



University of Urbino "Carlo Bo"
Department of Biomolecular Sciences
Section of Clinical Biochemistry and Molecular Genetics

MY RESEARCH EXPERIENCE ON CELLFOOD™

Dr. Serena Benedetti, PhD



The story begins in 2008...

- Prof. Franco Canestrari (University of Urbino, Italy) meets Giorgio Terziani (Eurodream, La Spezia, Italy), who introduces him to the nutritional supplement Cellfood™.
- A research collaboration arises in order to evaluate the in vitro antioxidant properties of Cellfood.
- After more than one year of fruitful research, results are published in an international scientific journal.

What we evaluated...

Food and Chemical Toxicology 49 (2011) 2292–2298

Contents lists available at ScienceDirect

Food and Chemical Toxicology

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

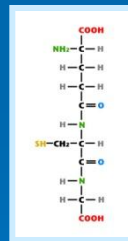
The antioxidant protection of CELLFOOD[®] against oxidative damage *in vitro*

Serena Benedetti^{a,*}, Simona Catalani^a, Francesco Palma^b, Franco Canestrari^a

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Targets of oxidation

Biomolecules



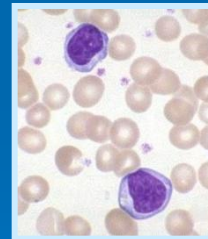
GSH



DNA



Erythrocytes



Lymphocytes

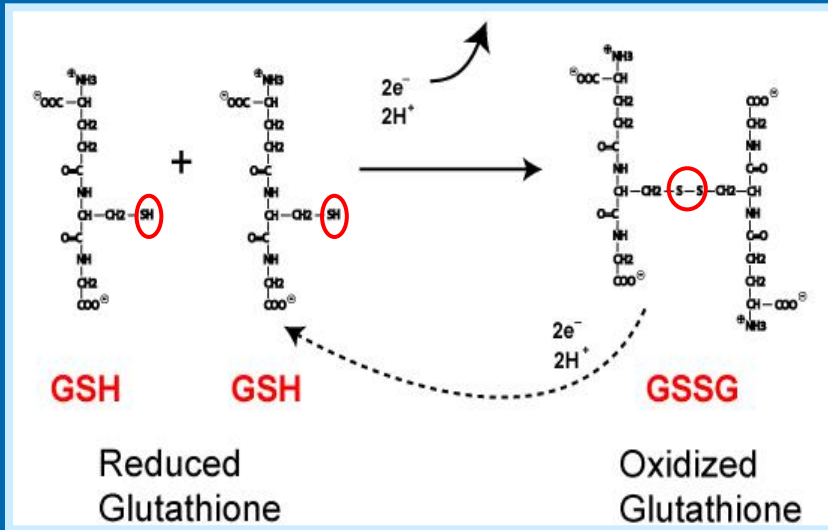


Cells

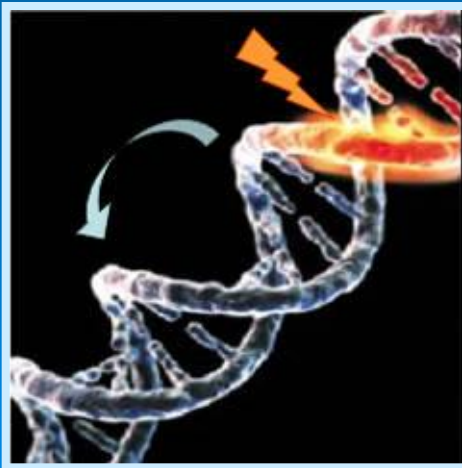
Physiological oxidants

Hydrogen peroxide - Peroxyl radicals - Hypochlorous acid

What we found...

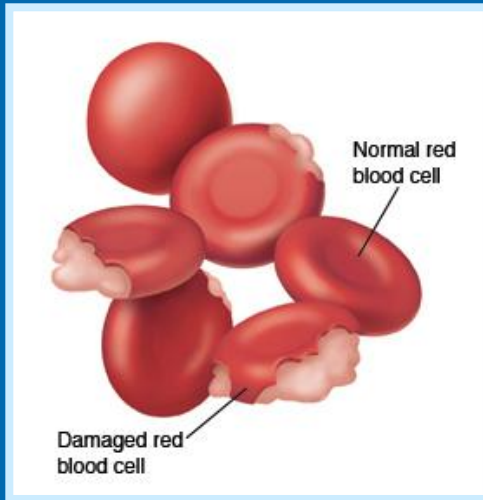


Cellfood protects glutathione (GSH) from oxidation (GSSG), thus preserving the endogenous antioxidant defence system.



