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BOOTCAMP

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TITLE

Identification and Analysis of Novel Metabolic Biomarkers in COVID-19: A Pathway-Based Approach

Noorul Jaasim N

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PROBLEM STATEMENT

Problem:

- Limited understanding of molecular markers for COVID-19 progression and severity.
- Need for reliable biomarkers to predict disease outcomes and guide treatment decisions.
- Challenges in early identification of high-risk patients.

Impact on Stakeholders:

- Healthcare Providers
- Patients
- Researchers

INTRODUCTION

Purpose of the Project:

- To identify and characterize novel molecular biomarkers for COVID-19.
- To analyse the clinical significance of differentially expressed genes.
- To understand the biological pathways involved in COVID-19 pathogenesis.

Importance of the Project:

- Aids in early detection and prognosis of COVID-19.
- Potential for improving patient stratification.
- Contributes to understanding disease mechanisms.

JUSTIFICATION

Significance of the Problem:

- Current limitations in predicting COVID-19 severity and progression.
- Need for molecular markers to guide clinical decision-making.
- Gap in understanding metabolic alterations during COVID-19 infection.

Need for Investigation:

- All identified genes show significant differential expression ($p < 0.05$).
- Multiple metabolic pathways affected (lipid, cholesterol, purine metabolism).
- Potential for therapeutic targeting and patient monitoring.

BACKGROUND

Context:

- COVID-19 pathogenesis involves multiple metabolic and inflammatory pathways.
- Gene expression changes can indicate disease severity and progression.
- Biomarkers needed for better disease management.

Literature review:

- Although there are studies that talk about COVID-19 severity and mortality, very few discuss the gene expression levels and in turn the biomarkers for the disease.
- This project aims to address this gap by providing potential biomarkers from the chosen dataset.

OBJECTIVES

Project Goals	Expected Outcomes
Identify significantly altered genes in COVID-19 patients.	Panel of potential biomarker candidates.
Analyse biological pathways and functions of identified genes.	Understanding of pathway interactions.
Evaluate potential clinical significance and applications.	Clinical significance assessment.
Establish correlations between gene expression and disease parameters.	Foundation for future validation studies.

INSIGHTS

Personal Discoveries:

- Learnt how different analytical approaches (statistical, functional, clinical) complement each other in biomarker research.
- Recognised how visualisation tools like Tableau can represent complex data into meaningful insights.

Real-world Impact:

- Potential for developing targeted therapies based on the pathways identified.
- Identified biomarkers could bring up new and effective diagnostic tests.

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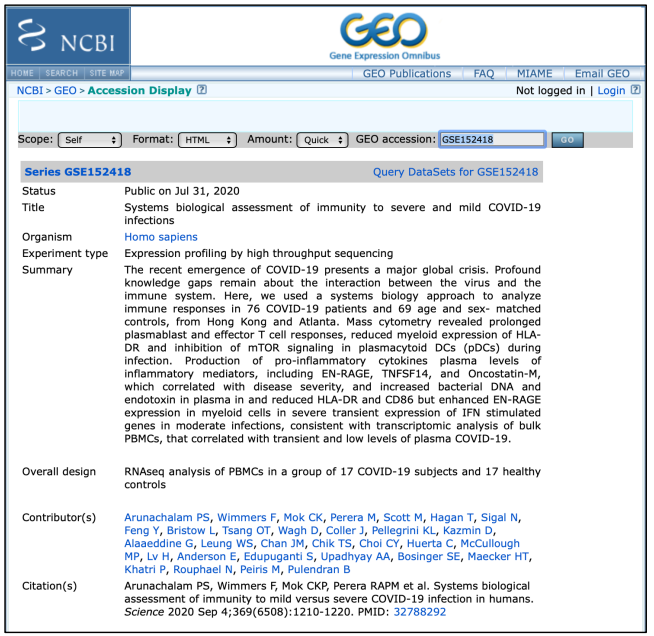
DATA COLLECTION

- **Study Design:** The dataset includes gene expression data from 17 COVID-19 patients and 17 healthy controls.
- **Differential Gene Expression:** A total of 2,080 genes were screened, with 1,905 identified as upregulated and 175 downregulated in COVID-19 patients compared to healthy controls.
- **Potential Biomarkers and Therapeutic Targets:** The findings from GSE152418 contribute to identifying potential biomarkers for COVID-19, which could aid in diagnosis and treatment strategies.



NCBI

Gene Expression Omnibus

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Scope: Self Format: HTML Amount: Quick GEO accession: GSE152418 GO

