BRIEF ARTICLES

TSPAN1 protein expression: A significant prognostic indicator for patients with colorectal adenocarcinoma

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Abstract

AIM: To determine if TSPAN1 overexpression is associated with clinicopathological and prognostic factors in human colorectal adenocarcinoma.

METHODS: Total RNA was extracted in 20 human adenocarcinoma tissues for TSPAN1 mRNA assay by RT-PCR. Eighty-eight specimens of human colorectal adenocarcinoma were surgically removed. TSPAN1 protein levels in cancer tissues were determined by immunohistochemistry using a polyclonal antibody against self-prepared TSPAN1. The correlation between TSPAN1 expression and the clinicopathological factors and the overall survival rate was analyzed by univariate and multivariate assay.

RESULTS: TSPAN1 mRNA was detected in 90.0% (18/20) of cancerous tissues. The light density of TSPAN1 mRNA expression levels was 0.89 ± 0.30 in adenocarcinoma by gel-image system. TSPAN1 protein expression was detected in 78.41% (69/88) and weakly expressed in 40% normal colorectal tissues. There were significant differences between colorectal adenocarcinoma and normal control epithelium (P < 0.05). TSPAN1 protein expression in colorectal cancerous tissue was significantly correlated with the histological grade, cell expression PCNA, lymph nodal metastasis and TNM staging of the disease. Patients with TSPAN1 protein overexpression had a significantly shorter survival period than that in patients with TSPAN1 protein negative or weak expression, respectively (P < 0.05). Furthermore, by multivariate analysis, TSPAN1 protein expression demonstrated an independent prognostic factor for human colorectal cancers (P < 0.05, relative risk 0.755; 95% confidence interval 0.302-1.208).

CONCLUSION: The expression of TSPAN1 gene is increased in colorectal carcinoma, suggesting that TSPAN1 might serve as an independent prognostic factor for the colorectal adenocarcinoma patients.

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Key words: TSPAN1; Colorectal adenocarcinoma; Semi-quantitative RT-PCR immunohistochemistry; Prognosis

INTRODUCTION

The colorectal carcinoma is one of the most common malignant neoplasms, ranking the fourth frequency in men and third in women[1]. Although the prognosis has slightly improved in the past years, colorectal cancer is still the second and third major common cause of
The incidence of colorectal cancer is the fourth in malignant tumor ranking in the United States, respectively. The incidence of colorectal cancer is the fourth in malignant tumor ranking in China, and it is increased dramatically in developing regions. The colorectal cancer is thought to result from a combination of environmental factors, diet, lifestyle, chronic inflammation and accumulation of specific genetic alterations. The pathogenesis and development of colorectal cancer involve multi-genes and multi-steps. Ogino et al. showed the occurrence of colorectal cancer involved in a series of gene mutations, microsatellite instability (MSI) and 18q loss of heterozygosity (LOH). The other molecules studied include MST1 (Mammalian sterile 20-like kinase). Replication protein (RPA), ELAV-like protein Huk and COX-2, α-catenin, β-catenin, α-ligatin, β-ligatin, Rho-a, etc. In fact, an established cascade of events leading to colorectal cancer development and progression is described by Vogelstein. The alteration of expression of these molecules often showed an obvious correlation with pathologic grading and clinical staging in colorectal cancer, which can be used as a biomarker for assessing prognosis. Currently, the assessment of prognosis is mainly based on pathological features of the tumor which is valuable to the triage of patients who will benefit from adjuvant therapy. The clinical pathological staging is the most popular standard prognostic approach for predicting the clinical outcome of colorectal cancer patients. The prognosis of colorectal cancer is closely related to the tumor TNM staging. However, patients with similar stages of the disease have various outcomes. Therefore, there is a need to identify useful prognostic molecular markers in guiding treatment decisions and/or in developing more effective treatments. TSPAN1 (GenBank Accession No. AF065388) is a new member of TM4SF, which is located at chromosome 1p34.1. It encodes a 241 amino acid protein. TSPAN1 was reported as a tumor-related gene recently. In several studies, TSPAN1 gene over-expression was detected in liver cancer, prostate cancer, gastric carcinoma and cervix cancer. It has been proposed that TSPAN1 plays a role in cell mitosis and/or cause cell abnormal differentiation. In this study, we examined fresh tumor tissues and histological sections of colorectal adenocarcinoma to determine the expression of TSPAN1 mRNA and protein, and analyzed the relationship between the gene expression and clinicopathological parameters. The result suggests that overexpression of TSPAN1 is correlated to the prognosis of colorectal cancer patients.

