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LETTER TO THE EDITOR

A glance upon Epigenetic and COVID-19

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Abstract: Epigenetics studies focused on SARS-CoV-2 infection to assist in the perception of pathophysiology can direct prospective approaches for the COVID-19 treatment. There is an intrinsic relationship between epigenetic marks and the adaptation of the immune system, which determines the outcome of the pathogen-host interaction. Recently, studies have shown that there is an increased expression of the ACE2 receptor in individuals with Lupus, the origin of this phenomenon is from DNA's methylation deregulation process that consequently, become this group more suitable to be infected by SARS-CoV-2. There is evidence for the use of some epigenetic modifiers known as Epidrugs, which might be a promising approach to be deeper investigated. Here we emphasize the importance of this glance upon Epigenetic and its modulators in the promising therapeutic in the COVID-19 disease context.

Key words: Epigenetic, COVID-19, SARS-CoV-2, Epidrugs.

In this letter, we would like to emphasize the relevance of a glance upon Epigenetics and its modulators in the context of COVID-19, to assist in the perception of pathophysiology and prospective approaches.

Epigenetics has been considered crucial for understanding the pathophysiology of infectious diseases, playing an essential role in the modulation of the immune system, in the development of inherited diseases, in cell dysregulation in neoplasms, and even in areas such as agriculture and ecology (Deans & Maggert 2015).

Currently, solid pieces of evidence have been observed in an epigenetic mechanism, the methylation of ACE2 promoter CpG islands, behind the regulation of Angiotensin II converting enzyme (ACE2) gene expression. The ACE2 gene is located in the chromosome X and this gene runs as a central regulator of blood pressure, in glycemia controlling (Donoghue et al. 2000) and has been proposed as a host receptor for SARS-CoV-2, allowing the virus entry into cells and infectivity (Zhou et al. 2020).

DNA methylation variability of the ACE2 gene and post-translational changes in histones are likely related to pathophysiological differences observed during SARS-CoV-2 infections in host tissues, as well as biological age and sex patterns (Chlamydas et al. 2020). In patients with Lupus, that presents an increased expression of the ACE2 receptor becoming this group more susceptible, also there is a DNA methylation deregulation process leading to T lymphocytes hyper-reactive due to a decrease in the methylation pattern, and increasing the transcriptional rate and impairing the inactivate of the X chromosomes (Gensterblum et al. 2018, Sawalha et al. 2020). Epigenetic T lymphocytes hyper-reactive profile in Lupus group would favor the worsening of the clinical picture in COVID-19 patient due to a more aggressive cytokine storm (Sawalha et al. 2020).

Interesting, Epigenetic regulation could elucidate the difference that has been observed in number and severity of COVID-19 among women and men. The ACE2 gene is on the X chromosome, and women are heterozygous for silenced/expressed X while men are hemizygous, as they have only one copy of chromosome X (Gemmati et al. 2020).

Another factor that alters the severity of COVID-19 is age. Age is one of the main drivers of variations in chromatin structure, distinguishing immune cell phenotypes and regulating inflammatory responses. Thus, it is evident that Epigenetic permeates the main aspects related to the outcome of COVID-19 (Salimi & Hamlyn 2020).

In this framework, some Epigenetic modulators such as curcumin, deferasirox, 8-hydroxyquinolines or sulforaphane, that have shown effects on ACE and Interferon genes silencing, in addition to having an effect on the transcriptional control of various inflammatory markers (Kaufman-Szymczyk et al. 2015), could be a very interesting therapeutic approach. Epigenetic modulations are reversible and responsive to the environment, so several epigenetic modulators have already been applied in the treatment of viral infections and cancers (Nehme et al. 2019).

It is a worldwide consensus that due to the dramatic situation of the SARS-CoV-2 pandemic, with overwhelming public health consequences, there is an imperative need to discover / rediscover potential therapeutic approaches.

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Natália Lopes de Freitas and Pedro Ricardo Gonçalves Azevedo contributed equally to data acquisition, writing, and discussion. Fabiana Brandão AS contributed to the conception, data acquisition and interpretation, discussion, and critically revised the manuscript. All authors gave their final approval and agree with all aspects of the work.