Integrative Network Biology Identifies Shared Transcriptional and miRNA Regulatory Hubs Linking Liver and Pancreatic Dysfunction in Metabolic Disease

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Abstract

Type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease (NAFLD), and dyslipidemia share common pathological mechanisms, including chronic inflammation, insulin resistance, extracellular matrix remodelling, and endothelial dysfunction, yet their integrated molecular signatures are not fully defined. In this study, an integrative bioinformatics approach was employed to identify shared molecular markers across these metabolic diseases. A tissue-specific gene co-expression network analysis of liver and pancreatic gene data was performed to identify common hub genes, followed by the construction of gene-miRNA and transcription factor (TF) regulatory networks using a network analyst. ICAM1 and COL3A1 were identified as key hub genes commonly dysregulated in liver and pancreatic tissues, implicating their roles in inflammatory and fibrotic processes respectively. Gene-miRNA network analysis identified hsa-miR-335-5p and hsa-miR-26b-5p as central regulators on the basis of node degree filter. Across NAFLD, T2DM, and dyslipidemia, dysregulated miRNA expression patterns were observed with hsa-miR-335-5p consistently upregulated and hsa-miR-26b-5p consistently downregulated. Additionally, TF-gene interaction analysis identified RELA, NFKB1, and SP1 as key transcriptional regulators, with NFKB1 and RELA influencing ICAM1 expression and SP1 regulating COL3A1 expression. These findings highlight the shared regulatory networks underlying metabolic diseases and suggest that ICAM1, COL3A1, and their associated miRNAs may represent potential biomarkers and therapeutic targets for integrated metabolic disease management.

Keywords

Dyslipidemia, miRNA, Non-alcoholic fatty liver disease, Transcription factor, Type 2 diabetes mellitus.