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MicroRNA-183 cluster plays an important role in hepatocellular carcinoma (HCC)

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Hepatocellular carcinoma (HCC) a primary liver cancer is the second leading cause of cancer related deaths worldwide. Molecular mechanisms of HCC pathogenesis are complex involving epigenetic alterations including miRNAs. MiR-183-96-182 cluster is consistently reported to be up regulated in HCC. Hence, the present study evaluated the role of miR-183-96-182 cluster and its diagnostic potential in HCC. Expression of miR-183-96-182 cluster in cells and tissues of HCC was determined and its functional characterization carried out in HCC cells. Target genes for miR-183-96-182 cluster were identified and validated. Temporal analysis of 183-96-182 cluster in liver and plasma of diethylnitrosamine induced HCC rat model was done. Serum levels of 183-96-182 cluster in different categories of HBV infected patients during the progression of liver disease to HCC were determined. Our results showed up regulation of miR-183-96-182 cluster in various cell lines and tumor tissues of HCC. Molecular mechanism behind functional role of miR-183-96-182 cluster in cell viability, migration and invasion involved regulation of ETS2 and EGR1 expression by hsa-miR-182-5p and hsa-miR-183-5p in Hep3B cells respectively. miR-183-96-182 cluster was found to be significantly up regulated in liver tissues and plasma of DEN treated Wistar rats. Interestingly, levels of hsa-miR-182 and hsa-miR-96 were found to distinguish between HCC and normal subjects whereas levels of miR-96 could distinguish CHB and control subjects as determined by ROC curve indicating their diagnostic potential. The present study suggested that up regulated miR-183-96-182 cluster has a role in liver disease progression and elevated levels of plasma of miR-183 and miR-96 indicated their biomarker potential.

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