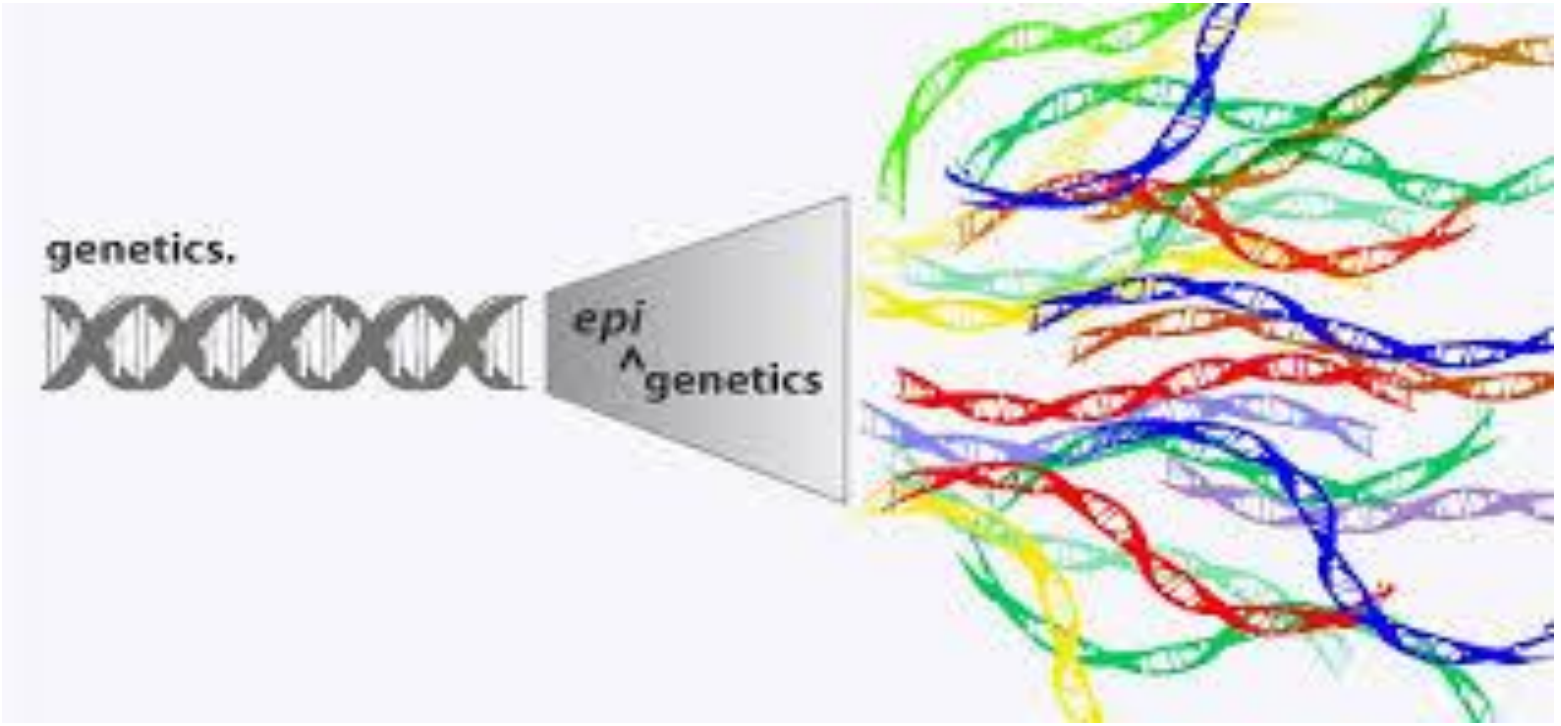
بسم الله الرحمن الرحيم

السلام عليكم ورحمة الله وبركاته

Genetics and Epigenetics



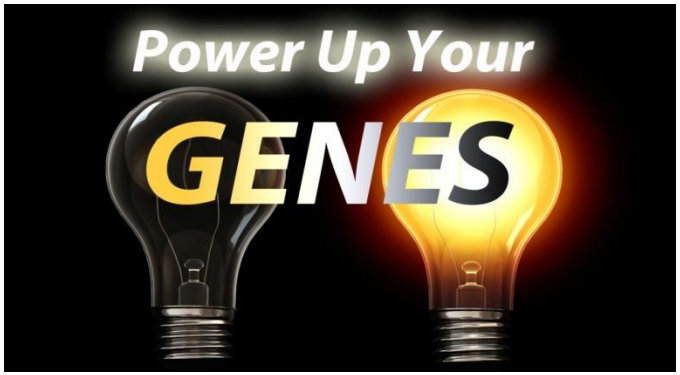
Prof.Dr. Khadiga Abougabal

Clinical & Chemical Pathology Department

Faculty of Medicine

Beni-Suef University

Powering Up Our Healthy Genes!



Q: What genes do we want to power up and what genes do we want to turn off?

The human genome has **23,000** genes that influence **40-60** trillion cells of the body.

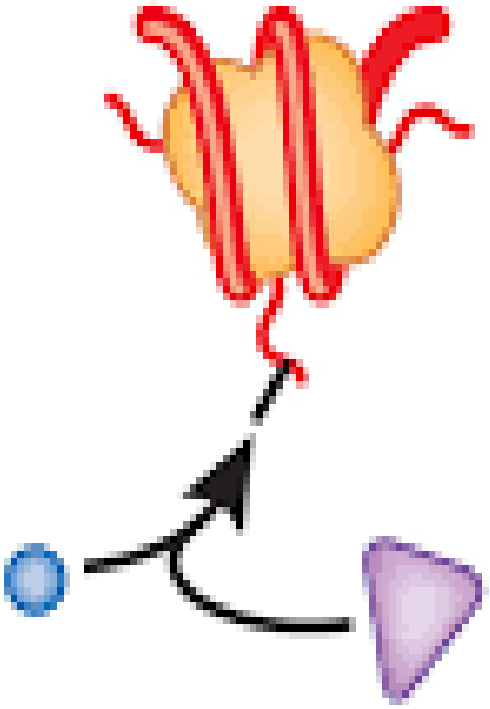
The more precise question is, is it possible to program my genes favorably?

Yes! Contrary to popular thinking, the current medical view of prevention of bad expressed genes like BRCA, is to **use the scalpel to remove the breasts of women that express positively**.

What many people are not aware of is BRCA expresses on other types of cancers that involve major organs. These ***organs cannot be surgically removed*** as the only treatment as they are critical to survival.

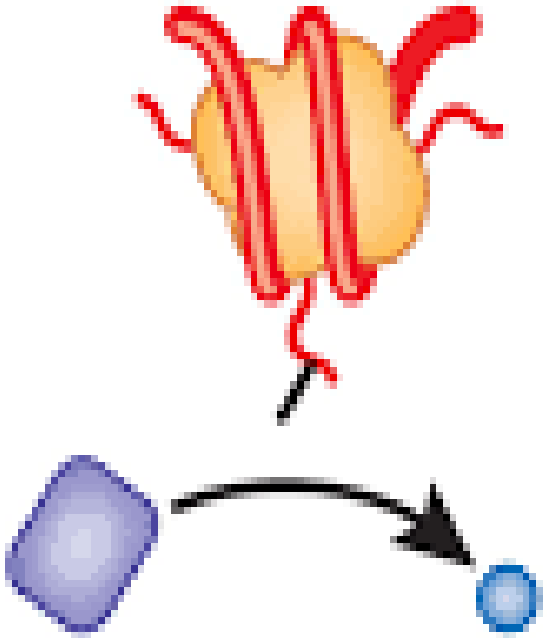
Surely, we must do better than this with all of the ***intelligence of genetics and epigenetics***. Yet, institutionalized medicine continues to inform us that personalized medicine is simply a better ***genetic matching of target specific drugs*** and better ways of matching chemotherapy, radiation and surgery.

