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Circulating ncRNAs as promising non-invasive molecular biomarkers of HCC

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Human hepatocellular carcinoma (HCC) is the most frequent primary tumor of the liver and is the third cause of cancer-related deaths. The prognosis of HCC is poor and thus the identification of novel molecular biomarkers for the early diagnosis in at-high risk patients is needed. Circulating ncRNAs (including lncRNAs and miRNAs more and less than 200 nt long respectively) have been detected in different human body fluids, including serum, plasma and urine. In order to identify promising circulating diagnostic molecular biomarkers, we measured the levels of selected ncRNAs in plasma from HCC patients. We previously found that miR-23b-3p resulted down-regulated in HCC tissues respect to their matched peri-tumoral (PT) counterparts. Here, we found that the levels of plasma circulating miR-23b-3p measured by ddPCR were significantly lower in HCC patients (n=25) respect to healthy subjects (n=37) and the ROC analysis displayed a discrete capability of miR-23b-3p to discriminate HCC from controls individuals (AUC=0.67; p=0.019). The same trend of dysregulation was observed for plasma circulating miR-126-3p, that we previously found significantly down-regulated in primary HCCs. The ROC curve analysis performed on 25 controls and 25 HCC patients supported the diagnostic potential of circulating miR-126-3p (AUC= 0.78; *P*-value= 0.0007). In the same cohort, the expression levels of the tumor suppressor lncRNA GAS5 were significantly lower in HCC patients compared to healthy subjects. The ROC curve analysis evidenced a good diagnostic potential of GAS5 (AUC= 0.72; *P*-value= 0.007). Finally, a preliminary study conducted on a small cohort of patients treated with sorafenib (an oral multikinase inhibitor used to treat the advanced HCC) evidenced that miR-23b-3p and miR-126-3p could be possible circulating biomarkers for the prediction of resistance and response to sorafenib. In conclusion, our results contribute to identify potential novel non-invasive biomarkers of diagnosis and response to therapy in liquid biopsies of HCC patients.