SIONG
SOCIETÀ ITALIANA OTONEUROGERIATRIA

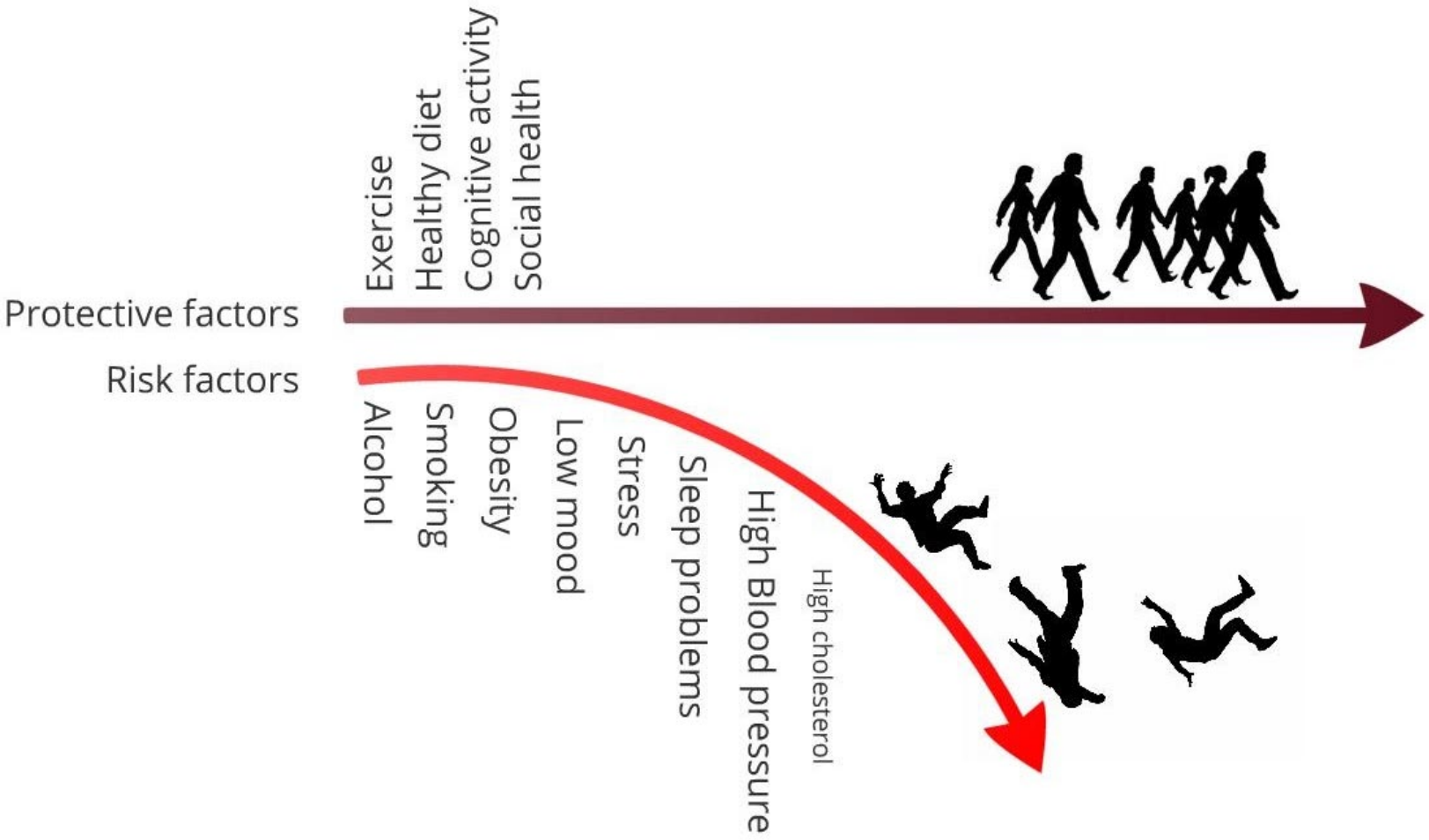
5° Congresso Nazionale

"La LGCI: dai markers biologici ai danni organici"

Markers biologici nell'Inflammaging

Pietro Gareri, MD, PhD
Geriatra ASP Catanzaro
CDCD Catanzaro Lido

Risk and protective factors for brain aging



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BACKGROUND: COGNITIVE DECLINE

Pathophysiological Mechanisms and Unmet Needs

THE CONTINUUM OF COGNITIVE DECLINE

Normal cognitive aging → Increasing impairment

Normal Cognitive Aging	Subjective Cognitive Decline	Mild Cognitive Impairment (MCI)	Dementia
Subjective forgetfulness	Subjective complaints	Objective cognitive decline	Progressive cognitive decline
Normal function	Normal objective performance	Preserved daily function	Loss of autonomy

KEY CLINICAL ENTITIES

- Amnestic / non-amnestic MCI
- Vascular cognitive impairment (VCI)
- Mixed pathologies
- Lewy body disease
- Frontotemporal dementia
- Alzheimer's disease

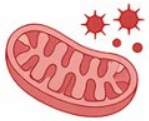
PATHOPHYSIOLOGICAL MECHANISMS INVOLVED IN COGNITIVE DECLINE

NEUROINFLAMMATION

Activated microglia and astrocytes release pro-inflammatory cytokines (IL-1β, IL-6, TNF-α)

- Chronic inflammation
- Synaptic dysfunction
- Neuronal damage

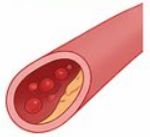
OXIDATIVE STRESS



Reactive oxygen species (ROS)

- Lipid peroxidation
- DNA damage
- Protein oxidation
- Mitochondrial injury

VASCULAR DYSFUNCTION



Cerebral small vessel disease, hypoperfusion

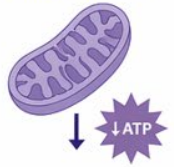
- Endothelial dysfunction
- Reduced cerebral blood flow
- Blood–brain barrier disruption

CHOLINERGIC DYSFUNCTION

Reduced acetylcholine synthesis and release

- Impaired attention
- Memory deficits
- Executive dysfunction

MITOCHONDRIAL DYSFUNCTION & ENERGY FAILURE



- Impaired energy metabolism
- Increased apoptosis
- Synaptic failure

RESULTING CONSEQUENCES

Neuronal loss and synaptic degeneration

Cognitive impairment (memory, attention, executive functions, language)

Functional decline and loss of independence

UNMET NEEDS IN THE MANAGEMENT OF COGNITIVE DECLINE

LIMITED EFFECTIVE THERAPIES

- Few disease-modifying treatments
- Mainly symptomatic therapies

EARLY DIAGNOSIS CHALLENGES

- Biomarkers not routinely available
- Heterogeneous clinical presentations

NON-COGNITIVE SYMPTOMS

- Mood disorders
- Sleep disturbances
- Apathy, irritability
- Often under-recognized and undertreated

PATIENT COMPLEXITY

- Advanced age
- Frailty
- Multimorbidity
- Polypharmacy

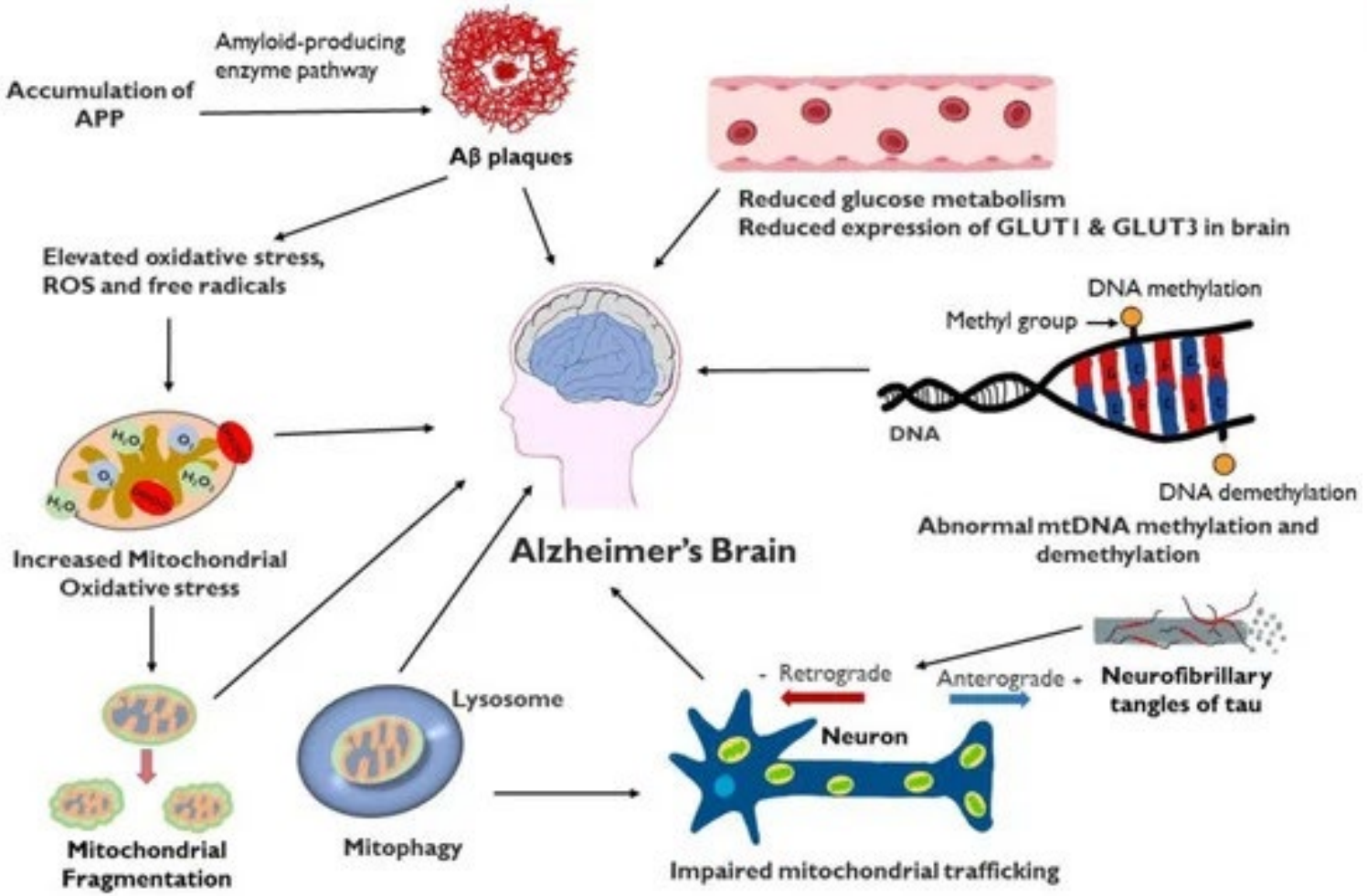
LACK OF INTEGRATED APPROACHES

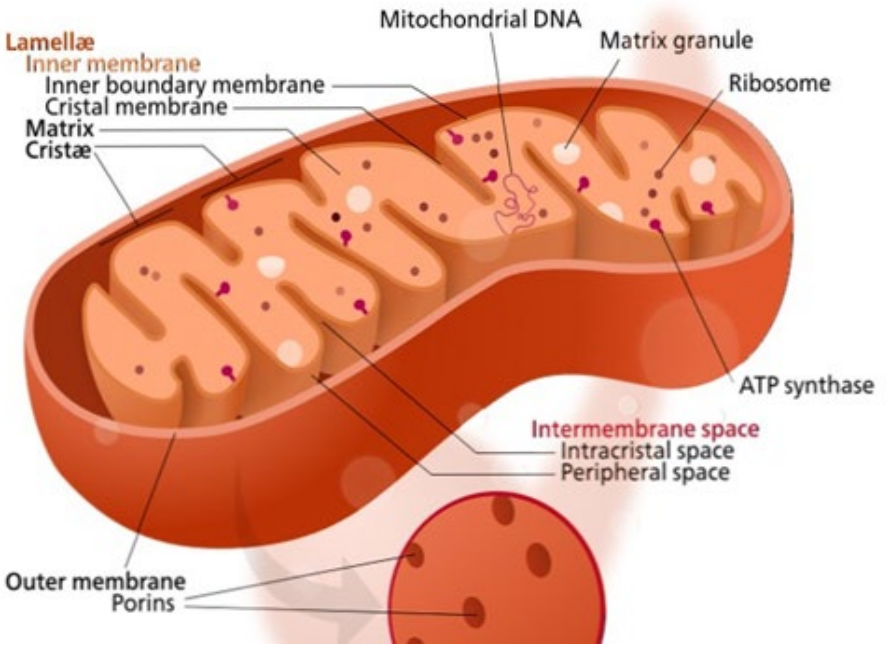
- Fragmented care
- Need for multimodal and personalized strategies