Cellfood protects DNA from oxidation, thus preserving nucleic acid integrity and genetic information (\rightarrow **cancer prevention**).

What we found...



Cellfood protects erythrocytes from oxidation, thus preserving them against oxidative emolysis.



Cellfood protects lymphocytes from oxidation, preventing free radical formation and cellular oxidative stress.

In the same year...

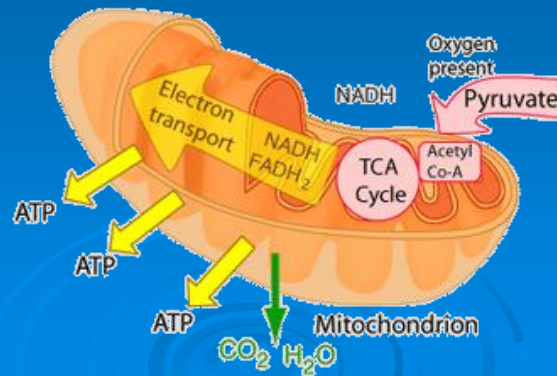
E. FERRERO¹, A. FULGENZI², D. BELLONI¹, C. FOGLENTI³, M.E. FERRERO²

J Physiol Pharmacol. 2011 Jun;62(3):287-93.

CELLFOOD™ IMPROVES RESPIRATORY METABOLISM OF ENDOTHELIAL CELLS AND INHIBITS HYPOXIA-INDUCED ROS GENERATION

¹Myeloma Unit, San Raffaele Scientific Institute, Milan, Italy; ²Dipartimento di Morfologia Umana e Scienze Biomediche - Citta Studi, Universita degli Studi di Milano, Milan, Italy; ³Clinical Cardiovascular Biology Laboratory, San Raffaele Scientific Institute, Milan, Italy

Cellfood administration to endothelial cells leads to **increased oxygen consumption and energy production** indicating an improvement of mitochondrial respiration.



CELLFOOD UNIQUE FEATURE

Modulator of cellular oxygen consumption, thus obtaining **full benefits from cell oxygenation** (i.e. energy production) **without incurring in possible adverse effects** associated with oxygen consumption (i.e. free radical production and oxidative damage).



Valuable adjuvant in the prevention and treatment of various physiological and pathological conditions related to oxidative stress

(i.e. intense aerobic exercise, cardiovascular risk, neurodegeneration and cancer).

In vivo confirmations...

CELLFOOD AND ENDURANCE SPORTS



Thanks to the **wide availability of oxygen to muscle cells** and the enhancement of energy production during prolonged aerobic activities:

- Cellfood counteracts hypoxia-related acidosis by reducing lactate levels and delaying the onset of fatigue,
- Cellfood improves cardiorespiratory parameters and athletic performances.

In vivo confirmations...

CELLFOOD AND CARDIOVASCULAR RISK

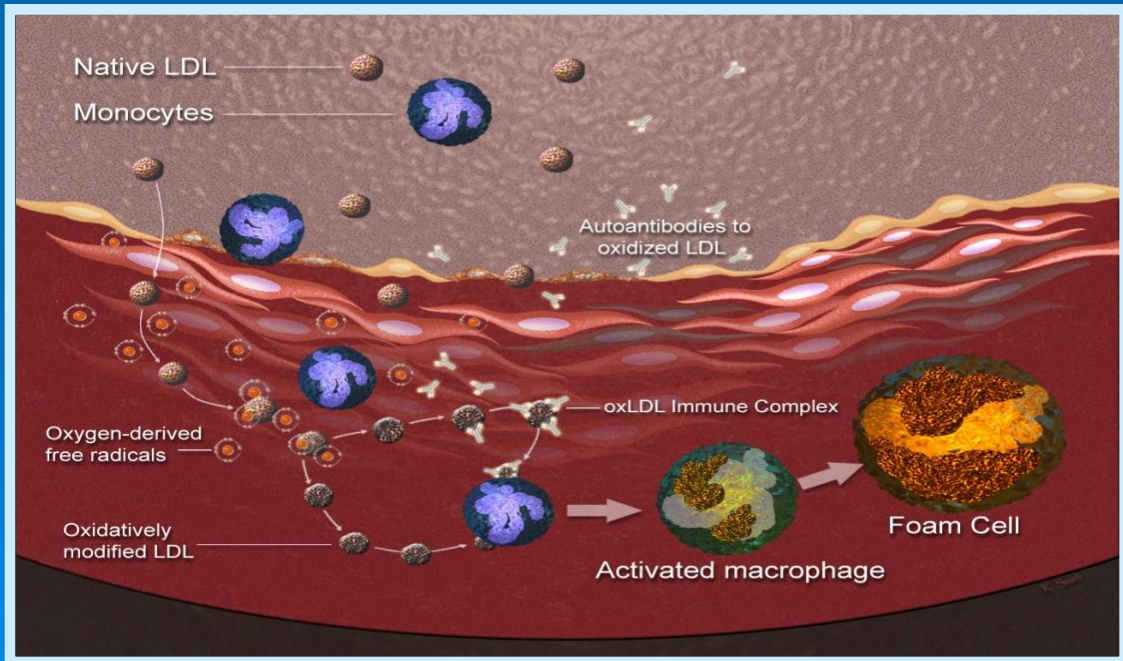
Cellfood administration to osteopenic women significantly reduces the serum levels of oxidized LDL (oxLDL), which are markers of oxidative damage to circulating lipoproteins responsible for the formation of the atheromatous plaque.