Writing



Acetylases,
methylases,
phosphorylases

Erasing

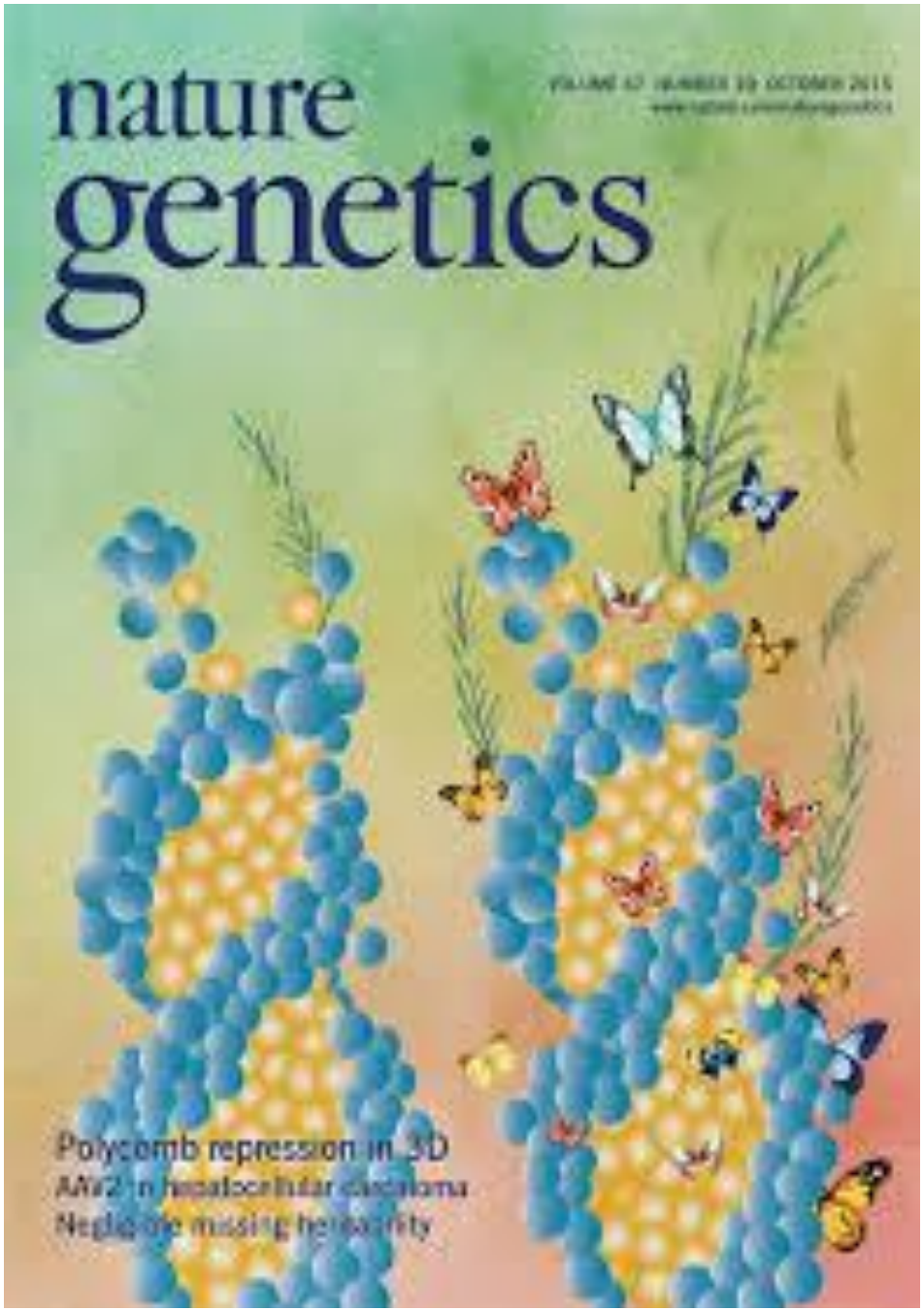


Deacetylases,
demethylases,
phosphatases

Reading

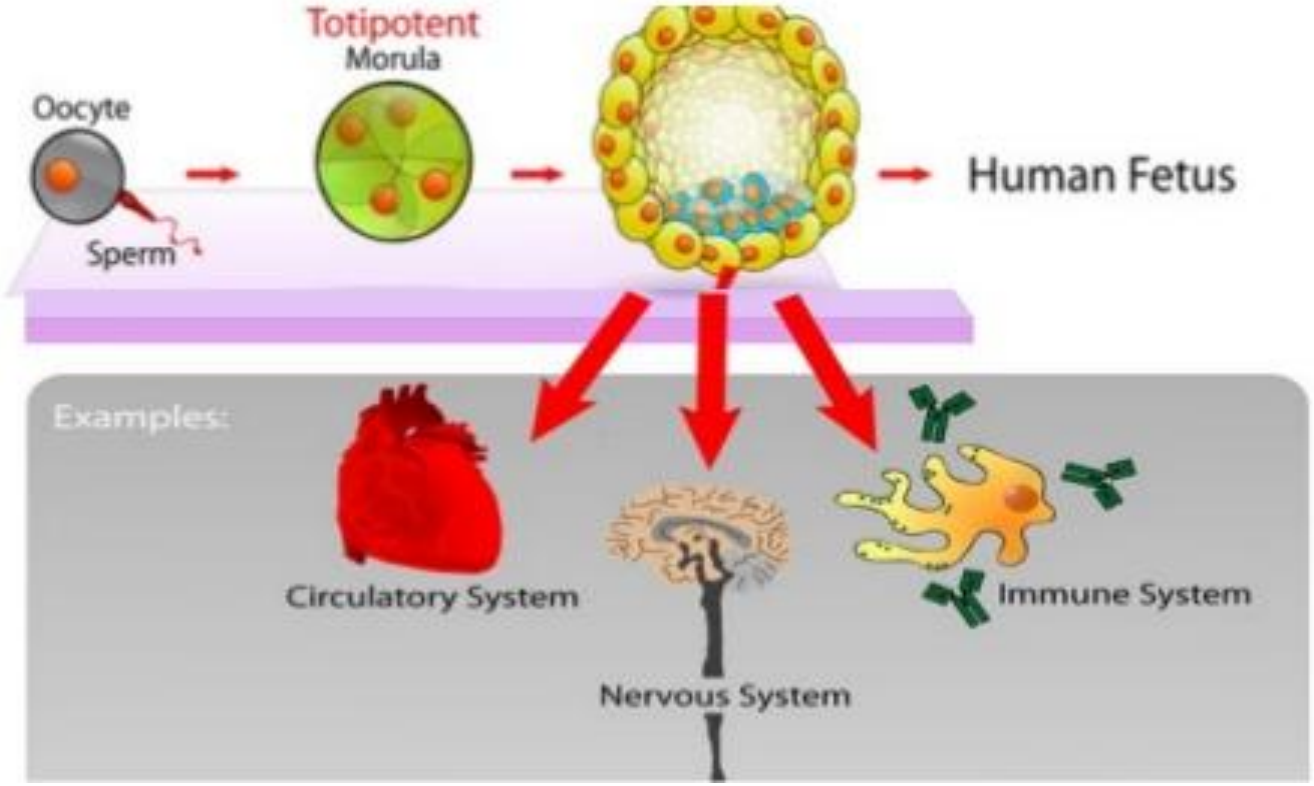
Bromodomain,
chromodomain,
PHD finger,
WD40 repeat

- Applications that inhibit the *accelerated aging process*, inhibiting the negative expressions resulting in *mutations* that cause serious disease and enhancing the expressed health and survival of healthy human cells and their *vital function* is where the personalized value is.



Definition of Epigenetics

- **Changes in gene expression or phenotype that don't involve changes to the DNA sequence**[1]
- **Its defined as heritable changes in gene activity and expression that occur without alteration in DNA sequence** [2]



OR: Non-genetic events which result in stable and heritable gene expression patterns

Epigenetics is simply a science of programming and such programming could contain accelerated enhancing or correcting value or unfavorable glitches.

علم التخلق هو مجرد علم البرمجة و هذه البرامج يمكن أن تحتوي على تسارع تعزيز أو تصحيح قيمة أو مواطن الخلل غير المواتية .

Example: Obesity

- Excess fat accumulation occurs when energy intake exceeds energy expenditure, although individuals *respond differently* to this imbalance owing to *genetic predisposition*.

- The goal of obesity research is to elucidate pathways and mechanisms that control obesity and to improve prevention, management and therapy.

