CONGRESSO NAZIONALE

78

FIMMG-METIS 2021

MEDICINA GENERALE

CONVENZIONATA, DIRITTO DELL'INDIVIDUO.

RESIDENZIALE E VIDEOCONFERENZA
4 OTTOBRE 2021
9 OTTOBRE 2021

FAD ASINCRONE
12 OTTOBRE 2021
15 NOVEMBRE 2021

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FIMMG® Federazione Italiana Medici di Famiglia

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SOCIETA' SCIENTIFICA DEI MEDICI

CONGRESSO NAZIONALE
FIMMG-METIS 2021

Stress ossidativo, immunità e nutrizione

Lorenzo M Donini

FIMMG
Federazione Italiana Medici di Famiglia

Metis
DI MEDICINA GENERALE
SOCIETA' SCIENTIFICA DEI MEDICI

SIMPeSV
Società Italiana di Medicina di Prevenzione e degli Stili di Vita

SAPIENZA
UNIVERSITÀ DI ROMA

Life Sciences 256 (2020) 117900

Contents lists available at ScienceDirect

Life Sciences

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Review article

The immune system and COVID-19: Friend or foe?

Fereshteh Yazdanpanah[a,b], Michael R. Hamblin[c,d,e], Nima Rezaei[b,f,g,*]

1. Following **entry of SARS-CoV-2** into the cell, the viral RNA genome is transferred from the envelope into the cytoplasm and the translation process begins.

- After **replication** of the RNA new viral particles are formed, by incorporating part of the host cell membrane in the new viral envelope.

2. Infected lung epithelial cells produce interleukin IL-8 which acts as a chemoattractant for neutrophils and T lymphocytes (**innate immune response**):

- Virus particles containing single-stranded ssRNA, act as pathogen-associated molecular patterns (PAMPs), and provoke a strong innate immune response after recognition by Toll-like receptor 7 (TLR7), which is expressed on monocyte-macrophages and dendritic cells (DC).
- TLR7 can activate several signaling pathways and transcription factors, such as Janus kinase transducers (JAK/STAT), nuclear factor κB (NF-κB), activator protein 1 (AP-1), interferon response factor 3 (IRF3), and IRF7.
- This signaling cascade leads to increased secretion of pro-inflammatory cytokines, like IL-1, IL-6, monocyte chemo attractant protein-1 (MCP-1), MIP-1A, tumor necrosis factor α (TNF-α) and ultimately interferon 1 (IFN1).
- Furthermore, neutrophils are rapidly recruited to sites of infection, where they kill viruses by an oxidative burst, defensin secretion, and neutrophil extracellular traps (NETs).

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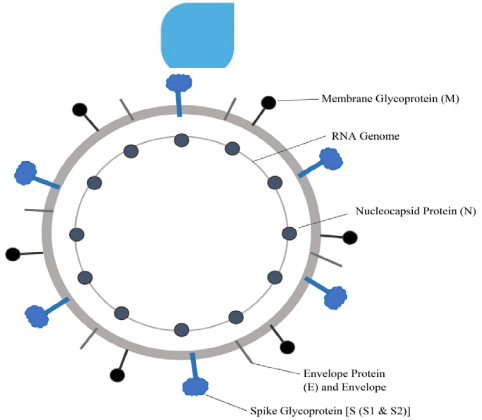
3. In the next stage, Ag presentation stimulates **adaptive immune responses** (both humoral and cellular immunity) that are triggered involving T and B lymphocytes and culminate in approximately 7–14 days after infection.

- Following the representation of antigens by APCs to the CD4+ and CD8+ T-cells, pro-inflammatory cytokines are produced via the NF-κB signaling pathway.
- Activated B cells secrete virus-specific antibodies, while Ag-specific T cytotoxic cells kill virus-infected cells.
- Additionally, Th17 cells, neutrophils, and granulocytes secrete IL-17, which in turn stimulates production of IL-1, IL-6, IL-8, MCP-1, Gro-a, GCSF, GM-CSF, TNF-α, and PGE2.
- All these mediators can increase the recruitment of neutrophils, monocytes, and other immune cells.



- Infected lung epithelial cells produce interleukin IL-8 which acts as a chemoattractant for neutrophils and T lymphocytes (**innate immune response**)
- In the next stage, Ag presentation stimulates **adaptive immune responses** (both humoral and cellular immunity) that are triggered involving T and B lymphocytes and culminate in approximately 7–14 days after infection.

- ROS are produced during viral infections and significantly affect both the **production of oxidizing agents and the synthesis of antioxidant enzymes.**
- Viral infections affect the production of mitochondrial ROS because viruses can induce or inhibit various mitochondrial processes in a highly specific way so that they can replicate and produce progeny

High number of critically ill patients and increased mortality in patients with **underlying diseases** (such as hypertension and diabetes) has been proven.

- T2DM can include a hyperinflammatory state with a low-grade inflammatory activity that causes long-term immune system stimulation, along with adipose tissue side effects on the immune system, which ultimately drives an immune imbalance.
- due to the overexpression of ACE2 in islet cells of the pancreas, SARS-CoV-2 may be a diabetogenic virus that causes severe instability in the blood glucose levels of diabetes patients, which worsens the inflammatory imbalance.

