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Aberrant Genome-Wide DNA Methylation Profiles of Peripheral Blood Mononuclear Cells from Patients Hospitalized with COVID-19

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Abstract : To date, more than 275 million people worldwide have been diagnosed with COVID-19 and the rapid spread of the omicron variant suggests many millions more will soon become infected. Many infections are asymptomatic, while others result in mild to moderate illness. Unfortunately, some infected individuals exhibit more serious symptoms including respiratory distress, thrombosis, cardiovascular disease, multi-organ failure, cognitive difficulties, and, in roughly 2% of cases, death. Studies indicate other coronaviruses can alter the host cell's epigenetic profile and lead to alterations in the immune response. To better understand the mechanism(s) by which SARS-CoV-2 infection causes serious illness, DNA methylation profiles in peripheral blood mononuclear cells (PBMCs) from 90 hospitalized severely ill COVID-19 patients were compared to profiles from uninfected control subjects. Exploratory epigenome-wide DNA methylation analyses were performed using multiplexed methylated DNA immunoprecipitation (MeDIP) followed by pathway enrichment analysis. The findings demonstrated significant DNA methylation changes in infected individuals as compared to uninfected controls. Pathway analysis indicated that apoptosis, cell cycle control, Toll-like receptors (TLR), cytokine interactions, and T cell differentiation were among the most affected metabolic processes. In addition, changes in specific gene methylation were compared to SARS-CoV-2 induced changes in RNA expression using published RNA-seq data from 3 patients with severe COVID-19. These findings demonstrate significant correlations between differentially methylated and differentially expressed genes in a number of critical pathways.

Keywords : COVID19, epigenetics, DNA mathylation, viral infection
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