구연발표 I-2

Tumor Suppressor Gene Expression Correlates with Gastric Cancer Prognosis

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Purpose: The loss of tumor suppressor gene (TSG) is a key event in many human cancers, including gastric carcinoma. Many TSG candidates have been studied, but their roles in gastric carcinogenesis remain unclear. The aim of this study was to clarify the clinical significances of TSG expressions in gastric carcinoma.

Methods: The expressions of various TSG candidates (p53, E-cadherin, FHIT, smad4, rb, VHL, PTEN, MGMT, p16, KAI1), as well as other proteins (bcl-2, MUC1, MUC2, MUC5AC, MUC6, CEA, CD44, b-catenin, C-erbB2 and cyclin B2), were evaluated immunohistochemically in 329 consecutive gastric carcinomas using the tissue array method.

Results: The overexpression of p53 and MUC1 ($p<0.01$) and the loss of expression of smad4 ($p=0.04$), FHIT ($p=0.03$), MGMT ($p=0.01$), E-cadherin, KAI1 and PTEN ($p<0.01$) were found to be significantly associated with poor gastric carcinoma prognosis. Seven out of 8 survival-associated proteins were ascertained to belong to protein products of tumor suppressor genes. Therefore, the gastric carcinomas were divided into 5 groups according to the grade of alteration in TSG expression. No TSG expression loss was found in 32 cases (TSG1), one TSG loss in 47 cases (TSG2), two in 67 cases (TSG3), three or four in 64 (TSG4), and five, six, or seven in 38 (TSG5). The grade of TSG expression was confirmed to be significantly associated with WHO classification ($p=0.04$), pTNM stage, lymphatic invasion and patient survival ($p<0.01$ for the latter three). By multivariate analysis, the grade of TSG expression was found to be significantly and independently associated with patient survival ($p<0.01$).

Conclusion: The findings of this study suggest that the cumulative loss of TSG expression in gastric carcinoma is important in determining patient survival.