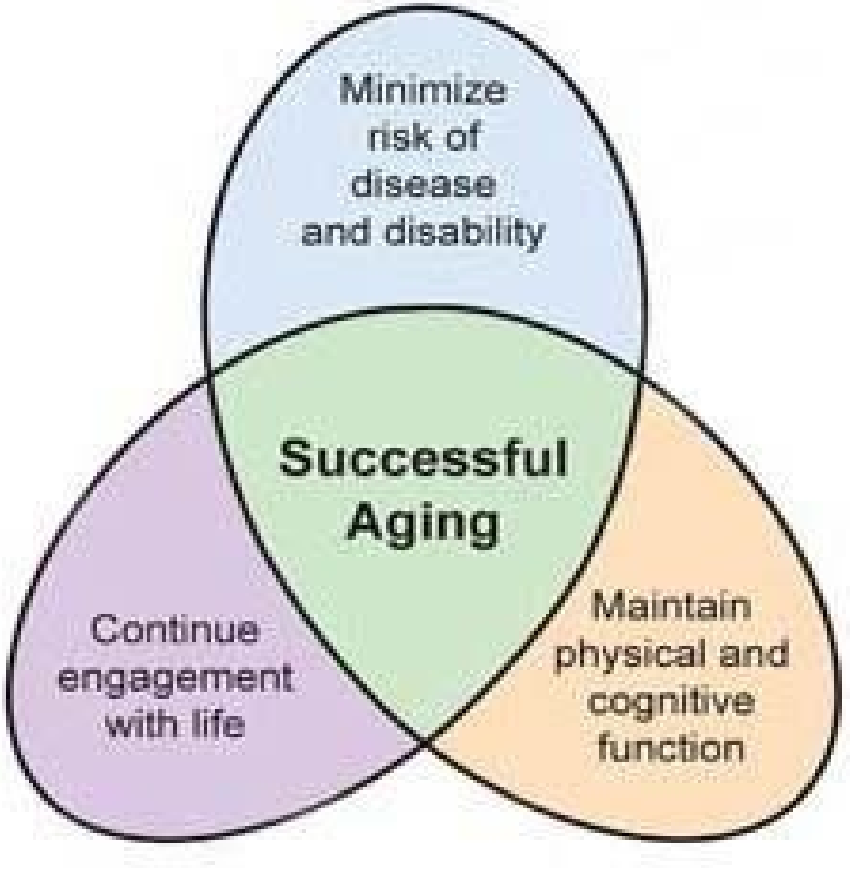
Ageing

Successful Aging[1]

The Gerontologist
Vol. 37, No. 4, 433–440

John W. Rowe, MD[2] and Robert L. Kahn, PhD[3]

Successful aging is **multidimensional**, encompassing the **avoidance of disease and disability**, the maintenance of **high physical and cognitive function**, and sustained **engagement in social and productive activities.**



nutrients

Nutrients 2016, 8, 338; doi:10.3390/nu8060338

MDPI

Review

Biomarkers of Aging: From Function to Molecular Biology

Karl-Heinz Wagner [1,2,*], David Cameron-Smith [3], Barbara Wessner [1,4] and Bernhard Franzke [1]

- **Aging** is the most profound risk factor for almost all **non-communicable diseases**, including cardiovascular diseases, cancer, diabetes and neurological diseases.

- The proposed mechanisms that contribute to the aging process and the development of these chronic, age-associated diseases include **DNA damage, alterations in gene and non-coding RNA expression, genotoxicity, oxidative stress**, and the incidence of **shorter telomeres.**

nutrients

Nutrients 2016, *8*, 338; doi:10.3390/nu8060338

MDPI

Review

Biomarkers of Aging: From Function to Molecular Biology

Karl-Heinz Wagner [1,2,*], David Cameron-Smith [3], Barbara Wessner [1,4] and Bernhard Franzke [1]

Table 1. Summary of putative biomarkers of aging.

Physical Function and Anthropometry		
	Practicability of Measurement	**Outcome Prediction**
Walking speed	High	Mortality
Chair stand	High	Mortality
Standing balance	High	Mortality
Grip strength	High	Mortality CVD Cognitive impairment
Body Mass Index	High	Mortality CVD Cognitive decline
Waist circumference	High	Mortality CVD
Muscle mass	High	Mortality
Blood-based candidate markers		
	Practicability of measurement	**Outcome prediction**
Inflammation IL-6, TNF-a, CRP	moderate to high	Mortality, grip strength
Network analysis of inflammatory markers	moderate	Mortality
Glucose metabolism: HbA1c, plasma glucose	moderate	Mortality, CVD
Adipokines	moderate	Mortality (moderate prediction) Aging/frailty
Thyroid hormones	moderate	Mortality/morbidity (moderate prediction)
Vitamin D	low	Mortality/multimorbidity Cognitive impairment
NT-proBNP Troponin	moderate	Mortality/multimorbidity Cognitive impairment

nutrients

Nutrients 2016, 8, 338; doi:10.3390/nu8060338

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Review

Biomarkers of Aging: From Function to Molecular Biology

Karl-Heinz Wagner [1,2,*], David Cameron-Smith [3], Barbara Wessner [1,4] and Bernhard Franzke [1]

Molecular/DNA based markers		
	Practicability of measurement	Outcome prediction
DNA/chromsomal damage	low	Aging (moderate prediction)
Telomere length	low	Mortality (moderate prediction)
DNA repair	low	-
Novel markers		
	Practicability of measurement	Outcome prediction
Bilirubin (mainly unconjugated bilirubin)	moderate to high	CVD, CVD-related mortality
Advanced glycation end products	low	CVD
Metallothioneins	low	Aging brain
DNA methylation	low	-
MicroRNAs	low	CVD aging (moderate prediction)

Ageing and immune system

Mechanisms of Ageing and Development xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Mechanisms of Ageing and Development

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

Review

Nutrition, diet and immunosenescence

Mònica Maijó [a,1], Sarah J. Clements [a,1], Kamal Ivory [a], Claudio Nicoletti [a], Simon R. Carding [a,b,*]

- **Immunosenescence**: ageing is associated with the **functional decline** of the immune system and **ability to defend** against infection by environmental pathogens, **vaccine failure**, and an increased incidence of **autoimmunity and cancer.**

