Using Genetics to Personalize Lifestyle

Michele L Neil DO, FACOI

Disclosures

- SPEAK INTERNATIONALLY FOR
  -DNA LIFE

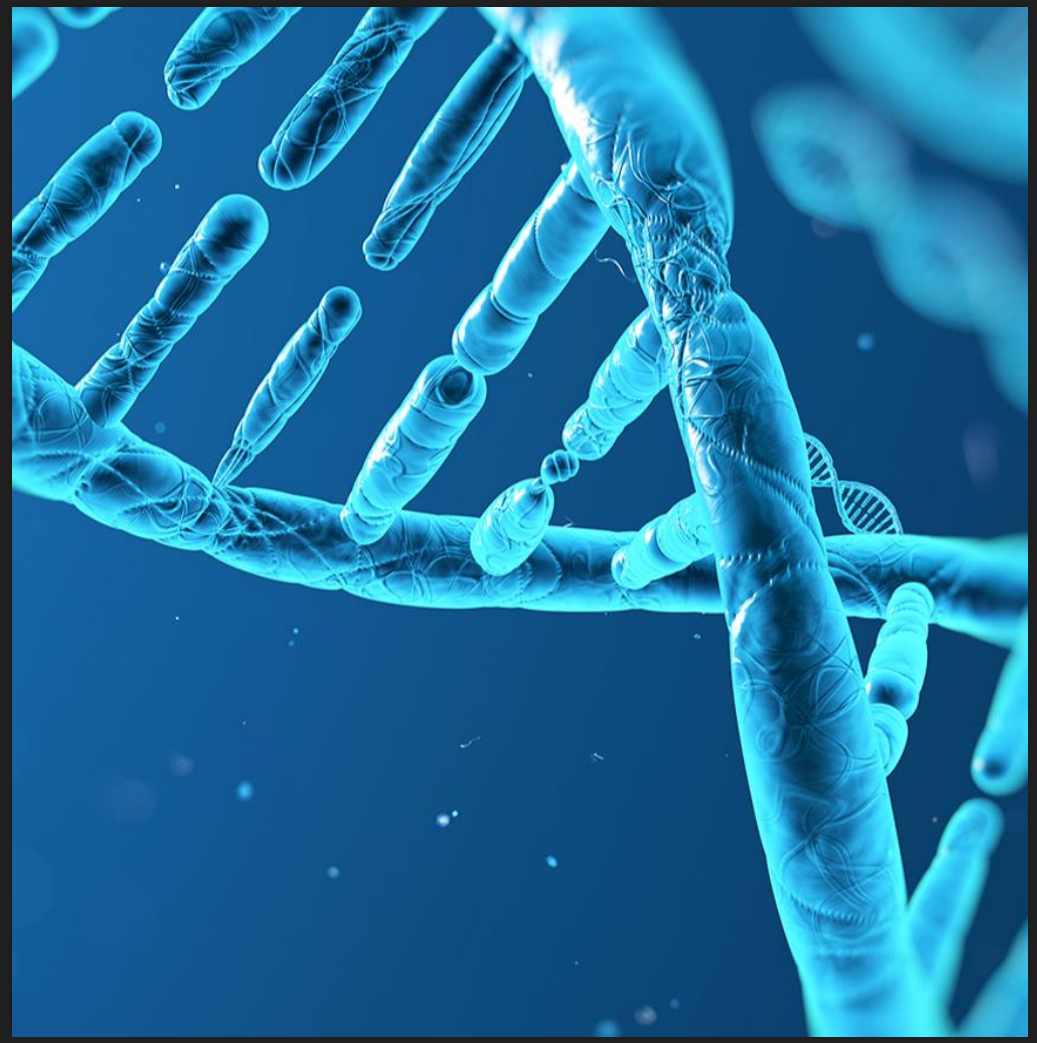
OBJECTIVES

- Genetics the future of health care
- Genetics basics
- Overview of just a few of the many areas of high interest using genetics to guide a patient to optimal wellness
  - -Obesity
  - -Detoxification
  - -Inflammation
- Usage in clinical practice

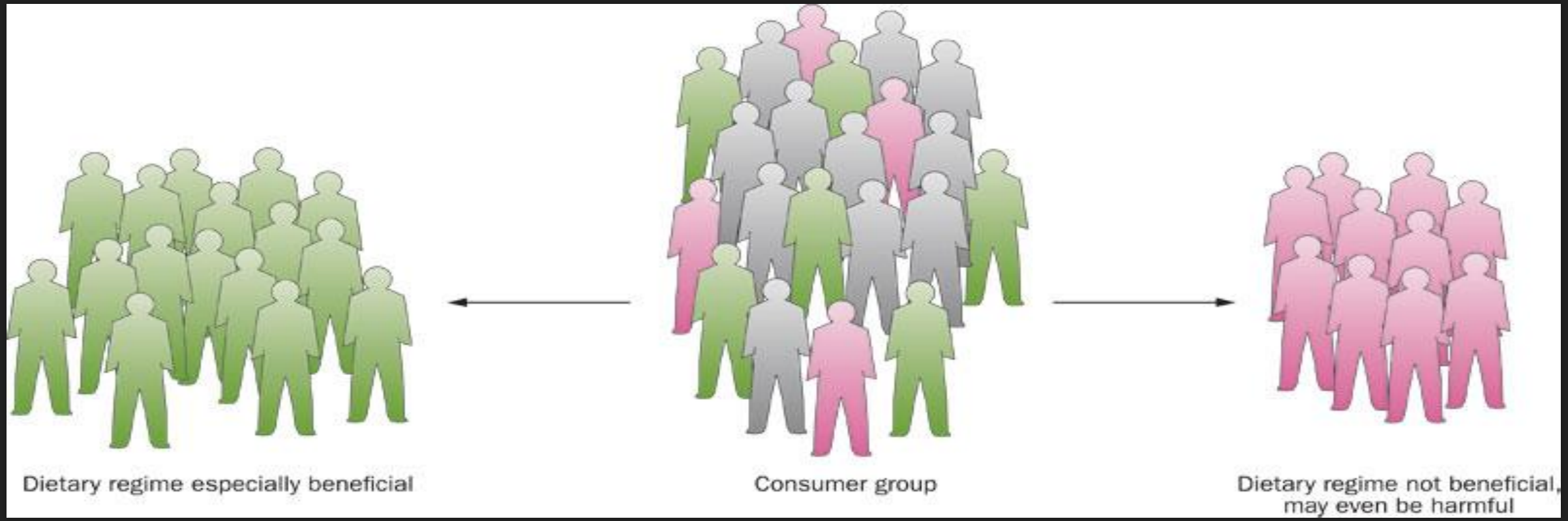
Personalization is the future Including Health Care

- No need for trial and error
- Avoid ‘Assumptions’ Based on family member
- Avoid confusing new ‘Fads’ in which to waste time
- Employ a comprehensive functional approach
- What is the most personalized approach to knowing?

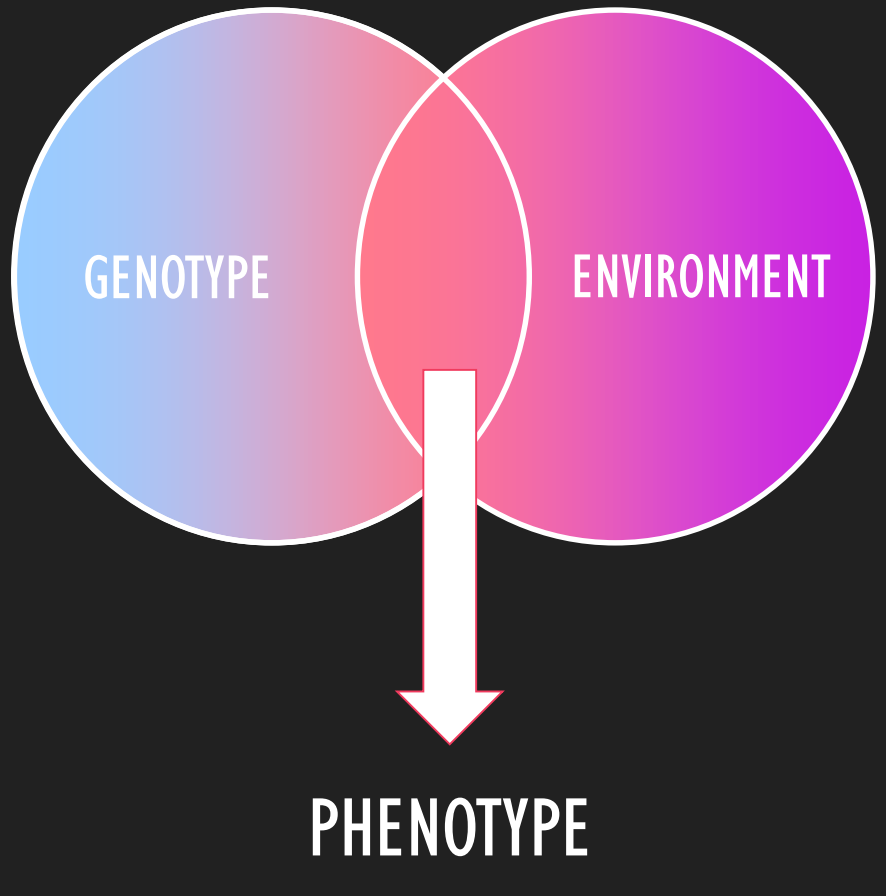
Pioneering the new Frontier in Health and Wellness with DNA



