Circulating Exosomal miRNAs Involved in the Pathogenesis of Children's Nonalcoholic Steatohepatitis

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Abstract

Background: The incidence of children non-alcoholic fatty liver disease (NAFLD) increased rapidly paralleled with the global burden of obesity and diabetes. Although most patients are nonalcoholic fatty liver, there are still a small part of them will progress to nonalcoholic steatohepatitis (NASH), fibrosis and cirrhosis. However, the diagnosis of NASH is based on the highly invasive tissue biopsy, so reliable circulating biomarkers are urgently needed. Exosomal miRNAs have attracted attention to provide further insights into NASH, and it may serve as biomarkers of children NASH.

Methods: Circulating exosomes were isolated from children diagnosed as NASH (n=3) and age matched health control (n=3) according to the protocol of RiboTM Exosome Isolation Reagent (for plasma or serum). Illumina HiSeqTM 2500 was performed to analyze the differential expression of exosomal miRNAs between the two groups. Bioinformatics analysis was applied to identify the molecular signature differences and search for potential biomarkers.

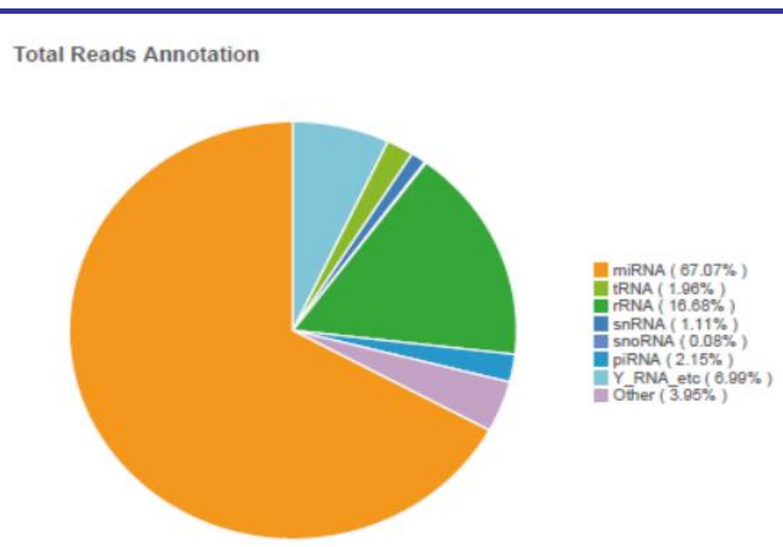


Figure 1. RNA distribution in exosomes

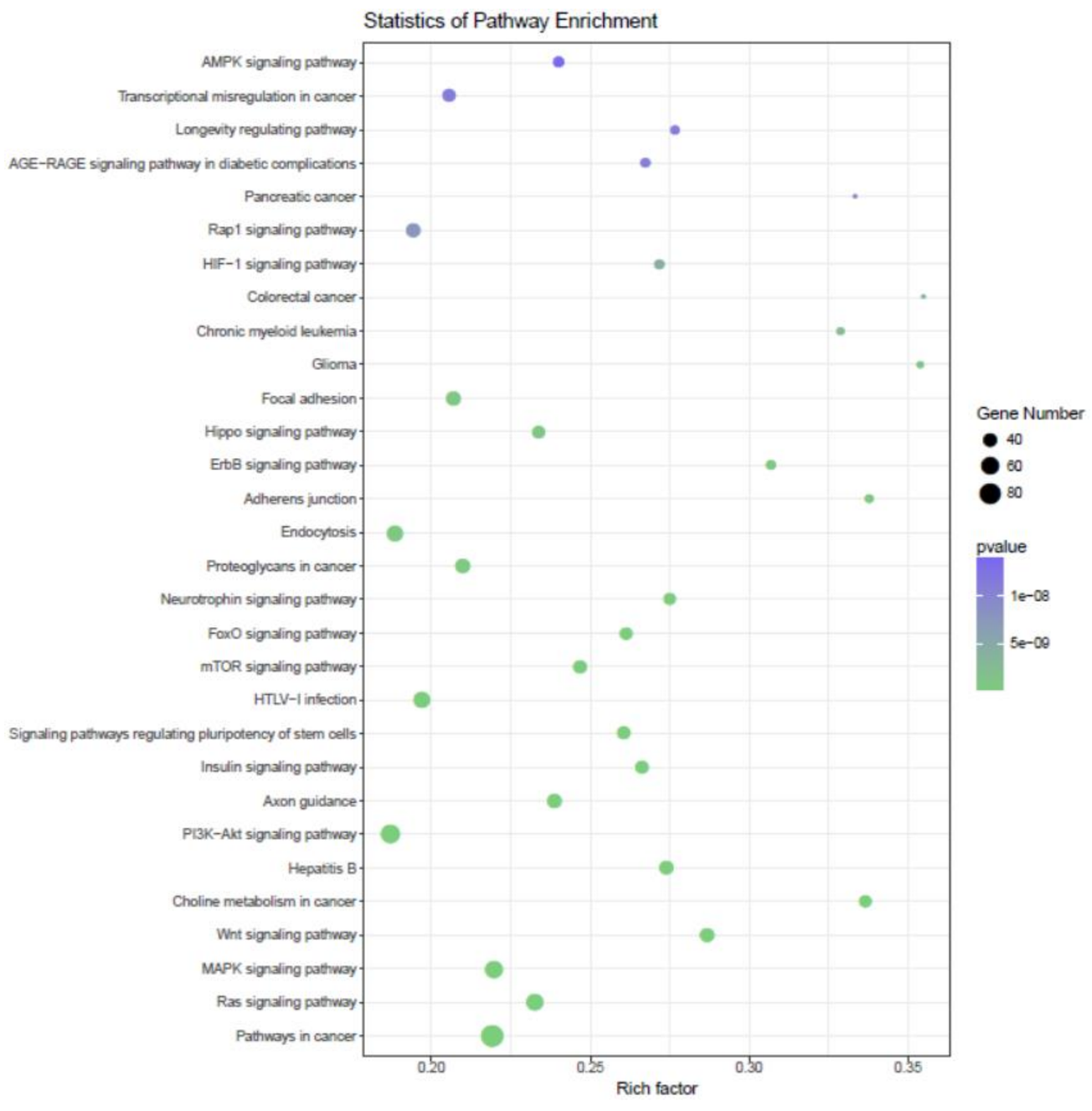
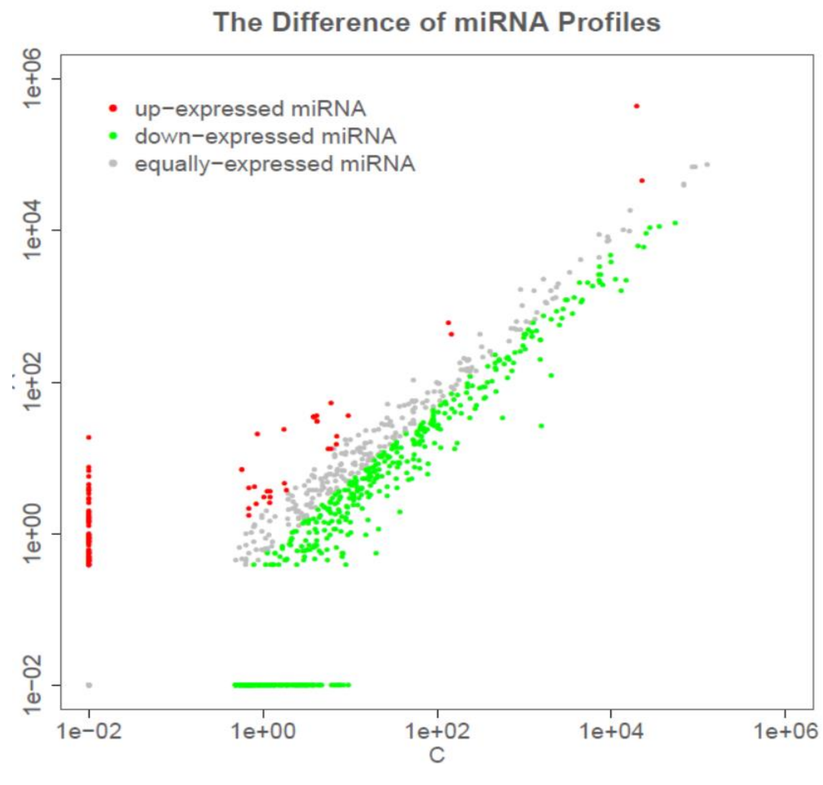


Figure 3. Keeg pathway analysis



Fgure 2. The differential expression of exosomal miRNAs between NASH and normal controls

Results: Exosomes were validated by NTA and flow cytometry (CD81 and CD63). With Illumina HiSeqTM 2500, 40 miRNAs were differentially expressed (| log2(fold change) | ≥1, P<0.05). Among which, miRNA122 was up-regulated while miRNA133a-5p was down-regulated most significantly. Gene Ontology (GO) annotation analysis showed these miRNAs involved in biological process, cellular components and molecular function. Pathway analysis revealed that PI3K−Akt signaling pathway, pathways in cancer and MAPK signaling pathway were significantly correlated with NAFLD.

Conclusions: 40 differentially circulating exosomal miRNAs were identified between NASH and health control group, which may involved in the pathogenesis of NASH and can be used as a potential biomarker for diagnosis of children NASH.

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