[BIOINFO 2024]

Differential Analysis of mRNA COVID-19 Vaccines in Muocarditis Patients through scRNA-seq and scATAC-seq Data

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This study aimed to investigate the differences in immune responses between recipients of two mRNA COVID-19 vaccines, Pfizer and Moderna, with a particular focus on understanding the mechanisms associated with the rare side effect of myocarditis. We concentrated on individual cell-level gene expression, underlying biological mechanisms, and chromatin accessibility patterns. To achieve this, we integrated single-cell RNA sequencing (scRNA-seq) and single-cell assay for transposase-accessible chromatin sequencing (scATAC-seq) to analyze the transcriptome profiles of peripheral blood mononuclear cells (PBMCs) from Pfizer and Moderna vaccine recipients, both before and after vaccination, as well as from individuals who developed myocarditis.

We employed Seurat and Signac for processing and analyzing scRNA-seq and scATAC-seq data. Cell type identification was initially performed using SingleR, followed by manual annotation based on additional reference datasets to ensure precise classification. For differential expression analysis, we compared gene expression between Pfizer and Moderna groups in T cells. Additionally, motif analysis and transcription factor identification were conducted using Signac and TRRUST to explore regulatory mechanisms linked to vaccine response.

Differential expression analysis identified higher expression of T cell-related genes, including key MHC Class I genes such as HLA-A, HLA-B, and HLA-C, in the Moderna group. Motif analysis revealed that the MA0162.4 transcription factor motif exhibited increased activation in the Pfizer group compared to the Moderna group, as demonstrated by chromVAR analysis. This indicates a higher binding potential of transcription factors associated with this motif in the Pfizer group. Furthermore, RNA expression analysis showed a significant elevation in EGR1 gene expression in the Pfizer group, further supporting the differential regulatory mechanisms between the two vaccine groups. Overall, our results suggest that while Moderna induces stronger T cell responses through MHC Class I gene expression, Pfizer may be more associated with transcription factor activation, particularly EGR1, which has been linked to cardiovascular diseases such as myocarditis.

These findings provide insights into gene expression changes induced by mRNA vaccination and

their potential connection to myocarditis and immune responses. Further investigation is needed to better understand these associations and improve strategies for preventing and managing myocarditis.