25TH NATIONAL & 11TH INTERNATIONAL ANNUAL CONGRESS
ON RESEARCH AND TECHNOLOGY OF IRANIAN MEDICAL SCIENCES STUDENTS
URMIA UNIVERSITY OF MEDICAL SCIENCES, URMIA, IRAN

Bulk RNA Sequencing-Based Drug Repurposing in Systemic Lupus Erythematosus

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Citation:
Abdali N, Tahmasebian S, Vaghf A. Bulk RNA Sequencing-Based Drug Repurposing in Systemic Lupus Erythematosus. *Iranian biomedical journal* 2024; 28(7): 305.

ABSTRACT

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting many body organs, especially the skin, joints, blood, kidneys, and central nervous system. It is estimated that 14.6 to 50.8 cases of SLE per 100,000 women in the United States are of reproductive age, making it one of the most prevalent autoimmune illnesses in this group. Drug repurposing is a valuable substitute method for identifying drug uses. RNA sequencing, or RNA-seq, is one of the most effective techniques for determining the varied gene expression profiles of diseases in response to specific medications is.

Methods and Materials: Our study employed a computational drug repurposing pipeline to identify drugs based on differential gene expression signatures associated with SLE, derived from RNA-seq data. We compared the transcriptional profile of peripheral blood mononuclear cells from healthy controls and SLE patients using accession code GSE131525 from the Gene Expression Omnibus (GEO) database. Whole peripheral blood mononuclear cells were collected from blood samples of healthy subjects (n = 3) and SLE subjects (n = 3). B cells, $CD4^+$, $CD8^+$, and other T cells were processed and cryopreserved from each blood sample. Monocytes were isolated, resulting in 36 blood samples from healthy individuals and 36 from lupus patients, which were subsequently categorized into healthy and diseased groups for analysis. Differentially expressed genes (DEGs) between samples from subjects with SLE and healthy individuals were identified using GEO2R. Then, the Library of Integrated Network-Based Signatures (LINCS) database was used to discover potential drugs that could reverse the expression of DEGs. A review of significant literature and studies from DrugBank led to the selection of the top-ranked drugs with the highest *p* values. The study identified 250 genes commonly affected by the disease; among these, genes with $|\log2FC| \geq 1$ and a *p* value of ≤0.05 were classified as DEGs, comprising 128 up-regulated genes and 122 down-regulated genes.

Results: The RNA-seq data analysis showed that methocarbamol can effectively treat lupus. The medicine methocarbamol impacts the *CA* gene. When the gene network associated with this gene was constructed, it was observed that the *CA2* and *STAT4* genes were particularly closely linked to the gene; hence, medications that impact these two genes may also affect the *CA* gene.

Conclusion and Discussion: Methocarbamol is a central nervous system depressant that is prescribed in conjunction with rest and physical therapy to alleviate discomfort associated with various acute musculoskeletal conditions. Its mechanism of action may involve the inhibition of spinal polysynaptic reflexes, a reduction in neurotransmission within spinal and supraspinal polysynaptic pathways, and an extension of the duration cell resistance.

Keywords: Methods, RNA sequence analysis, Systemic lupus erythematosus