L. VIGNA¹, F. DE LISO²,
C. NOVEMBRINO²,
R. DE GIUSEPPE³,
R. MAIAVACCA², C. DE VITA³,
F. BAMONTI³

PROGRESS IN NUTRITION
VOL. 15, N. 3, 163-174, 2013

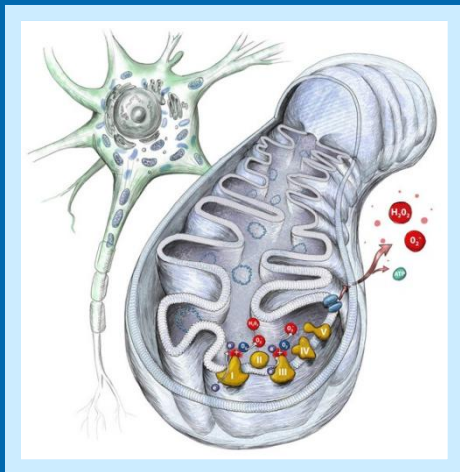
TITLE

Evaluating effects of a natural supplementation on metabolic-nutritional-oxidative status in osteopenic women: a pilot study



In vivo confirmations...

CELLFOOD AND NEURODEGENERATION



High oxygen consumption and free radical production in neuronal cells.



High susceptibility to oxidative damage and neurodegeneration.

Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 281510, 9 pages
<http://dx.doi.org/10.1155/2014/281510>



Clinical Study

Improvement of Oxidative and Metabolic Parameters by Cellfood Administration in Patients Affected by Neurodegenerative Diseases on Chelation Treatment

Alessandro Fulgenzi,¹ Rachele De Giuseppe,² Fabrizia Bamonti,² and Maria Elena Ferrero¹

¹ Department of Biomedical Sciences for Health, University of Milan, Via L. Mangiagalli 31, 20133 Milan, Italy

² Department of Biomedical, Surgical and Dental Sciences, University of Milan and Haematology-Oncology and BMT Unit, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via F. Sforza 33, 20122 Milan, Italy

Journal of Inorganic Biochemistry 152 (2015) 214–218

Contents lists available at ScienceDirect

Journal of Inorganic Biochemistry

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



ELSEVIER



Efficacy of chelation therapy to remove aluminium intoxication

Alessandro Fulgenzi^a, Rachele De Giuseppe^b, Fabrizia Bamonti^b, Daniele Vietti^a, Maria Elena Ferrero^a

^a Department of Biomedical Sciences for Health, University of the Study of Milan, Milan, Italy

^b Department of Biomedical, Surgical and Dental Sciences University of the Study of Milan, Haematology-Oncology and BMT Unit, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy



In vivo confirmations...

CELLFOOD AND NEURODEGENERATION

In patients on chelation therapy suffering from neurodegenerative diseases, Cellfood administration in combination with EDTA leads to:

- significant reduction of aluminium intoxication,
- improvement of clinical symptoms,
- significant decrement of reactive oxygen species (ROS), oxLDL, and homocysteine serum levels,
- significant increment of vitamin B12, folate, and GSH serum levels, and of total antioxidant capacity (TAC).

