Decoding Molecular Shifts in Late-Stage ALD: Opposing Gene Expression and Metabolic Trends Revealed Through RNA-Seq Analysis

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Purpose: Alcohol-related liver disease (ALD) is a leading cause of liver failure worldwide. This study aims to identify differentially expressed genes and affected biological pathways in late-stage liver transplant patients with ethanol-induced liver damage, providing new insights into the molecular mechanisms underlying disease progression. Procedure: RNA-Seq analysis was performed on liver tissue samples from 5 ALD patients and 5 healthy controls. Raw sequencing data was processed using the GreatLake supercomputer for alignment and quantification. Differential gene expression analysis was conducted using DESeq in R, followed by Gene Set Enrichment Analysis (GSEA) for GO term pathway exploration. Observations/Data/Results: Thousands of differentially expressed genes (DEGs) were identified. Notably, SAA and S100 gene families were downregulated in patients—contrary to previous literature. GO term analysis revealed that metabolic pathways were predominantly downregulated, while developmental processes were upregulated in the patient group, suggesting a shift in biological priorities during late-stage disease. Conclusions: Our findings reveal unexpected gene regulation patterns in ethanol-induced liver disease and suggest a potential reprogramming of metabolic and developmental pathways during advanced stages. These insights may refine future diagnostic and therapeutic approaches for ALD.

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