MECHANISMS OF TOXICITY - OXIDATIVE STRESS - METHODOLOGICAL ASPECTS OF OXIDATIVE STRESS AND ANTIOXIDANT ACTIVITY ASSESSMENT

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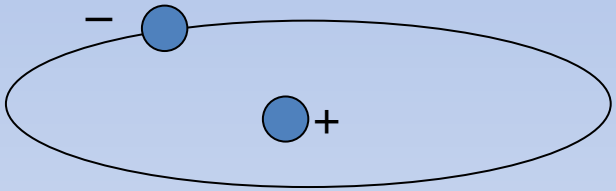
JAMES BOND AND FREE RADICALS

James Bond and Free Radicals.flv

Free Radicals

- **A free radical is an atom (or group of atoms) capable of independent existence (hence the term “free”) that contains one or more unpaired electrons.**

- **Free radicals are**
  - **small**
  - **diffusible**
  - **unstable**
  - **very reactive**
  - **short-lived**



Free Radicals

- **Free radicals may be electrically neutral or either positively or negatively charged.**
- **They attack sites of increased electron density such as:**
  - **the nitrogen atom present in proteins and DNA**
  - **carbon-carbon double bonds present in polyunsaturated fatty acids and phospholipids**
- **Produce additional free radical, often reactive intermediates.**
- **Free radicals can participate in chain reactions in which a single free radical initiation event can be propagated to damage multiple molecules.**

Common Notations and Abbreviations for Free Radicals

Species Systematic	IUPAC Name	Alternative/Comments
O^{-}	oxide(1-)	hydroxyl radical without proton
$O_2^{\bullet -}$	dioxide(1-)	superoxide
O_3	trioxygen	ozone
O_3^{-}	trioxide(1-)	ozonide
$HO^{\bullet}$	hydroxyl	not hydroxy, hydroxide is OH^{-}
$HO_2^{\bullet}$	hydrogen dioxide	hydrodioxyl, or hydroperoxyl, but perhydroxyl does not make sense
HO_2^{-}	hydrogen dioxide(1-)	hydrogenperoxide(1-)
H_2O_2	hydrogen peroxide	
$RO^{\bullet}$	alkoxyl	not alkoxy
$ROO^{\bullet}$	alkyldioxyl	alkylperoxyl not peroxy
ROOH		alkyl hydroperoxide
$ONOO^{-}$	oxoperoxonitrate (1-)	peroxynitrite
ONOOH	hydrogen oxoperoxonitrate	peroxynitrous acid
$NO^{\bullet}$	nitrogen monoxide	nitric oxide

Reactive Oxygen Species (ROS)

- **Reactive oxygen species (ROS) are free radicals containing oxygen.**
- **ROS include also non-radical species which can lead to the production of ROS (e.g. H_2O_2).**

Oxygen and Reactive Oxygen Species (ROS)

- **Oxygen, or molecular oxygen, is vital for survival of all aerobic organisms.**

- **During aerobic metabolism, in normal cells, 30–32 molecules of adenosine triphosphate (ATP) are generated from one molecule of oxygen. During this process, oxygen is reduced into water (4 electron reduction).**

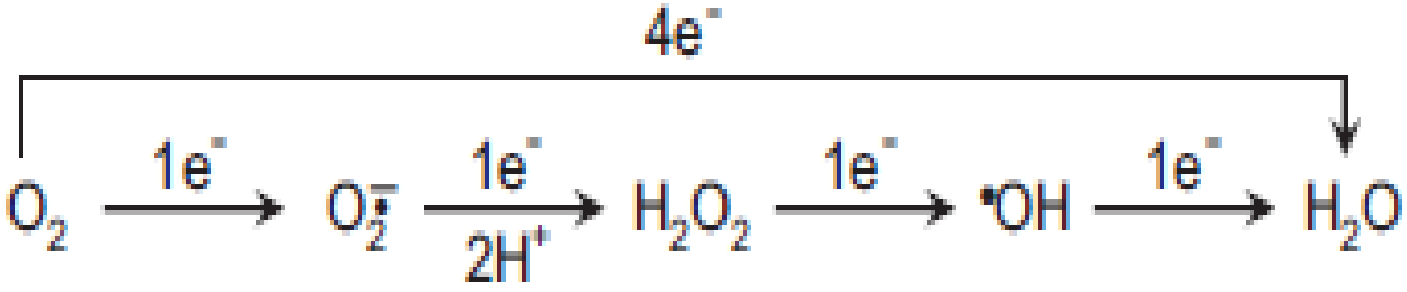


Fig. 1. Sequential reduction of O_2 to H_2O.

Oxygen and Reactive Oxygen Species (ROS)

- **In a perfect world, cells will use oxygen to produce ATP and water without any toxic byproducts or ROS.**
- **However, due to damage to mitochondria, in pathophysiological conditions or during mitochondrial dysfunction, the electron-transport mechanism in the mitochondrial respiratory chain is impaired.**
- **This leads to reactive oxygen species formation (e.g., superoxide anion) from one-electron reduction of oxygen.**

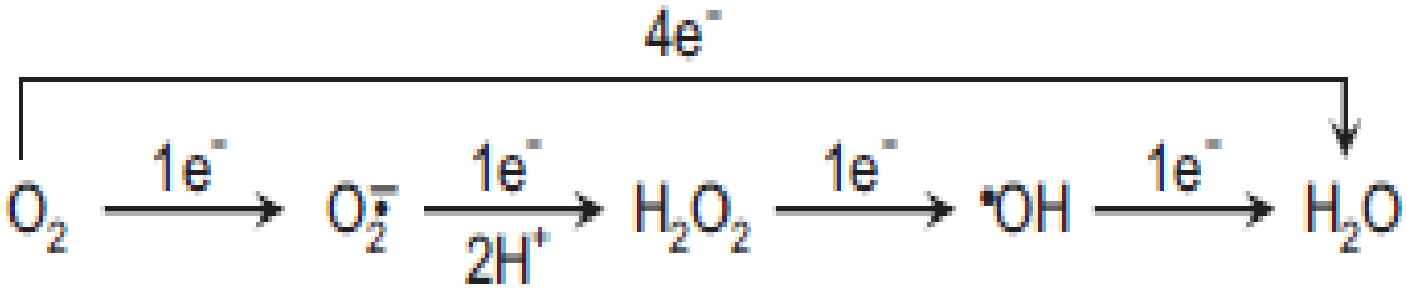


Fig. 1. Sequential reduction of O_2 to H_2O.

ROS

- Superoxide ($O_2^{\bullet -}$) is a free radical (species with a single electron).

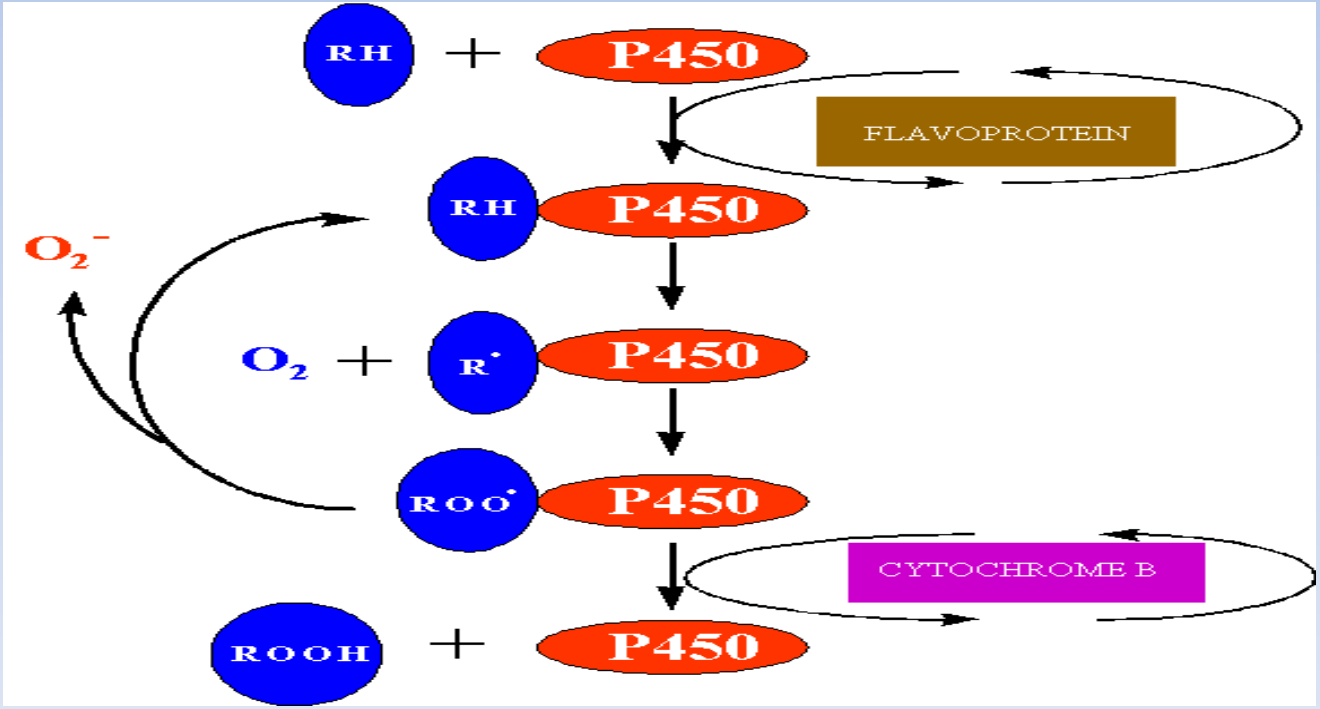
Sources of Superoxide Radical

The following table lists the most important reactions within the cell that generate superoxide anion ($O_2^{\cdot -}$).

Source	*Pathophysiological Significance*
• *Enzymic reactions*	
- xanthine oxidase	Intestinal ischemia/reperfusion
- NADH oxidase	Present in leukocytes: bactericidal activity
- NADPH-cytochrome P450 reductase	
• *Cellular sources*	
- leukocytes and macrophages	Bactericidal activity
- mitochondrial electron transfer	
- microsomal monooxygenase	
• *Environmental factors*	
- ultraviolet light	
- X rays	
- toxic chemicals	
- aromatic hydroxylamines	
- aromatic nitro compounds	
- insecticides, such as paraquat	
- chemotherapeutic agents, such as quinones	

Sources of superoxide radical

- Cytochrome P450 reacts first with its organic substrate, RH.
- The complex is reduced by a flavoprotein to form a radical intermediate that can readily react with triplet oxygen because each has one unpaired electron. This oxygenated complex may be reduced by cytochrome b or occasionally the complex may decompose releasing superoxide radical.



Sources of Hydroxyl Radical

•Hydrogen peroxide (H_2O_2) is not a free radical, but is a precursor of free radicals.

• UV radiation causes the hemolytic cleavage of the oxygen-oxygen of hydrogen peroxide bond to form hydroxyl radicals (OH●).

• Redox metal ions (Fe^{2+} or Cu^{+}) react with hydrogen peroxide to generate hydroxyl radicals (OH●) (the Fenton reaction).

$$Fe^{++} + H_2O_2 \rightarrow Fe^{+++} + HO^- + \mathbf{HO^{\cdot}}$$

• In terms of reactivity with biological constituents (nucleic acids, proteins, and lipids), hydroxyl radicals are the most reactive, and the life time of this species in the presence of most biological constituents is extremely short (10^{-9} s).

Free Radicals: Positive Effects

- **The presence of low concentrations of free radicals is important for normal cellular redox status, immune function, and intracellular signalling.**

- **Immune system: neutrophils and macrophages use ROS to destroy engulfed microorganisms. For example, $O_2^{\cdot -}$ radicals are powerful oxidizing agents that degrade microbes.**

- **Can serve as second messengers or modify oxidation-reduction (redox) states.**

- **Involved in some enzyme activation.**

- **Play an essential role in muscle contraction.**

Free Radicals: Negative Effects

- **However, excessive production can provoke inflammation or altered cellular functions through:**
  - **lipid peroxidation**
  - **protein modification**
  - **DNA modification**

- **These effects compromise cell function leading to cell death by necrosis or apoptosis.**

Oxidative stress

- **Oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage.**

- **Disturbances in the normal redox state of cells can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA.**

- **Further, some reactive oxidative species act as cellular messengers in redox signaling. Thus, oxidative stress can cause disruptions in normal mechanisms of cellular signaling.**

- **In humans, oxidative stress is thought to be involved in the development of cancer, Parkinson's disease, Alzheimer's disease,atherosclerosis, heart failure, myocardial infarction, fragile X syndrome, Sickle Cell Disease, vitiligo, autism, chronic fatigue syndrome etc.**

- **Short-term oxidative stress may also be important in enhancement of antioxidant mechanisms by induction of a process named hormesis.**

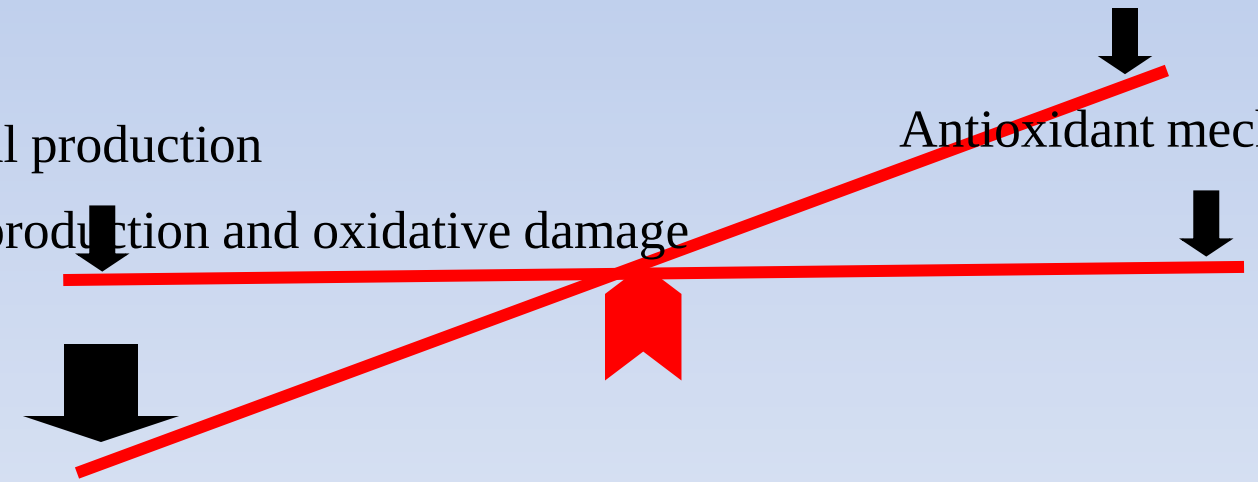
Oxidative stress

Decrease in antioxidant mechanisms

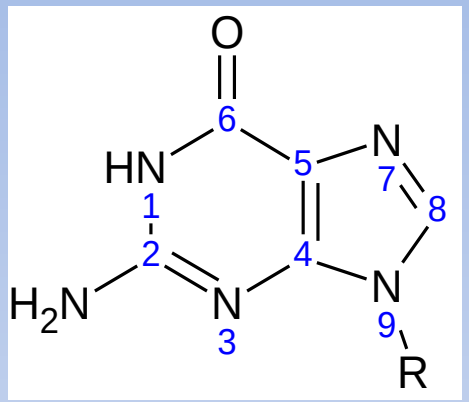
Antioxidant mechanisms

Free radical production

Free radical production and oxidative damage

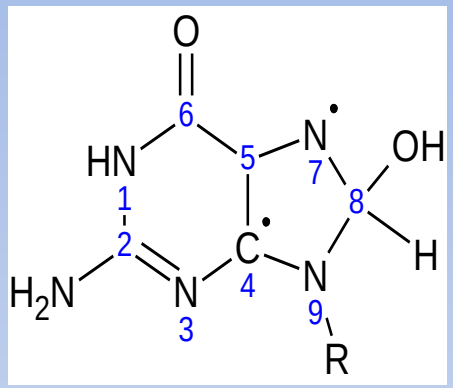


Free radicals can cause damage to DNA

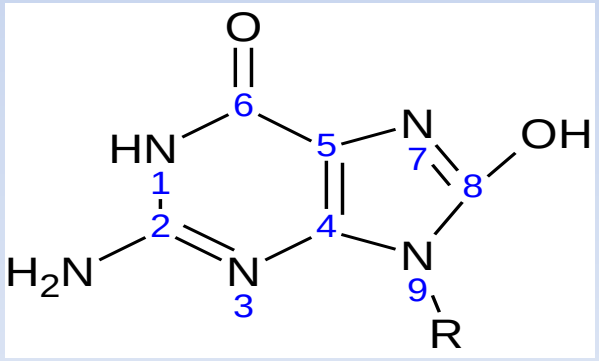


Guanine

OH•



+ e^- + H^+



8-OH-Guanine

OXIDATIVE DAMAGE TO DNA

•Activated oxygen and agents that generate oxygen free radicals, such as ionizing radiation, induce numerous lesions in DNA that cause deletions, mutations and other lethal genetic effects.

• Degradation of the base will produce numerous products, including 8-hydroxyguanine, hydroxymethyl urea, urea, thymine glycol, thymine and adenine ring-opened and -saturated products.

• Characterization of this damage to DNA has indicated that both the sugar and the base moieties are susceptible to oxidation, causing base degradation and single strand breakage.

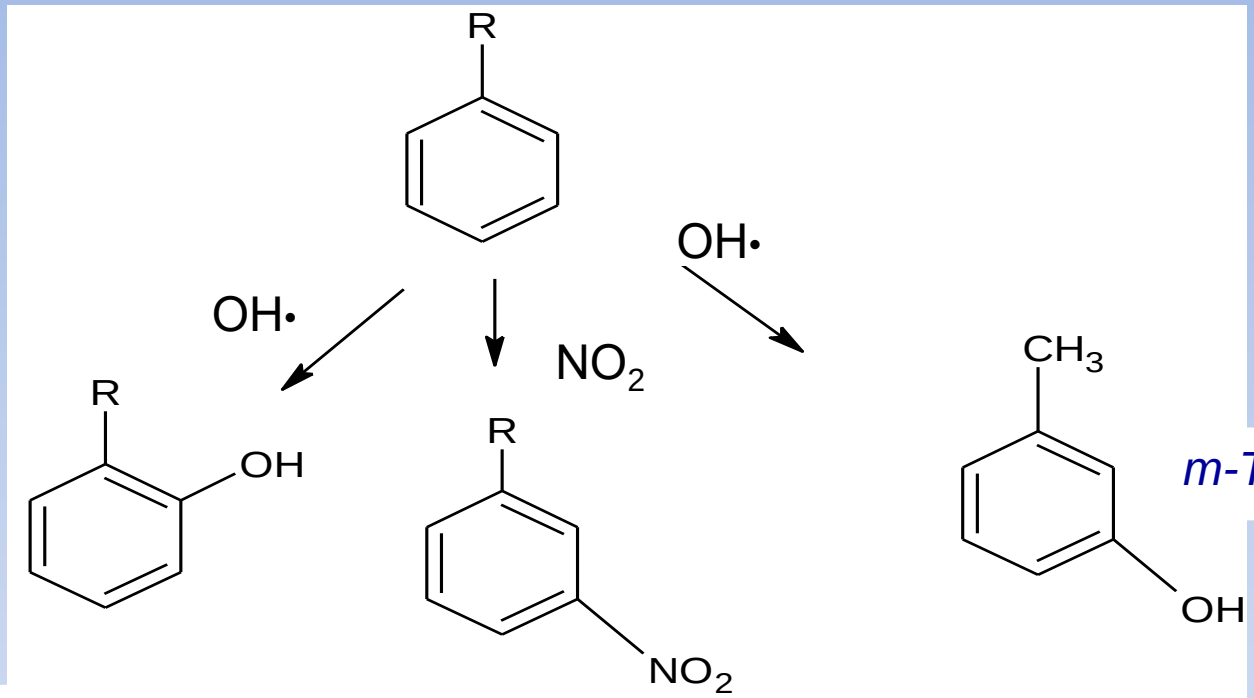
- **8-oxodeoxy- guanosine may act as a promutagen or may alter the methylation of adjacent cytosine, and thus it may lead to cancer development.**

- **ROS have also been shown to activate mutations in human Ras proto-oncogene, and to induce mutation in the p53 tumour-suppressor gene.**

- **The oxidative damage of mitochondrial DNA also involves base modification and strand breaks, which leads to formation of abnormal components of the electron transport chain.**
- **This results in the generation of more ROS through increased leakage of electrons, and cell damage.**
- **Thus, oxidative damage to mitochondrial DNA may promote cancer and aging.**

Free radicals can cause damage to proteins

Phenylananine



o-Tyrosine

3-Nitrophenylananine

m-Tyrosine

OXIDATIVE DAMAGE TO PROTEINS

- **Oxidative attack on proteins results in site-specific amino acid modifications, fragmentation of the peptide chain, aggregation of cross-linked reaction products, altered electrical charge and increased susceptibility to proteolysis.**

- **Sulphur containing amino acids, and thiol groups specifically, are very susceptible sites.**

- **Thus, oxidative attack on proteins destroys the structure, functions of essential proteins and enzymes and whole cell metabolism is blocked.**

- **For example, in the process of cataractogenesis, oxidative modification plays a significant role in cross-linking of crystalline lens protein, leading to high-molecular-weight aggregates, loss of solubility, and lens opacity.**

- **Lipofuscin – an aggregate of peroxidized lipid and proteins – accumulates in lysosomes of aged cells, Alzheimer's disease brain cells, and iron overloaded hepatocytes.**

Lipid peroxidation chain reactions

- **Propagation of one free radical generates another free radical in the neighbouring molecules→chain reaction→destruction of architechture and integrity of the membranes.**

- **Cell membranes, which are structurally made up of large amounts of polyunsaturated fatty acids, are highly susceptible to oxidative attack , and consequently, changes in membrane fluidity, permeability, and cellular metabolic functions are caused.**

- **Moreover, lipid peroxyl radicals react with proteins, and nucleic acids; thereby propagating the transfer of electrons and bringing about the oxidation of substrates.**

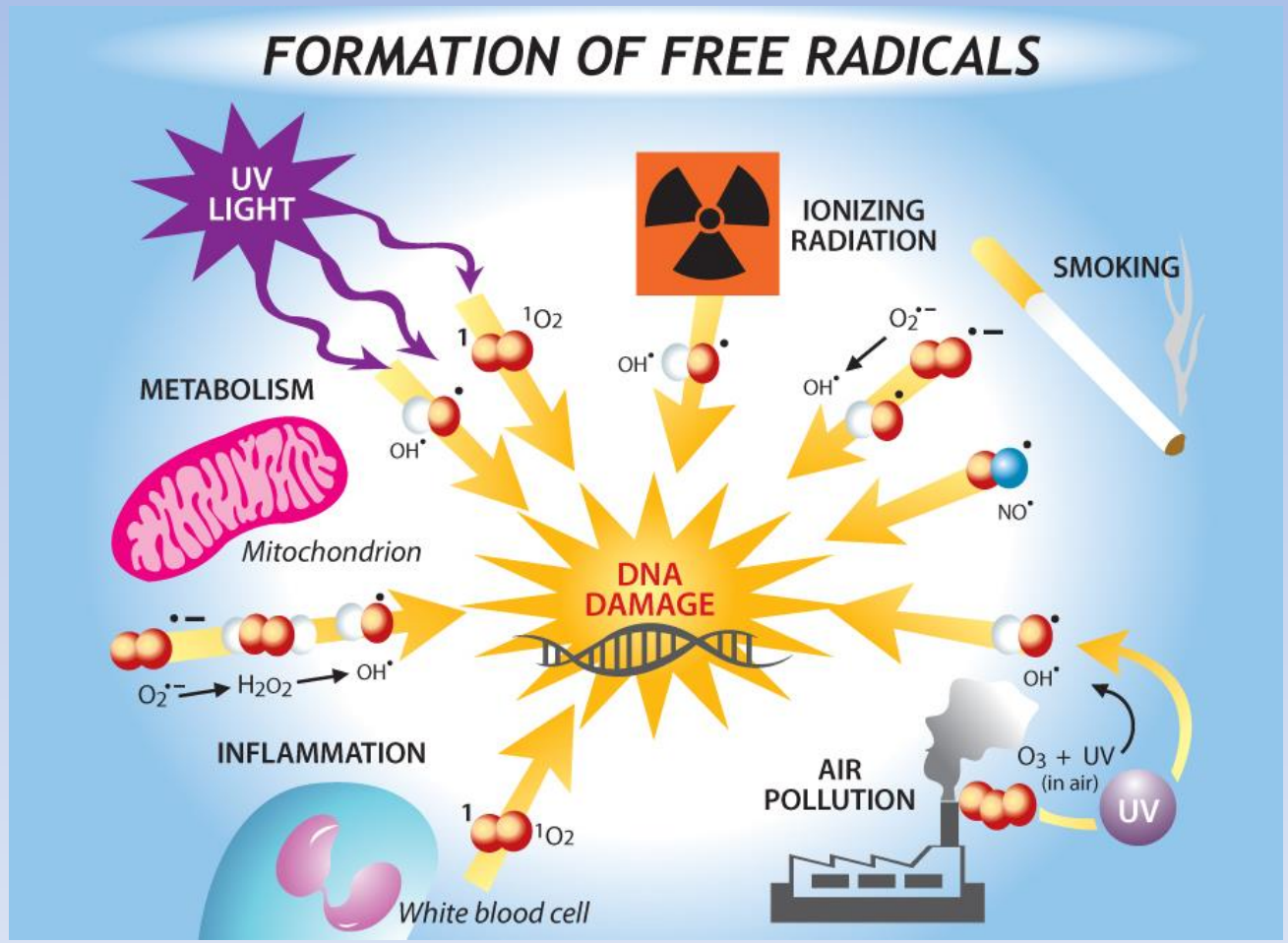
$$LH + R\bullet \rightarrow L\bullet + RH$$

$$L\bullet + O_2 \rightarrow LOO\bullet$$

$$LOO\bullet + LH \rightarrow LOOH + L\bullet$$

$$LOOH \rightarrow LOO\bullet, LO\bullet, RCHO$$

Causes of oxidative stress



Causes of oxidative stress

- **Diet is one of the most important causes for the formation of free radicals in the organism. For example, the junk foods are full of sugars and unsaturated lipids leading to the formation of free radicals.**
- **Also, foods containing additives like colors, preservatives or artificial sweeteners can also lead to the formation of free radicals in the body.**

- **Chemicals such as those used for household cleaning purposes, pesticides, cosmetics, perfumes and creams have also been found to cause the formation of free radicals in the body.**

- **The chemicals (e.g. pesticides, incectisides) sprayed in the fields are also sources of radical formation.**

Causes of oxidative stress

- **Pollution, especially that of the air, is another factor which leads to the rise of free radicals in the body.**
- **For example, smoke from cigarette, factory chimneys and automobiles can cause the formation of free radicals.**
- **Due to the increase in the pollution levels worldwide, the ozone layer is getting depleted. This leads to increase in harmful UV rays that enter into the atmosphere of the earth. These UV rays may cause free radical production in the body, and thus it may lead to skin diseases and premature aging.**

Causes of oxidative stress

- **Pharmaceutical drugs may also lead to the formation of free radicals. For example, certain drugs have compounds that bind to unstable biomolecules and form free radicals in the body.**

- **Physical and emotional stress also has been found to be a cause for the formation of free radicals in the organism.**

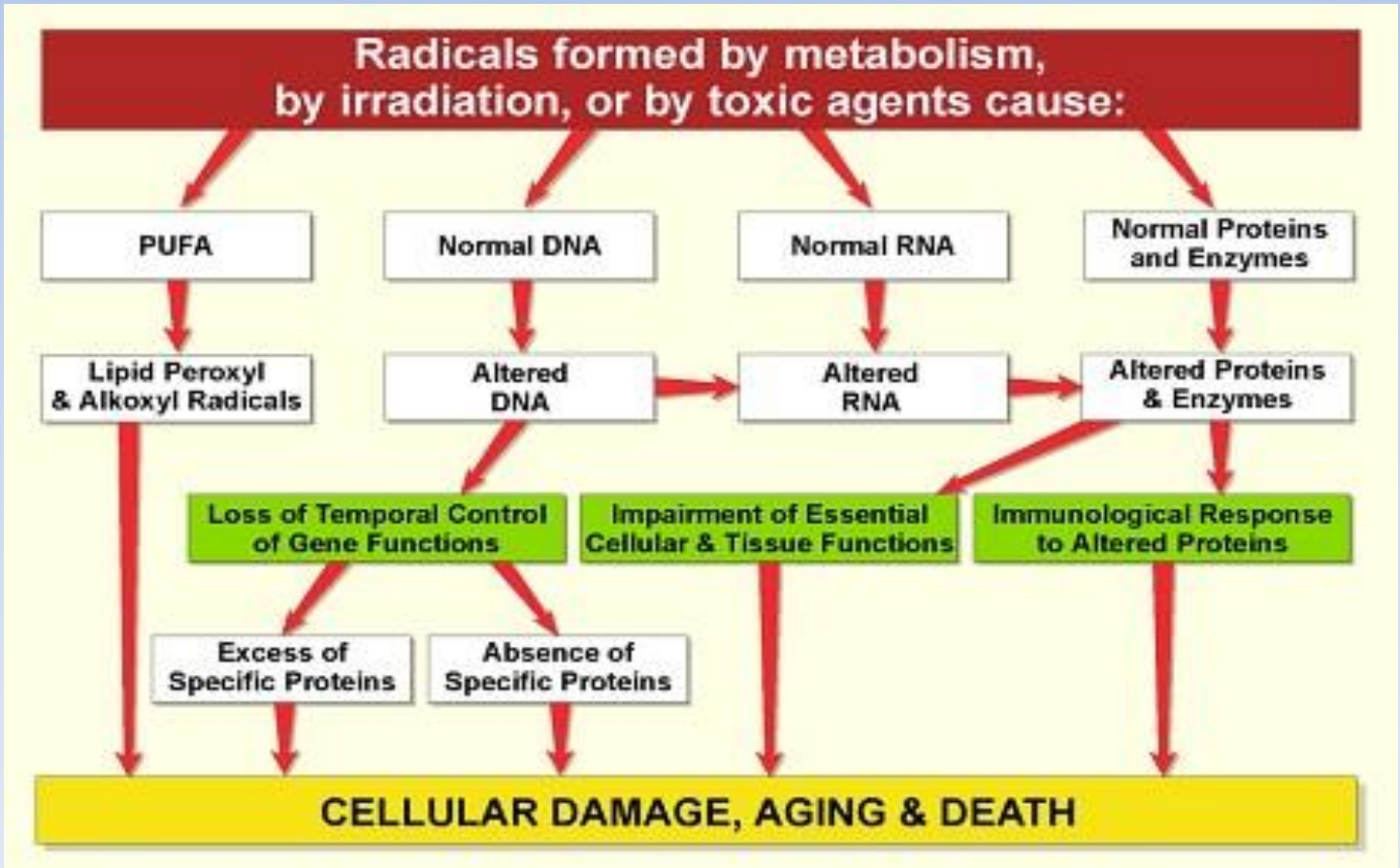
OXIDATIVE STRESS AND DISEASES

- **Oxidative stress has been implicated in various pathological conditions involving:**
  - **Aging**
  - **Cancer**
  - **Cardiovascular disease (atherosclerosis)**
  - **Neurogenerative diseases (Alzheimer, Parkinson)**

OXIDATIVE STRESS AND AGING

- Damage to cellular macromolecules via free radical production in aerobic organisms is a major determinant of life span.

- Thus, increases in ROS lead to pre-mature aging, pathological conditions and even death.

