

# Molecular signatures associated with lithium treatment in bipolar disorder patients - a transcriptomic approach

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## Introduction

Bipolar disorder (BD) is a severe psychiatric condition affecting 2.4% of the global population, leading to significant disability and an increased risk of suicide in young people. Lithium (Li) is the first-line treatment for BD, but its molecular mechanisms are not fully understood.

The R-LiNK project integrates clinical, biological, and neuroimaging data to study lithium's effects in BP. Within this framework, we applied differential expression (DE) and WGCNA analyses to explore Li's impact on the transcriptomic profiles of BD patients before (TP0) and after 3 months (TP3) of Li treatment.

## Methods

Blood samples from 127 BD patients were collected at TP0 and TP3. RNA was sequenced using the Illumina NextSeq2000 system.

Transcript quantification was performed with Salmon, and differential expression analysis was conducted with DESeq2 correcting for unwanted variation factors estimated by RUVg. Transcripts with a fold-change of  $\pm 1.2$  and a q-value  $< 0.1$  were classified as DE genes and used for pathway analysis with Ingenuity Pathway Analysis.

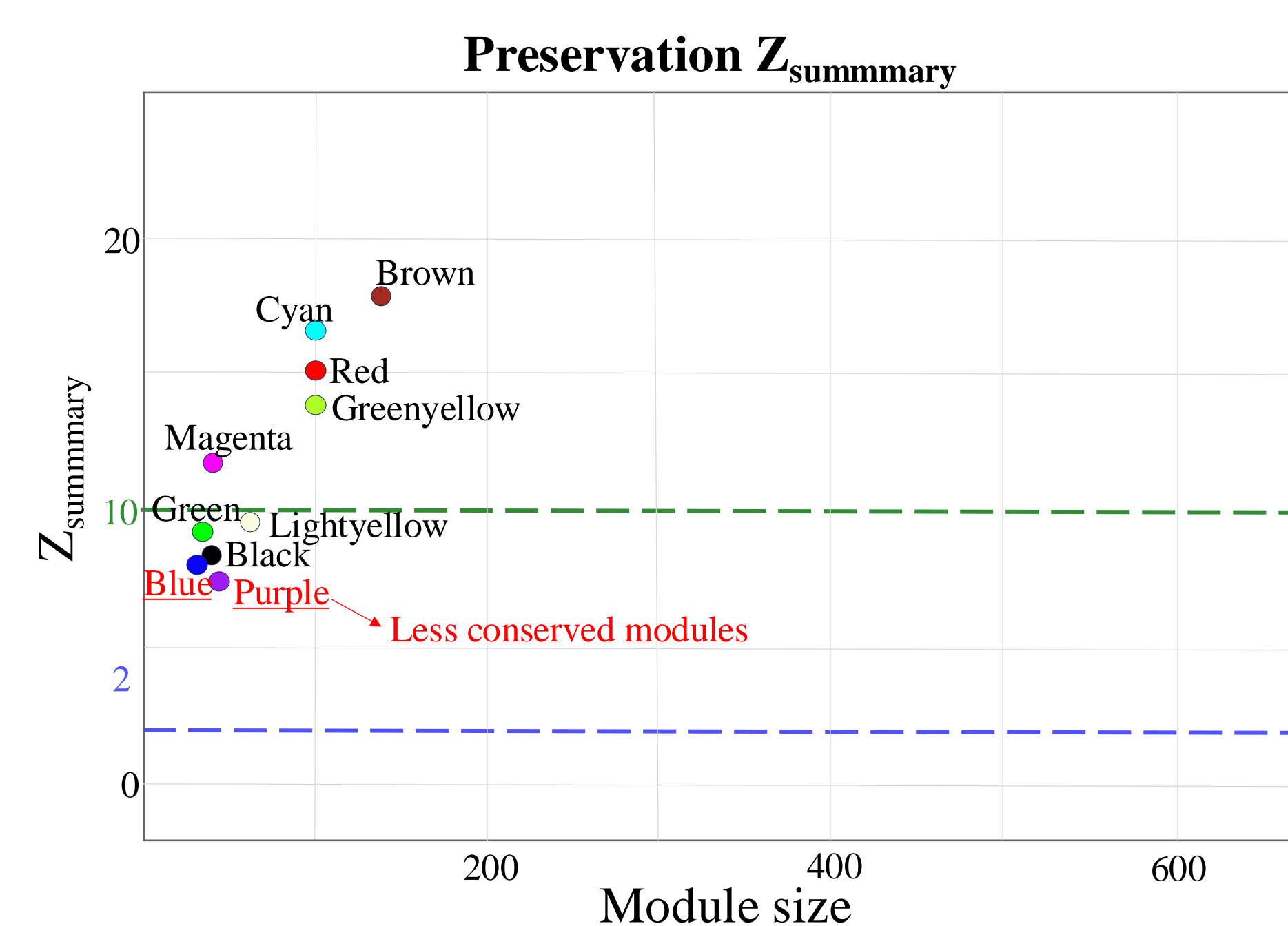
Weighted gene co-expression networks preservation analysis was performed using BioNERO, with the WGCNA algorithm. The TP0 data set was used as the training set, while TP3 served as the test set. The two least preserved modules, with Zsummary values in the range of 2 to 10, were used for further pathway analysis with Ingenuity Pathway Analysis (IPA).