Here we review recent advances in identifying factors contributing to obesity susceptibility. We focus on:

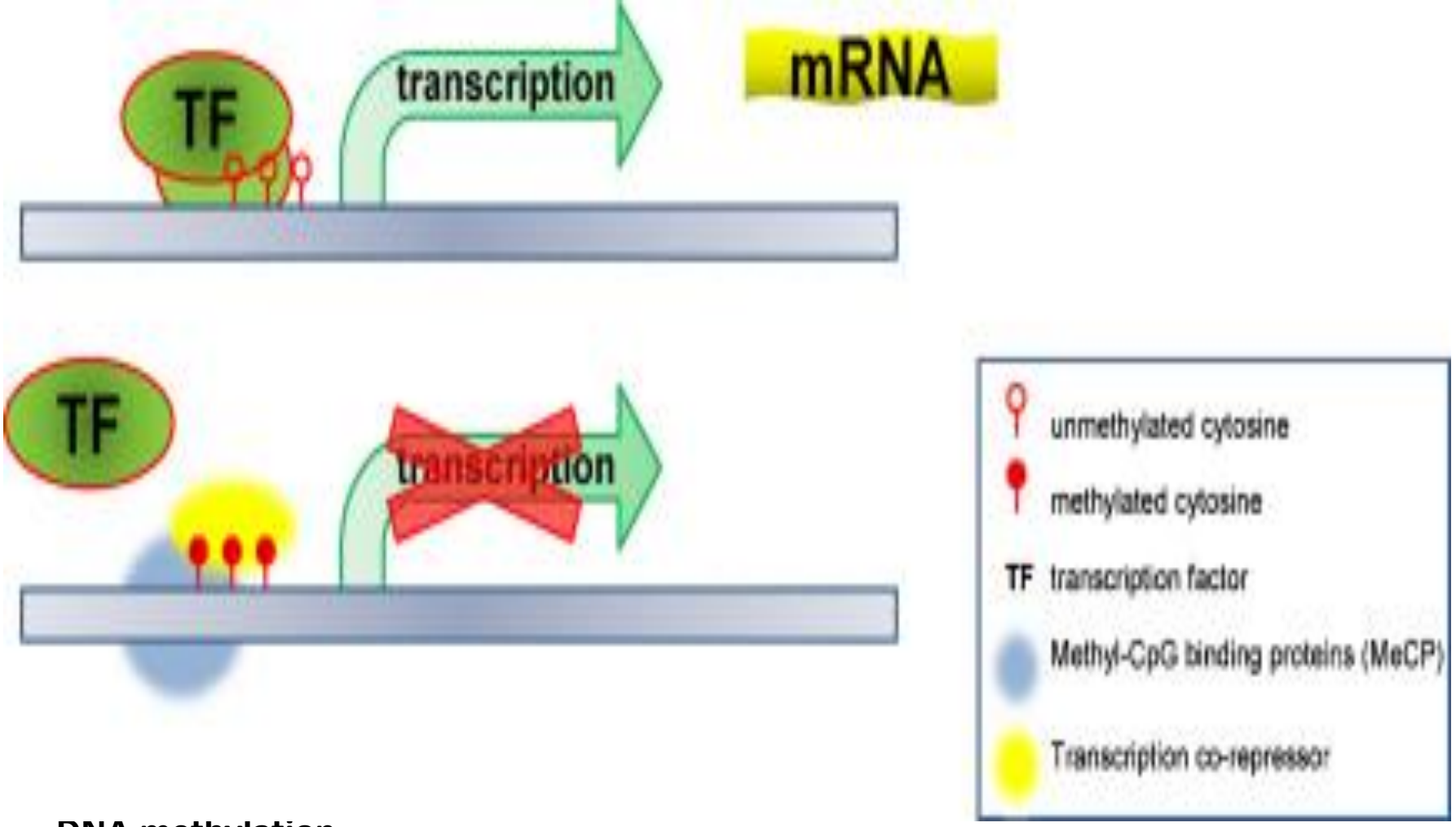
(a) Recent successes in identification of genetic variation affecting obesity trait susceptibility;

(b)emerging evidence connecting epigenetic (heritable changes which affect gene function but do not modify DNA sequence) events with obesity.

Mediators of genomic imprinting:

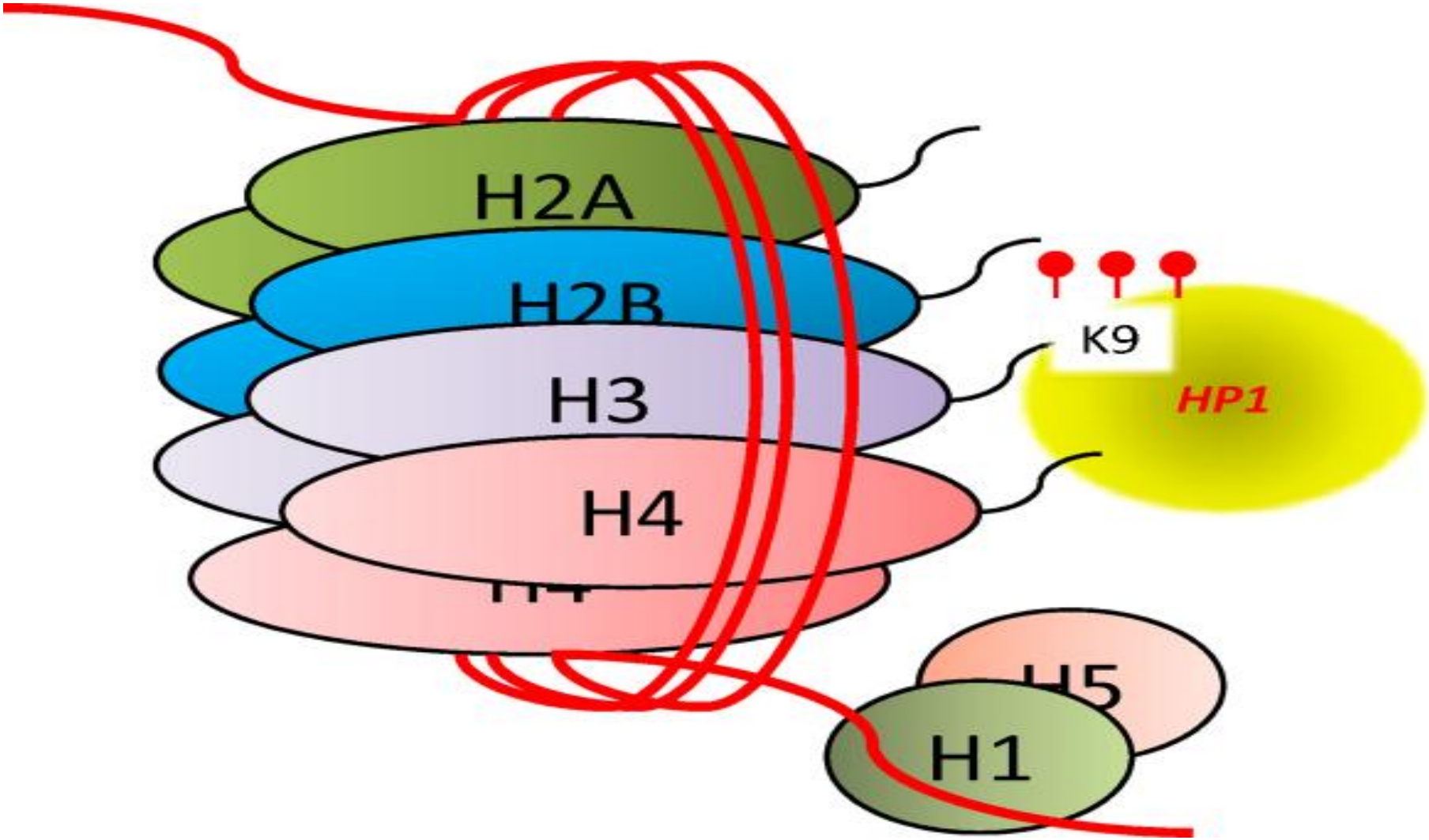
1- DNA methylation

2- Histone modification



(١) DNA methylation

Genomic imprinting is mediated by DNA methylation as exemplified in the *H19* and *IGF2* loci. Methylation is a widespread feature of the genome, and is obtained through the addition of a methyl group (CH3) to a cytosine positioned next to a guanine nucleotide (CpGs), usually in regions with a high presence of CpG dinucleotides (>60%). Methylation in a promoter region results in the repression (silencing) اسكات of gene expression this effect may be achieved by a number of mechanisms including: obstructing access to transcription factors/activators and recruitment of co-repressors (like histone deacetylases) which alter chromatin structure resulting in failure to initiate transcription



(٢)Histone modification. This simplified diagram of a nucleosome shows a histone octamer “bead” surrounded by a DNA strand and try-methylation at lysine-9, this kind of modification exemplifies modifications found at promoter regions of silenced genes.

