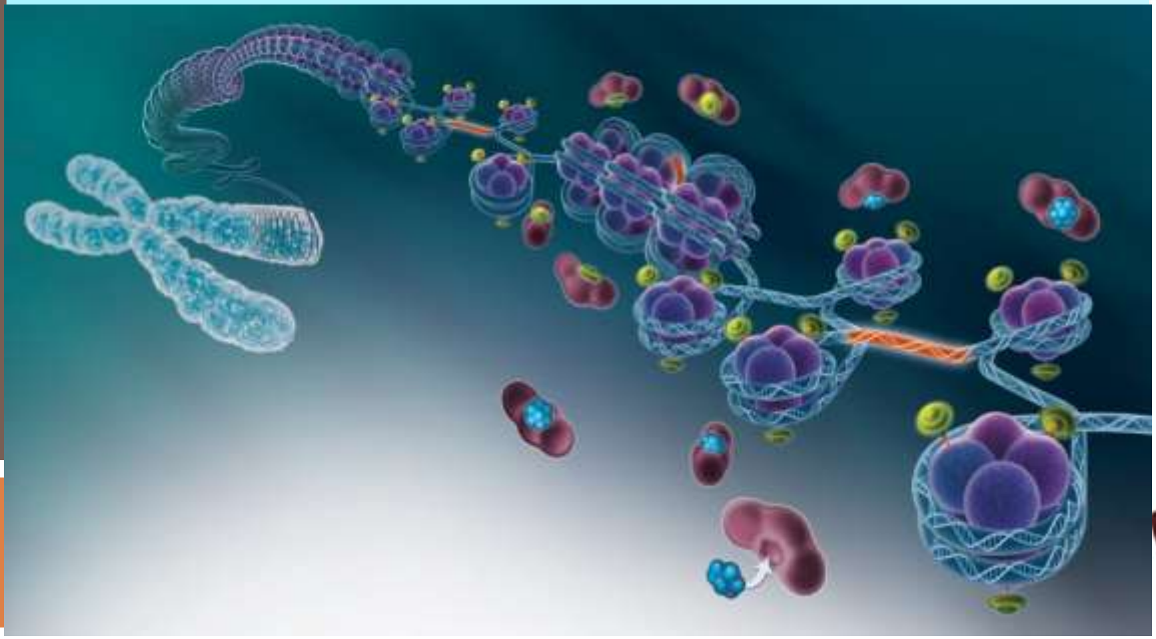
End of Part 2

Any Question Please?!



First Section

Part 3:
Affecting Epigenetic patterns as a way of nutrient gene interaction



Polyphenols

- **Flavonoids**
  - **Resveratrol (3,5,4’-trihydroxy-trans-stilbene)**
  - **Phytoalexins**
  - **Tea catechins/epicatechins**
    - epicatechin (EC),
    - epicatechin-3-gallate (ECG),
    - epigallocatechin (EGC),
    - epigallocatechin-3-gallate (EGC

