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NON-CODING RNAs AS EMERGING BIOMARKERS FOR HUMAN DISEASES:

NEW INSIGHTS AND ANALYTICAL STRATEGIES

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MiR-193a-3p and miR-23b-3p in human hepatocellular carcinoma: from biological function to potential biomedical application

Grossi I.[1], *Ferracin M.*[2] *, Guerriero P.*[3], *Negrini M.*[3], *Manganelli M. 1 , Molfino S.*[4], *Nazario P.*[4], *Salvi A.*[1], *De Petro G.*[1]

Hepatocellular carcinoma (HCC) is the most common liver cancer and the third cause of cancer related death. The identification of molecular biomarkers useful in the early diagnosis and prognosis of HCC remains a challenge. MicroRNAs (miRs) play roles in almost all aspects of cancer biology and have emerged as valuable candidates with clinical potential in cancer. Previously, we have demonstrated that miR-193a-3p and miR-23b-3p exert tumor-suppressor functions and DNA methylation is involved in the down-regulation of miR-23b-3p in HCC cell lines. Further we explored the potential clinical significance of miR-193a-3p and miR-23b-3p in HCC. To this purpose, we evaluated the levels of miR-23b-3p and miR-193a-3p in tissue and liquid biopsies from HCC patients.

The expression levels of miR-23b-3p and miR-193a-3p were significantly down-regulated in HCC tissues versus their matched peritumoral tissues (PT) in a cohort of HCC patients (n=59, n=67, respectively). Interestingly, high miR-193a-3p level in HCCs was associated with longer OS and DFS of patients.

In addition, in a subset of 30 HCC cases, we found a negative trend between miR-23b-3p (but not miR-193a-3p) expression and DNA methylation confirming that miR-23b-3p is partially down-regulated by DNA methylation in HCC. Concerning the circulating levels of the selected miRs, we used the droplet digital PCR for the detection of miR-23b-3p and miR-193a-3p in the plasma from untreated 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, it was associated with tumor grading, and the ROC curve indicated its diagnostic relevance (AUC=0.68).

miR-193a-3p was undetectable in the plasma samples. Overall, these data highlight the promising translational value of miR-193a-3p and miR-23b-3p in HCC. A multicentric study has already been planned and the recruitment of HCC patients is ongoing to determine the levels of tissue miR-193a- 3p and circulating miR-23b-3p in a larger cohort of HCC patients and to sustain the prognostic and diagnostic value of these miRs in HCC.

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