Mechanisms of Ageing and Development xxx (2014) xxx–xxx

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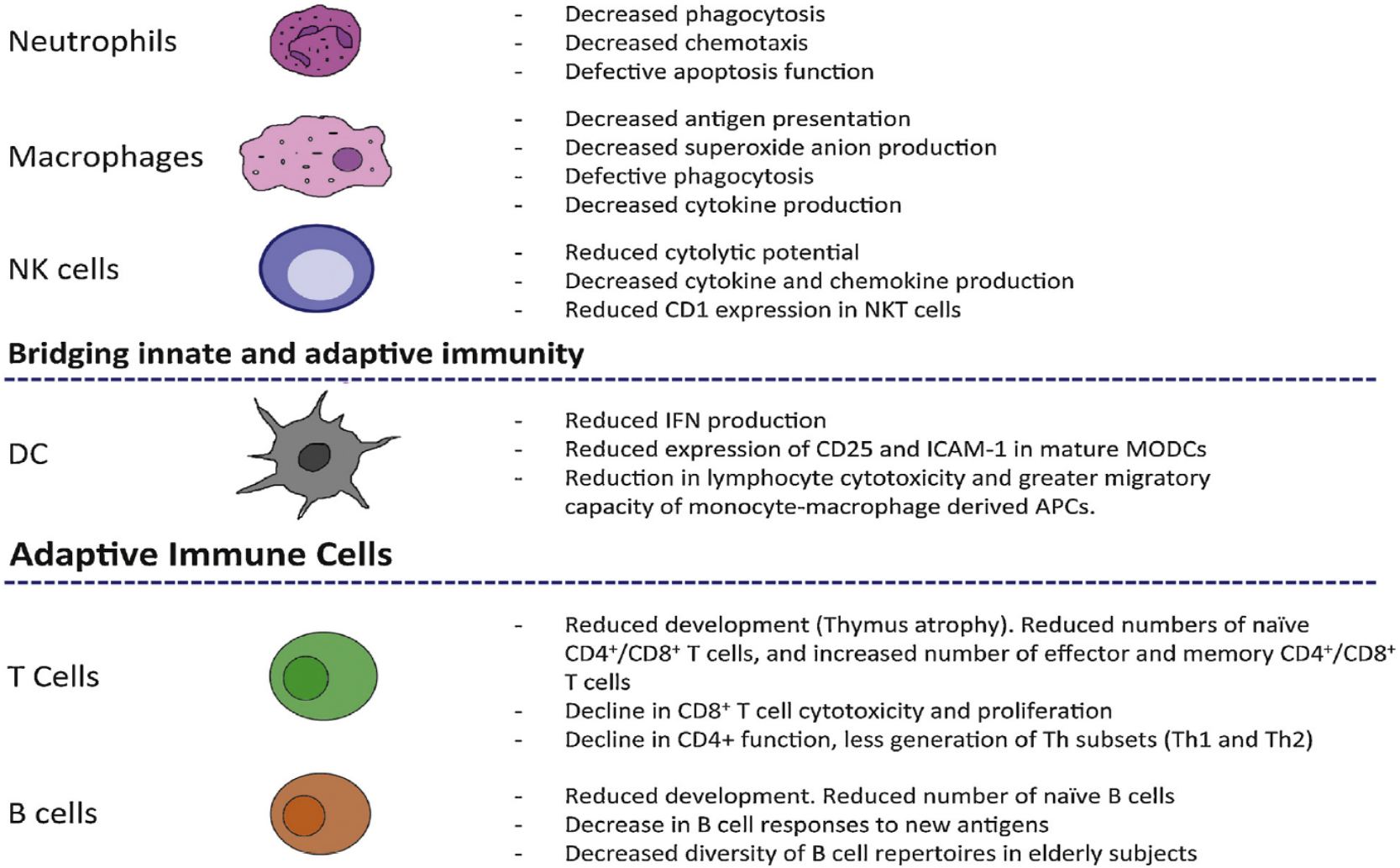

Fig. 1. Age-associated changes observed in innate and adaptive immune cell populations. Decreased cellular function in old age has been documented in neutrophils, macrophages, NK cells, monocyte-derived (MO) and dendritic cells (DCs). And a reduced development of T and B cells as well an impaired functionality of theses populations in elderly people.

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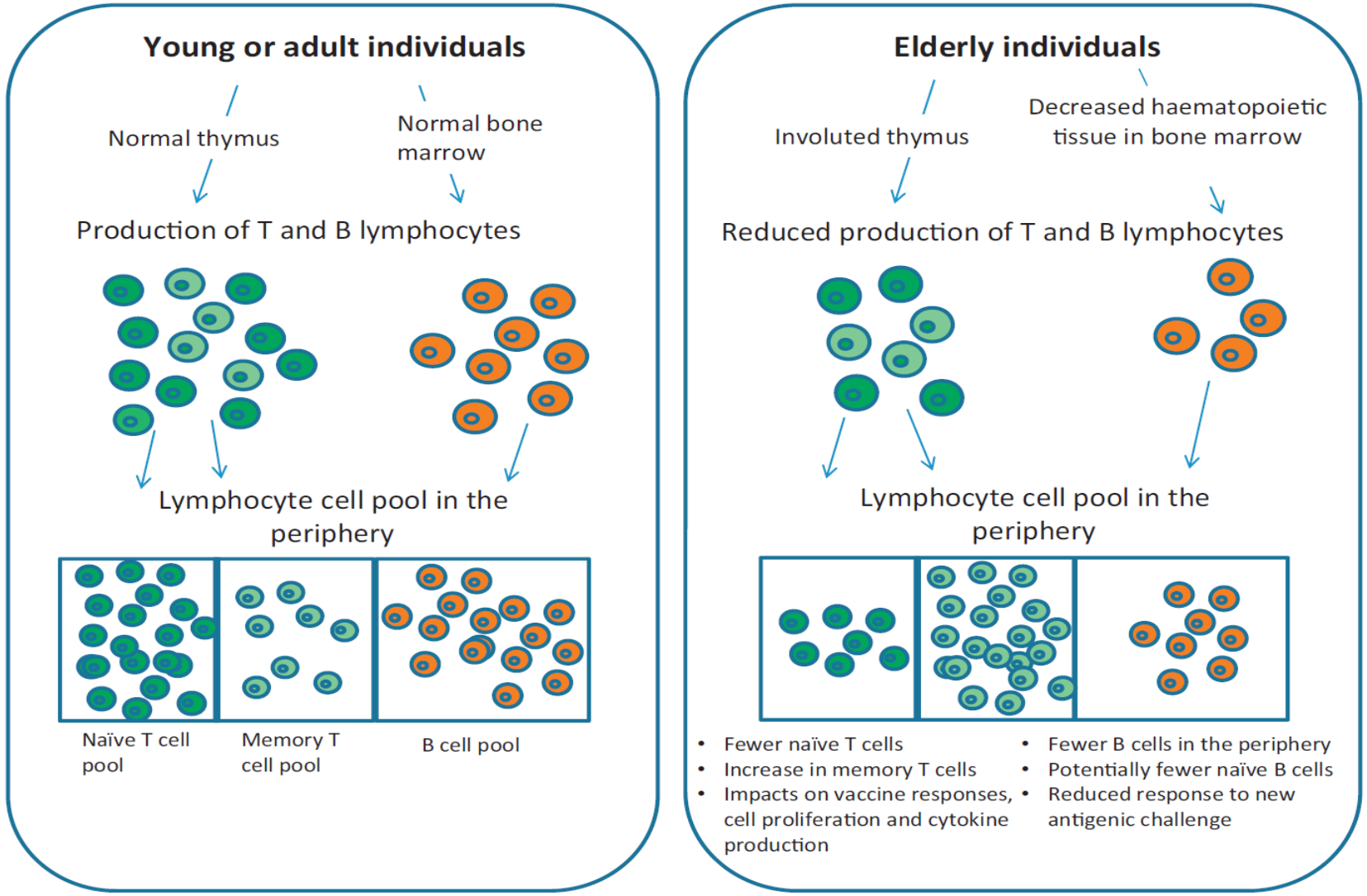