Personalized “Health” Care

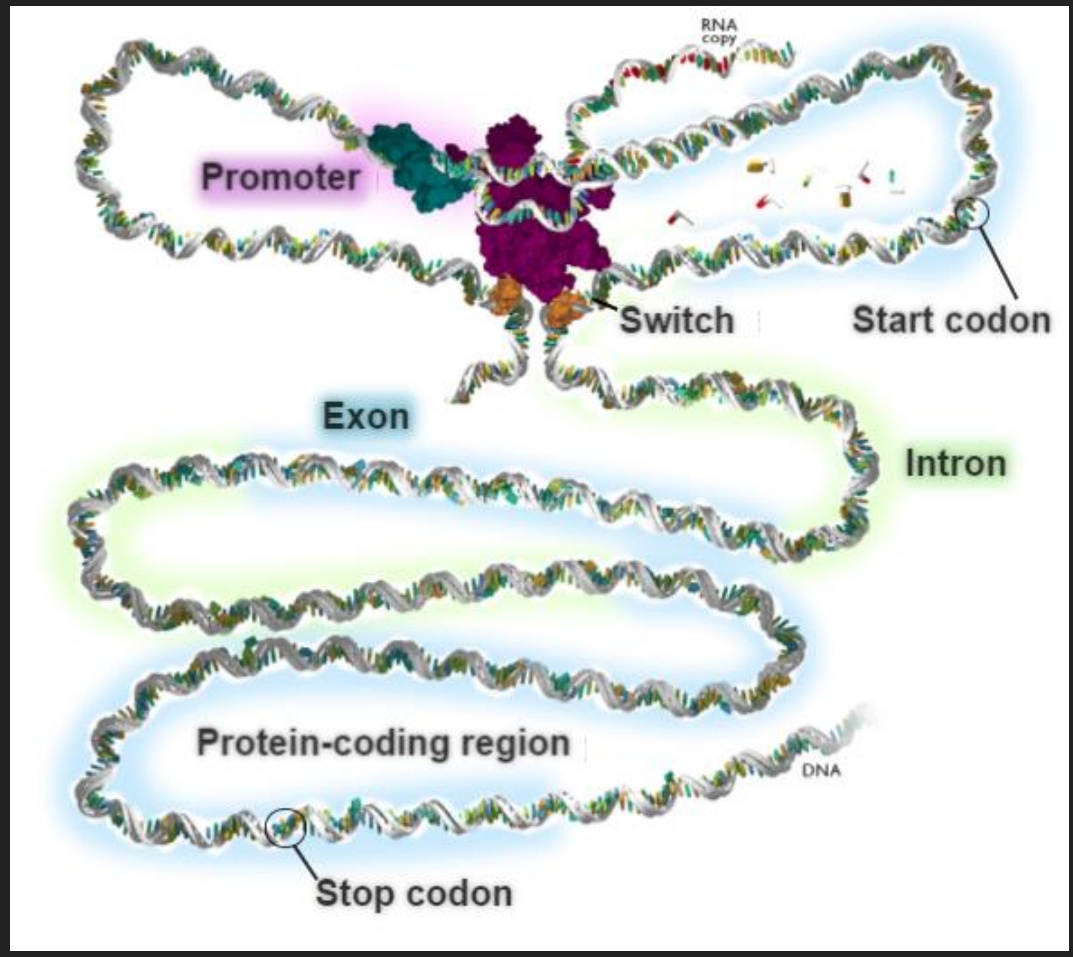


Personalized “Health” Care



What we know about DNA

- Gene- encodes for protein
- Genome – the complete book of genes in our DNA
- Chromosome



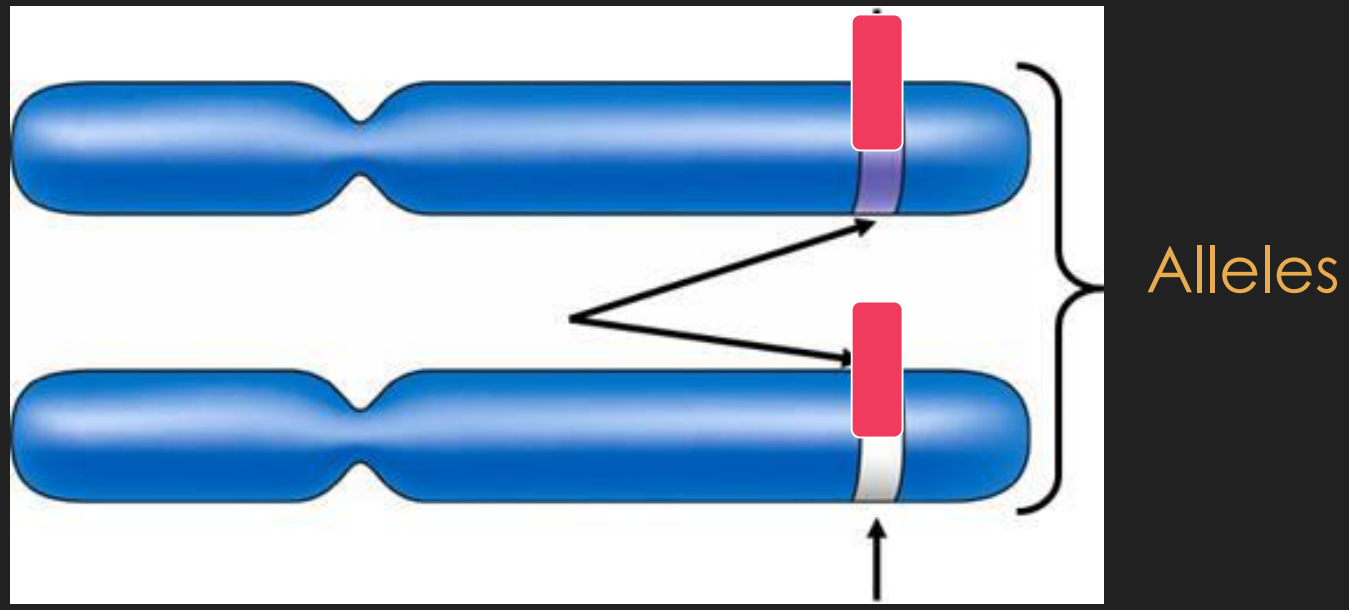
Terminology

- Nucleotide
  Subunit of DNA/RNA consisting of base pairs

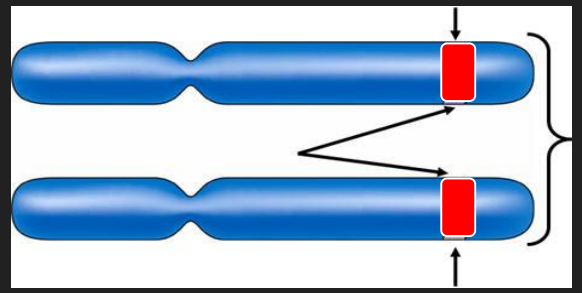
- Codon
  A sequence of 3 nucleotides that codes for a certain AA

- SNP:
  FAT
  HAT
  CAT

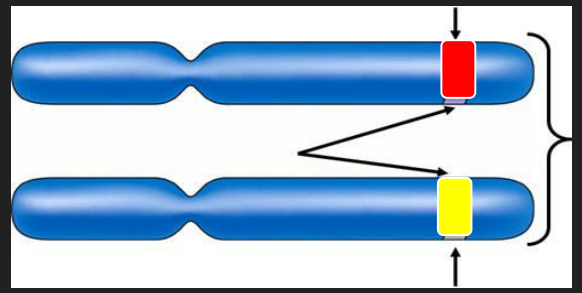
• Allele



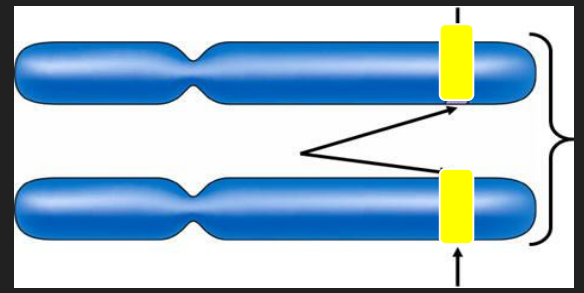
Terminology



Wild Type:



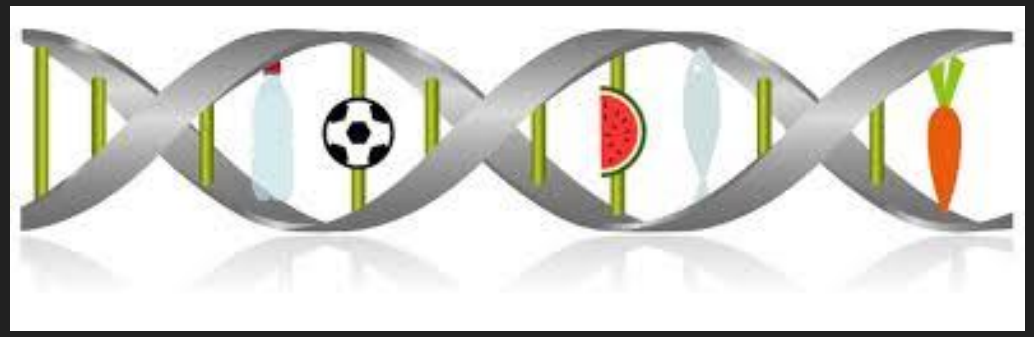
Heterozygote:



Homozygote:

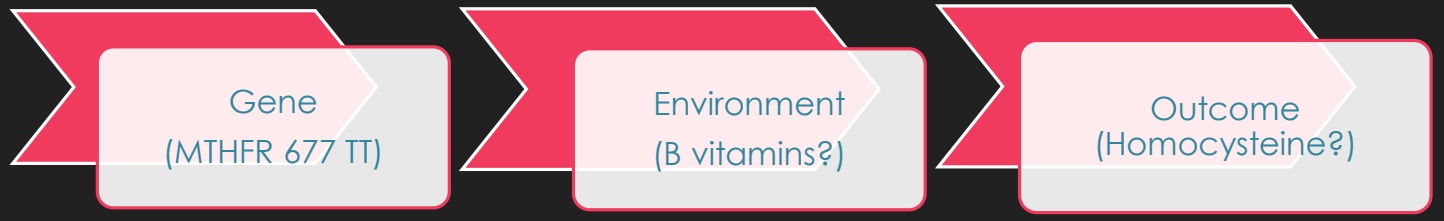
Nutritional genomics, nutrigenetics, & nutrigenomics

- Nutritional genomics is a science studying the relationship between human genome, nutrition and health.



