



**PROGETTO FORMATIVO
AZIENDALE
RESIDENZIALE**

**Recenti acquisizioni in nutrizione clinica:
ruolo degli ambulatori nutrizionali Sian nella
prevenzione delle malattie**

Nutrizione e stress ossidativo

Dr. Andrea Bolner – CSOx Villa Margherita - Vicenza



Ossigeno è Vita: la storia
della vita sulla Terra, sin
dagli albori, è storia di
relazione con l'ambiente



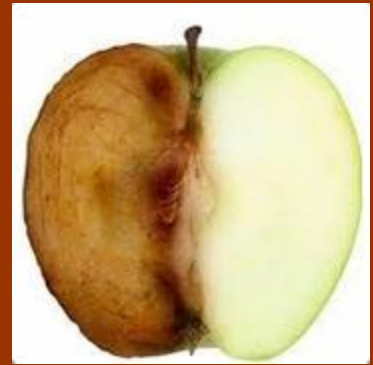
Ossigenato o Ossidato?

O_2 è indispensabile alla vita ma condiziona i viventi che devono adattare il loro metabolismo ad un ambiente pro-ossidante



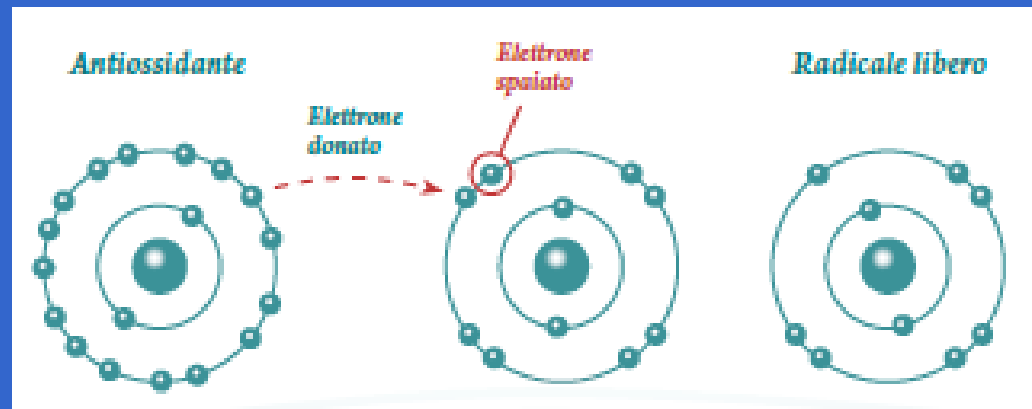
GOOD

BAD



COSA SONO I RADICALI LIBERI?

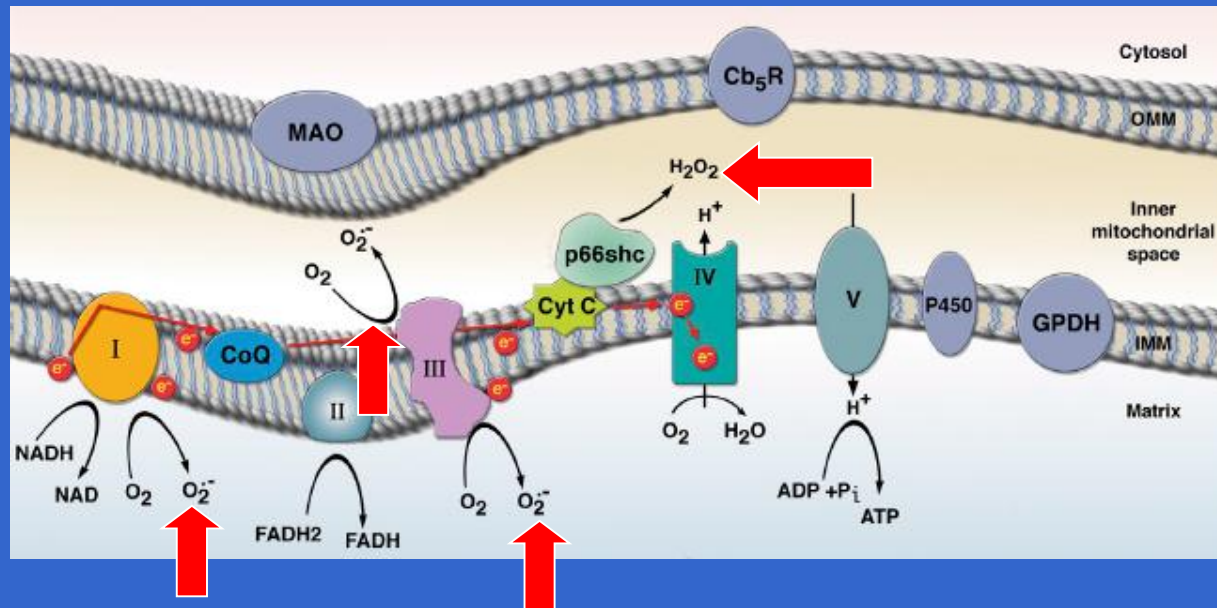
“...specie chimiche capaci di *esistenza indipendente* che contengono uno o più *elettroni spaiati* sull'orbitale più esterno...”



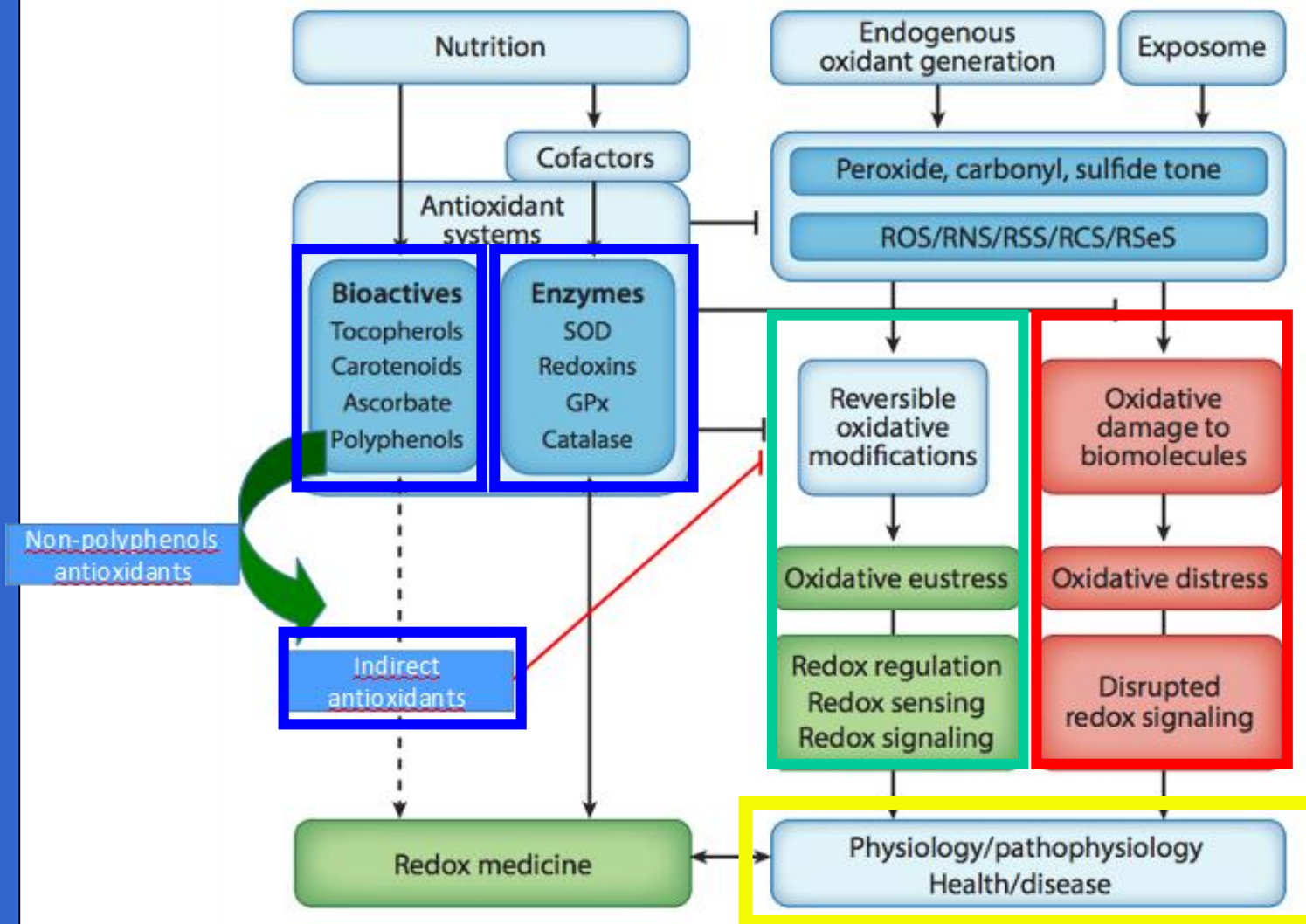
Stress ossidativo: ruolo fisiologico di ROS e RNS

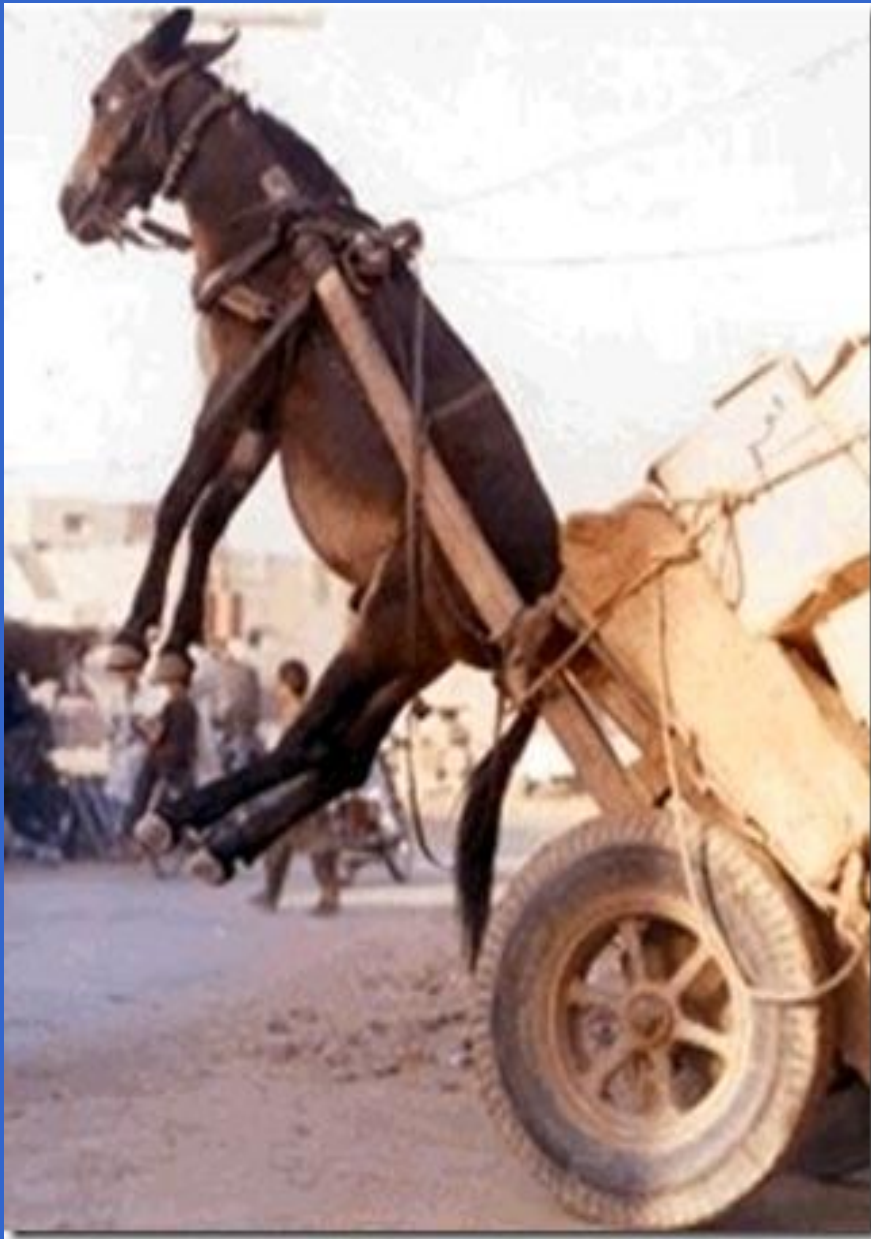
PRINCIPALI SORGENTI

- Enzimi di membrana NADPH dipendenti
- Enzimi metabolismo intracellulare: xantina ossidasi, cicloossigenasi, lipossigenasi
- Mitochondri