Functional and Integrative Dynamics

There are six functional dynamics namely genes, metabolism (methylation), immunity, inflammation, detoxification and hormones (endocrine and neuroendocrine). The seventh dynamic is an integrative dynamic that addresses the sensitivities and vulnerabilities that are observed in the six functional dynamics and a plan is then generated.

هناك ستة وظائف ديناميكية وهي الجينات ، والتمثيل الغذائي (مثيلة) ، والحصانة ، والتهاب ، وإزالة السموم والهرمونات (الغدد الصماء و الغدد الصم العصبية) . ديناميكية السابعة هي ديناميكية متكاملة تعالج حساسيات ونقاط الضعف التي لوحظت في ديناميكيات الوظيفية الستة و يتم إنشاء خطة الجين .

The Common Problem that impact health and epigenetic programming.

- Protecting healthy DNA (Methylation disturbances)
- Inhibited cellular energetics (metabolism and mitochondrial function)
- Deprivation of nutrition leading macro and micronutrient depletion
- Exposure to toxic agents and decreased ability to detoxify
- Innate immune defense slow to respond or under extreme stress
- Increased vulnerability for autoimmune reactions
- Increased vulnerability for prolonged inflammation
- Enzyme deficiencies that impair digestion, balanced metabolism and cell protection
- Cardio-methylation protection and lipid metabolism disturbances
- Body clock, stress maladaptation and neurotransmitter disturbance
- Reduced protection of the brain and CNS leading to neurodegenerative change
- Mood fluctuations caused by neuroendocrine shifts

وراثية وجينية = Genetic and Epigenetic

- These are some of the crucial factors that have adverse influence on epigenetics and cause unfavorable or “bad” mutations. Bad mutations are not necessarily in the form of SNP’s (Single Nucleotide Polymorphisms). SNP’s may not have any associated negativity and may demonstrate aspects of favorable adaptation.
- Uncorrected factors like above will increase bad signaling and harm DNA.
- There is evidence that point in the direction of favorable activity associated with the SNP occurring for positive benefit and protective adaptation.

Bad Mutations

- Vulnerable DNA causes epigenetic stress and is the culprit leading to unfavorable mutations and initiating oncogene activation and expression. Simply, vulnerable DNA is DNA that has been hit by an adverse force, exposure, cell environment stress and / or process of aging. Vulnerable DNA can be evident at birth of a new cell line. In other words, cell progeny can have vulnerable or “bad” DNA from the start.

- Often, these cells that express “bad,” DNA are labeled with antigens that demonstrate movement toward altered cell expressions that can initiate disease and premature aging. Cells that have vulnerable or “bad” DNA are prime to cause cancerous mutations if permitted to live, replicate and expand.

Cell Protection Basics

- When a cell is exposed to harm, vital components of the cell including the nucleus, mitochondria, endoplasmic reticulum, Golgi and cell membrane are stressed. The nucleus is the command center, the mitochondria is the power house, the endoplasmic reticulum is the factory for protein manufacturing directed by the nucleus and powered by the mitochondria, the Golgi is the shipping and distribution center. DNA is the foundation of it all.

- Bad DNA! Bad Cell!, BAD Proteins!, Bad Shipping and Distribution!, No Protection!, Faulty and Disastrous Function! Bad Offspring! I'm sure you get the picture. Human chromosomes house all of the genes. Chromosomes can undergo remodeling that is either favorable or unfavorable. The process of this remodeling is known as telomere maintenance. Telomeres can either elongate or can become stunted. The process is directed by DNA sequencing.

