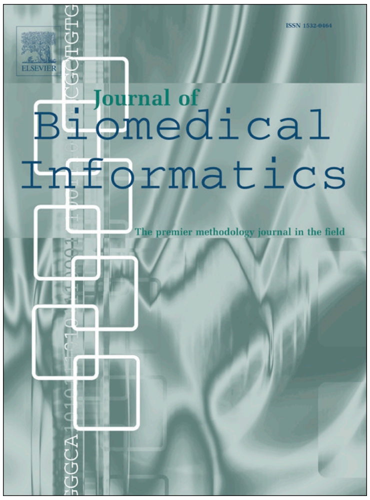

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miR2Pathway: A Novel Analytical Method to Discover MicroRNA-mediated Dysregulated Pathways Involved in Hepatocellular Carcinoma

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Abstract

MicroRNAs (miRNAs) are small, non-coding RNAs involved in the regulation of gene expression at a post-transcriptional level. Recent studies have shown miRNAs as key regulators of a variety of biological processes, such as proliferation, differentiation, apoptosis, metabolism, etc. Aberrantly expressed miRNAs influence individual gene expression level, but rewired miRNA-mRNA connections can influence the activity of biological pathways. Here, we define rewired miRNA-mRNA connections as the differential (rewiring) effects on the activity of biological pathways between hepatocellular carcinoma (HCC) and normal phenotypes. Our work presented here uses a PageRank-based approach to measure the degree of miRNA-mediated dysregulation of biological pathways between HCC and normal samples based on rewired miRNA-mRNA connections. In our study, we regard the degree of miRNA-mediated dysregulation of biological pathways as disease risk of biological pathways. Therefore, we propose a new method, miR2Pathway, to measure and rank the degree of miRNA-mediated dysregulation of biological pathways by measuring the total differential influence of miRNAs on the activity of pathways between HCC and normal states. miR2Pathway proposed here systematically shows the first evidence for a mechanism of biological pathways being dysregulated by rewired miRNA-mRNA connections, and provides new insight into exploring mechanisms behind HCC. Thus, miR2Pathway is a novel method to identify and rank miRNA-dysregulated pathways in HCC.

Keywords: Topological analysis, PageRank, Biological pathways, MicroRNAs, Hepatocellular carcinoma, miR2Pathway

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