LIMITED REAL-WORLD EVIDENCE

- Few data from routine clinical practice
- Heterogeneity of study populations

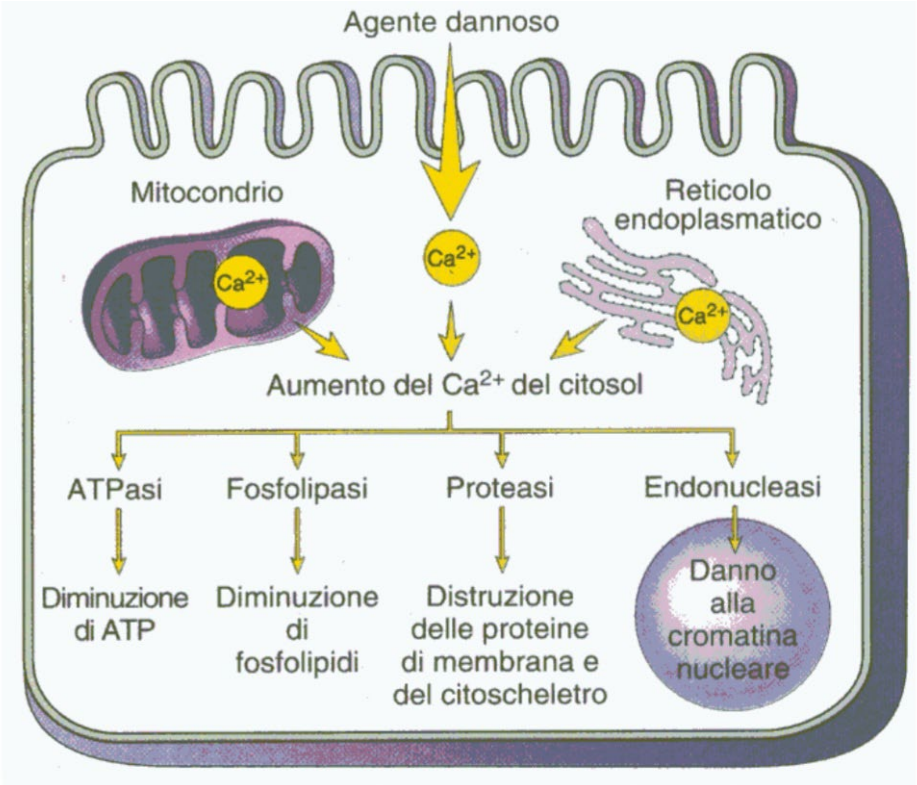
Cognitive decline is a multifactorial process driven by complex biological mechanisms and associated with major unmet needs. An integrated, multimodal and patient-centered approach is essential to improve outcomes.


Amyloid-producing enzyme pathway
Accumulation of APP
Aβ plaques
Reduced glucose metabolism
Reduced expression of GLUT1 & GLUT3 in brain
Elevated oxidative stress, ROS and free radicals
DNA methylation
Methyl group
DNA
DNA demethylation
Abnormal mtDNA methylation and demethylation
Increased Mitochondrial Oxidative stress
Alzheimer's Brain
Retrograde
Anterograde
Neurofibrillary tangles of tau
Lysosome
Neuron
Mitochondrial Fragmentation
Mitophagy
Impaired mitochondrial trafficking


Lamellæ
Inner membrane
Inner boundary membrane
Cristal membrane
Matrix
Cristæ
Mitochondrial DNA
Matrix granule
Ribosome
ATP synthase
Intermembrane space
Intracristal space
Peripheral space
Outer membrane
Porins

L'eccitotossicità del glutammato può causare danni ai mitocondri, infatti:

- l'aumento dei livelli di GLU porta ad un eccesso di calcio intracellulare che a sua volta può danneggiare i mitocondri ed innescare la morte neuronale
- L'eccessivo calcio intracellulare può alterare la permeabilità della membrana mitocondriale, causando rilascio di ROS e compromissione della funzione respiratoria mitocondriale.
- La disfunzione mitocondriale ed eccesso di calcio possono innescare la via apoptotica, necrosi, morte neuronale come nella SLA, ictus, traumi cranici e malattie neurodegenerative, Alzheimer.

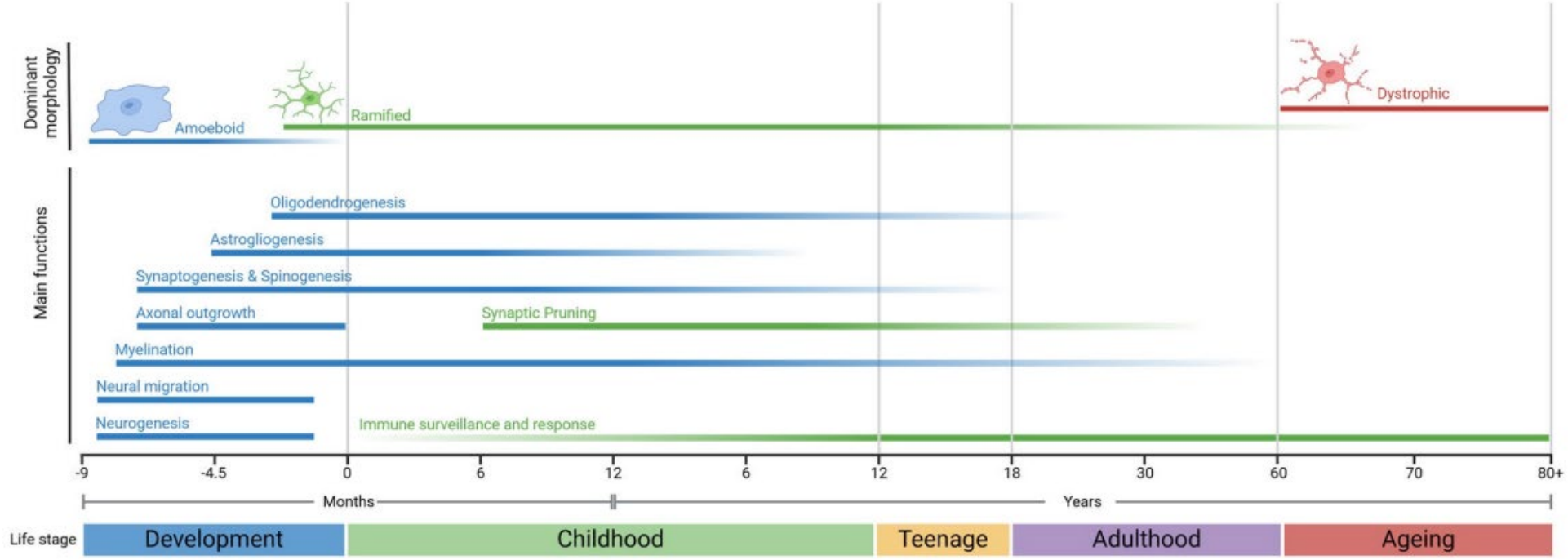


La reattività microgliale alla base di patologie neuroinfiammatorie dell'anziano

The Hallmarks of Ageing in Microglia

Laura Carr[1] · Sanam Mustafa[1,2] · Lyndsey E. Collins-Praino[1,2]

2025 doi.org/10.1007/s10571-025-01564-y



Recenti evidenze riportano che nella fase di senescenza, la microglia assume la morfologia **distrofica**: questo rappresenta il **fenotipo più reattivo** della microglia, che determina risposte più accentuate e tempi più lunghi per la risoluzione dello stato neuroinfiammatorio.

Neuroinflammation — a common thread in neurological disorders

*Nils Erik Gilhus[1,2] and Günther Deuschl[3,4]**

Inflammatory processes contribute to neurological disorders, and many therapeutic breakthroughs in neurological disease have been immune-targeted. The choice of neuroinflammation as the theme for the 5th European Academy of Neurology Congress in 2019 and of this Focus issue highlights its importance to neurologists across the discipline.

NATURE REVIEWS | NEUROLOGY
https://doi.org/10.1038/ s41582-019-0227-8

La Neuroinfiammazione come motore attivo delle patologie neurodegenerative

Disordini cronici neurodegenerativi
(Amor and others 2014; Freeman and Ting 2016; Iadecola and Anrather 2011; McGeer and McGeer 2013; Ransohoff 2016)

Patologie demielinizzanti
(Psenicka et al., 2021)

Stroke
(Jayaraj et al., 2019)

Patologie neuropsichiatriche
(Castanon and others 2015; Najjar and others 2013; Theoharides and others 2015b; Wohleb and others 2016)

Disturbo dello Spettro Autistico
(Noriega and Savelkoul, 2014; Theoharides and others 2016)

Epilessia
(Patel et al 2019)

Patologie dei motoneuroni
(Philips et al., 2011)

Trauma cranico
(Simon et al., 2017)

Mast cells, glia and neuroinflammation: partners in crime?

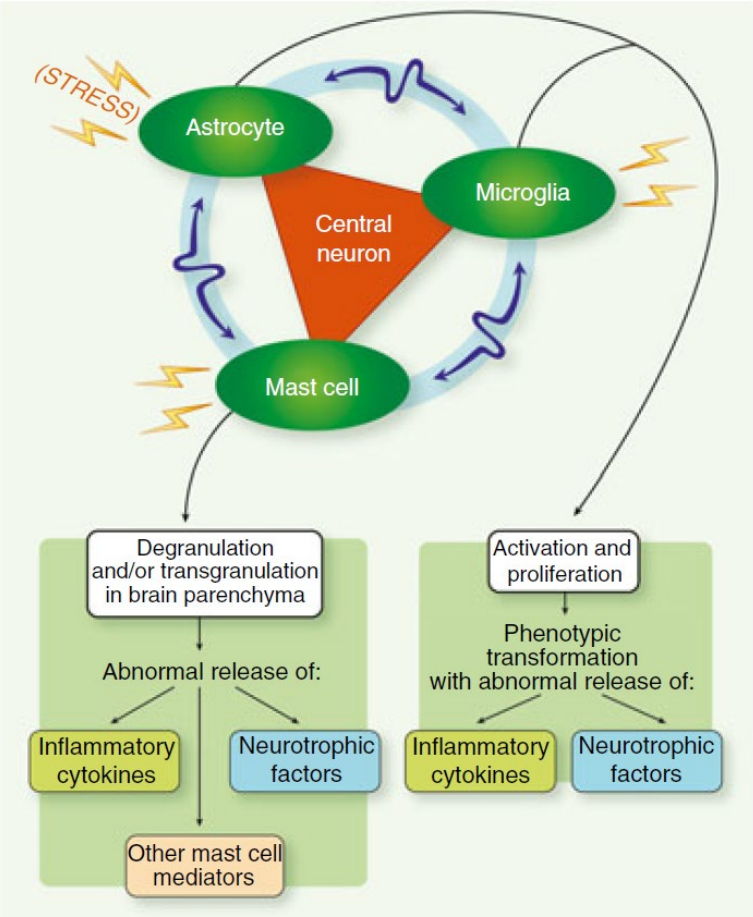
Stephen D. Skaper, Laura Facci and Pietro Giusti

Dipartimento di Scienze del Farmaco, Largo 'Egidio Meneghetti' 2, Università degli Studi di Padova, Padova, Italy

doi:10.1111/imm.12170

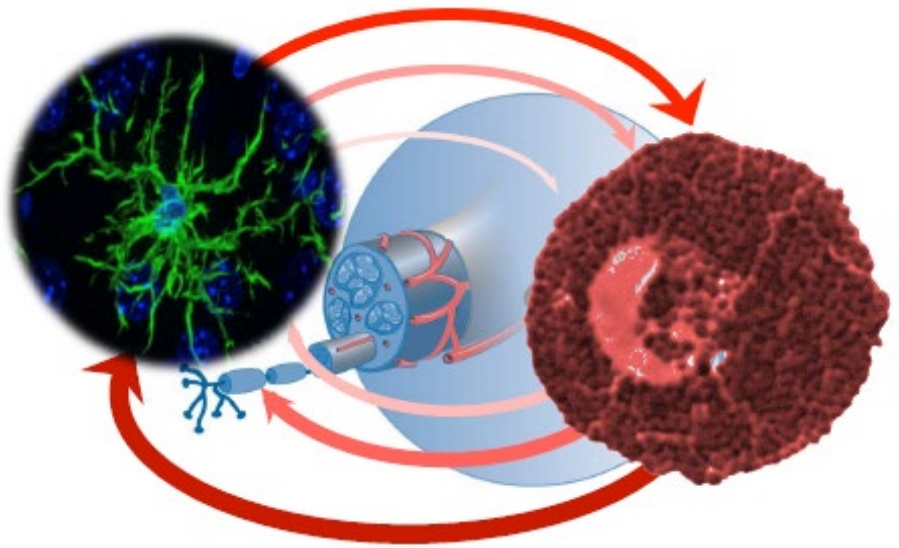
Neuroinfiammazione

Inadeguata regolazione delle **cellule non neuronali (mastociti, microglia e astrociti)** dovuta a stimoli esogeni e/o endogeni eccessivi e persistenti che alterano la funzione neuronale centrale.



cross-talk

comunicazione bidirezionale sincrona



Mast cells, glia and neuroinflammation: partners in crime?
Skaper SD, Facci L, Giusti P.
Immunology. 2014 Mar;141(3):314-27. Review.