  - **Genistein**
- Phenolic Acids
- Lignans
- Stilbenes

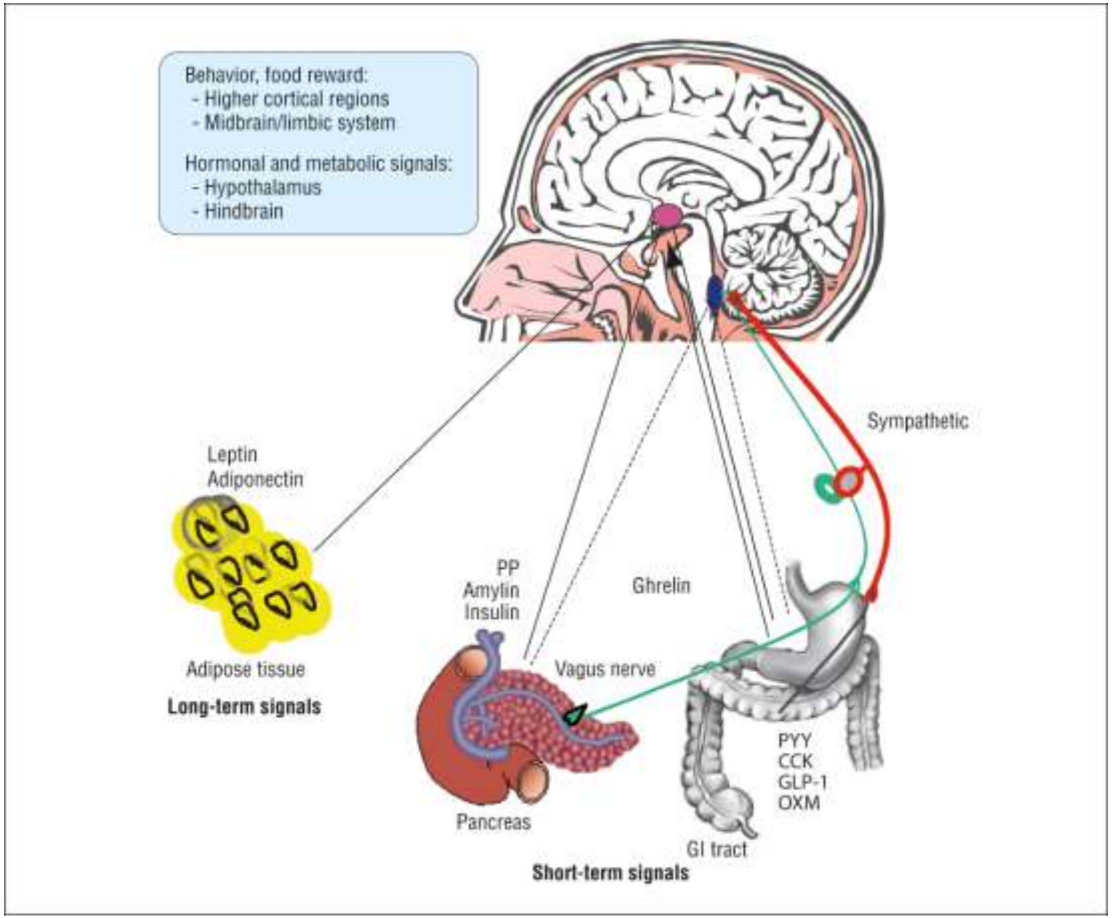
Flavonoids & interaction with genome

- acting via:
  - Alter concentrations of reactive oxygen species
  - The klotho gene, transcription factors
  - Effect on intercellular signaling molecules including nitrous oxide and pro-inflammatory cytokines
  - **Epigenetic mechanisms**
- Studied on:
  - Aging process
  - Cancer
  - Cardiovascular disease

Epigenetic Changes and Diet

Body Response to Nutritional State of Diet

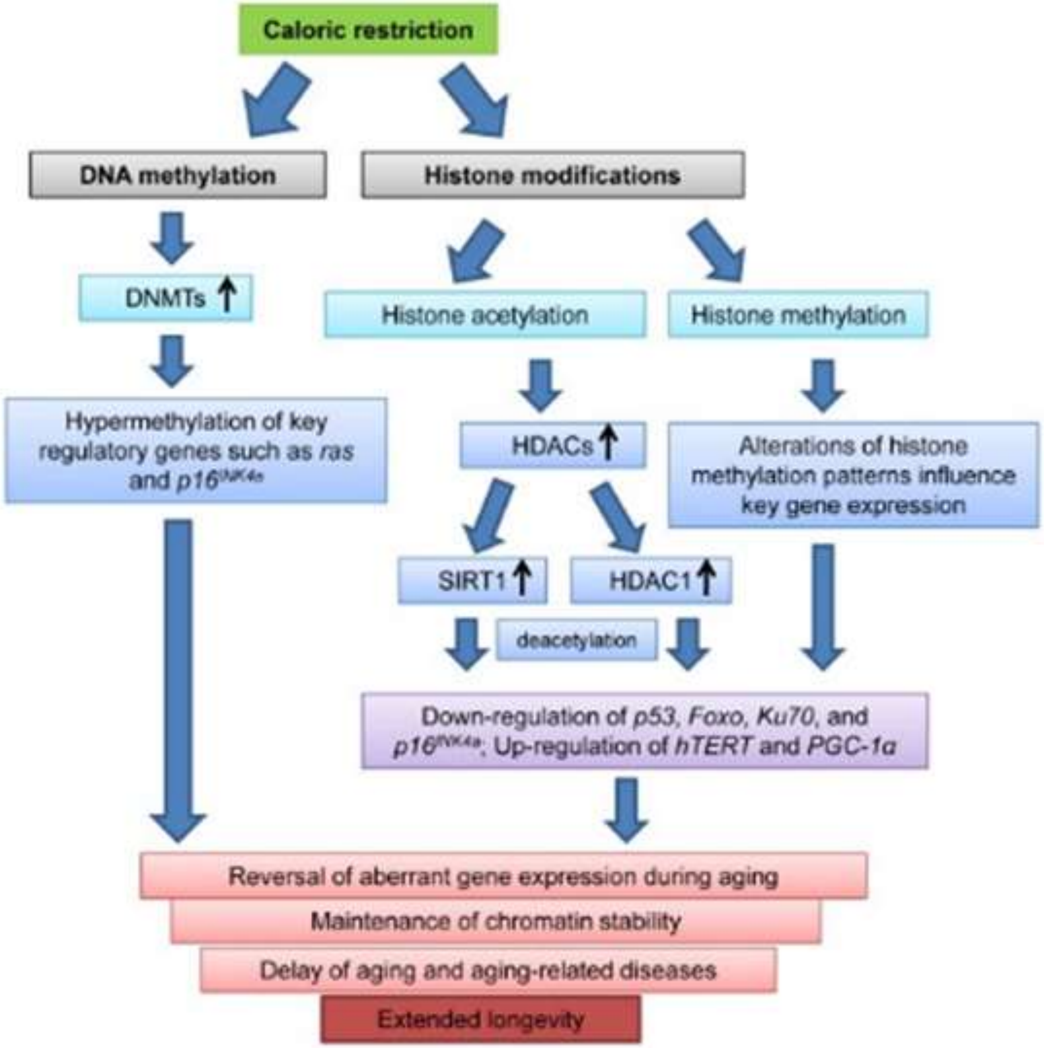
- Nutritional changes → a complex signaling
  - Obesity → resistance to the anorexigenic signals