Fig. 2. Effects of age on the production and distribution of lymphocytes. Modified from Dorshkind et al. (2009) and Nikolich-Zugich (2008). Young and adult individuals present a normal T and B cell production. In contrast, elderly people have a decreased production of naïve T and B cells and an increase in the memory T cell poll. These changes result from decreased T-cell production from involuted thymus and an increase in the homeostatic cycling that drives proliferating naïve T cells into memory cells, and from a decline in the bone marrow function producing fewer B cell precursors (Dunn-Walters and Ademokun, 2010).

Mechanisms of Ageing and Development xxx (2014) xxx–xxx

JOURNAL OF PROTEOMICS 74 (2011) 2313–2323

available at www.sciencedirect.com

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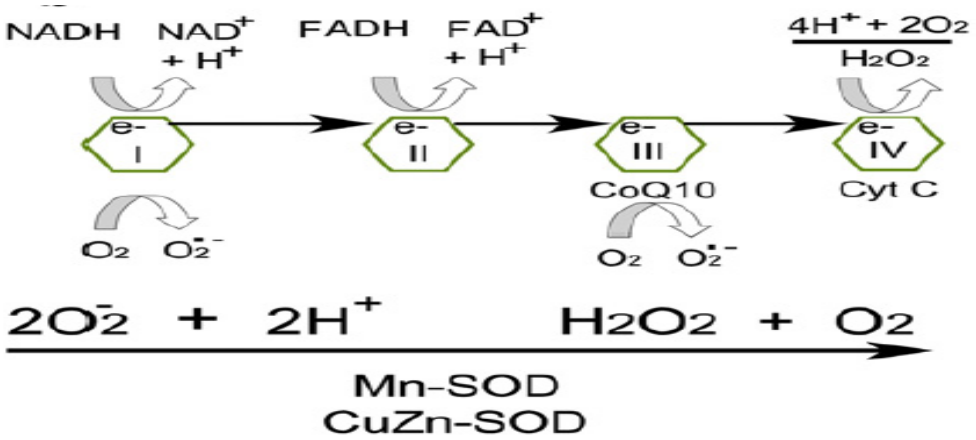
www.elsevier.com/locate/jprot

Review

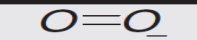
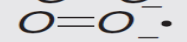
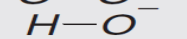
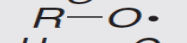
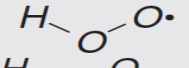
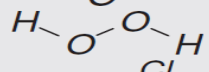
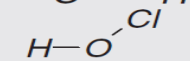
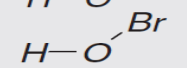
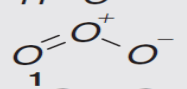
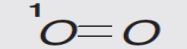
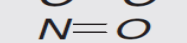
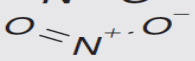
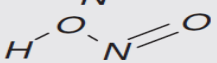
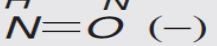
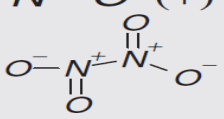
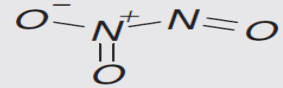
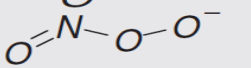
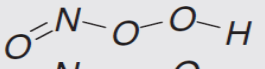
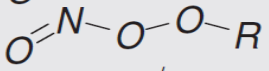
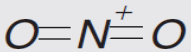
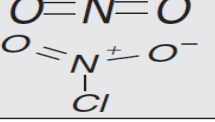
Oxidative stress, inflamm-aging and immunosenescence

Elvira S. Cannizzo[a], Cristina C. Clement[a], Ranjit Sahu[a], Carlo Follo[a], Laura Santambrogio[a,b,]*



- Free radicals are molecules in which the outer electron orbital contains a solitary unpaired electron (hydrogen (H•), nitric oxide (NO•), hydroxyl radical (•OH), peroxyl radicals (RO2), alkoxyl radicals (RO•), transition metals (copper and iron) or two unpaired electrons (the diatomic oxygen molecule O2, and its superoxide (O•−2).
- Most are generally quite unstable and readily induce the non-enzymatic oxidation of biomolecules (proteins, carbohydrates, lipids and nucleic acids).

Table 1 – Reactive oxygen species (ROS) and reactive nitrogen species (RNS) generated in cells and tissues.

Oxygen (O_2)	
Superoxide anion (O_2^-)	
Hydroxyl radical (HO^-)	
Peroxyl radical (ROO^-)	
Alkoxyl radical (RO^-)	
Hydroperoxyl radical (HOO^-)	
Hydrogen peroxide (H_2O_2)	
Hypochlorous acid (HOCl)	
Hypobromous acid (HOBr)	
Ozone (O_3)	
Singlet ($^1O_2$)	
Nitric oxide (NO)	
Nitrogen dioxide (NO_2)	
Nitrous acid (HNO)	
Nitrosyl anion (NO-)	
Nitrosyl cation (NO+)	
Dinitrogen tetraoxide (N_2O4)	
Dinitrogen trioxide (N_2O_3)	
Peroxynitrite (ONOO)	
Peroxynitrous acid (ONOOH)	
Alkyl peroxynitrites (ROONO)	
Nitronium cation (NO_2^+)	
Nitryl chloride (NO_2Cl)	

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PROTEOMICS

Review

Oxidative stress, inflamm-aging and immunosenescence

Elvira S. Cannizzo[a], Cristina C. Clement[a], Ranjit Sahu[a], Carlo Follo[a], Laura Santambrogio[a,b,]*

Within the cells there are three major sources of free radical formation:

1. **Oxidative metabolism:** In the mitochondrial respiratory chain (series of protein complexes that transfer electrons via redox reactions coupled with the transfer of protons creating an electrochemical proton gradient that drives the synthesis of ATP), the forward and reverse transport of electrons is coupled with the formation of reactive oxygen species (ROS).
2. **Oxidative burst:** neutrophils, macrophages, dendritic cells and monocytes release ROS, as part of their innate immune function towards different pathogens. The “oxidative burst” is a metabolic pathway, quiescent in resting cells, which is set in motion upon microbe invasion. Its role is to produce strong oxidizing agents that function as highly reactive microbicidal components.
3. **Environment:** Free radicals are commonly produced by a series of environmental factors including alcohol, cigarette smoke, dietary factors, some medications, UV light and ionizing radiations.