Inflammaging

- 'Inflammaging' refers to the chronic, low-grade inflammation that characterizes aging

- Inflammaging is macrophage centered, involves several tissues and organs, including the gut microbiota, and is characterized by a complex balance between pro- and anti-inflammatory responses

- The major source of inflammatory stimuli is represented by endogenous/self, misplaced, or altered molecules resulting from damaged and/or dead cells and organelles, recognized by receptors of the innate immune system

- While their production is physiological and increases with age, their disposal by the proteasome via autophagy and/or mitophagy progressively declines. This 'autoreactive/autoimmune' process fuels the onset or progression of chronic diseases that can accelerate and propagate the aging process locally and systemically

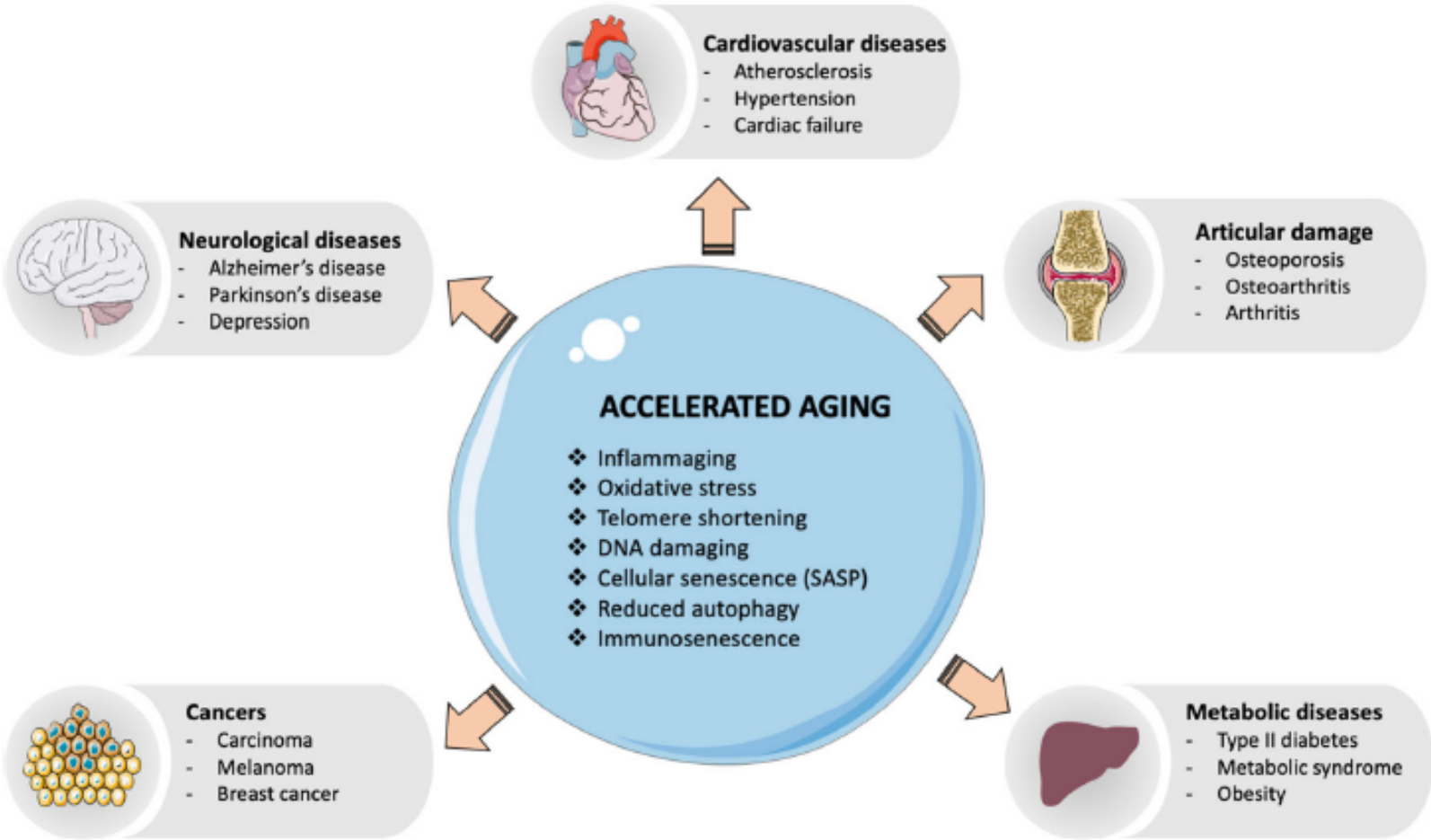
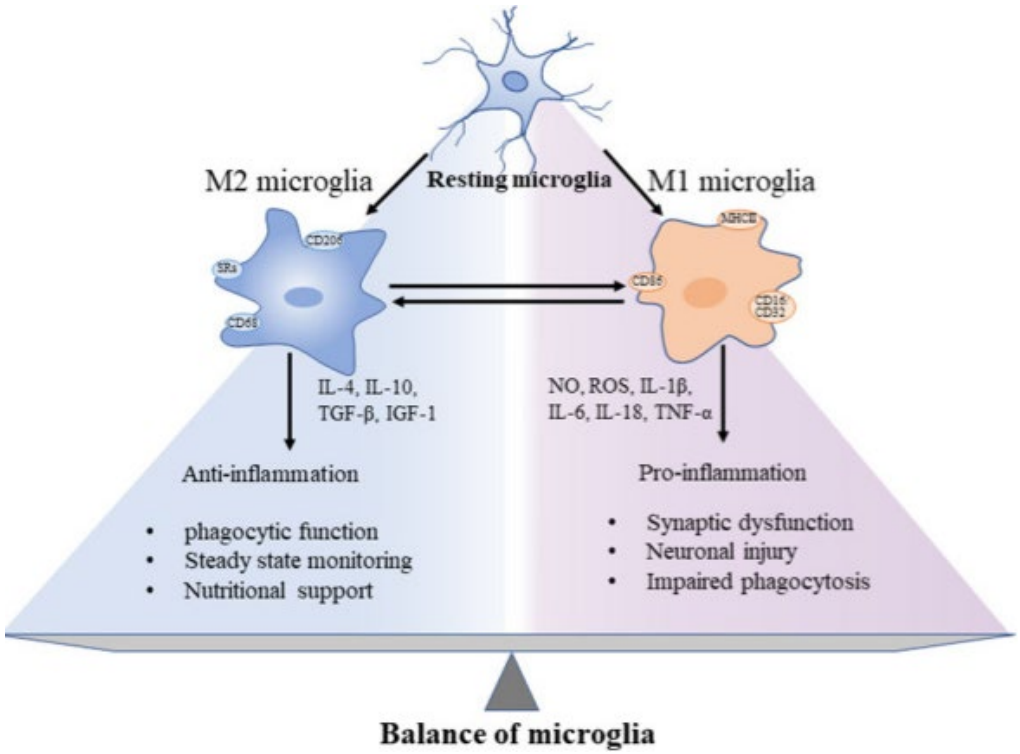


Fig. 1 Multiple mechanisms of accelerated aging are similarly found in age-related diseases. Abbreviations: CMV, cytomegalovirus; SASP, senescence-associated secretory phenotype

Il processo di attivazione microgliale è un fenomeno complesso, caratterizzato dall'acquisizione di diversi fenotipi funzionali, schematicamente rappresentati dai fenotipi M1 e M2, associati rispettivamente a funzioni neuro-tossiche e neuro-protettive.



The effects of microglia-associated neuroinflammation on Alzheimer's disease

Cuicui Wang [1], Shuai Zong [1], Xiaolin Cui [2], Xueying Wang [1], Shuang Wu [2], Le Wang [1], Yingchao Liu [1], Zhiming Lu [1]

Affiliations + expand

PMID: 36911732 PMCID: PMC9992739 DOI: 10.3389/fimmu.2023.1117172

Key Inflammatory Markers

- **C-Reactive Protein (CRP):** Produced by the liver in response to inflammation; it is generally considered the most common and sensitive first-line test.
- **Erythrocyte Sedimentation Rate (ESR):** Measures how quickly red blood cells fall to the bottom of a test tube, with faster rates indicating higher inflammation.
- **Procalcitonin (PCT):** Often used to detect bacterial infections and guide antibiotic treatment
- **Plasma Viscosity (PV):** Measures the thickness of the blood, which increases with inflammation.
- **Other Markers:** Includes serum amyloid A, fibrinogen, and cytokines like interleukins (IL-6).

Cell type/subset	Age-related alterations	Molecular pathways & mechanisms
Naïve CD4$^+$ T cells	Reduced pool size, impaired homeostasis, increased IL-7-driven AKT activation	Decreased FOXO1 activity reduces IL-7R/CCR7; reduced TCR signaling due to miR-181a loss and increased DUSP6; sustained AKT-mTORC1 and ERK signaling skews toward short-lived effector differentiation; increased chromatin accessibility at effector gene loci (BATF, T-BET); telomerase activity loss and telomere shortening;
Naïve CD8$^+$ T cells	Reduced quiescence, increased homeostatic proliferation, effector-like features	Reduced NRF1 expression; decreased IL-7R/CCR7 expression due to FOXO1 inhibition; excessive AKT activation; epigenetic remodeling (DNA methylation, histone modification) leads to central memory-like phenotype
Memory CD4$^+$ T cells	Effector memory cells expansion, increased IFN-γ production, proliferative capacity reduced, telomere erosion	Increased accessibility to BATF and T-BET, EOMES transcription factors; demethylation and overexpression of effector genes; increased IL-15 sensitivity; altered metabolic programming (reduced glycolysis, increased ROS)
Memory CD8$^+$ T cells	Senescent/exhausted phenotype accumulation, inhibitory receptor upregulation (PD-1, CTLA-4, KLRG1), reduced cytotoxicity	TOX-driven exhaustion program; persistent antigenic stimulation; increased SASP; mTORC1 hyperactivation
Effector CD4$^+$ T cells	Skewed differentiation toward Th17/Th1, increased IL-2Rα, TIM3, granzyme B expression	Sustained AKT-mTORC1 and ERK signaling; BLIMP1, RUNX3 upregulation; downregulation of TCF1, LEF1, IL-7R, CD62L, CD27; increased miR-21 expression; impaired lysosomal activity; increased SIRT1 expression leads to replication stress and cell cycle arrest
Regulatory T cells (Treg)	Increased natural Treg frequency, decreased inducibility from precursors, impaired suppressive function, altered cytokine profile	Increased Foxp3 expression; altered IL-10 and TGF-β signaling; epigenetic changes affecting Treg stability
B cell progenitors	Reduced early B cell progenitors (EBPs), impaired lineage commitment	Epigenetic changes in HSCs and B cell precursors; increased ERK MAPK activity; reduced RAGs and surrogate light chain (lambda-5) expression; impaired Notch signaling
Mature B cells	Reduced turnover, impaired class-switch recombination and somatic hypermutation, diminished antibody diversity/affinity	Reduced E2A due to increased mRNA degradation; altered BCR signaling; increased Glut1 expression and glucose uptake; persistent antigenic stimulation leads to age-associated B cell expansion (ABCs); epigenetic changes affecting memory/plasma cell differentiation
Plasma cells	Reduced long-lived plasma cells, decreased antibody secretion	Impaired metabolic reprogramming; decreased transcription factors expression (e.g., BLIMP1, XBP1); reduced survival signals (BAFF, APRIL)
Memory B cells	Reduced pool size, impaired recall responses, increased autoreactivity, expansion of ABCs	Epigenetic remodeling; altered BCR and TLR signaling; upregulation of pro-inflammatory cytokines (TNF-α, IL-6); impaired class-switch recombination
Age-associated B cells (ABCs)	Expansion in aged individuals, pro-inflammatory/autoimmune phenotype, increased cytokine and autoantibody production	TLR7/9 signaling and persistent antigenic stimulation; metabolic reprogramming (increased glycolysis, OXPHOS); epigenetic changes reinforce inflammatory gene expression; impaired negative selection of autoreactive clones

TABLE 4 Cytokine production by T and B cell subsets in inflammaging.

