Mapping peripheral biological pathways associated with long-lasting effect of early life stress: a transcriptomic set-based approach

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Abstract

➢ Adversities in early life may leave long-lasting neurobiological alterations, increasing the risk of developing psychiatric disorders in later life.

➢ Emerging evidence has suggested that stress in early life can interfere with neuroendocrine and immunological cascades through genetic and epigenetic modifications, determining long-term consequences on brain morphology, functioning and behaviour.

➢ By using a transcriptomic approach, the aim of this study is to identify potential peripheral biological signatures associated with early life stress and the risk of developing mental disorders in a cohort of children and adolescents.

Keywords: Transcriptomics, Early life stress, Psychiatric disorders.

Methods

➢ Through a transcriptome approach, we analysed blood mRNA expression of a sample of 606 children and adolescents screened for high risk of developing mental disorders at two different time-points.

➢ After quality and concentration evaluation, RNA-Seq libraries were sequenced on a NextSeq2000 platform (Illumina).

➢ Bioinformatic analyses included a quality control of raw data using the FASTQC software and MultiQC tool. Raw reads were counted by using Salmon.

➢ Differential expression analysis was performed by DESeq2 (q-value < 0.1, FC cut-off of ± |1.2|), applying a preliminary filter to include only genes with a minimum count of 10 in the smallest experimental group.
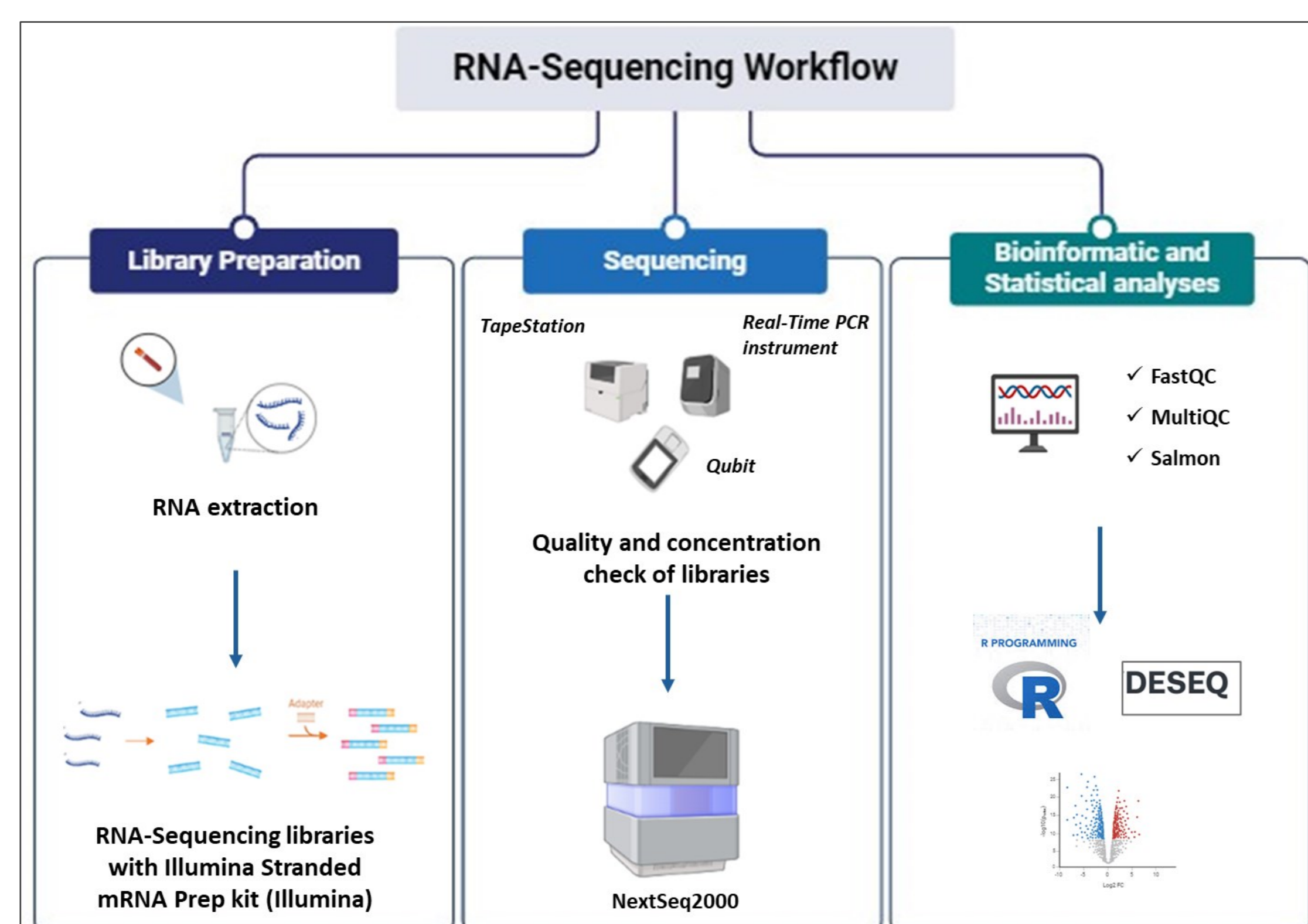

Results

➢ FASTQC Per Base Sequence Quality. The average quality for the nucleotide obtained a high score for most of our samples.

