Proteomic study identified APC-binding protein EB1 as a novel biomarker for malignant potentials of colorectal cancer

Yutaka Sugihara, Hirokazu Taniguchi, Daisuke Kubota, Hiroshi Ichikawa, Takeshi Tomonaga, Shin Fujita, Tadashi Kondo

We conducted proteomic study to reveal proteome backgrounds of CRC and identify biomarkers to assess the malignant potentials of CRC.

Surgically resected normal and tumor tissues from 59 CRC patients were examined by two-dimensional difference gel electrophoresis (2D-DIGE) with Cydye DIGE Fluor saturation dye and our original large format gel apparatus (1). We performed immunostaining to validate protein expression, and examined the relation between protein expression and clinical parameters. Moreover, *in vitro* RNAi assays were carried out to evaluate the association of cancer characteristics such as cell proliferation and invasion.

We found that APC-binding protein EB1 (EB1) had higher expression in tumor tissues (47 of 59 cases), compared with normal ones. We previously reported the clinical utilities of EB1 in hepatocellular carcinoma (2). Although a possible utility of EB1 as a plasma biomarker in CRC was suggested (3), EB1 was not implemented with malignant potentials of CRC. Following immunohistochemical studies revealed that EB1 was rarely overexpressed in colorectal adenoma (3 of 19 cases), and overexpression of EB1 was observed in tumor tissues from 150 of 176 CRC cases examined. Univariate and multivariate analyses in 132 CRC cases which we could use for survival analysis indicated that nuclear EB1 was associated with lymph node metastasis, lymphovascular invasion and venous invasion. Moreover, silencing of EB1 resulted in the reduced cell proliferation and invasion.

In conclusion, we found the association of EB1 with malignant potentials of CRC. EB1 is worth further investigated for its clinical utilities.

Keywords:

Colorectal cancer / 2D-DIGE

References

- 1. Kondo T et al, Nat Prot 2006;1(6):2940-56.
- 2. Orimo T et al, Hepatology 2008;48(6):1851-63.
- 3. Ladd J et al, Cancer Prev Res 2012 Epub ahead of print

*This presentation is accepted in J Proteomics.

Sugihara Y, Taniguchi H, Kushima R, Tsuta H, Kubota D, Ichikawa H, Sakamoto K, Nakamura Y, Tomonaga T, Fujita S, Kondo T. Proteomic-based identification of the APC-binding protein EB1 as a candidate of novel tissue biomarker and therapeutic target for colorectal cancer. J Proteomics, in press 2012