Calorie Restriction in Humans

Caloric restriction → Altering epigenetic processes via:

- DNA methylation
- Histone modification



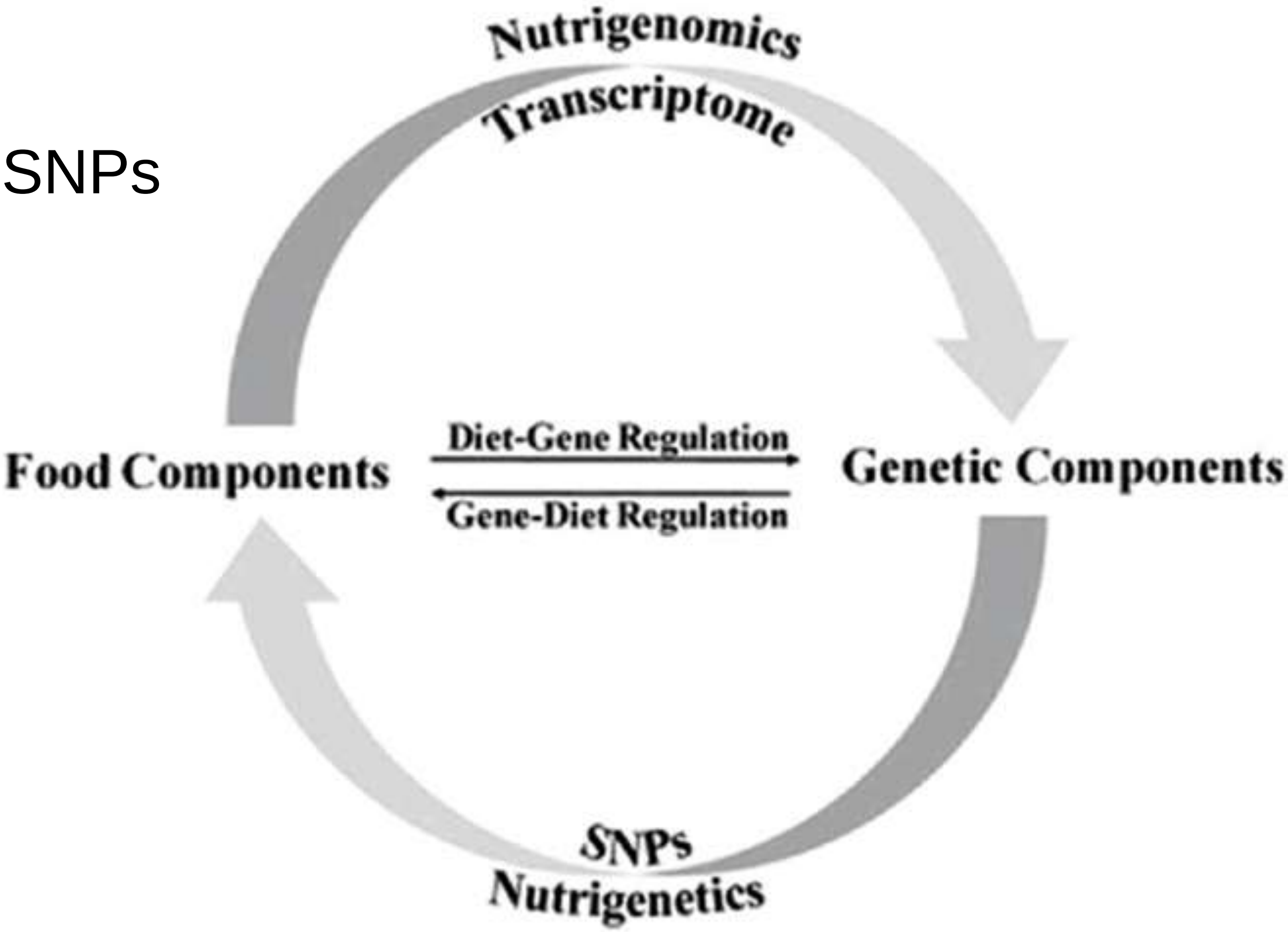
Conclusion of First Section ?!