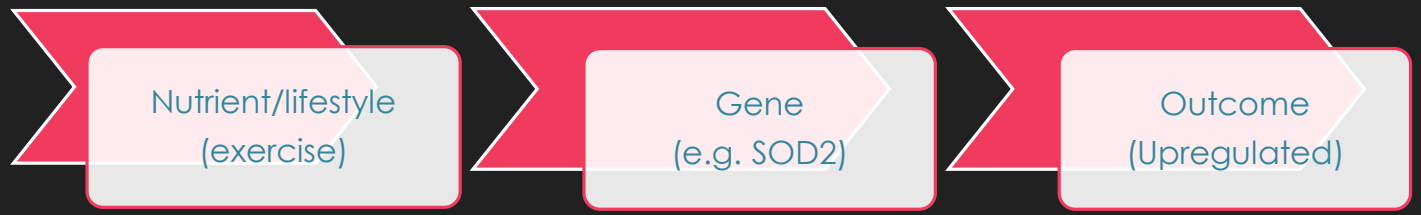
Nutrigenetic diet-gene interactions

Nutrigenetics



Nutrigenomic diet-gene interactions

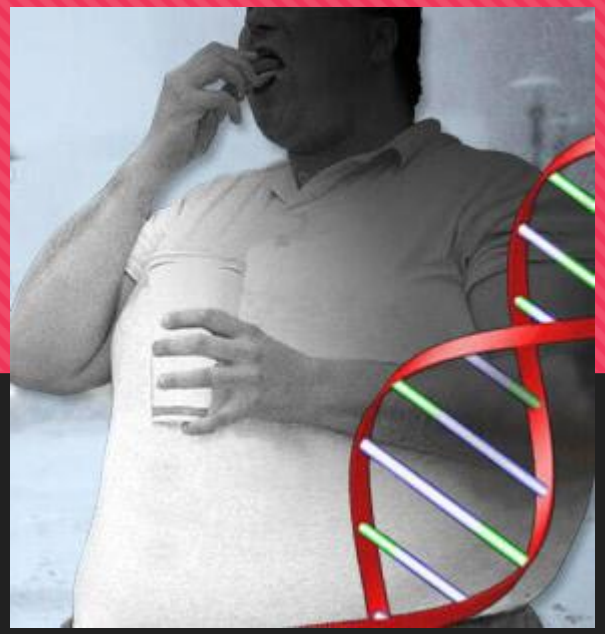
Nutrigenomics



Personalizing Medicine in these areas

- Obesity
- Detoxification
- Inflammation

Genetics and Obesity



- Obesity affects the majority
- 4 decades earlier there was a prevalence of about 13% (food pyramid?)
- The development of obesity has an evident environmental contribution, but has shown by heritability estimates of 40-70%

-Curr Diab Rep. 2010 Dec; 10(6): 498-505

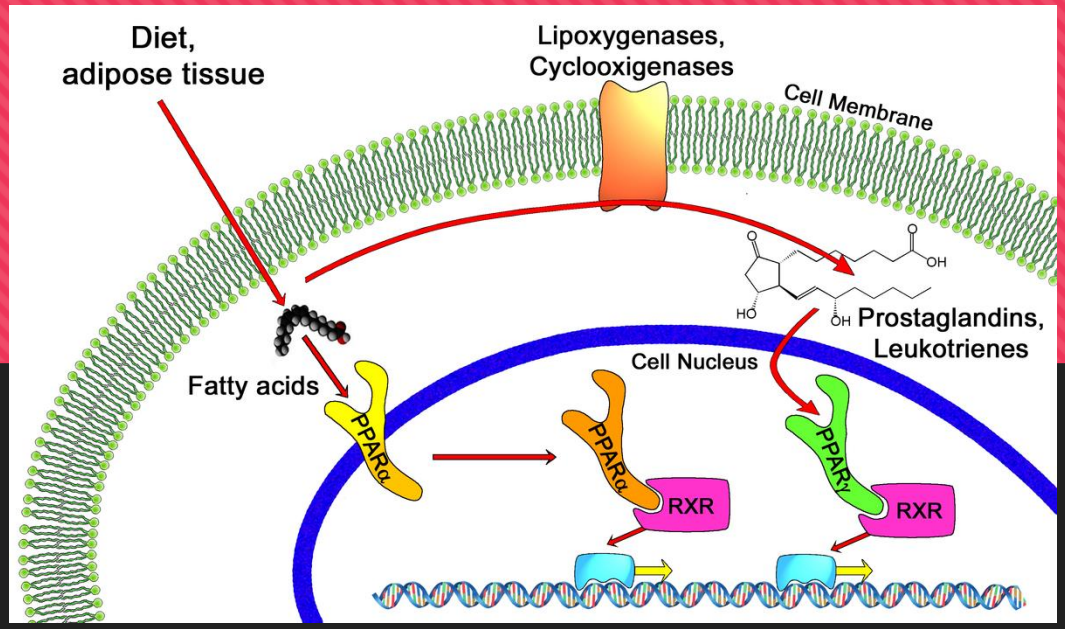
- Common misperception is that exercise is a major component to weight loss
- Truth: Nutrition is far more important for weight than is exercise

FTO T>A

- 16% of the population have 2 copies of the A allele (the risk allele)
- 1 copy carries about 3x risk of obesity and with 2 copies 6x risk
- Present in several metabolically active tissues
- Involved in fat cell differentiation and fat storage by making more white fat than brown

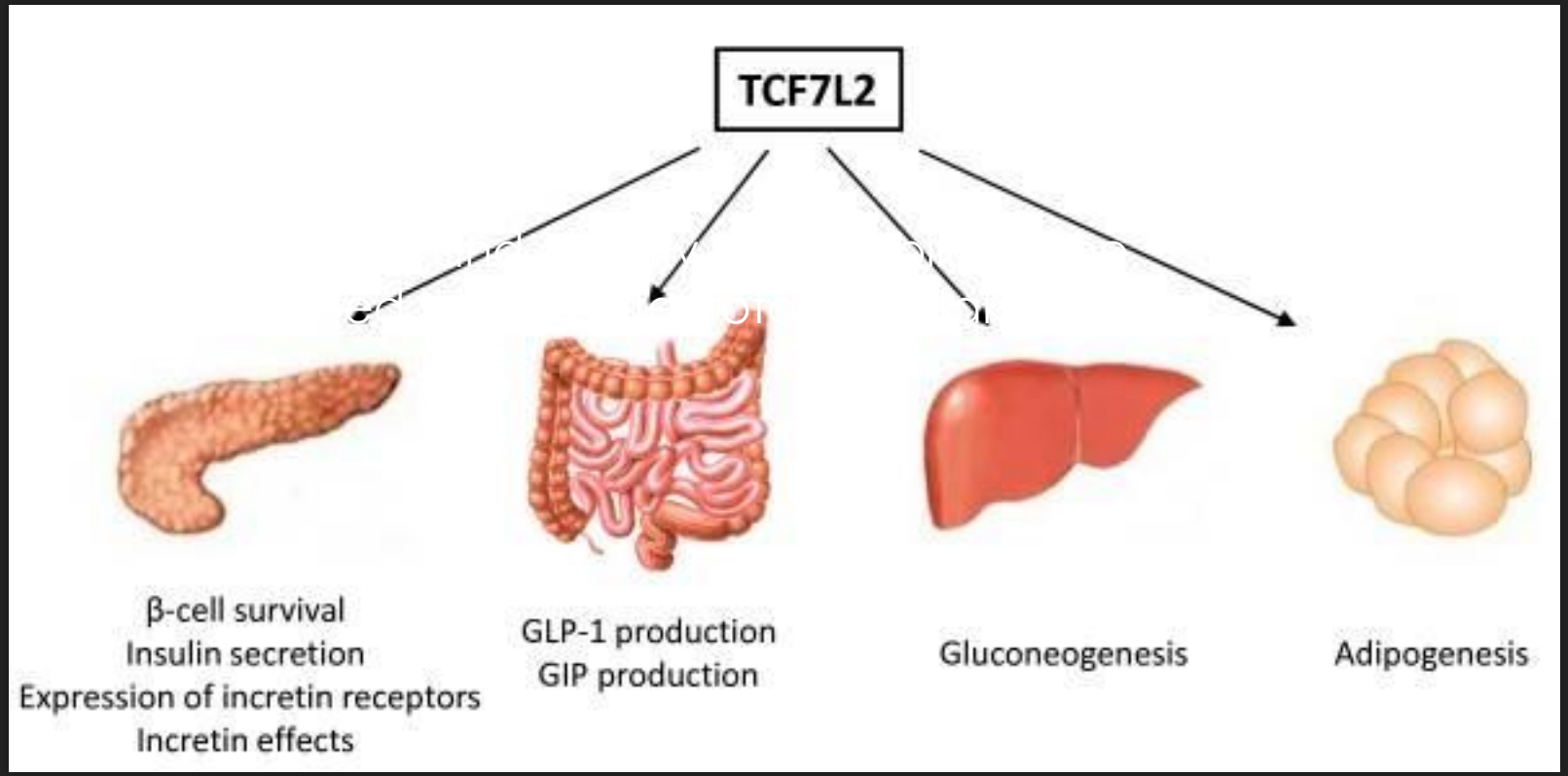
- Treatment: Awareness around meals - behavioral modification, setting the glycemic load and index, adequate physical activity

