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Received: July 15, 2020; Published: August 14, 2020

*Keywords:* SARS-CoV-2 and COVID-19 Global Pandemic; Nutritional Status; Immune System; Mitochondria; Vitamins; Amino Acids; Industry 4.0 and Sustainable and Modern Food Systems

On 7<sup>th</sup> January 2020, subsequently a collection of specimen with pneumonia of unexplained cause in Wuhan, Hubei Province, China, researchers screened an original coronavirus, suddenly denominated Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1] and COVID- 19, the inferred disease. SARS-CoV-2 speedly spread worldwide, considering its contagiousness/virulence earmark and boosted by globalization, it was transported everywhere faster than a virus had ever done previously. On March 11th, 2020 the World Health Organization declared COVID-19 a global pandemic [2]. Within the old European continent, my country-Italy-was early and severely involved, with a critical spread of the contamination and an uncontestable number of deceased [3], up to this date, unfortunately, more than 35.000 victims. The SARS-CoV-2-caused COVID-19 pandemic has culminated in an annihilating behave towards to human society in terms of well-being, economy, and style of living [3]. The Italian Government introduced progressive mitigation measurements on March 9 [4-6] and March 11 [7], 2020, to drastically restrict social interactions and prevent virus diffusion. All European countries learned from the Italian lesson and to immediately adopt very restrictive rules to limit viral diffusion, ensure appropriate health-system feedback, and reduce mortality [5]. Supposing the virus commonly first attacks and encroaches the lung and respiratory system tissue, in extremis, main part major organs in the body are, at the present moment, established to be negatively impacted frequently leading to severe systemic failure in part of elderly population [8]. Pre-existing pathological circumstances or comorbidities, for instance, geriatrics are a primary conjecture for untimely death and elevated morbidity and mortality [3]. The immobilization due to hospitalization and bed rest and the physical inactivity due to sustained quarantine and social distancing can downregulate the competence of different organs to resist to viral infection and expand the risk of injury to the immune, respiratory, cardiovascular, musculoskeletal systems and, last but not least, the possibility of seriously damaging the brain [8]. The cellular mechanisms and danger of this "second wave" effect of COVID-19 to the human body, along with the effects of aging, proper nutrition, and regular physical activity are reviewed by Woods and colleagues, see reference [3]. While much remains to be known about the COVID-19, the influence of this pandemic on nutrition and dietary intake has already gone beyond the individual and the community to reach national and global levels. The main goal of these recommendations is to maintain the physical and mental health of individuals, resilience of communities and national and global food security [8]. Intriguing clues display that dietary habits are affected by conditions of stress, distress, and emotional disturbance, whereby elevated distress levels are associated with unhealthy dietary patterns and indigent and underprivileged standard of the nutritional therapy [9,10]. The typical denominator that drives most of the dietetics and dietary guidelines and endorsement to combat viral infections, as well as COVID-19, is situated