Series GSE152418 Query DataSets for GSE152418

Status	Public on Jul 31, 2020
Title	Systems biological assessment of immunity to severe and mild COVID-19 infections
Organism	Homo sapiens
Experiment type	Expression profiling by high throughput sequencing
Summary	The recent emergence of COVID-19 presents a major global crisis. Profound knowledge gaps remain about the interaction between the virus and the immune system. Here, we used a systems biology approach to analyze immune responses in 76 COVID-19 patients and 69 age and sex- matched controls, from Hong Kong and Atlanta. Mass cytometry revealed prolonged plasmablast and effector T cell responses, reduced myeloid expression of HLA-DR and inhibition of mTOR signaling in plasmacytoid DCs (pDCs) during infection. Production of pro-inflammatory cytokines plasma levels of inflammatory mediators, including EN-RAGE, TNFSF14, and Oncostatin-M, which correlated with disease severity, and increased bacterial DNA and endotoxin in plasma in and reduced HLA-DR and CD86 but enhanced EN-RAGE expression in myeloid cells in severe transient expression of IFN stimulated genes in moderate infections, consistent with transcriptomic analysis of bulk PBMCs, that correlated with transient and low levels of plasma COVID-19.
Overall design	RNAseq analysis of PBMCs in a group of 17 COVID-19 subjects and 17 healthy controls
Contributor(s)	Arunachalam PS, Wimmers F, Mok CK, Perera M, Scott M, Hagan T, Sigal N, Feng Y, Bristow L, Tsang OT, Wagh D, Coller J, Pellegrini KL, Kazmin D, Alaaeddine G, Leung WS, Chan JM, Chik TS, Choi CY, Huerta C, McCullough MP, Lv H, Anderson E, Edupuganti S, Upadhyay AA, Bosinger SE, Maecker HT, Khatri P, Rouphael N, Peiris M, Pulendran B
Citation(s)	Arunachalam PS, Wimmers F, Mok CKP, Perera RAPM et al. Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans. *Science* 2020 Sep 4;369(6508):1210-1220. PMID: 32788292

DATA ANALYSIS

1. Statistical Analysis:
- Fold change calculation
- P-value determination (< 0.05)
- Significance testing

2. Visualisation Methods:
- Gene expression level plots
- Fold change vs. P-value correlation analysis
- Tableau dashboard creation

3. Functional Categorisation:
- Pathway analysis
- Biological process classification

RESULTS

1. Gene Expression Analysis:

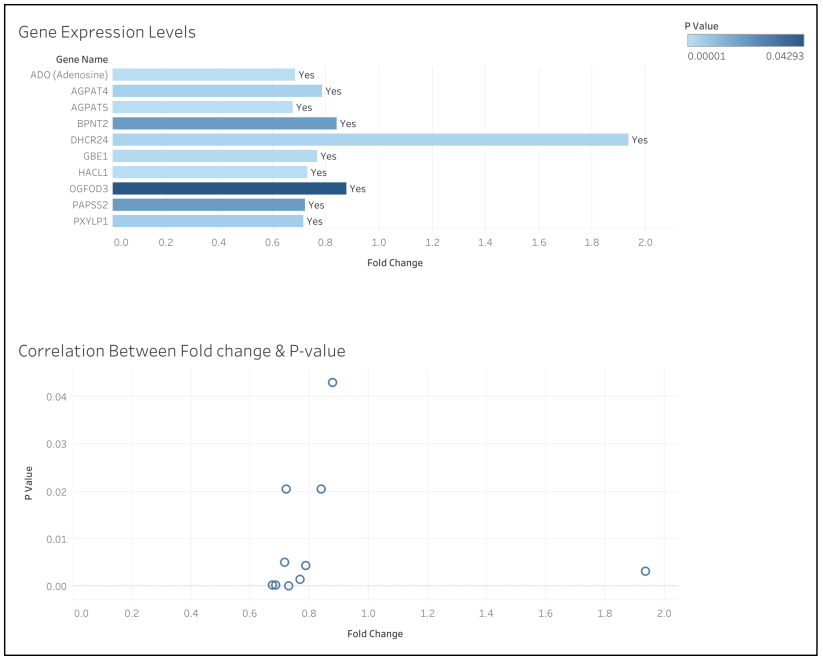
- DHCR24 showed highest upregulation (FC: 1.93).
- ADO showed significant downregulation (FC: 0.68).
- All genes showed statistical significance ($p < 0.05$).

2. Functional Categories Identified:

- Metabolic pathways (cholesterol, lipid, purine).
- Signalling pathways (oxygen sensing, sulfation).
- Structural components (glycogen, GAG metabolism).

3. Visualisation Insights:

- Clear correlation between fold change and p-values.
- Distinct expression patterns across genes.
- Pathway-specific clustering of genes.



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DISCUSSION

Interpretation and Rationale:

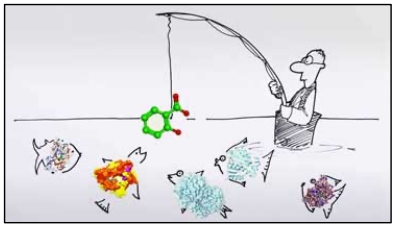
1. Pathway Analysis:

- Multiple metabolic pathways affected in COVID-19.
- Strong involvement of lipid and cholesterol metabolism.
- Significant role of oxygen sensing and sulfation pathways.

2. Clinical Relevance:

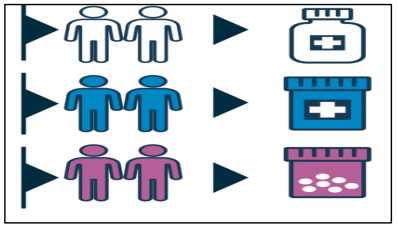
- DHCR24: Potential marker for immune response.
- ADO: Indicator for hypoxic conditions.
- AGPAT5/4: Markers for membrane integrity.

Target Identification



Therapeutic Applications

Patient Stratification



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LIMITATIONS

Limitations:

- Analysis based on gene expression data only.
- Need for protein-level validation.
- Need for experimental validation of predicted interactions.

Impact on Results:

- Findings need validation in larger datasets.
- Clinical significance requires further testing.
- Potential confounding factors are not addressed in the study.

CONCLUSIONS

Key Discoveries:

- Identified 10 significantly altered genes in COVID-19.
- DHCR24 shows highest upregulation (FC: 1.94).
- Multiple metabolic pathways affected.

Research Recommendations:

- Validation in larger patient cohorts.
- Proceed with protein-level studies.
- Clinical trials for therapeutic targeting.

Thank You

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