PPARG C>G



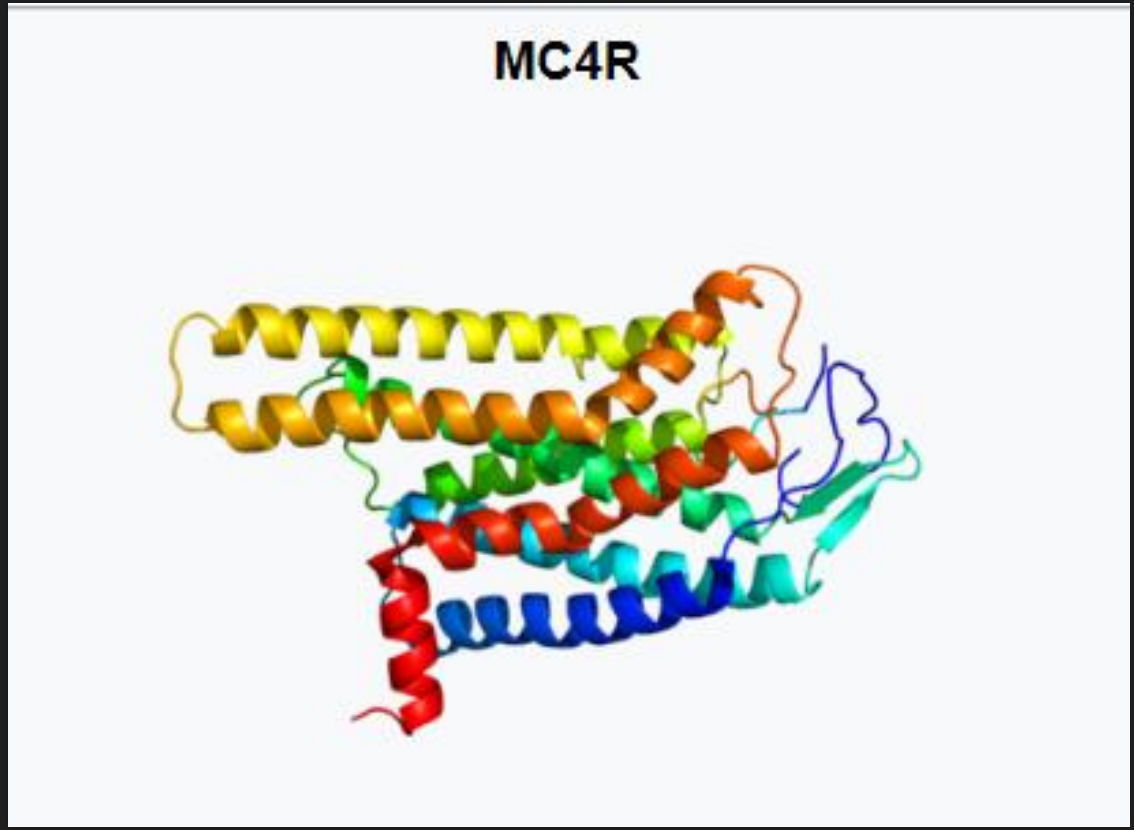
- Expressed abundantly in fat cells and plays a key role in adipogenesis
- PPARG are lipid sensing transcription factors that are known for modulating energy metabolism, lipid storage, transport and inflammation.
- PPARG regulates fatty acid storage and glucose metabolism

TCF7L2 C>T


TCF7L2
β-cell survival
Insulin secretion
Expression of incretin receptors
Incretin effects
GLP-1 production
GIP production
Gluconeogenesis
Adipogenesis

