Induction of apurinic endonuclease 1 overexpression by endoplasmic reticulum stress in hepatoma cells

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Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide with poor prognosis due to resistance to conventional chemotherapy and limited efficacy of radiotherapy. Previous study have indicated that induction of endoplasmic reticulum stress or apurinic endonuclease 1 (APE1) were observed in many tumors. Therefore, the aim of this study was to investigate the relationship between endoplasmic reticulum (ER stress) and APE1 in hepatocellular carcinoma. Here we show that the expression of APE1 during ER stress in HepG2 and Huh-7 cell lines. Tunicamycin or brefeldin A, two ER stress inducers, increased APE1 and GRP78, ER stress marker, expression in HepG2 and Huh-7 cells. Induction of APE1 expression was through transcription level in response to ER stress. We found APE1 nuclear localization during ER stress by using immunofluorescence assay in HepG2 cells. Furthermore, expression of Hepatitis B virus pre-S2\textDelta large mutant surface protein (pre-S2\textDelta), ER stress-induced protein, also increased GRP78 and APE1 expression in normal hepatocyte NeHepLxHT cell line. Similarly, tumor sample showed higher expression of APE1 in ER stress-correlated liver cancer tissue in vivo. Our result demonstrates that ER stress and HBV pre-S2\textDelta increased APE1 expression which may plays an important role in resistance to chemotherapeutic agents or tumor development. Therefore, these data provide an important chemotherapeutic strategy in ER stress and HBV pre-S2\textDelta-associated tumor.

Key words: Hepatocellular carcinoma, Huh-7, HepG2, NeHepLxHT, hepatitis B virus, Hepatitis B virus pre-S2\textDelta large mutant surface protein, Endoplasmic reticulum stress, apurinic endonuclease 1, GRP78.