Diet

Psychological state

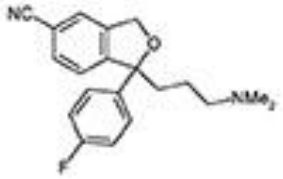
Diurnal/Seasonal correlations

Social Interactions

Disease exposure

Alternative medicine

Toxic Chemicals



Therapeutic Drugs

Drugs of Abuse

Microbiome

Exercise

Financial Status

EPIGENETIC MODULATION

GENETIC

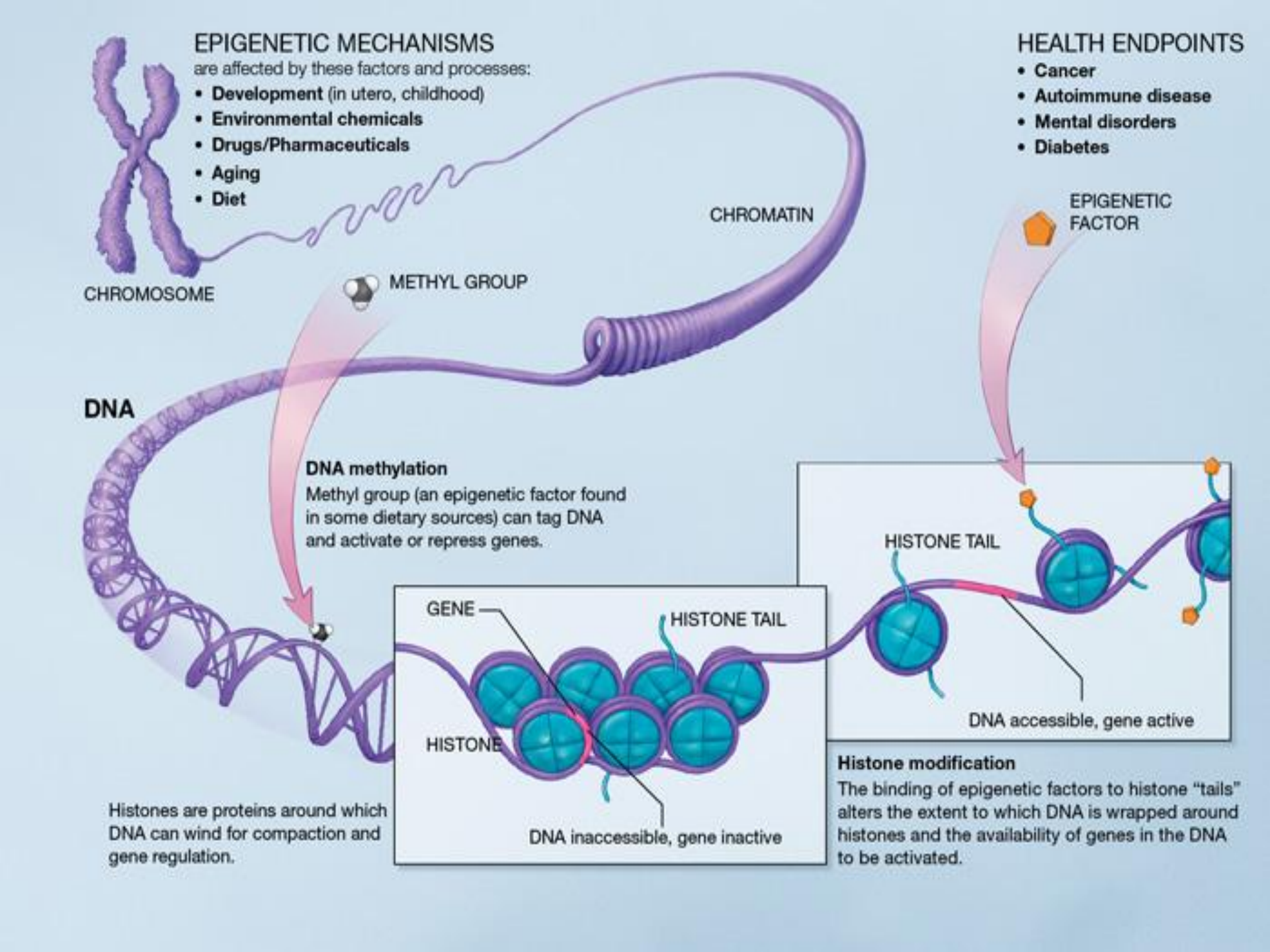
MODULATION

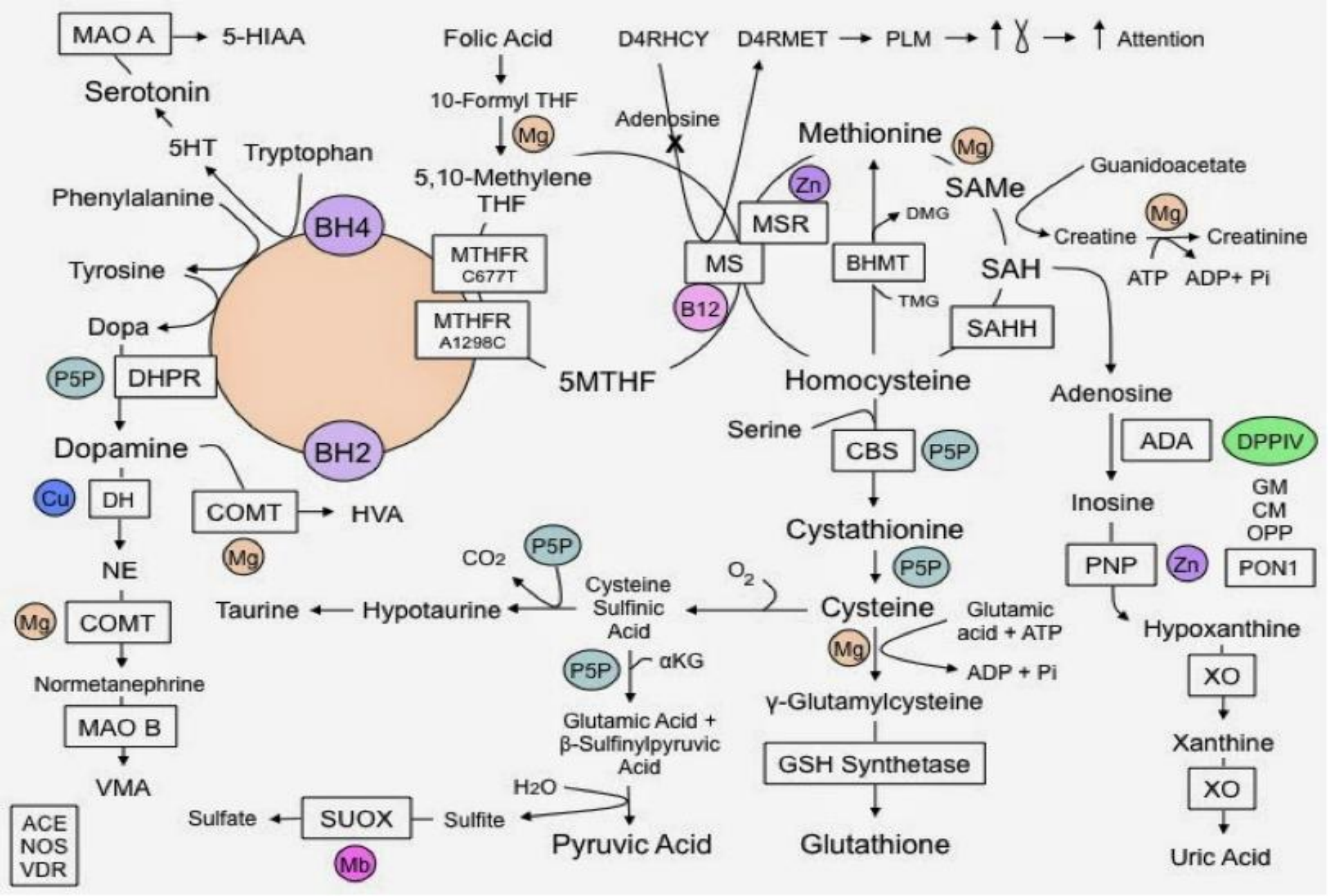
Cancer Cells, DNA and Telomeres

- Altered DNA sequencing leads to cancer mutations. Cancer cells reproduce at a furious pace. Telomere maintenance is the process by which they do this, they quickly reach the ends of their telomeric “ropes,” and need to find a way to lengthen them again in order to keep going.
- Successful cancer cells are the ones that have evolved mutations that exploit one of the cell’s two systems for renewing telomeres: either a primary system called telomerase, or in a few cases an “alternative” system appropriately called Alternative Lengthening of Telomeres (ALT). If a nascent cancer can’t find a way to seize hold of the telomerase-lengthening machinery, their telomeres will run down, their chromosomes will fray, and the cell will be destroyed before it can kill us.

Basics on DNA Methylation Hypomethylation and Hypermethylation

- Simply, methylation is the mechanism by which DNA is in homeostasis (healthy sequencing) or in harmful dysfunctional sequencing. **Hypomethylation** (decreased or low) and **Hypermethylation** (increased or high) are the two extremes that initiate harmful consequences upon DNA and ultimately lead to and result in unfavorable conditions and change in DNA sequencing performance.
- Ultimately, this leads to unfavorable function and potentially bad signals altering cell health and survival, predisposing new cell lines to “bad” mutations.


EPIGENETIC MECHANISMS
are affected by these factors and processes:
• Development (in utero, childhood)
• Environmental chemicals
• Drugs/Pharmaceuticals
• Aging
• Diet
HEALTH ENDPOINTS
• Cancer
• Autoimmune disease
• Mental disorders
• Diabetes
CHROMOSOME
CHROMATIN
METHYL GROUP
EPIGENETIC FACTOR
DNA
DNA methylation
Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.
GENE
HISTONE TAIL
HISTONE
DNA inaccessible, gene inactive
HISTONE TAIL
DNA accessible, gene active
Histones are proteins around which DNA can wind for compaction and gene regulation.
Histone modification
The binding of epigenetic factors to histone "tails" alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.

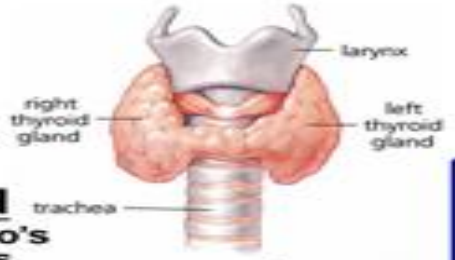


Methylation is not a simple process it is set by your genetics and epigenetics!

- Epigenetics can be used positively in personalized health and medicine to design more intelligent strategies to encourage favorable improvements regarding gene expressions. Currently, westernized medicine (institutionalized) focuses in upon the diagnostic and risk values rather than the personalized applications.

- It is crucial to know that dynamic alterations affecting the sequencing of DNA within the cell can initiate either protective or damaging action. DNA methylation is an example of such a process.

Tissues of The Body Affected By Autoimmune Attack



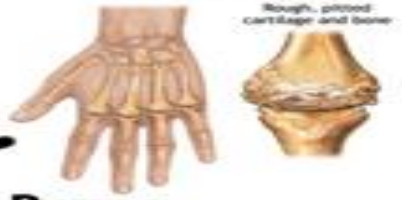
Thyroid
Hashimoto's Thyroiditis
Graves Disease

Triggers
1. Stress
2. Hormones
3. Metals
4. Food Antigens
5. Pesticides & Poisons

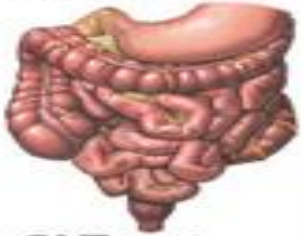
Brain
Multiple Sclerosis
Autism
Guillain-Barre Syndrome
Psychological