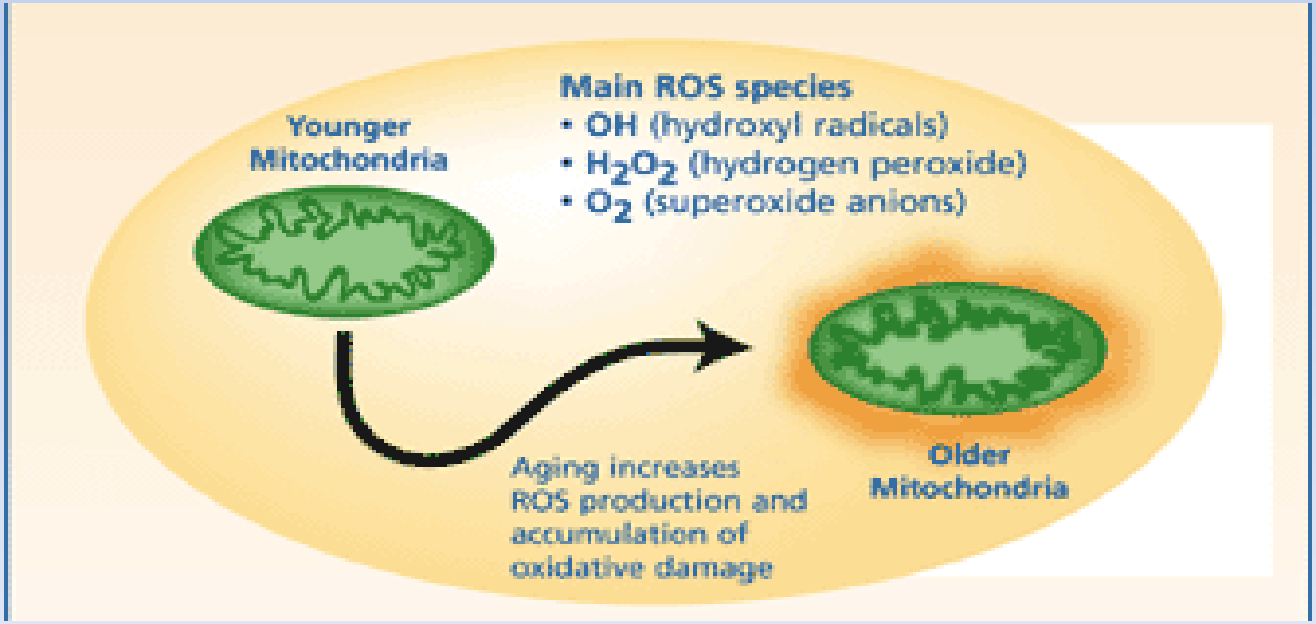


OXIDATIVE STRESS AND AGING

- Mitochondria are the critical component in control of aging.

- Electrons leaking from the electron transport chain (ETC) produce ROS, and these molecules can then damage ETC components and mitochondrial DNA, leading to further increases in intracellular ROS levels and a decline in mitochondrial function.

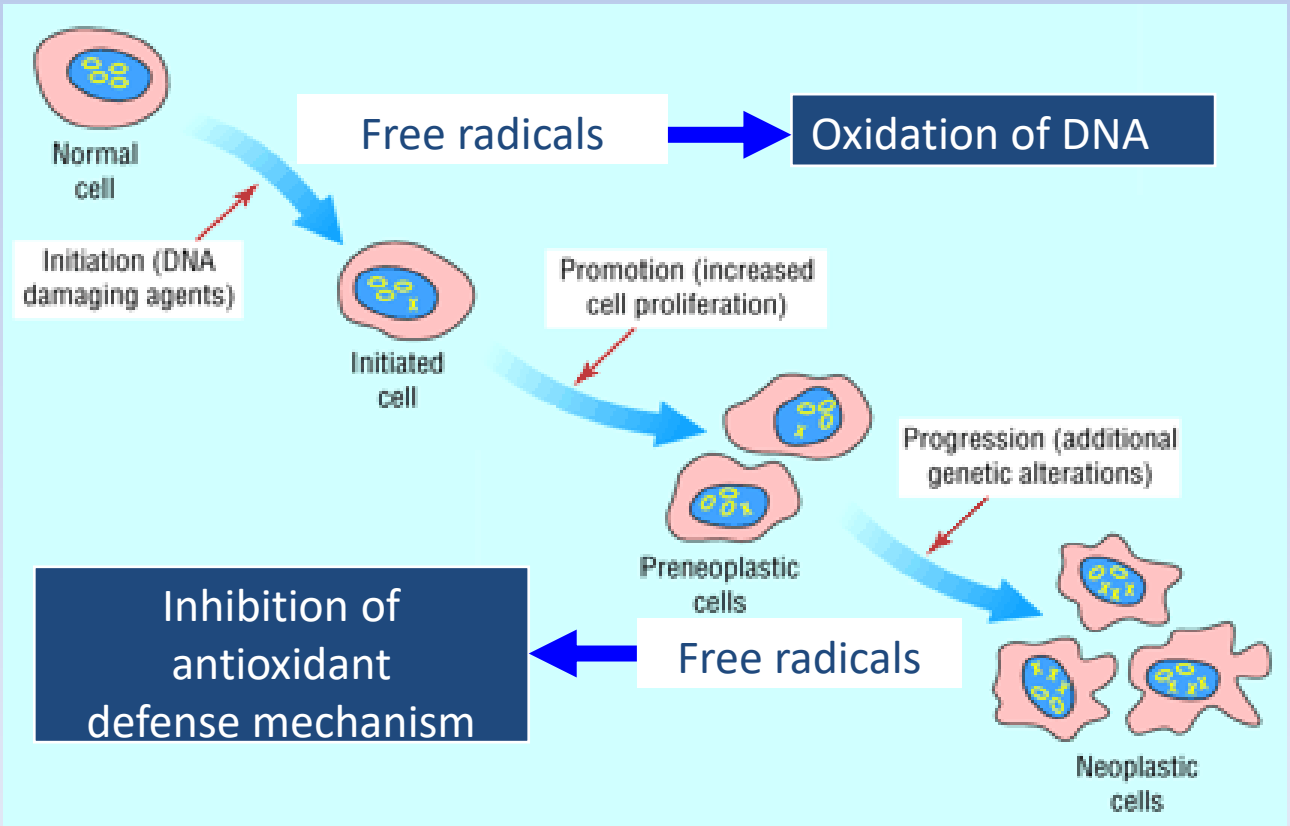
- Also, mitochondrial DNA damage is increased with aging.



OXIDATIVE STRESS AND CANCER

- **Cancer almost certainly stems from damage in the form of DNA mutation due to oxidative stress.**

- **ROS produced from oxidative stress, activate signal transduction pathways, leading to the transcription of genes involved in cell growth regulatory pathways.**



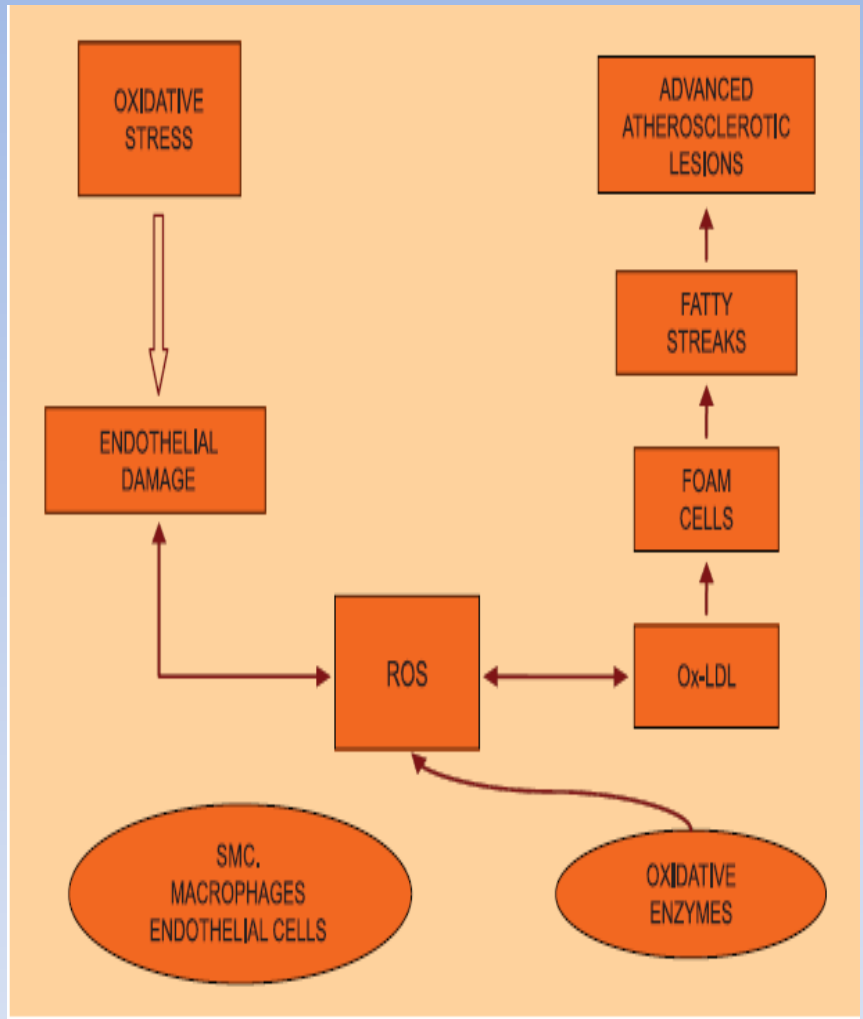
OXIDATIVE STRESS AND ATHEROSLCEROSIS

- The production of ROS is believed to induce endothelial dysfunction, an initial step of atherogenesis.

- The main sources of oxidative substances and ROS in atherosclerotic vessels are macrophages and smooth muscle cells.

- Oxidative stress leads to oxidation of LDL (ox-LDL).

- The increased production of ROS reduces the production and consequently the bioavailability of NO, leading to vasoconstriction, platelet aggregation and adhesion of neutrophils to the endothelium.



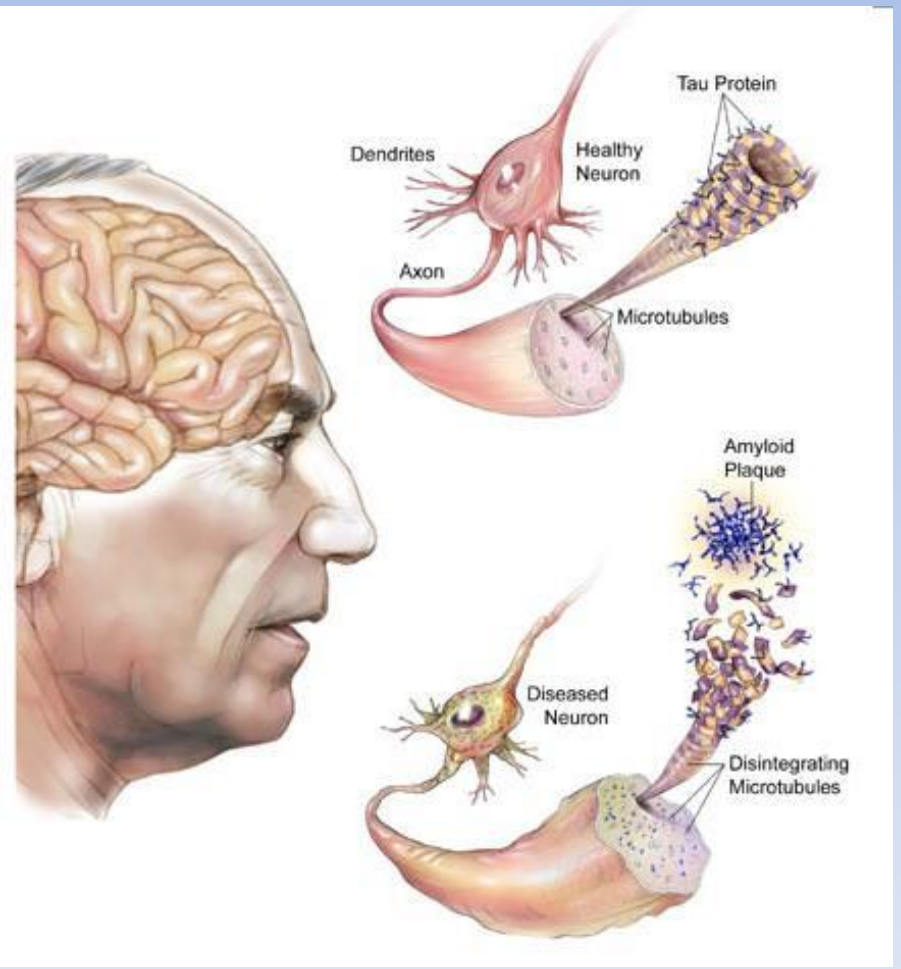
OXIDATIVE STRESS AND NEUROLOGICAL DISORDERS

- **The brain is particularly vulnerable to oxidative damage because of its high oxygen utilisation, its high content of oxidisable polyunsaturated fatty acids, and the presence of redox-active metals (Cu, Fe).**

- **Oxidative stress increases with age, and therefore it can be considered as an important causative factor in several neurodegenerative diseases**

Alzheimer's disease

- **The brains of patients with Alzheimer's disease (AD) show a significant extent of oxidative damage associated with a marked accumulation of amyloid- peptide (A), the main constituent of senile plaques in brain, as well as deposition of neurofibrillary tangles and neuropil threads.**



Normal Aging, Mutations

↓

Elevation of β-amyloid

↓

β-amyloid polymerization

↓

Production of ROS

↓

Lipid peroxidation

↓

Tau protein formation

↓

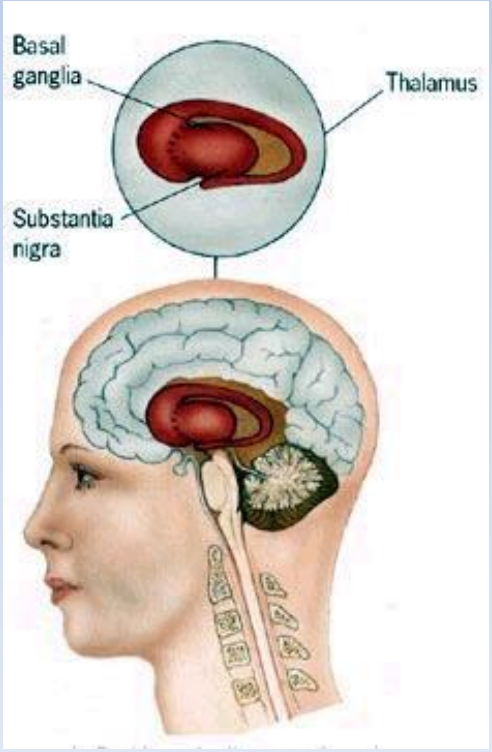
Neuronal dysfunction

Parkinson's disease

- **Parkinson's disease (PD) involves a selective loss of neurons in an area of the midbrain called the substantia nigra.**

- **The cells of the substantia nigra use dopamine (a neurotransmitter-chemical messenger between brain and nerve cells) to communicate with the cells in another region of the brain called the stratium.**

- **Thus, a reduction in nigral dopamine levels results in a decrease in stratial dopamine that is believed to cause PD symptoms.**



Increased hydrogen peroxide formation increases dopamine oxidation.

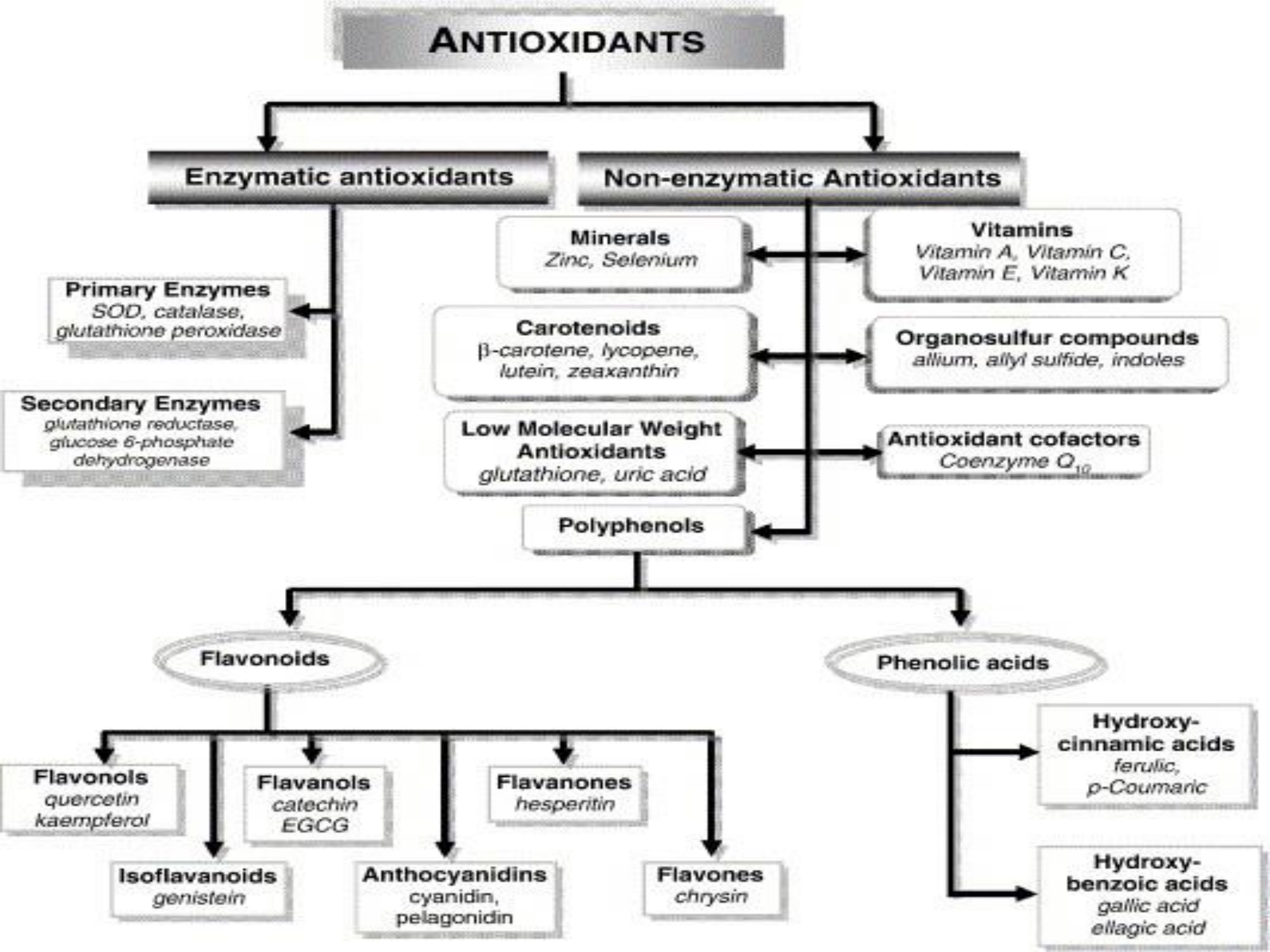
Decreased glutathione level in substantia nigra.

Formation of hydroxy radical by increased iron concentration in substantia nigra.

Increased lipid peroxidation in substantia nigra.

Antioxidant Defense System

- Superoxide dismutase
- Catalase
- Glutathione
- Antioxidants in diet
- Food supplements


ANTIOXIDANTS
Enzymatic antioxidants
Non-enzymatic Antioxidants
Primary Enzymes
SOD, catalase, glutathione peroxidase
Secondary Enzymes
glutathione reductase, glucose 6-phosphate dehydrogenase
Minerals
Zinc, Selenium
Vitamins
Vitamin A, Vitamin C, Vitamin E, Vitamin K
Carotenoids
β-carotene, lycopene, lutein, zeaxanthin
Organosulfur compounds
allium, allyl sulfide, indoles
Low Molecular Weight Antioxidants
glutathione, uric acid
Antioxidant cofactors
Coenzyme Q_{10}
Polyphenols
Flavonoids
Phenolic acids
Flavonols
quercetin kaempferol
Flavanols
catechin EGCG
Flavanones
hesperitin
Isoflavanoids
genistein
Anthocyanidins
cyanidin, pelagonidin
Flavones
chrysin
Hydroxy-cinnamic acids
ferulic, p-Coumaric
Hydroxy-benzoic acids
gallic acid ellagic acid

Antioxidant Enzymes

SUPEROXIDE DISMUTASE (SOD)

- **SOD catalyses the dismutation of superoxide to hydrogen peroxide and oxygen.**

Antioxidant Enzymes

CATALASE

- **Catalase is an heme-containing enzyme that catalyses the dismutation of hydrogen peroxide into water and oxygen.**

- **It is found in all aerobic eukaryotes and is important in the removal of hydrogen peroxide generated in peroxisomes (microbodies) by oxidases involved in ß-oxidation of fatty acids, the glyoxylate cycle and purine catabolism.**

$$2\,H_2O_2 \rightarrow 2H_2O + O_2$$

Antioxidant Enzymes

- **Glutathione Peroxidase (GSH PX) – The biochemical function of glutathione peroxidase is to reduce lipid hydroperoxides to their corresponding alcohols and to reduce free hydrogen peroxide to water.**

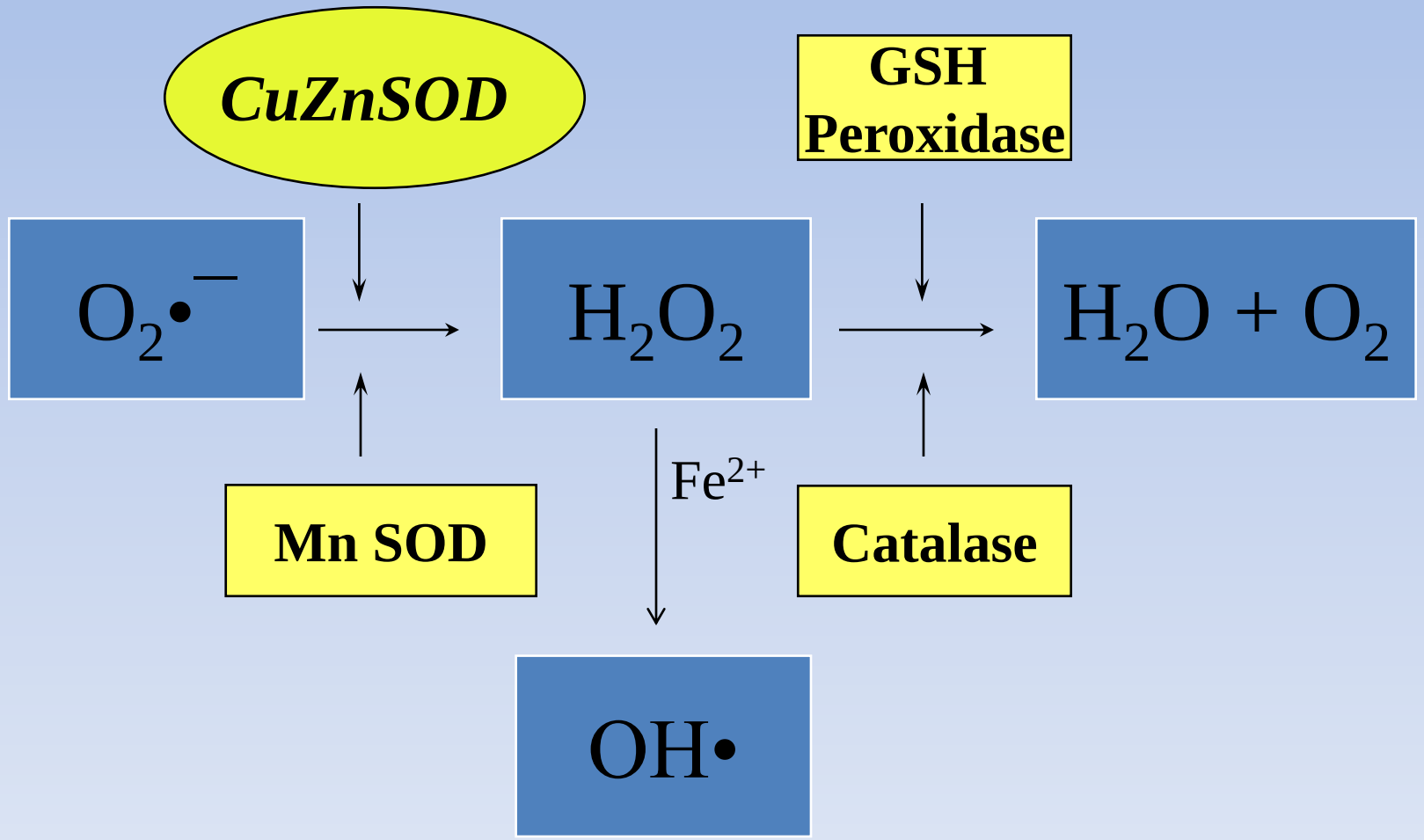
- **It requires reduced glutathione (GSH) as substrate and produces oxidized glutathione (GSSG) as product.**

- **It is a cytosolic enzyme.**

- **The main reaction that glutathione peroxidase catalyzes is:**

$$2GSH + H_2O_2 \rightarrow GSSG + 2H_2O$$

Oxygen Radical Defense Enzymes

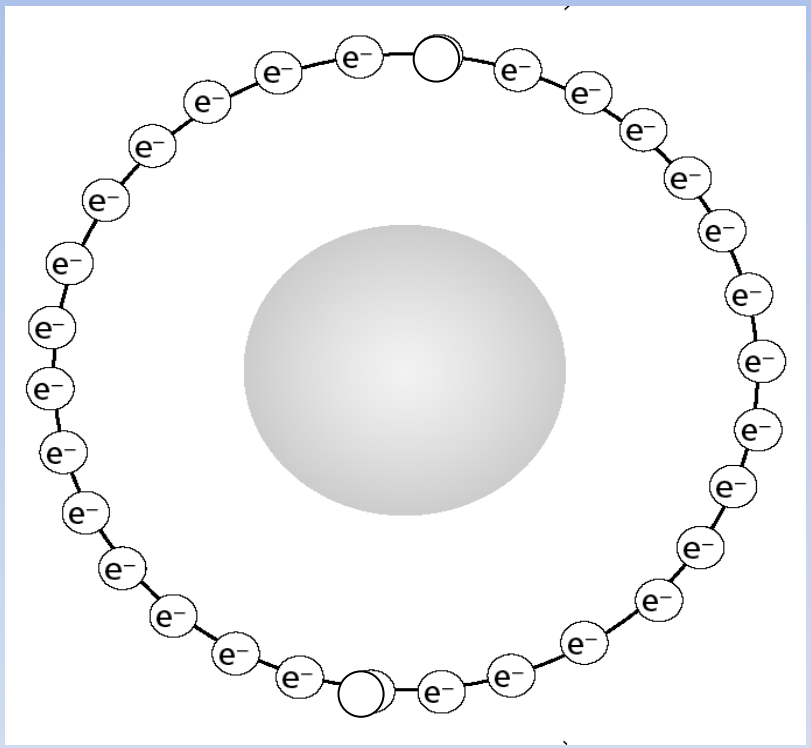


Antioxidants

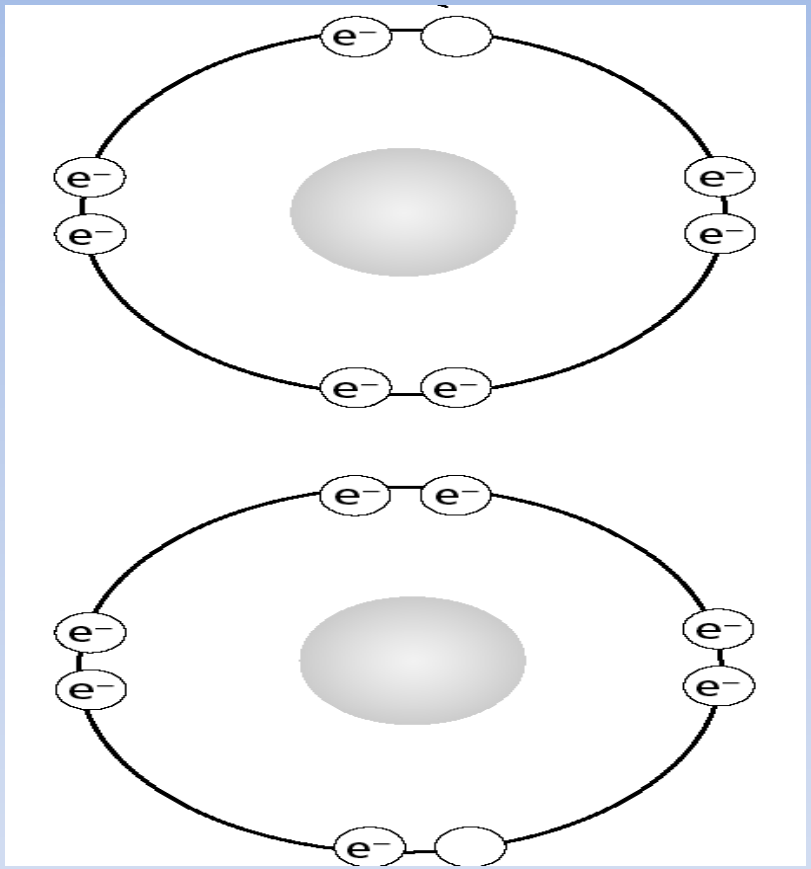
- To counteract oxidative stress, the body has a number of antioxidant molecules.
- Antioxidants scavenge free radicals that can harm our cells.
- Our body's ability to produce antioxidants is controlled by our genetic makeup and influenced by our exposure to environmental factors, such as diet and smoking.
- We can help our body to defend itself by increasing our dietary intake of antioxidants.
- Thus, antioxidants are widely used in dietary supplements and have been investigated for the prevention of diseases such as cancer and coronary heart disease.
- However, recent clinical trials showed that the intake of some antioxidants has no benefit on health, and even suggested that excess supplementation with certain antioxidants may be harmful.

Antioxidants

- Prevent the transfer of electron from O_2 to other molecules.
- Stabilize free radicals.
- Terminate free radical reactions.