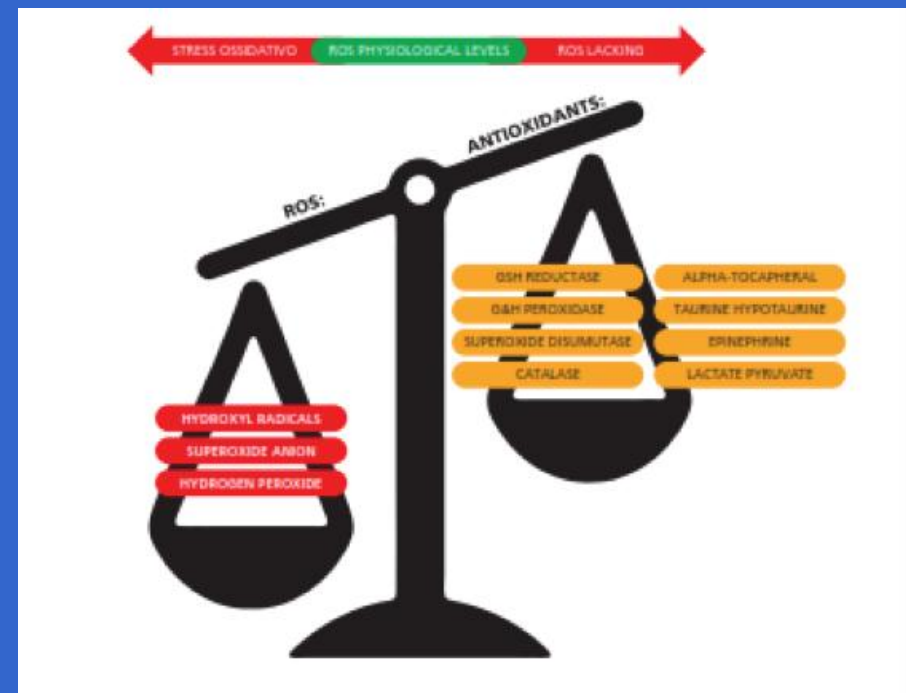


Synoptic view of oxidative stress and its relation to nutrition and redox medicine



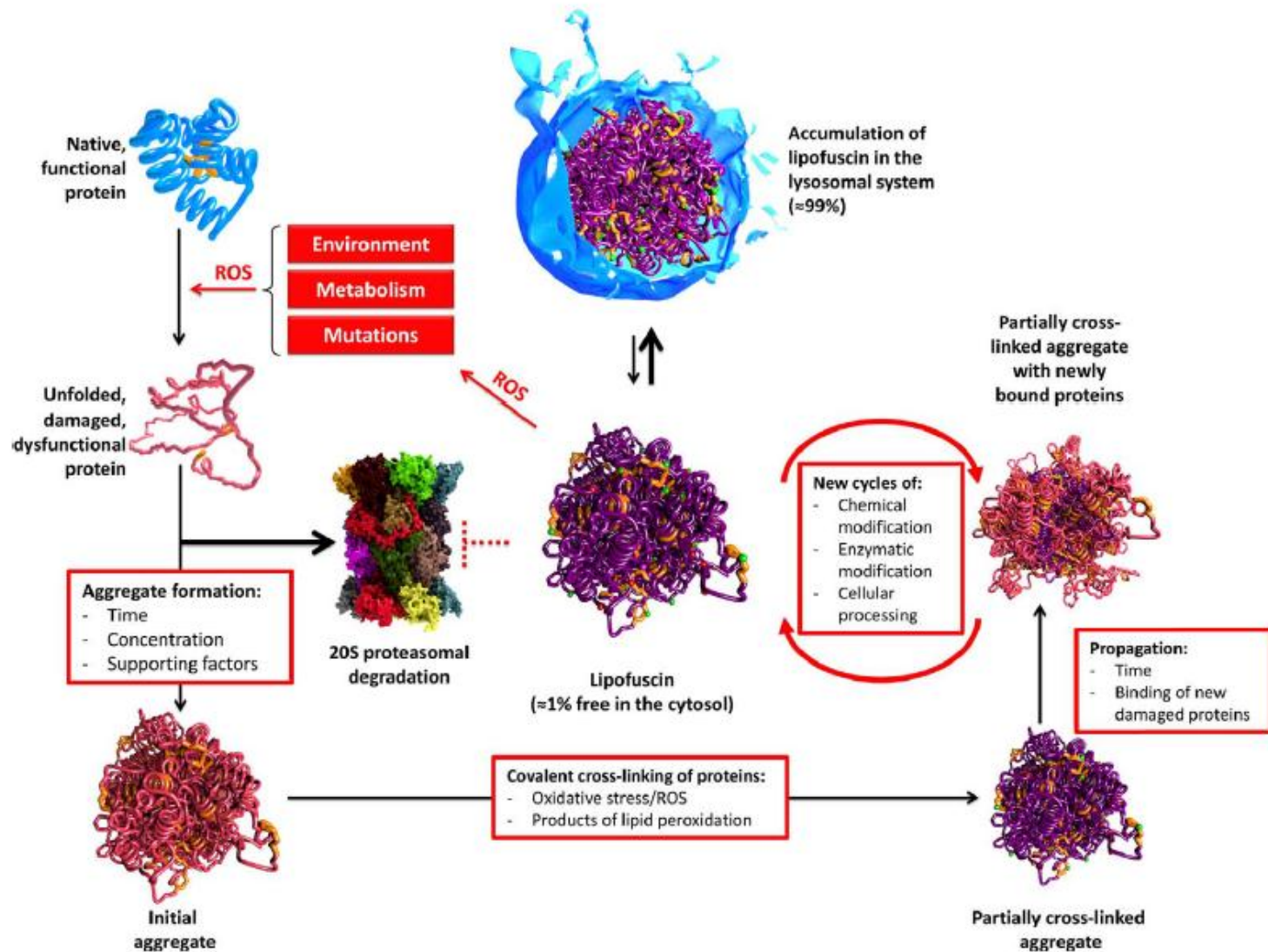


Come si origina lo sbilancio ossidativo?

