



# UNIVERSITÀ DEGLI STUDI DI TORINO

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## **Clinical evaluation of circulating microRNAs as potential biomarkers of hepatocellular carcinoma in patients with chronic HBV infection**

G.P. Caviglia<sup>1</sup>, M.L. Abate<sup>1</sup>, E. Petrini<sup>2</sup>, S. Gaia<sup>2</sup>, P. Manzini<sup>3</sup>, P. Carucci<sup>2</sup>, M. Rizzetto<sup>1,2</sup>, A. Smedile<sup>1,2</sup>

<sup>1</sup>*Department of Medical Sciences, University of Turin, Turin, Italy*

<sup>2</sup>*Department of Gastroenterology and Hepatology, Città della Salute e della Scienza Hospital, Turin, Italy*

<sup>3</sup>*Blood Bank, Città della Salute e della Scienza Hospital, Turin, Italy*

**Introduction.** Several studies showed that aberrant miRNA expression is associated with development and progression of hepatocellular carcinoma (HCC).

**Aim.** To examine whether some commonly deregulated miRNAs (miR-122, miR-21, miR-221 and miR-16) in HBV-related HCC may serve as diagnostic markers.

**Materials and Methods.** Serum expression of miR-122, miR-21, miR-221 and miR-16 was evaluated by real-time quantitative RT-PCR in 33 patients with HBV-related HCC (61±10 years; F/M=4/29), 30 patients with HBV-related cirrhosis (53±11 years; F/M=11/19) and 27 blood donors as healthy controls (54±8 years; F/M=9/18).

**Results.** Median levels of miR-16, miR-122 and miR-221 were significantly different in patients with HCC or cirrhosis compared to healthy controls ( $p<0.001$ ) whereas, only miR-122 levels differed in patients with HCC from cirrhotic patients ( $p=0.024$ ). miR-122 levels were significantly higher in patients with multifocal HCC than in patients with a single lesion ( $p=0.024$ ). Expression levels of miR-21 were similar in the 3 groups. Area under the curve (AUC) analysis showed that serum levels of miR-122, miR-122+miR-221, miR-122+miR-16 and miR-122+miR-221+miR-16, are able to differentiate patients with HCC from patients with cirrhosis (AUC=0.675; AUC=0.704; AUC=0.681; AUC=0.703, respectively). Moreover, miR-16, miR-122 and miR-221, alone or in combination, were able to discriminate patients with HCC or cirrhosis from healthy controls (AUC>0.9). In addition, a correlation between miR-122 levels and HCC nodules number ( $R=0.390$ ;  $p=0.036$ ), and between miR-16 and miR-122 levels, and ALT values ( $R=-0.464$ ,  $p=0.034$ ;  $R=0.449$ ,  $p=0.536$ , respectively) was found.

**Conclusions.** Among the four microRNAs analyzed, only miR-122 significantly discriminates patients with HCC from cirrhotic patients and patients with HCC or cirrhosis from controls. miR-122 appears to reflect liver necro-inflammation, since we observed a positive correlation with ALT levels. Moreover, the correlation between miR-122 expression levels and HCC with multi-nodules, suggests the possible use of this miRNA for tumor stadiation. Nevertheless, miR-122 AUC values were not sufficiently high for HCC screening purposes.