Subset	Hallmark cytokines produced	Role in inflammaging and aging-related shift	Plasticity/Notes
Th1	IFN-γ, TNF-α, IL-2	IFN-γ and TNF-α maintained or increased with age, especially women and with chronic inflammation; can cause chronic inflammation, tissue damage	Th1/Th17 hybrid cells in chronic inflammation; IFN-γ by CD8$^+$ T cells and ABCs
Th2	IL-4, IL-5, IL-13	Reduced differentiation and cytokine output; IL-4 and IL-13 may cause chronic inflammation	Th2/Th17 hybrid states in chronic inflammation
Th17	IL-17A, IL-17F, IL-21, IL-22, TNF-α, IL-6	Relative preservation or increase with age; Th17 dominance and increased IL-17/IL-22, tissue damage, autoimmunity	Highly plastic; can convert to Th1 or Th2; Th17/Th1 and Th17/Th2 hybrid cells
Treg	IL-10, TGF-β, IL-35	Increased frequency in aging with impaired suppressive function and altered cytokine profile	Can lose FoxP3 and acquire effector cytokine production
Tfh	IL-21, IL-4, IL-10	Supports B cell help and antibody production; may be reduced with age	Shares features and cytokines with Th17; promote autoimmunity
Cytotoxic CD8$^+$ T cells	IFN-γ, TNF-α, perforin, granzyme B	Accumulate as senescent/exhausted cells with altered cytokine output	Senescent CD8$^+$ T cells can gain NK-like properties
Memory B cells (Be1, Be2, GM-CSF$^+$, IRA B cells)	IL-6, TNF-α, IFN-γ, GM-CSF, LT, IL-10	Memory B cells and ABCs expand with age, producing more pro-inflammatory cytokines can promote inflammaging and autoimmunity	B cell cytokine profile depends on activation context; Be1 (promote Th1), Be2 (promote Th2); IRA B cells (GM-CSF$^+$) support innate responses
Plasma cells	IL-10, (occasionally IL-6, TNF-α)	Reduced IL-10 in aged plasma cells; impaired anti-inflammatory feedback	Survival and cytokine production depend on signals from Tfh
Age-associated B cells (ABCs)	IL-6, TNF-α, IFN-γ, GM-CSF, autoantibodies	Expanded in aging and chronic inflammation; pro-inflammatory cytokines and autoantibodies; can promote inflammaging and autoimmunity	Driven by TLR7/9 and persistent antigenic stimulation; T-bet$^+$, CD11c$^+$ phenotype

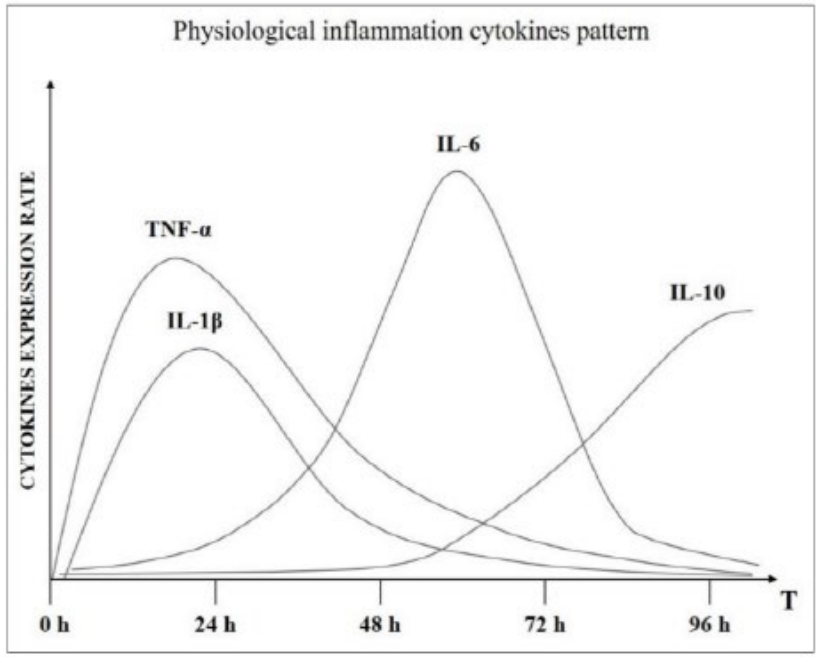

Neuroinflammation in Alzheimer's disease
Michael T Heneka, Monica J Carson, Joseph El Khoury, Gary E Landreth, Frederic Brosseron, Douglas L Feinstein, Andreas H Jacobs, Tony Wyss-Coray, Javier Vitorica, Richard M Ransohoff, Karl Herrup, Sally A Frautschy, Bente Finsen, Guy C Brown, Alexei Verkhratsky, Koji Yamanaka, Jari Koistinaho, Eicke Latz, Annett Halle, Gabor C Petzold, Terrence Town, Dave Morgan, Mari L Shinohara, V Hugh Perry, Clive Holmes, Nicolas G Bazan, David J Brooks, Stéphane Hunot, Bertrand Joseph, Nikolaus Deigendesch, Olga Garaschuk, Erik Boddeke, Charles A Dinarello, John C Breitner, Greg M Cole, Douglas T Golenbock, Markus P Kummer
Neuroinflammation and oxidative stress: Co-conspirators in the pathology of Parkinson's disease
Juliet M. Taylor *, Bevan S. Main, Peter J. Crack
Neuroinflammation: A common denominator for stroke, multiple sclerosis and Alzheimer's disease
Helga E. de Vries , Markus Schwaninger
Neuroinflammation in motor neuron disease
Okiru Komine and Koji Yamanaka
Neuroinflammation in Stroke
U. Dirnagl
B. Elger
(Editors)
The far-reaching scope of neuroinflammation after traumatic brain injury
Dennis W. Simon, Mandy J. McGeachy, Hülya Bayır, Robert S. B. Clark, David J. Loane and Patrick M. Kochanek

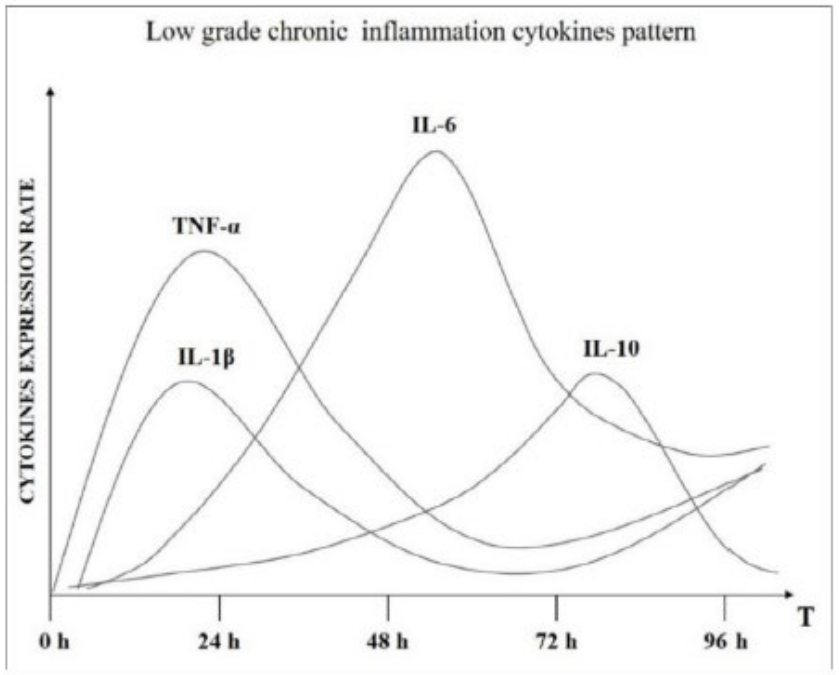
International Journal of Molecular Sciences
MDPI

Review

Regulation of Inflammatory Reaction in Health and Disease

Massimo Fioranelli [1,*], Maria Grazia Roccia [1], Dana Flavin [2] and Linda Cota [2]





The main mechanism of LGCI onset is based on the nuclear translocation of the transcription factor NF-kB. The activation of transcription and translation of specific pro-inflammatory genes is manifested by the release IL-1, TNF-α, and IL-6. At the same time, the oxidative damage produced by the inflammatory trigger reduces the production of AMPK, a fundamental inhibitory control factor of NF-kB translocation. The negative control function on the inflammatory cascade is thus lost.