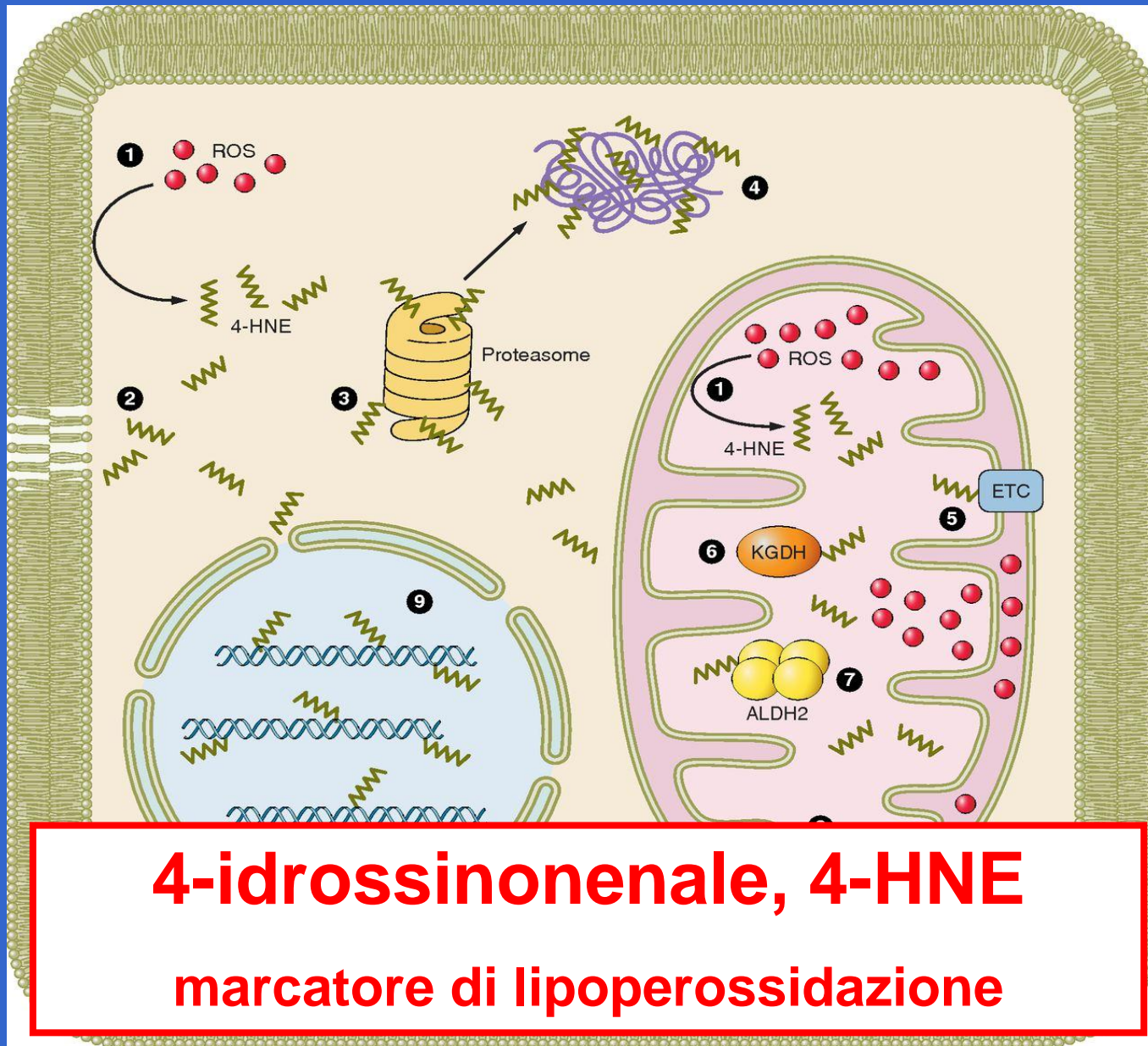


Sbilancio ossidativo e proteine

I. Korovila et al.

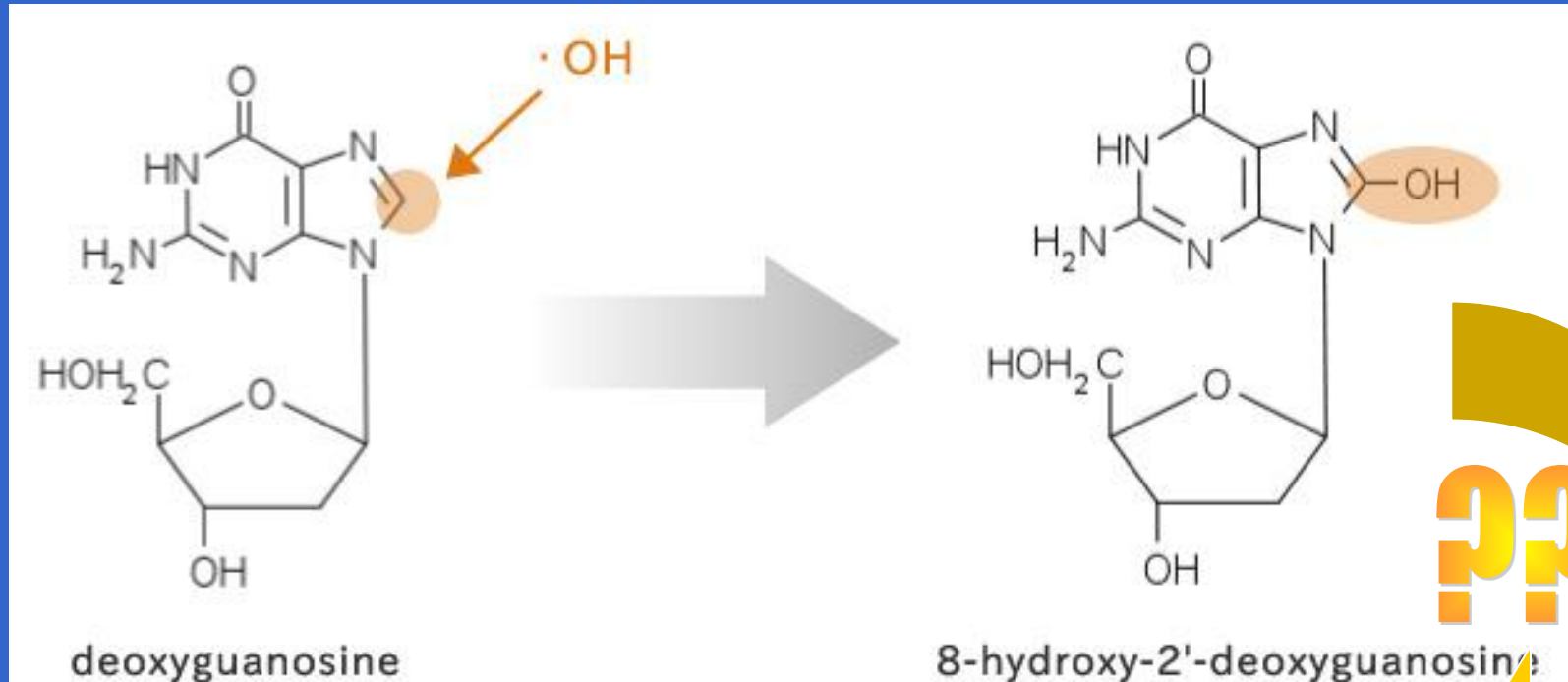


Sbilancio ossidativo e lipidi



4-idrossinonenale, 4-HNE
marcatore di lipoperossidazione

Sbilancio ossidativo e DNA

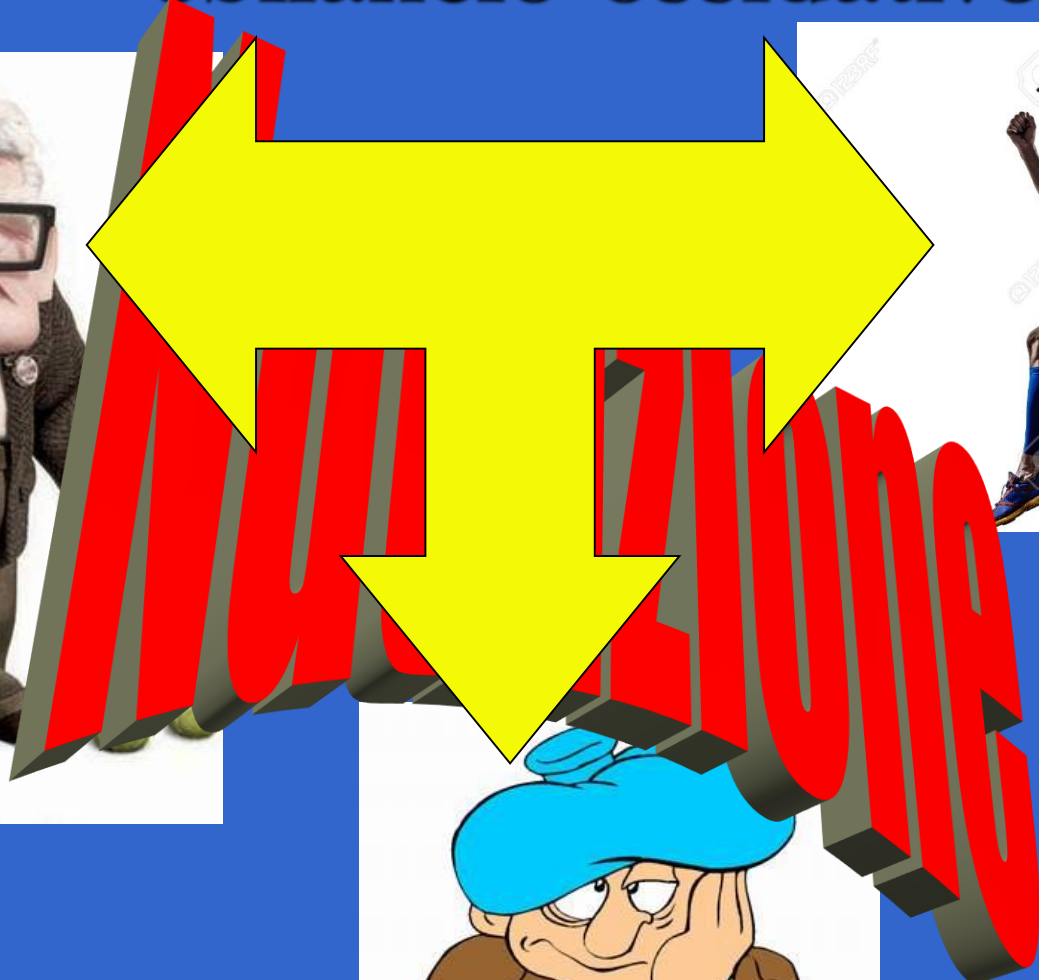


8-idrossi deossi guanosina,

8-OHdG

marcatore di danno ossidativo sul DNA

Perché studiare lo sbilancio-ossidativo?