➢ Salmon Fragment Length Distribution. Most of our samples showed a similar and overlapping fragment length distribution. Percentage and million reads values were considered suitable for transcriptomic analyses.
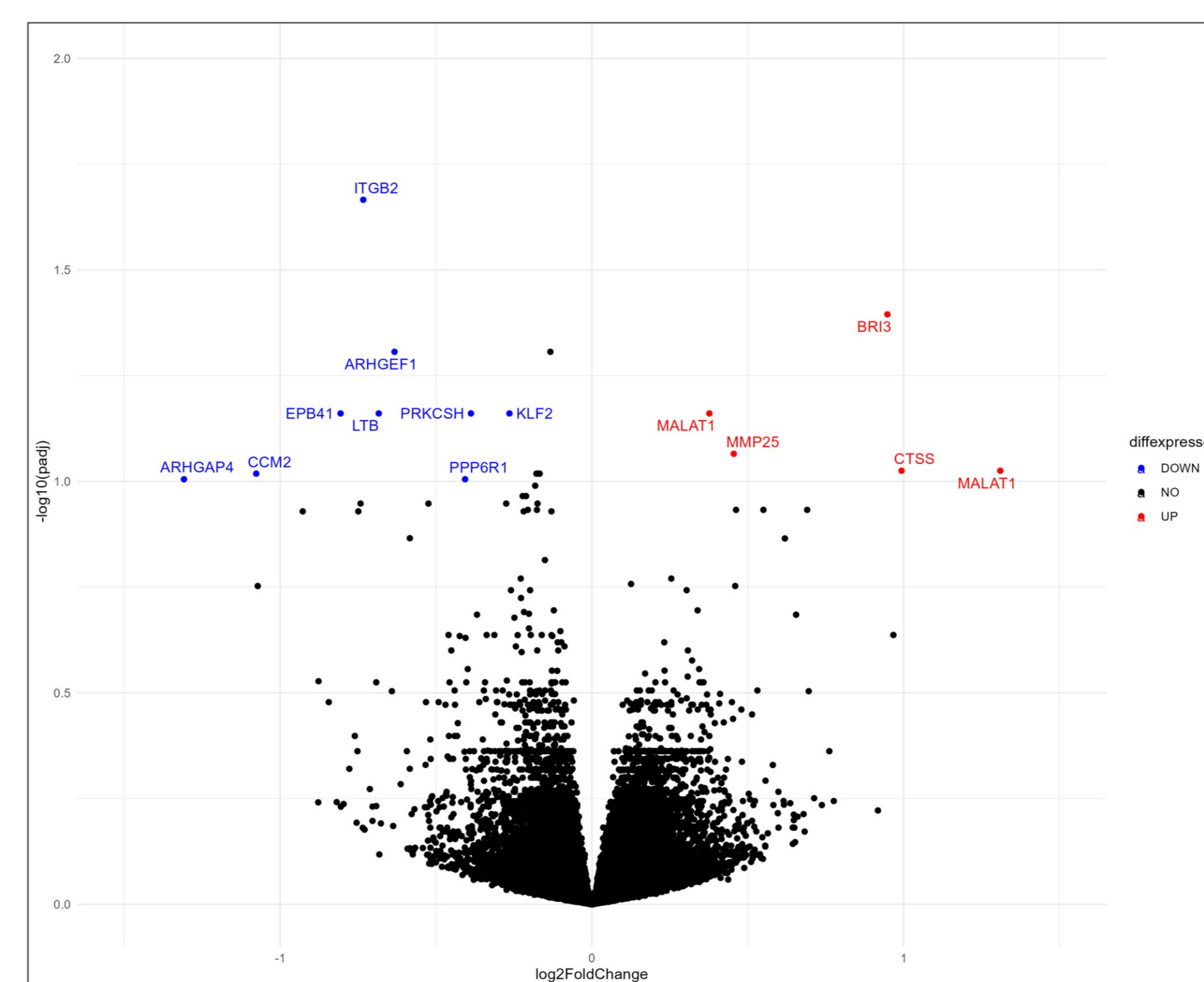
Volcano plot for the comparison _High Risk vs Random group _T0_

