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Short Communication

A mild oxidative stress could modulate the Nrf2 pathway in CoVid-19 patients

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Abstract

Due to the technical difficult in built up a stable vaccine against some viruses whose structure change with multiple mutations, the possibility of overcoming the problem could be an indirect approach. As proposed by some authors, the system medicine science suggests the possibility to act counteracting the mechanism induced by the pathogen rather than acts directly against the virus exploiting the hormesis phenomenon. Indeed, most of the COVID-19 fatalities are a consequence of the cytokine storm because of the strong oxidative stress and inflammation induced by an exaggerated response of the immune system. While a vaccine is addressed to simulate the image of the virus and to induce a humoral protection, the indirect approach trough a mild oxidative stress simulates the effect induced by the virus itself promoting the activation of defence mechanisms which in turn could favor the healing of the patients..

One of the most common defence against viral infections is vaccination [1]. As known, a vaccine is a form attenuated or killed of the active pathogen that stimulates the immune system to kill the microorganism and to prevent future infections. Unfortunately, the difficult in developing a functional vaccine in the cases of a frequent mutation of the virus require new strategy and long time for its preparation. In the case of the COVID-19 pandemic novel RNA vaccines are being investigated [2]. Moreover, the rapidity of the diffusion of the SARS CoVid-2 pandemic require relevant and rapid efforts that could rise some limitations and failure in obtaining a functional vaccine [3].

Some interesting data proposed by Yuen et al [4] are related to the reduced pathogenicity of SARS-CoV-2 probably because of adaptation on humans. As suggested by the same authors, will be particularly important to elucidate the ability of SARS-CoV-2 in modulating the antiviral and the proinflammatory responses trough nuclear factor erythroid 2 p45-related factor 2 (Nrf2) and NLRP3 inflammasome activation. The importance of the Nrf2 pathway on the homeostasis of the cells regarding an excessive oxidative stress is a well confirmed data [5,6]. Recently, Cuadrado et al, in an excellent paper published in 2018 [7], described the complexity of a group of illnesses reported as "***diseasome***" which share the same mechanism linked to the transcription of Nrf2. ***"Interestingly, this network includes heterogeneous phenotypes such as autoimmune, respiratory, digestive, cardiovascular, metabolic, and neurodegenerative diseases, along with cancer and many other conditions"***. Furthermore, in their paper the authors described the importance of system medicine as an interdisciplinary field of study that looks at the systems of the human body as part of an "integrated whole", incorporating biochemical, physiological, and environment interactions. Thus, they applied this method to Nrf2 by cross-validating its position in a protein-protein interaction network (the Nrf2 interactome) functionally linked to chronic inflammation and oxidative stress. To our opinion, the fact that the strong inflammation and the severe conditions induced in a high number of patients by the SARS-CoV-2 could be a consequence of the unbalance of the Nrf2 pathway, could open new horizons. Indeed, some oxidative therapies able to induce a controlled and brief oxidation status have been demonstrated to be powerful modulator of the Nrf2 pathway [8,9]. Furthermore, recent reports based on clinical randomized studies following the induction of brief and controlled oxidative stress are indicative of potentially useful effects against the severity of the COVID-19 disease [10,11]. Recently, other works have suggested that the pharmacological activation of Nrf2 could be a possible strategy against Covid-19 [12] reinforcing the hypothesis that Nrf2 activators could represent a possible tool at least to alleviate the clinical outcome of this terrible pandemic.

More studies will be needed to clearly demonstrate the relationship of the Nrf2

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modulation and the COVID-19 induced cytokine storm. However, at the light of the huge diffusion of this pandemic and the absence of a real therapeutic strategy or vaccination, we think that an indirect approach, throughout oxidative interventions, could help in reducing the severe progression of the infection.

Conflict of Interest

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