Anioxidants



Free radicals

Antioxidant Quenchers

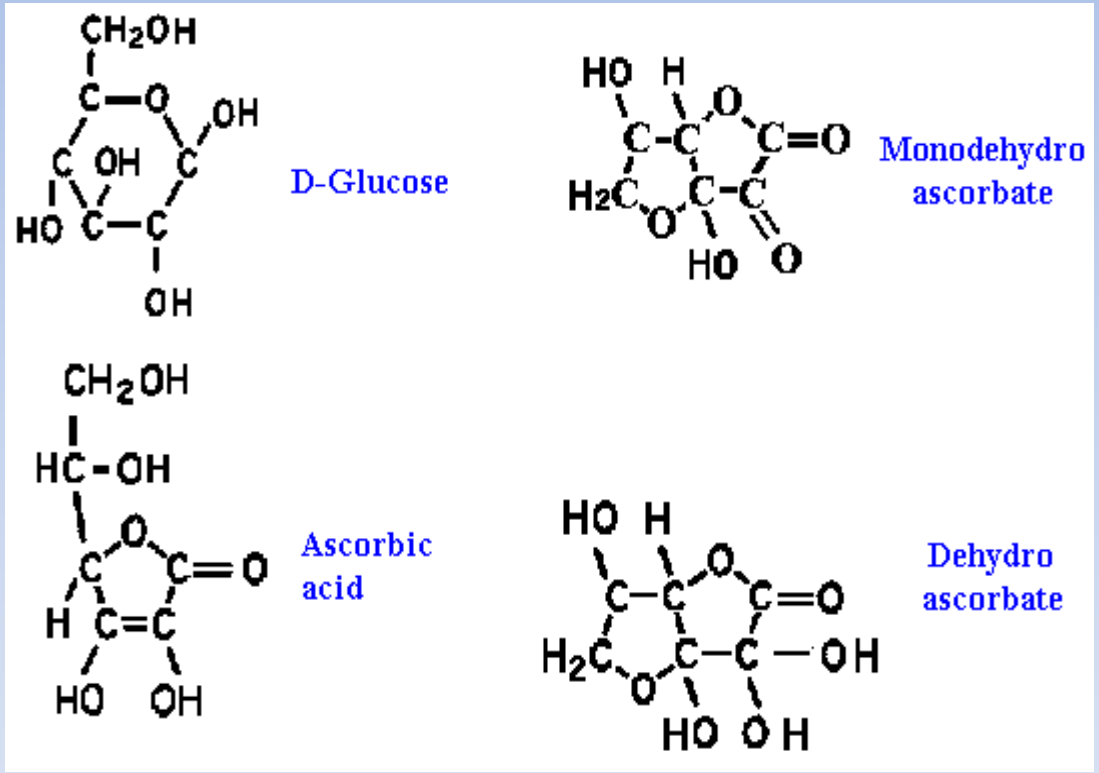
- **Cellular proteins which chelate pro-oxidant minerals (iron and copper or others).**
- **Transferrin – iron transport protein.**
- **Ferritin – iron storage protein.**
- **Metallothionein – minerals and heavy metals (Zn/Cu/Cd/Hg).**
- **Ceruloplasmin – copper transport and storage**
- **Uric acid in plasma**

Antioxidants From Food

- **Antioxidant nutrients – vitamin E, vitamin C, (vitamin A?), beta-carotene.**
- **Phytochemicals – antioxidants from plants.**

Ascorbic acid

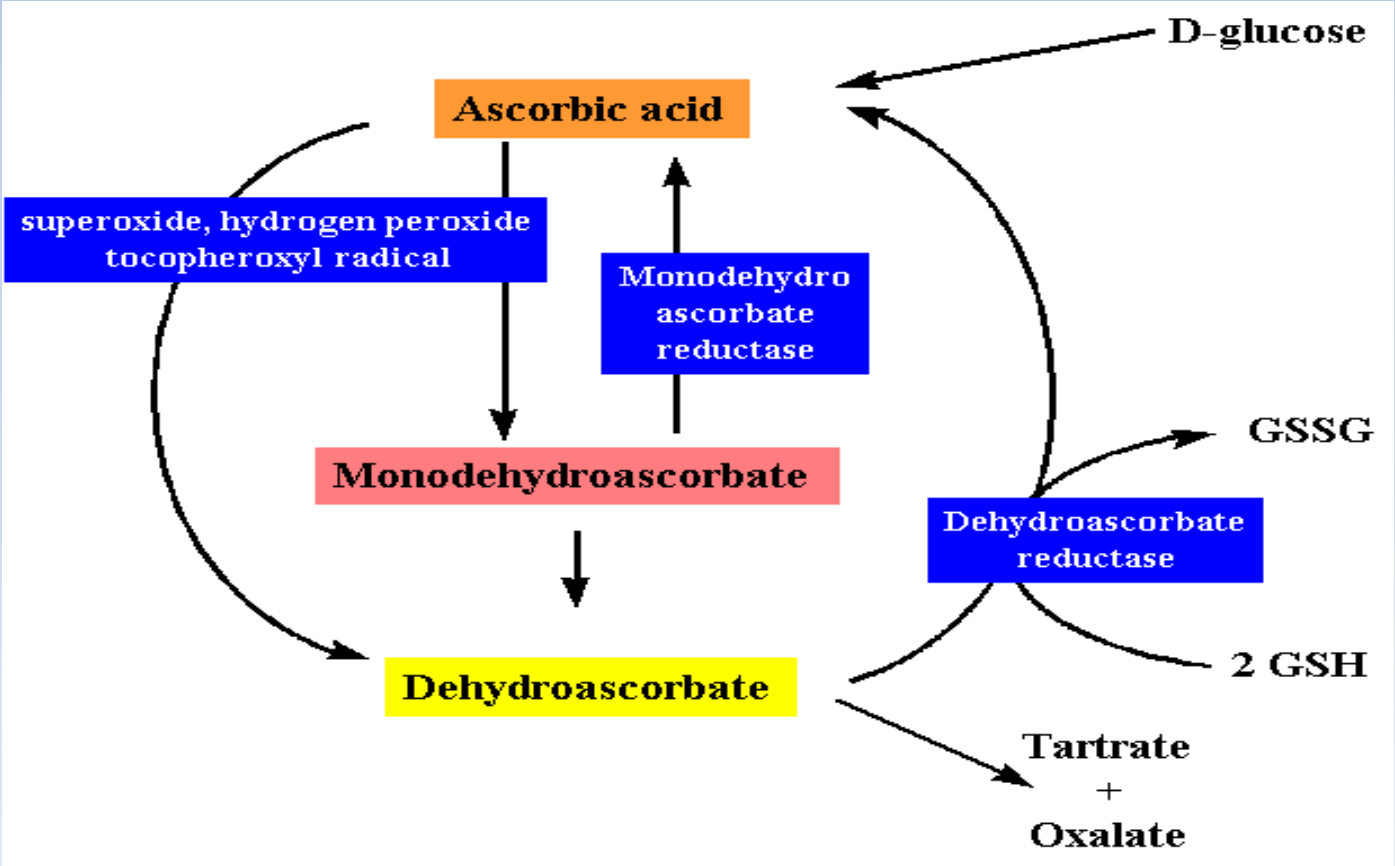
- L-ascorbic acid (vitamin C) is an important vitamin in the human diet and is abundant in plant tissues.
- Ascorbate functions as a reductant for many free radicals, thereby minimising the damage caused by oxidative stress



Structure of ascorbic acid and its metabolites

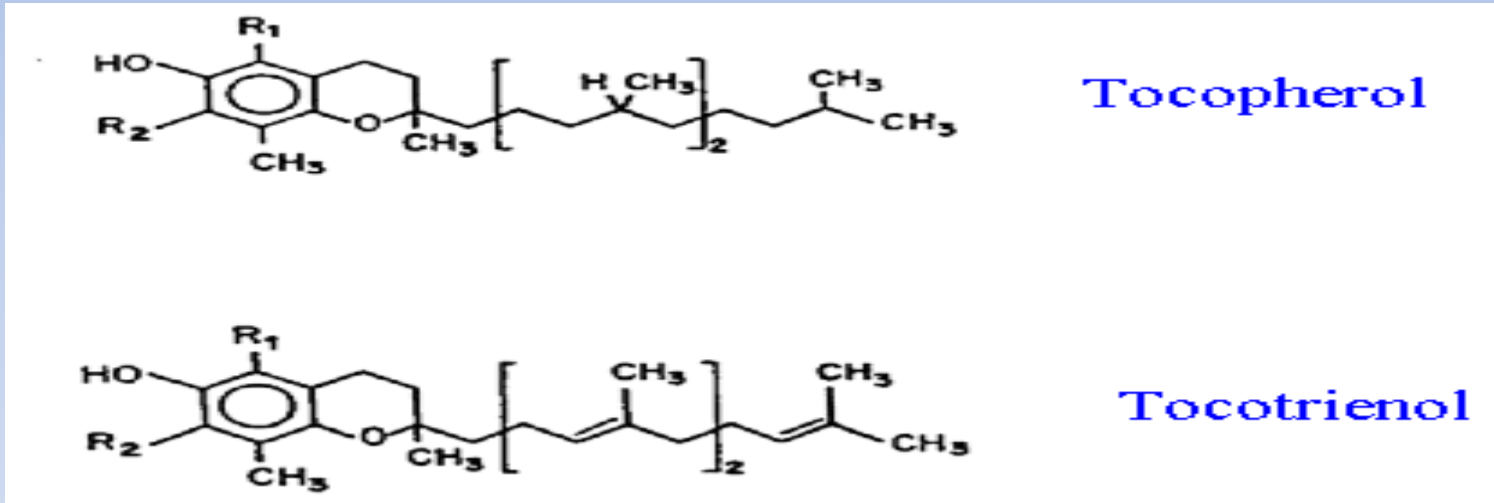
- **Ascorbic acid can directly scavenge oxygen free radicals with and without enzyme catalysts and can indirectly scavenge them by recycling tocopherol to the reduced form.**

- **By reacting with activated oxygen more readily than any other aqueous component, ascorbate protects critical macromolecules from oxidative damage.**



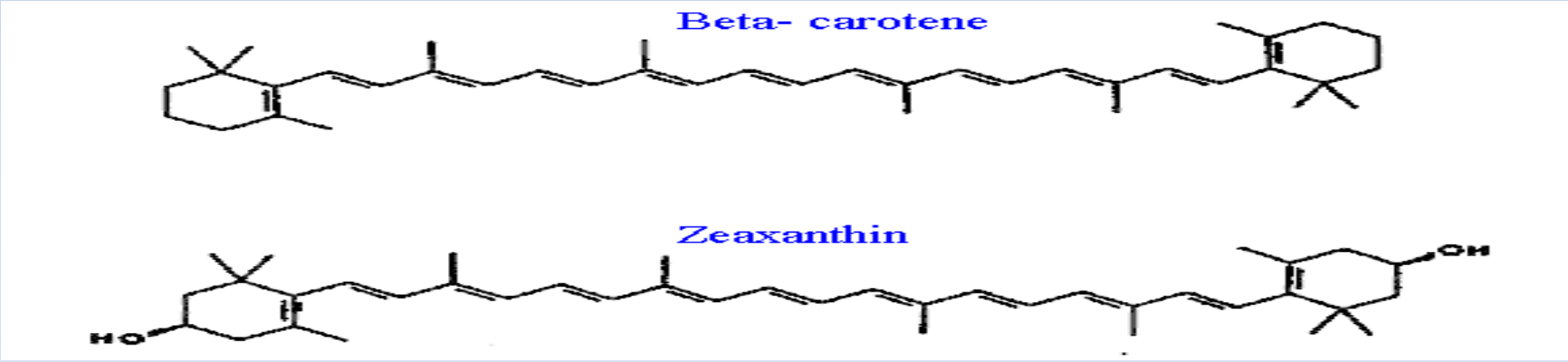
Tocopherol

- **The tocopherol (vitamin E), have been studied extensively in mammalian research as membrane stabiliser and multifaceted antioxidant, that scavenge oxygen free radicals, lipid peroxy radicals, and singlet oxygen.**



Carotenoids

- Carotenoids are C40 isoprenoids and tetraterpenes that are located in the plastids of both photosynthetic and non-photosynthetic plant tissues.
- In chloroplasts, the carotenoids function as accessory pigments in light harvesting.
- More important role is carotenoids' ability to scavenge free radicals.



Structure of two common carotenoids found in plants, β-carotene and zeaxanthin.

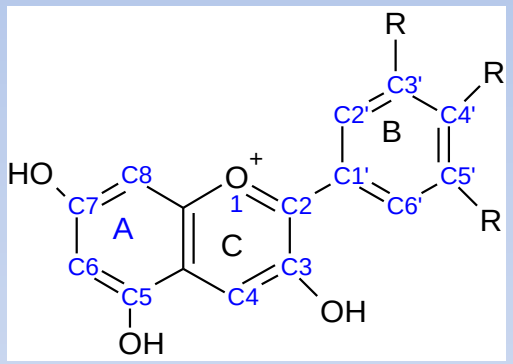
Plant polyphenols

- **Plant polyphenols are a large and heterogenous category of chemical compounds produced as secondary metabolites by plants.**

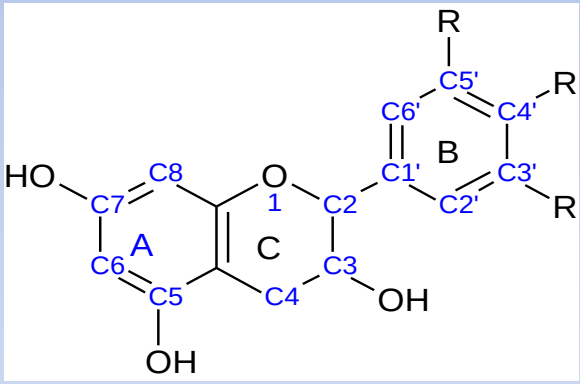
- **The known polyphenols are estimated to be more than 8000.**

- **The major characteristic of plant polyphenols is their benzoic ring associated with one or more hydroxyl groups.**

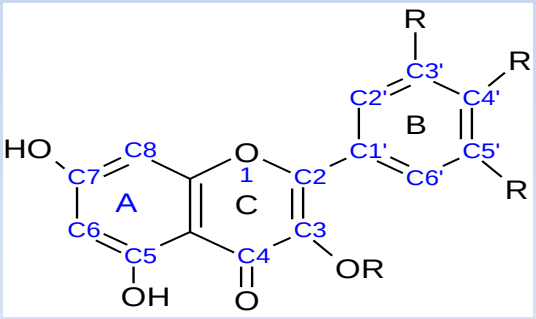
- **The largest polyphenolic category is the flavonoids.**



Flavonols

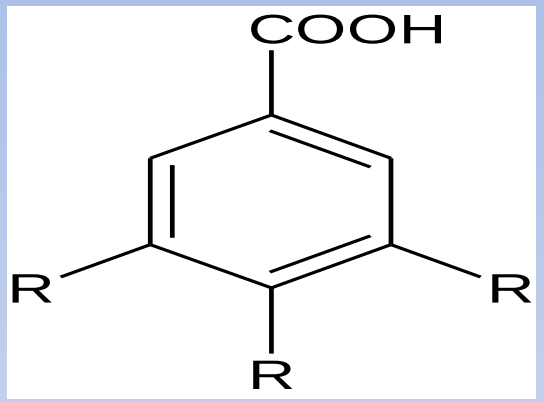


Flavanols

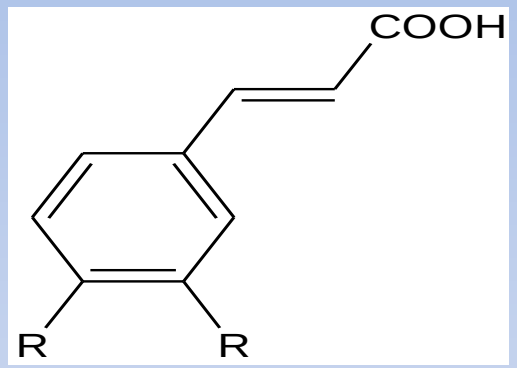


Anthocyanidins

- **Another polyphenolic category is the polyphenolic acids.**

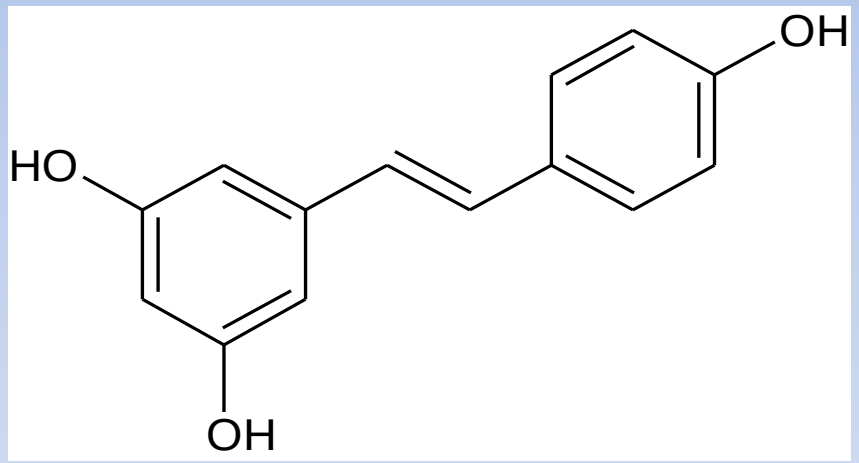


Hydroxybenzoic acid



Hydroxycinnamic acid

•The third most important polyphenolic category is the stilbenes found mainly in grapes.



trans-resveratrol

Antioxidant mechanisms of plant polyphenols

i) Direct scavenging of free radicals

$$POH + RO\bullet \rightarrow PO\bullet + ROH$$

POH: polyphenol, RO•: free radical,
PO•: polyphenolic radical

$$PO\bullet + RO\bullet \rightarrow ROOP$$

ii) Chelation of metal ions

Fenton reaction

$$H_2O_2 + Fe^{2+} \text{ (ή } Cu^{1+}) \rightarrow OH^- + OH\bullet + Fe^{3+} \text{ (ή } Cu^{2+})$$

Haber-Weiss reaction

$$O_2\bullet^- + H_2O_2 \rightarrow OH^- + OH\bullet + O_2$$

Antioxidant mechanisms of plant polyphenols

iii) Inhibit the activity of enzymes producing free radicals.

iv) Induce antioxidant enzymes.

v) Interact with the Antioxidant response element (ARE).

ARE exists in the promoter region of several antioxidant enzymes and play important role in the regulation of their expression.

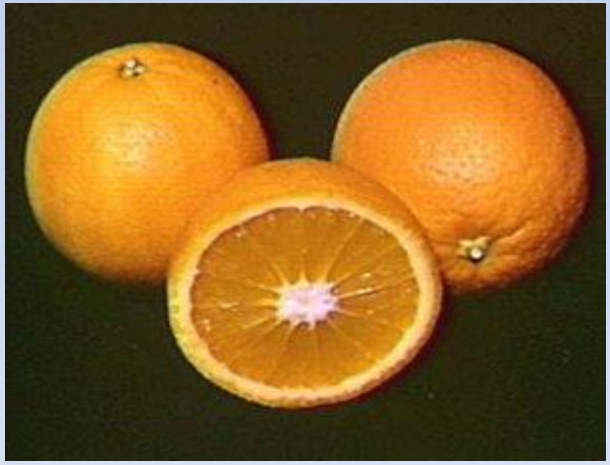
Foods and antioxidants

Tomatoes

- Tomatoes contain a pigment called lycopene that is responsible for their red colour but is also a powerful antioxidant.
- Tomatoes in all their forms are a major source of lycopene, including tomato products like canned tomatoes, tomato soup, tomato juice.
- Lycopene is also highly concentrated in watermelon.

Citrus fruits

- **Oranges, grapefruit, lemons and limes possess many natural substances that appear to be important in disease protection, such as carotenoids, flavonoids, terpenes, limonoids and coumarins.**
- **It is always better to eat the fruit whole in its natural form, because some of the potency is lost when the juice is extracted.**

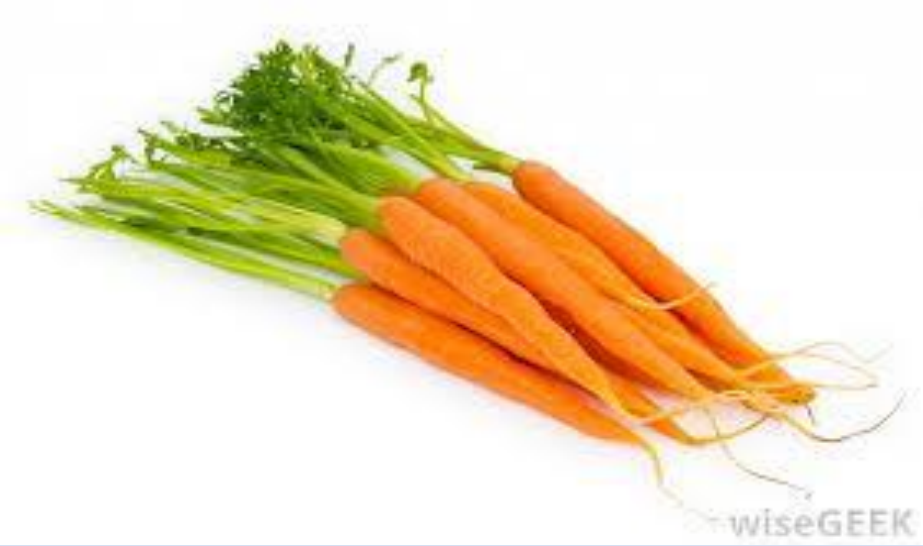


Tea

- Black tea, green tea and oolong teas have antioxidant properties. All three varieties come from the plant Camellia sinenis.
- Common brands of black tea contain antioxidants, but by far the most potent source is green tea (jasmine tea) which contains the antioxidant catechin.
- Black tea has only 10 per cent as many antioxidants as green tea.
- Oolong tea has 40 per cent as many antioxidants as green tea.
- This because some of the catechins are destroyed when green tea is processed (baked and fermented) to make black tea.

Carrots

- **Beta-carotene is an orange pigment with strong antioxidant properties .**
- **It is also found concentrated in deep orange and green vegetables.**



Conclusion

- **A vast body of information is accumulated concerning antioxidants, and their protective effects from ROS and their damaging effects.**

- **However, reactive oxygen species also have useful cellular functions, such as redox signaling. Thus, the function of antioxidant systems is not to remove oxidants entirely, but instead to keep them at an optimum level.**

Antioxidants vs Free Radicals - Immune System.flv

ASSESSMENT
OF FREE RADICAL SCAVENGING ACTIVITY

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Current Opinion in Toxicology

A battery of translational biomarkers for the assessment of the *in vitro* and *in vivo* antioxidant action of plant polyphenolic compounds: The biomarker issue

Aristidis Veskoukis, Efthalia Kerasioti, Alexandros Priftis, Paraskevi Kouka, Ypatios Spanidis, Sotiria Makri and Dimitrios Kouretas

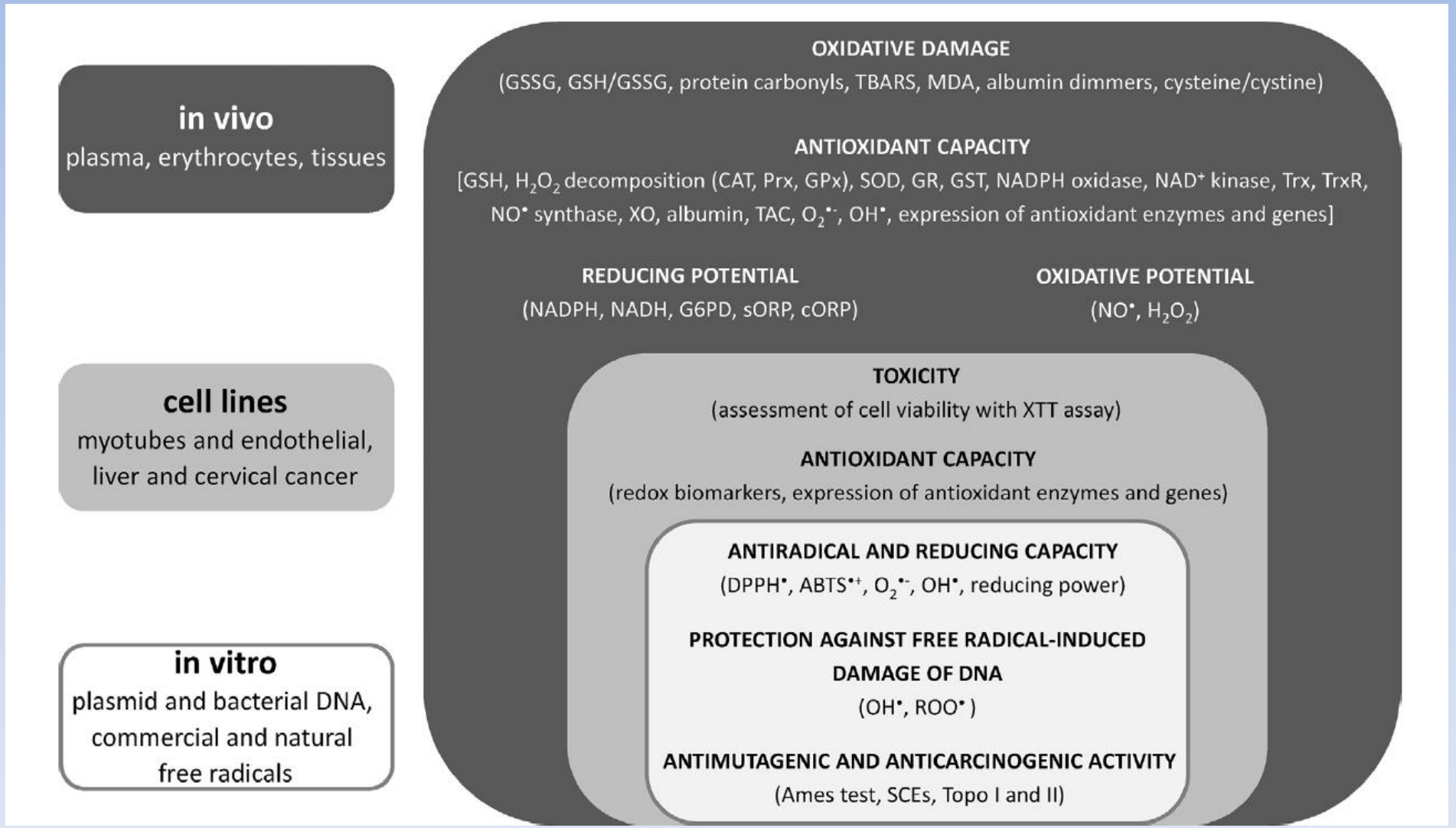
Abstract

Over the last decades, the scientific findings stressing the beneficial health implications of plant-derived compounds (i.e., plant extracts rich in polyphenols) have been increased

For a complete overview see the Issue and the Editorial

https://doi.org/10.1016/j.cotox.2018.10.001

The proposed battery of translational biomarkers for the characterization of a plant-derived compound in vitro, in cell culture environment and in vivo as well, in order to holistically reveal its biological action.



ΜΕΘΟΔΟΛΟΓΙΑ

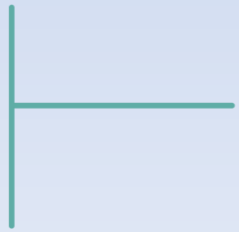
ΠΙΣΤΟΠΟΙΗΣΗ ΧΑΡΑΚΤΗΡΙΣΤΙΚΩΝ ΑΝΑ ΠΡΟΪΟΝ

ΠΡΟΣΔΙΟΡΙΣΜΟΣ

	Εξουδετέρωσης ριζών			Συνολικής αναγωγικής δύναμης	Αναστολής		Εξουδετέρωσης ριζών $O_2^{\bullet}$	Αναγωγικής ικανότητας έναντι του χαλκού
	$ABTS^{+\bullet}$	$DPPH^{\bullet}$	$OH^{\bullet}$		Θραύσεων προκαλούμενων από ελεύθερες ρίζες στο DNA	Λιπιδικής υπεροξείδωσης		
Μέγιστη Βαθμολογία ανά **μέθοδο**:	3 ΜΟΝΑΔΕΣ	3 ΜΟΝΑΔΕΣ	3 ΜΟΝΑΔΕΣ	3 ΜΟΝΑΔΕΣ	4 ΜΟΝΑΔΕΣ	4 ΜΟΝΑΔΕΣ	4 ΜΟΝΑΔΕΣ	4 ΜΟΝΑΔΕΣ
	4 βασικοί μέθοδοι				Επιλογή 2 από τις 4 μεθόδους, αναλόγως την κατηγορία προϊόντος			

Μέγιστη Βαθμολογία ανά **προϊόν**:

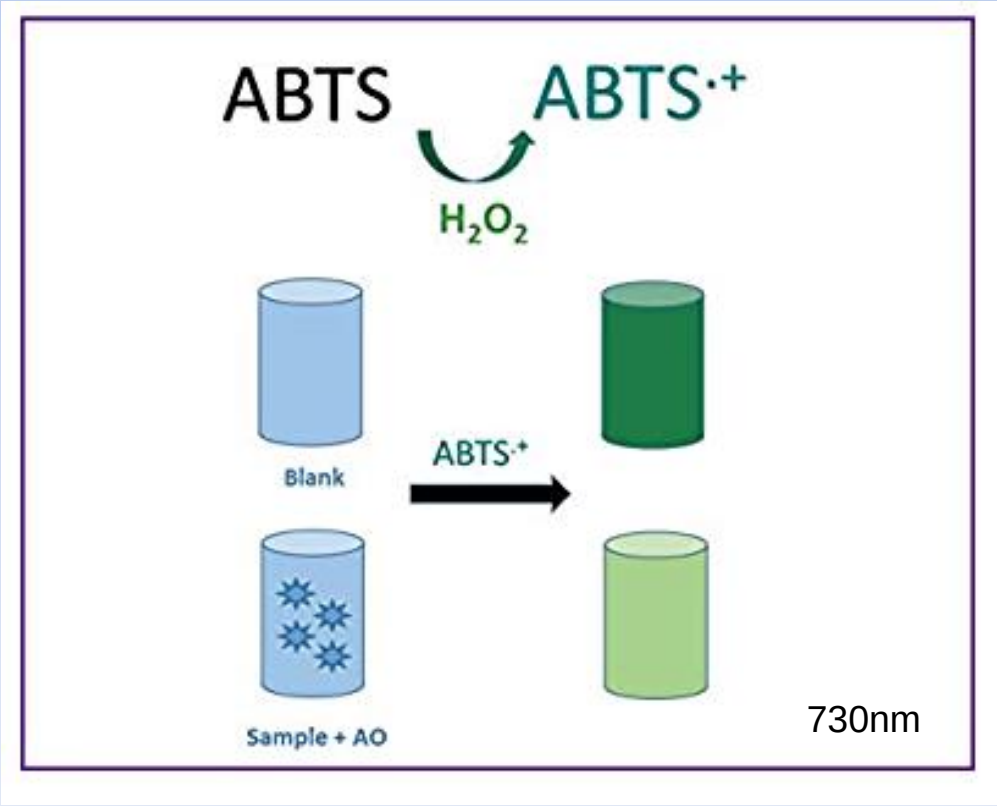
12 ΜΟΝΑΔΕΣ + 8 ΜΟΝΑΔΕΣ



AFQ 20

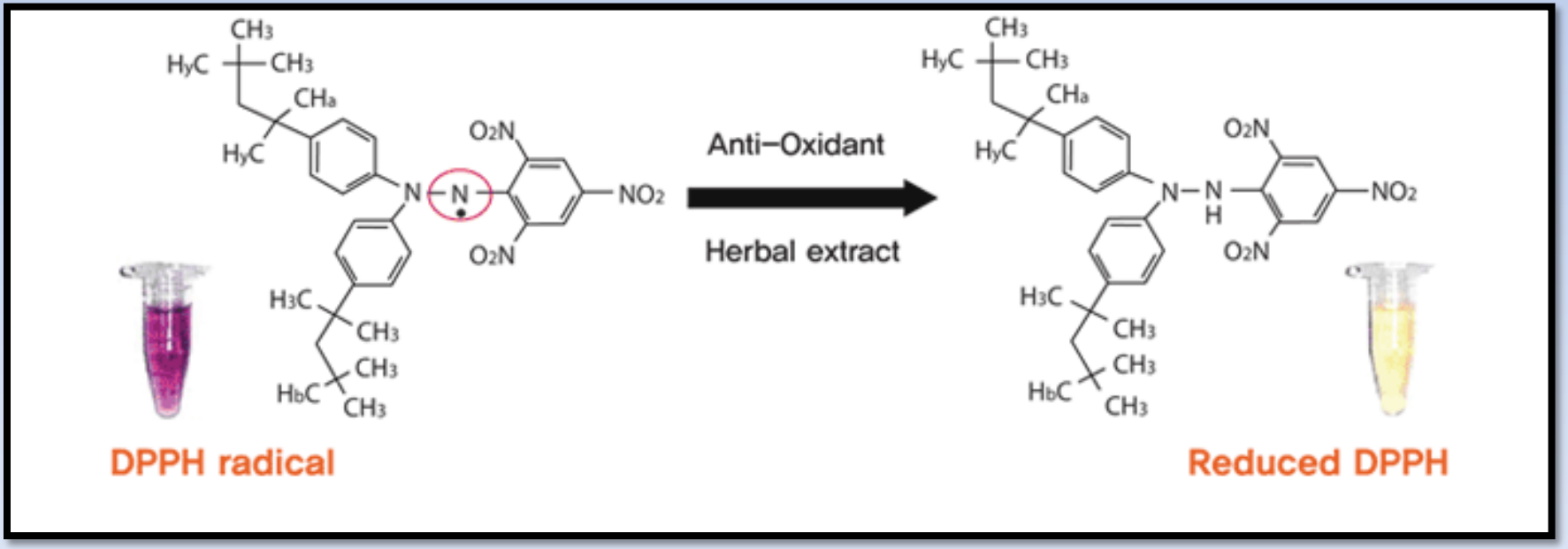
Determination of ABTS $^{+}$ •Radical Neutralization

This method examines the ability of a specific amount of sample to neutralize a specific amount of ABTS + •radical. This radical is an artificial substance produced in the laboratory and is widely used to assess the antioxidant capacity of hydrophilic components of products.