Blood
Leukemia
Lupus
Hemolytic
Dysglycemia

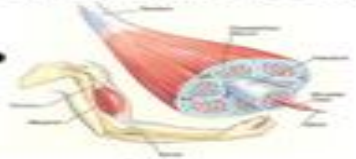
Autoimmune Disorder



Bones
Rheumatoid Arthristis
Ankylosing Spondylitis
Polymyalgia Rheumatica



GI Tract
Celiac
Chron's Disease
Ulceratic Colitis

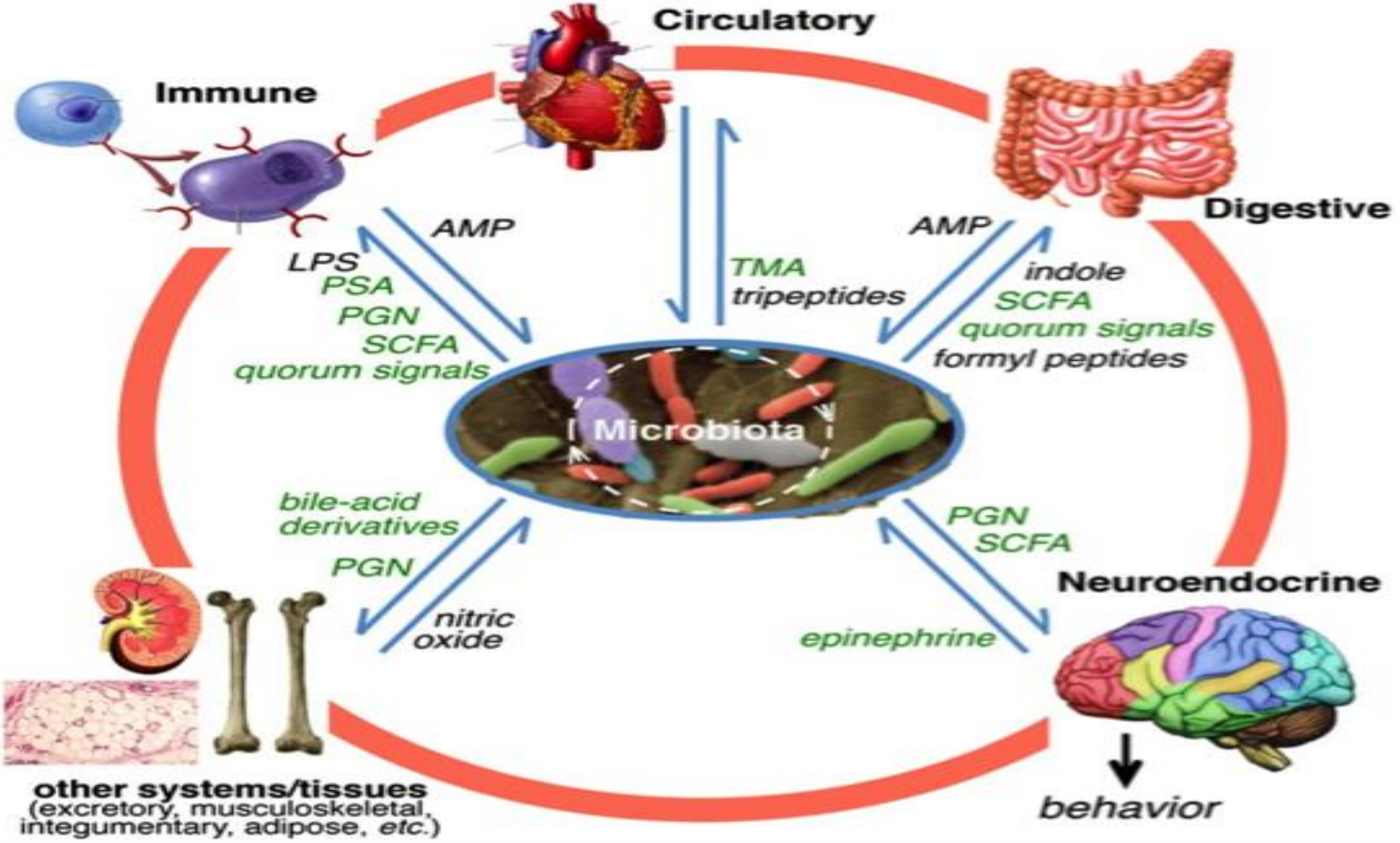


Muscles
Fibromyalgia
Muscular Dystrophy

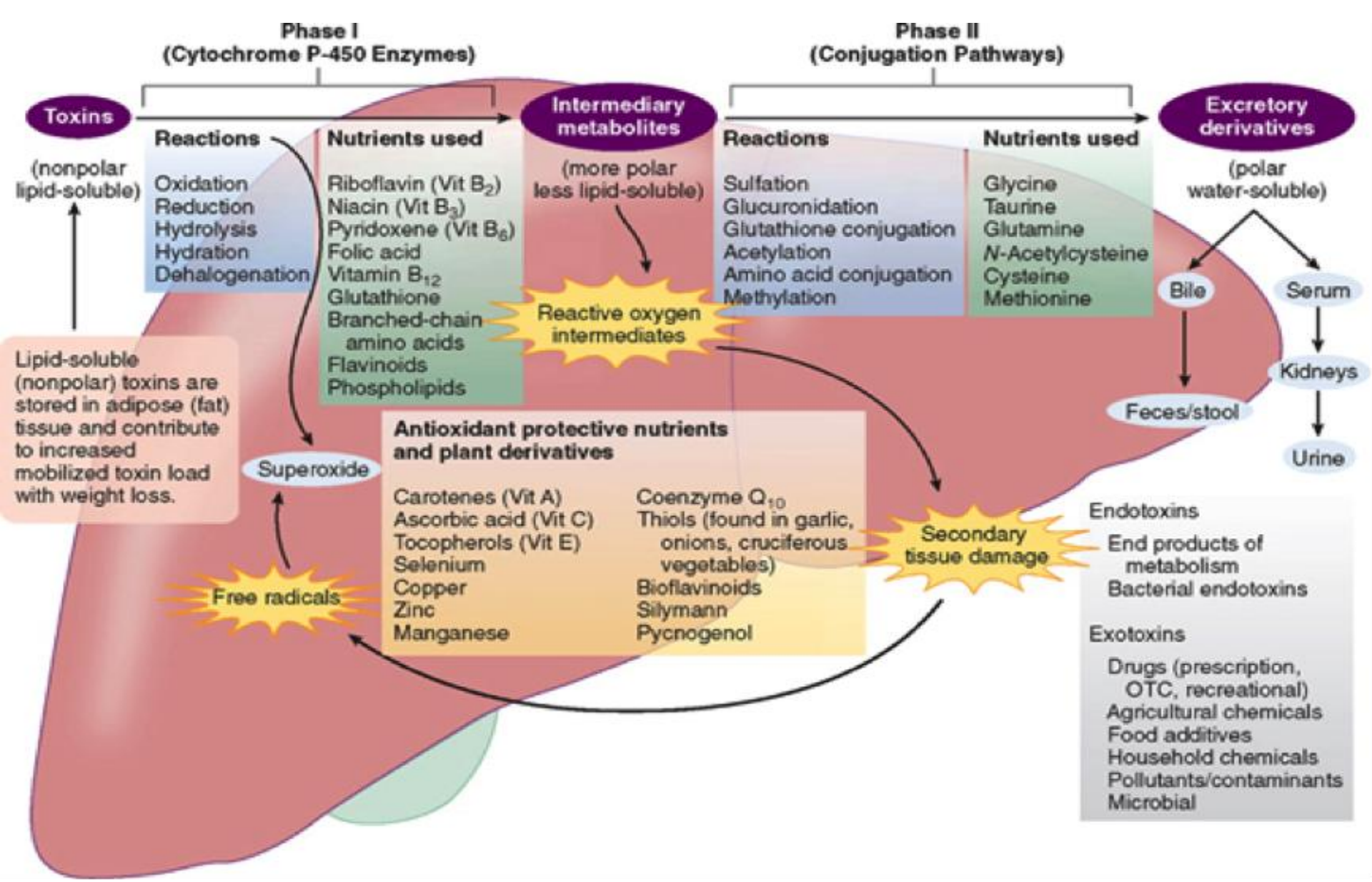
Nerves
Peripheral Neuropathy
Diabetic Neuropathy

