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Identification of critical TF-miRNA-mRNA regulation loops for colorectal cancer metastasis

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ABSTRACT. To explore the potential cause of colorectal cancer metastasis, gene expression profiles, GSE21510, and miRNA expression profiles, GSE48074, were downloaded from the Gene Expression Omnibus database. Differentially expressed genes in metastatic colorectal and non metastatic colorectal cancer compared with the normal samples were identified via the limma package in R. The differentially expressed miRNAs in colorectal cancer samples with lymph node metastasis compared with those without lymph node metastasis were screened out by the some method. Differentially expressed genes that were upregulated in colorectal cancer samples with distant metastasis in comparison to that in samples without distant metastasis and normal samples were considered to play important roles in colorectal cancer metastasis. Functional enrichment analysis of these genes was conducted using the Database for Annotation, Visualization, and Integrated Discovery v6.7. Biological processes related to cell differentiation and cell proliferation were significantly enriched. TF (transcription factor)-miRNA-mRNA regulation loops were constructed by using the starBase and ChIPBase databases. Finally, six critical regulation loops were screened out. They were composed of two

TFs, two miRNAs, and three mRNAs. Some of these TFs, mRNAs, or miRNAs have previously been identified as critical targets in colorectal cancer metastasis. Additionally, several new targets were identified in our study, which may be helpful to improve metastatic colorectal cancer treatment.

Key words: ChIPBase; Colorectal cancer; DAVID; TF-miRNA-mRNA; Gene Expression Omnibus; StarBase