P.A50

Profiling of miR-98-5p, miR-130a-3p, and miR-1246 levels in tissue and liquid biopsies of patients with hepatocellular carcinoma

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Hepatocellular carcinoma (HCC) is the most common primary liver malignancy. Its non-invasive early diagnosis and prognosis remain challenging partially due to the lack of reliable circulating biomarkers. Recently, the content of extracellular vesicles (EVs), particularly miRNAs, has emerged as a source of candidate biomarkers.
To identify novel molecular indicators for early diagnosis and prognosis in HCC patients we have performed RNA-seq analysis on plasmatic EVs from a discovery cohort consisting of 10 healthy individuals, 10 patients with liver cirrhosis, and 10 HCC patients. Among the miRNAs detected at different levels across the three groups, we selected miR-98-5p, miR-130a-3p, and miR-1246 for further investigations. Their levels have been determined by droplet digital PCR (ddPCR) in an independent validation cohort of 20 HCC patients, 20 patients with cirrhosis and 20 healthy individuals. Quantification was performed in plasmatic EVs, plasma, peritumoral and tumoral tissues obtained from biopsy specimens.
In plasmatic EVs, miR-98-5p was significantly upregulated in HCC patients compared to cirrhotic patients. miR-1246 showed a similar trend. In tissue biopsies, miR-130a-3p was downregulated in HCC tissues compared to peritumoral tissues, while miR-98-5p and miR-1246 showed comparable levels. Notably, miR-98-5p and miR-130a-3p levels in EVs positively correlated with their expression levels in tissue biopsies. These results may suggest that miR-98-5p and miR-130a-3p levels in EVs are at least partially released by hepatic tissue. Furthermore, miR-130a-3p displayed a significant inverse correlation between tissue expression levels and plasma levels, as well as between plasmatic EVs and plasma levels. These results may support the hypothesis that miR-130a-3p is preferentially secreted into the circulation by hepatic tissue *via* EVs.
In conclusion, our results would indicate that miR-98-5p, miR-130a-3p, and miR-1246 may cover potential translational role in HCC.