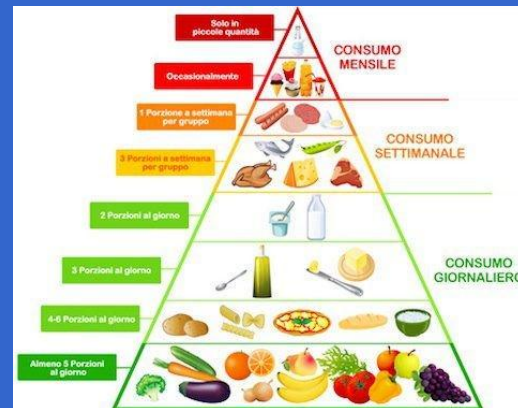


Nutrizione e sbilancio ossidativo

- **Apporto calorico**



- **Nutrienti**



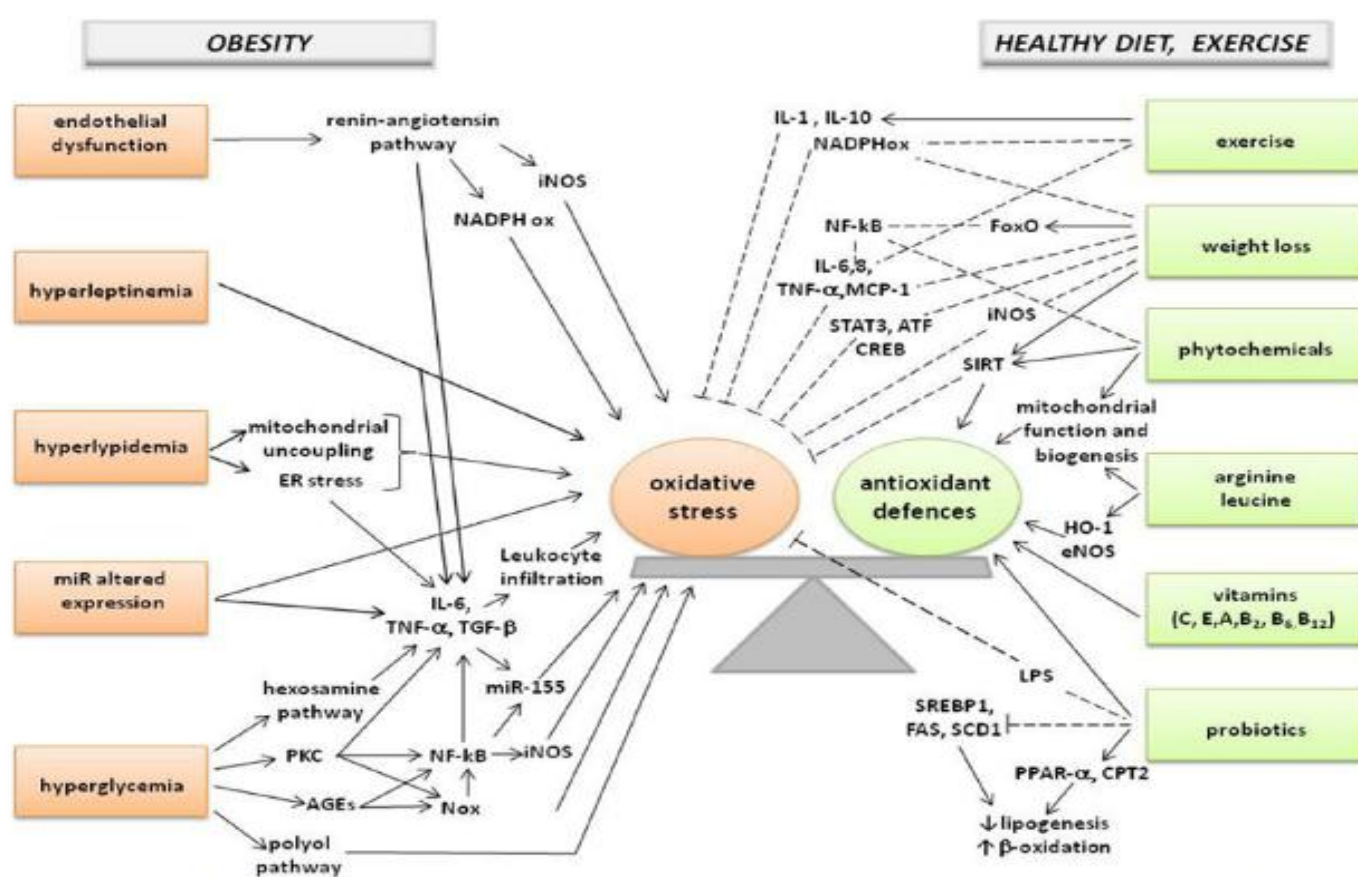
- **Integrazione**



- **Microbiota**

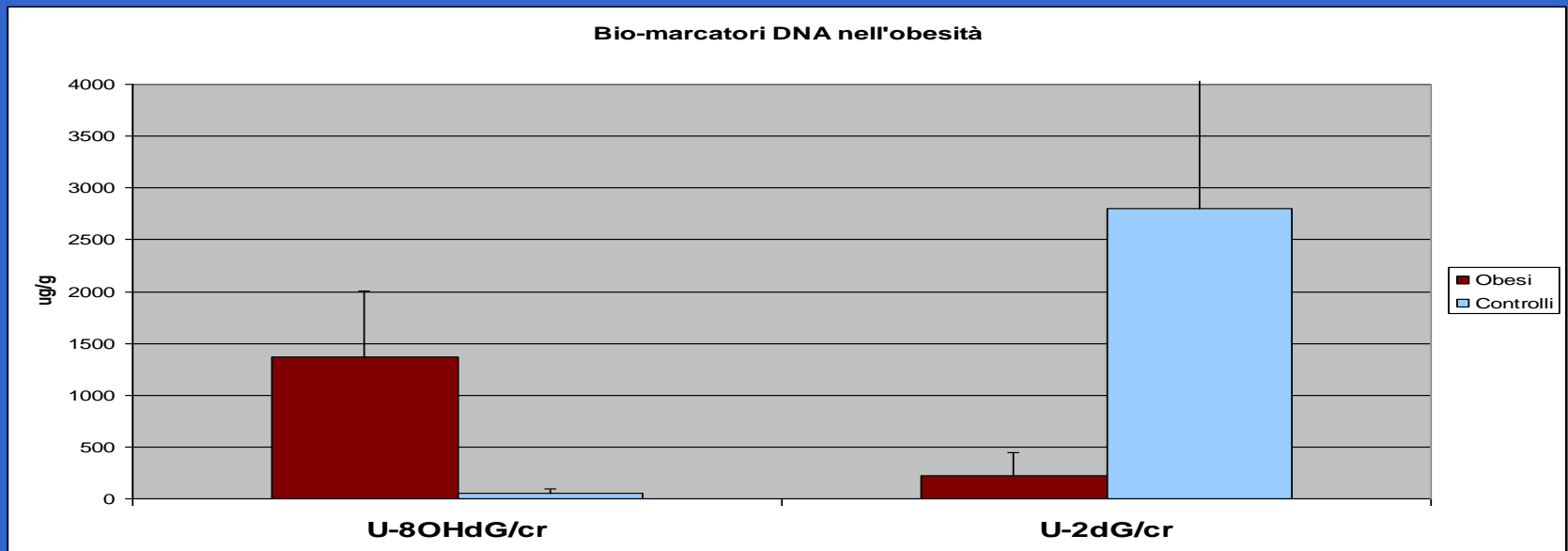
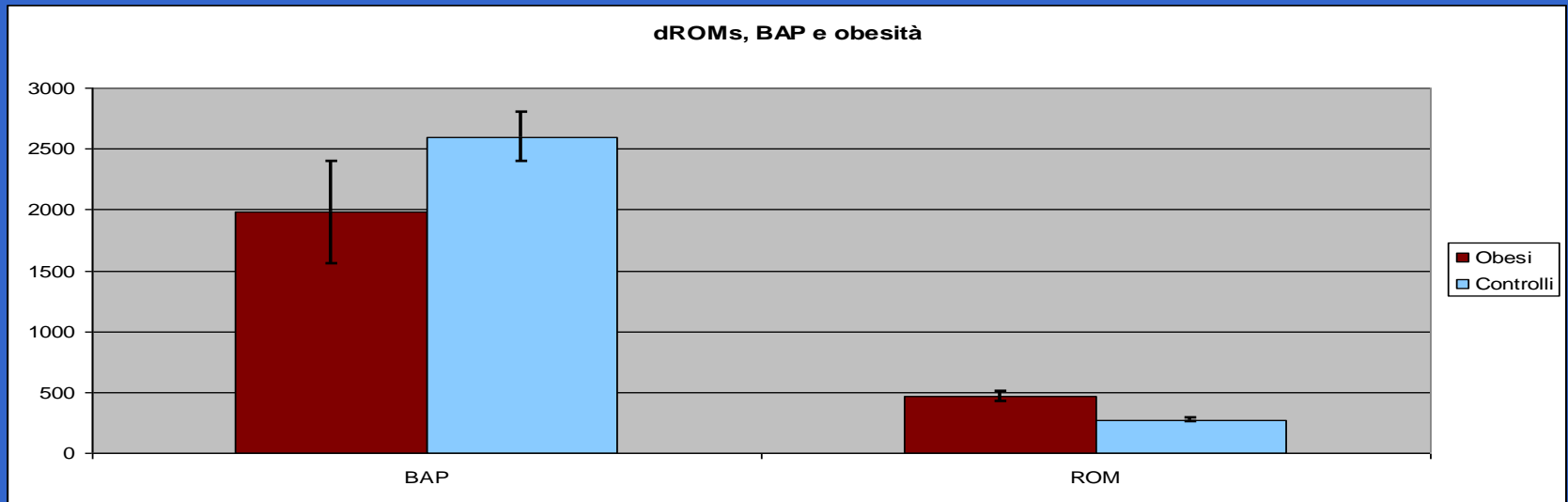


Apporto calorico

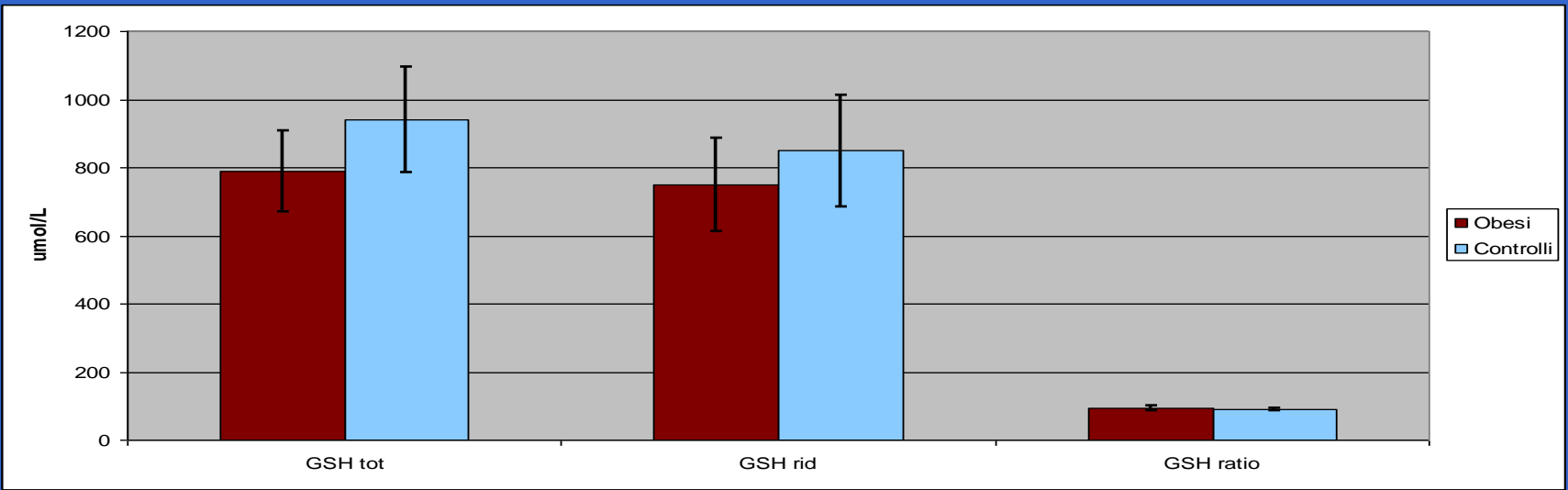
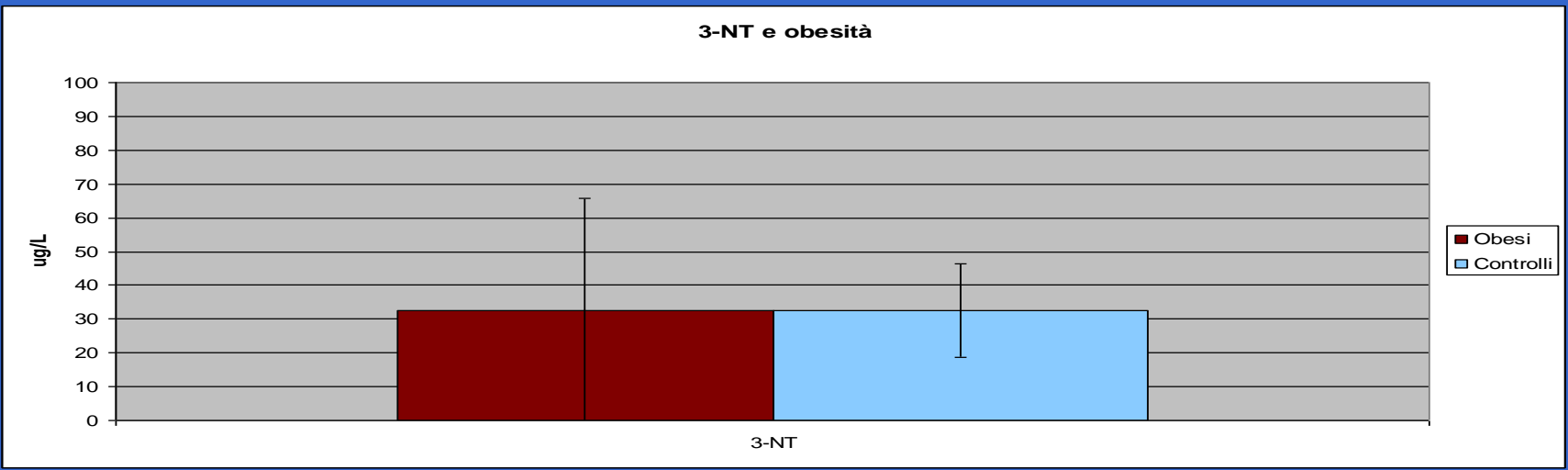


AGEs: advanced glycation end products; ATF: NF-κB, activating transcription factor; CPT2: carnitine palmitoyltransferase 2; CREB: cyclic AMP response element binding; ER: endoplasmic reticulum; FAS: fatty acid synthase; FoxO: forkhead box, sub-group O; HO-1: heme oxygenase-1; iNOS: inducible nitric oxide synthase; LPS: lipopolysaccharide MCP-1: monocyte chemotactic protein-1; miR: microRNA; NF-κB: nuclear factor-κB; Nox: NADPH oxidase; PKC: protein kinase C; PPAR-α: peroxisome proliferator-activated receptor-α; SCD1: stearoyl-CoA desaturase-1; SIRT: sirtuin; SREBP1: sucrose responsive element binding protein1; STAT3: signal transducer and activator of transcription 3; TGF-β: transforming growth factor-β; TNF-α: tumor necrosis factor-α.