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- As aging progresses the **biochemical imbalance** between the formation and clearance of free radicals, generates a state often referred to as “oxidative stress”.
- The resulting increased amount of unstable and highly reactive free radicals will lead to
  - **oxidative protein** modifications, including direct AA modifications by hydroxylation and formation of carbonyl derivatives (aldehyde and ketonic groups on AA side chains), protein nitrosylation, or indirect AA modifications;

  ⇒ protein fragmentation, sub-unit dissociation, unfolding, and exposure of hydrophobic residues and aggregation ⇒ overall loss of function
  - **peroxidated lipids**
  - products from **glycation and glycoxidation**

Mechanisms of Ageing and Development xxx (2014) xxx–xxx

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Mechanisms of Ageing and Development

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

Review

Nutrition, diet and immunosenescence

Mònica Maijó [a,1], Sarah J. Clements [a,1], Kamal Ivory [a], Claudio Nicoletti [a], Simon R. Carding [a,b,*]

- The ageing organism is characterized by a low grade chronic inflammation that results from alterations in the balance of production of pro-inflammatory versus anti-inflammatory mediators and cytokines and is termed '**inflammaging**'.

- Inflammaging is under **genetic control** and is detrimental for **longevity** due to long term tissue damage.

- Inflammaging is believed to be a consequence of a **cumulative lifetime exposure to antigenic load** caused by both clinical and subclinical infections as well as exposure to non-infective antigens

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PROTEOMICS

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Oxidative stress, inflamm-aging and immunosenescence

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Two major pathways promotes inflammaging secondary to oxidative damage produced by free radicals:

- **Toll-like-receptors (TLRs)** binding to pathogen-associated molecular pattern molecules (PAMPs) activates an orchestrated innate immune response aimed at eradicating the invading pathogen
  - increased ROS production and post-translationally modified molecules activate the TLR8 and TLR2 pathway initiating an inflammatory response whose key mediators are IL-1, IL6 and TNFα
- **NLRP-3 inflammosome** is a cytosolic multiprotein complex that, upon assembly with caspase 1, has the enzymatic ability to cleave pro-IL-1 and pro-IL-18 into active cytokines activation
  - Nalp3 inflammasome has been shown to be directly activated by the presence of sustained amounts of ROS

Nutritional status and the immune system

frontiers in Immunology
REVIEW
published: 16 May 2018
doi: 10.3389/fimmu.2018.01055

Changes in Nutritional Status Impact Immune Cell Metabolism and Function

*Yazan Alwarawrah[1], Kaitlin Kiernan[2] and Nancie J. MacIver[1,2,3]**

Immune Cells affected by changes in Nutritional Status

- **The hormone and cytokine changes seen in response to obesity and malnutrition are closely linked to changes in immune cell populations.**

- Several types of immune cells residing in the **adipose tissue** (macrophages, neutrophils, mast cells, B and T lymphocytes, T-reg cells) are affected by changes in the cytokine and hormone levels and in turn contribute to altered cytokine production in states of under- or overnutrition.
- These adipose tissue- localized immune cells can be affected by changes in nutritional status through both paracrine effects (due to their proximity to adipocytes) and systemic/endocrine effects of secreted adipose factors.

- In contrast to the effects of obesity on immune cells, **malnutrition** leads to a *decrease* in immune cell number (total, CD4+ and CD8+ T cells).

REVIEW
published: 16 May 2018
doi: 10.3389/fimmu.2018.01065

Changes in Nutritional Status Impact Immune Cell Metabolism and Function

*Yazan Alwarawrah[1], Kaitlin Kiernan[2] and Nancie J. MacIver[1,2,3]**

Molecule	Class	Obesity	Malnutrition	Secreted by	Immune function
Leptin	Adipocytokine	Increased	Decreased	Adipocytes	Pleiotropic hormone with many targets and many functions in immune cells Induces Th1 and Th17 polarization
Adiponectin	Adipocytokine	Decreased	Conflicting reports—may be context-dependent	Adipocytes	Polarization of monocytes and macrophages toward M2 phenotype Suppresses NK cell, eosinophil, neutrophil, γδ T cell, and dendritic cell activation and inflammatory cytokine production
Resistin	Adipocytokine	Increased	No clear correlation; more investigation needed	Adipocytes, macrophages	Stimulates the production of TNF-α and IL-12 in macrophages
Visfatin	Adipocytokine	Increased	No clear correlation; more investigation needed	Adipocytes	Stimulates the production of TNF-α, IL-1β, and IL-6
TNF-α	Cytokine	Increased	Mixed results, may depend on context	Adipocytes	Neutrophil chemotaxis
IL-1β	Cytokine	Increased	Mixed results, may depend on context	Non-adipocyte cells in adipose tissue	Stimulates macrophage activity
IL-6	Cytokine	Increased	Decreased	Adipocytes, macrophages	Recruitment of macrophages; polarization toward pro-inflammatory classically activated macrophages
IL-8	Cytokine	Increased	Decreased	Adipocytes, macrophages	Induces neutrophil chemotaxis
IL-10	Cytokine	Mixed—may be context-dependent	Increased	Treg cells, iNKT cells, DCs, adipocytes, macrophages	Broad anti-inflammatory function
IL-33	Cytokine	Decreased	Increased	DCs, macrophages, epithelial cells	Maintains adipose tissue-resident Treg cell function, promotes Th2 response, promotes alternatively activated macrophage polarization
IL-1RA	Cytokine	Increased	Unknown	Macrophages, epithelial cells	Inhibits IL-1α and IL-1β activity
MCP-1	Chemokine	Increased	Increased	Macrophages, adipocytes	Macrophage recruitment
MIF	Chemokine	Increased	Decreased	Adipocytes, lymphocytes	Inhibits macrophage migration
MIP-1α	Chemokine	Increased	Unknown	Adipocytes	Enhances macrophage migration
MIP-1β	Chemokine	Increased	Unknown	Adipocytes	Enhances macrophage migration

frontiers in Immunology

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REVIEW
published: 16 May 2018
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Changes in Nutritional Status Impact Immune Cell Metabolism and Function

