METFORMIN MODULATES ALTERNATIVE SPLICING THROUGH RNA PROCESSING PATHWAYS RELATED TO CODING AND LONG NON-CODING GENES

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Introduction and Objectives

Alternative splicing is a highly regulated process that generates multiple RNA isoforms from the same transcriptionally active region, and much of the eukaryote transcript diversity is related to it. Imbalances on the splicing mechanism are present in various human diseases and drugs for these diseases are known to act as modulators of that imbalance and to alter patient's gene expression.

Here we used results from publicly available high-throughput RNA-seq data of human hepatocytes treated with metformin, the first line oral therapy for type II Diabetes, to identify: metformin effects on the splicing machinery and differentially expressed spliced variants, especially those with a significant effect on gene expression compared to vehicle-control.

Methods

Transcript quantification

Splicing analysis

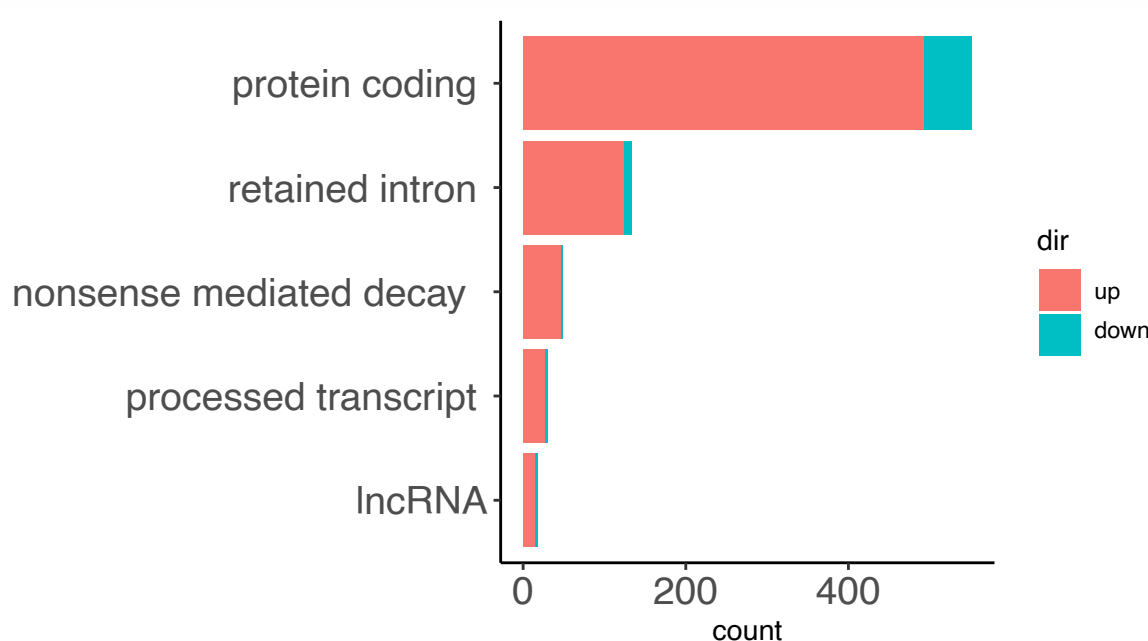Gene-set enrichment (GSE)

Network analysis

Results

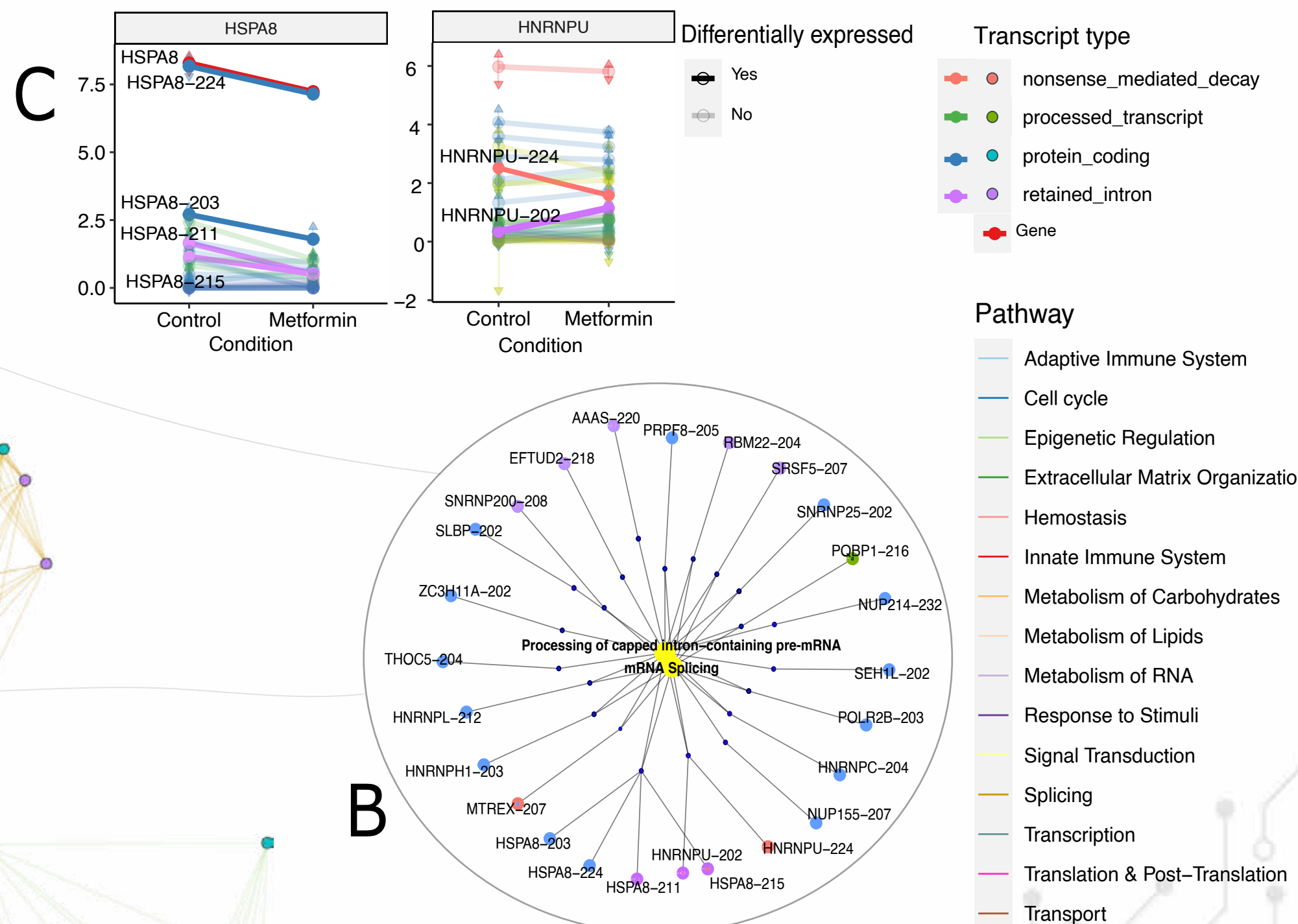Fig. 1: Quantification of all differentially expressed transcripts grouped by their type

Fig. 2: Network analysis of (A) all differentially expressed transcripts connected by their pathways. (B) Highlight of splicing related pathways, showing high number of transcripts with retained introns in those processes. (C) Transcript levels of two genes which are essential for tho splicing process, a isoform switch can be seen on the **right**.