Determination of DPPH• Radical Neutralization

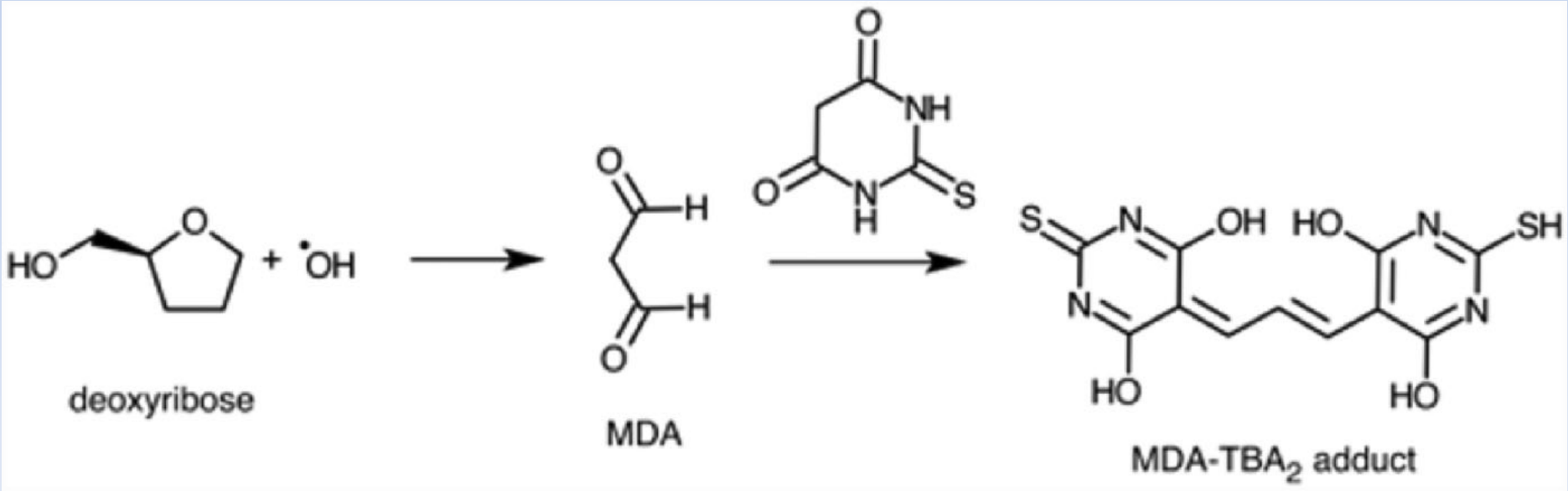
This method examines the ability of a specific amount of sample to neutralize a specific amount of DPPH• radical. This radical is an artificial substance produced in the laboratory and is widely used to assess the antioxidant capacity of hydrophilic and partially lipophilic components of products.



Determination of OH• radical Neutralization

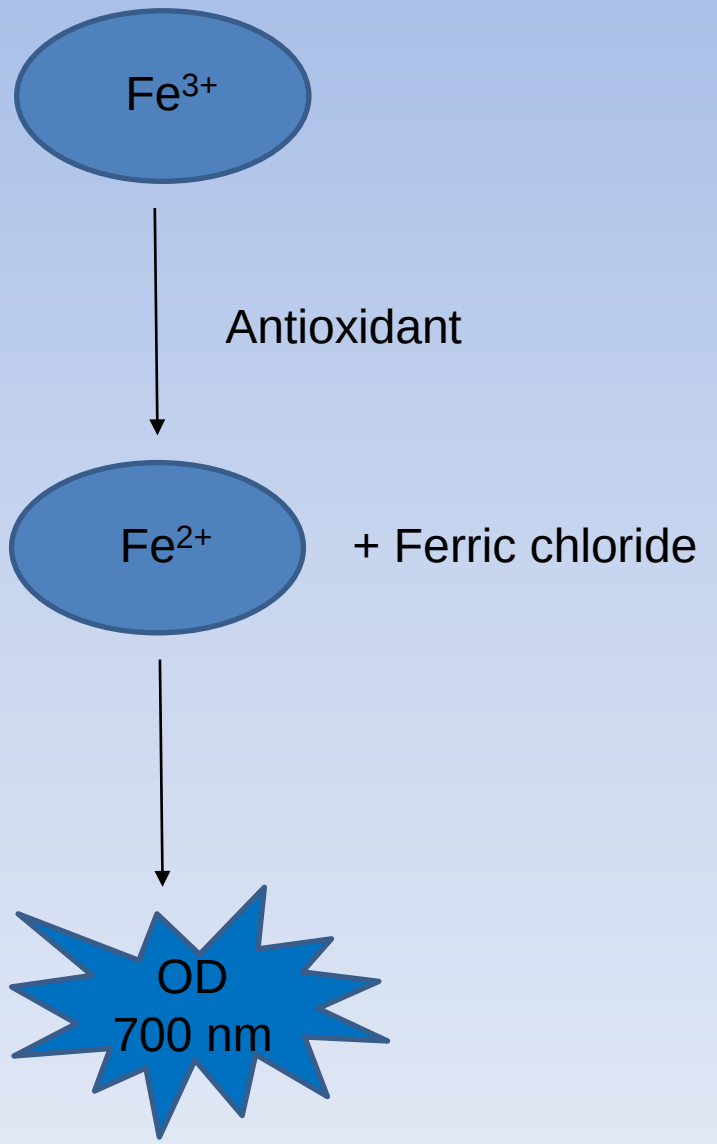
Fenton reaction

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + {}^{\bullet}OH + OH^-$$



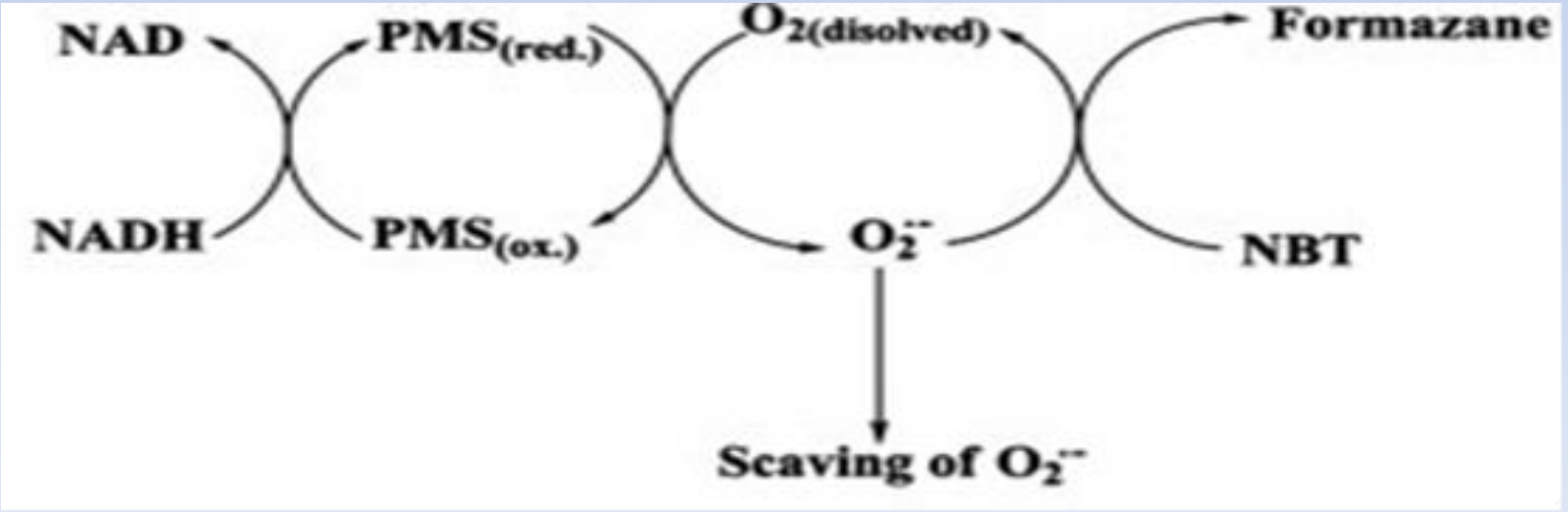
Determination of total reducing power

This method examines the ability of the product to create a (reducing) environment capable of converting potentially dangerous free radicals into inactive ones. This protects various biomolecules (eg DNA, fats, proteins) from possible damage. This method shows a general assessment of the antioxidant capacity of a product.



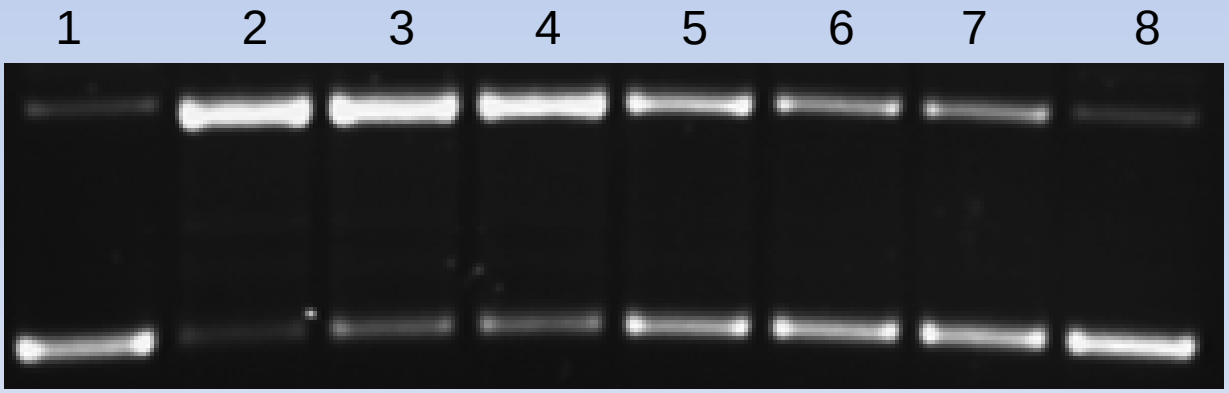
Determination of O2• Radical Neutralization

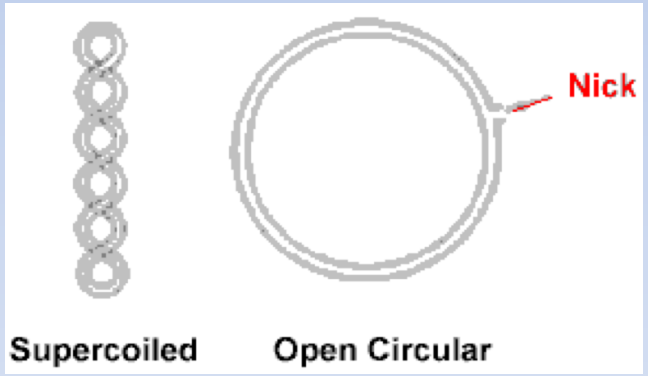
This method examines the ability of a specific amount of sample to neutralize a specific amount of O2• radical. This radical is produced in normal and pathological conditions in the human body. Its overproduction in combination with its reduced neutralization by the body can lead to damage of various biomolecules (e.g. DNA, fats, proteins).The assessment of the ability of the product under evaluation to neutralize this radical is very important.



Determination of inhibition of DNA breaks due to free radicals

This method examines the protective ability of the product against DNA damage. ROO• radical causes DNA to break down, causing irreparable damage to it. With this method we exclusively control the DNA-protective activity of the product under evaluation.

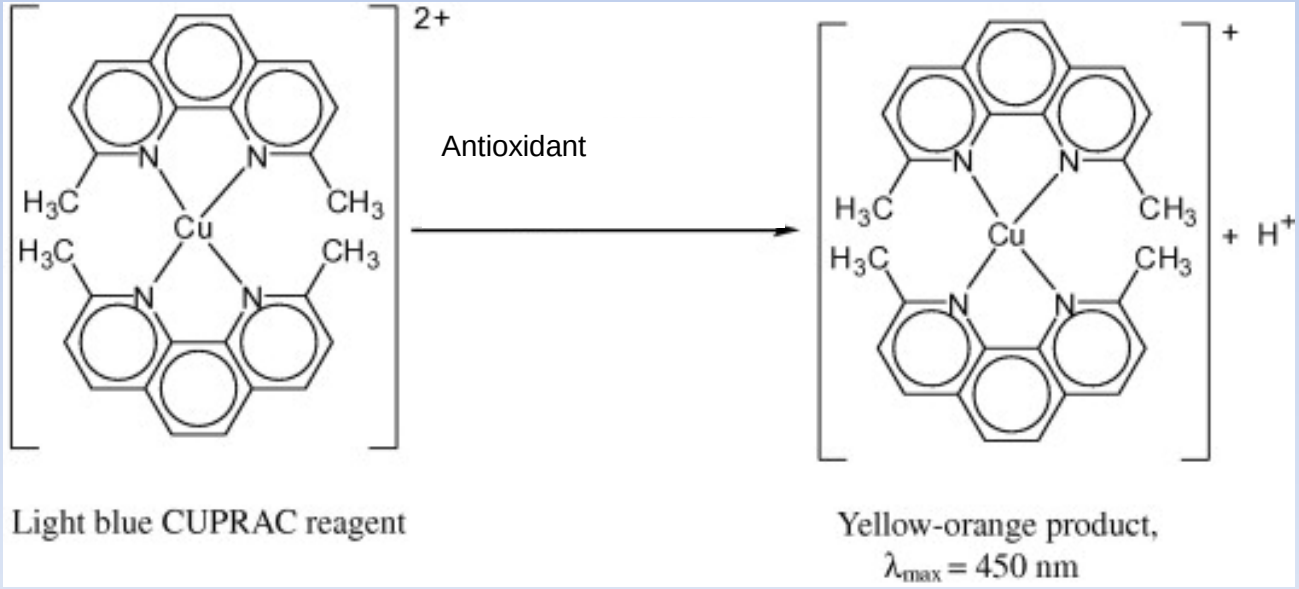




1: control
2: Plasmid + οξειδωτικός παράγοντας
3-7: Plasmid + αντιοξειδωτικός παράγοντας
8: Αντιοξειδωτικός παράγοντας

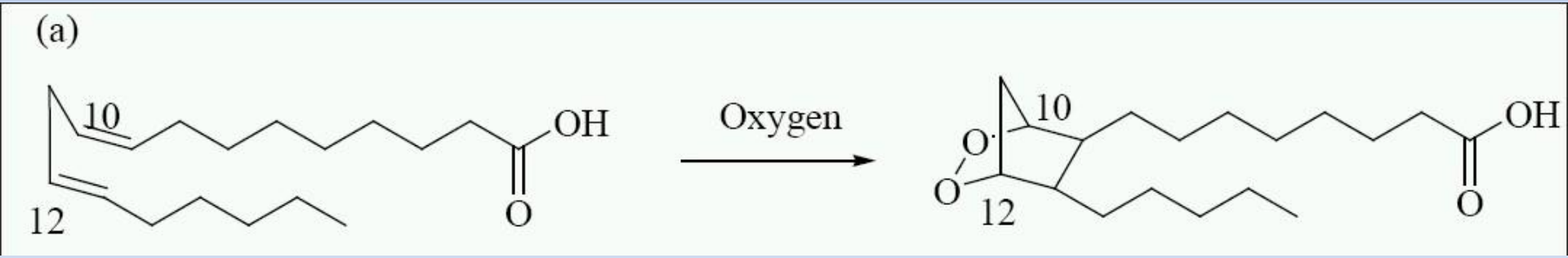
Determination of reductive ability against copper

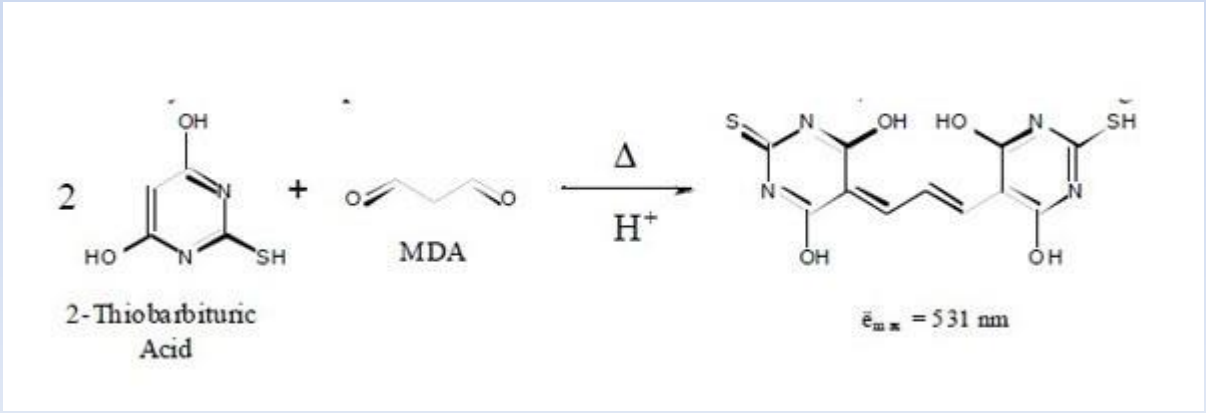
This method examines the ability of the product to reduce oxidized copper. It provides us with information concerning the product's ability to create a reducing environment capable of neutralizing free radicals.



Determination of lipid peroxidation inhibition

This method examines the protecting ability of the product against the peroxidation of lipids, i.e. the damage caused by free radicals in lipids. Lipids are particularly sensitive to oxidative modifications which can lead to disruption of the normal functioning of their metabolism.





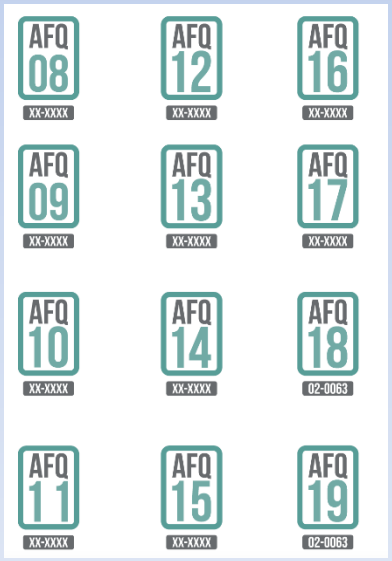
Παράδειγμα

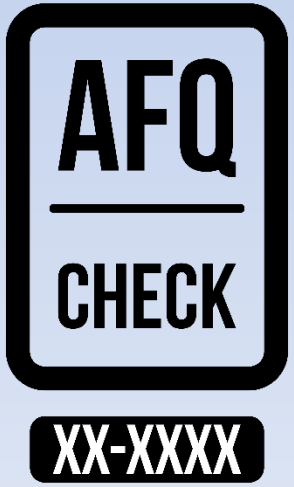
	Ειδική Δράση ανά μέθοδο								Αθροιστική Δράση
	1	2	3	4	5	6	7	8	
Μέλι 1	1,5	1,1	1,8	2,1	3,2	3			12,7
Μέλι 2	1,3	1,4	1,7	2,2	2,4	2,6			11,6
Μέλι 3	1,0	0,8	1,1	1,4	1,7	1,4			7,4
Μέλι 4	2,8	2,4	2,9	2,7	3,5	3,7			18
Μέλι 5	2,1	2,3	1,9	2,2	3,1	3,4			15
Μέλι 6	1,9	2	2,6	1,6	2,4	1,8			12,3
Βέλτιστη τιμή	**3**	**3**	**3**	**3**	**4**	**4**			**20**

1. Determination of ABTS + •Radical Neutralization
2. Determination of DPPH• Radical Neutralization
3. Determination of OH•radical Neutralization
4. Determination of total reducing power
5. Determination of O2• Radical Neutralization
6. Determination of inhibition of DNA breaks due to free radicals
7. Determination of reductive ability against copper
8. Determination of lipid peroxidation inhibition

EUIPO

ΓΡΑΦΕΙΟ ΔΙΑΝΟΗΤΙΚΗΣ ΙΔΙΟΚΤΗΣΙΑΣ
ΤΗΣ ΕΥΡΩΠΑΪΚΗΣ ΕΝΩΣΗΣ

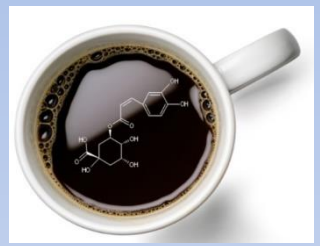




Σύγκριση αντιοξειδωτικών

1 ποτήρι χυμό ρόδι

=



3 κούπες (espresso)
1 κούπα (φραπέ)

=

5 ποτήρια κόκκινο κρασί

=

17 ποτήρια χυμό (τυποποιημένο)

23 ποτήρια μπύρα

=

50 ποτήρια λευκό κρασί

=

100 ποτήρια γάλα

Αντιοξειδωτικά βοτάνων

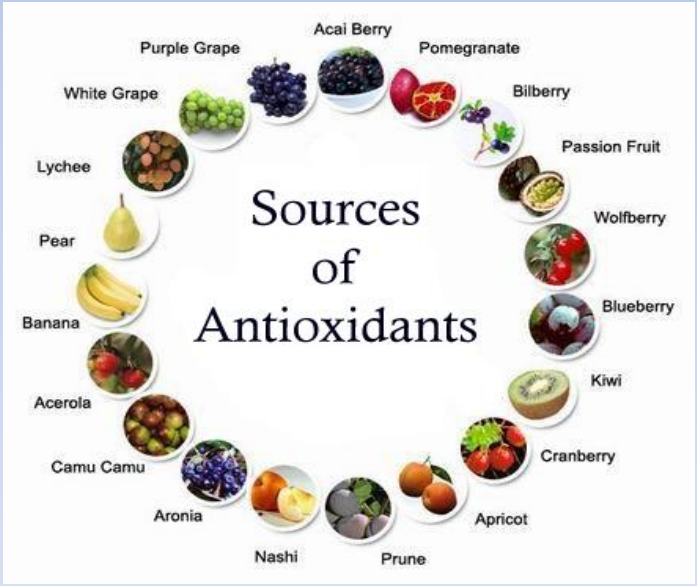
Βότανο	Μονάδες/ml	Μονάδες/ 200ml
Τσάι του βουνού	0,51	102
Βασιλικός	3,51	702
Ιβίσκος	1,65	330
Αντωνιάδα	2,82	564
Λουίζα	6,39	1278
Δυόσμος	5,63	1126
Θρουμπί	3,22	644
Λαδανιά	8,27	1654
Θυμάρι	8,16	1632
Φασκόμηλο	8,03	1606
Χαμομήλι	0,92	184
Ματζουράνα	3,79	758
Δενδρολίβανο	3,42	684
Δίκταμο	6,68	1336

Διάφορα τρόφιμα δίνουν διαφορετικά επίπεδα αντιοξειδωτικών

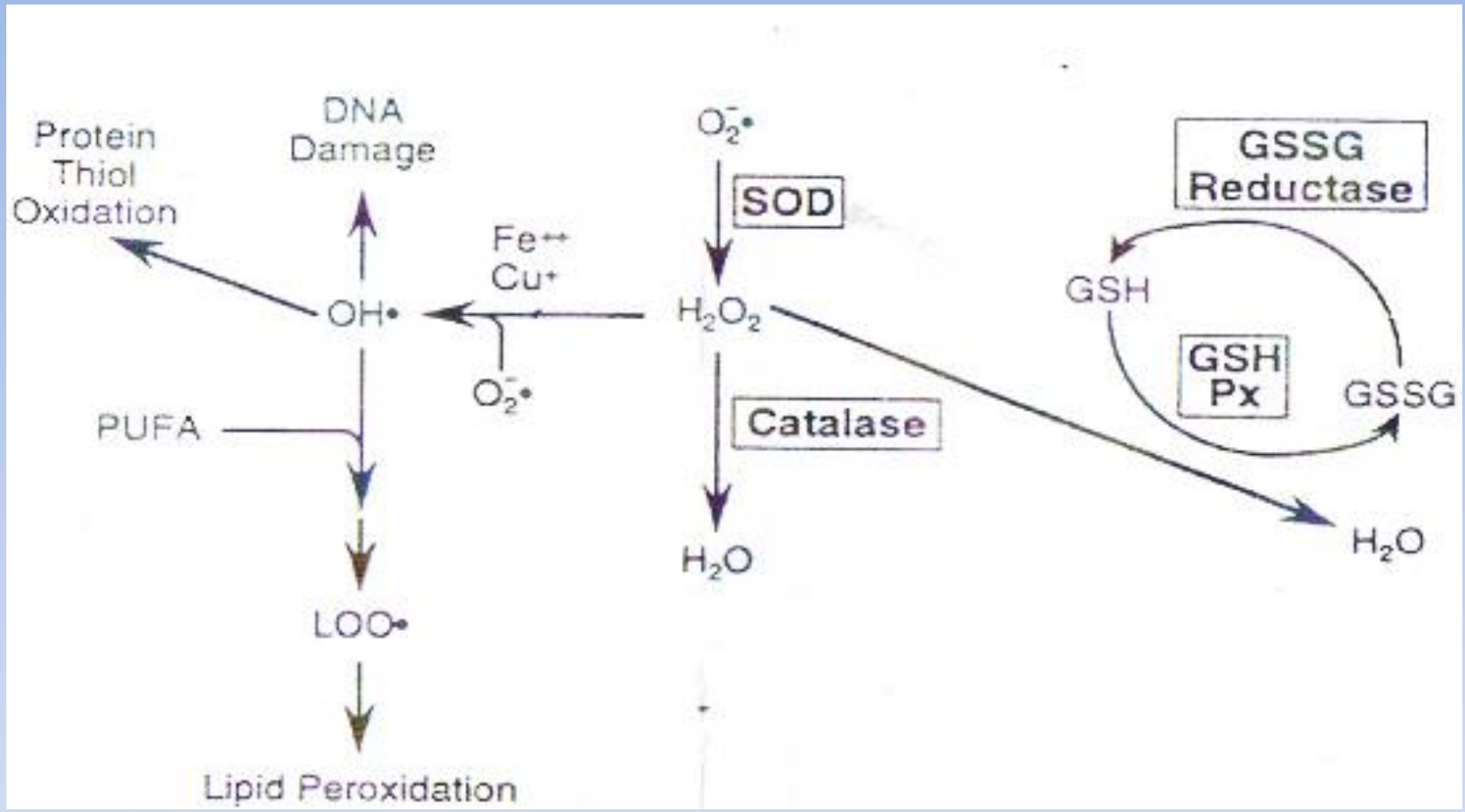
	Υγρό	Αντιοξειδωτική ικανότητα ανά δόση (200ml Χυμοί, 30ml Espresso, 45ml Greek coffee, 250ml Instant & Filtered coffee, 200ml ανά ποτήρι γάλατος και κρασιού, 330ml Μπύρα)
Χυμοί	Apple-Orange-Carrot	366-550
	Peach	144-352
	9 fruits	660-1202
	Pomegranate	3860-14280
	Apple-Pomegranate-Grape-Orange	2380-4340
	Orange	224-880
Καφέδες	Espresso	1807,5-3489
	Instant coffee	7062-10775
	Greek coffee	735,8-1285
	Filtered coffee	1522-1841
Άλλα	Milk	66-98
	White Wine	160
	Blonde Beer	396

Διάφορα τρόφιμα δίνουν διαφορετικά επίπεδα αντιοξειδωτικών

	Φαγητά	Αντιοξειδωτική δράση 300 gr (μmol DPPH)
1	Ξιφίας - πατατοσαλάτα	1200
2	Παστίτσιο	1047
3	Αγκινάρα - Αρακάς	2418
4	Λαχανόρυζο	894
5	Αρακάς - Ντομάτα Λαδερός	1080
6	Σουτζουκάκι Σμυρναίικο	1110
7	Σπανάκι - Ρεβύθι	1305
8	Πατάτες φούρνου	687
9	Κριθαράκι - Ντομάτα - Μοσχάρι	873
10	Αρνί - Κριθαράκι	1230
11	Γίγαντες	1215
12	Κοτόπουλο - Μουστάρδα	1389
13	Μπάμιες - Ντομάτα	1875
14	Ντομάτες γεμιστές	753
15	Μπιφτέκι κοτόπουλο	1665
16	Μοσχάρι κοκκινιστό	2886
17	Μουσακάς	1470

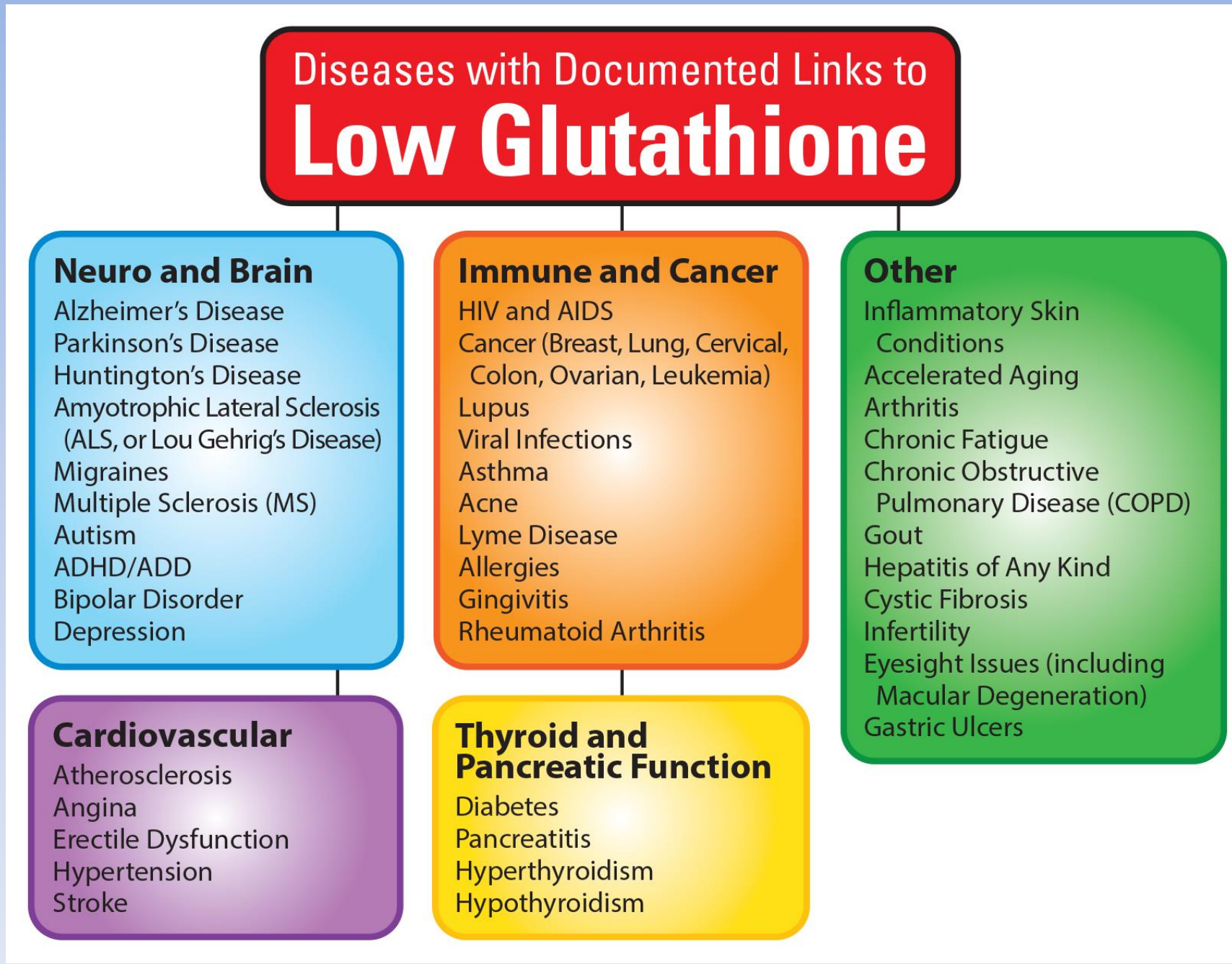


Personalized Nutrition Plans based on Measurement of Specific Redox Biomarkers in Human Blood

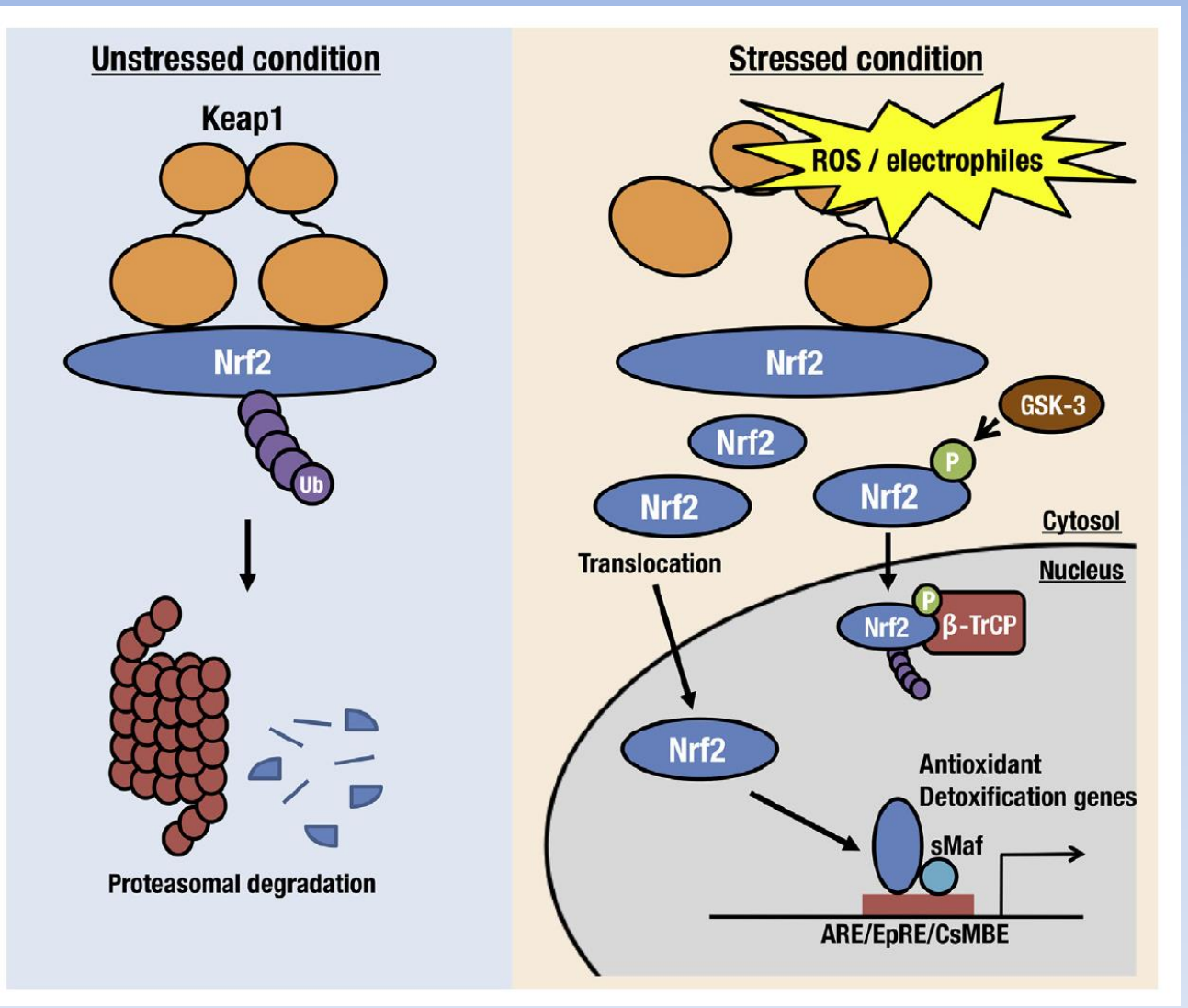


Mylonas, C. and Kouretas, D. (1999) Lipid Peroxidation and Tissue Damage. In Vivo, 13, 295-309.