MC4R T>C

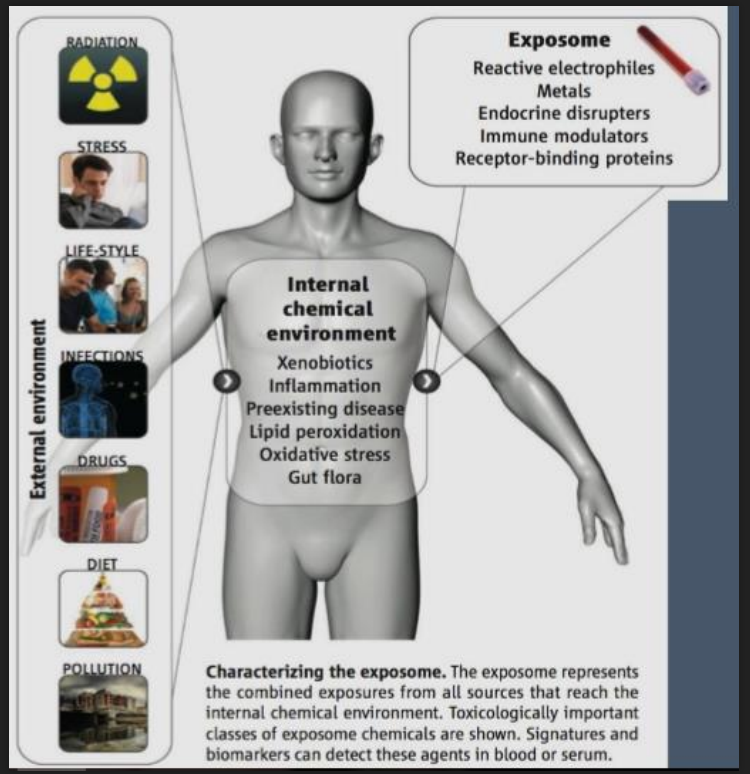
- DEATH BY “BUFFET” GENE
- TREATMENT: BEHAVIORAL MODIFICATION



Obesity Gene in Clinical Practice

- FTO
- PPARG
- TCF7L2
- MC4R

Detoxification



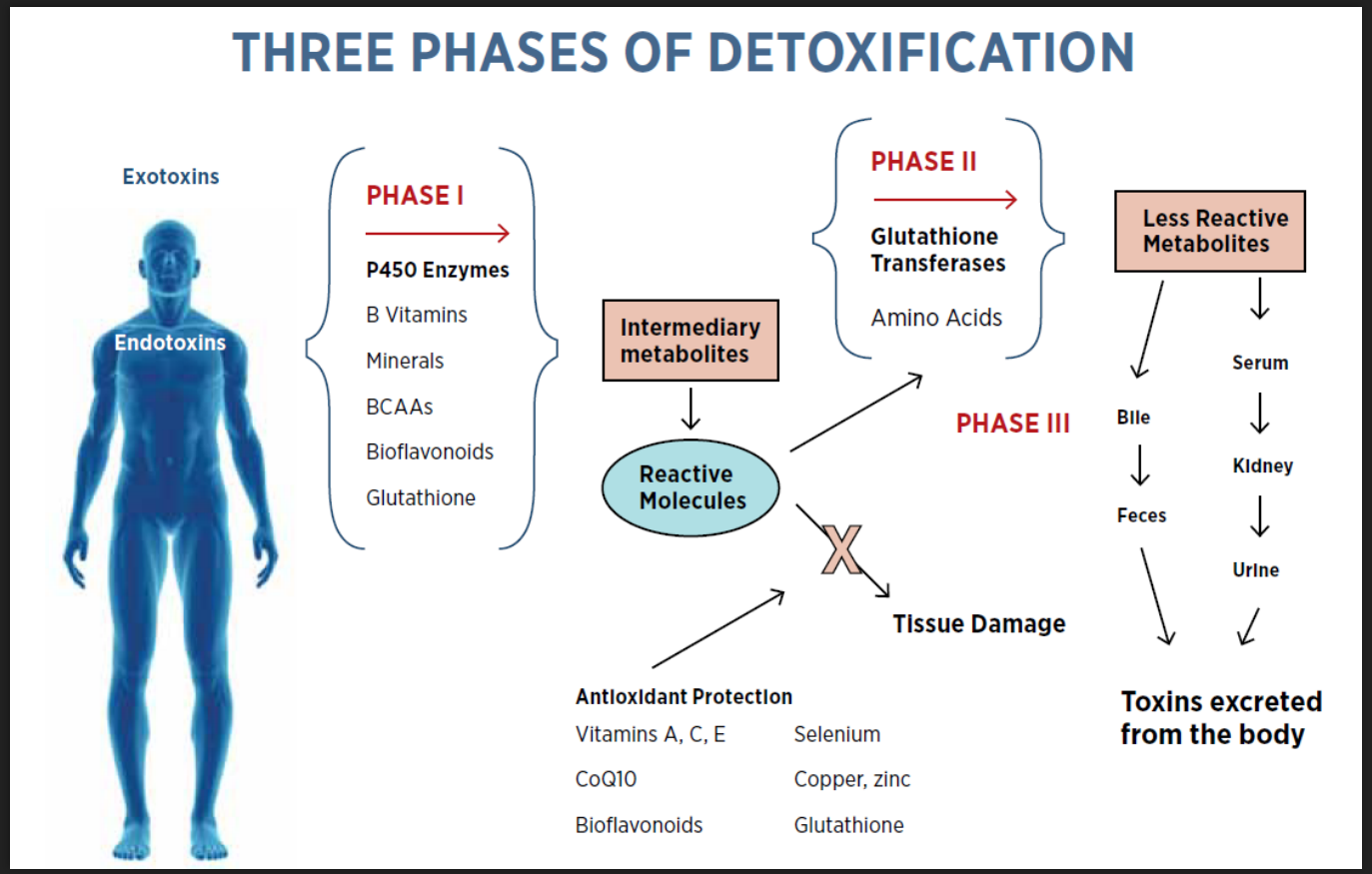
TOTAL TOXIC BURDEN

- Results from

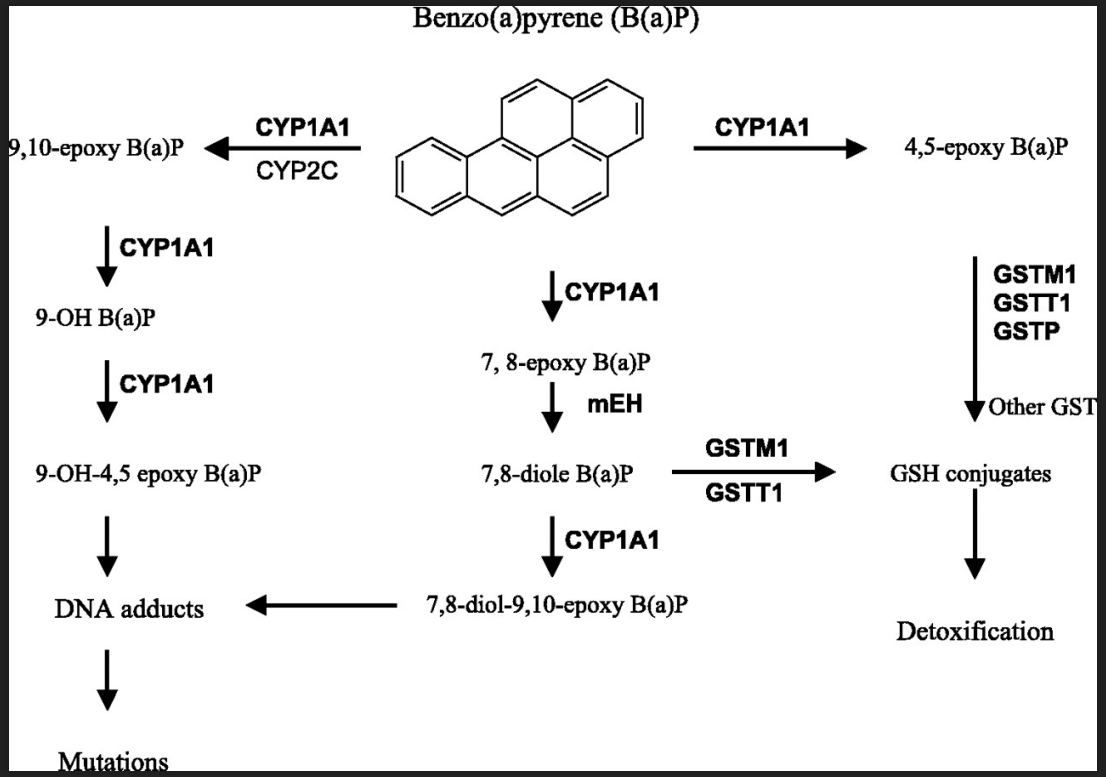
  TOTOAL TOXIC EXPOSURE – ABILITITY TO BIOTRANSFORM AND EXCRETE

- Internal enzyme systems are always at work

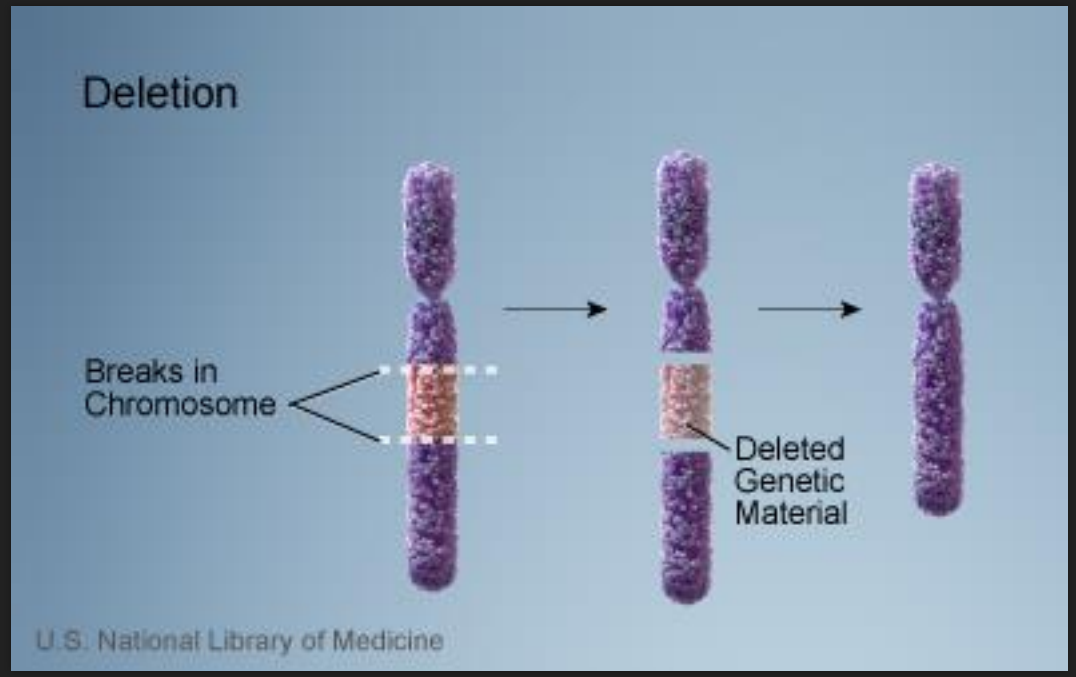
Phases of Detoxification



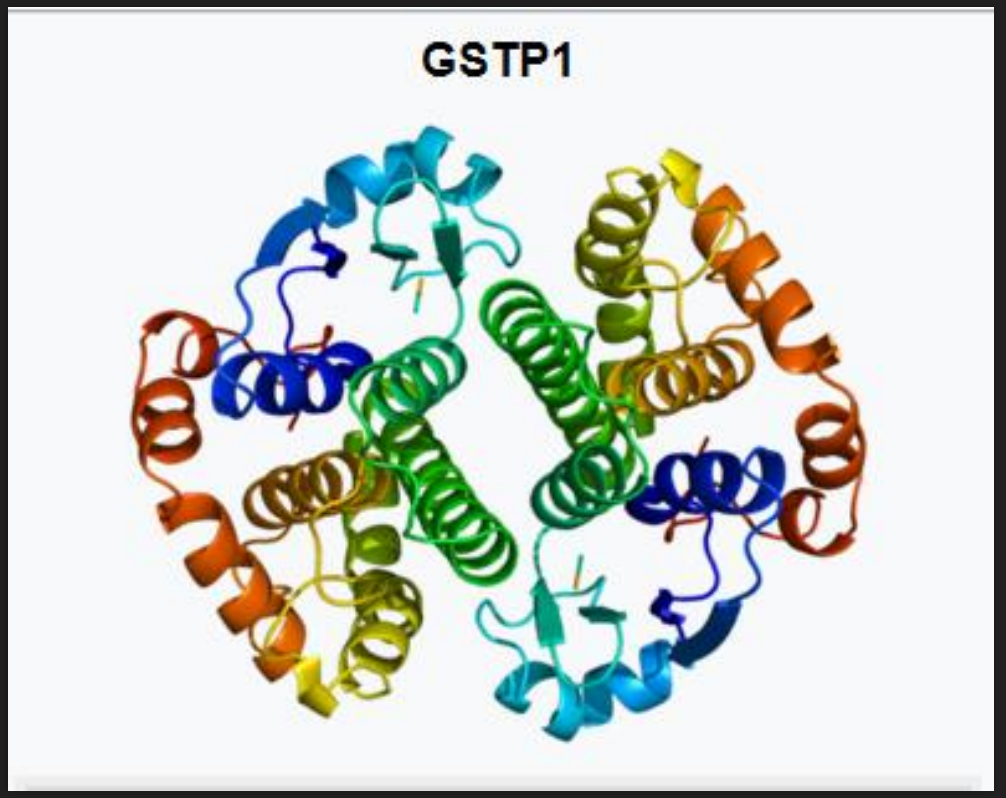
CYP1A1 Cytochrome P450



GSTMI GSTT1


Deletion
Breaks in Chromosome
Deleted Genetic Material
U.S. National Library of Medicine