31

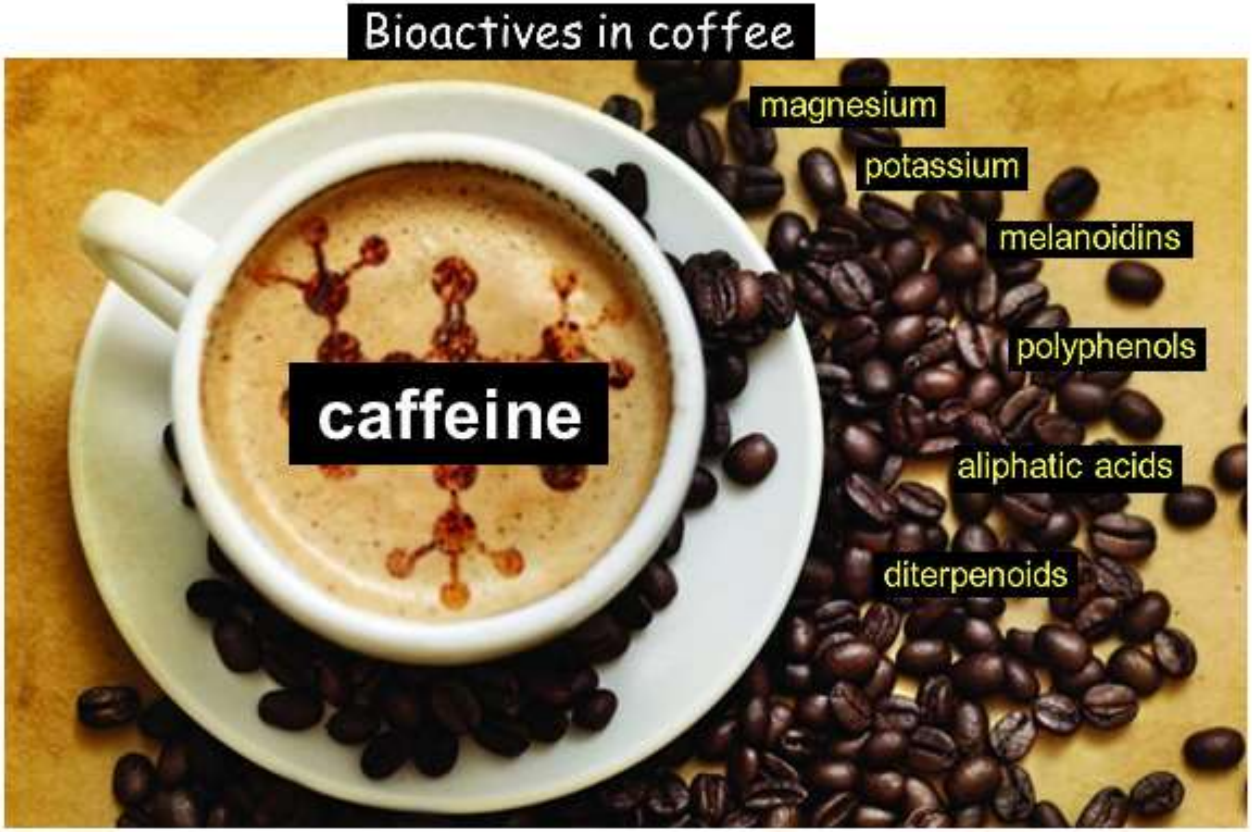
Section 2:
Nutrigenetics

Nutrigenetics

- Definition
- Variations and SNPs

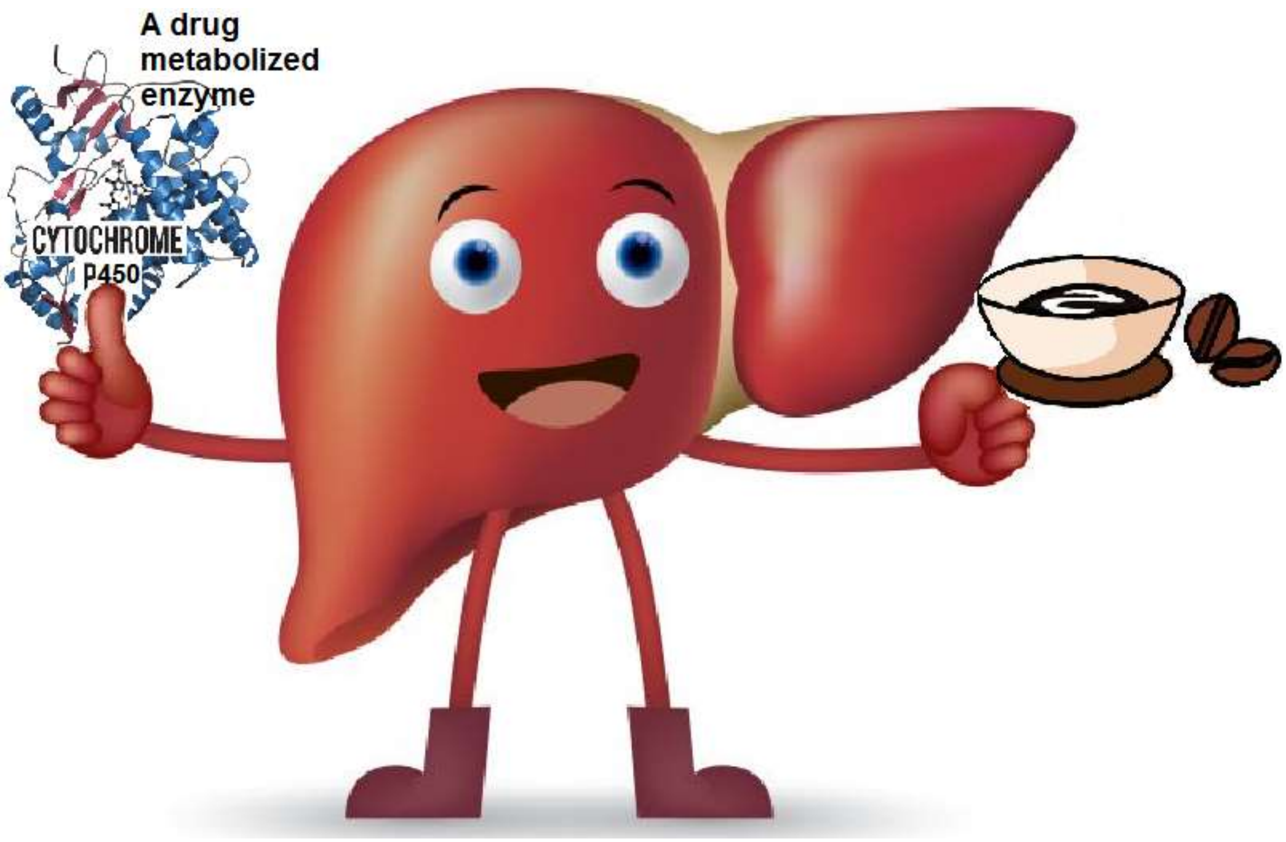


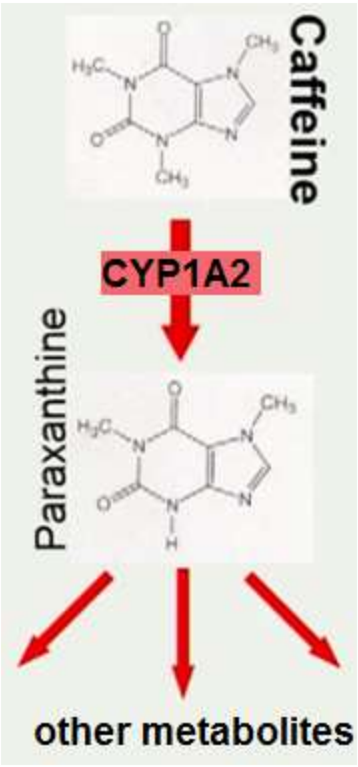
Coffee Story



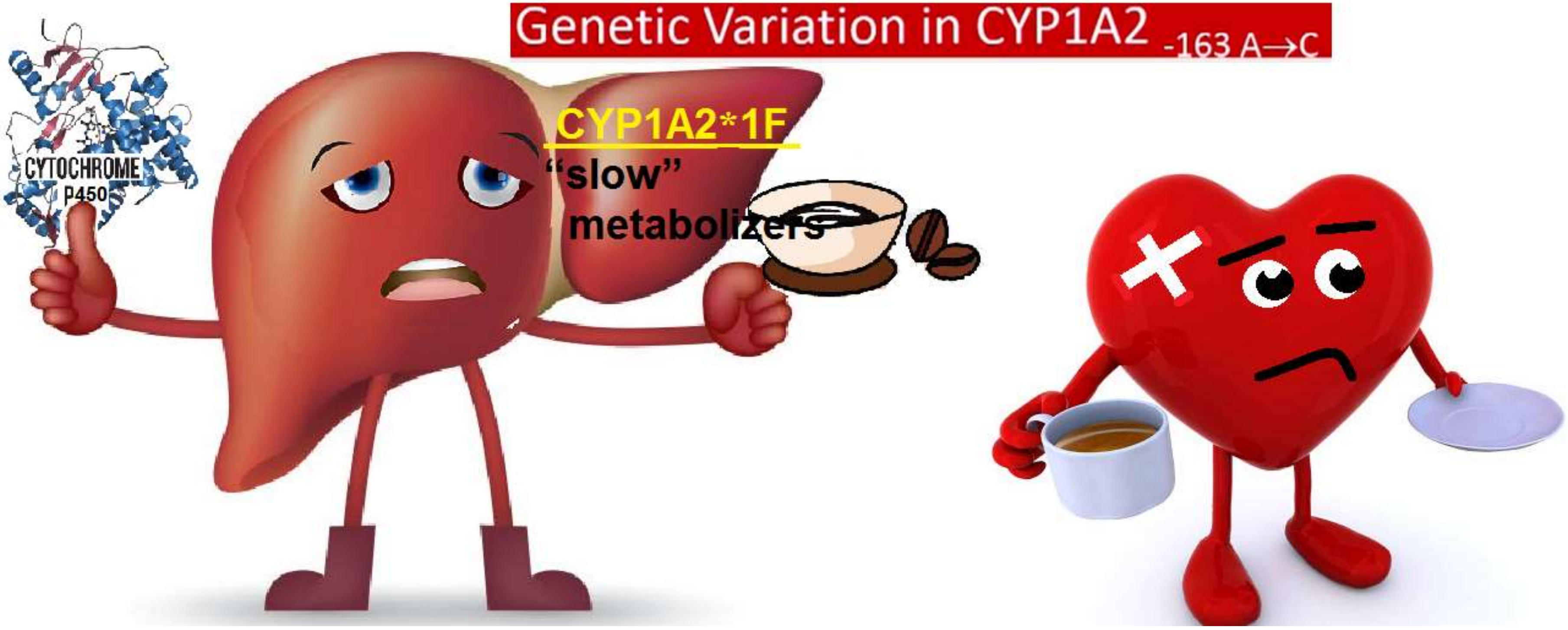
Metabolizing the Caffeine

- polymorphic cytochrome P450 1A2 enzyme (CYP1A2)





Polymorphism of CYP1A2



Polymorphism of CYP1A2 Cont'd.