*Yazan Alwarawrah[1], Kaitlin Kiernan[2] and Nancie J. MacIver[1,2,3]**

Effect of Nutritional Status on Immune Cell Metabolism

- Although it is clear that systemic metabolism influences immune cell function, we are only just starting to understand how changes in nutrition can influence metabolism at the cellular level.
- There is a **link between cellular metabolism and function** for several types of immune cells. In particular T cell metabolism can influence T cell differentiation and function, whereas changes in T cell function can likewise influence T cell metabolism.
- **Energy requirements and aerobic glycolysis** (glucose uptake, glycolysis, and reduction of pyruvate to lactate) regulation is controlled by several key signaling pathways and transcription factors and essential for optimal immune function.

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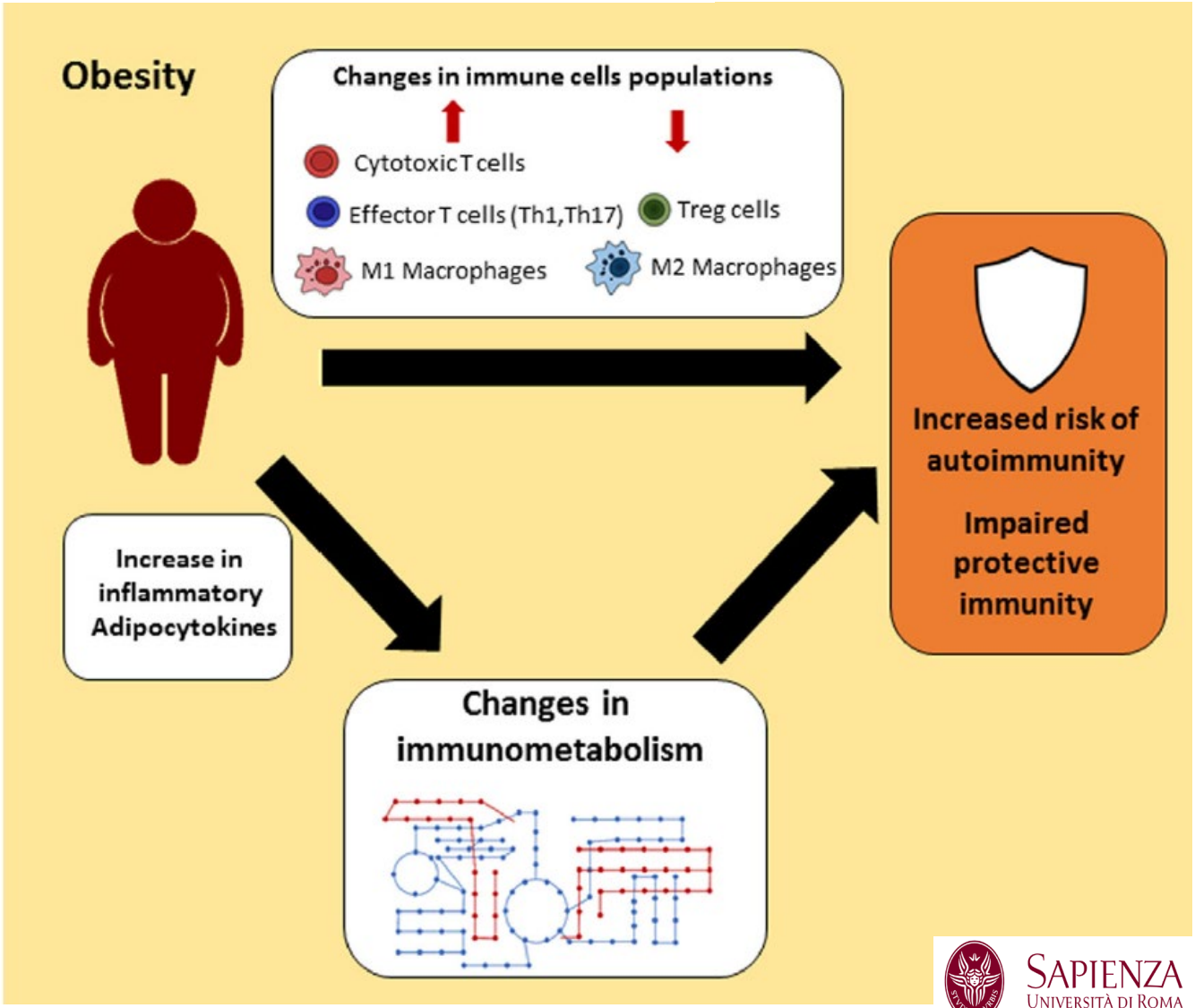
*Yazan Alwarawrah[1], Kaitlin Kiernan[2] and Nancie J. MacIver[1,2,3]**

Links between nutritional status, immune metabolism, and immune function.
In settings of extreme nutritional status (obesity or malnutrition), changes in immune cell populations, hormones, and cytokine levels lead to alternations in immune cell metabolism, which thereby influence immune function