GSTP1 A>G



NQO1 C>T

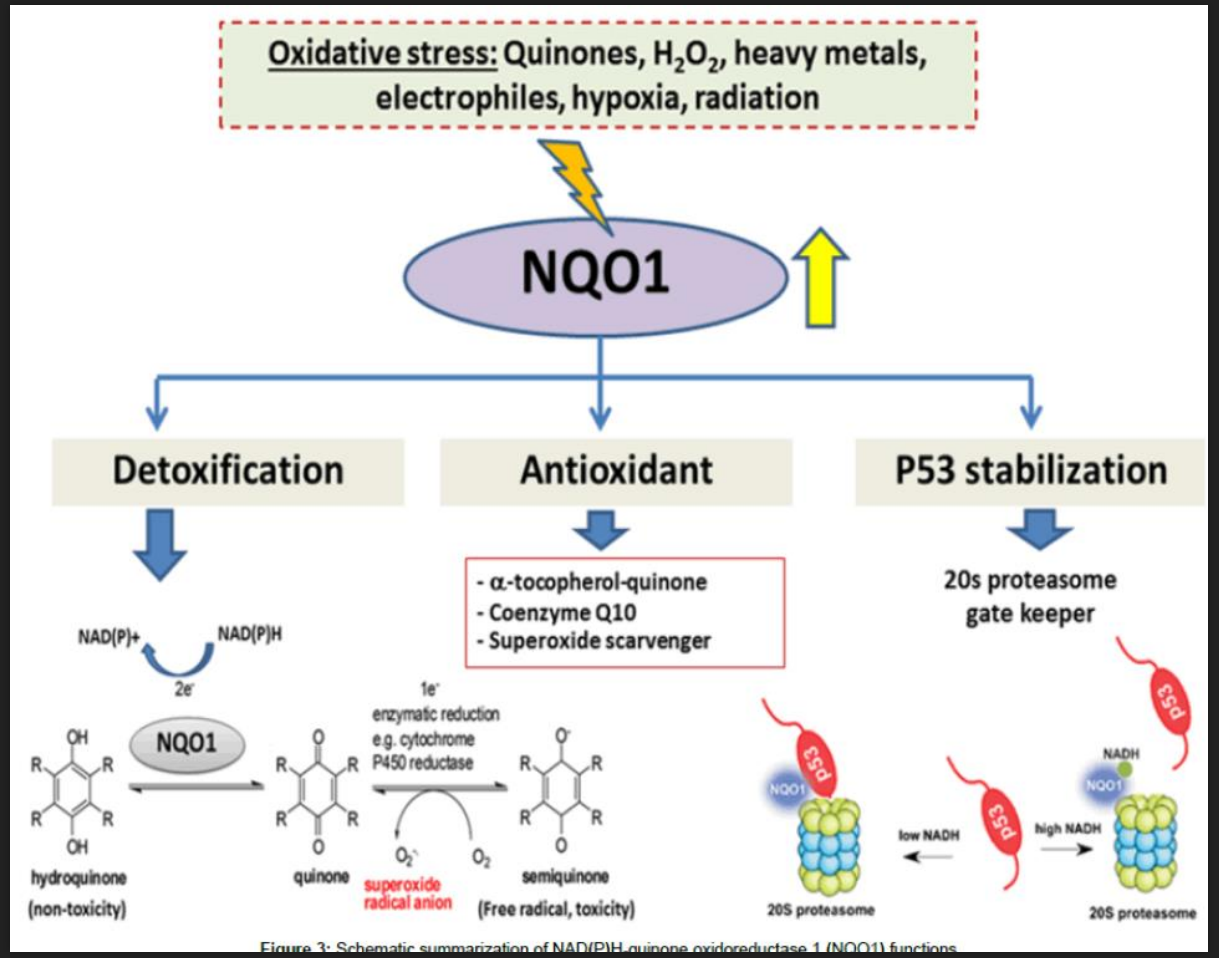
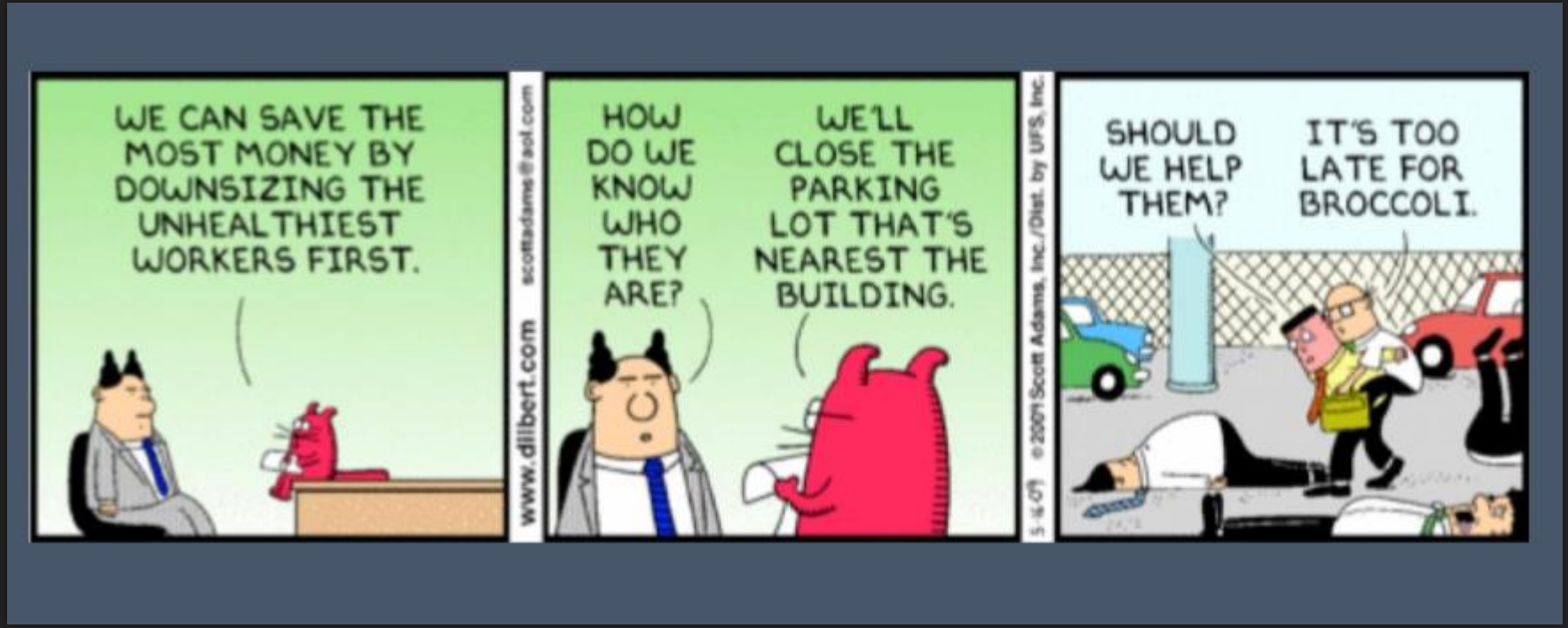


Figure 3: Schematic summarization of NAD(P)H-quinone oxidoreductase 1 (NQO1) functions

