Is Up-Regulation Gene Expression of the Certain Genes During the Viral Respiratory Tract Infection Would Have Any Influence in Pathogenesis of the SAR-CoV-2 Infection?

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Novel coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is characterized as a pandemic by WHO. Differential expression analysis takes the normalized read count data and performing statistical analysis to discover quantitative changes in expression levels between experimental groups and give DEGs from functional genomics experiments which depend on the scale and intent of the experiment. Some commonly used technologies are real-time PCR, microarray analysis, next-generation sequencing, and RNA-seq. Our study aimed to look for the differential expressed genes in viral respiratory tract infection. Furthermore, we wanted to consider these genes expression to be noticed during the current pandemic infection SARS-CoV-2 patients as most of the viral respiratory tract infections have the same pathogenesis and disease pattern. These genes were found to be up-regulated in the study during the viral respiratory tract infection and which might be helpful in understanding the pathogenesis, disease management, drug, and vaccines developed for the current COVID-19 infection. Our study is a bioinformatics based analysis on the NCBI GSE68310 dataset, which is a microarray dataset for different respiratory viral infections. We got different down and up-regulated DEGs through limma package utilizing GEO2R of the NCBI and $P<0.05$, and log fold change (FC)> one was used as the cut-off criteria. α-Defensins rectify acute lung injury (ALI) by LRP-mediated loss of capillary-epithelial barrier function, implying a probable new method to intervention (1). Defensins have an effective immunomodulatory effect that can modify inborn and flexible immune reactions to viral infection. There are a few cases where data shows paradoxical desertion from defensin neutralization or development of viral infection. (2). LILRA3 role is currently unidentified and can cohere human leukocyte antigen (HLA) class I. Consequently, assuming that it excretes, then the LILRA3 might weaken the interaction of membrane-bound LILRs (such as LILRB1, an inhibitory receptor expressed on effector and memory CD8 T cells) with their HLA ligands, hence tempering immune reactions and prompting vulnerability to disease. (3,4,5). LILRA3 was also reported up-regulated in the PBMCs from patients with SARS. Concentrating this gene in SAR-COV-2 patients will allow for new approaches for producing novel diagnostics and treatments for this new lethal disease (6). IGLL1 gene encodes one of the surrogate light chain subunits and belongs to the immunoglobulin gene superfamily. This gene does not go through rearrange. Alterations in this gene can lead to B cell deficiency and Agammaglobulinemia (7). Up until now, the 7 Primary Antibody Deficiencies (PAD) patients with the COVID-19 virus have been found. Five of those seven have had Common Variable Immune Deficiencies (CVIDs), two of them have been affected with Agammaglobulinemia, one with X-linked Agammaglobulinemia (XLA) and one with Autosomal Recessive Agammaglobulinemia (ARA) (8). Examining this gene in COVID patients can assist in finding probable signs of new therapeutic targets. Numerous RPs work with viral mRNA and proteins to take part in viral protein biosynthesis and control the imitation and contamination of viruses in host cells. This gene expression needs to be checked during COVID-19 because many of the communications are important for viral conversion and imitation, which encourage viral

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infection and growth. The antiviral approach established on RPs will be used as models for additional studies (9). Over the past few decades, it has been highly valued that the enzyme phospholipase A2 (PLA 2) is a significant aspect of lung diseases that include inflammation (10). Annexins (ANXs) are a family of calcium and phospholipid cohering proteins with immune-regulatory functions in viral infections, lung injury, and inflammation. Recent recognition of the role of ANXs in modifying IAV infection and host reactions will allow the upcoming progress of additional compelling antiviral therapies (11). The LST1 gene is constitutively expressed in leukocytes and dendritic cells, and it is categorized by broad alternative merging and can act as an immune-regulator while protein expression of LST1 on the cell surface of mononuclear cells, and they display an inhibitory outcome on lymphocyte proliferation of two LST1 proteins (12). New studies have shown the value of Fc-mediated antibody effector functions in protection and pathogenesis equally for several infectious agents. Fc-mediated antibody effector operates for the reasonable design of secure and efficient vaccines and monoclonal antibody rehabilitations against RSV. (13). Thus, it is vital to study the FCGR3B gene during the COVID-19 infection. The novel coronavirus SARS-CoV-2, causing the new infectious coronavirus disease-2019 (COVID-19), is currently spreading rapidly around the world; it has been recently declared as a pandemic by WHO. Recent clinical observation suggests that patient age, male sex, and certain chronic medical conditions (e.g., cardiovascular disease, diabetes, COPD) seem to represent a risk for the infection of SARS-CoV-2 and higher disease severity1. There is currently no biological marker known to predict the susceptibility to COVID-19. (14). Our results and previous research on these genes suggest that DEFA1B, LILRA3, IGLL1, ANXA4, LST1, and FCGR3B expression might be up-regulated in COVID-19 and other viral respiratory tract infections. Consequently, the up-regulation of these genes would facilitate infection with COVID-19. We, therefore, hypothesize these mentioned genes up-regulation might increase the risk of developing severe and fatal COVID-19. If this hypothesis were to be confirmed, it could lead to a conflict regarding the pathogenesis of the different viral respiratory tract infections and SARS-CoV-2 because previously, the up-regulation of these above stated are not linked with the pathogenesis of the COVID-19. Furthermore, these genes are not used in research for disease management, drug development, and vaccine production of COVID-19. A further aspect that should be investigated is the genetic predisposition for an increased risk of SARS-CoV-2 infection, which might be due to these listed genes or else other human respiratory system-related genes expression at the time of SARS-CoV-2 and VRTIs. DEFA1B, LILRA3, IGLL1, ANXA4, LST1, and FCGR3B would be a good candidate for the development of novel, host-directed therapeutics to improve COVID-19 disease management as they are tested for different VRTIs disease management in previous studies. Summarizing this information, the sensitivity of an individual might result from a variation in the gene expression profile of these genes and other respiration or pulmonary system-related genes during the VRTI plus COVID-19 infection. We suggest that patients with upregulation of the genes and other pulmonary system linked gens are at higher risk for severe COVID-19 infection and, therefore, patients' gene expression profile should be monitored during the infections as some genes' down or up-regulation will impact the pathogenesis and mortality rate of the COVID-19. Based on a different articles search engine on April 09, 2020, we did not find any study that shows the stated genes and other gene expression profile which are related to the lungs or pulmonary system of the patient at the time of SARS-CoV-2 and other VRTIs. Therefore, such studies would not only provide a suitable approach for the understanding and disease management of COVID-19 and other VRTIs but would also prove valuable in the development of the drug and vaccine for the SARS-CoV-2 or other VRTIs.

Table 1. Stated down-regulated DEGs gens in the GSE68310 dataset

ID	Gene Symbol	*P*	LogFc
Up-regulated			
ILMN_1725661	DEFA1B	1.01E-03	1.8148
ILMN_1661631	LILRA3	9.84E-07	1.7185
ILMN_2393765	IGLL1	1.07E-04	1.6647
ILMN_1711408	ANXA4	7.63E-06	1.276
ILMN_1718936	LST1	9.03E-13	1.2365
ILMN_1728639	FCGR3B	1.59E-06	1.2244

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