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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 cancer, and its non-invasive early diagnosis and prognosis remain challenging partially due to the limited availability of reliable circulating biomarkers. Extracellular vesicles (EVs), particularly their miRNA cargo, have recently emerged as promising candidate biomarkers.
To identify novel molecular indicators for HCC, RNA-sequencing was performed on plasmatic EVs from a discovery cohort of 10 healthy individuals, 10 patients with cirrhosis, and 10 HCC patients. Among the miRNAs at significant different levels, miR-98-5p, miR-130a-3p, and miR-1246 were selected for validation. Their levels were quantified by droplet digital PCR (ddPCR) in an independent cohort of 29 HCC patients, 30 cirrhotic patients, and 20 healthy subjects. Quantitation was performed in plasmatic EVs, plasma, peritumoral and tumoral tissues obtained from biopsy specimens.
In plasmatic EVs, miR-130a-3p and miR-98-5p were significantly downregulated in HCC patients compared to healthy subjects, whereas miR-1246 was markedly upregulated in HCC patients respect to cirrhotic patients. In tissue biopsies, miR-130a-3p was reduced in HCC tissues compared to peritumoral, while miR-98-5p and miR-1246 showed the opposite trend. In plasma, all three miRNAs were significantly elevated in HCC patients compared to those with liver cirrhosis. Notably, higher plasmatic levels of miR-130a-3p and miR-1246 were associated with improved overall survival. Patients with histological grade 2 tumors exhibited higher levels of miR-130a-3p than those with grade 3 tumors, and individuals without relapse showed increased miR-1246 levels compared to relapsed cases. Likewise, elevated plasma miR-98-5p correlated with prolonged disease-free survival.
These findings suggest that miR-98-5p, miR-130a-3p, and miR-1246 may act as potential biomarkers and they might contribute to stratify the patients with different outcome, prognosis and clinical features.