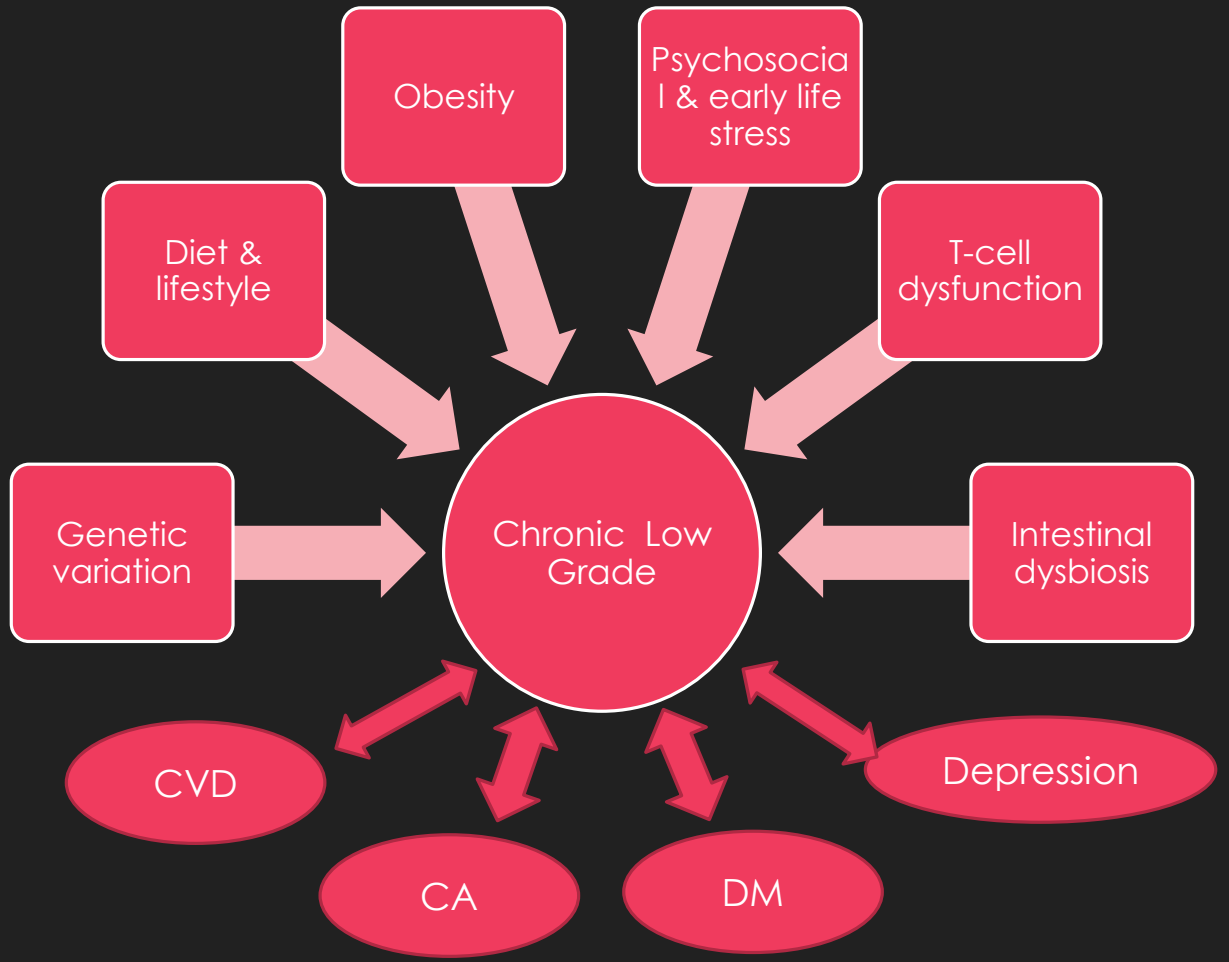
Detox solutions

- Solution to pollution
- Targeted nutrition
- Hydration
- Adequate nutrient support as cofactors
- Down regulate inflammation with Omega 3 support
- Sweat/ Infra-red
- Cruciferous vegetables
- Sulfurophane

Not the "Optimum" Detox Plan



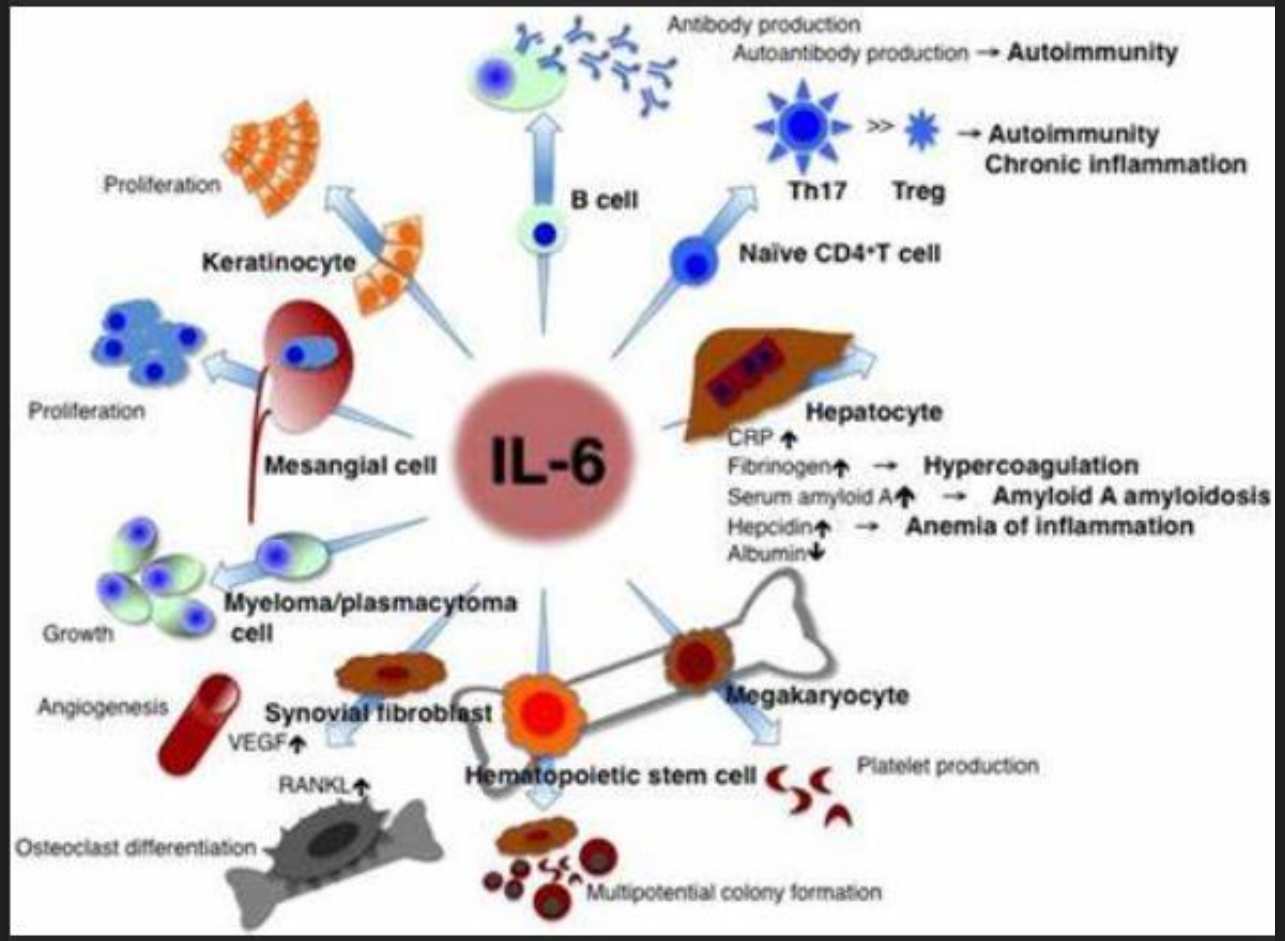
Inflammation



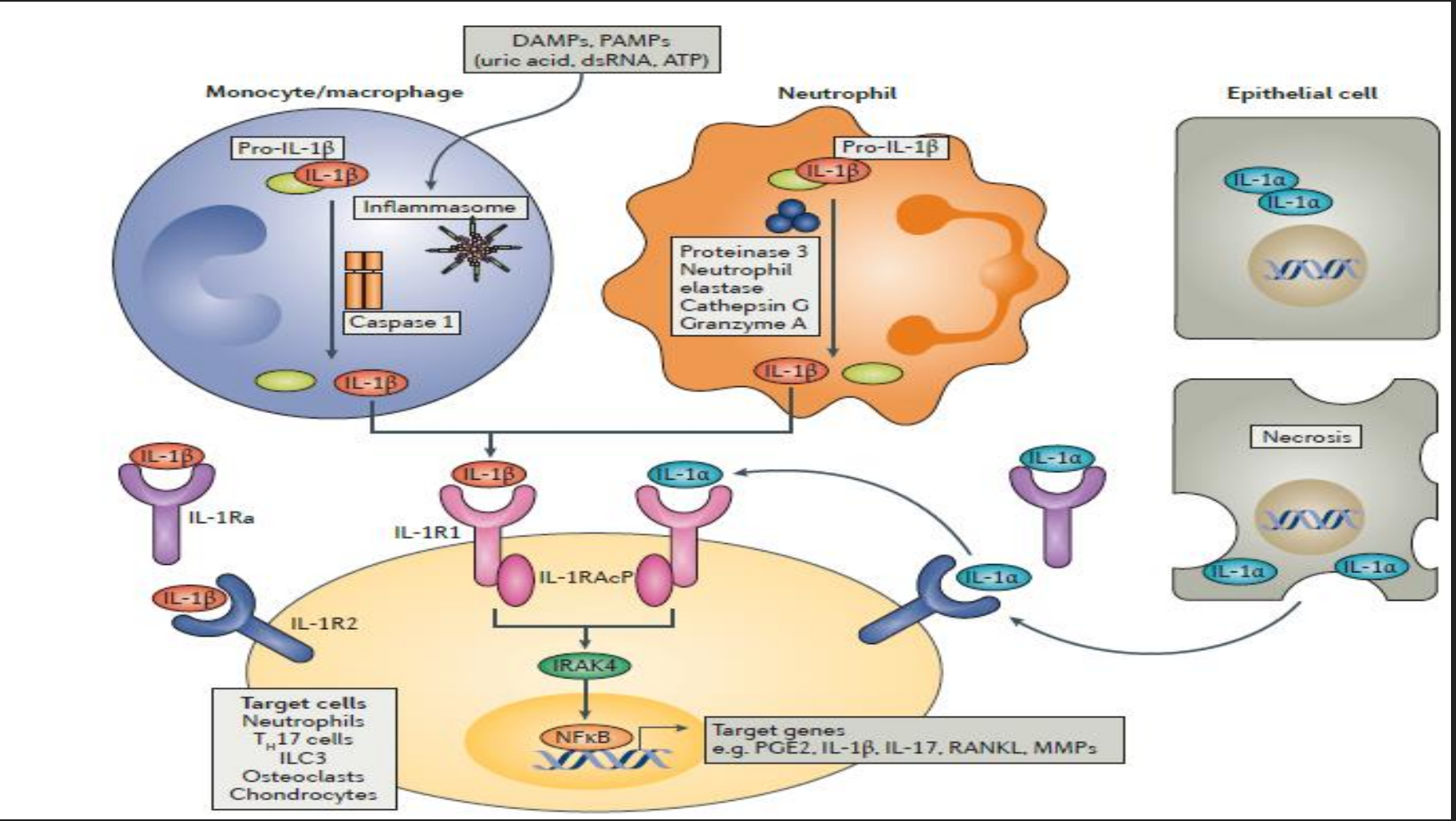
APOE4

- 20% of the population have at least 1 copy of the E4 allele
- One copy may show a 3-fold increase risk of Alzheimer's and 16-fold with 2 copies
- ApoE4 stimulates the faster degradation of insulin degrading enzyme and in a high sugar diet what is left of the enzyme will be forced to be focused on insulin and not amyloid B
- High risk of Cardiovascular disease- 40-50 % in the presence on 1allele