Obesità e sbilancio ossidativo 1

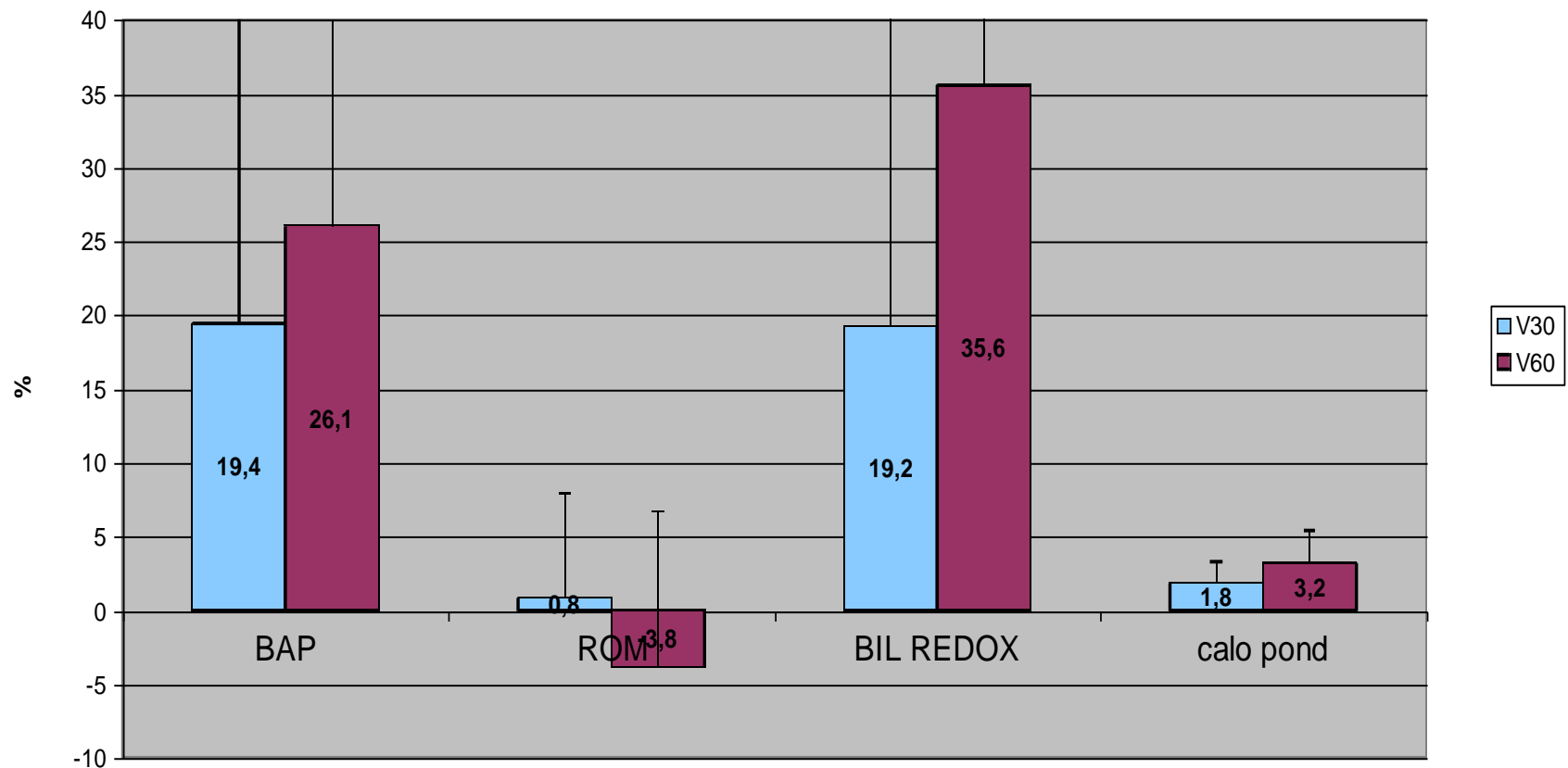


Obesità e sbilancio ossidativo 2



Restrizione calorica – SIAN 2017

Delta % vs basale

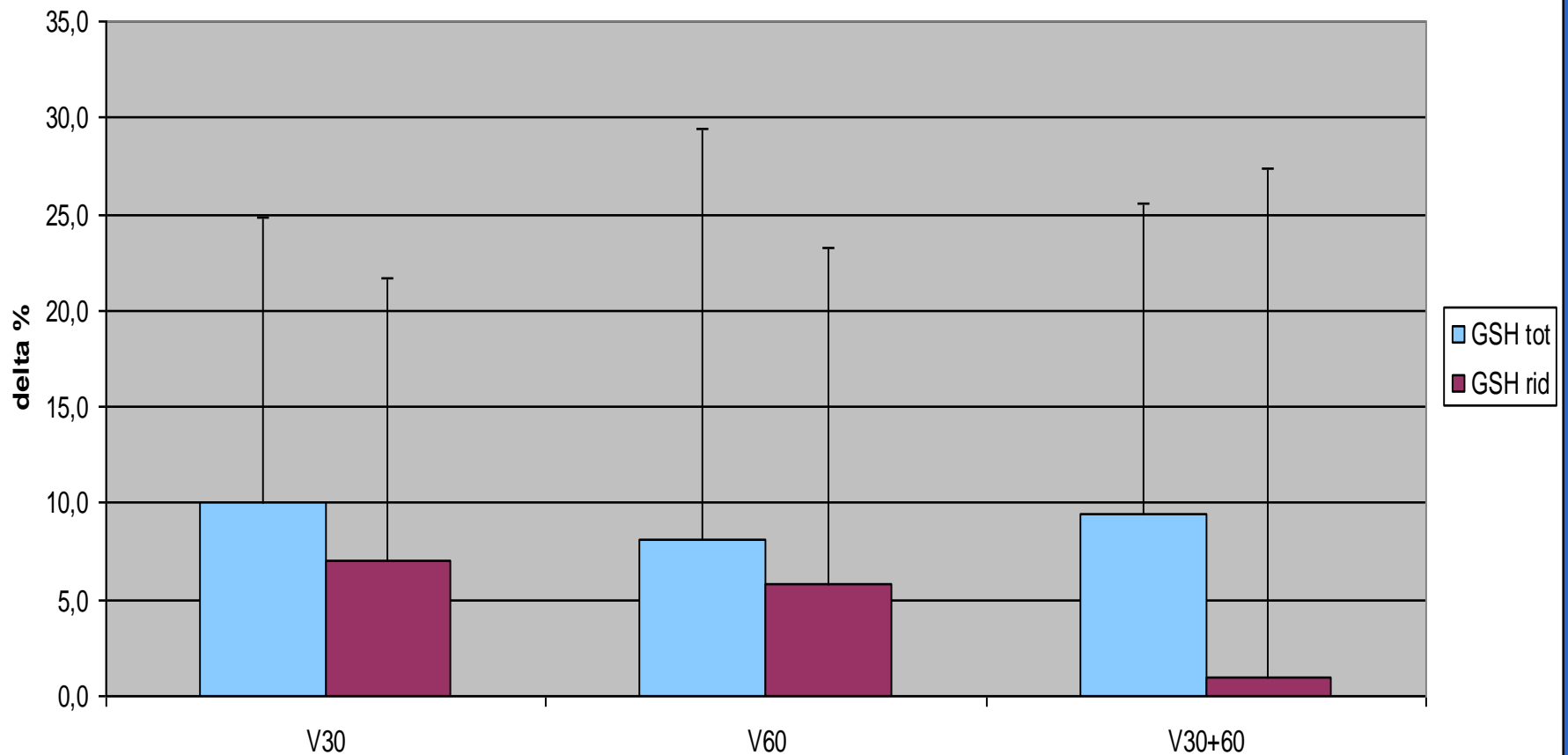


Restrizione calorica – SIAN 2017



Restrizione calorica – SIAN 2017

GSH e Restrizione calorica



Nutrienti anti-ROS

Int. J. Mol. Sci. **2015**, *16*, 22636-22661; doi:10.3390/ijms160922636

Review

ω -3 Fatty Acids and Cardiovascular Diseases: Effects, Mechanisms and Dietary Relevance

Hanne K. Maehre *, Ida-Johanne Jensen, Edel O. Elvevoll and Karl-Erik Eilertsen

Norwegian College of Fishery Science Faculty of Biosciences, Fisheries and Economics,

Table 3. Overview of dietary recommendations regarding the *n*-3 fatty acids.

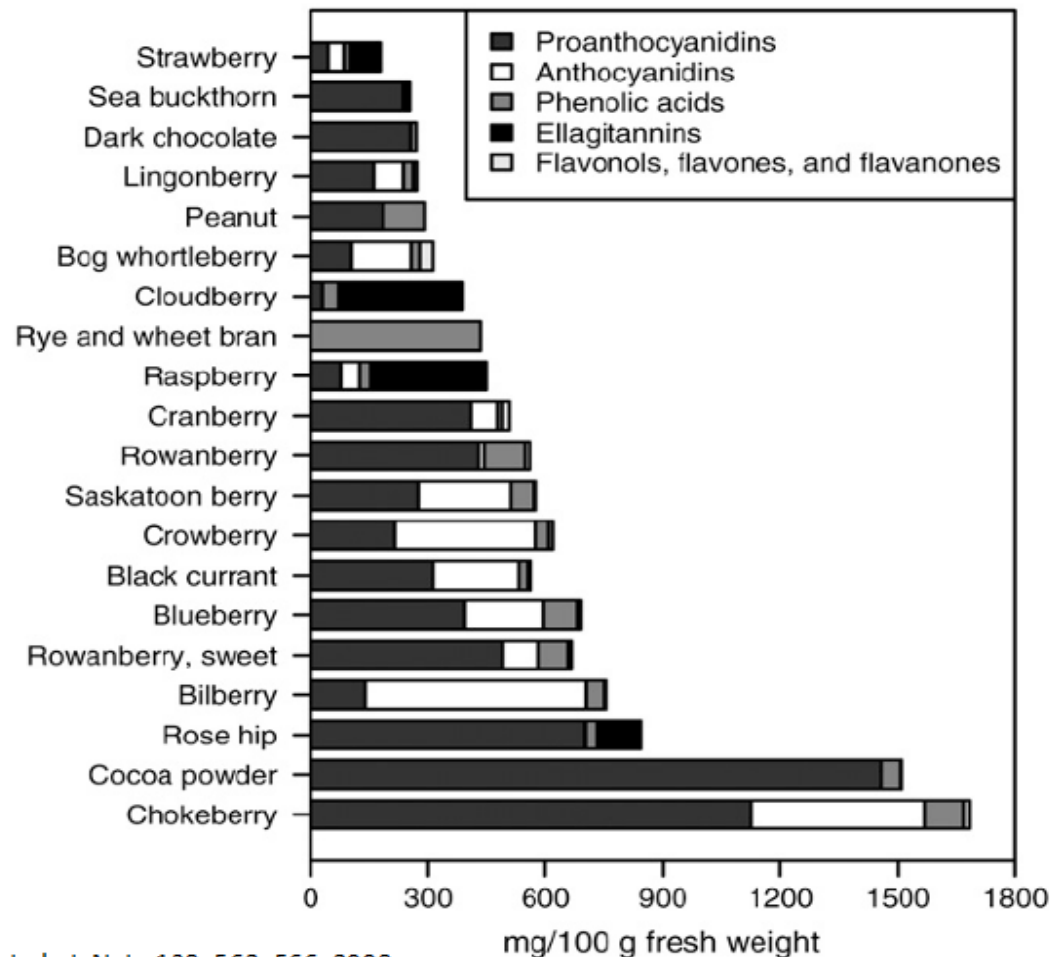
Authority/Organization	Country/Region	Year	Recommendation	Reference
The American Heart Association	USA	2015	A variety of (preferably fatty) fish at least twice a week	[137]
The Norwegian Directorate of Health/VKM	Norway	2014	Fish as dinner at least 2–3 times per week	[91]
Food and Agricultural Organization of the United Nations (FAO)/World Health Organization (WHO)	World	2011	At least 1–2 100 g servings of fatty fish per week	[136]
European Food Safety Association (EFSA)	Europe	2010	250 mg EPA + DHA daily	[138]
Scientific Advisory Committee for Nutrition (SACN)	UK	2004	450 mg EPA + DHA daily	[139]
International Society for the Study of Fatty Acids and Lipids (ISSFAL)	UK/Europe	2004	500 mg EPA + DHA daily	[140]

Nutrienti antiossidanti diretti

NUTRIENTE	RUOLO
Vitamina E	Neutralizza i radicali liberi mano a mano che si formano
Vitamina K	Accetta e dona H^+ ed e^-
Carotene	Accetta e dona H^+ ed e^-
Vitamina C	Accetta e dona H^+ ed e^-
Selenio	Viene incorporato come seleniocisteina nella glutatione perossidasi
Rame, zinco	Cofattori della superossido dismutasi citosolica
Manganese	Cofattore della superossido dismutasi mitocondriale

