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Implication of diverse stemness in clinical manifestations of hepatocellular carcinoma

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Cumulating evidence suggests that hepatocellular carcinoma (HCC) can be derived from cancer stem cells (CSCs), which are regarded as the origins for tumor metastasis, chemoresistance and post-treatment recurrence. Different markers, including CD13, CD24, CD44, CD90, CD133 and EpCAM, have been reported as specific surface markers to enrich CSCs in HCC. Many of them are not only surface markers but also functionally implicated in tumor development and progression. For example, CD13 helps HCC cells escape chemotherapies by both inducing cells into dormancy and reduces ROS accumulation, DNA damages and cell death. CD24 facilitates the activation of STAT3-mediated signaling which subsequently induces the expression of NANOG, a critical stemness transcription factor, endowing tumor cells with stemness traits. EpCAM, a cell adhesion molecule connecting to the actin cytoskeleton via b-actinin, involves the regulation of cell proliferation. HCC positive for EpCAM and AFP display distinct features of CSCs and have a poor outcome and high metastasis as comparing with HCC negative for both EpCAM and AFP. On the other hand, EpCAM and CD90 independently express in distinct subgroups of HCCs with different cell phenotypes and clinical manifestations. EpCAM+ cells have features of epithelial cells with active proliferation, whereas CD90+ cells have those of vascular endothelial cells with high invasiveness. Clinically, EpCAM is associated with poorly differentiated HCC and high serum AFP, whereas CD90 is linked to a high incidence of metastasis. In cultured HCC cells, CD90+ cells enhanced the motility of EpCAM+ cells via the activation of TGF- β signaling. The complexed roles of these CSC surface markers not only imply diverse origins of CSCs but also indicate a different degree of de-differentiation during the carcinogenesis of hepatocytes, which contributes to the heterogeneous responses to anti-cancer therapies in HCC patients.

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Vitamin D status predicts outcome of chronic liver disease

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Vitamin D and its role in immunity, inflammation and chronic disease pathogenesis has been the subject of many scientific investigations. The progression of the chronic liver disease (CLD) to cirrhosis is the result of an imbalance between the production and dissolution of the extracellular matrix. Development of liver fibrosis in the setting of chronic hepatic inflammation and injury is orchestrated by many cell types, including hepatic stellate cells (HSCs). The significance of vitamin D deficiency in CLD and cirrhosis is emerging in the literature. We systematically evaluated the literature for the relationship of vitamin D to fibrogenic liver disease by utilizing PubMed, SCOPUS, Embase, Cochrane Database, OVID and Lilacs as part of a search protocol. Low vitamin D status predicts progression of non-alcohol fatty liver disease (NAFLD) to non-alcoholic steatohepatitis (NASH) and then to cirrhosis and appears to predict survival. Low vitamin D status contributes to resistance to anti-viral therapy for viral hepatitis with improved response rates in those having vitamin D sufficiency. This session will review the literature, the putative mechanisms for vitamin D's apparent effect on CLD outcome and the importance of monitoring of serum 25-hydroxyvitamin D levels for prognostication and intervention.

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