• 9 genes down-regulated
• 5 genes up-regulated
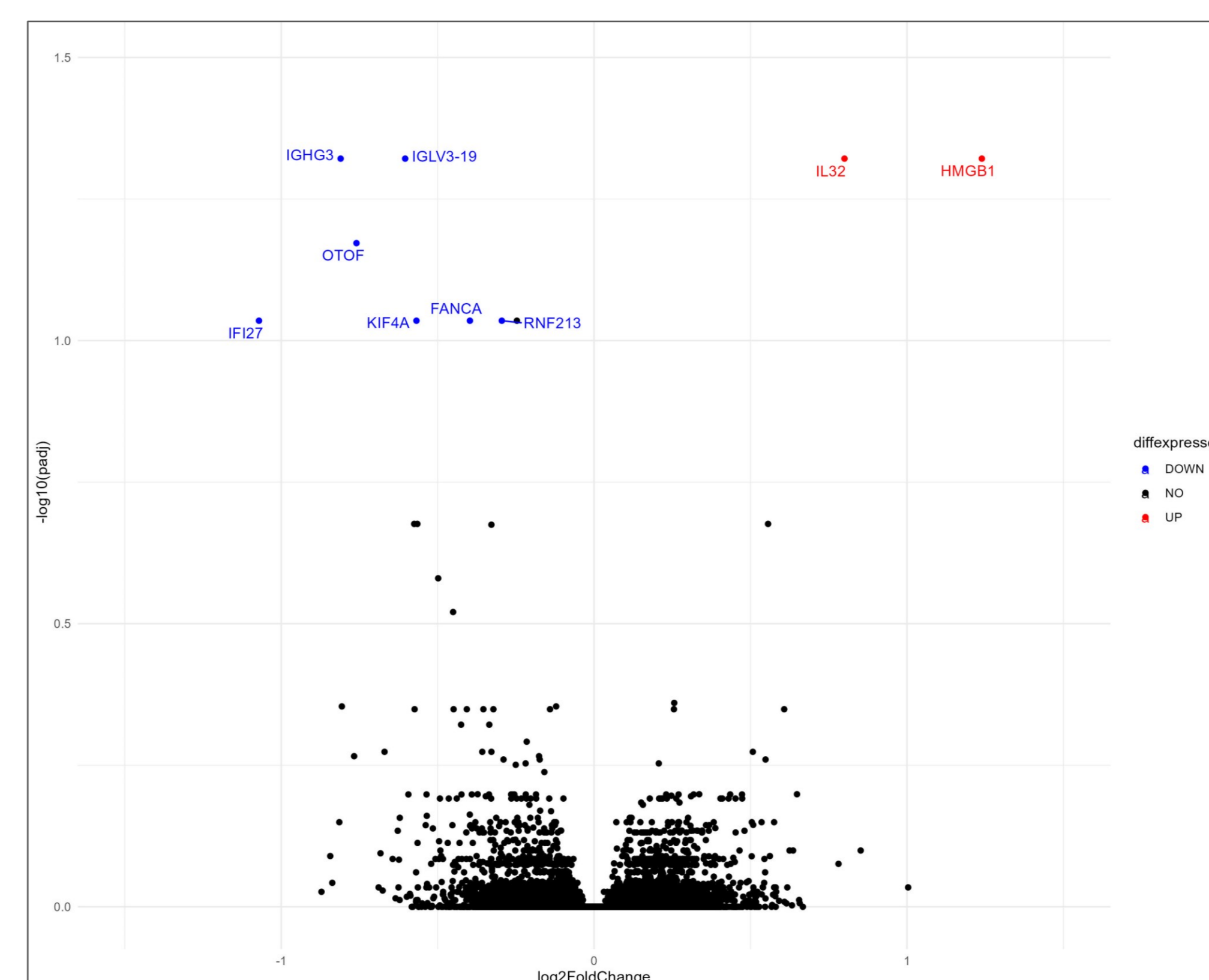
Volcano plot for the comparison _High Risk vs Random group _T1_

• 7 genes down-regulated
• 2 genes up-regulated

Conclusion

This study provides a specific transcriptomic workflow with related bioinformatic software for RNA-seq analysis, revealing significant changes in the gene expression in individuals with a high risk for psychiatric disorders compared to random group, both at baseline (T0) and at follow-up (T1).

These results may represent a first step toward a better understanding of the potential role of genes and biological pathways in the early development of psychiatric symptoms with the final goal of identifying novel biomarkers for effective therapeutic strategies.