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Low-Gra
Mechan

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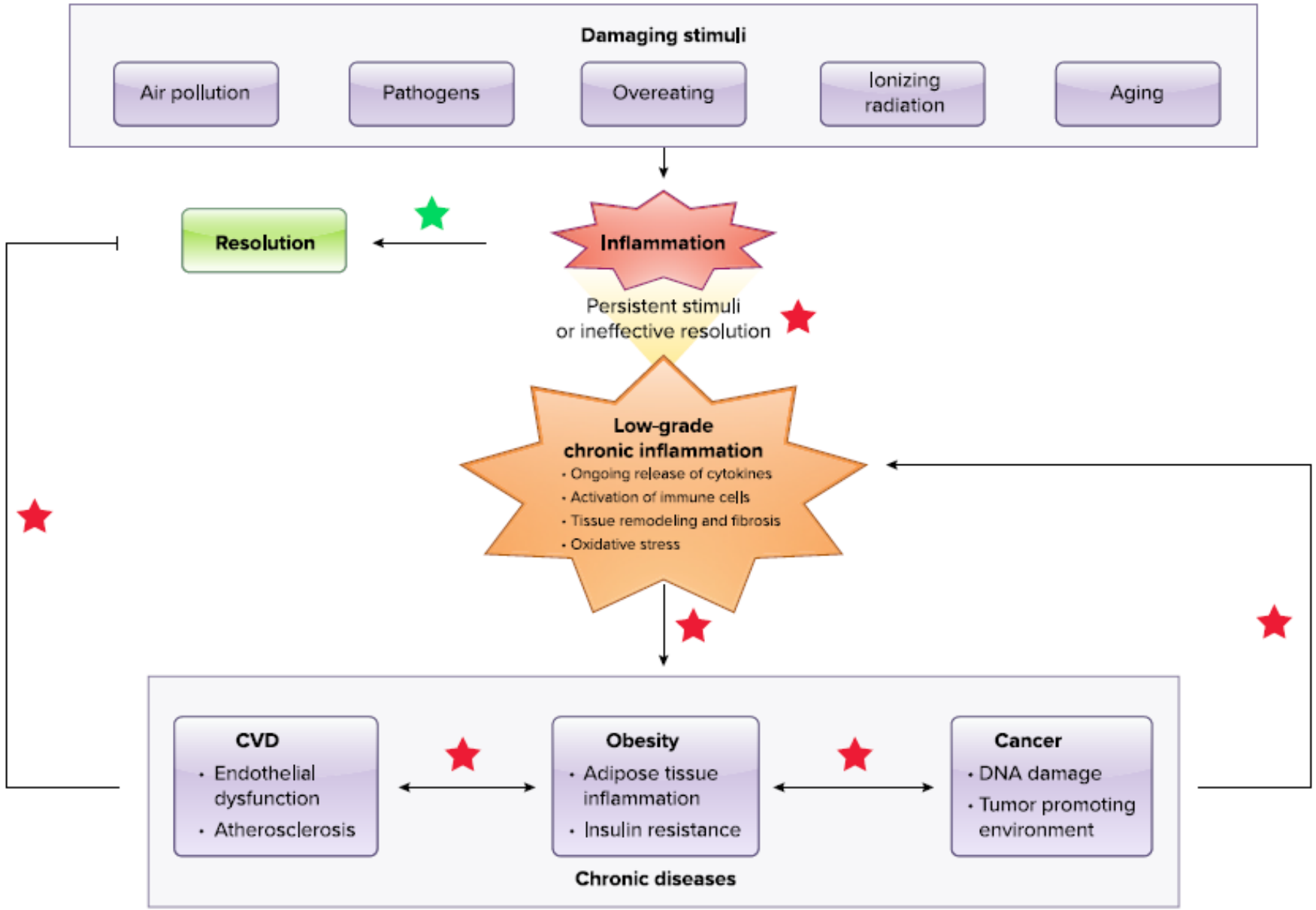
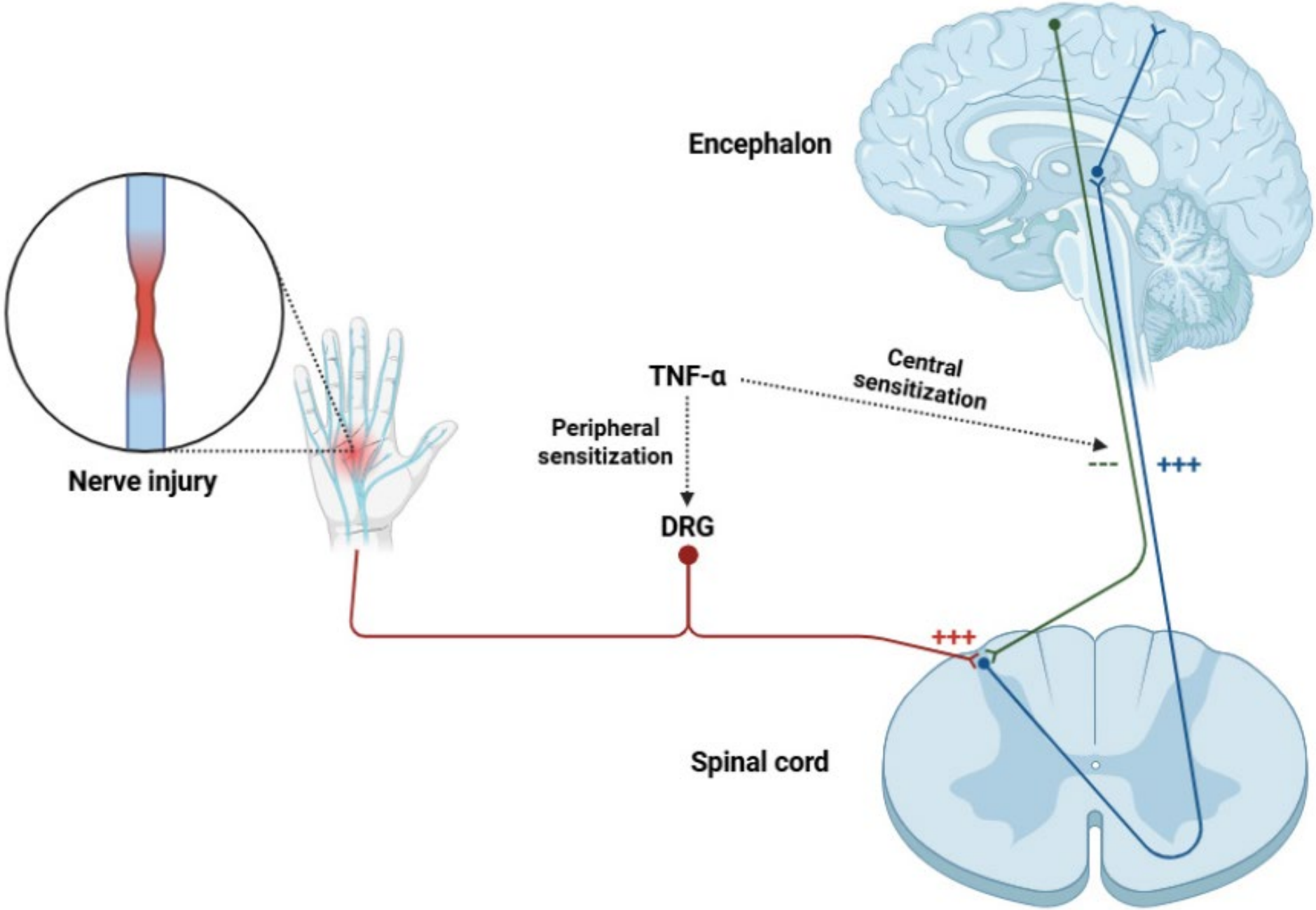



Encephalon
TNF-α
Central sensitization
Peripheral sensitization

+++
DRG
Nerve injury
+++
Spinal cord

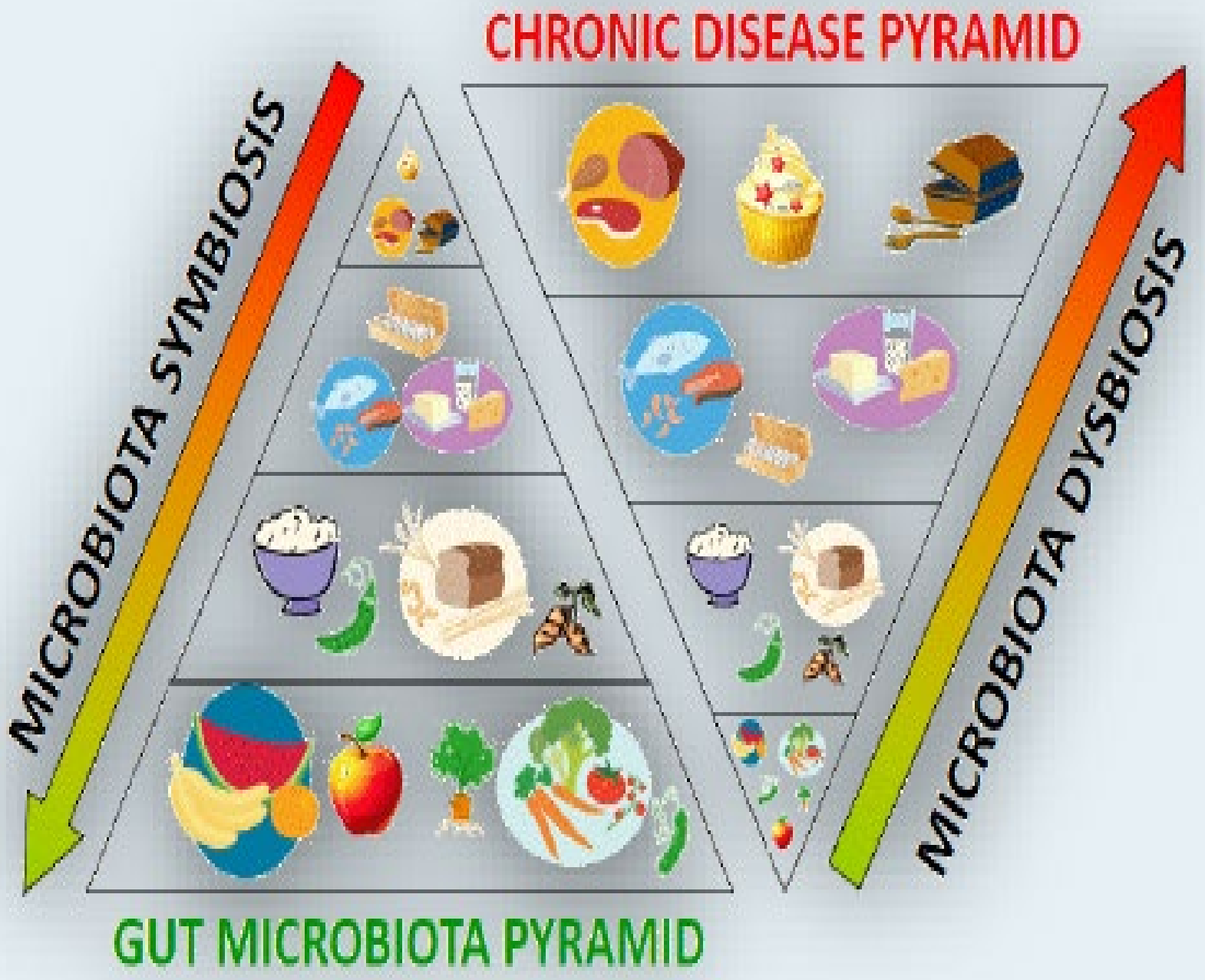
Abstract

The role of oxidative stress and the use of biochemical biomarkers in the severity of COVID-19 was evaluated through a literature review (2020–2021) using scientific search engines such as PubMed, Science Direct, and Google Scholar. The search was limited to articles published in Spanish or English that reported on COVID-19 and its relationship with oxidative stress, following PRISMA-2020 guidelines. The search terms included oxidative stress, COVID-19, SARS-CoV-2, oxidative biomarkers, and oxidative damage. 93.5% of the selected studies were from the year 2021. These studies evaluated both oxidative stress biomarkers and oxidative damage biomarkers in COVID-19 patients. The reviewed studies reinforce the strong association of SARS-CoV-2 with oxidative stress and demonstrate how SARS-CoV-2-induced ROS production and disruption of the antioxidant defense system trigger a pro-inflammatory environment and cause severe tissue damage. In 64.7% of the studies, a combination of oxidative stress biomarkers (antioxidant and oxidative damage biomarkers) was used to assess COVID-19 severity. The most commonly used antioxidant biomarkers were thiols and total antioxidant capacity, followed by glutathione. The most commonly used oxidative damage biomarkers were malondialdehyde and peroxides, followed by advanced oxidation protein products. COVID-19 leads to a decrease in the antioxidant defense system, reflected by a decrease in antioxidant biomarkers and an increase in oxidative damage biomarkers.

• PAMP - *Pathogen-Associated Molecular Patterns* sono molecole strutturali essenziali tipiche dei microrganismi (batteri, virus, funghi) ma assenti nell'ospite, che fungono da "firma" per il riconoscimento da parte del sistema immunitario innato.

- Riconosciuti dai recettori PRR (come i TLR), attivano risposte infiammatorie e difese immediate.
- Sono essenziali per la sopravvivenza, la replicazione o l'infettività del patogeno
- Es. LPS, acidi lipoteicoici, flagellina, betaglucani, RNA a doppia catena, a catena singola, DNA non metilato

• DAMP - le cellule danneggiate o necrotiche rilasciano molecole endogene chiamate **DAMP (Damage-associated molecular patterns)**, o allarmine, che allertano il sistema immunitario in caso di traumi, ustioni o infezioni.

