Upregulation of Innate Immune Response Genes in a SARS-CoV-2 Nucleocapsid Protein Dependent Manner

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The coronavirus disease, caused by SARS-CoV-2, is arguably one of the greatest medical challenges of the past 100 years. Recent investigations have linked the nucleocapsid (N) protein of SARS-CoV-2 with the perturbation of host cellular processes by inhibiting the production of interferons and cytokines. In specifics, this study focuses on two consecutive mutations (R203K/G204R) (KR mutation) in the N protein which has been suspected to increase viral load and disease severity. This study profiled the expression of selected immune-related genes by RT-qPCR using RNA extracted from mutant as well as wildtype pseudovirus-infected cells, using non-infected cells as a control. Three trials were conducted for RNA extraction from HEK-293 cells, RNA quantification and quality analysis, reverse transcription to make cDNA, qPCR for selected target genes, and lastly, gene expression data analysis and interpretation. An increase in the level of the inflammatory transcripts in a KR mutationdependent manner as compared to the wildtype was made clear. The results inculcate that on average the selected immune response genes in the mutant infected cells were expressed 11 times more than the non-infected cells, whereas the wildtype infected cells were expressed 2.6 times more. This links an increased virality and disease severity to the KR mutation in the N protein. Ultimately, the findings in this study provides potential for widening the understanding of differential host immune responses to distinct viral genotypes and aiding in maximizing the efficacy of existing vaccines and modern-day therapeutics.

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