B-CELL TRANSLOCATION GENE 1 SERVES AS A NOVEL PROGNOSTIC INDICATOR OF HEPATOCELLULAR CARCINOMA

M. Kanda1, D. Shimizu1, H. Sugimoto1, H. Oya1, S. Hibino1, H. Takami1, R. Hashimoto1, Y. Okamura2, S. Yamada1, T. Fuji1, G. Nakayama1, M. Koike1, S. Nomoto1, M. Fujiwara1, Y. Kodera1

1Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, Nagoya, JAPAN
2Department of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Suntogun, Shizuoka, JAPAN

Aim: Although B-cell translocation gene 1 (BTG1) plays an important role in apoptosis and negatively regulates cell proliferation, BTG1 expression in hepatocellular carcinoma (HCC) has not been evaluated. The aim of this study was to clarify the role of BTG1 in the initiation of HCC carcinogenesis and progression.

Methods: BTG1 mRNA expression levels were determined for HCC cell lines and 151 surgical specimen pairs using a quantitative real-time reverse transcription polymerase chain reaction assay. The mutational and methylation statuses of HCC cell lines were analyzed via high-resolution melting analysis and direct sequencing analysis to explore the regulatory mechanisms of BTG1 expression. The expression and distribution of the BTG1 protein in liver tissues were evaluated using immunohistochemistry.

Results: Decreased expression of BTG1 mRNA was confirmed in the majority of HCC cell lines (89%) and clinical HCC tissues (85%) compared with non-cancerous liver tissues. Mutations or promoter hypermethylation of BTG1 were not identified in HCC cell lines. BTG1 mRNA expression levels were not influenced by background liver status. The pattern of BTG1 protein expression was consistent with that of BTG1 mRNA. Downregulation of BTG1 mRNA in HCC was significantly associated with shorter disease-specific and recurrence-free survival rates. Multivariate analysis of disease-specific survival rates identified BTG1 mRNA downregulation as an independent prognostic factor for HCC (hazard ratio 2.12, 95% confidence interval 1.12 – 4.04, P = 0.022).

Conclusions: Our results indicate that altered BTG1 expression might affect hepatocarcinogenesis and may represent a novel biomarker for HCC carcinogenesis and progression.

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