Condition	GSH	TBARS	CATALASE	TAC	CARBONYLS	Literature
Cancer	↓15-30%	↑50-100%	↓12-50%	↓10-30%	↑20-50%	Badjatia et al.,2010; Kumaraguruparan et al.,2002
Cardiovascular	↓17-37%	↑100-142%	↓60-70%	↓20-30%	↑100-140%	Singh et al.,2015; Noichri1 et al.,2013;Flores-Mateo et al.,2009
Kidney failure	↓25-35%	↑120-150%	↓30-40%	↓30-40%	↑50-70%	Santangelo et al.,2004; Simmons et al.,2005; Aziz et al.,2013
Diabetes	↓15-20%	↑50-60%	↓25-30%	↓30-40%	↑50-70%	Stambouli et al., 2015; Maellaro et al.,2011; Goth et al.,2001

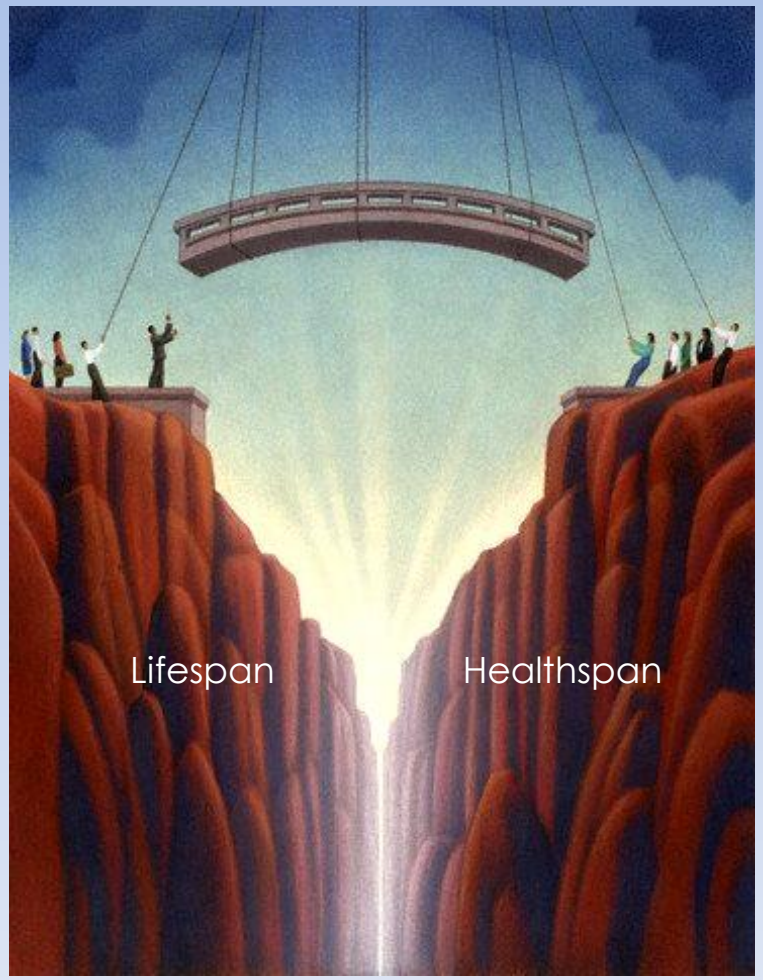

Diseases with Documented Links to
Low Glutathione
Neuro and Brain
Alzheimer's Disease
Parkinson's Disease
Huntington's Disease
Amyotrophic Lateral Sclerosis (ALS, or Lou Gehrig's Disease)
Migraines
Multiple Sclerosis (MS)
Autism
ADHD/ADD
Bipolar Disorder
Depression
Immune and Cancer
HIV and AIDS
Cancer (Breast, Lung, Cervical, Colon, Ovarian, Leukemia)
Lupus
Viral Infections
Asthma
Acne
Lyme Disease
Allergies
Gingivitis
Rheumatoid Arthritis
Other
Inflammatory Skin Conditions
Accelerated Aging
Arthritis
Chronic Fatigue
Chronic Obstructive Pulmonary Disease (COPD)
Gout
Hepatitis of Any Kind
Cystic Fibrosis
Infertility
Eyesight Issues (including Macular Degeneration)
Gastric Ulcers
Cardiovascular
Atherosclerosis
Angina
Erectile Dysfunction
Hypertension
Stroke
Thyroid and Pancreatic Function
Diabetes
Pancreatitis
Hyperthyroidism
Hypothyroidism

Nrf2 pathway

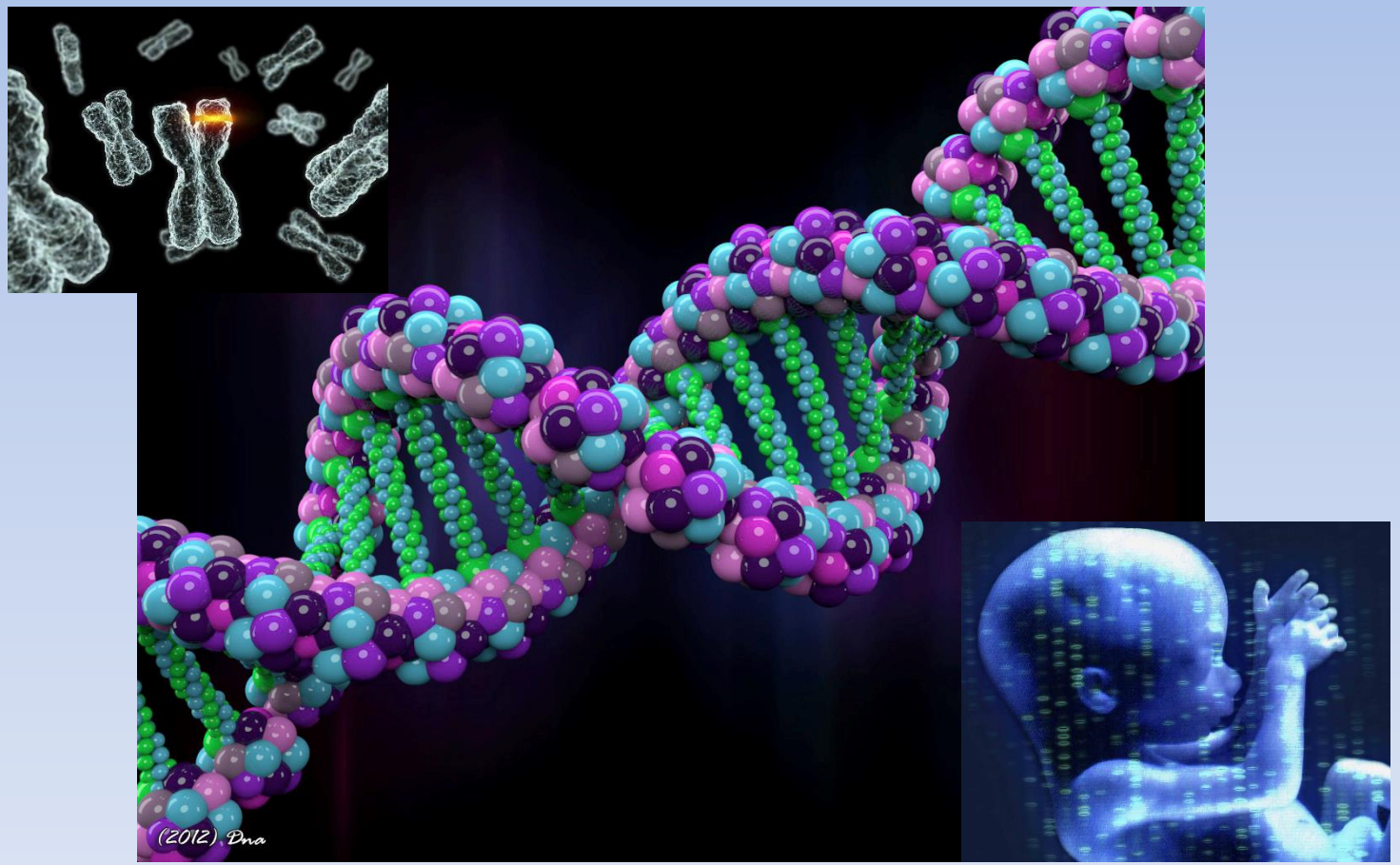


Overview of redox regulation by Keap1–Nrf2 system in toxicology and cancer Mikiko Suzuki, Akihito Otsuki, Nadine Keleku-Lukwete and Masayuki Yamamoto. Current Opinion in Toxicology 2016, 1:29–36

Is There a Way to Bridge the Gap Between Lifespan and Healthspan?



Is Your Lifespan (and/or Healthspan) "Programmed" in Your Genes?



Genetics

Your Genetic Make-up Influences Life Expectancy

A glance at your family tree may indicate whether you have a tendency to live a long, healthy life

Family History

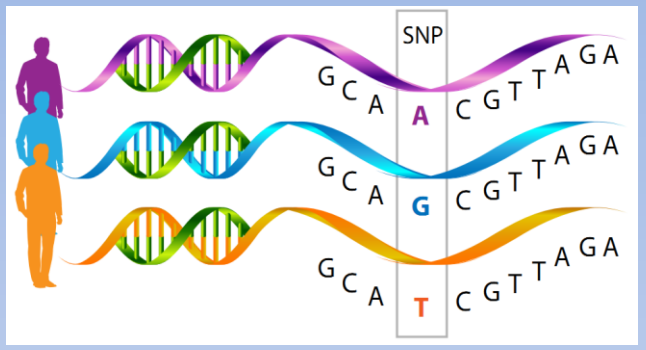
1. Exceptional longevity (1 to 3 decades longer than average) tends to run in families

2. Siblings of "super-centenarians" tend to live longer than average

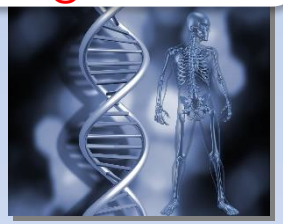
What Does Genetic Analysis of Exceptionally Long-lived People Reveal About Longevity?

There are "nodes" of exceptionally long-lived people throughout the world

Genome Analysis [with "single nucleotide polymorphisms" (SNPs)] of Exceptionally Long-lived People Reveal…



Complex Genetic Signatures



19 different genetic groupings

Very Few Genes Consistently Involved

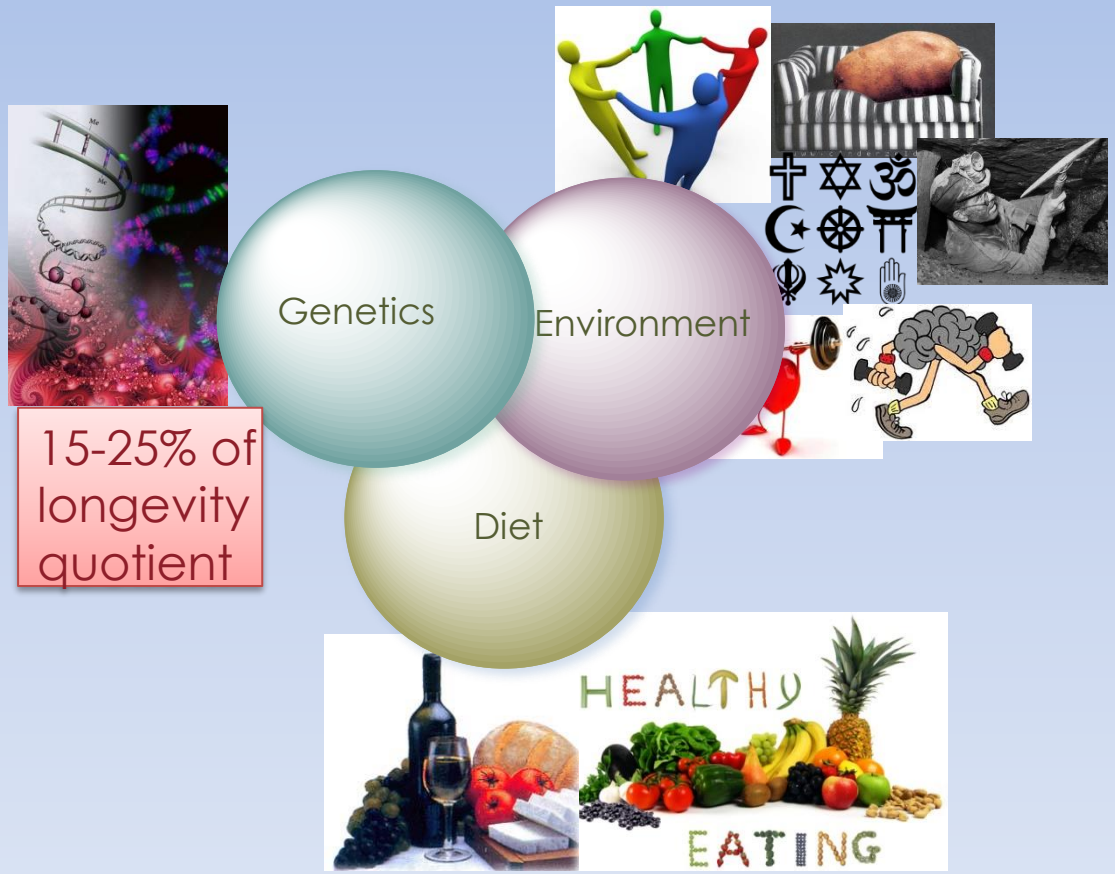
- FOXO3A
- APOE
- Many SNPs

No Genes Associated With Diseases

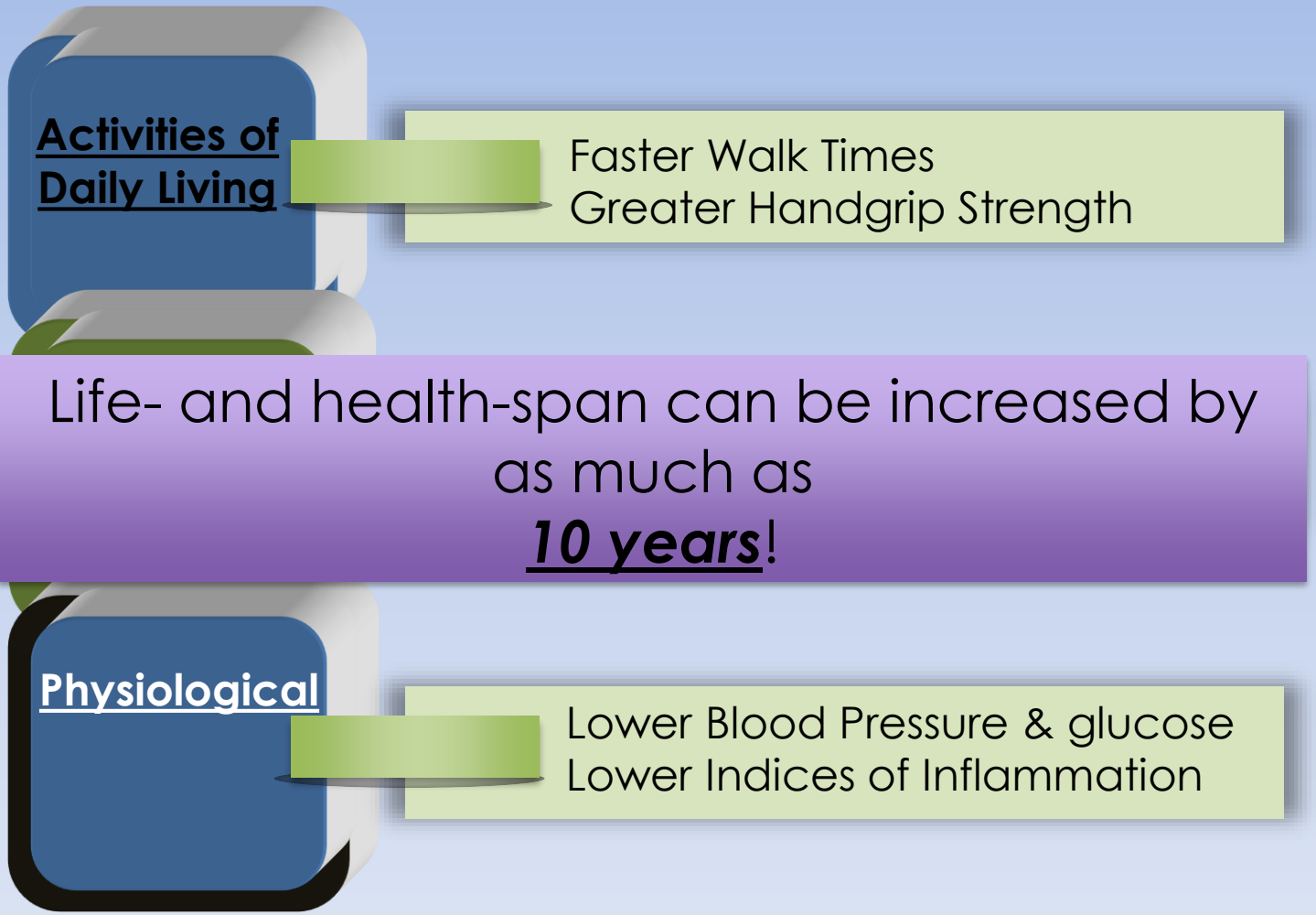
Longevity genes confer resiliency

Genes do not solely govern whether you will live longer than an average lifespan

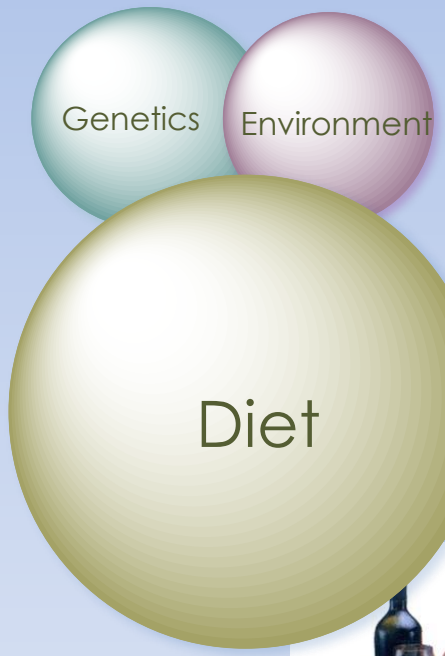
Genetic Analysis Suggests that Environment & Diet are the Major Determinants for Healthy Aging



Accentuating Positive Lifestyle Factors & Eliminating the Adverse Ones Promotes Healthy Aging



Diet is the Largest Factor Affecting Longevity and Healthy Aging



Nutrient influence on healthy aging is being extensively studied in humans and in many animal models of aging

THE 3 PILLARS OF METABOLIC HEALTH

1ST PILLAR

Consumption of plant – derived products rich in polyphenols promotes healthy lifespan

What is the quantity of antioxidants for a personalized nutrition regime?

ELSEVIER

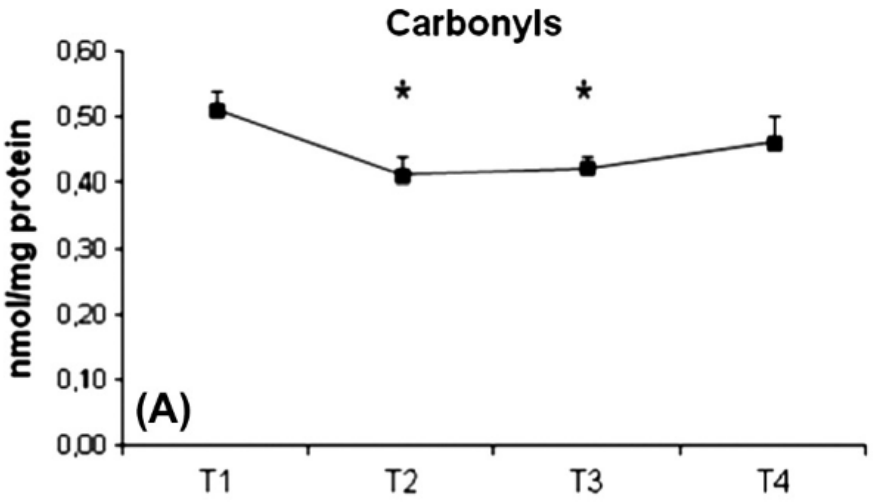
Food and Chemical Toxicology

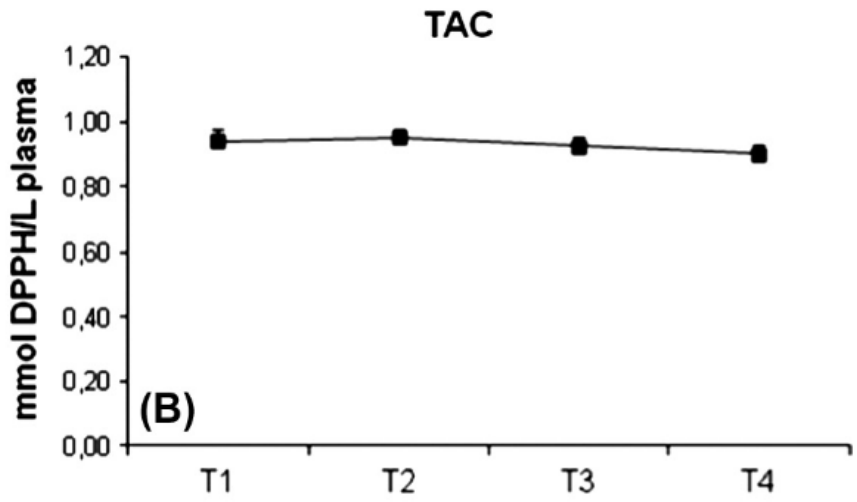
Volume 73, November 2014, Pages 1-6

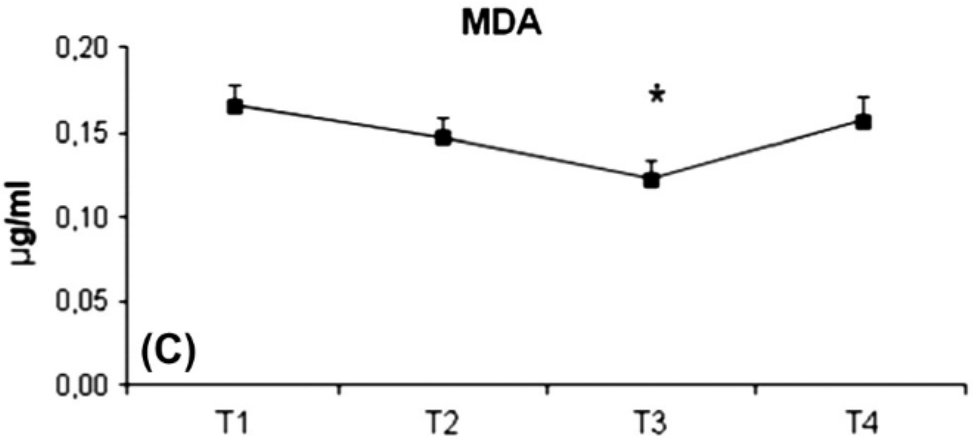
Pomegranate juice consumption increases GSH levels and reduces lipid and protein oxidation in human blood

Chrysoula M. Matthaiou [b], Nikolaos Goutzourelas [a], Dimitrios Stagos [a], Eleni Sarafoglou [a], Athanasios Jamurtas [c], Sofia D. Koulocheri [b], Serkos A. Haroutounian [b], Aristidis M. Tsatsakis [d], Dimitrios Kouretas [a]

https://doi.org/10.1016/j.fct.2014.07.027

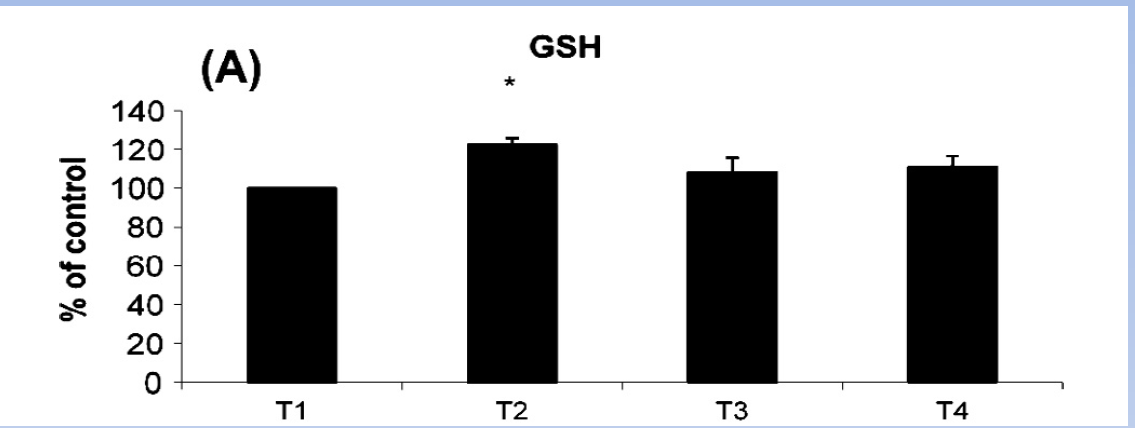






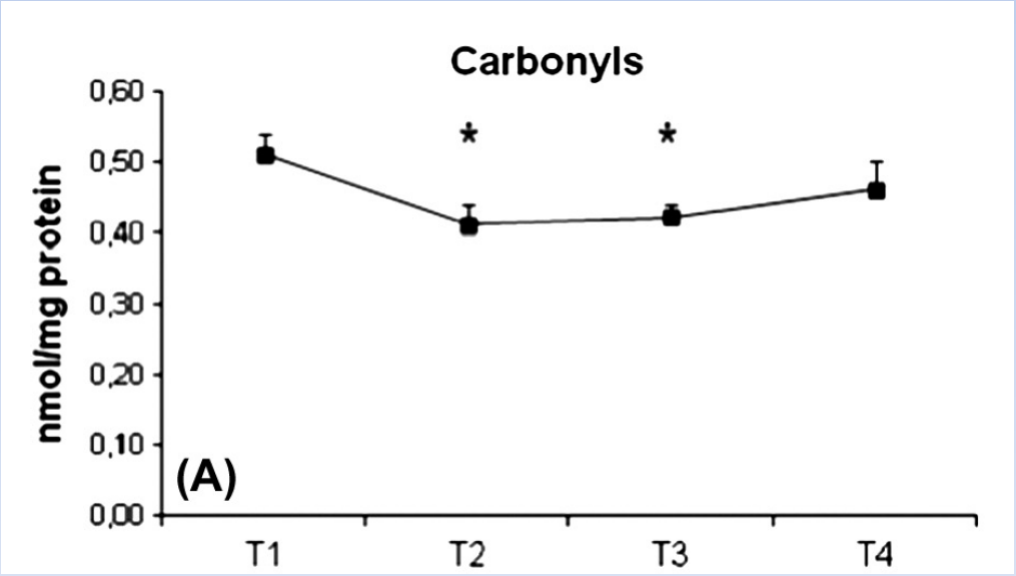
T1: BEFORE JUICE
T2: IMMEDIATELY AFTER STOPPING JUICE (2 WEEKS)