## Results

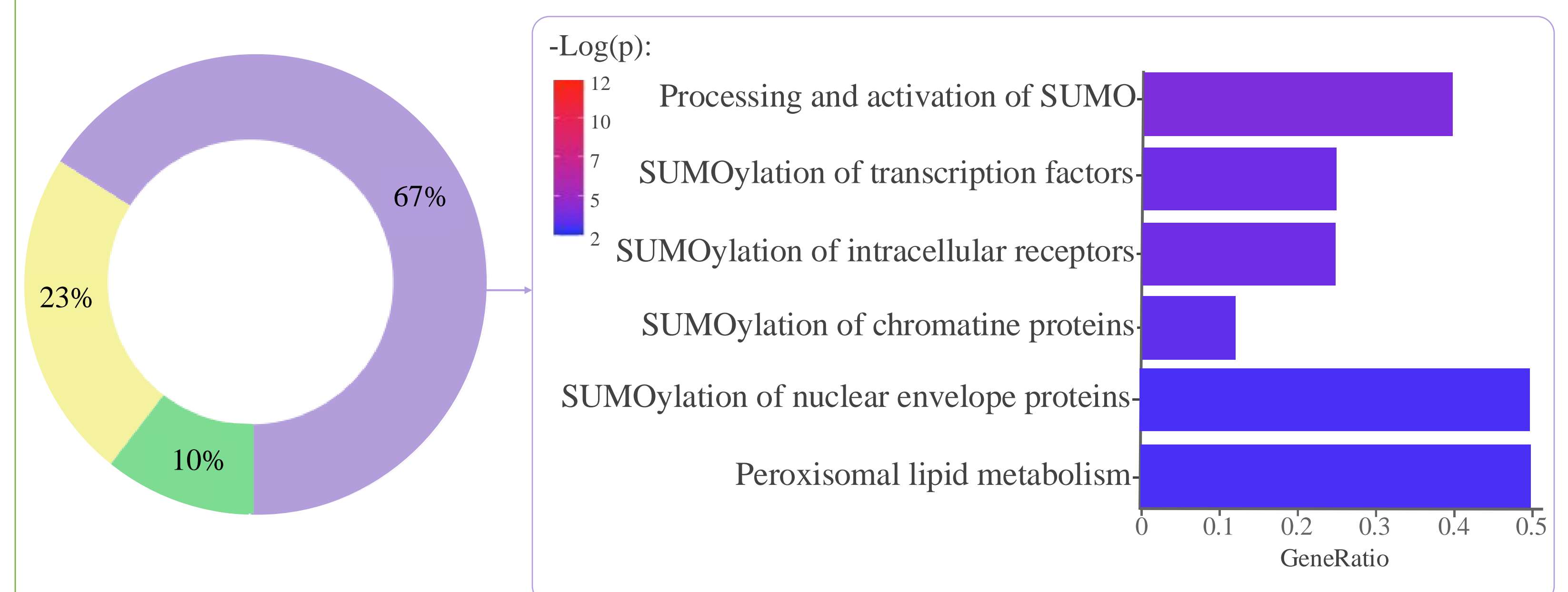
DE analyses showed that Lithium treatment reduced inflammation, inhibit metabolic pathways, and activate coagulation and blood-related pathways



