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# مطالعه بیوانفورماتیکی بیان ژن در بیماران کووید ۱۹ با استفاده از DAVID

# Bioinformatic study on gene expression status in COVID-19 patients using DAVID

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## Abstract

Investigating the differential expression of genes in COVID 19 patients and healthy people is one of the ways to identify the function of the virus in the host cell. High-throughput technologies such as RNA-Seq enable the expression of a large number of genes to be compared simultaneously. The real-time PCR is a standard and accurate method of measuring gene expression, which can be used for a limited number of genes. Since the outbreak of Covid-19, many studies have been conducted to determine the expression status of genes in patients. The purpose of this study was to investigate the function of over expressed genes in these studies through the DAVID website. The result of this study emphasizes the role of the *ACE2* gene in the entry of the Corona virus into the host cell.

Keywords: Gene expression, Covid-19, Gene ontology, DAVID

## Introduction

Covid-19 disease is caused by coronavirus 2 and has spread all over the world. Due to the complexities of the functioning of the virus in the human cells, no effective medicine has been found against it (Alabboud and Javadmanesh, 2020). Gene expression studies have shown that

several genes and biological pathways are involved in the body's defense system against viruses. Accurate knowledge of these pathways can ultimately help to find effective drugs and vaccines against the virus (Ilieva et al., 2022). RNA-Seq technology provides a better understanding of the disease biology by determining all involved genes. Since the outbreak of the COVID-19 disease, several studies have been conducted on the expression of genes related to the immune system in patients, and their results have determined the biological pathways involved in the disease. The aim of the present study was to study the gene ontology of over-expressed genes in the lung tissue of patient infected with the COVID-19.

**Materials and Methods**

In this study, articles related to gene expression in Covid-19 patients were collected, and genes that were differentially expressed larger than 2.5 fold in patients compared to healthy individuals were selected (Bass et al., 2021; Cao et al., 2021; Chakraborty et al., 2021; Moni et al., 2021; Gomez-Carballa et al., 2022; Jabeen et al., 2022; Maulding et al., 2022). The gene names were converted to the "official gene symbol" format by DAVID in the Gene Format Conversion section of the DAVID Bioinformatic Resources server (http://david.ncifcrf.gov). Then functional annotations, gene ontology and pathways which were evaluated considering no change in defaults of the server.

**Results and Discussion**

In total, 137 up-regulated genes in patients were selected which showed above 2.5 fold change. The result of the functional annotation of DAVID server included that these up-regulated gene were involved mainly in two disease clusters, six functional clusters, three ontology groups, three biological pathways and four protein domain clusters. A large number of genes interfere in functional annotation (Table 1). *CCL2*, *IFNG* and *TLR2* genes were present in the cluster of susceptibility to Mycobacterium tuberculosis disease. *JAK1* and *RUNX1* genes were identified in the pathway of susceptibility to leukemia. Furthermore, *TNFL4* and *TLR5* genes were identified in the pathway of SLE autoimmune disease.

Around 97% of the genes were involved in the functional pathways of cell wall proteins. A large number of genes were involved in the activity of the immune system and defending against the virus. Gene ontology showed the involvement of genes in several biological pathways such as NOD-Like Receptor Signaling Pathway, Toll-like Receptor Signaling Pathway, Influenza A and

Corona Virus Disease-COVID19. *TMPRSS2*, *ACE2* and *NRP1* genes are used by Corona virus to enter the cell. *ACE2* plays a very effective role in virus entry. However, other factors such as *TMPRSS2* expression are required (Figure 1). Furthermore, interferon immune responses and interferon-stimulating genes play an important role in cellular immunity, although cell type, virus type, and virus amount play a key role (Cao et al., 2021). The interaction of S-glycoprotein of the virus and the host's immune system and the activity of cytokines and chemokines play a key role in the severity of the disease (Chakraborty et al., 2021). High expression of pro-inflammatory genes, including *IL1R1*, *IL1R2* and *IL18R1*, as well as *FKBP5* and *S100A8*, which regulate the immune system of host, has been reported (Gomez-Carbella et al., 2022). The role of nasal epithelium has been highlighted in the severity of the disease. The involvement of *ACE2*, *TMPRSS2* and *NRP1* in the entry of the virus into the host cell can be studied more in the future.

**Table 1.** Annotation summary results from DAVID

| Term | Gene count | Percent % | *P*-value | Functional annotation |
|---|---|---|---|---|
| Innate immunity | 42 | 30.7 | 4.1E-32 | Biological process |
| Antiviral defense | 30 | 21.9 | 1.2E-31 | Biological process |
| Immunity | 47 | 34.3 | 2.0E-22 | Biological process |
| Inflammatory response | 23 | 16.8 | 3.5E-18 | Biological process |
| Chemotaxis | 12 | 8.8 | 3.7E-9 | Biological process |
| Host-Virus interaction | 17 | 12.4 | 5.0E-4 | Biological process |
| Secreted | 45 | 32.8 | 1.3E-10 | Cellular component |
| Cytokine | 17 | 12.4 | 2.8E-11 | Molecular function |
| Antimicrobial | 11 | 8 | 8.3E-8 | Molecular function |
| Antibiotic | 10 | 7.3 | 2.3E-7 | Molecular function |
| Disulfide bond | 64 | 46.7 | 5.5E-9 | Post- translational modification |

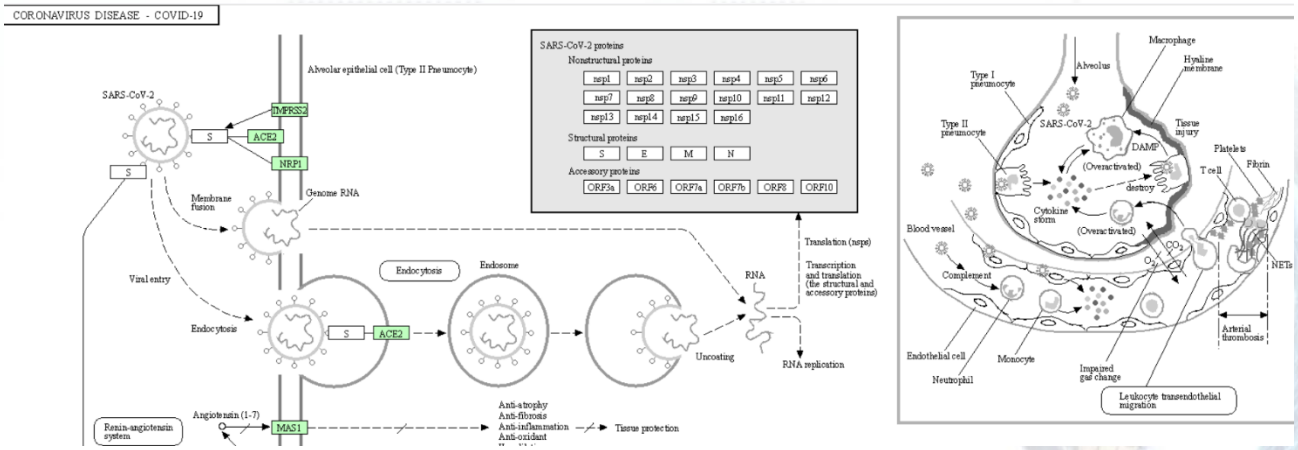


**Figure 1.** Biological pathway of Coronavirus Disease – COVID-19

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