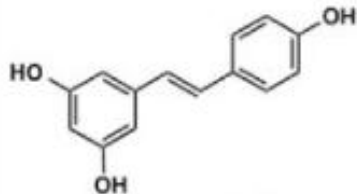
Nutrienti antiossidanti indiretti

The 20 food items with the highest total concentrations of polyphenols

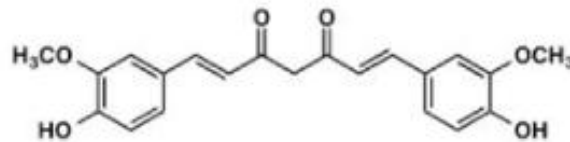


Products that have indirect antioxidant properties

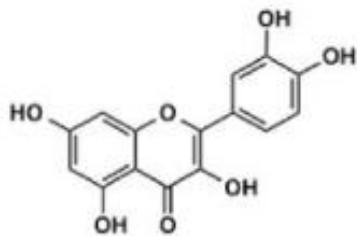
Polyphenols



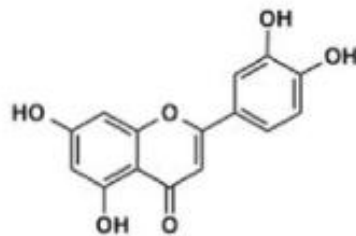
**Resveratrol
(Stilbene)**



**Curcumin
(Curcuminoid)**



**Quercetin
(Flavonol)**

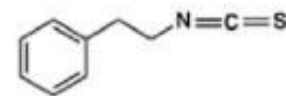


**Luteolin
(Flavone)**

Isothiocyanates



Sulforaphane



**Phenethyl
isothiocyanate**

Epithionitriles

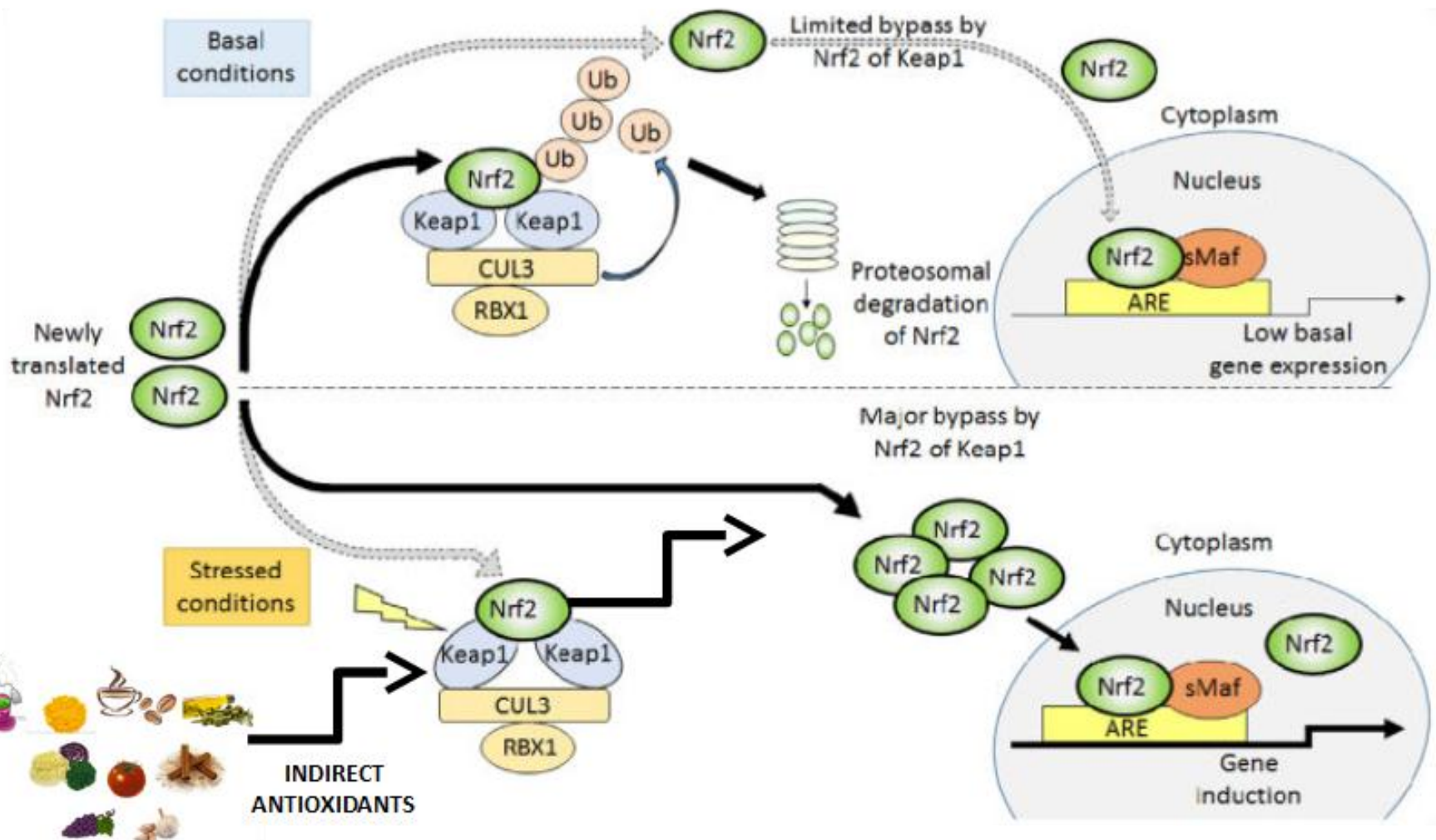


**1-cyano-2,3-
epithiopropene**



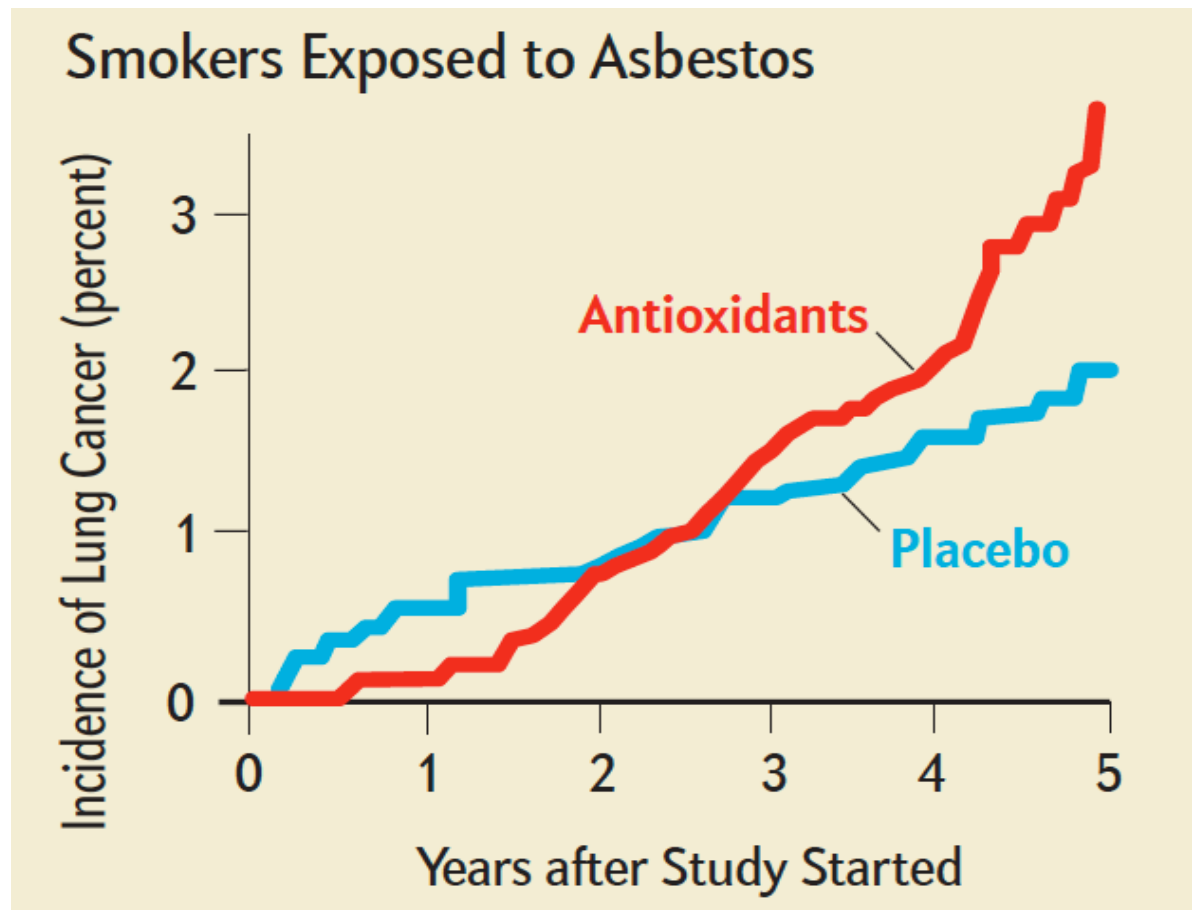
**1-cyano-2,3-
epithiobutane**

Regulation of Nrf2 by Keap1 under basal and stressed conditions



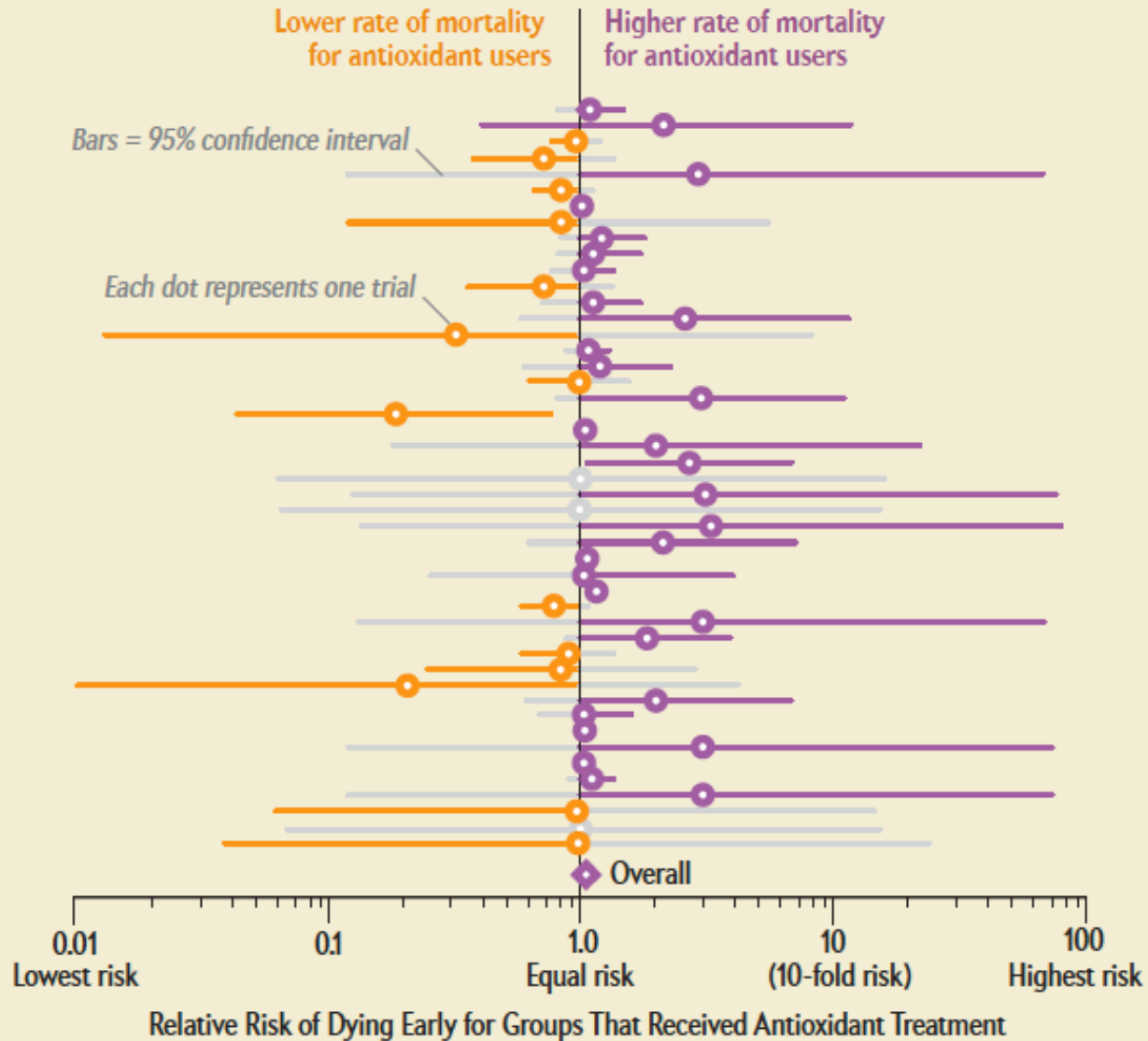
Integrazione e supplementazione

A 1996 study of some 18,000 men and women found 28% more lung cancers and 17% more deaths in group that was given beta-carotene and retinol compared with people who did not receive the antioxidants. The risk became clear particularly in heavy smokers and was strongest among smokers who had been exposed to asbestos.



