HCC-DERIVED MICROVESICLES ENRICHED IN ABNORMAL MIRNAS TARGETING CHROMOSOME OPEN READING FRAME GENES

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Aim: Hepatocellular carcinoma (HCC) is one of the most common malignancies. Microvesicles (MVs) are nano-particles shed by various cell types including tumor cells. MicroRNAs (miRNAs) within MVs in body fluids of HCC patients are rarely investigated.

Methods: Blood samples were obtained from HCC patients and healthy donors in Wuhan Union Hospital, Tongji Medical College, Huazhong University of Science and Technology from May to September in 2011. Our study was approved by the Ethics Committee of our University and all subjects signed informed consent. We determined miRNA expression profiles of HCC-derived MVs using Agilent miRNA microarray analysis. Putative target genes were predicted by bioinformatic software.

Results: We identified numerous dysregulated miRNAs in MVs from HCC patients compared with normal controls by microarray analysis. Specifically, 115 up-regulated and 127 down-expressed miRNAs were present in HCC-MVs, separately. Then, we analyzed putative target genes of the aberrantly expressed miRNAs by bioinformatic methods. We found that 802 chromosome open reading frame (Corf) genes were regulated by 101 altered MVs miRNAs, indicating that HCC-MVs were enriched with distinct sets of dysregulated miRNAs targeting Corf genes. It was worth noting that plenty of Corf genes were targeted by the same dysregulated MVs miRNAs, such as 419 Corf genes targeted by miR-940. Also, many abnormally expressed miRNAs targeted one Corf gene, such as 38 miRNAs targeted chromosome 1 open reading frame 116 (C1orf116). These findings showed that Corf genes were active and complex in HCC-MVs. It was reported that some members of Corf genes were involved in tumor development. For instance, miR-1182 targeted chromosome 6 open reading frame 61 (C1orf61) which was involved in tumorigenesis and metastasis. C1orf61 was up-regulated in hepatic cirrhosis tissues and was further up-regulated in primary HCC tumors. In addition, chromosome x open reading frame 66 (CXorf66) targeted by miR-1290 was abnormally up-regulated in leukemia, and was down-regulated in liver and prostate cancer.

Conclusions: In conclusion, we demonstrated for the first time that HCC-MVs were enriched with dysregulated miRNAs targeting Corf genes, indicating that miRNAs regulating Corf genes were active in HCC-MVs. And these Corf genes were complex and might function together in HCC.

Disclosure: All authors have declared no conflicts of interest.