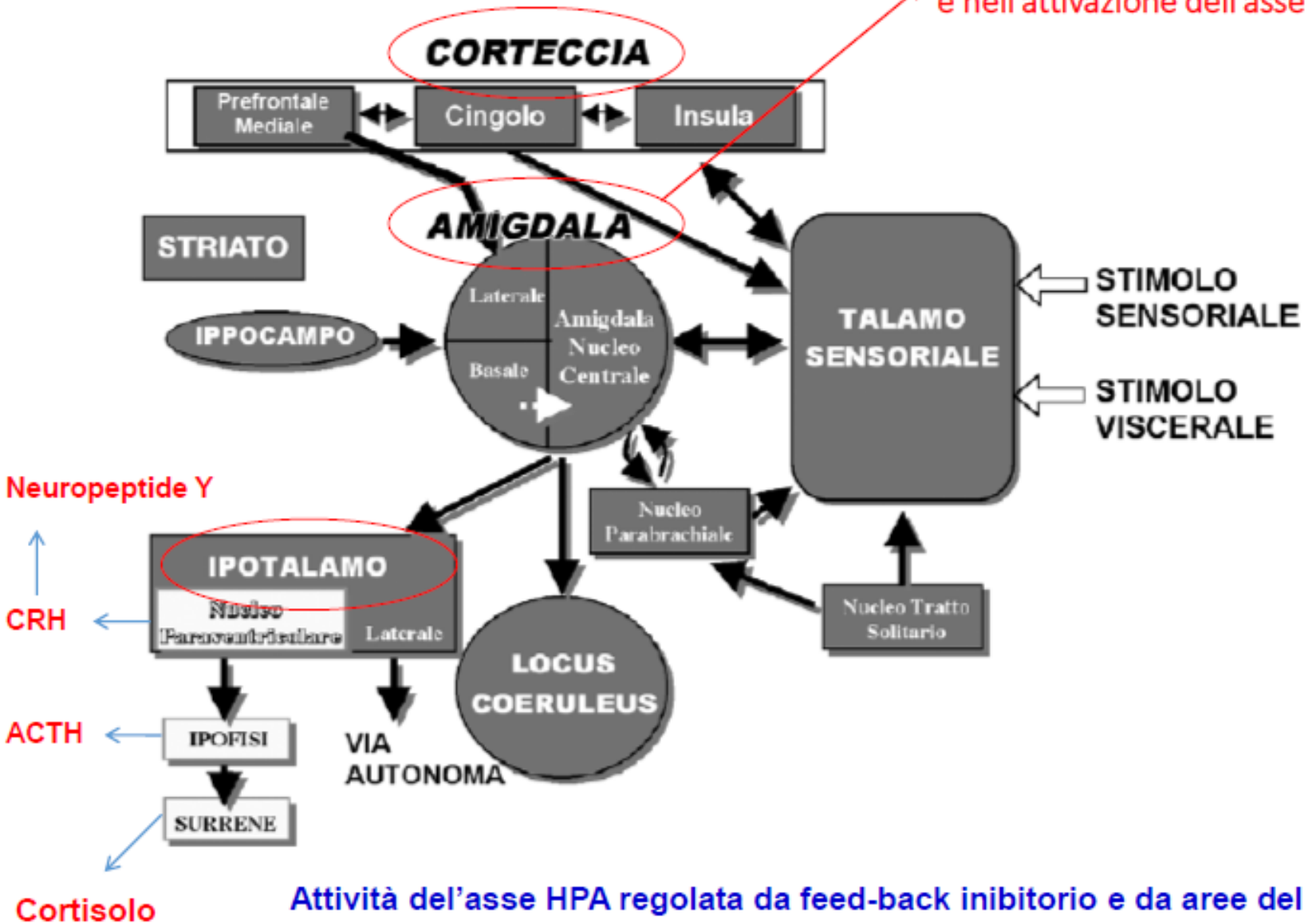


Indolo e scatolo sono metaboliti prodotti dalla flora batterica intestinale, in particolare durante processi di putrefazione di diete ricche di proteine e povere di fibre.

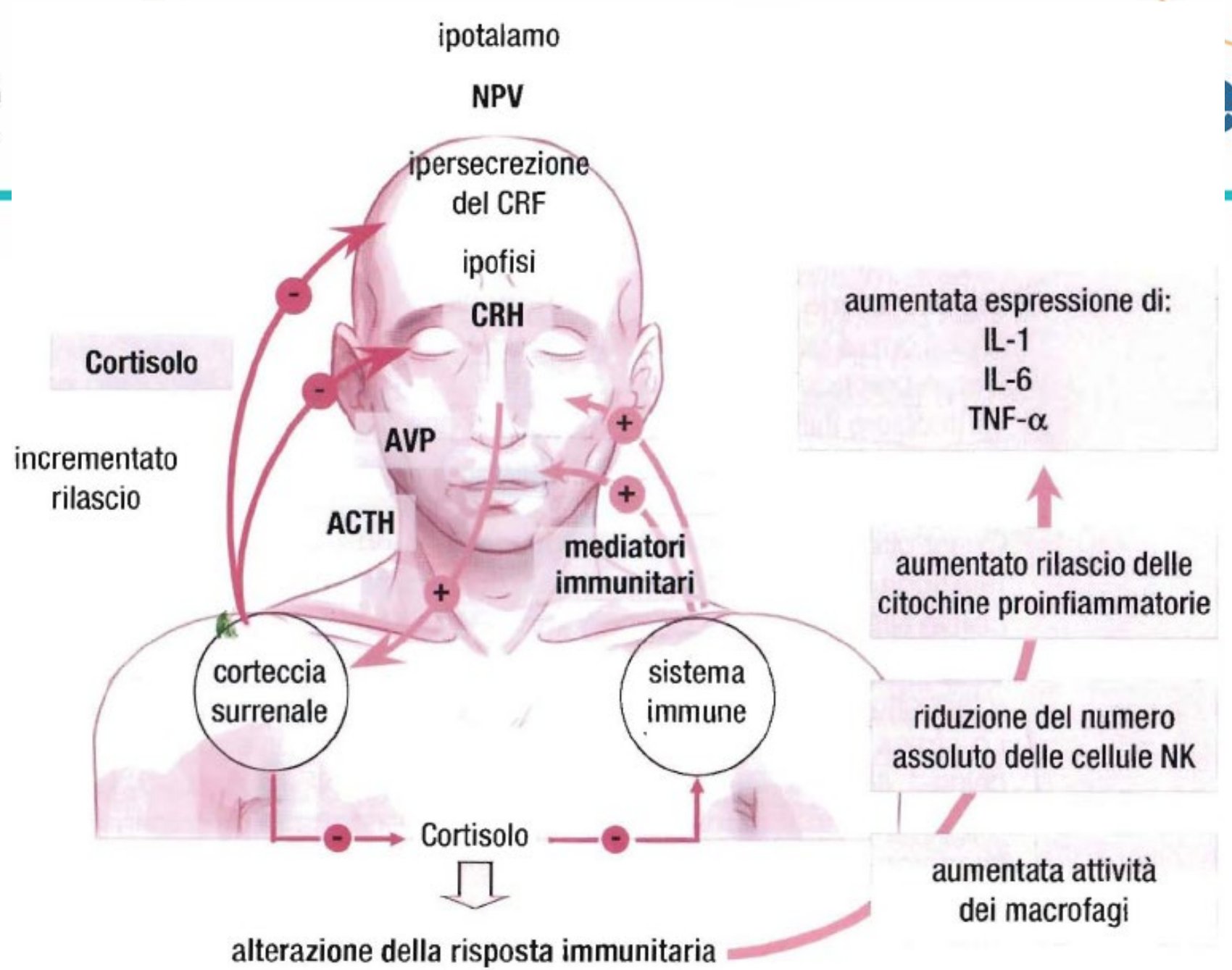
Valori elevati di queste sostanze nelle urine (misurati con il *disbiosi test*) indicano un'alterazione del microbiota che può avere un ruolo chiave nel favorire la neuroinfiammazione attraverso l'asse intestino-cervello.

I metaboliti della putrefazione favoriscono il rilascio di citochine pro-infiammatorie

Ruolo nell'ansia, nella paura
e nell'attivazione dell'asse HPA



Attività dell'asse HPA regolata da feed-back inibitorio e da aree del sistema limbico quali ippocampo, corteccia prefrontale ed amigdala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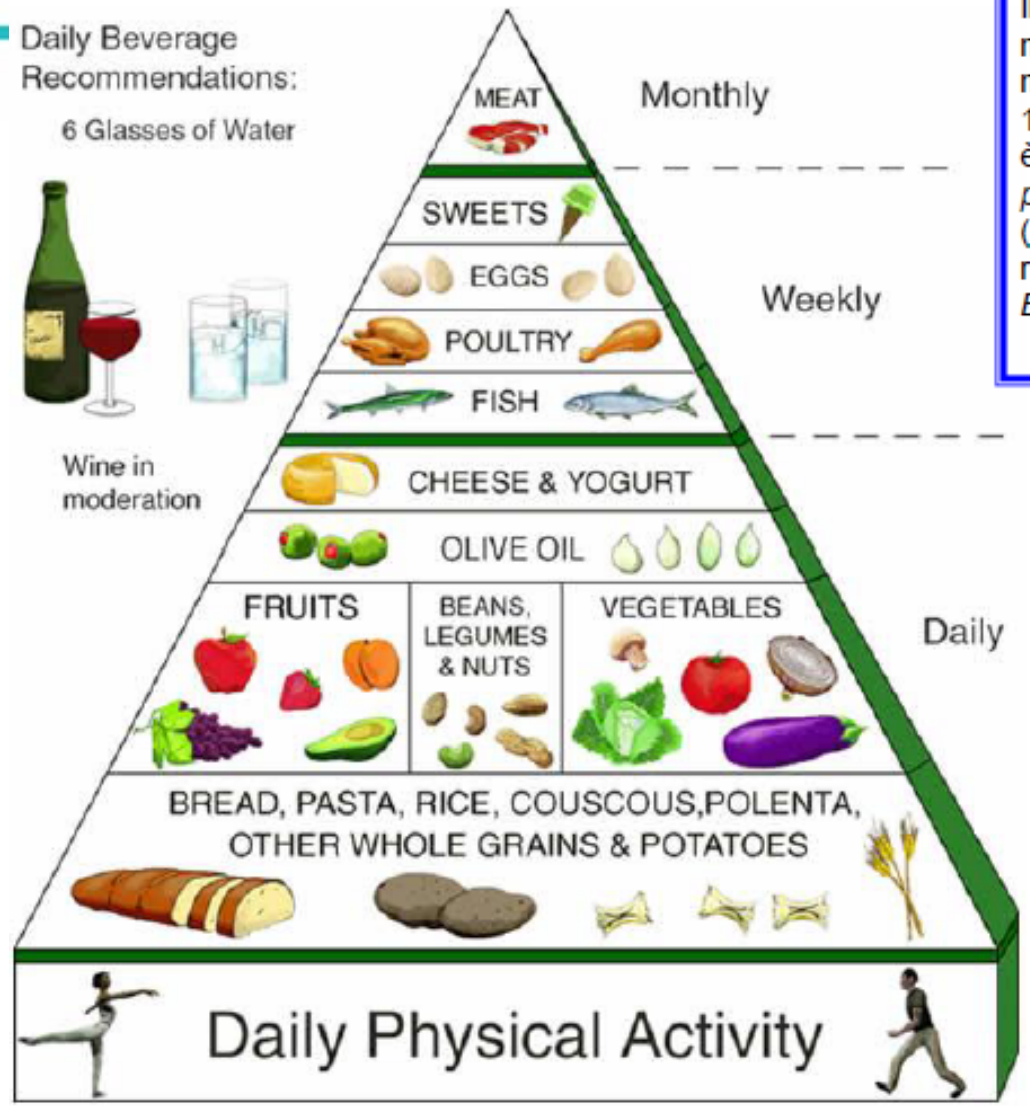
ipersecrezione del CRF
ipofisi
CRH
Cortisolo
incrementato rilascio
AVP
ACTH
mediatori immunitari
corteccia surrenale
sistema immune
Cortisolo
alterazione della risposta immunitaria
aumentata espressione di:
IL-1
IL-6
TNF-α
aumentato rilascio delle citochine proinfiammatorie
riduzione del numero assoluto delle cellule NK
aumentata attività dei macrofagi