JAMA. 2006 Mar 8;295(10):1135-41.

Coffee, CYP1A2 genotype, and risk of myocardial infarction.

Cornelis MC[1], El-Sohemy A, Kabagambe EK, Campos H.

Author information

Cancer Epidemiol Biomarkers Prev. 2007 May;16(5):912-6.

The CYP1A2 genotype modifies the association between coffee consumption and breast cancer risk among BRCA1 mutation carriers.

Kotsopoulos J[1], Ghadirian P, El-Sohemy A, Lynch HT, Snyder C, Daly M, Domchek S, Randall S, Karlan B, Zhang P, Zhang S, Sun P, Narod SA.

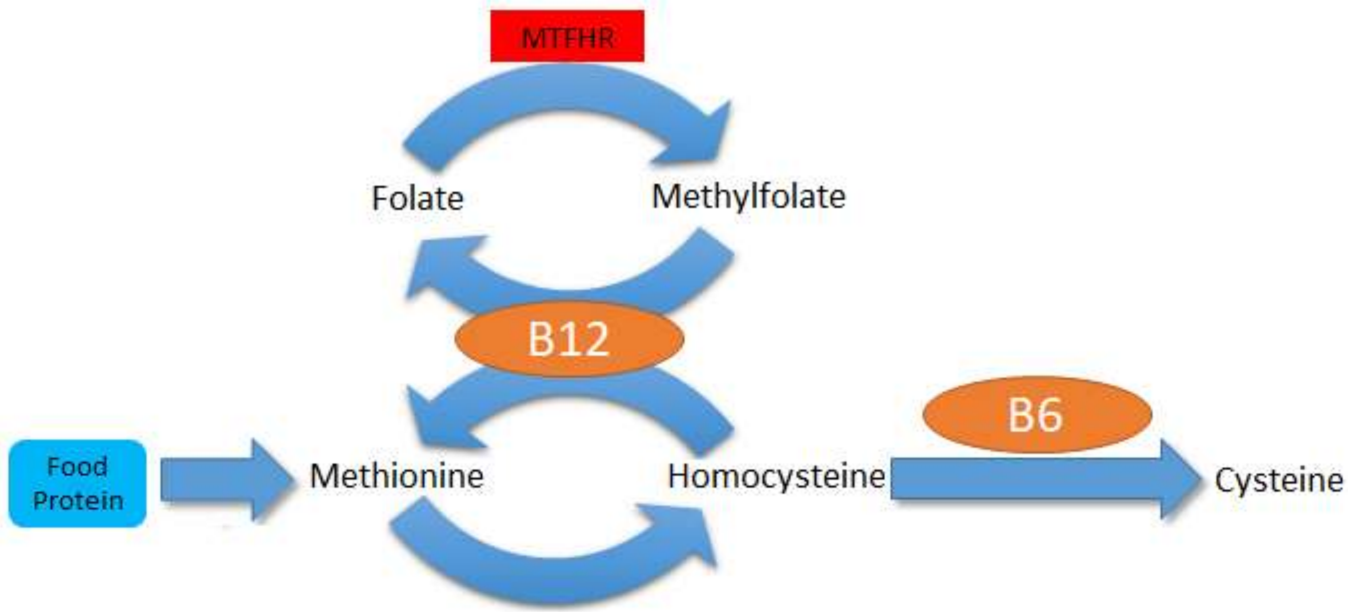
J Hypertens. 2009 Aug;27(8):1594-601. doi: 10.1097/HJH.0b013e32832ba850.

CYP1A2 genotype modifies the association between coffee intake and the risk of hypertension.

Palatini P[1], Ceolotto G, Ragazzo F, Dorigatti F, Saladini F, Papparella I, Mos L, Zanata G, Santonastaso M.