T3: A WEEK AFTER THE JUICE ADMINISTRATION
T4: 3 WEEKS AFTER STOPPING JUICE ADMINISTRATION



Statistically significant increase in GSH with pomegranate juice for 2 weeks

Statistically significant decrease in protein carbonyls with pomegranate juice for 2 weeks and maintained for 1 month



antioxidants

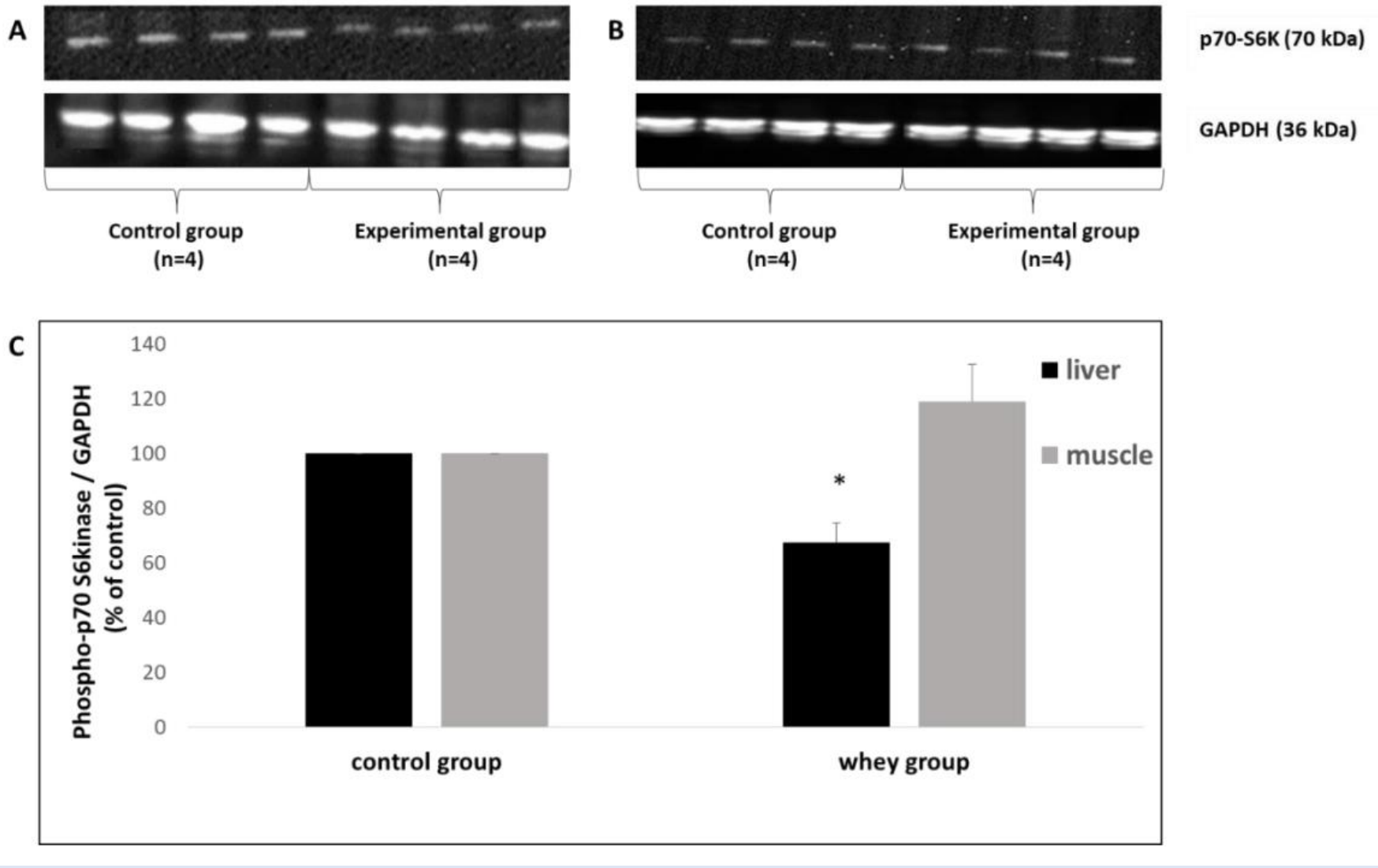
MDPI

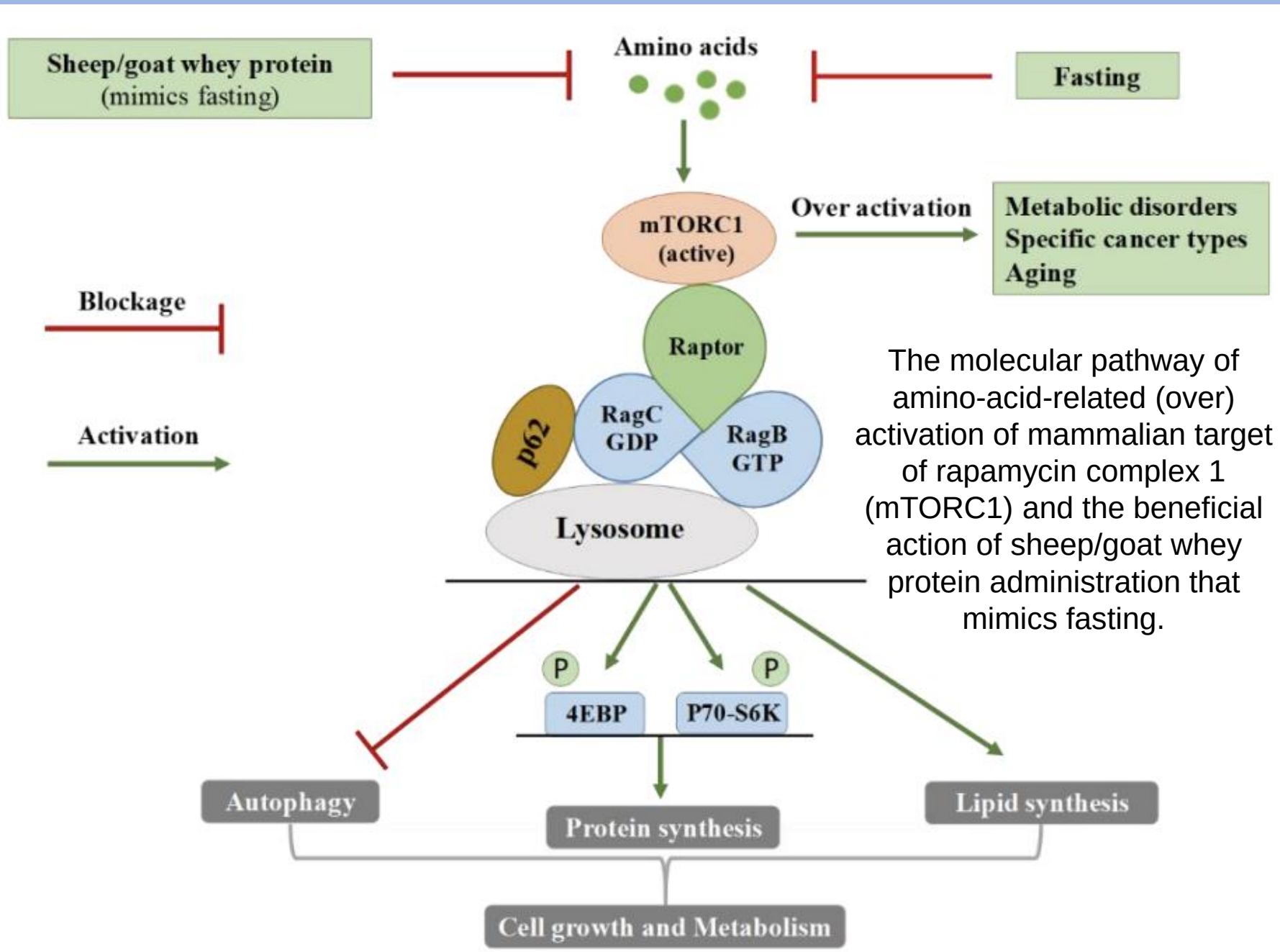
Article

The Strong Antioxidant Sheep/Goat Whey Protein Protects Against mTOR Overactivation in Rats: A Mode of Action Mimicking Fasting

Efthalia Kerasioti [1], Aristidis Veskoukis [1], Christina Virgiliou [2,3], Georgios Theodoridis [2,3], Ioannis Taitzoglou [4] and Dimitrios Kouretas [1,*]

Sheep/Goat Whey Protein inactivates of mTOR



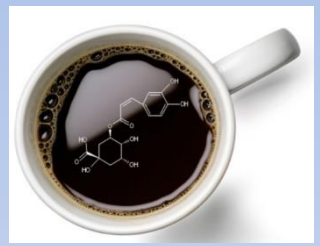


The molecular pathway of amino-acid-related (over) activation of mammalian target of rapamycin complex 1 (mTORC1) and the beneficial action of sheep/goat whey protein administration that mimics fasting.

Comparison of antioxidants

1 glass of pomegranate juice

=



3 cups espresso
1 cup instant coffee

=

5 glasses of red wine

=

17 cups of juice

23 glasses of beer

=

50 glasses of white wine

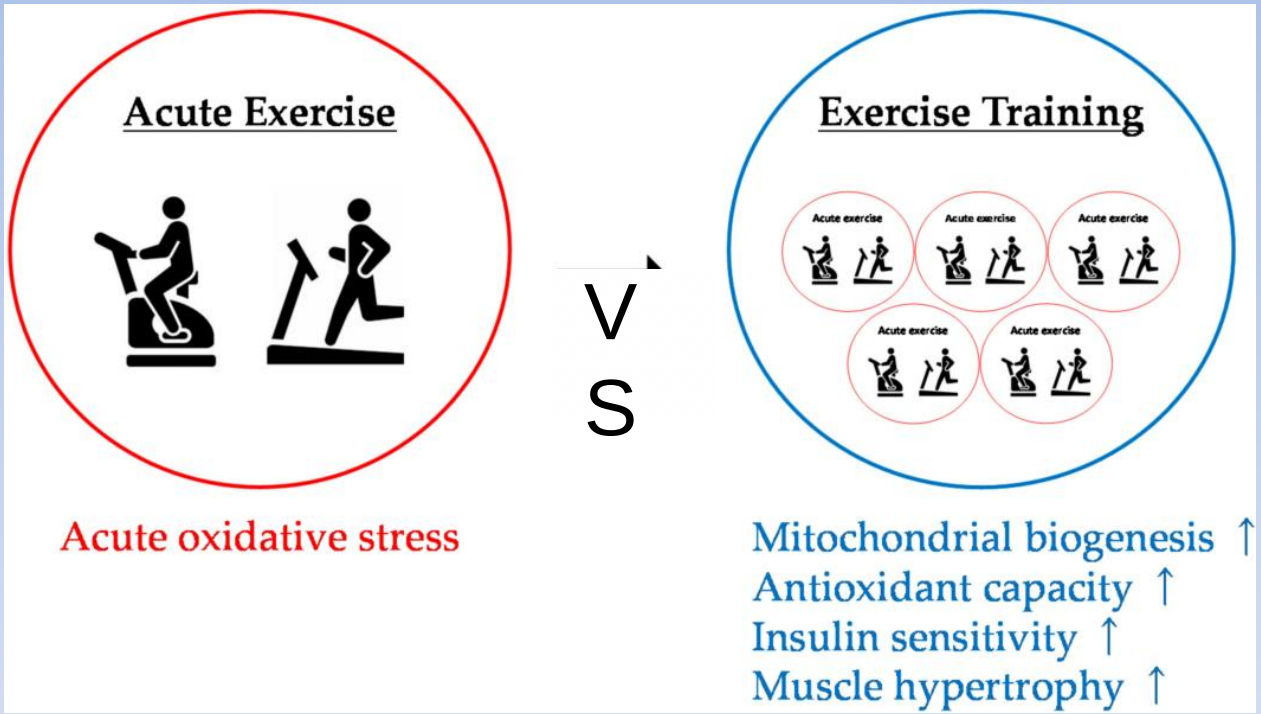
=

100 glasses of milk

2nd PILLAR

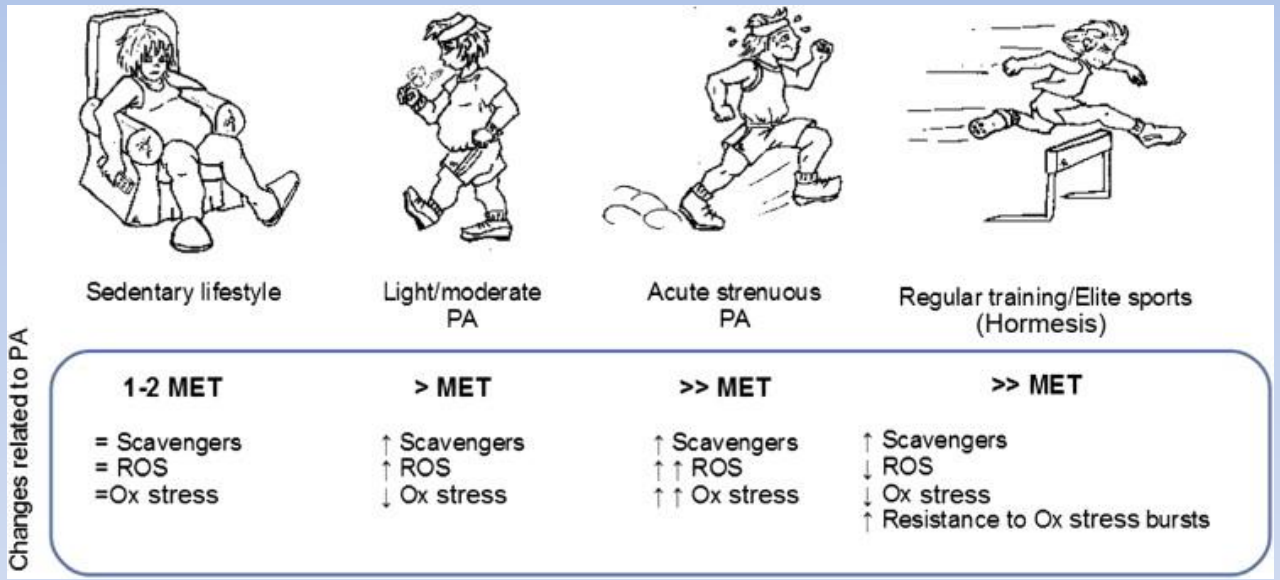
Exercise promotes healthy lifespan

Reactive species and physiological adaptations to endurance training



Takuji Kawamura, Isao Muraoka. Exercise-Induced Oxidative Stress and the Effects of Antioxidant Intake from a Physiological Viewpoint. Chemistry, MedicinePublished in Antioxidants 2018. DOI:10.3390/antiox7090119

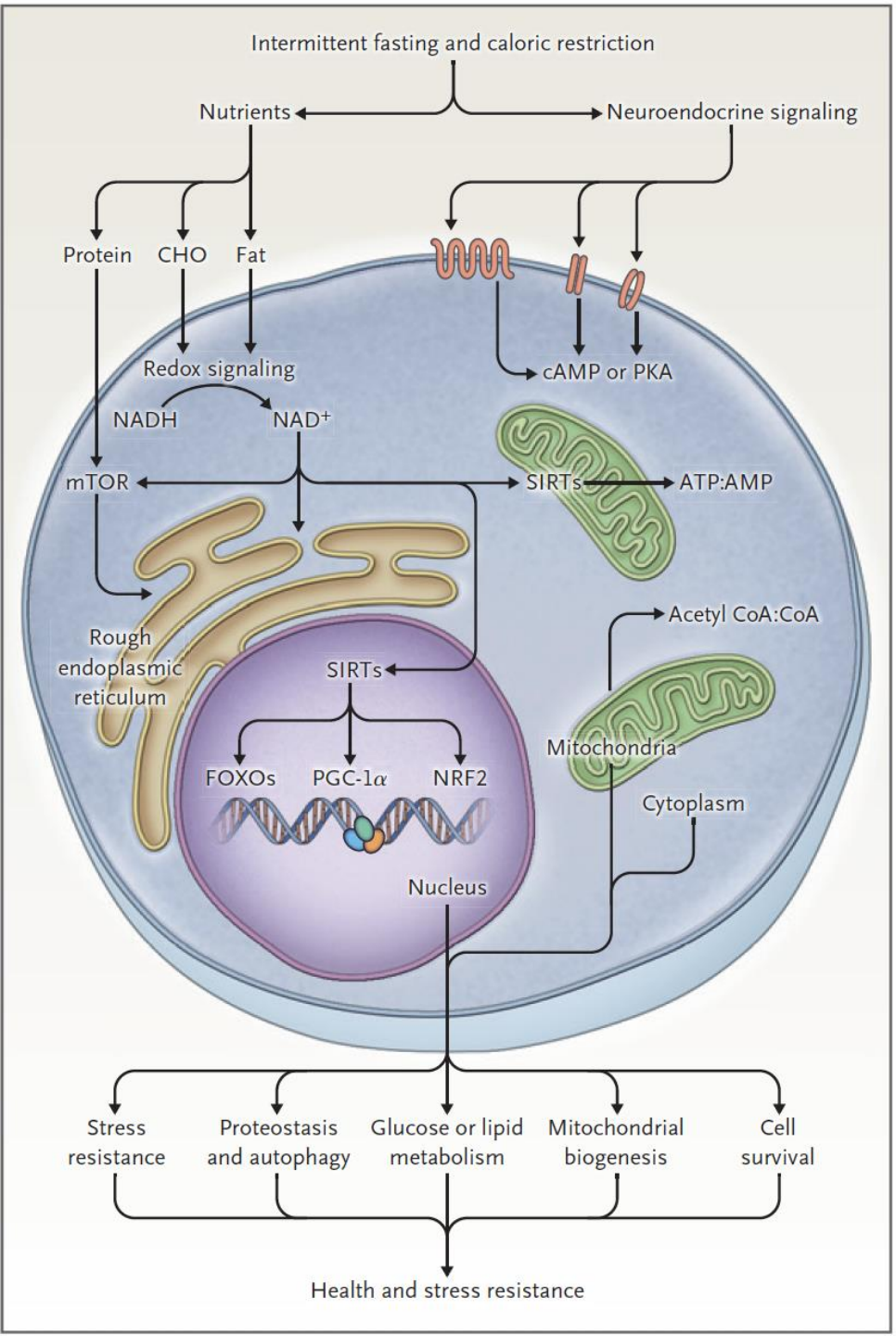
Effects of physical activity on oxidative stress status



Alessandro PingitoreM.D.,Giuseppina Pace PereiraLimaPh.D., FrancescaMastorciPh.D., AlfredoQuinonesM.D., GiorgioIervasiM.D., CristinaVassallePh.D. Exercise and oxidative stress: Potential effects of antioxidant dietary strategies in sports. Volume 31, Issues 7–8, July–August 2015, Pages 916-922

3RD PILLAR

Fasting induces metabolic shift and promotes healthy lifespan



Fasting and health

Cellular Responses to Energy Restriction That Integrate Cycles of Feeding and Fasting with Metabolism.

Effects of Intermittent Fasting on Health, Aging, and Disease. Rafael de Cabo, Ph.D., and Mark P. Mattson, Ph.D. N Engl J Med 2019;381:2541-51. DOI: 10.1056/NEJMra1905136

Buchinger Wilhelmi Clinic

antioxidants

MDPI

Article

Influence of Long-Term Fasting on Blood Redox Status in Humans

Françoise Wilhelmi de Toledo [1,*,†], Franziska Grundler [1,2,†], Nikolaos Goutzourelas [3], Fotios Tekos [3], Eleni Vassi [3], Robin Mesnage [4] and Demetrios Kouretas [3,*]

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4 Gene Expression and Therapy Group, King's College London, Faculty of Life Sciences & Medicine, Department of Medical and Molecular Genetics, 8th Floor, Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT, UK; robin.mesnage@kcl.ac.uk
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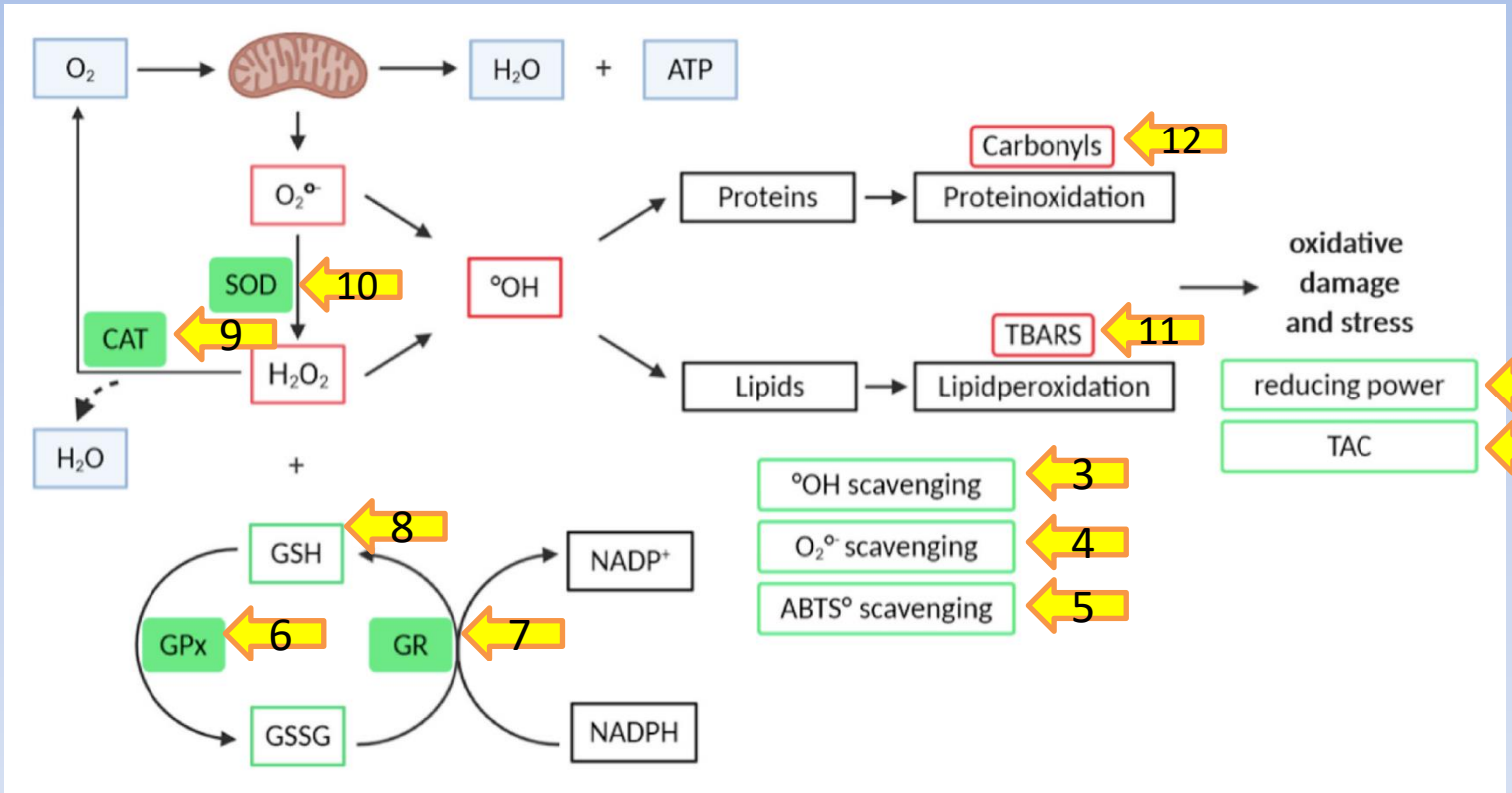
† These authors contributed equally to this work.

Received: 16 April 2020; Accepted: 4 June 2020; Published: 6 June 2020

check for updates

Overview of the measured redox parameters



Parameters	Baseline
Age, years	57.0 (±10.5)
Female, n	68 (62%)
Male, n	41 (38%)

antioxidants

MDPI

Article

Influence of Long-Term Fasting on Blood Redox Status in Humans

Françoise Wilhelmi de Toledo [1,*,†], Franziska Grundler [1,2,†], Nikolaos Goutzourelas [3], Fotios Tekos [3], Eleni Vassi [3], Robin Mesnage [4] and Demetrios Kouretas [3,*]

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2 Charité–Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt–Universität zu Berlin and Berlin Institute of Health, 10117 Berlin, Germany
3 Department of Biochemistry-Biotechnology, School of Health Sciences, University of Thessaly, Viopolis, 41500 Larissa, Greece; nikgkoutz@gmail.com (N.G.); fotis.tekos@gmail.com (F.T.); elenhva.97@outlook.com.gr (E.V.)
4 Gene Expression and Therapy Group, King's College London, Faculty of Life Sciences & Medicine, Department of Medical and Molecular Genetics, 8th Floor, Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT, UK; robin.mesnage@kcl.ac.uk
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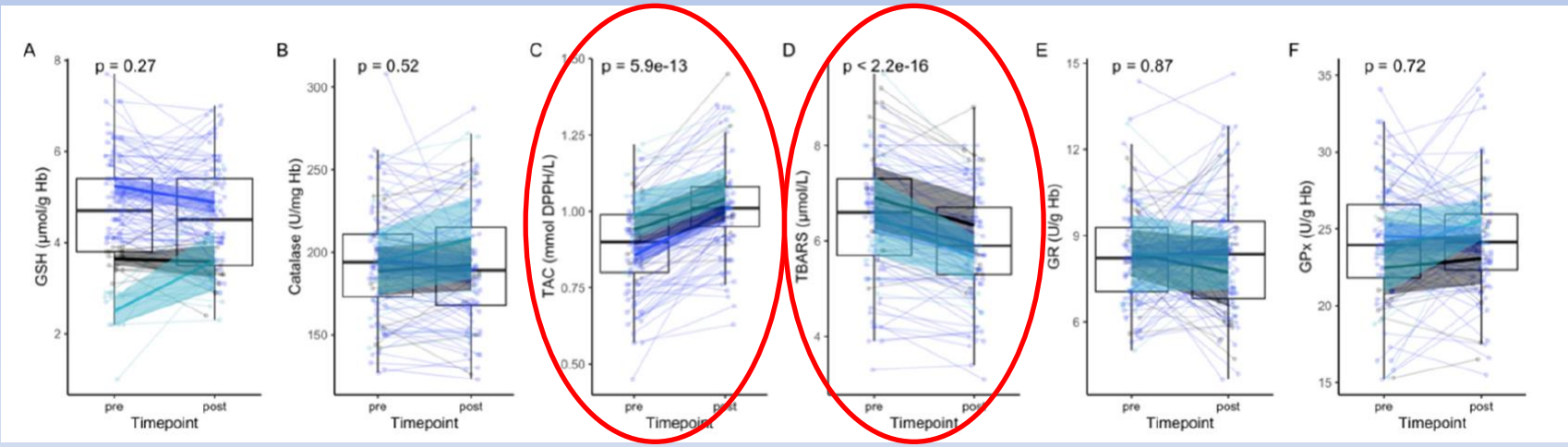
† These authors contributed equally to this work.

Received: 16 April 2020; Accepted: 4 June 2020; Published: 6 June 2020

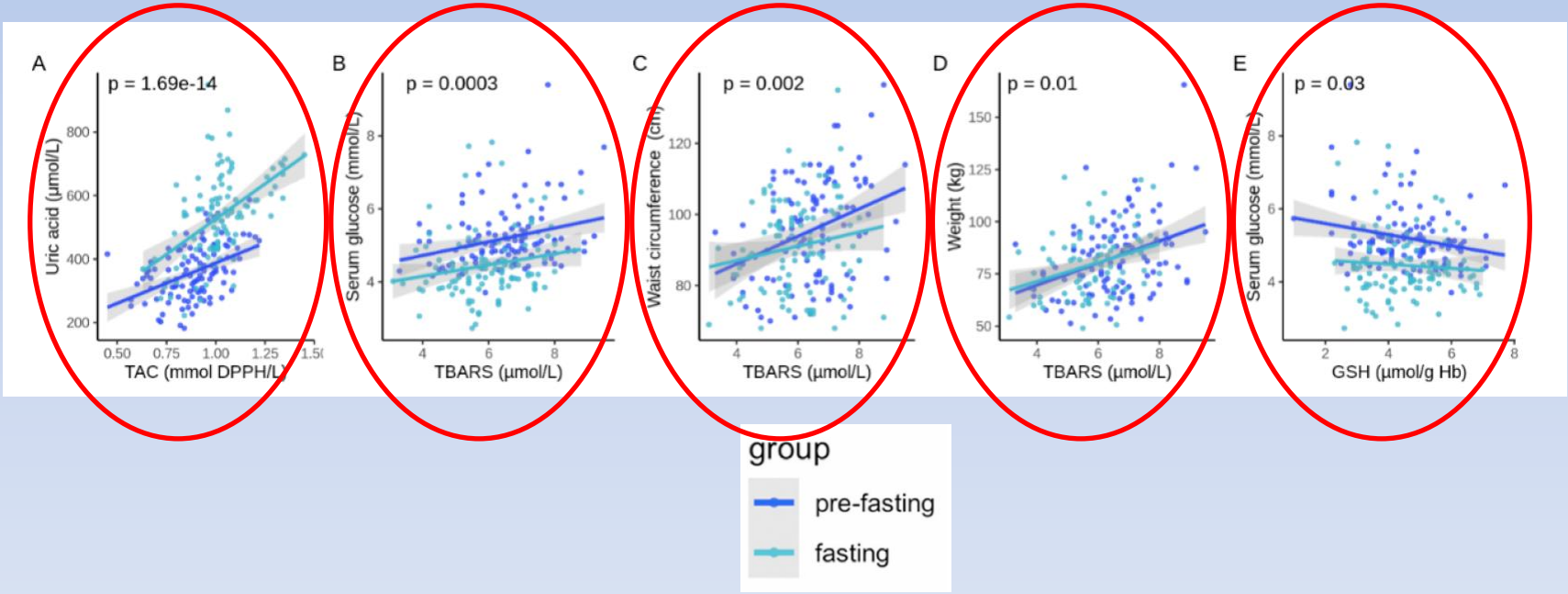
The effects of the 10-day fast on the mean levels of redox biomarkers



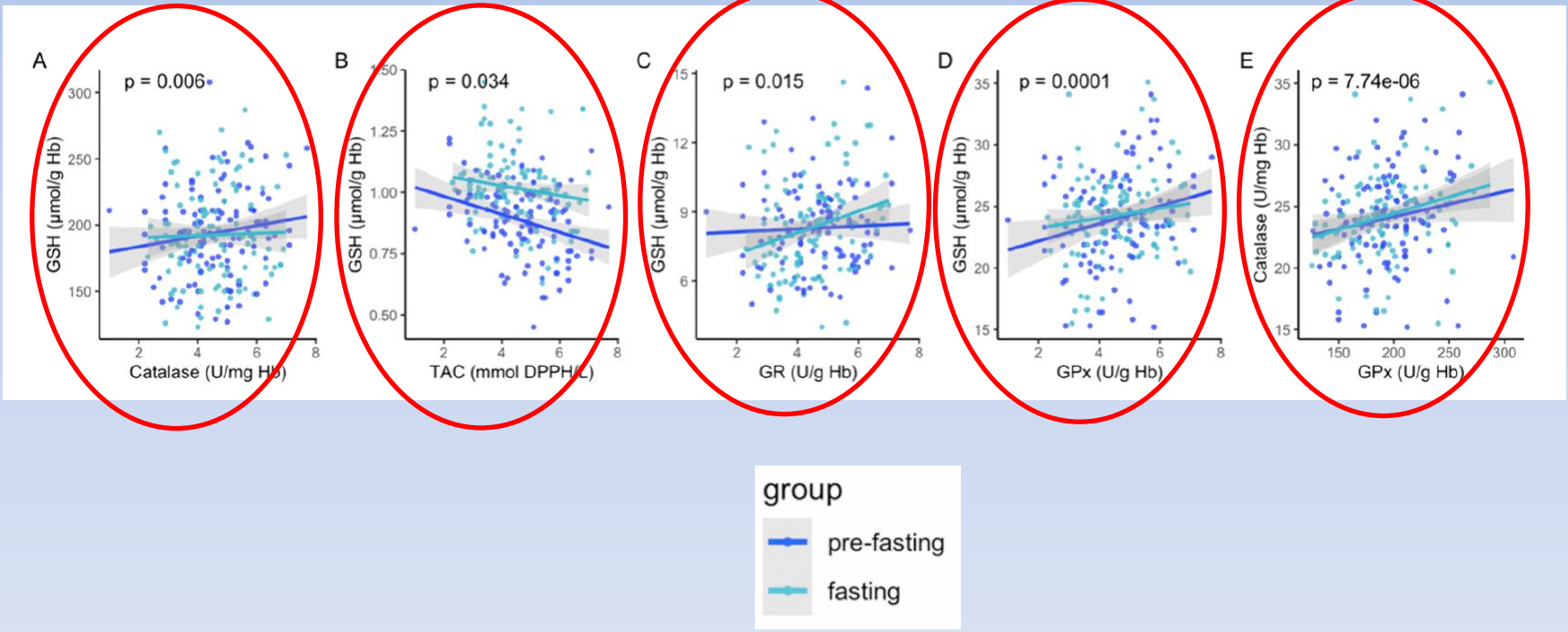
GSH levels:

- Increase → light blue
- Decrease → dark blue
- Unchanged →black

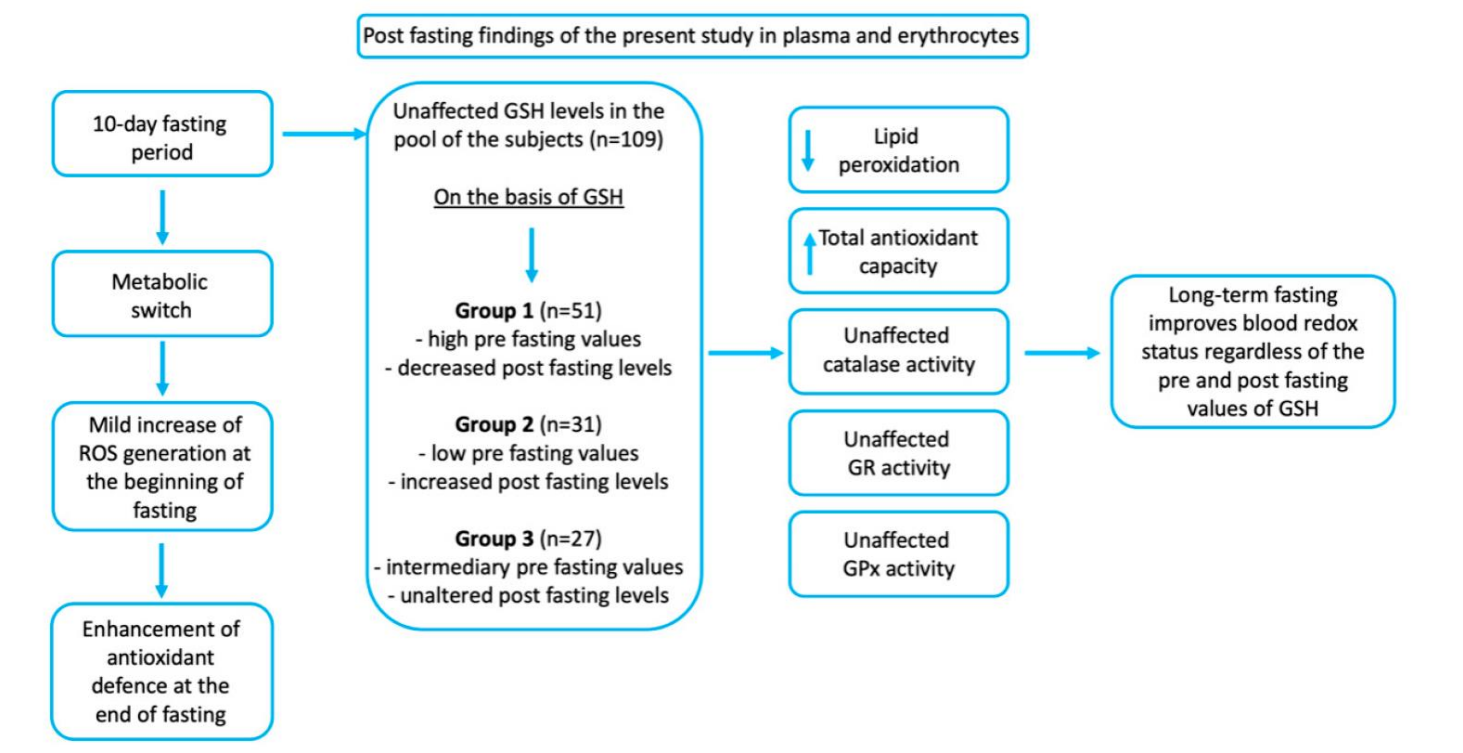
Changes in redox parameters during fasting were associated with changes in clinical parameters



Associations between the different redox parameters measured in this study



The beneficial effects of long-term fasting and the findings of the present study



Food and Chemical Toxicology 145 (2020) 111701

Contents lists available at ScienceDirect

Food and Chemical Toxicology

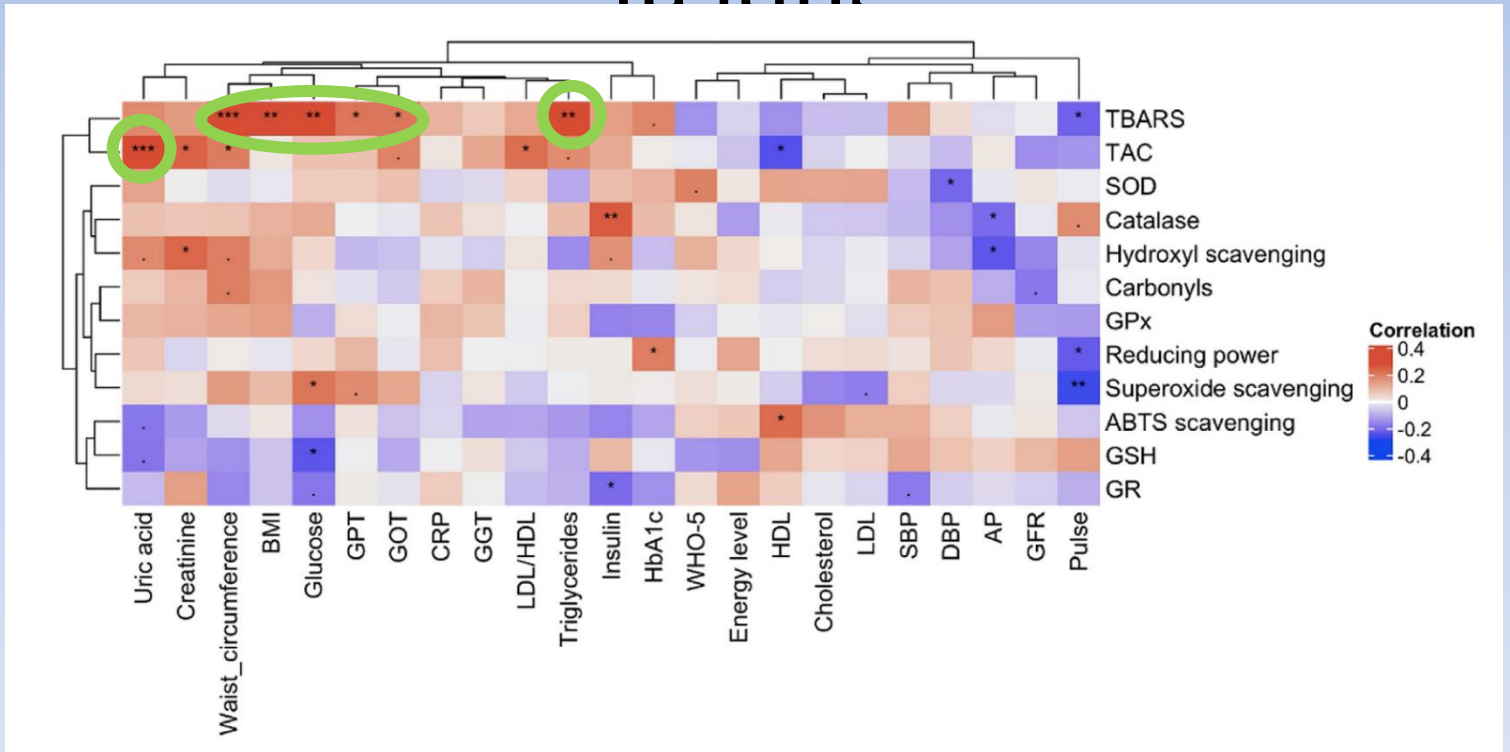
journal homepage: www.elsevier.com/locate/foodchemtox

Interplay between oxidative damage, the redox status, and metabolic biomarkers during long-term fasting

Franziska Grundler [a,b,1], Robin Mesnage [c,1], Nikolaos Goutzourelas [d], Fotios Tekos [d], Sotiria Makri [d], Michel Brack [e], Demetrios Kouretas [d,2,*], Françoise Wilhelmi de Toledo [a,2]

[a] Buchinger Wilhelmi Clinic, 88662, Überlingen, Germany
[b] Charité–Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt–Universität zu Berlin and Berlin Institute of Health, 10117, Berlin, Germany
[c] Gene Expression and Therapy Group, King's College London, Faculty of Life Sciences & Medicine, Department of Medical and Molecular Genetics, 8th Floor, Tower Wing, Guy's Hospital, Great Maze Pond, London, SE1 9RT, UK
[d] Department of Biochemistry-Biotechnology, School of Health Sciences, University of Thessaly, Viopolis, 41500, Larissa, Greece
[e] The Oxidative Stress College Paris, 75007, Paris, France

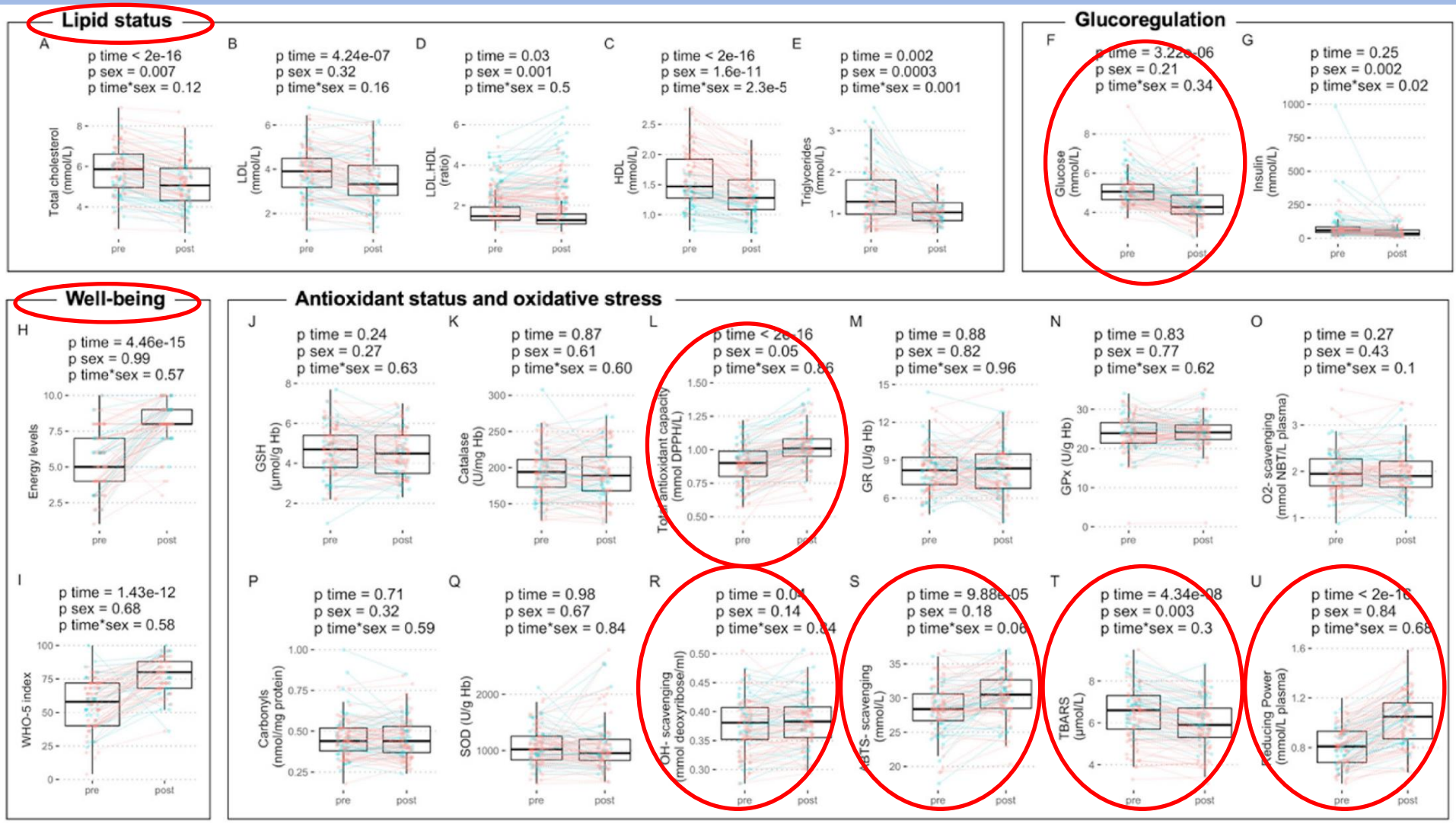
Redox parameters correlate with metabolic parameters before fasting



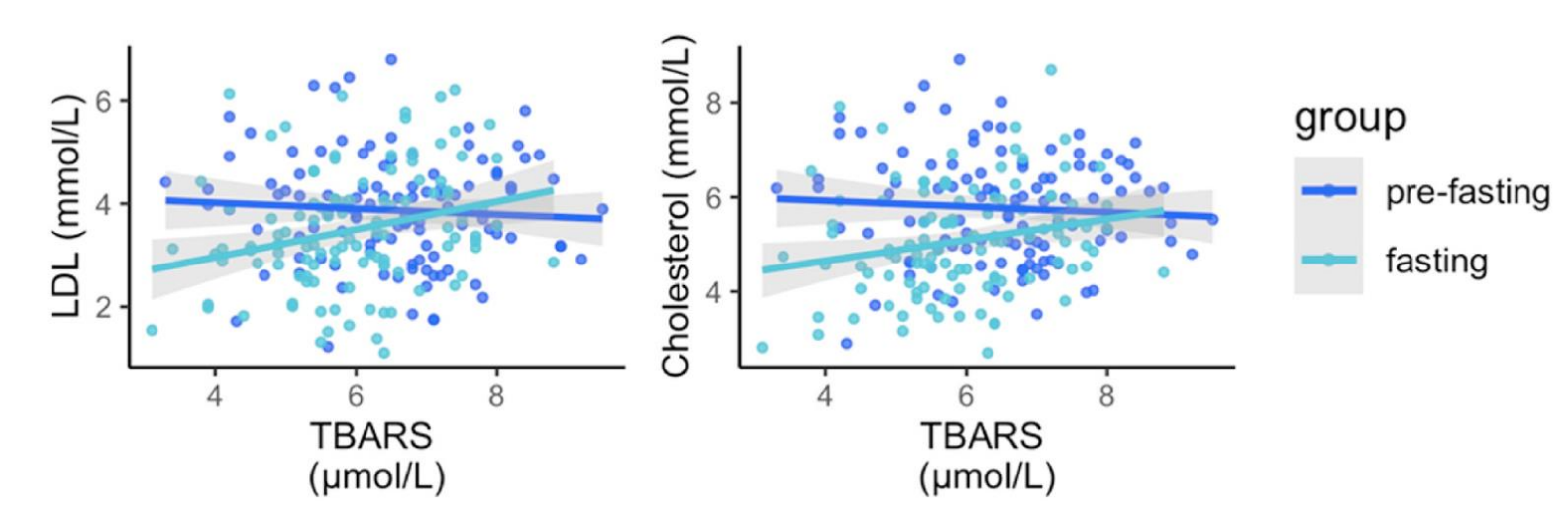
* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$


Lipid status
A
p time < 2e-16
p sex = 0.007
p time*sex = 0.12
Total cholesterol (mmol/L)
B
p time = 4.24e-07
p sex = 0.32
p time*sex = 0.16
LDL (mmol/L)
D
p time = 0.03
p sex = 0.001
p time*sex = 0.5
LDL.HDL (ratio)
C
p time < 2e-16
p sex = 1.6e-11
p time*sex = 2.3e-5
HDL (mmol/L)
E
p time = 0.002
p sex = 0.0003
p time*sex = 0.001
Triglycerides (mmol/L)
Glucoregulation
F
p time = 3.22e-06
p sex = 0.21
p time*sex = 0.34
Glucose (mmol/L)
G
p time = 0.25
p sex = 0.002
p time*sex = 0.02
Insulin (mmol/L)
Well-being
H
p time = 4.46e-15
p sex = 0.99
p time*sex = 0.57
Energy levels
I
p time = 1.43e-12
p sex = 0.68
p time*sex = 0.58
WHO-5 index
Antioxidant status and oxidative stress
J
p time = 0.24
p sex = 0.27
p time*sex = 0.63
GSH (µmol/g Hb)
K
p time = 0.87
p sex = 0.61
p time*sex = 0.60
Catalase (U/mg Hb)
L
p time < 2e-16
p sex = 0.05
p time*sex = 0.86
Total antioxidant capacity (mmol DPPH/L)
M
p time = 0.88
p sex = 0.82
p time*sex = 0.96
GR (U/g Hb)
N
p time = 0.83
p sex = 0.77
p time*sex = 0.62
GPx (U/g Hb)
O
p time = 0.27
p sex = 0.43
p time*sex = 0.1
O2- scavenging (mmol NBT/L plasma)
P
p time = 0.71
p sex = 0.32
p time*sex = 0.59
Carbonyls (nmol/mg protein)
Q
p time = 0.98
p sex = 0.67
p time*sex = 0.84
SOD (U/g Hb)
R
p time = 0.04
p sex = 0.14
p time*sex = 0.84
OH- scavenging (mmol deoxyribose/ml)
S
p time = 9.88e-05
p sex = 0.18
p time*sex = 0.06
ABTS- scavenging (mmol/L)
T
p time = 4.34e-08
p sex = 0.003
p time*sex = 0.3
TBARS (µmol/L)
U
p time < 2e-16
p sex = 0.84
p time*sex = 0.68
Reducing Power (mmol/L plasma)
pre
post

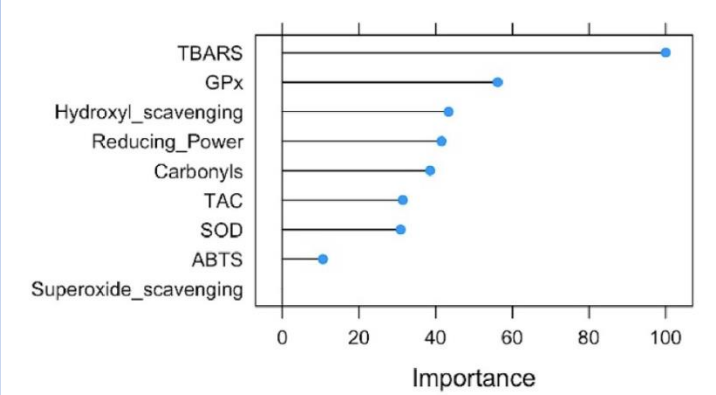
Lipid peroxidation levels affects the effects of long-term fasting on the normalization of lipid levels



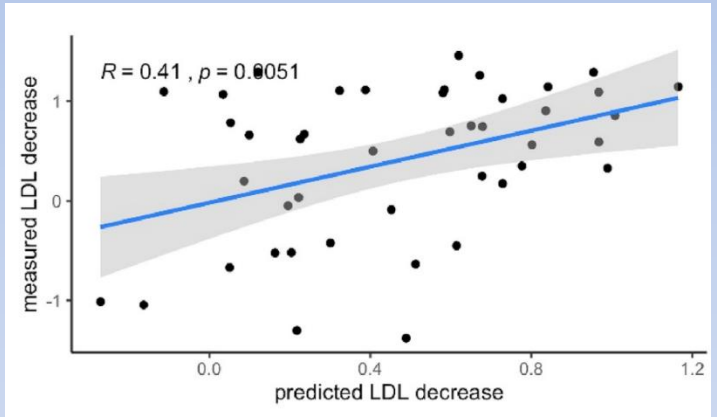
Important findings

Pre-Fasting TBARS levels can lead to individualized fasting interventions

A machine learning algorithm using a combination of antioxidant parameters measured at baseline can predict changes in markers of metabolic health caused by long-term fasting



The redox parameters that contribute to the predictive ability of the model



The values predicted by the model on an independent test set correlate well with the measured decrease in LDL during fasting

Human biomarker measurement services

HOLISTIC EVALUATION OF BLOOD REDOX STATUS MEASURING A WIDE RANGE OF BIOMARKERS, BEFORE AND AFTER A PROPOSED NUTRITIONAL SCHEME

We measure the following biomarkers

- **Control of antioxidants**
  - GSH (reduced glutathione),
  - TAC (total antioxidant capacity),
  - Reducing Power,
  - ABTS Radical scavenging
  - Hydroxyl Radical scavenging
  - Superoxide Radical scavenging
- **Control of critical gene products**
  - Catalase,
  - GPx (glutathione peroxidase),
  - SOD (peroxidase dismutase),
  - GR (glutathione reductase) – enzymatic antioxidants that are involved in protecting the cell against free radicals.
- **Control of oxidative damage products**
  - TBARS (lipid peroxidation),
  - Protein Carbonyls (oxidative protein damage)-the end products of free radical action.

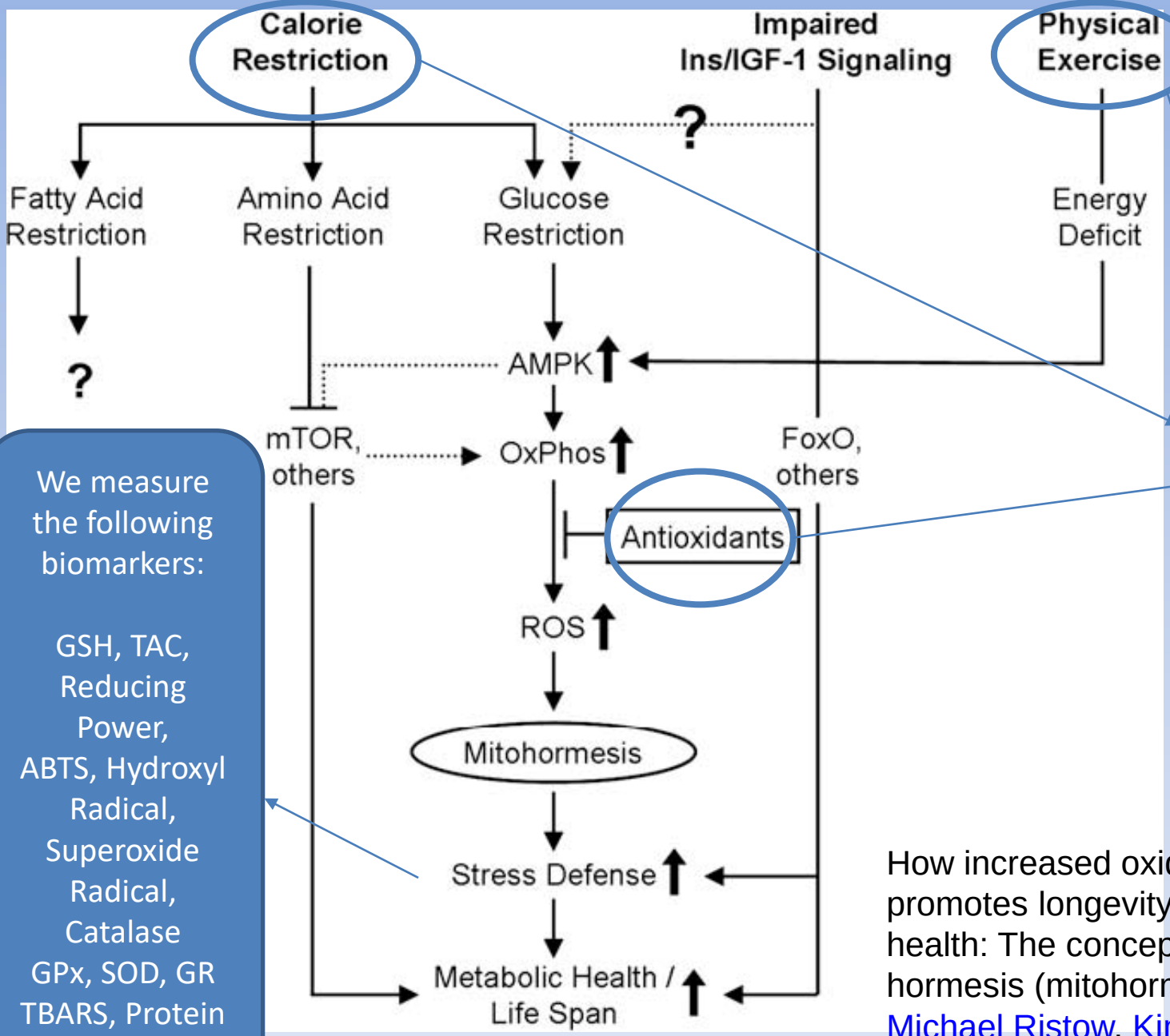
The effect of personalized nutrition on human redox status is evaluated and human health is improved

Antioxidant consumption, exercise and fasting regulate baseline gsh levels in blood and improve human redox status

1ST PILLAR

2ND PILLAR

3ND PILLAR



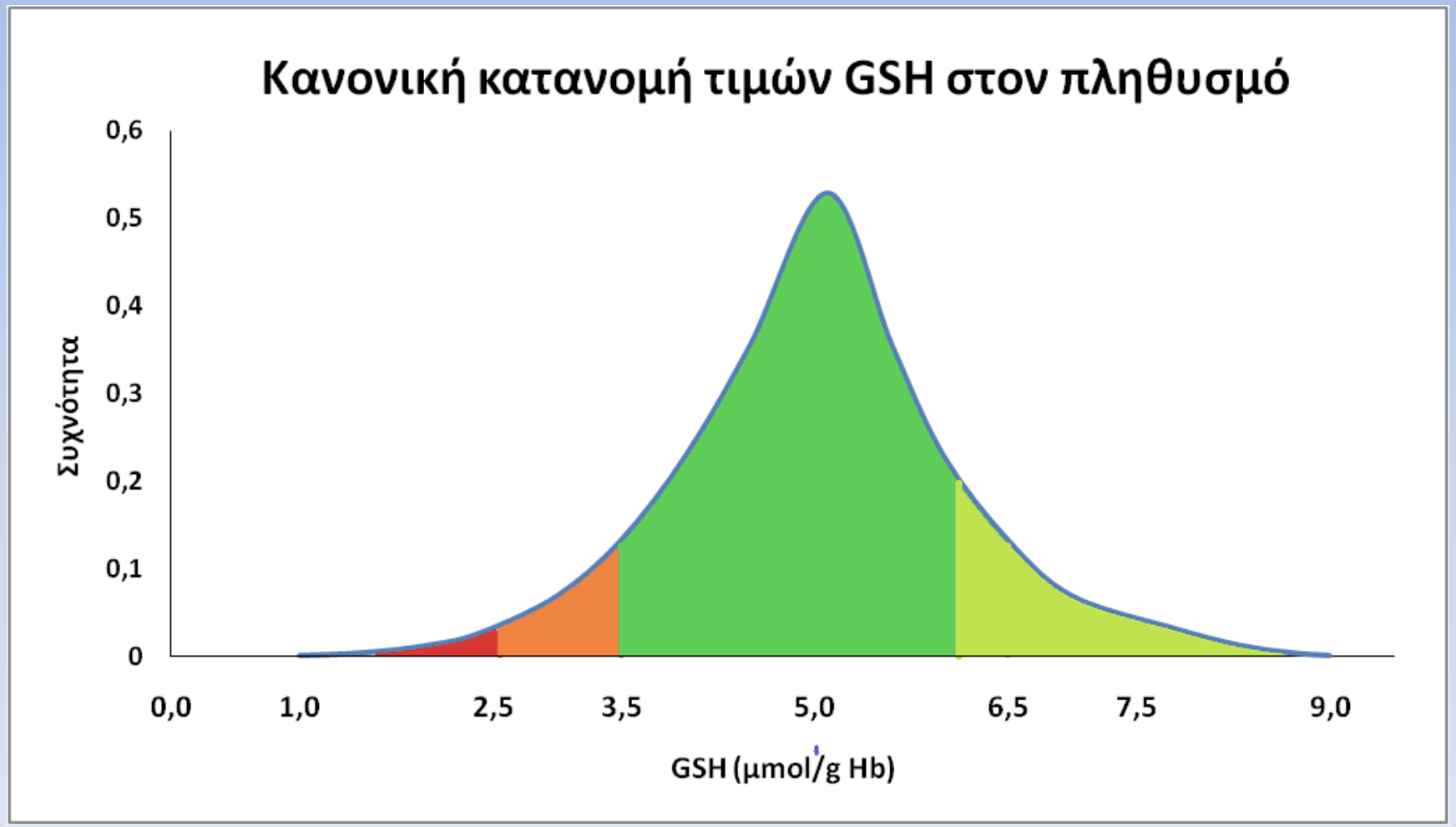
We measure the following biomarkers:

GSH, TAC, Reducing Power, ABTS, Hydroxyl Radical, Superoxide Radical, Catalase GPx, SOD, GR TBARS, Protein Carbonyls

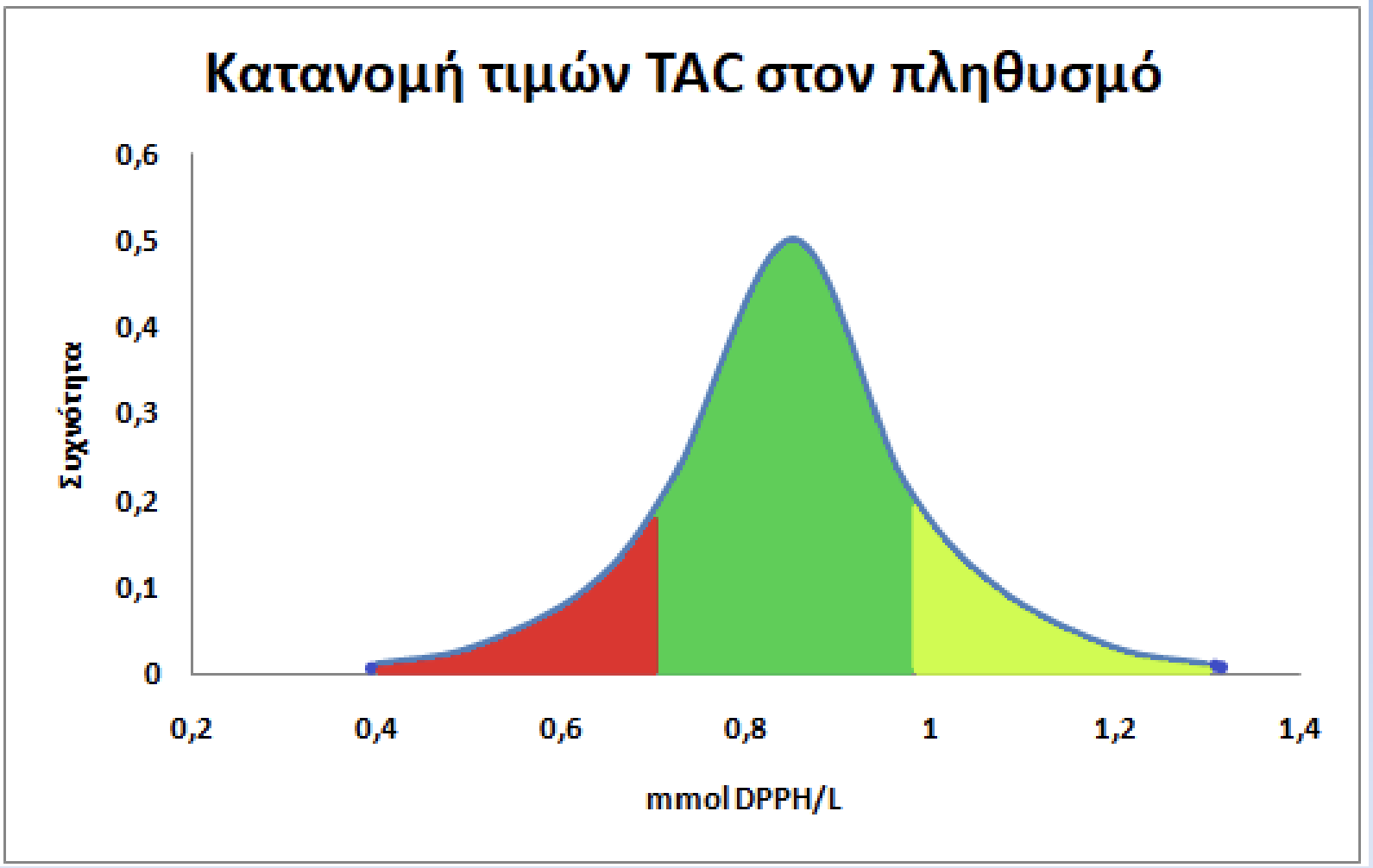
The 3 Pillars of metabolic health

How increased oxidative stress promotes longevity and metabolic health: The concept of mitochondrial hormesis (mitohormesis) Michael Ristow, Kim Zarse. Biology, Medicine. Published in Experimental Gerontology 2010

