Hepatocellular carcinoma risk-stratification based on ASGR1 in circulating epithelial cells for cancer interception

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Abstract

The lack of diagnostic and prognostic biomarkers in hepatocellular carcinoma impedes performance of precision medicine in this tumor type. The aim of this study was to identify phenotypic and genetic heterogeneity of circulating epithelial cells (CECs) based on asialoglycoprotein receptor 1 (ASGR1) and miR-122-5p expression as potential diagnostic and prognostic tools in patients with hepatocellular carcinoma (HCC) and liver cirrhosis (LC). Peripheral blood samples were extracted from LC and HCC patients at different disease stages. CECs were isolated using positive immunomagnetic selection. Genetic and phenotypical characterizations were done by double immunocytochemistry for cytokeratin (CK) and ASGR1 or by in-situ hybridization with miR-122-5p and cells were visualized by confocal microscopy. Presence of CECs increased HCC risk by 2.58 times however this was only significant (p=0.028) for patients with previous LC and not for those without prior LC (p=0.23). Furthermore, the number of CECs lacking ASGR1 expression significantly (p=0.014; r=0.23) correlated with HCC incidence and absence of miR-122-5p expression. Finally, overall survival was significantly greater (p=0.018) for patients at earlier cancer stages but this difference was only maintained in the group with presence of CECs (p=0.021) whereas progression-free survival was influenced by absence of ASGR1 expression. Identification and characterization of CECs by ASGR1 and/or miR-122-5p expression might be a cancer interception tool in LC patients as it was shown to be an independent prognostic and risk-stratification marker in LC and early disease stage HCC patients.

Keywords: Hepatocellular carcinoma, liver cirrhosis, circulating tumor cells, precision medicine, cancer interception.