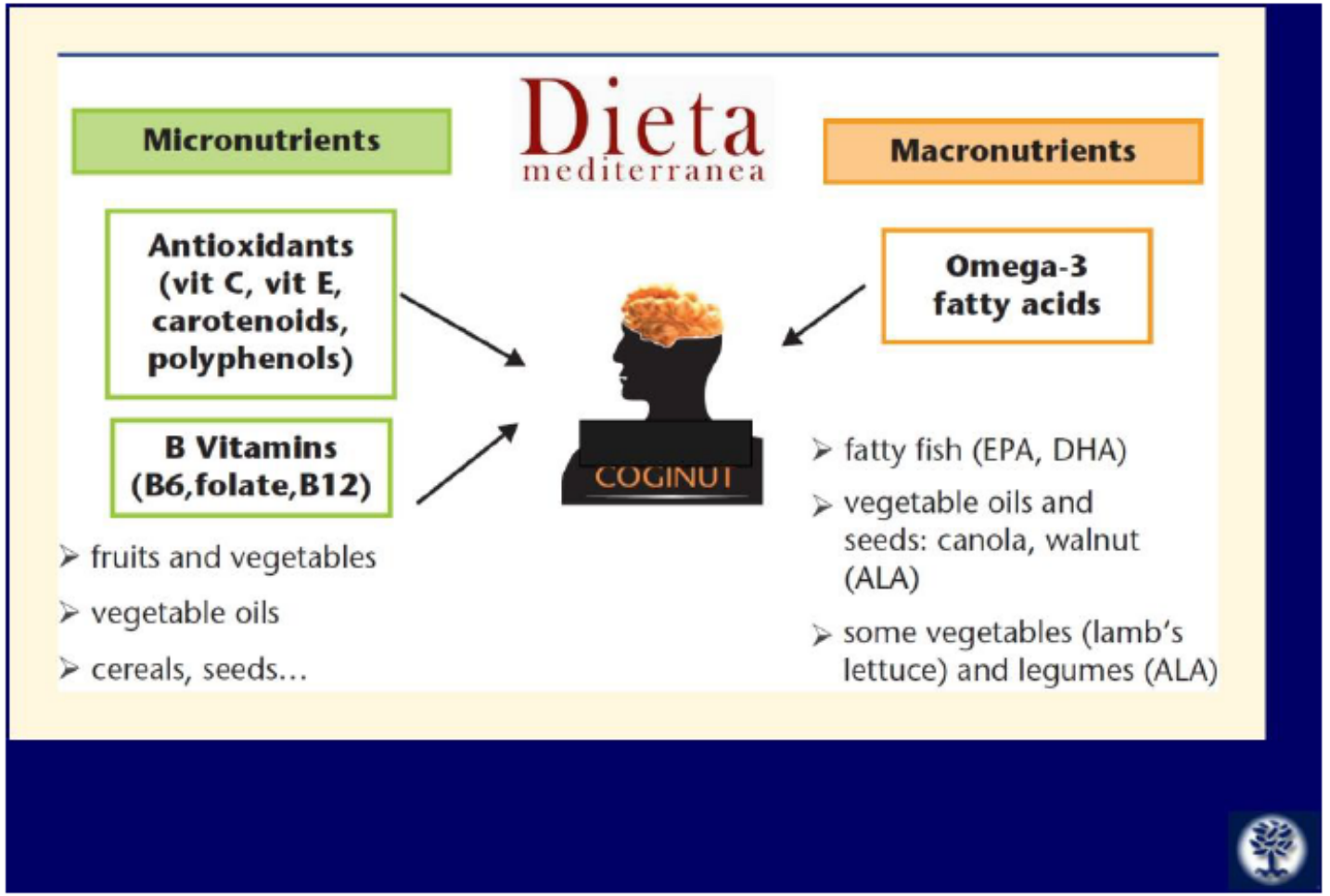
La dieta mediterranea: patrimonio culturale dell' umanità dal 2010

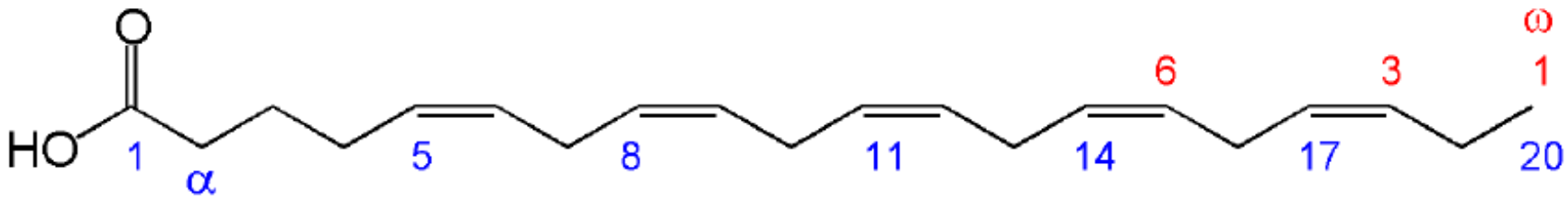


Il primo a intuire la connessione tra alimentazione e malattie del ricambio, quali diabete, bulimia, obesità, fu il medico nutrizionista italiano ***Lorenzo Piroddi*** (Genova 1911-1999). Considerato il "padre" della dieta mediterranea è anche autore del libro *Cucina Mediterranea. Ingredienti, principi dietetici e ricette al sapore di sole*. Ancel Keys (1904-2004) si fece promotore dell'ampio programma di ricerca noto come *Seven Countries Study* e autore del libro *Eat well and stay well, the Mediterranean way*.

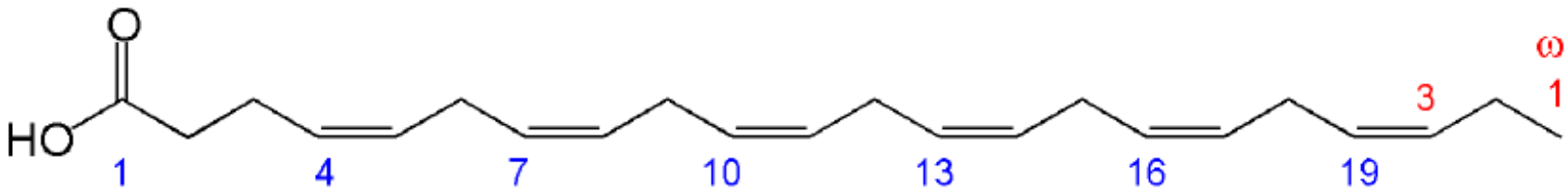
frutta, legumi, ortaggi, pesce e olio d'oliva

Dieta mediterranea e funzioni cognitive





EPA = eicosapentaenoic acid (20 carbons and 5 double bonds)

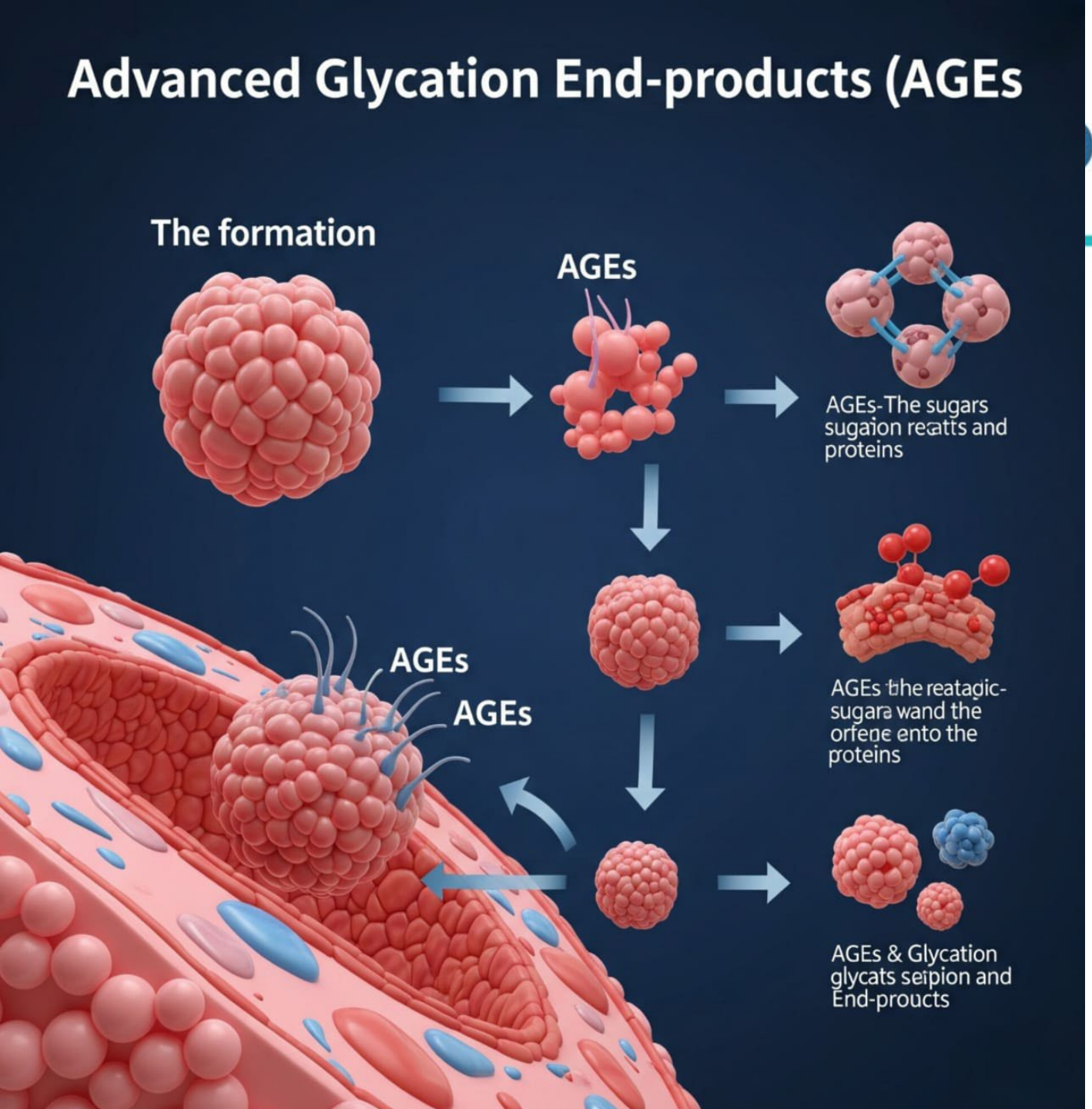


DHA = docosahexaenoic acid (22 carbons and 6 double bonds)

- Cognitive functions
- Mood
- Immune functions
- Antiarrhythmic effects
- Cardiovascular risk reduction
- Lipid Metabolism improvement
- Modulation of platelet aggregation
- Muscle and Bone Health
- Antioxidant activity

Gareri P. Omega-3 Long-Chain Polyunsaturated Fatty Acids in the Elderly: A Review2022; OBM Geriatrics, Vol. 6, Issue 2, pp 1-18

- **MGO (Metilgliossale)**, **Albumina Glicata**, **BAFF** e **PAF** sono marcatori molecolari utilizzati per valutare l'infiammazione cronica, la glicazione (danni da zuccheri) e l'infiammazione legata all'alimentazione.
- Vengono comunemente misurati attraverso test innovativi, come il *Glyco Test* o il *Recaller Test* (Food Inflammation Test), per prevenire malattie metaboliche, cardiovascolari e infiammatorie.



Nazionale

Advanced Glycation End Products (AGEs) are a group of compounds that form through non-enzymatic reactions between reducing sugars and amino acids, proteins, or lipids. This process is known as glycation and is primarily driven by the Maillard reaction, which occurs during cooking and food processing, especially at high temperatures.

The accumulation of AGEs is associated with several health issues, including:

Diabetes and its complications: AGEs contribute to insulin resistance and vascular complications in diabetic patients.

Cardiovascular diseases: AGEs can promote inflammation and oxidative stress, leading to vascular damage and atherosclerosis.

Neurodegenerative disorders: There is evidence linking AGEs to conditions like Alzheimer's disease due to their role in inflammation and oxidative damage.