Κανονική κατανομή σε δείγμα 5.000 ατόμων



Κανονική κατανομή σε δείγμα 5.000 ατόμων



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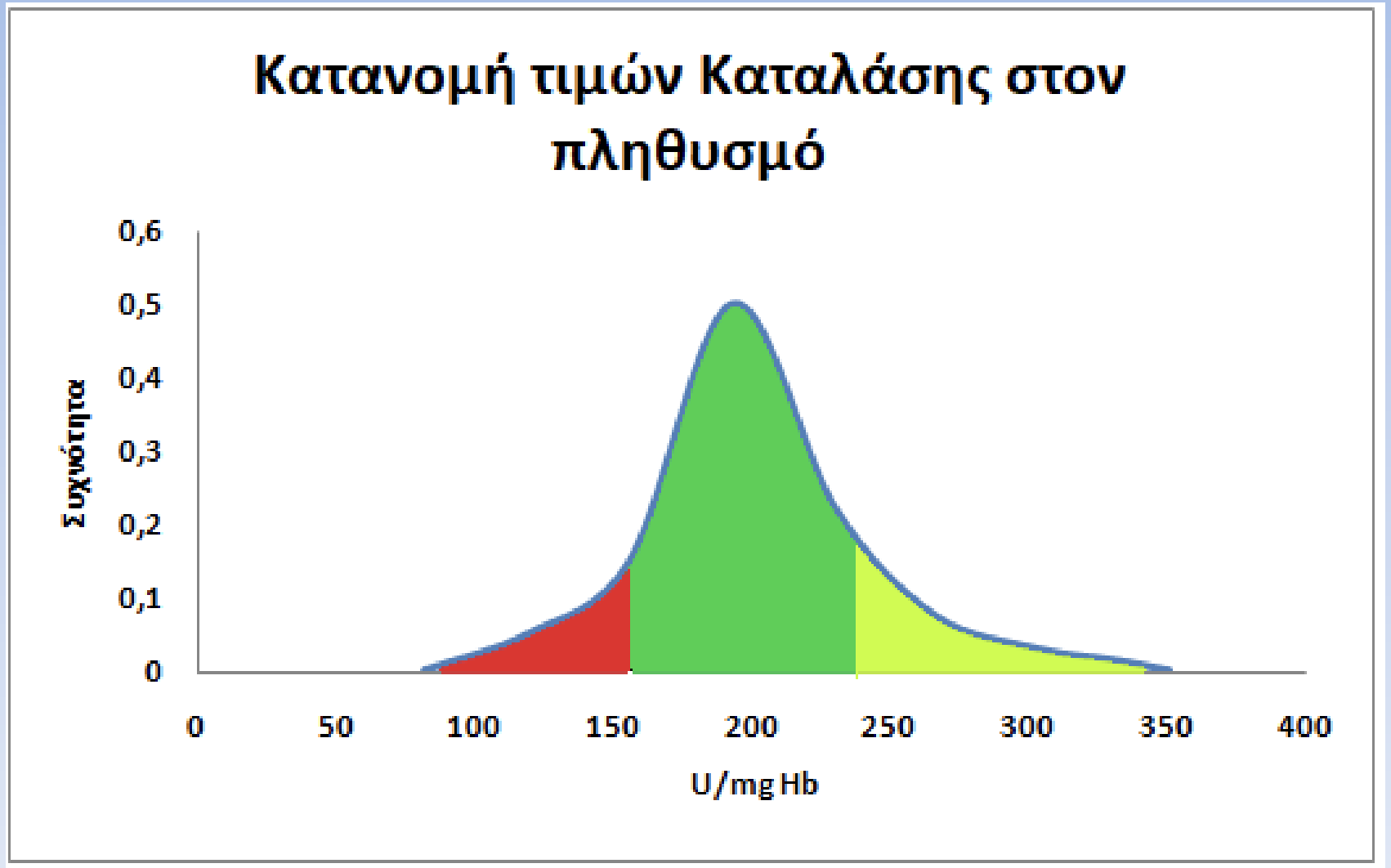

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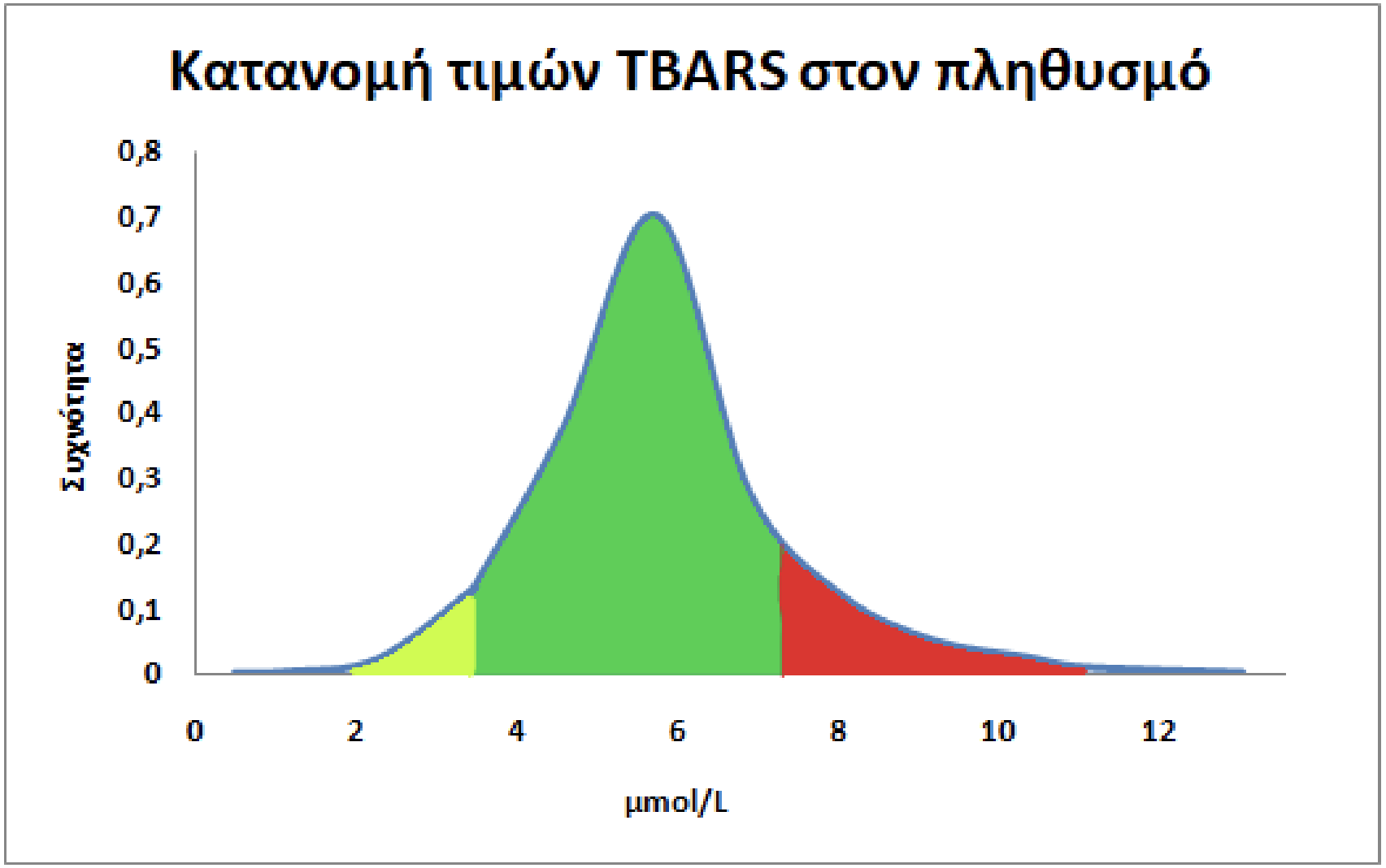
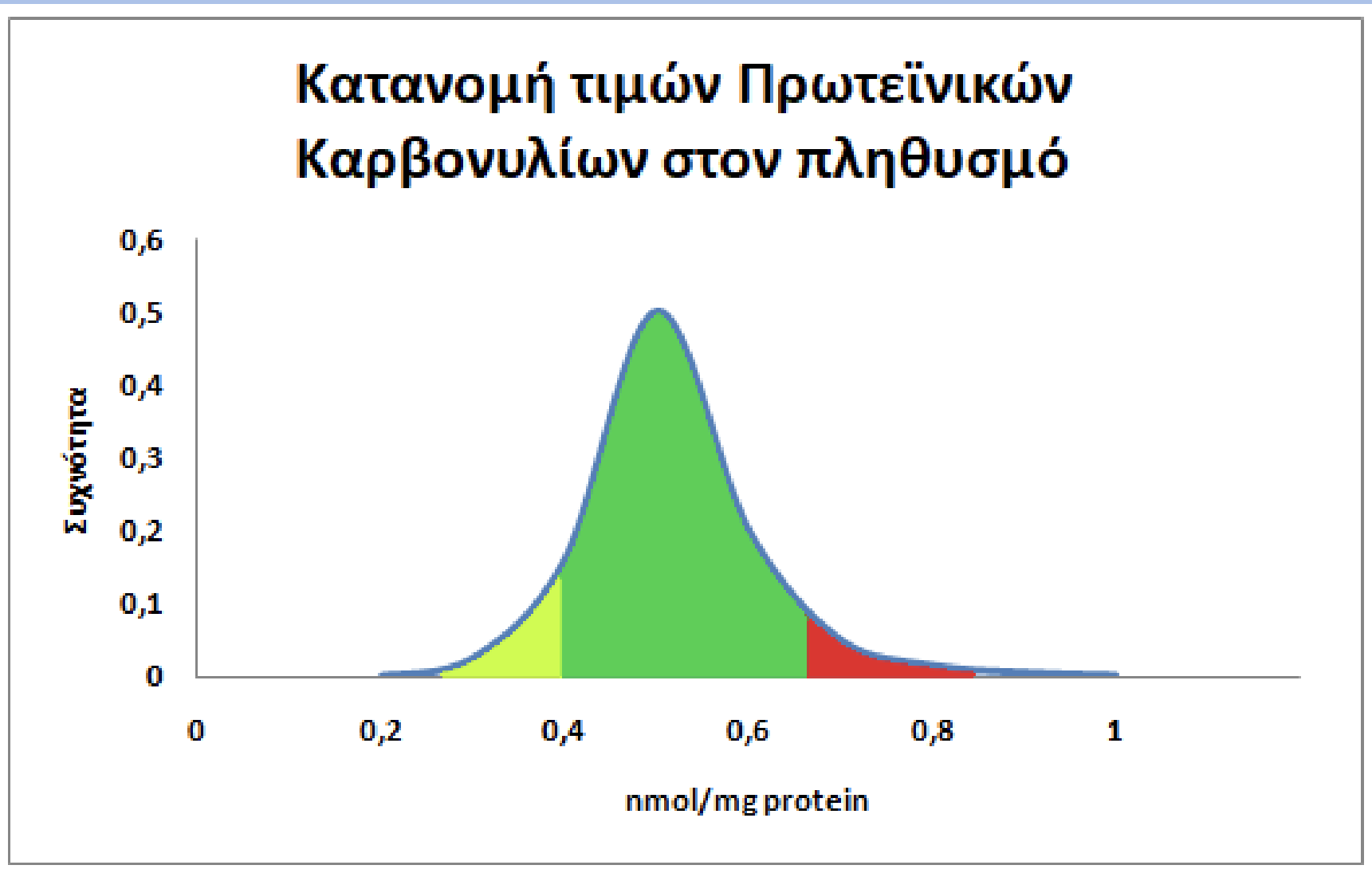
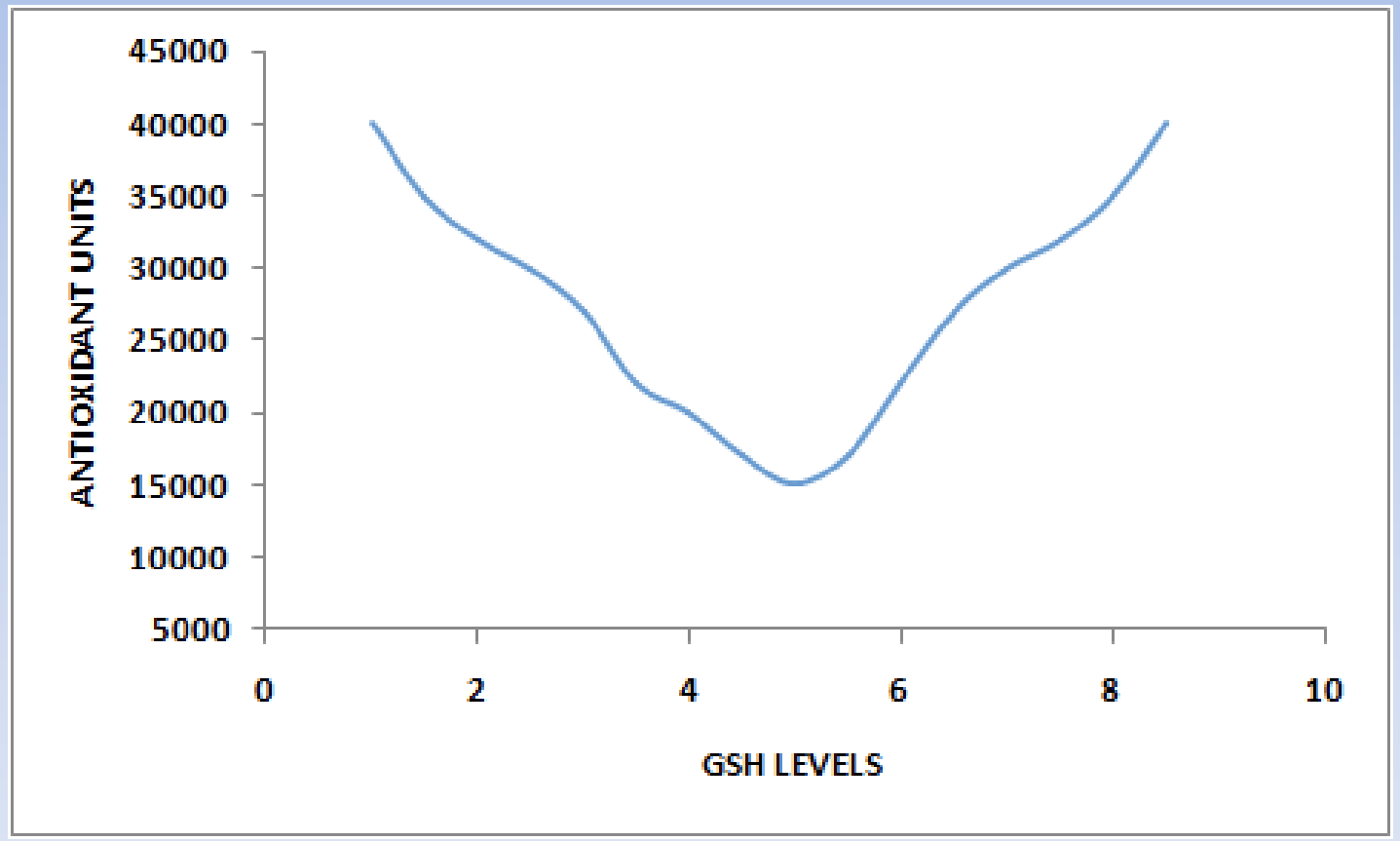


Κανονική κατανομή σε δείγμα 5.000 ατόμων



Η ανάγκη για αντιοξειδωτικά από τη διατροφή σε σχέση με τα ενδογενή επίπεδα GSH που εντοπίστηκαν στο δείγμα αίματος



antioxidants

MDPI

Review

The Importance of Redox Status in the Frame of Lifestyle Approaches and the Genetics of the Lung Innate Immune Molecules, SP-A1 and SP-A2, on Differential Outcomes of COVID-19 Infection

Fotios Tekos [1,†], Zoi Skaperda [1,†], Nikolaos Goutzourelas [1], David S. Phelps [2], Joanna Floros [2,3] and Demetrios Kouretas [1,*]

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Obesity - a risk factor for increased COVID-19 prevalence, severity and lethality (Review)

DEMETRIOS PETRAKIS[1], DENISA MARGINĂ[2*], KONSTANTINOS TSAROUHAS[3*], FOTIOS TEKOS[4], MIRIANA STAN[5], DRAGANA NIKITOVIC[6], DEMETRIOS KOURETAS[4], DEMETRIOS A. SPANDIDOS[7] and ARISTIDIS TSATSAKIS[1]

[1]Laboratory of Toxicology, Medical School, University of Crete, 71409 Heraklion, Greece; [2]'Carol Davila' University of Medicine and Pharmacy, Faculty of Pharmacy, Department of Biochemistry, 020956 Bucharest, Romania; [3]Department of Cardiology, University Hospital of Larissa, 41110 Larissa; [4]Department of Biochemistry-Biotechnology, University of Thessaly, 41500 Larissa, Greece; [5]'Carol Davila' University of Medicine and Pharmacy, Faculty of Pharmacy, Department of Toxicology, 020956 Bucharest, Romania; [6]Laboratory of Histology-Embryology, School of Medicine, University of Crete, 71003 Heraklion; [7]Laboratory of Clinical Virology, Medical School, University of Crete, 71110 Heraklion, Greece

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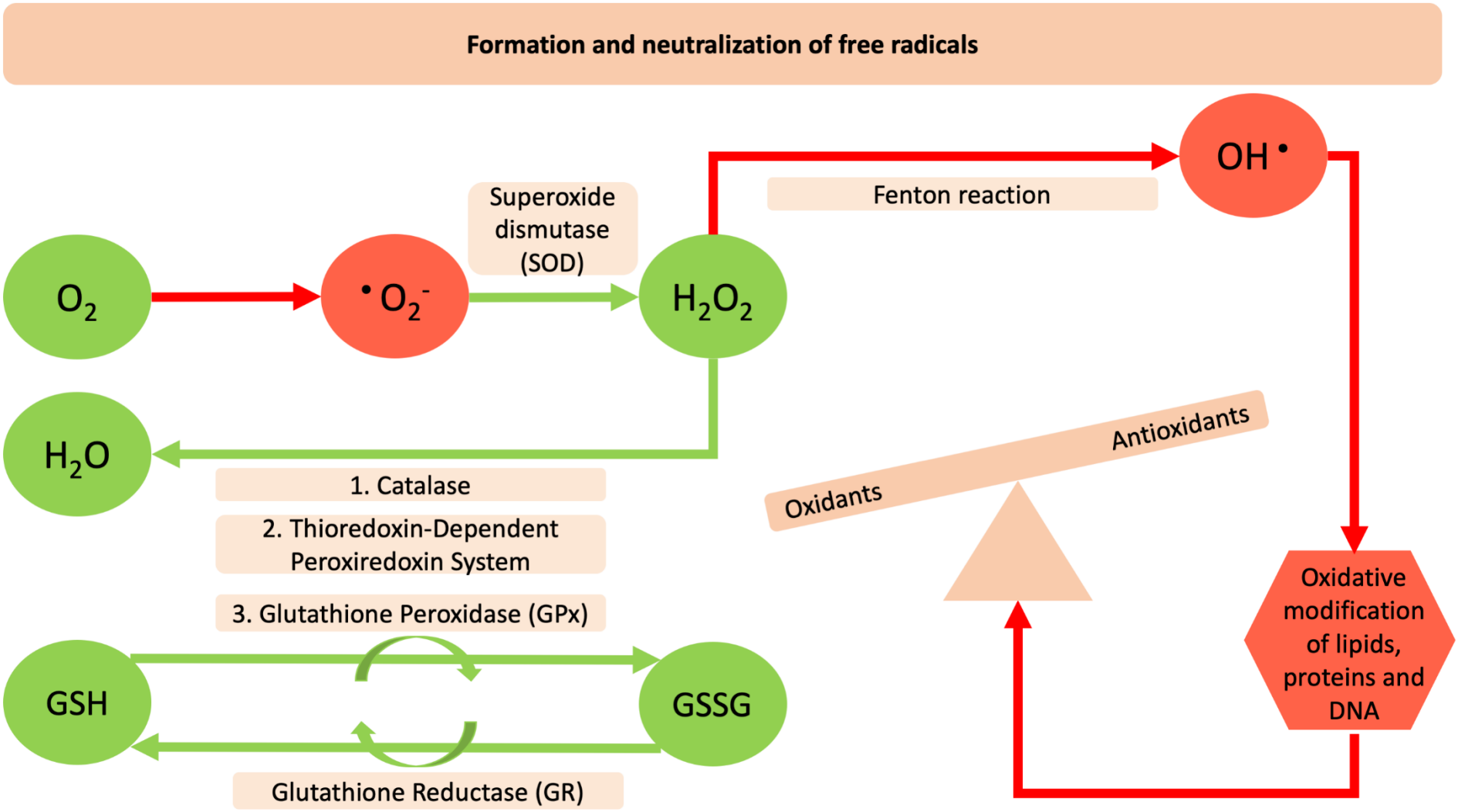
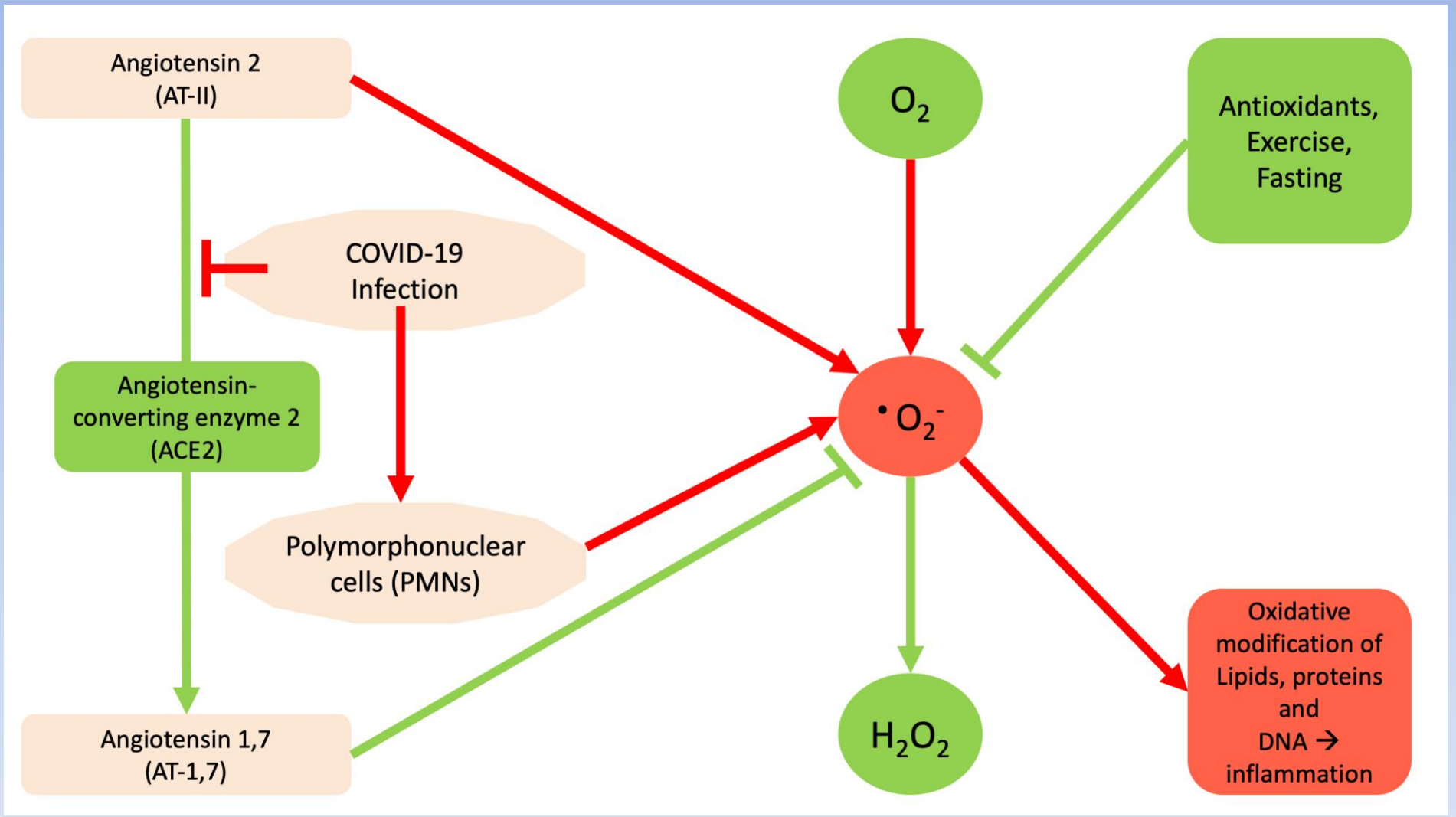
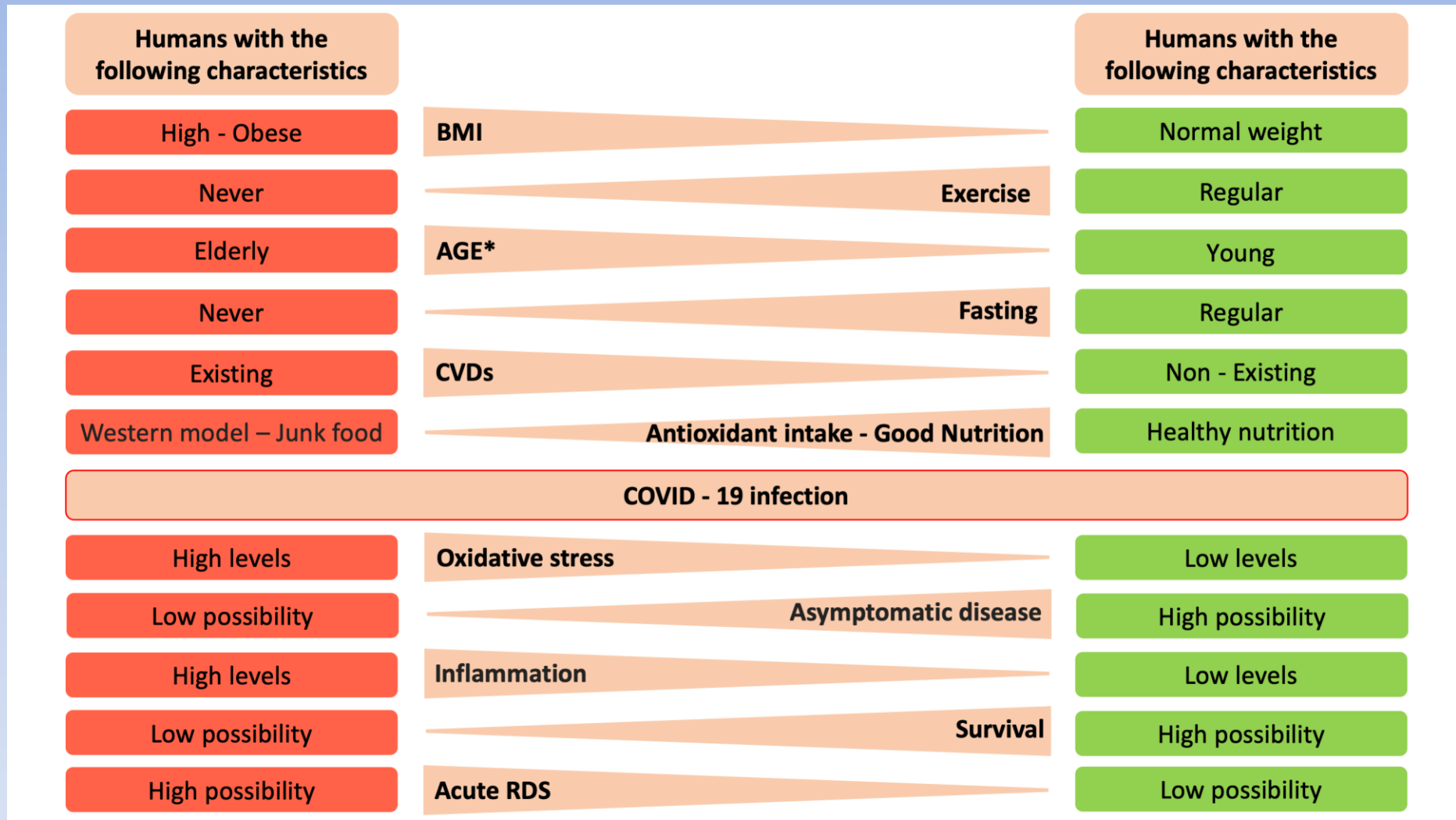
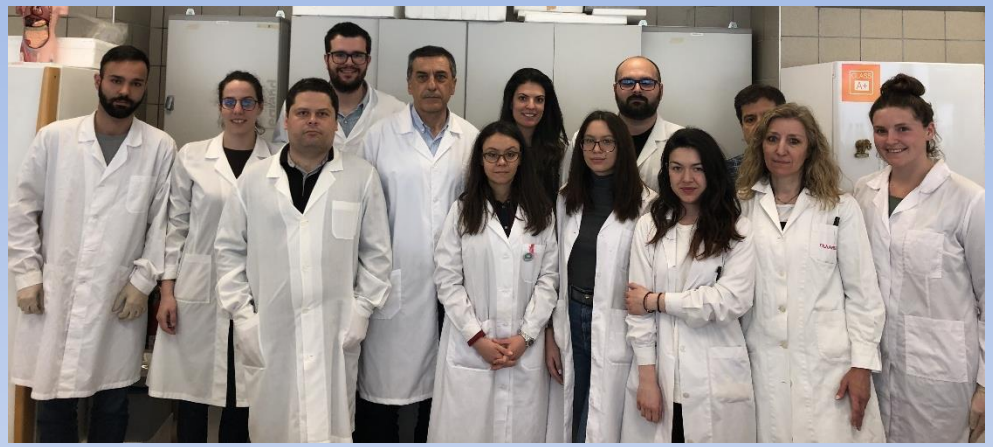

Formation and neutralization of free radicals
O_2
$^{\bullet}O_2^-$
Superoxide dismutase (SOD)
H_2O_2
$OH^{\bullet}$
Fenton reaction
H_2O
1. Catalase
2. Thioredoxin-Dependent Peroxiredoxin System
3. Glutathione Peroxidase (GPx)
GSH
GSSG
Glutathione Reductase (GR)
Oxidants
Antioxidants
Oxidative modification of lipids, proteins and DNA


Angiotensin 2
(AT-II)
O_2
Antioxidants,
Exercise,
Fasting
COVID-19
Infection
Angiotensin-
converting enzyme 2
(ACE2)
$^{\bullet}O_2^-$
Polymorphonuclear
cells (PMNs)
Oxidative
modification of
Lipids, proteins
and
DNA →
inflammation
H_2O_2
Angiotensin 1,7
(AT-1,7)


Humans with the following characteristics
Humans with the following characteristics
High - Obese
BMI
Normal weight
Never
Exercise
Regular
Elderly
AGE*
Young
Never
Fasting
Regular
Existing
CVDs
Non - Existing
Western model – Junk food
Antioxidant intake - Good Nutrition
Healthy nutrition
COVID - 19 infection
High levels
Oxidative stress
Low levels
Low possibility
Asymptomatic disease
High possibility
High levels
Inflammation
Low levels
Low possibility
Survival
High possibility
High possibility
Acute RDS
Low possibility



ΕΡΓΑΣΤΗΡΙΟ
Φυσιολογίας
Ζωϊκών
Οργανισμών

ΤΜΗΜΑ
Βιοχημείας &
Βιοτεχνολογίας
ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ

Thank you