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Introduction: Hyper-functional platelets are increasingly recognized as important players in cancer progression and metastasis and have been proposed as potential therapeutic target in multiple types of cancers. Whether this could be considered in patients with cirrhosis and hepatocellular carcinoma (HCC) is currently unknown as platelet function in these patients has not yet been investigated.
Aim: To evaluate platelet function in patients with cirrhosis and HCC.
Materials and Methods: Patients with cirrhosis with and without HCC were prospectively recruited over a 6 months period. Platelet aggregation, a marker of platelet function, was assessed by impedance whole blood aggregometry with adenosine diphosphate (ADP), arachidonic acid (ASPI), and thrombin receptor agonist peptide (TRAP) stimulation.
Results: One-hundred patients with cirrhosis were recruited (50 with and 50 without HCC). As shown in the table, severity of cirrhosis and platelet count were comparable between the groups. Patients with HCC demonstrated higher ADP-, ASPI-, and TRAP- induced platelet-aggregation, all indicative of platelet hyper-function. Remarkably, HCC-driven platelet hyper-function was confirmed after adjusting the analysis for severity of cirrhosis and thrombocytopenia.
Conclusion: In patients with cirrhosis, HCC is associated with a significantly increased platelet aggregation. Further studies are required to evaluate whether inhibition of hyper-functional platelets can mitigate HCC-related morbidity and mortality in patients with cirrhosis.

	HCC (n=50)	No HCC (n=50)	
Age, years	65 (58-69)	61 (55-71)	
Male gender, %	80	66	
Child class A/B/C, %	46/36/18	58/26/16	
MELD	11 (8-16)	10 (8-14)	
Platelet count*, x10^9/L	90 (64-124)	110 (67-140)	
Alpha-fetoprotein, ng/mL	9 (4-47)	3 (2-4)	
History of previous treatment(s) for HCC, %	45	-	
Multinodular, %	68	-	
Total tumor volume, cm^3	9 (5-16)	-	
BCLC staging 0/A/B/C/D, %	10/19/57/8/6	-	
			p value
Platelet aggregation, AUC			
ADP	45 (35-68)	28 (18-43)	<0.001
ASPI	47 (29-62)	28 (18-45)	<0.001
TRAP	85 (66-121)	75 (52-94)	0.01

Median values reported with 25th and 75th percentile values in parenthesis.
Abbreviations: MELD: Model for End-Stage Liver Disease; HCC: hepatocellular carcinoma; BCLC: Barcelona Clinic Liver Cancer; AUC: area under curve.
*When patients with and without HCC were matched according to Child class, those with HCC demonstrated a significantly higher platelet count in Child A and B but not in Child C class.

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Circulating microRNA-23b-3p and tissue microRNA-193a-3p as promising molecular biomarkers in human hepatocellular carcinoma

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MicroRNAs (miRs) are small non-coding RNAs that act mainly as negative regulators of gene expression. The dysregulation of miRs is clearly implicated in cancer. Because of their release and stability in body fluids (*i.e.* serum and plasma), miRs have received growing attention as biomarkers in cancer, including hepatocellular carcinoma (HCC). Recently, we have demonstrated that miR-193a-3p and miR-23b-3p exert a tumor-suppressor role in HCC. Here, we shifted our attention from the biological to the potential clinical significance of miR-193a-3p and miR-23b-3p exploring their diagnostic and prognostic value in HCC. The expression levels of miR-193a-3p and -23b-3p resulted significantly down-regulated in primary HCCs compared to their matched peritumoral (PT) counterparts in a cohort of HCC patients (n=67, n=59, respectively) as indicated by stem-loop qPCR results. Interestingly, high miR-193a-3p level in HCCs was associated with longer OS and DFS of patients. It is known that the expression of miRs can be regulated by DNA methylation and the alteration of this epigenetic mark may occur in cancer. For this purpose, we verified the DNA methylation level of the CpG islands identified near the miRs coding sequences using the methylation-specific PCR. An inverse trend between miR-23b-3p (but not miR-193a-3p) expression and DNA methylation was observed in a subset of 30 HCC cases and cells. Finally, to explore the potential role of these miRs as circulating biomarkers of HCC, we used the droplet digital PCR for the detection of miR-23b-3p and miR-193a-3p in the plasma from HCC patients (n=25) and healthy subjects (n=37). The plasmatic level of miR-23b-3p was significantly lower in HCC patients respect to controls and it was associated with tumor grading; while miR-193a-3p resulted undetectable in the plasma samples. Further analyses are ongoing to investigate the potential role of circulating miR-23b-3p as a non-invasive biomarker of response to therapy in HCC patients.

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Copper chelation as a new treatment strategy to counteract hepatocellular carcinoma

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Introduction: Hepatocellular carcinoma (HCC) represents the third most frequent cause of cancer death. HCC carries an extremely poor prognosis since it is often diagnosed at advanced stages, restricting efficient therapeutic options to either surgical resection or transplantation. Hence, it is urgent to develop new and more effective therapeutic strategies to defeat HCC.
Biometals, in particular copper, are emerging as important regulators of several physiological and pathological processes,