MTHFR (methyltetrahydrofolate reductase)

- A common polymorphism:
  - **C677T SNP (Ala^{222}Val)**



  - plasma homocysteine

TAS1R2

Genetic variation in *TAS1R2* (Ile191Val) is associated with consumption of sugars in overweight and obese individuals in 2 distinct populations[1–3]

Karen M Eny, Thomas MS Wolever, Paul N Corey, and Ahmed El-Sohemy

Nutrition Journal

BioMed Central

Research

Open Access

Improved weight management using genetic information to personalize a calorie controlled diet

Ioannis Arkadianos[1], Ana M Valdes[2], Efstathios Marinos[3], Anna Florou[1], Rosalynn D Gill[4] and Keith A Grimaldi*[4]

Address: [1]The Dr Arkadianos Clinic, Messogion Av, Athens, Greece, [2]Twin Research Unit, King's College London, UK, [3]Biomedical Engineering Laboratory, National Technical University of Athens, Greece and [4]Sciona Inc, Boulder, 80302, Colorado, USA

Email: Ioannis Arkadianos - idc.diet@eexi.gr; Ana M Valdes - ana.valdes@kcl.ac.uk; Efstathios Marinos - smarin@biomed.ntua.gr; Anna Florou - tsurekia@gmail.com; Rosalynn D Gill - rgill-garrison@sciona.com; Keith A Grimaldi* - kgrimaldi@sciona.com

* Corresponding author

Table 2: Genes and polymorphisms tested in the nutrigenetic patient group.

Gene	Gene symbol	Polymorphism	% homozygote wild type	% heterozygote	% homozygote variant	HWE p <
Angiotensin I converting enzyme	*ACE*	INS/DEL	14.6%	48.8%	36.6%	0.99
Apolipoprotein C-III	*APOC3*	3175C>G	73.3%	20.0%	6.7%	0.17
Cystathionine-beta-synthase	*CBS*	699C>T	53.5%	41.9%	4.7%	0.81
Cholesteryl ester transfer protein	*CETP*	279G>A	48.8%	39.5%	11.6%	0.86
Collagen, type I, alpha 1	*COLIA1*	G Sp1 T	58.1%	34.9%	7.0%	0.94
Glutathione S-transferase M1	*GSTM1*	Deletion (*)	52.0%	0.0%	48.0%	N/A
Glutathione S-transferase pi	*GSTP1*	313A>G	57.8%	33.3%	8.9%	0.68
		341C>T	56.8%	34.1%	9.1%	1.00
Glutathione S-transferase theta 1	*GSTT1*	Deletion (*)	86.0%	0.0%	14.0%	N/A
Interleukin 6	*IL6*	-174G>C	66.7%	33.3%	0.0%	0.37
		-634G>C	86.0%	14.0%	0.0%	0.89
Lipoprotein lipase	*LPL*	1595C>G	69.8%	27.9%	2.3%	1.00
5-methyltetrahydrofolate-homocysteine methyltransferase reductase	*MTRR*	66A>G	19.0%	45.2%	35.7%	0.90
5,10-methylenetetrahydrofolate reductase	*MTHFR*	1298A>C	34.0%	48.9%	17.0%	1.00
		677 C>T	48.0%	44.0%	8.0%	0.95
5-methyltetrahydrofolate-homocysteine methyltransferase	*MTR*	2756A>G	59.5%	33.3%	7.1%	0.86
Nitric oxide synthase 3 (endothelial cell)	*NOS3*	894G>T	44.2%	44.2%	11.6%	1.00
Peroxisome proliferator-activated receptor gamma	*PPARG*	Pro12Ala	75.6%	15.6%	8.9%	**0.02**
Superoxide dismutase 2, mitochondrial	*SOD2*	-28C>T	10.0%	54.0%	36.0%	0.57
Superoxide dismutase 3, extracellular	*SOD3*	760C>G	100.0%	0.0%	0.0%	1.00
Tumor necrosis factor	*TNF*α	-308G>A	71.1%	24.4%	4.4%	0.72
Vitamin D receptor	*VDR*	C TaqI T	23.3%	46.5%	30.2%	0.91
		T BsmI C	23.3%	46.5%	30.2%	0.91
		T FokI C	11.6%	58.1%	30.2%	0.41

Genotype frequencies in the study group and p-values for Hardy Weinberg Equilibrium (HWE) are shown. (*) the assay only measured presence or absence of the deletion so a HWE test is not applicable.

Association of polymorphic genes with response to nutrients

- *TAS1R2 (Ile191Val)*
- *Glucose transporter type 2 (Glut-2)*
- *Tumor necrosis factor-alpha (TNF-α)*
- *Catechol-O-Methyltransferase enzyme (COMT)*
- *Apolipoprotein E (APO E)*
- *APOC3*
- *APOA1*
- *…*

