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High Expression of Electron Transport Chain Genes in Blood Cells of Patient with SARS-Cov-2 Infection

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Abstract

Transcriptome analysis has emerged as the go-to tool in the post-genomic era to perform unbiased comprehensive analysis of gene expression of many cell types and organisms. To this end, the next-generation sequencing powered RNA-seq technology is dominant, and provides many researchers with a powerful tool to interrogate gene expression at the whole-genome level. In this work, the RNA-seq transcriptome of blood cells of a 43 year-old male COVID-19 positive patient was analyzed with an in-house MATLAB transcriptome analysis software. Results emanating from a partial 10000 reads analysis reveal the high expression of electron transport chain genes in blood cells of patient with COVID-19. Genes include different subunits of NADH dehydrogenase and cytochrome c oxidase. Given electron transport chain important role in generating ATP for cells, it may be possible that high expression of electron transport chain genes may prime the immune cells to synthesize proteins and produce cytokines to mount an initial response to SARS-CoV-2 infection. Overall, RNA-seq transcriptome analysis of blood cells has illuminated that blood cells are primed for energy metabolism for possible powering of protein synthesis and cytokine production through activating expression of genes of the electron transport chain.

Keywords: Electron transport chain, SARS-CoV-2, RNA-seq, transcriptome analysis, blood cells.

Subject areas: Genomics, molecular biology, bioinformatics, computational biology, systems biology.

Gene expression analysis is the key tool for biologists to characterise the molecular fingerprint of cellular phenotypes as well as explore its mechanistic basis (Lowe et al., 2017). Transcriptome analysis technology has blossomed in the last decade to help reveal, in increasingly finer detail, the patterns in gene expression that underpins particular cellular behaviour (Chen et al., 2021; Kotliar et al., 2019). In this regard, RNA-seq enabled by next-generation sequencing technology is the dominant technology in the field (Hong et al., 2020; Stark et al., 2019; Wang et al., 2020; Marco-Puche et al., 2019).

This work uses published transcriptome data generated by RNA-seq to understand the gene expression pattern of blood cells of a 43 year-old male COVID-19 patient who tested positive through reverse transcriptase quantitative polymerase chain reaction (RT-qPCR). Transcriptome data was downloaded from Array Express (Accession number: E-MTAB-10022), while the annotated human genome was downloaded from Genbank. An in-house MATLAB transcriptome analysis software (Ng, 2021) was subsequently used to align a partial set of 10000 reads to genes in the human genome to help generate a map of the gene expression pattern of blood cells in patient with SARS-CoV-2 infection.

Results revealed high expression of electron transport genes in blood cells of the patient who tested positive for SARS-CoV-2 (Table 1). Specifically, different subunits of NADH dehydrogenase and cytochrome c oxidase were highly expressed. Given the role of the electron transport chain in generating ATP, there is a possibility that these genes were upregulated in expression in order to provide the energy currency needed for downstream protein synthesis and cytokine production. These steps are necessary for mounting an initial response against SARS-CoV-2 infection.

Gene	Product	Count
COX1	cytochrome c oxidase subunit I	78
ND1	NADH dehydrogenase subunit 1	52
ND4	NADH dehydrogenase subunit 4	51
ND2	NADH dehydrogenase subunit 2	44
ATP6	ATP synthase F0 subunit 6	28
CYTB	cytochrome b	26
COX3	cytochrome c oxidase subunit III	24
ND5	NADH dehydrogenase subunit 5	23
COX2	cytochrome c oxidase subunit II	20

Table 1: Partial RNA-seq transcriptome of blood cells of 43 year-old male patient with SARS-CoV-2 infection

From another perspective, there is also possibility that the resultant high expression of electron transport chain genes may be due to infection of blood cells by SARS-CoV-2. But, recent results that indicated lack of viral mRNA transcripts in blood cells of COVID-19 patient suggests that this is not a likely scenario (Ng, 2021). Hence, the earlier hypothesis of cellular upregulation of electron transport gene expression to help prepare a store of ATP to power protein synthesis and cytokine production for mounting an immune response against the virus may be more plausible.

Overall, gene expression analysis is usually the first tool for probing the mechanistic basis of an observed cellular phenotype, as well as providing the molecular information to link cellular behaviour to transcriptional activities. Application of RNA-seq transcriptome analysis to blood cells of COVID-19 patient reveal, in a partial analysis, that genes encoding the electron transport chain were highly expressed. Given the role of NADH dehydrogenase and cytochrome c oxidase in generating ATP, a plausible scenario in which blood cells are priming for protein synthesis and cytokine production with energy currency from ATP may be playing out at the cellular level to help mount an immune response against SARS-CoV-2 infection.

Conflicts of interest

The author declares no conflicts of interest.

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