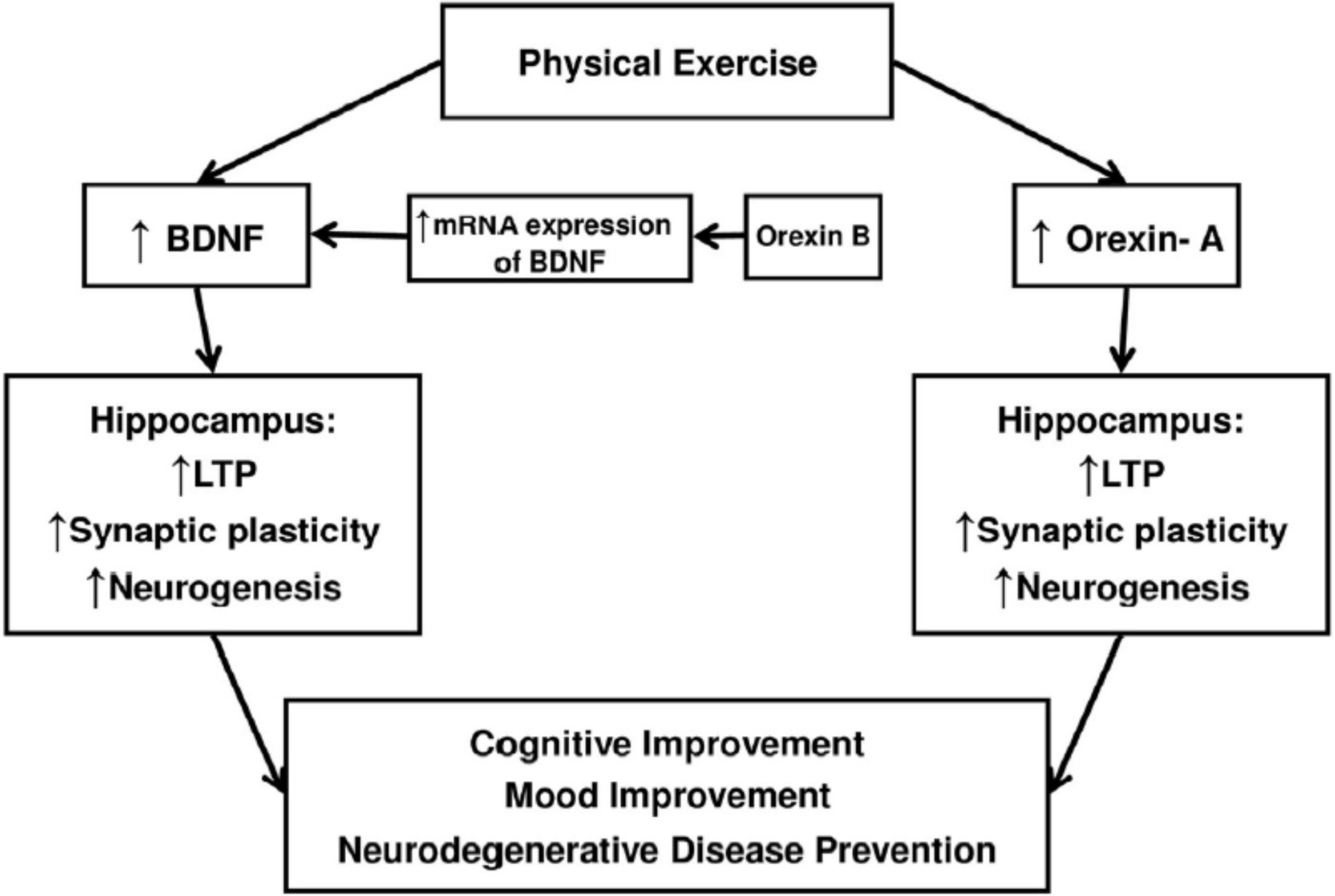
Attività fisica

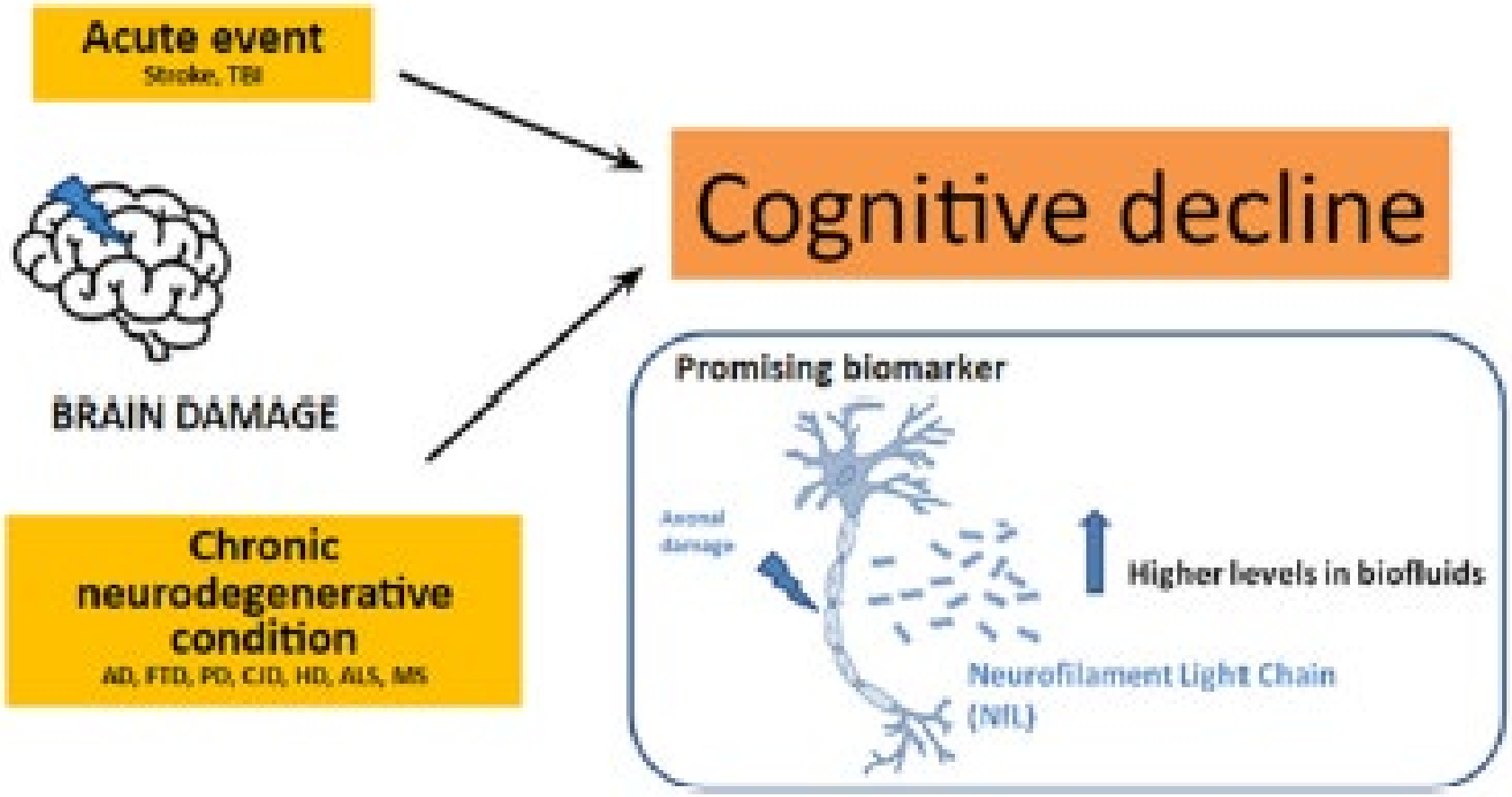
L'attività fisica promuove l'attivazione del fattore di **trascrizione PGC-1** alfa citoplasmatico, che a livello nucleare promuove la trascrizione di alcune miochine muscolari, **come l'erisina**, la quale agisce a vari livelli:

- a livello del SNC promuove la sintesi del fattore neurotrofico cerebrale BDNF;

- A livello delle cellule immunitarie promuove la sintesi di citochine anti-infiammatorie come la IL-10;

- aumenta la sensibilità periferica all'insulina e quindi riduce la insulino-resistenza


Physical Exercise
↑ BDNF
↑mRNA expression of BDNF
Orexin B
↑ Orexin- A
Hippocampus:
↑LTP
↑Synaptic plasticity
↑Neurogenesis
Hippocampus:
↑LTP
↑Synaptic plasticity
↑Neurogenesis
Cognitive Improvement
Mood Improvement
Neurodegenerative Disease Prevention


Acute event
Stroke, TBI
BRAIN DAMAGE
Chronic neurodegenerative condition
AD, FTD, PD, CJD, HD, ALS, MS
Cognitive decline
Promising biomarker
Axonal damage
Higher levels in biofluids
Neurofilament Light Chain (NfL)

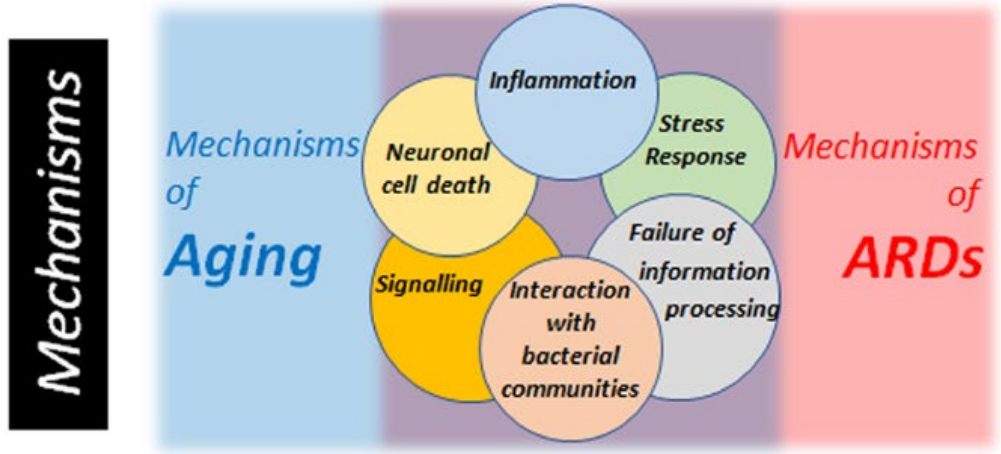
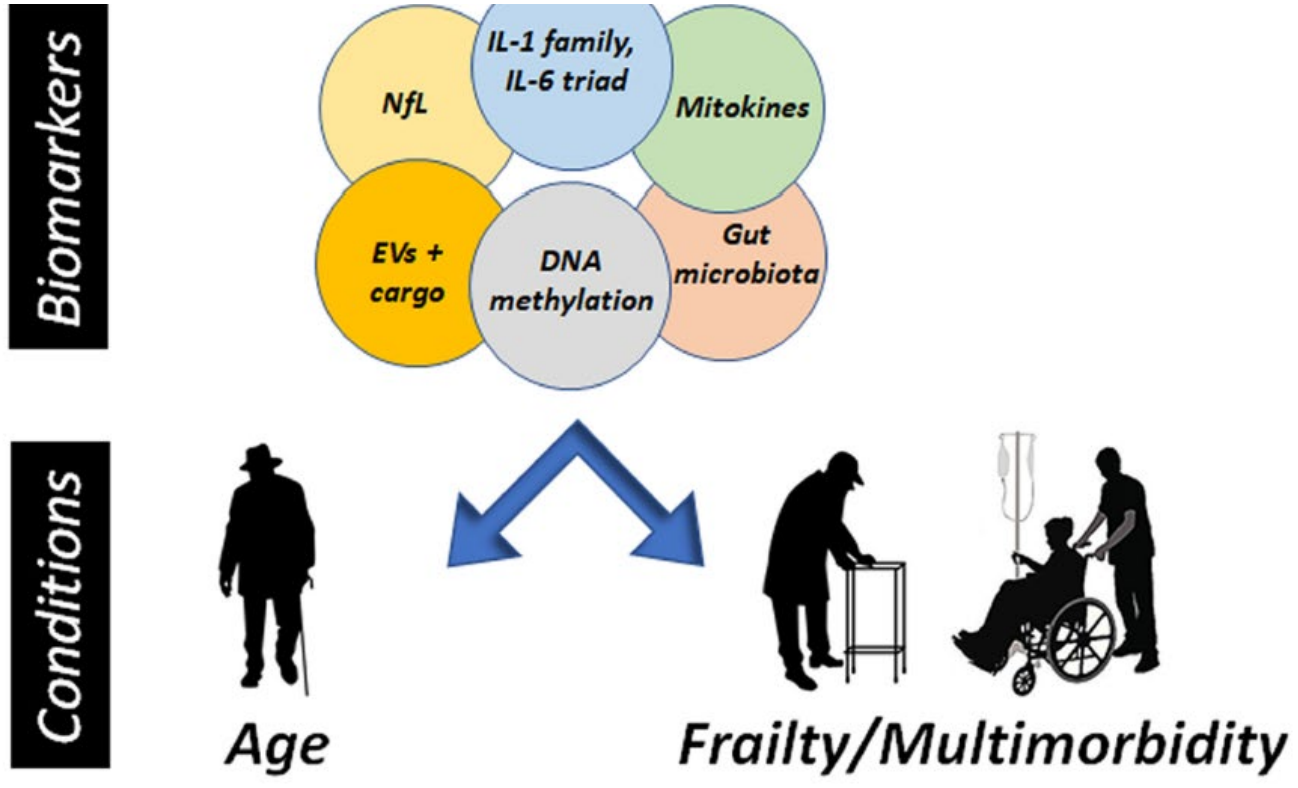


Fig. 2. Biomarkers of age can be also biomarkers for frailty and multimorbidity. According to Geroscience, basic molecular mechanisms are shared between aging and age-related diseases (ARD). We have considered in this review some selected biomarkers related to those mechanisms, and discussed available evidence that they can be useful also to identify frail or multimorbid patients.



Essere Medici:

Non solo scienza…

Non solo tecnica…

Ma anche..PRESENZA