Lungs
Asthma
Wegener's Granulomatosis

Skin
Eczema
Psoriasis
Scleroderma
Vitiligo

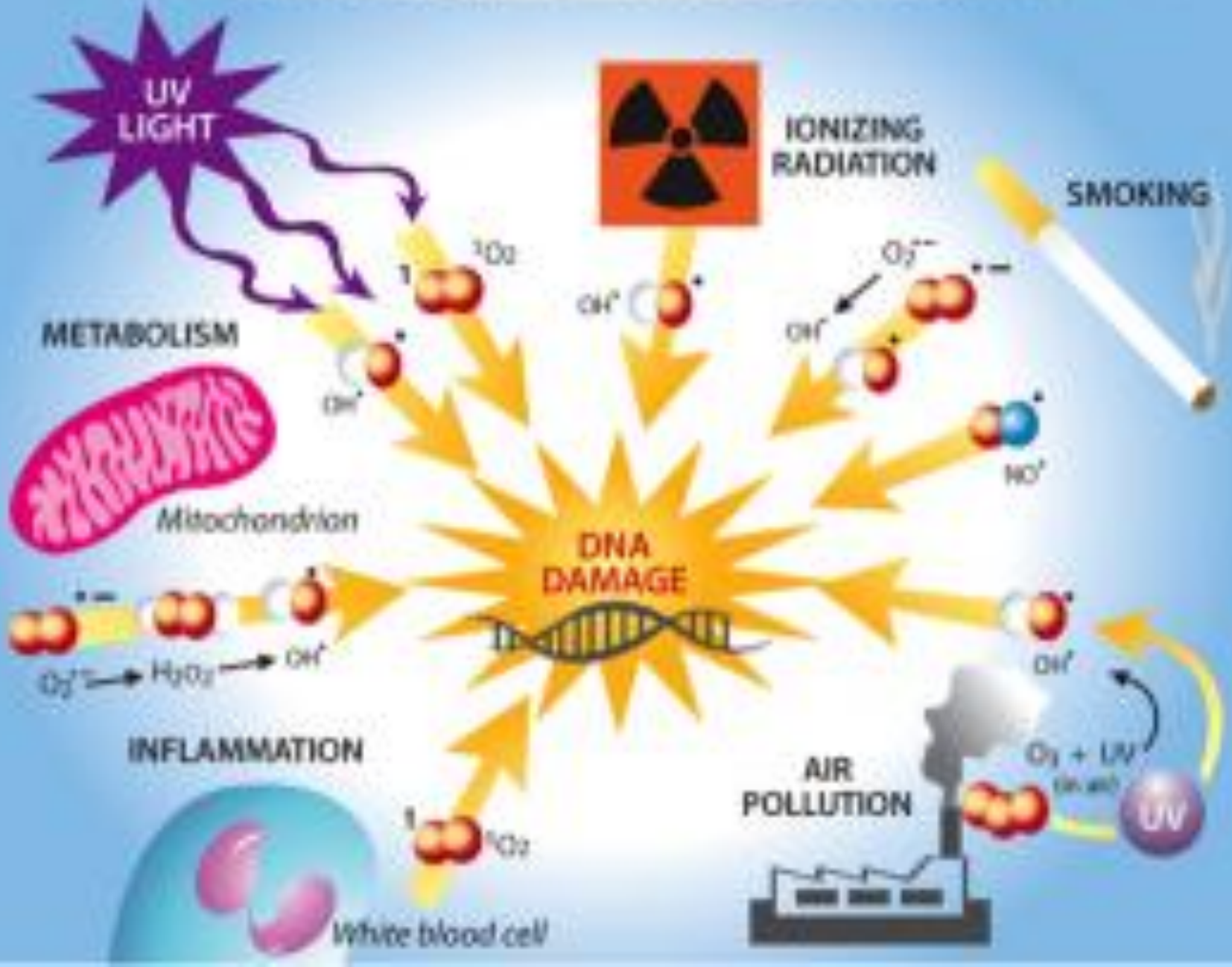


- *This figure demonstrates the influence of virobiota and microbiota have on immunity, digestion, brain function, heart and circulation, musculoskeletal and skin. Disturbances in this balance can lead to adverse epigenetic signaling, autoimmunity and chronic inflammatory changes that can contribute to degenerative disease, cancer and premature aging.*



This figure demonstrates the exposures, detoxification path and nutrients involved in elimination and protection of the body. Efficient detoxification ensures enhanced epigenetic signals involved in protective adaptation.

FORMATION OF FREE RADICALS



ANTIOXIDANTS

Enzymatic antioxidants

Superoxide dismutase (SOD)

Catalase (CAT)

Glutathione peroxidase (GPx)

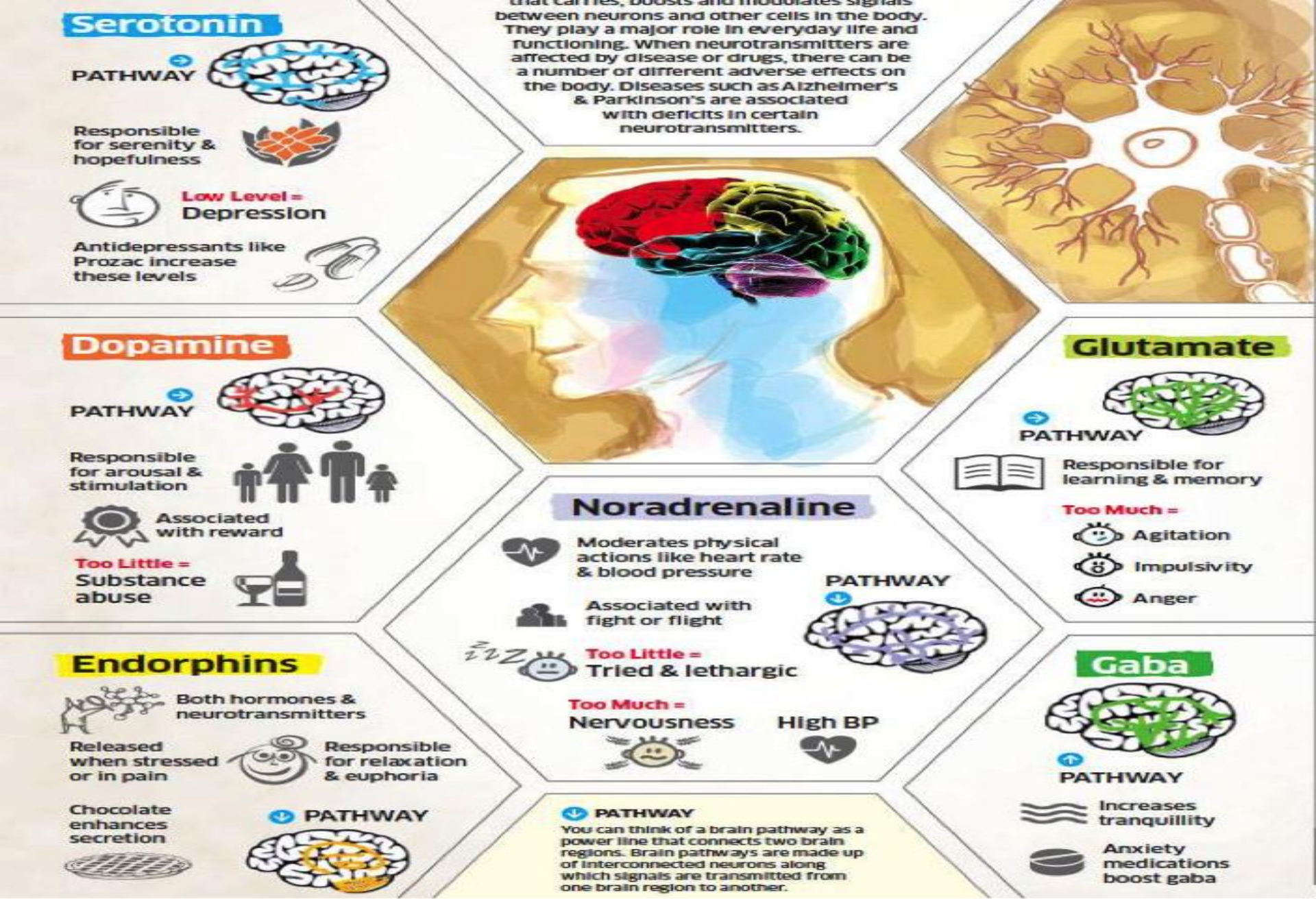
Glutathione reductase (GR)

Glutathione-S-transferase (GST)