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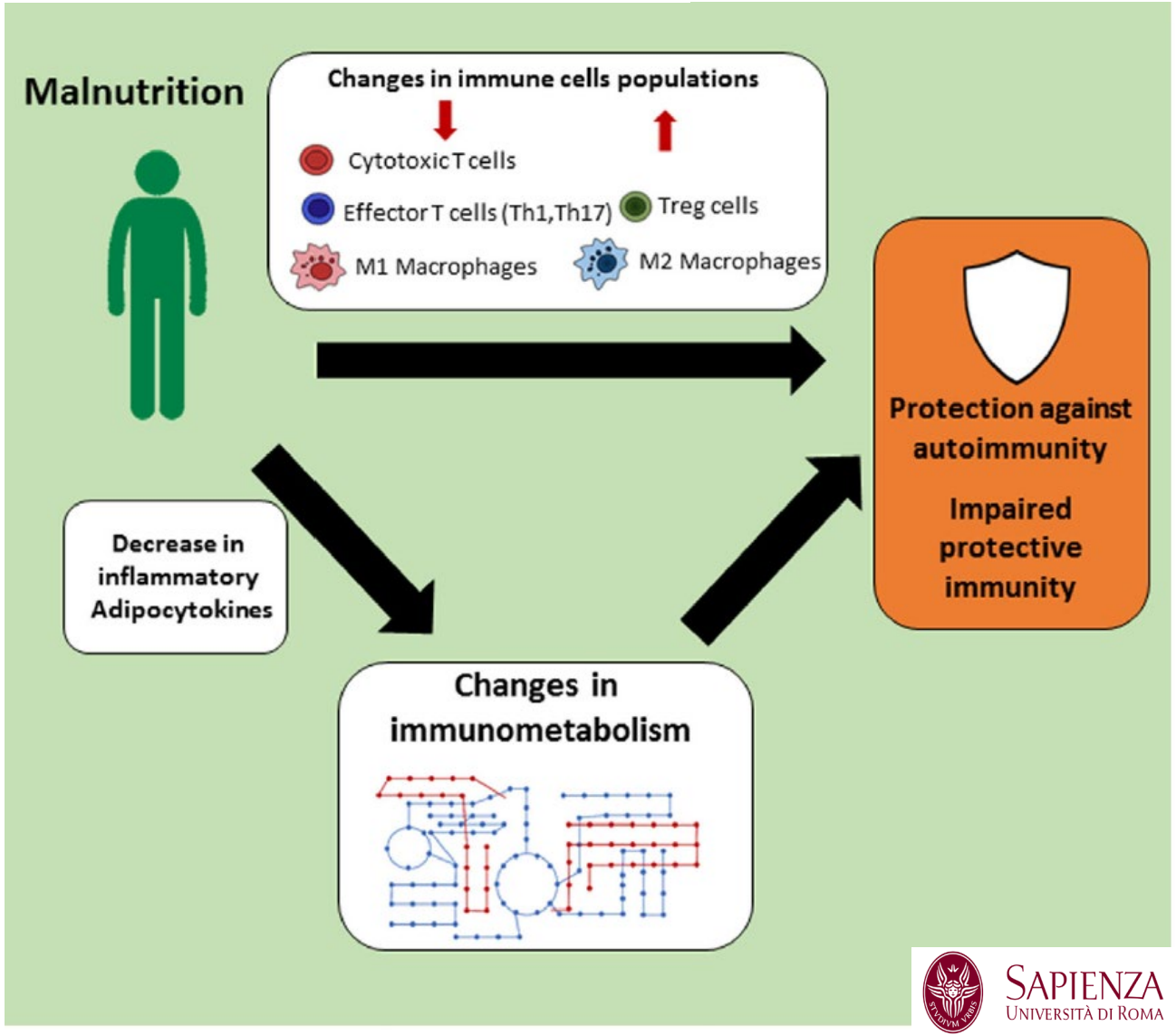

Modulation of immune system through nutritional intervention

Mechanisms of Ageing and Development xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Mechanisms of Ageing and Development

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Review

Nutrition, diet and immunosenescence

Mònica Maijó [a,1], Sarah J. Clements [a,1], Kamal Ivory [a], Claudio Nicoletti [a], Simon R. Carding [a,b,*]

- **Vit E.** In animal models it can enhance T cell functions by directly influencing membrane integrity and signal transduction and indirectly by reducing production of suppressive factors such as PGE2 by macrophages.
  - Different studies have reported beneficial effects of vitamin E supplementation in healthy elderly people. However, responses to vitamin E supplementation are influenced by individual factors such as genetic background and previous immune (high basal levels of cytokine production).

- **Carotenoids** (β-carotene, lycopene and lutein) are linked to enhanced immune function and bactericidal activity.

- **Zinc.** Several studies have shown beneficial effects of supplementation on cell-mediated immunity (delayed type hypersensitivity, lymphocyte populaytions production) and humoral responses in elderly people.

antioxidants

MDPI

Antioxidants **2020**, *9*, 897; doi:10.3390/antiox9090897

Review

Implications of Oxidative Stress and Potential Role of Mitochondrial Dysfunction in COVID-19: Therapeutic Effects of Vitamin D

Natalia de las Heras [1,*], Virna Margarita Martín Giménez [2], León Ferder [3], Walter Manucha [4,5] and Vicente Lahera [1]

Vitamin D may act as an antioxidant by mitochondrial function stabilization

- reduction in H_2O_2 levels accumulated in cardiac tissue and the increase in **superoxide dismutase and catalase** activities as antioxidant mechanisms
- decrease in **cellular apoptosis and autophagy-mediated** by the adequate maintenance of mitochondrial function and the reduction in $O_2^{\bullet}$ production
- upregulation of the AKT/UCP2 signaling pathway (reduction of oxidative stress induced by high glucose levels in human renal tubular cell line) ⇐ increasing the activity of **superoxide dismutase and MMP and decreasing malondialdehyde levels**

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- **N-3 PUFA** have anti-inflammatory properties inhibiting formation of eicosanoids (thromboxane A2) required for platelet aggregation and clot formation, proinflammatory cytokines (IL-1b, TNF-a, IL-6), chemokines (IL-8, MCP-1), adhesion molecules (ICAM-1, VCAM-1, selectins), and reactive oxygen and nitrogen species.
- They also suppress both innate (mainly inflammation) and adaptive (T cell mediated) immune responses, which can impair immunity to infectious and neoplastic diseases.

- In the elderly it is important to consider the possible drawbacks of n-3 PUFA supplementation in individuals that have impaired immune responses, and that high doses of n-3 PUFAs can increase lipid peroxidation and suppress IL-2 production and lymphocyte proliferation in older women.

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- **Polyphenols** may influence the production of key cytokines (IL-12, IL-10 and IL-1b), B cell function, increase production of protective IgA and IgG, and partially restore the function of aged macrophages.

- **Probiotics.** Certain strains improve innate immune responses such as phagocytosis and cytotoxicity in ageing people thus reducing the incidence and severity of infectious diseases in the elderly.