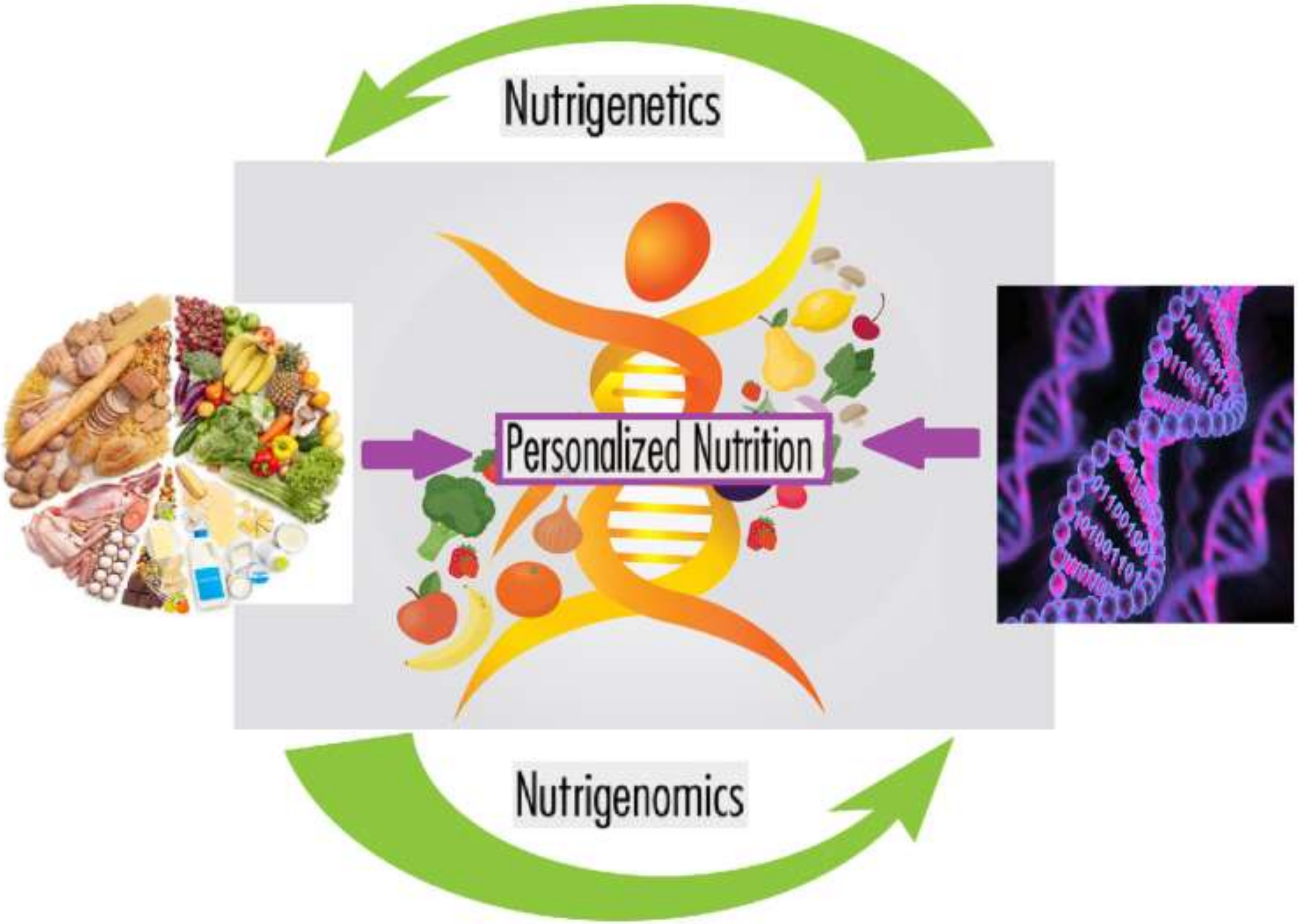
End of the second section ….

Third Section

FUTURE PROSPECTS

Disease Prevention & Health Promotion

Personalized Nutrition



Forth Section

What I have learned?

The Forth Section Cont'd.

- Food sends informational signals to the genes.

- Your genes are not your destiny.

- Food influence ingested behavior.

Food is more than calories,
Food is information !

The Forth Section Cont'd.

- What's your definition of nutrigenomics and nutrigenetics?
- How Personalized Nutrition can be helpful in health promotion and disease prevention
- Nutrients and gene expression can lead to epigenetic altering?
- How nutrients can act as informational signals for our body?

Main References:

- Malavolta M, Mocchegiani E, editors. Molecular Basis of Nutrition and Aging: A Volume in the Molecular Nutrition Series. Academic Press; 2016 Apr 15.
- Fenech M, El-Sohemy A, Cahill L, Ferguson LR, French TA, Tai ES, Milner J, Koh WP, Xie L, Zucker M, Buckley M. Nutrigenetics and nutrigenomics: viewpoints on the current status and applications in nutrition research and practice. Lifestyle Genomics. 2011;4(2):69-89.
- Ramos-Lopez O, Milagro FI, Allayee H, Chmurzynska A, Choi MS, Curi R, De Caterina R, Ferguson LR, Goni L, Kang JX, Kohlmeier M. Guide for current nutrigenetic, nutrigenomic, and nutriepigenetic approaches for precision nutrition involving the prevention and management of chronic diseases associated with obesity. Lifestyle Genomics. 2017;10(1-2):43-62.
- Cornelis MC, El-Sohemy A, Kabagambe EK, Campos H. Coffee, CYP1A2 genotype, and risk of myocardial infarction. Jama. 2006 Mar 8;295(10):1135-41.

Thanks

For your

attention