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MiRNA-dependent regulation of ERBB signaling pathway genes in patients with NASH

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NAFLD occupies a leading position among internal diseases, and its prevalence among adult population of Russia is 37 %. The development of NAFLD is associated with obesity, type 2 diabetes, dyslipidemia, and metabolic syndrome. Recently, there is increasing evidence for the role of miRNA in the development of metabolic disorders.
In our study, we first comprehensively analyzed the miRNA profile in NAFLD. Screening of miRNAs in the blood serum of the studied patients revealed that miRNAs are differentially expressed at different stages of NAFLD. MiRWalk algorithms were used to identify genes potentially deregulated by differentially expressed miRNAs and to functionally enrich (GSEA) the obtained gene sets using the KEGG and REACTOME databases. One of the pathways yielded was the ERBB signaling pathway, which leads to the mobilization of various metabolic pathways. A total of 58 ERBB pathway genes were predicted to be targets of miRNAs that are elevated in NASH patients. Of particular interest are ERBB4 and its ligand NRG4, which are most likely targeted by miRNA-15b, miRNA-222-3p, miRNA-423-5p, and mir-23a-5p. Investigating the mechanisms of the little-studied miRNA-dependent regulation of the ERBB signaling in the liver is important for finding new participants in the pathogenesis of liver diseases and/or their diagnostic markers.
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