The story continues in 2011...

A new research collaboration arises between:

- Eurodream,
 - University of Urbino,
 - “Regina Elena” National Cancer Institute (Rome),
- in order to evaluate the in vitro antiproliferative properties of Cellfood.



Catalani, Battistelli, Canestrari, Benedetti, Galati, Terziani.
SANA Exhibition, Bologna, 2012.

Two scientific papers are published...

Catalani et al. *Journal of Experimental & Clinical Cancer Research* 2013, **32**:63
<http://www.jeccr.com/content/32/1/63>



Journal of Experimental &
Clinical Cancer Research

RESEARCH

Open Access

Metabolism modifications and apoptosis induction after Cellfood™ administration to leukemia cell lines

Simona Catalani¹, Valentina Carbonaro¹, Francesco Palma², Marselina Arshakyan², Rossella Galati³, Barbara Nuvoli³, Serafina Battistelli¹, Franco Canestrari¹ and Serena Benedetti^{1*}

Cellfood
antiproliferative activity
on hematologic cancer
cells (leukemia).

Nuvoli et al. *Journal of Experimental & Clinical Cancer Research* 2014, **33**:24
<http://www.jeccr.com/content/33/1/24>



Journal of Experimental &
Clinical Cancer Research

RESEARCH

Open Access

CELLFOOD™ induces apoptosis in human mesothelioma and colorectal cancer cells by modulating p53, c-myc and pAkt signaling pathways

Barbara Nuvoli¹, Raffaella Santoro¹, Simona Catalani², Serafina Battistelli², Serena Benedetti², Franco Canestrari² and Rossella Galati^{1*}

Cellfood
antiproliferative activity
on solid-tumor cancer
cells (carcinomas).

What we evaluated...

CANCER CELL LINES

Jurkat: acute lymphoblastic leukemia

U937: acute myeloid leukemia

K562: chronic myeloid leukemia

IM1, IM2, NCI2452, MSTO211, MPP89: mesotelioma

M14, ME1007: melanoma

SKRB3, MCF7: breast carcinoma

HCT116: colon carcinoma

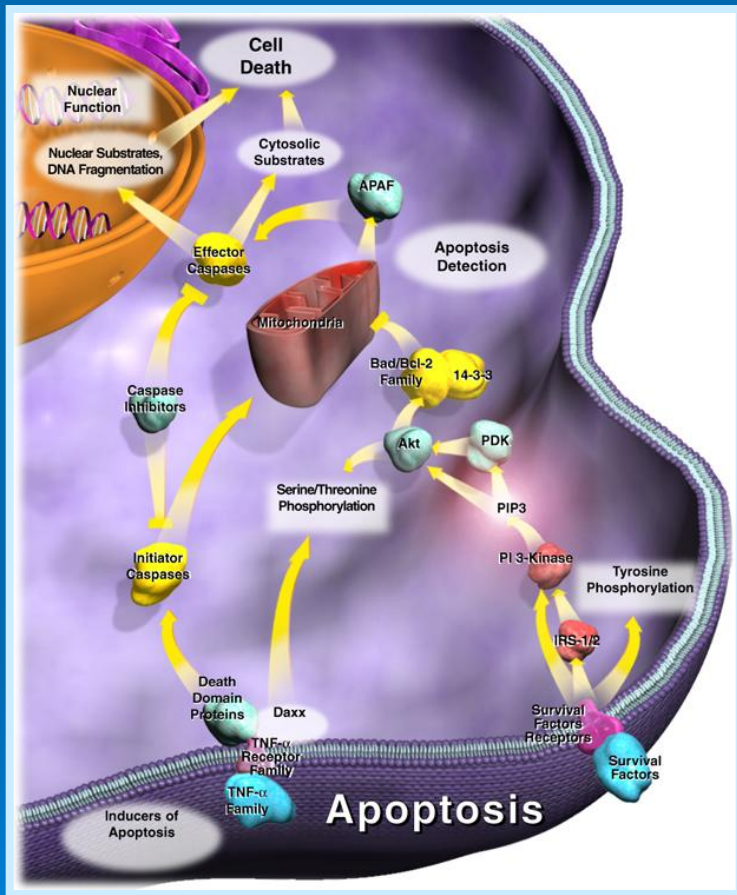
H1650, H1975, H1299: lung carcinoma

EJ: bladder carcinoma



**Tumor cell incubation with CELLFOOD (5 μ l/ml)
for 24, 48, and 72 hours.**

What we evaluated...