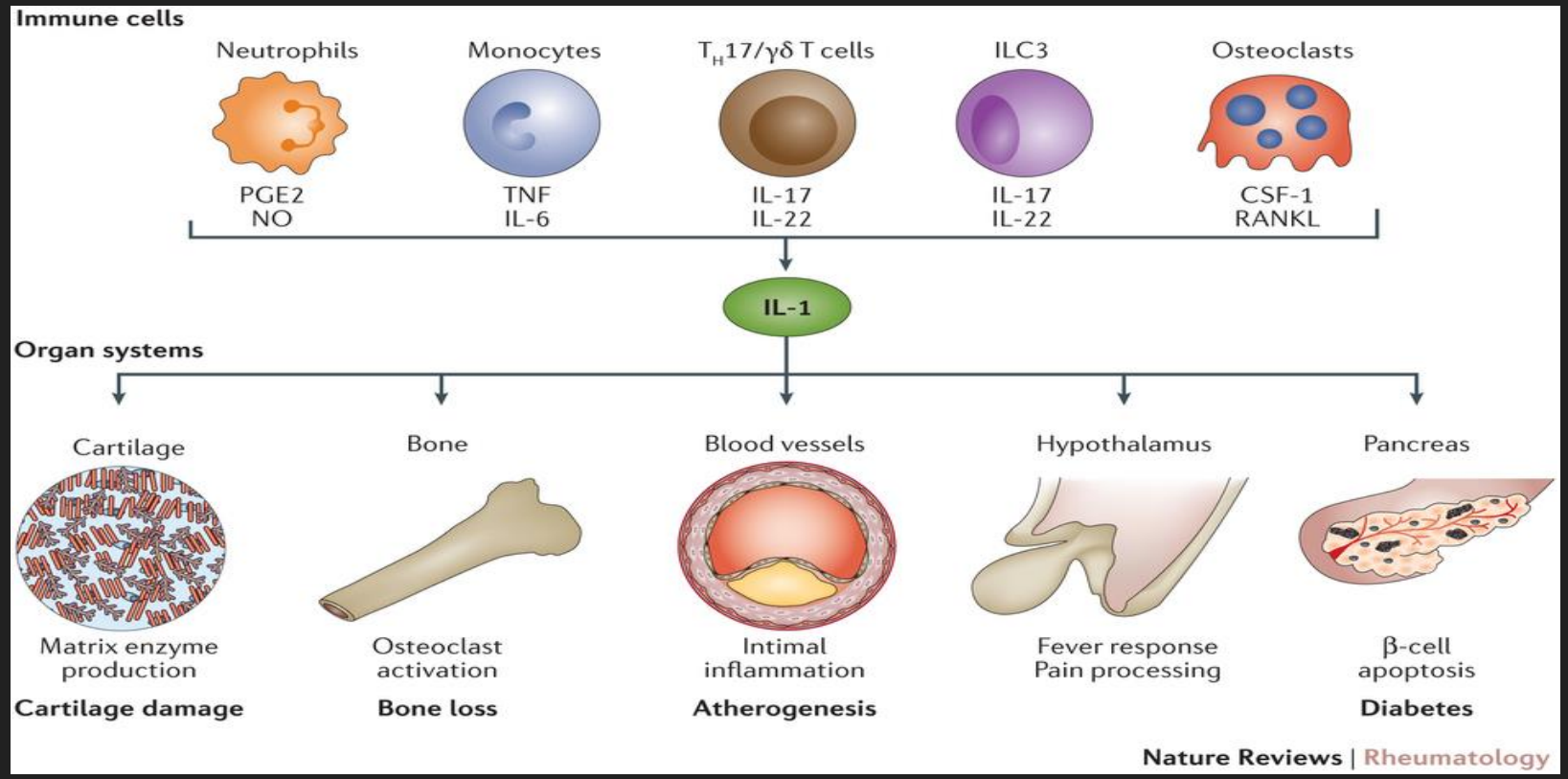
IL-6 G>T


Antibody production
Autoantibody production → Autoimmunity
B cell
Th17
Treg
>>
→ Autoimmunity
Chronic inflammation
Naïve CD4+T cell
Proliferation
Keratinocyte
Proliferation
Mesangial cell
IL-6
Hepatocyte
CRP↑
Fibrinogen↑ → Hypercoagulation
Serum amyloid A↑ → Amyloid A amyloidosis
Hepcidin↑ → Anemia of inflammation
Albumin↓
Growth
Myeloma/plasmacytoma cell
Angiogenesis
VEGF↑
Synovial fibroblast
Megakaryocyte
Hematopoietic stem cell
Platelet production
RANKL↑
Osteoclast differentiation
Multipotential colony formation

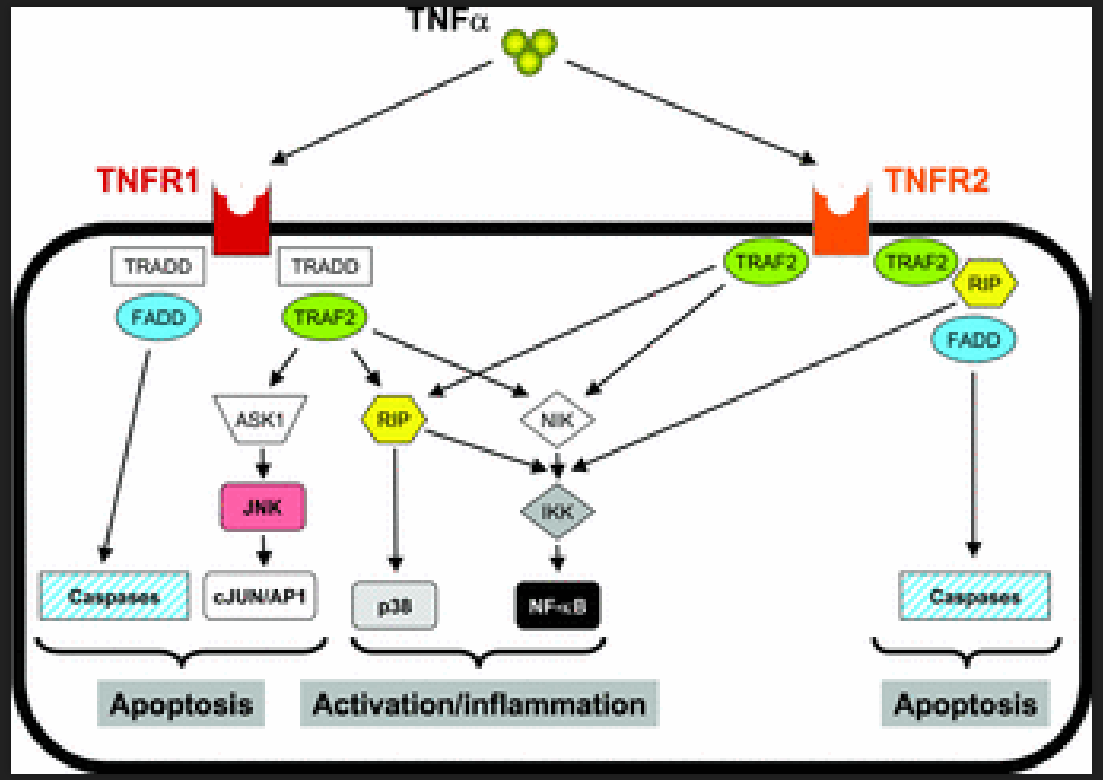
IL-1: Activation & signalling



Interleukin 1



TNFa G>A


TNFα
TNFR1
TNFR2
TRADD
TRADD
FADD
TRAF2
TRAF2
TRAF2
RIP
FADD
ASK1
RIP
NIK
JNK
IKK
Caspases
cJUN/AP1
p38
NFκB
Caspases
Apoptosis
Activation/inflammation
Apoptosis

Final thoughts on Inflammation

- Inflammation is not bad but can become problematic in an inflammatory environment
- Optimize an anti-inflammatory nutritional protocol
- Heal a leaky gut- can take years
- Detox on a routine basis
- Optimize omega 3 index
- Exercise appropriately
- Anti inflammatory additions to food as spices
- Infra red heat
- Adequate sleep
- What about spreading out vaccines?
- Minimize blue light exposure

Summary

- Genes have changed 2 % in 10,000 years
- They have evolved to help us survive
- It is the rapidly changing environment that is constantly put on the genes that creates expression
- This has resulted in a mismatched relationship with equally mismatched diseases
- Just because you were born with a certain set of genes does not mean negative issues
- Knowing your genes can help you stay out of harms way and lend proof to the fact that lifestyle matters every day and all the time