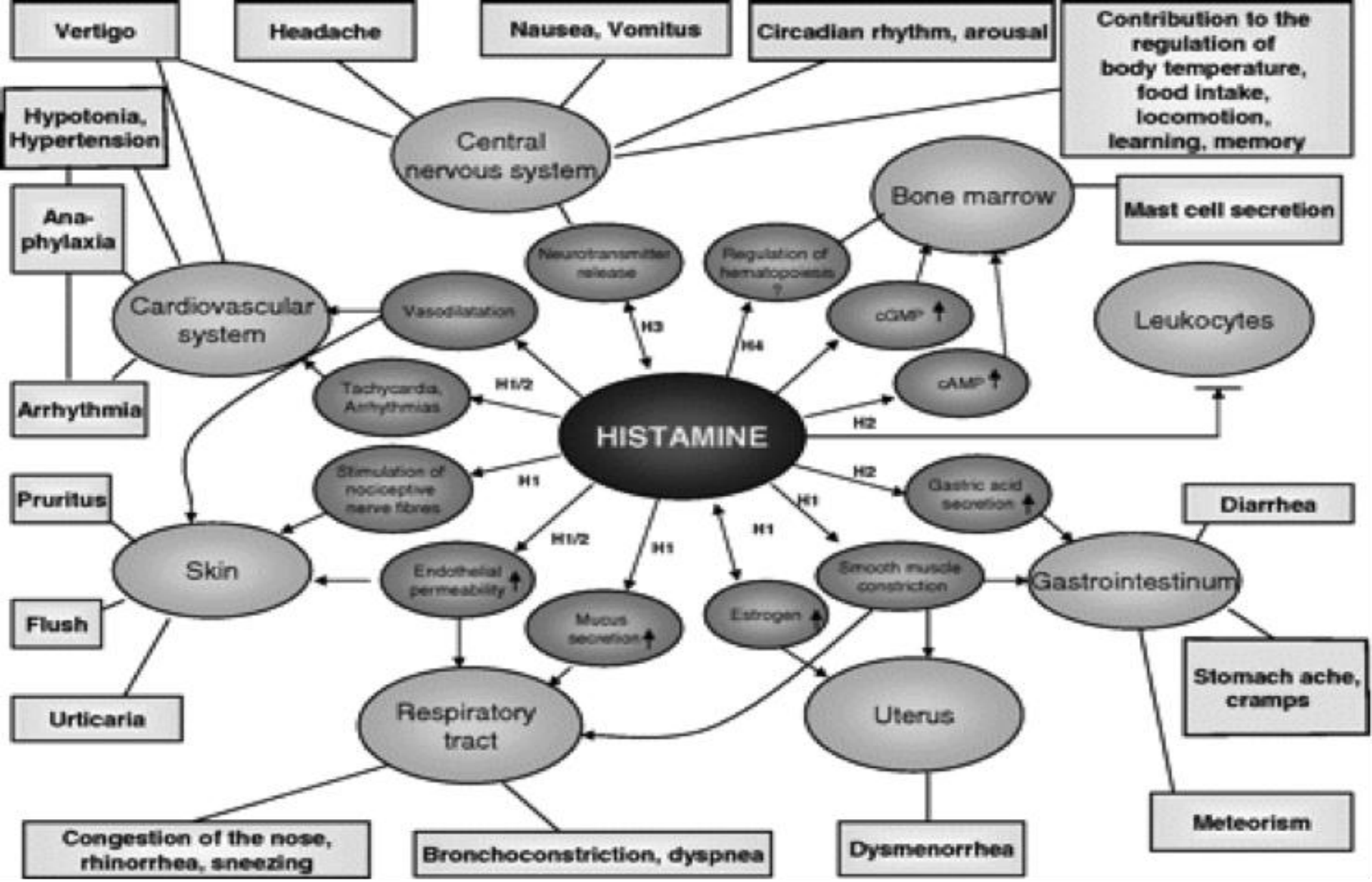
Non-enzymatic antioxidants

Vitamin E	Flavonoids	Albumin	Haptoglobin
Vitamin C	Melatonin	Glutathione	Ceruloplasmin
Vitamin A	Uric acid	Ubiquinone	Transferrin
α-Lipoic acid	Bilirubin	Selenium	Lactoferrin

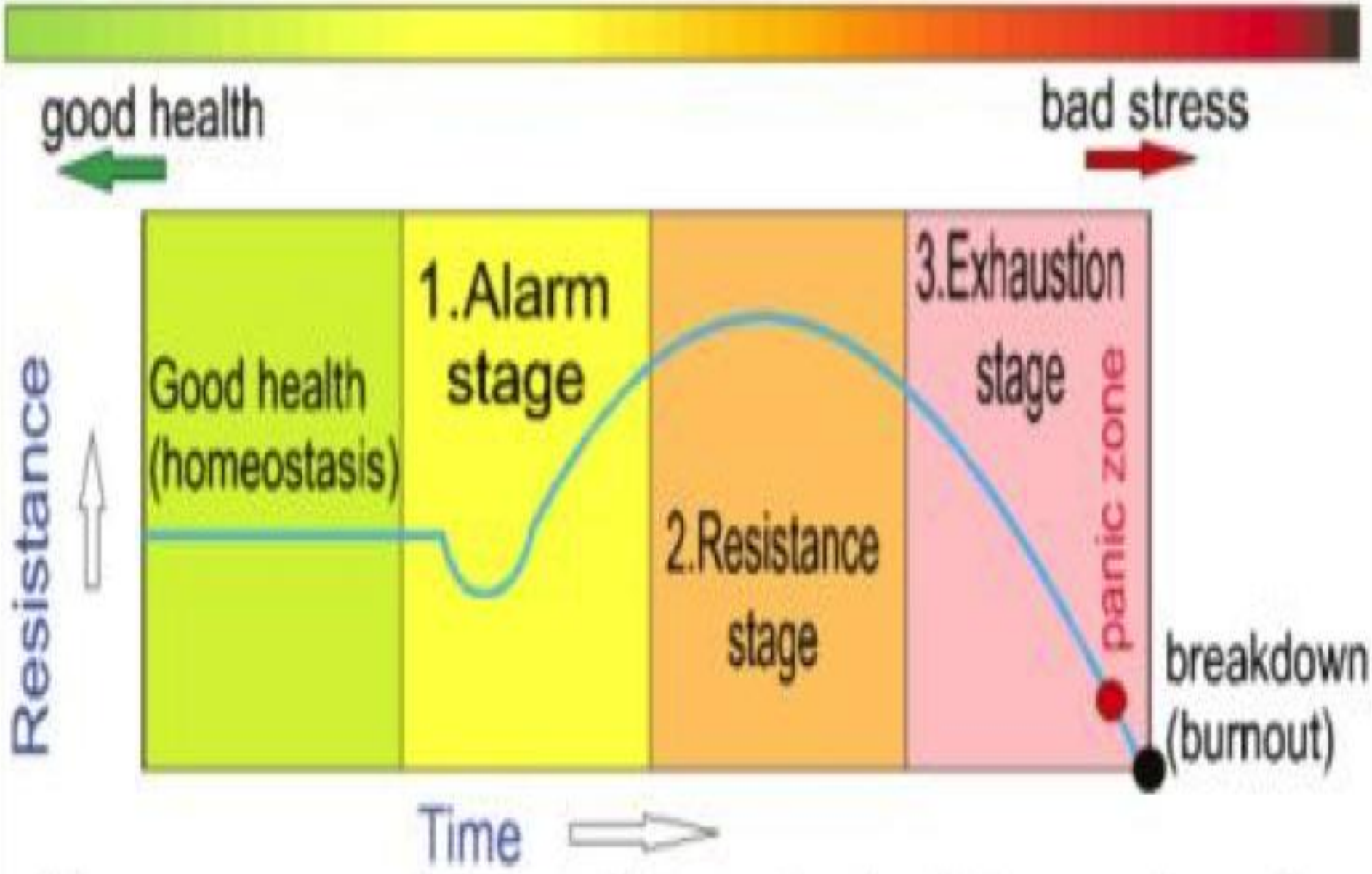
- *Both of these diagrams why the need for specific replacement of antioxidant and better pro-oxidant defenses are crucial to cellular defenses and epigenetic signals that enhance protection.*



Neurotransmitter and hormone relationships are crucial to keeping complete brain and body balance and are integrally involved in favorable epigenetics.



Histamine is involved in many interactions in many systems of the body. As you can see from above the brain and central nervous system is very sensitive to histamine and many symptoms are associated with it.



Stress curve and phases (General adaptation syndrome)

Closing Thoughts

- With increasing knowledge in genetics and epigenetics there will be more precise monitoring and solutions in the future. This is the most powerful direction in health and wellness an individual can pursue.

- Personalized genetics and epigenetics are not a thing of the future it is now.