- **Prebiotics** (FOS, galactooligosaccharides) have been shown to enhance immune function in the frail elderly with reductions in IL-6 and TNF-a mRNA.

nutrients Nutrients 2020, 12, 1562; doi:10.3390/nu12061562 MDPI

Review

Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis

Mohammed Iddir [1,†], Alex Brito [1,2,†], Giulia Dingeo [3], Sofia Sosa Fernandez Del Campo [1], Hanen Samouda [1], Michael R. La Frano [4,5] and Torsten Bohn [1,*]

diet that positively impacts immune function must contain

- adequate amounts of protein, particularly including glutamine, arginine and BCAA;
- high omega-3 versus lower saturated, trans fat, and omega-6 fatty acids,
- low refined sugars,
- high fiber content such as whole grains, and
- micronutrients including vitamins A, D, C, E, B, Zn, Se and Fe, as well as phytochemicals.

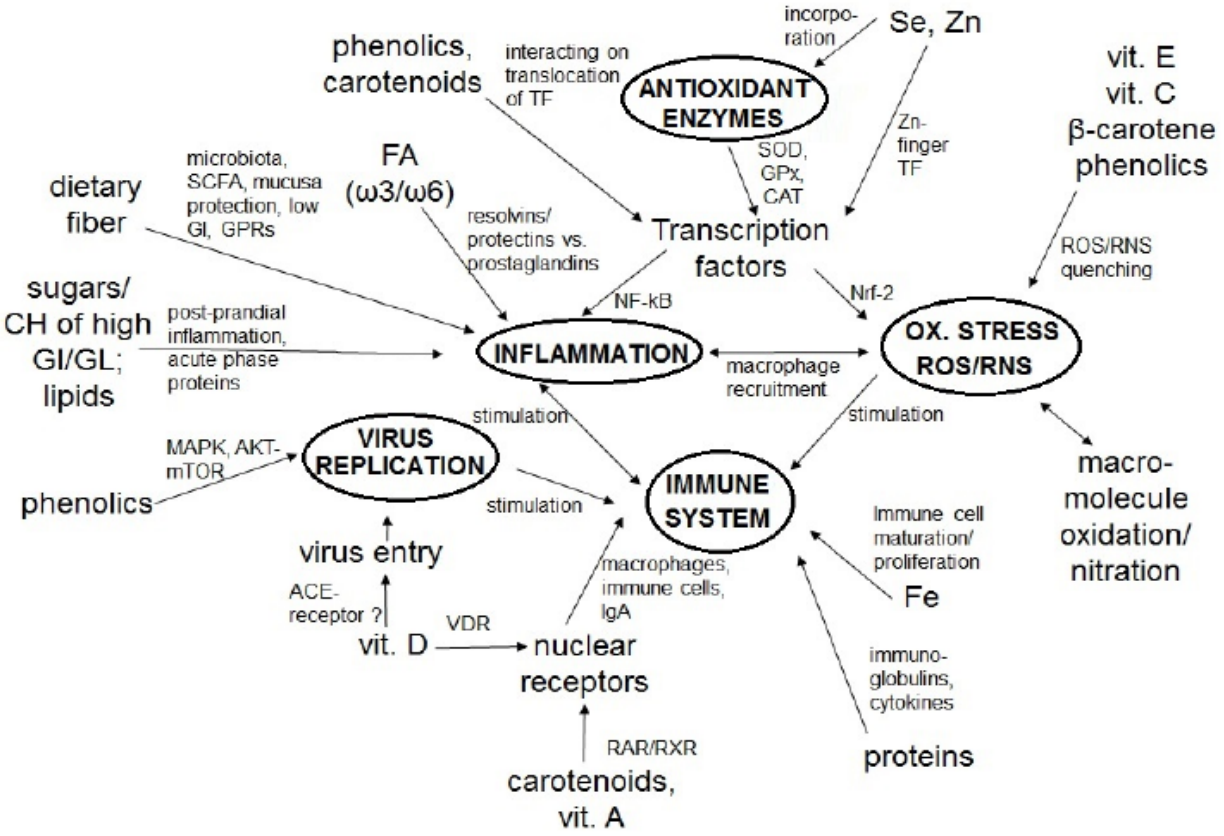

Figure 1. Schematic diagram showing interactions between selected dietary constituents, the immune system, and viral infection. *Abbreviations:* CH: carbohydrates; GALT: gut-associated lymphoid tissue; GPRs: G-protein-coupled receptors; FA: fatty acids; GI/GL: glycemic index/load; RAR/RXR: retinoic acid receptor/retinoid X receptor; SCFA: short-chain fatty acids; TF: transcription factors; VDR: vitamin D receptor.

Gli studi che hanno valutato l'effetto di integratori sull'assetto immunitario sono spesso caratterizzati da importanti limiti metodologici:

- selezione del campione molto variabile (comorbosità, status infiammatorio,…)
- bassa potenza statistica
- influenza dell'alimentazione spesso non considerata
- dosaggio della sostanza variabile (da integratore a farmacologica)

REJUVENATION RESEARCH
Volume 10, Number 3, 2007

DOI: 10.1089/rej.2007.0596

Nutrition as a Determinant of Successful Aging: Description of the Quebec Longitudinal Study NuAge and Results from Cross-Sectional Pilot Studies

Pierrette Gaudreau,[1] José A Morais,[2] Bryna Shatenstein,[3] Katherine Gray-Donald,[4] Abdel Khalil,[5] Isabelle Dionne,[5] Guylaine Ferland,[3] Tamàs Fülöp,[5] Danielle Jacques,[5] Marie-Jeanne Kergoat,[3] Daniel Tessier,[5] Richard Wagner,[5] and Hélène Payette[5]

- Daily consumption of several **antioxidant-rich foods** (fruits, vegetables, corn products, nuts, cocoa-containing products, green tea, and red wine) may help maintaining antioxidant defenses as measured by circulating total antioxidant status (TAS) and vitamin C.
- Dietary supplements (vitamins A, C, E and/or Se) were not associated with either TAS or vitamin C variation of circulating levels.

- Whether or not higher antioxidant levels exert a positive impact on the maintenance of physiologic functions, particularly the immune and endocrine somatotroph functions, and functional autonomy, will have to be established in a longitudinal perspective.

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- **Mediterranean diet** (MD) has a beneficial influence on several age-related diseases and improves immune responses.

- The MD has been shown to influence **cellular and circulating levels of inflammatory biomarkers**:
  - reducing plasma concentrations of inflammatory biomarkers (sICAM-1, sVCAM-1, SE-selectin, and CRP)
  - down-regulating CD49d and CD40 expression among circulating monocytes
  - increasing the levels of anti-inflammatory cytokines (IL-10)
  - reducing the production of pro-inflammatory cytokines (IL-6, TNF-a and IL-12).

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