Bottom Line: Taking Some Vitamins Can Shorten Life Span

In 2007 researchers reviewed 68 of the most scientifically rigorous studies of vitamins and reported that pooling the data from the 47 trials with the least scientific bias resulted in a 5 percent increase in the rate of early death. Further analysis linked the increased risk to beta-carotene, vitamin A and vitamin E.



Integrazione e supplementazione

EDITORIAL

Annals of Internal Medicine

Enough Is Enough: Stop Wasting Money on Vitamin and Mineral Supplements

In conclusion, β -carotene, vitamin E, and possibly high doses of vitamin A supplements are harmful. Other antioxidants, folic acid and B vitamins, and multivitamin and mineral supplements are ineffective for preventing mortality or morbidity due to major chronic diseases.

We believe that the case is closed: supplementing the diet of well-nourished adults with (most) mineral or vitamin supplements **has no benefit and might even be harmful.**

These vitamins should not be used for chronic disease prevention.

Enough is enough.

Integrazione e supplementazione

CLINICAL GUIDELINE

Annals of Internal Medicine

Vitamin, Mineral, and Multivitamin Supplements for the Primary Prevention of Cardiovascular Disease and Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Recommendation.

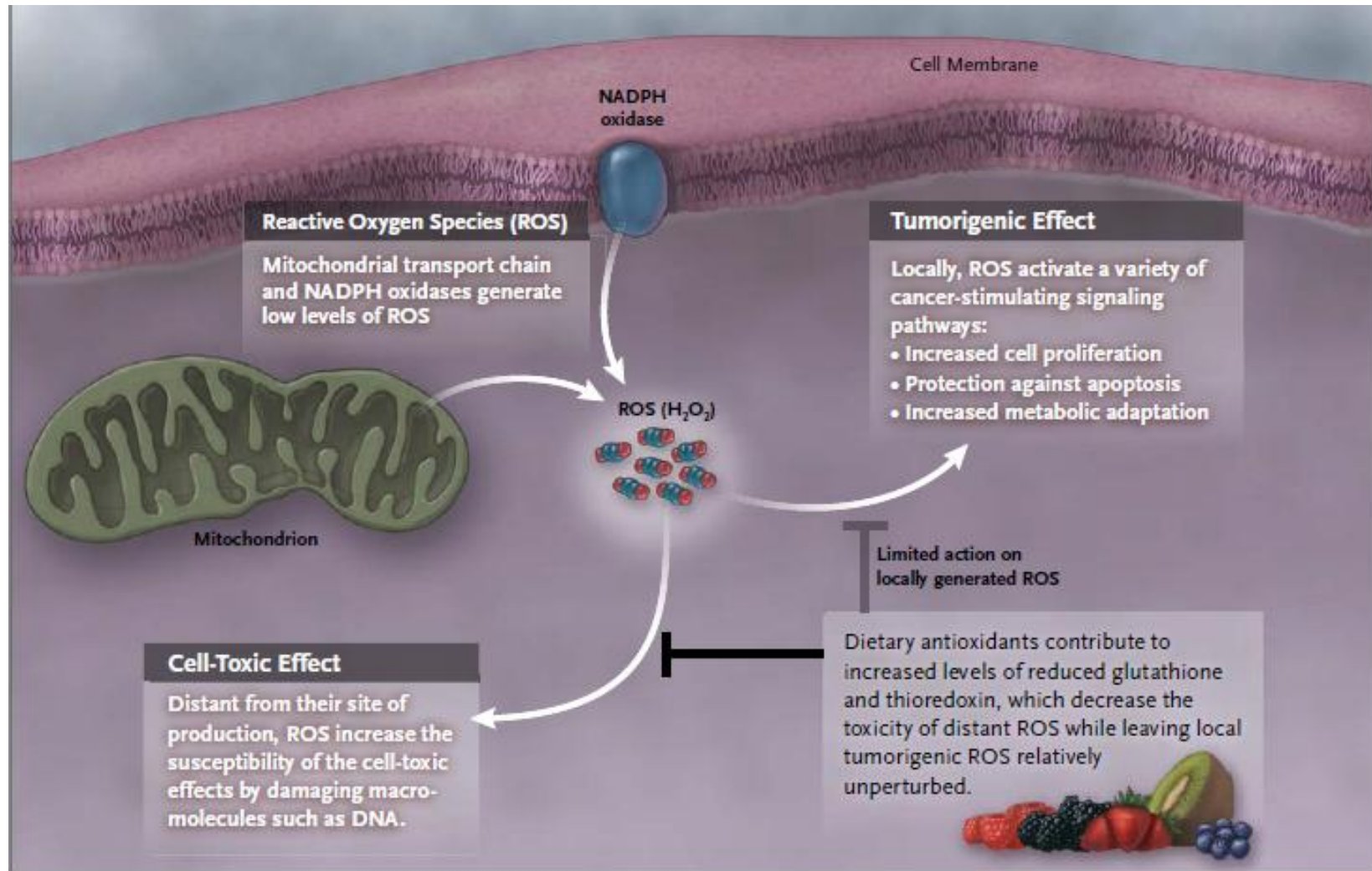
The USPSTF recommends against β -carotene or vitamin E supplements for the prevention of cardiovascular disease or cancer.

CLINICAL IMPLICATIONS OF BASIC RESEARCH

Elizabeth G. Phimister, Ph.D., *Editor*

The Promise and Perils of Antioxidants for Cancer Patients

Navdeep S. Chandel, Ph.D., and David A. Tuveson, M.D., Ph.D.



Approccio terapeutico

Gorrini et al., Nature Reviews (2013) 12, 931

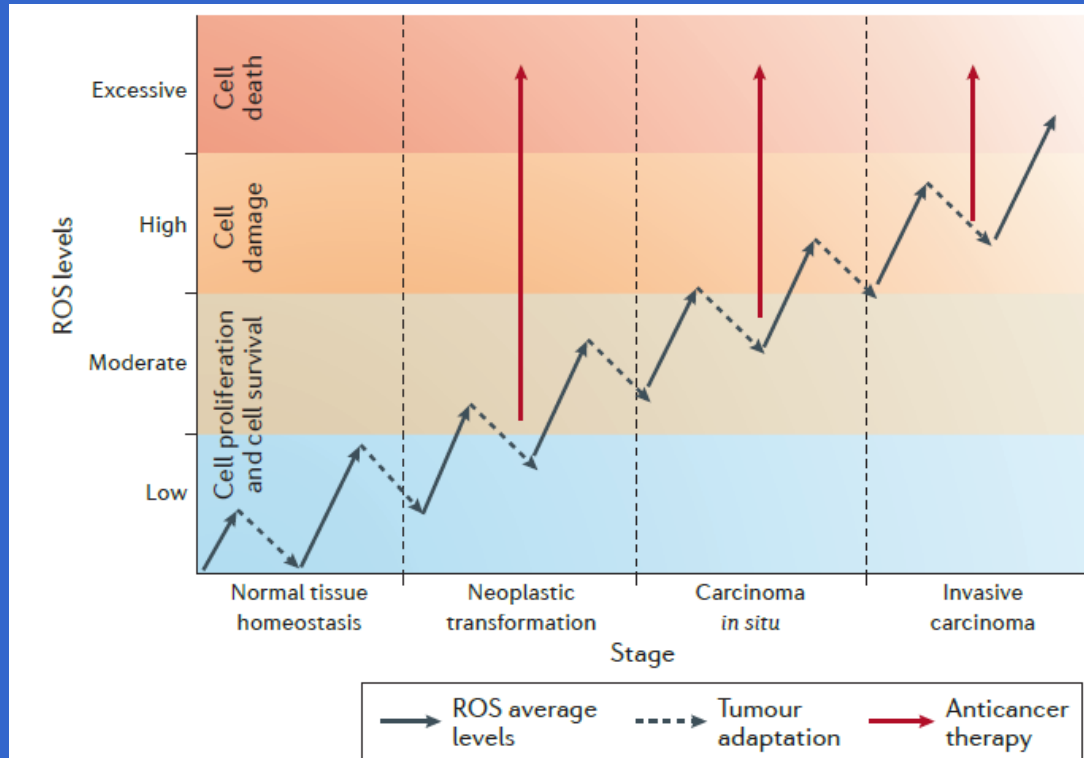


Figure 6 | **Interplay between ROS regulation and tumorigenesis at different stages.** During the transition phases from normal tissue to invasive carcinoma, cells experience a progressive increase in reactive oxygen species (ROS) levels owing to metabolic aberrations acquired following transformation (represented by the solid arrows)²⁰⁹. Cancer cells escape cell death and damage induced by high ROS levels by increasing their antioxidant defences that lower ROS levels (dashed arrows). We propose to target the antioxidant mechanisms of tumour adaptation by an anticancer therapy that forces the accumulation of excessive ROS and the induction of cell death (solid red arrows). This can be achieved by treating cancer cells either with ROS-inducing therapies or with antioxidant-inhibiting therapies.





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**

DNA

CHROMATIN

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

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.

Histones are proteins around which DNA can wind for compaction and gene regulation.

EPIGENETIC FACTOR



Vitamina C ed epigenetica

Annu Rev Nutr. 2015 July 17; 35: 545–564. doi:10.1146/annurev-nutr-071714-034228.

Regulation of the Epigenome by Vitamin C

Juan I. Young¹, Stephan Züchner¹, and Gaofeng Wang^{1,2,*}

¹John P. Hussman Institute for Human Genomics, Dr. John T. Macdonald Foundation
Department of Human Genetics, University of Miami Miller School of Medicine, Miami, Florida
33136

²Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida
33136

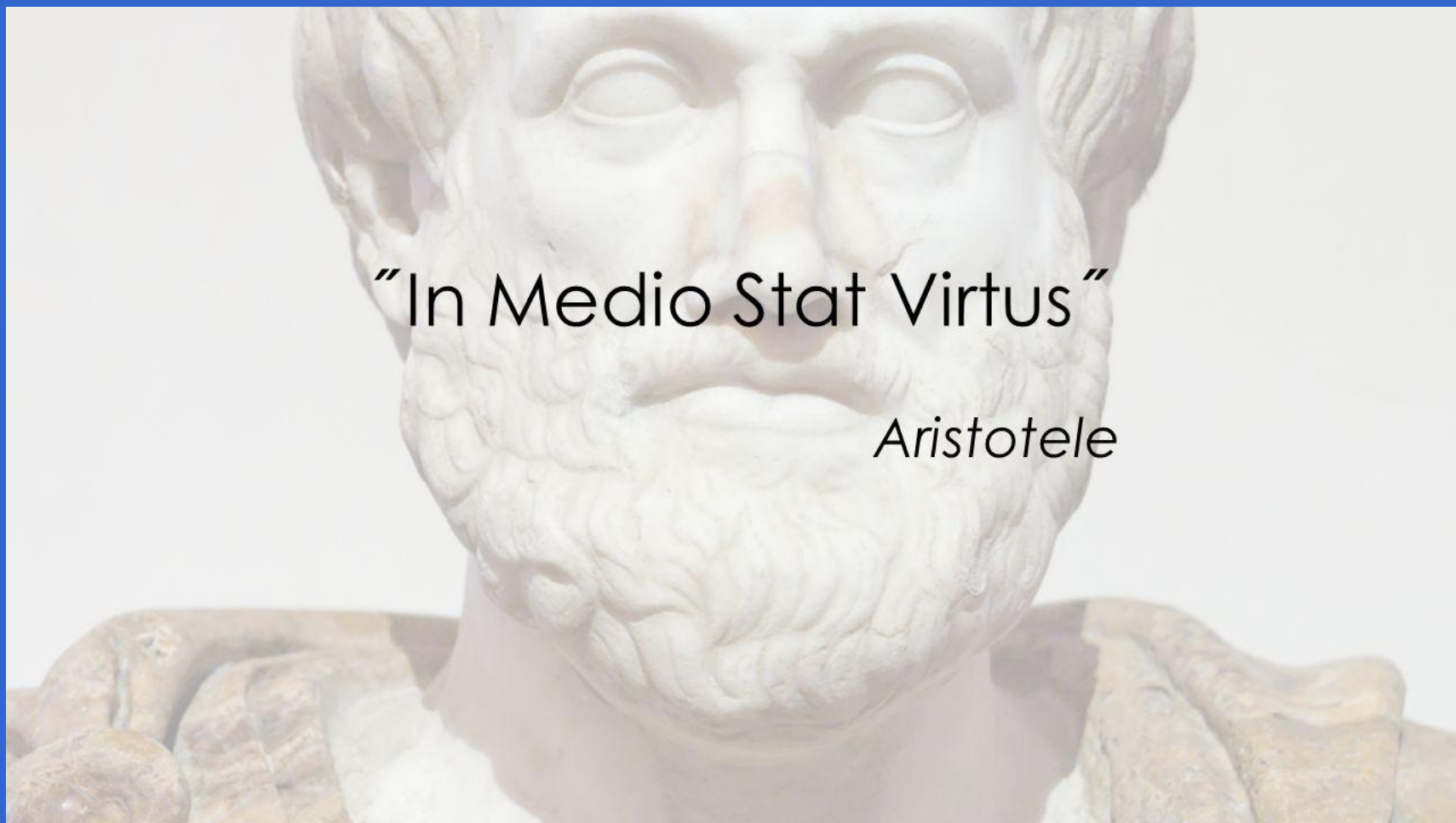
Abstract

Emerging evidence suggests that ascorbate, the dominant form of vitamin C under physiological pH conditions, influences the genome activity via regulating epigenomic processes. Ascorbate serves as a cofactor for ten-eleven translocation (TET) dioxygenases that catalyze the oxidation of 5-methylcytosine (5mC) into 5-hydroxymethylcytosine (5hmC), further to 5-formylcytosine (5fC) and 5-carboxylcytosine (5caC), which are ultimately replaced by unmodified cytosine. The JmjC domain-containing histone demethylases also require ascorbate as a cofactor for histone demethylation. Thus, by primarily participating in the demethylation of both DNA and histones, ascorbate appears to be a mediator of the interface between the genome and environment. Furthermore, redox status has a profound impact on the bioavailability of ascorbate in the nucleus. In order to bridge the gap between redox biology and genomics, we suggest an interdisciplinary research field that can be termed “Redox Genomics” to study dynamic redox processes in health and diseases. This review examines the evidence and potential molecular mechanism of ascorbate in demethylation of the genome, while highlighting potential epigenetic roles of ascorbate in various diseases.

Antiossidanti: sì o no?

"In Medio Stat Virtus"

Aristotele



Integrazione e supplementazione

Int. J. Mol. Sci. 2017, 18, 1583

6 of 14

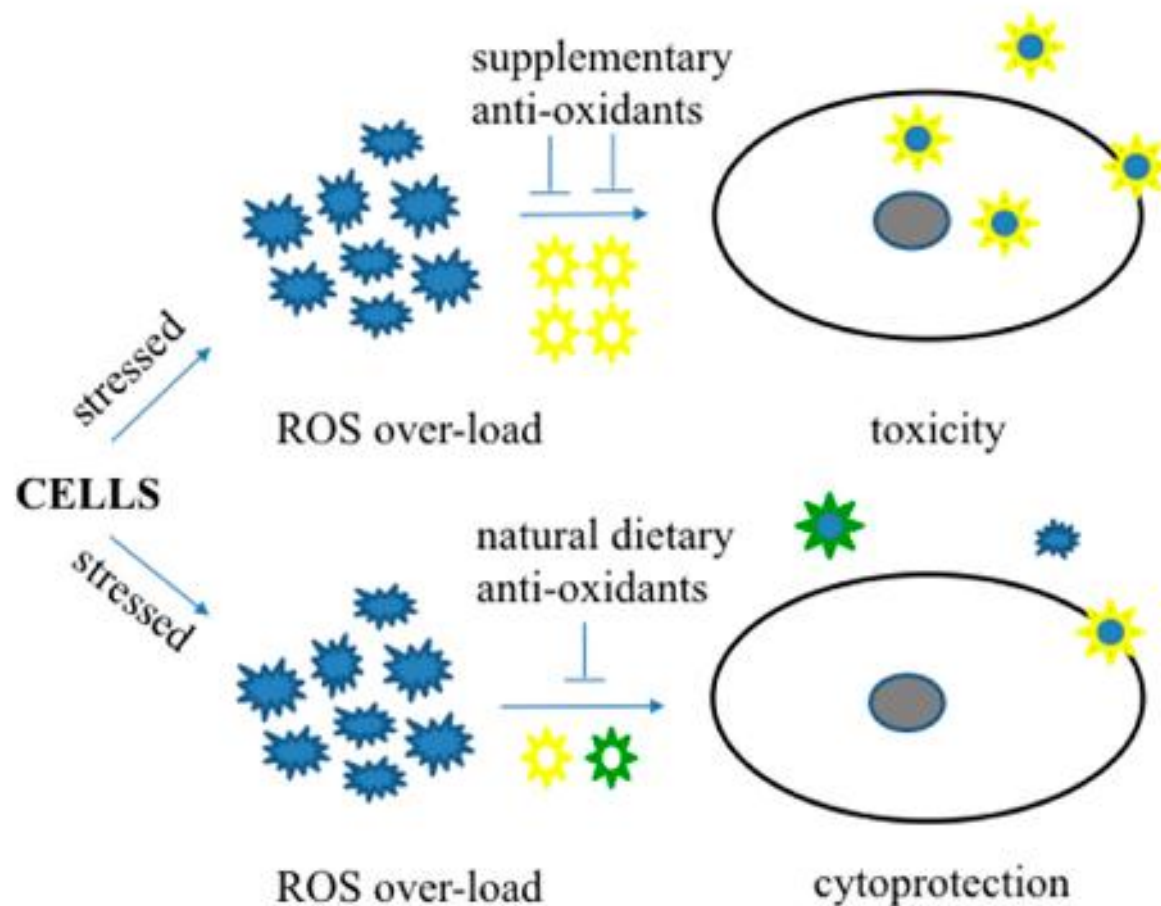


Figure 2. A schematic showing the beneficial roles of dietary anti-oxidants (moderate amounts of multiple anti-oxidants) and harmful roles of anti-oxidant supplements (higher amounts of individual anti-oxidant) during stressed conditions.



Review

Dietary Modulation of Oxidative Stress in Alzheimer's Disease

Arjun Thapa * and Nick J. Carroll *

Department of Chemical and Biological Engineering and the Center for Biomedical Engineering, University of New Mexico, Albuquerque, NM 87131, USA

* Correspondence: athapa@unm.edu (A.T.); ncarroll@unm.edu (N.J.C.);

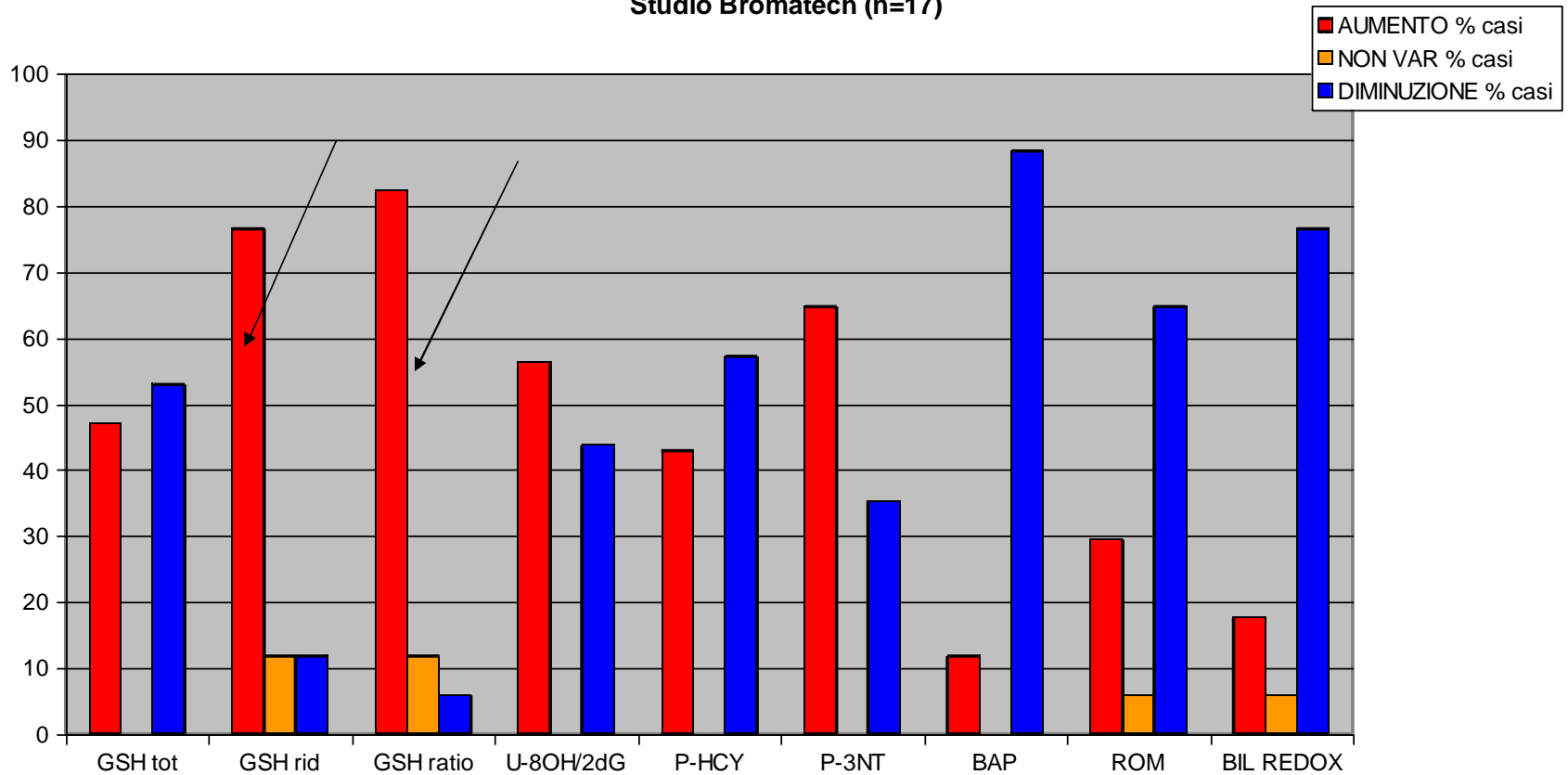
Tel.: +1-505-277-0752 (A.T.); +1-505-277-2803 (N.J.C.); Fax: +1-505-277-1979 (A.T. & N.J.C.)

Received: 16 June 2017; Accepted: 12 July 2017; Published: 21 July 2017

Natural fruit and vegetable products that are rich in anti-oxidants (flavonoids and polyphenols) are known as beneficial agents against aging-related disease and improving cognitive functions [29,50,67,69,82,102–104]. Therefore, dietary compounds are promising therapeutics for AD and other aging related degenerative diseases. However, currently available dietary supplementary formations have been ineffective in clinical trials as proposed. In fact, some of them even revealed negative side effects [64,65,85,88,98,105,106]. The benefits of several different kinds of natural compounds present in our balanced diet may potentially outweigh the supplementary risks. Fruits and vegetables are enriched with moderate amounts of multiple anti-oxidants and other essential elements. For example, one apple contains quercetin, kaempferol, myricitin, catechin, gallic acid, phloridzin, chlorogenic acid, procyanidin B2 molecules, minerals (calcium, magnesium, phosphorus, and iron), and fiber [95,107]. The individual or synergistic effects of varieties of compounds found in fruits and vegetables could play a transformative role in attenuating oxidative stress. Compounds such as highly

Probiotici e sbilanciamento ossidativo

Studio Bromatech (n=17)



Nutrizione e sbilancio ossidativo

- **Apporto calorico**



- **Nutrienti**



- **Integrazione**



- **Microbiota**



"Stile di vita"

**GRAZIE PER LA VOSTRA
PAZIENTE ATTENZIONE**