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within the connection between nutrition and immunity [9,11]. Literally, recent clinical data, highlight that nutrition has a wide and deep impact on people's immune system and disease susceptibility. It has recently been reported that precise nutrients or nutrient blend may influence the immune system through the stimulation of cells, alteration in the production of signaling molecules, and gene expression [9,12]. Additionally, food characteristics are significant determinants of gut microbial balance and consequently can shape the nature of immune responses in the individual [9,11]. Nutritional decline in energy, specific protein, and peculiar micronutrients are linked with depressed immune function and increased susceptibility to infection [9,13]. A suitable intake of vitamins, both hydrophobic i.e. A [14], D [15], E [16] and hydrophilic C [17], B, or Riboflavin [18-26], B, or Niacin [27-31], B, and B, is predominantly vital for the maintenance of immune function [9] together with an appropriate absorption of Fe++, Zn++ [32]. Accordingly, the solution for maintaining an adequate immune system is to avoid deficiencies of the healthy food that play a crucial role in immune cell triggering, synergy, differentiation, or functional and convenient expression. The nutritional status of humans being has for long been contemplated as a gauge of resilience against destabilization [9]. The condition of lockdown and confinement could also lead to erratic eating patterns and recurrent snacking, both of them are associated with greater caloric intake and expanded peril of obesity [3]. In this contest, patients with autoimmune diseases are at high risk of infections, due to endogenous (dysfunctional immune system) and external factors (i.e. immunosuppressants) [33,34]. Autoimmune convalescents under immunosuppressive pharmaceuticals could be prone to SARS-CoV-2 affliction; per contra, suspension of the ongoing conventional and biological therapy is contraindicated to avoid disease flares and the consequent increase in the infection risk [9,33]. By means of decreasing oxidative stress and enhancing immunity, nutritional support helps people to lower the risk of virus infection or to alleviate the symptom of COVID-19 [13,33,34]. An emerging concept in immunology is that remodelling of macrophage activities is pivotal in order to control and to direct their metabolism. Thus, rewiring of the Krebs cycle in macrophages sustains the gathering of bioactive metabolites that can promote proinflammatory or anti-inflammatory activities, but the underlying mechanisms are not fully understood. Recently, a study in *Nature* reports that the metabolite itaconate regulates the key anti-inflammatory transcription factor nuclear factor erythroid 2-related factor 2 (NRF2) in macrophages [35,36]. Macrophages that are the primary innate immune cells of the body, regulate wound healing by switching between M1 and M2 phenotypes in order to kill bacteria, clear apoptotic cell debris, stimulate angiogenesis, and deposit functional extracellular matrix. Though, a set of pathologies are characterized by macrophages that are stalled in a M1 state, and there is a need for different compounds (i.e. inhibitors) that can decrease M1 macrophage action. Previous research found that application of unsaturated fatty acids, glycolysis inhibitors, and L-glutamate anabolism/catabolism inhibitors decrease inflammatory gene and protein expression [37]. Also, it has been shown that M1 macrophages primarily rely on glycolysis for energy (ATP production via phosphorylation at the substrate level), while M2 macrophages rely on oxidative phosphorylation [35-38]. However, cells of macrophage lineage have to "pay the price" for making itaconate, and they lose the ability to perform mitochondrial substrate-level phosphorylation [38] Amino acids are fundamental building blocks supporting life. Their role in protein synthesis is well defined, but they contribute to be a host of other intracellular metabolic pathways, including ATP generation, nucleotide synthesis, and redox balance, to support cellular and organismal function. Immune cells critically depend on such pathways to acquire energy and biomass and to reprogram their metabolism upon activation to support growth, proliferation, and effector functions. Amino acid metabolism plays a key role in this metabolic rewiring, and it supports various immune cell functions beyond increased protein synthesis. Thus, amino acid metabolism promotes immune cell function, and improve immunity in pathological conditions [39]. The COVID-19 pandemic crisis has created a new era [40] while we are still trying to examine the contrecoup for humankind, financial system, and, afterwards, food formulation. Thus, both academic analysts and food sector experts will have to face many significant claiming i.e. ensuring food safety and food security, introducing Industry 4.0 tools to reduce losses and waste of food, inclusive of identifying alternative and safe protein sources that meet the nutritional expectations of customers [40-42]. At the same time, they should introduce innovations fast enough with the imminent economic crisis in the era of the COVID-19 pandemic, offering acceptable and economically competitive products and developing functional foods fortified with bioactive compounds and antioxidants that promote healthy microbiota [43-49] and support consumers' immune system [40-49]. There is undoubtedly a need to avoid "business as usual" practices, to think out of the box and accelerate efforts to develop sustainable and modern food systems [43-48,50]. Moreover, researchers have a little power but huge

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responsibilities. Thus, novel challenges of COVID-19 pandemic will be addressed in twenty-first century to those visionaries within the pioneering community of Nutritional Biochemists: researchers good will' at work, it is (y)our time! Because even those who go too fast are left behind if the rules of the game are rigged and the common good is not pursued. We are not "only a pawn in their game" but "We're gonna change the world" (Bob Dylan *ipse dixits* in his lyrics). Europe together with all culturally developed and innovative countries has a duty to show the way out of this trap. The gift of suffering will be a new vision of our planet where equanimity and sustainability will finally walk side by side.

All spirits are enslaved which serve things evil (Percy Bysshe Shelley).

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