CELL PROLIFERATION
(cell count and viability)

CELL METABOLISM
(HIF-1 α , GLUT-1, LDH, lactate)

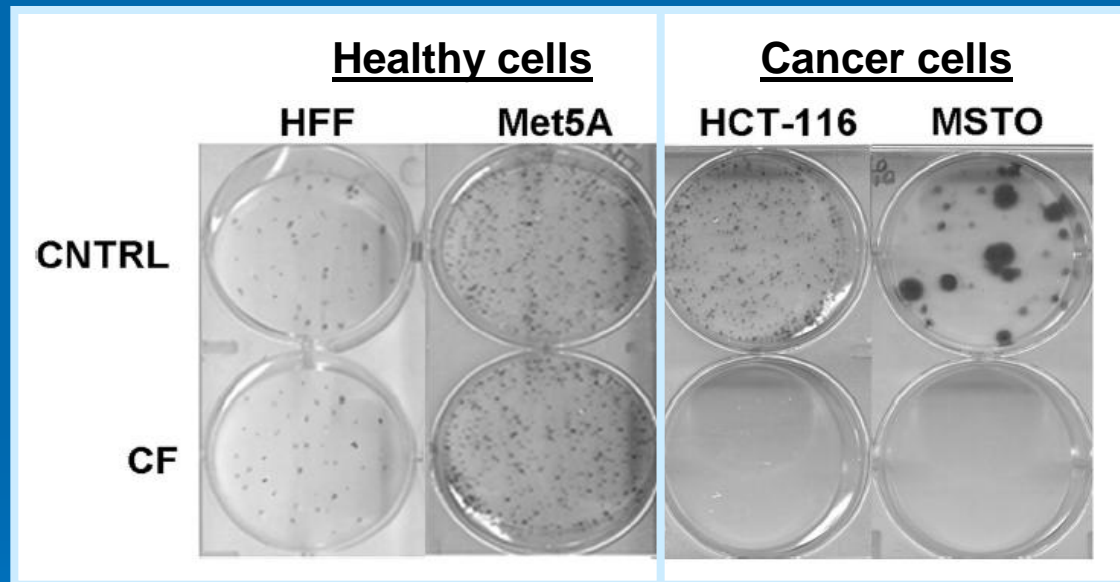
APOPTOSIS
(caspase-3, PARP, DNA laddering)

APOPTOSIS-RELATED PROTEINS
(p53, p21, p27, c-myc)

CELL SURVIVAL PATHWAYS
(Akt, Bcl-2)

What we found...

CELLFOOD INHIBITS CANCER CELL GROWTH WITHOUT AFFECTING HEALTHY CELLS



HFF and Met5A: fibroblast and mesothelio cell lines.

HCT-116 and MSTO: colon carcinoma and mesothelioma cell lines.

CNTR: untreated control cells.

CF: Cellfood-treated cells.

What we found...

CELLFOOD INHIBITS THE HYPOXIC FACTOR HIF-1 α ,
involved in the regulation of cancer cell metabolism and
apoptosis resistance.

Modulation of glucose metabolism
(glycolysis) after Cellfood
administration.

Inhibition of GLUT-1 expression,
lactate dehydrogenase activity and
lactate release.



Induction of apoptotic cell
death after Cellfood
administration.

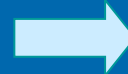
Activation of caspase-3
and induction of DNA
fragmentation.

What we found...

CELLFOOD INHIBITS THE ACTIVATION OF AKT, involved in cancer cell survival and apoptosis resistance.

Inhibition of cell survival pathways after Cellfood administration.

Increment of p53 expression and decrement of c-myc and bcl-2 expression.

