

NS5ABP37 Inhibits Liver Cancer by Impeding Lipogenesis and Cholesterogenesis

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Abstract : The molecular mechanism underlying nonalcoholic fatty liver disease (NAFLD) progression to hepatocellular carcinoma (HCC) remains unknown. In this study, immunohistochemistry staining result showed that NS5ABP37 protein expression decreased as with increasing degree of HCC malignancy. In agreement, NS5ABP37 protein overexpression significantly suppressed cell proliferation, caused G1/S cell cycle arrest, and induced apoptosis by increasing caspase-3/7 activity and cleaved caspase-3 levels. In addition, NS5ABP37 overexpression resulted in decreased intracellular TG and TC contents, with level reduction in SREBPs and downstream effectors. Furthermore, NS5ABP37 overexpression decreased SREBP1c and SREBP2 levels by inducing their respective promoters. Finally, ROS levels and ER-stress were both induced by NS5ABP37 overexpression. These findings together demonstrate that NS5ABP37 inhibits cancer cell proliferation and promotes apoptosis, by altering SREBP-dependent lipogenesis and cholesterogenesis in HepG2 cells and inducing oxidative stress and ER stress.

Keywords : NS5ABP37, liver cancer, lipid metabolism, oxidative stress, ER stress

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