HEP-11

PROMOTER METHYLATION OF *SFRP1* IS FREQUENT IN HEPATOCELLULAR CARCINOMA

Yu-Lueng Shih,[1,3] Wei-Kuo Chang,[1] Tsai-Yuan Hsieh,[1] You-Chen Chao,[1] Chung-Bao Hsieh,[2] Ya-Wen Lin[3]

[1]Division of Gastroenterology, Department of Internal Medicine, National Defense Medical Center, Tri-Service General Hospital, Taipei, Taiwan

[2]Division of General Surgery, Department of Surgery, National Defense Medical Center, Tri-Service General Hospital, Taipei, Taiwan

[3]Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan

BACKGROUND: The secreted frizzled-related protein 1 gene (*SFRP1*) encodes a Wnt/β-catenin signaling antagonist and is frequently inactivated by promoter methylation in many tumors. However, the role of *SFRP1* in hepatocellular carcinoma (HCC) is not clear. Therefore, we investigated whether methylation of the *SFRP1* promoter is common in HCC and whether it may influence *SFRP1* expression.

METHODS: Four HCC cell lines, 54 HCCs, 42 cirrhotic livers, 21 chronic hepatitis livers and 15 normal controls were analyzed for 1) *SFRP1* promoter methylation by methylation specific polymerase chain reaction (MS-PCR) and bisulfite sequencing, 2) *SFRP1* mRNA expression by quantitative reverse transcription PCR, and 3) loss of heterozygosity (LOH) by microsatellite markers flanking the *SFRP1* locus. We treated HCC cells with the demethylating agent 5-aza-2′-deoxycytidine to determine whether it could restore *SFRP1* expression.

RESULTS: *SFRP1* promoter methylation was observed in 75%, 48.2%, 21.4%, 14.3% and 0% in HCC cell lines, primary HCCs, cirrhosis livers, chronic hepatitis livers and normal controls, respectively. Methylation of *SFRP1* promoter region in HCCs increased significantly compared with control tissues. All samples with *SFRP1* methylation showed downregulation of *SFRP1* expression. Demethylation treatment with 5-aza-2′-deoxycytidine in HCC cells restored the *SFRP1* expression. Moreover, LOH markers D8S505 and D8S1722 were found to be 25% and 27.6% of the informative cases, respectively.

CONCLUSION: Our data suggest that promoter hypermethylation of *SFRP1* is a common event in HCCs, and this plays an important role in the regulation of *SFRP1* expression. In addition to methylation-mediated downregulation of *SFRP1*, LOH may also play a role.

Key words: hepatocellular carcinoma, *SFRP1*, promoter hypermethylation, loss of heterozygosity