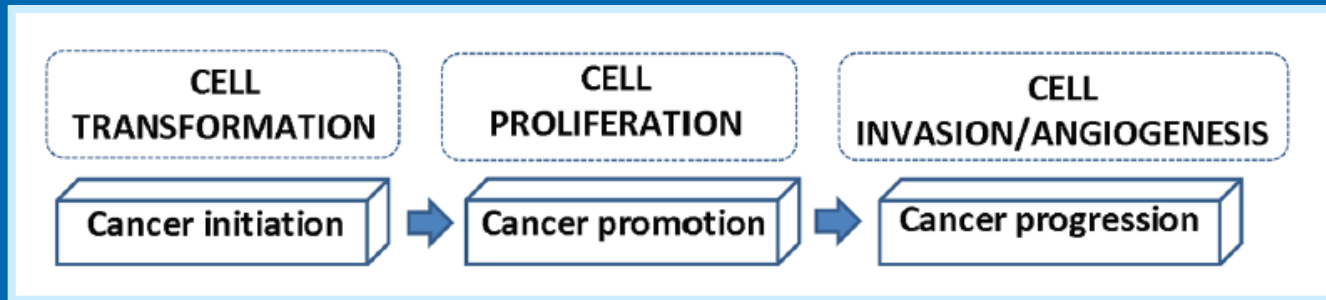


Induction of apoptotic cell death after Cellfood administration.

Activation of caspase-3 and cleavage of PARP.

CELLFOOD AND CANCER

Cellfood may affect all the three stages of carcinogenesis



Considering that...

The combination of metabolic regulators and inhibitors of signaling pathways is a rational approach to treat cancer.

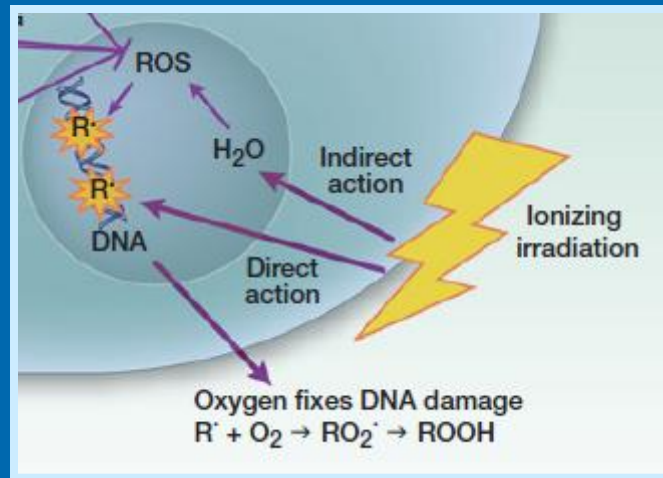
The long-term safety and tolerability of any chemopreventive compound for human consumption are a key issue.



CELLFOOD MAY BE OF GREAT CLINICAL UTILITY BOTH AS A CHEMOPREVENTIVE AGENT AND AS A SUPPORT TO STANDARD ANTINEOPLASTIC THERAPIES.

The story still continues in 2016...

Can **Cellfood sensitize cancer cells to radiotherapy** by counteracting hypoxia-related radioresistance?



Preliminary in vitro studies indicate that, in Cellfood-treated cancer cells, irradiation causes higher tumor cell mortality as compared to untreated irradiated cells.

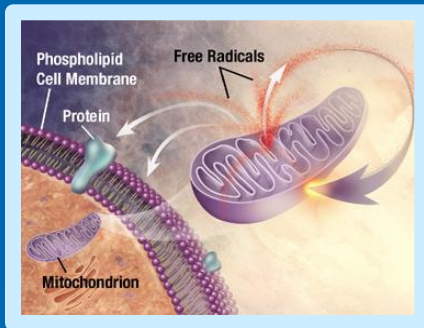
Waiting for in vivo studies...

Take home message... **Cellfood to rebalance**

Oxidative stress and hypoxia play a pathological role in many degenerative diseases, from neurodegeneration to cancer.

Cellfood, as unique oxygen modulator, may offer health benefits both in the prevention and treatment of these disorders.

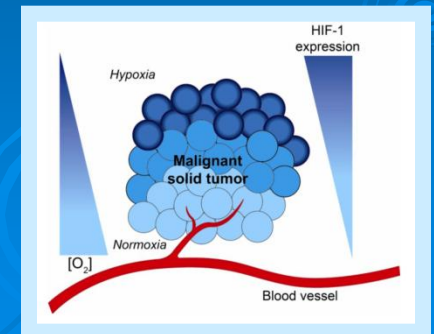
↑pO₂
HYPEROXIA



NORMOXIA



↓pO₂
HYPOXIA



THANK YOU ALL FOR YOUR KIND ATTENTION!

Thanks to my collaborators:



Department of Biomolecular Sciences

Dr. Simona Catalani, Prof. Francesco Palma, Prof. Serafina Battistelli, Prof. Franco Canestrari



Regina Elena National Cancer Institute

Dr. Rossella Galati, Dr. Barbara Nuvoli