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RUNX3 promoter methylation correlation with pathogenesis of hepatocellular carcinoma in Asians

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ABSTRACT. The aim of this study was to elucidate the role of *RUNX3* promoter methylation in the pathogenesis of hepatocellular carcinoma (HCC) among Asians. For this purpose, we performed a comprehensive search of Chinese and English language scientific literature databases using stringent selection criteria; ultimately, we identified relevant studies that specifically assessed the correlation between *RUNX3* promoter methylation and HCC. All data was retrieved and analyzed by two independent investigators using the STATA software (version 12.0). Initially, 132 studies (103 in Chinese, 29 in English) were retrieved; 122 were eliminated through a stepwise filtering process. Finally, 10 studies conducted in Asian populations (5 Chinese, 4 Japanese, 1 Korean) fulfilled all the inclusion criteria of our meta-analysis. The studies included 588 HCC patients (641 cancer tissues; 593 adjacent normal

tissues) and 184 healthy controls. We observed that *RUNX3* promoter methylation was significantly higher in cancer tissues than in adjacent normal tissues (RR = 6.35, 95%CI = 3.62-11.14, P < 0.001) and normal control tissues (RR = 17.31, 95%CI = 7.08-42.34, P < 0.001). *RUNX3* promoter methylation status did not differ significantly between patients with different TNM stages (RR = 0.88, 95%CI = 0.70-1.10, P = 0.269) and histological grades (RR = 0.86, 95%CI = 0.65-1.14, P = 0.304), suggesting that *RUNX3* promoter methylation is linked to the origin of HCC but not to its progression from non-metastatic to metastatic stages. This in turn indicated that *RUNX3* could be an early diagnostic marker distinguishing benign from malignant hepatocellular carcinoma.

Key words: Hepatocellular carcinoma; *RUNX3*; Methylation; Pathogenesis; Meta-analysis