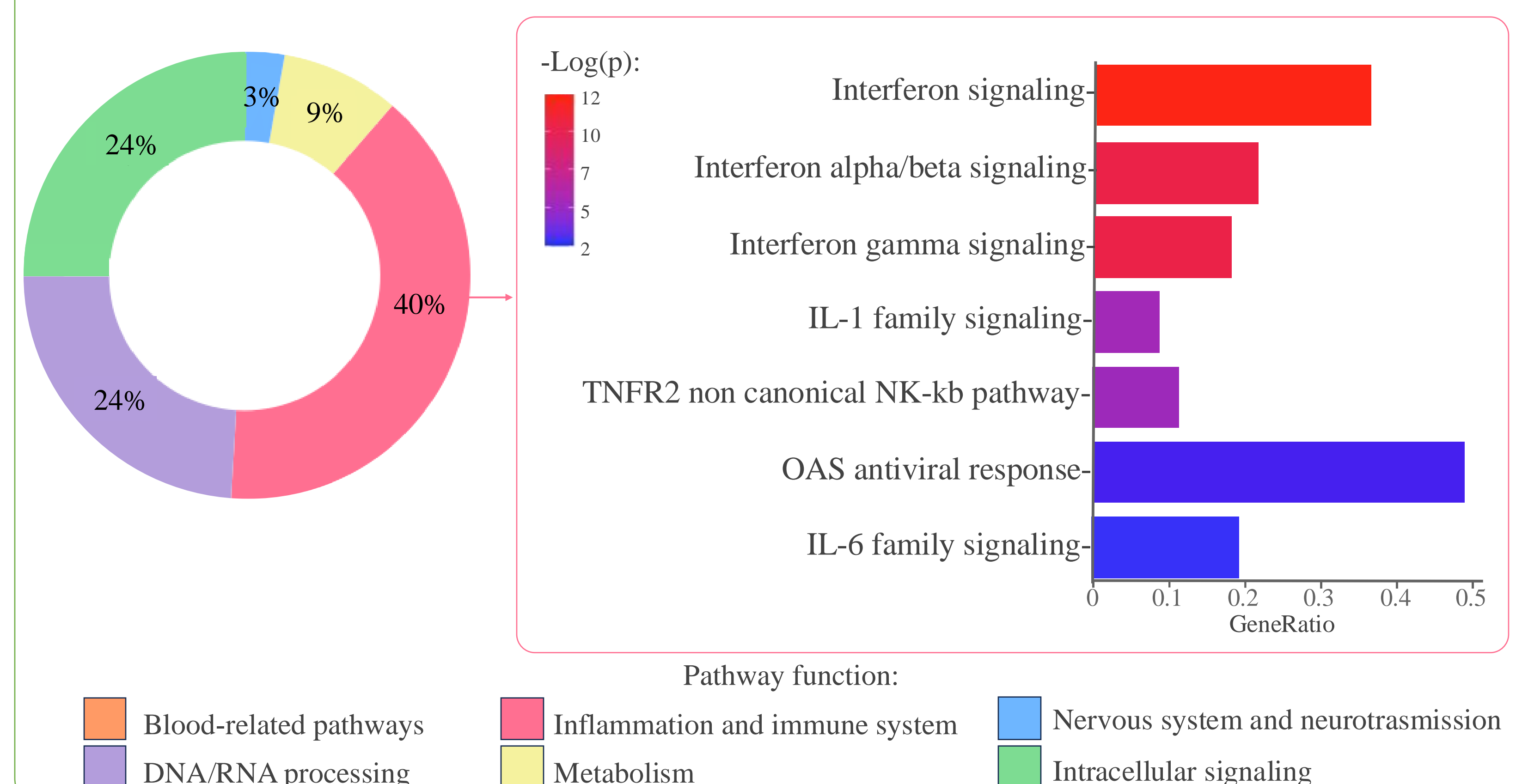
Preservation analysis



The blue module was associated with DNA/RNA processing pathways



The purple module was linked to inflammation



## Conclusion

These results suggested that lithium treatment might modulate the immune and the epigenetic systems. These effects might contribute to its mechanism of action and explain its therapeutic efficacy.

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