MATERIALS AND METHODS

Specimen

A total of 88 patients with colorectal adenocarcinoma, diagnosed and treated from January 1998 to April 2000 were investigated in this study. Of the 88 cases evaluated, 46.6% (41 cases) were rectum cancers, 30.1% (27 cases) were sigmoid colon cancers, 6.8% (6 cases) were descending colon cancers, 2.3% (2 cases) were transverse colon cancers and 13.6% (12 cases) were ascending colon cancers. The median age at the time of diagnosis was 62.2 years (range, 37-85). There were 50 male patients, 38 female patients. None of them had received chemotherapy or radiotherapy before diagnosis. After surgery, these patients with TMN stage II took oral 5-fluorouracil and patients with stage III-IV were subjected to 5-fluorouracil-based systemic chemotheraphy. In order to avoid bias, each case was diagnosed by two pathologists.

The clinicopathological data were determined according to the WHO classification and TNM cancer staging. The average size of the tumor was 4 cm (range from 1.5 to 7.6 cm), 54.5% (48 cases) were cauliflower/polypl type and 45.45% (40 cases) were ulcer/sclerotic type. Adenocarcinomas were graded predominantly on the basis of the extent of glandular appearances, and divided into well (lesions exhibit glandular structures in >95% of the tumor, grade 1, 15.9% or 14 cases), moderate (lesions have 50%-95% glands, grade 2, 44.31% or 39 cases) and poor differentiation (lesions have 5%-50% glands, grade 3, 39.77% or 35 cases). Tumor limited in submucosa (T1) and muscularis propria (T2) as stage I accounted for 32.95% (29 cases), tumor invaded through muscularis propria into subserosa or into non-peritonealized pericolic or perirectal tissues (T3) and tumor directly invades other organs or structures and/or perforates visceral peritoneum (T4) as stage II accounted for 29.54% (26 cases), and the tumor with metastasis in I-3 regional lymph nodes (N1-3) in any T as stage III and the tumor with distant metastasis (M) in any T and N as stage IV, III and IV accounted for 37.5% (33 cases). Vascular invasion in 26 cases (29.55%) demonstrated that vessel wall was occlusive or infiltrating damaged up to the complete destruction with a surrounding fibroinflammatory reaction. Such clinicopathological factors as perineural invasion and desmoplasia reaction were observed and analyzed as well. The proliferation level of cancer cells was evaluated based on the expression of PCNA in tumor parenchymas.

Semiquantitative reverse transcription-polymerase chain (RT-PCR)

Twenty cases of fresh colorectal cancer specimens were stored in -70°C refrigerator immediately after dissection for semi-quantitative RT-PCR with co-amplification of TSPAN1 gene and an internal control β-actin. Briefly, total RNA from tumor tissues was extracted with TRIZOL reagent and the reverse transcription was performed with Rneasy Kit (Clontech, CA, USA) according to previously published protocols. A 50 µL PCR reaction contains approximately 50 ng of human colorectal cancer ds-cDNA; 40 mmol/L Tricine-KOH, pH9.2; 15 mmol/L KOAc; 3.5 mmol/L Mg (OAc)₂; 0.2 µmol/L 5’ TSPAN1 primer (5’-CAG-CTT-CTT-CAT-CAC-GAA-CTC-ACT-G-3’); 0.2 µmol/L 3’ TSPAN1 primer (5’-ATC-CAC-CCA-GAG-GCT-CGT-CTG-ATT-TCA-CTC-3’); 0.1 µmol/L 5’ β-actin primer (5’-TTA-CAC-CCT-TTC-TTG-ACA-AAA-CCT-A-3’);
0.1 μmol/L 3′-actin primer (5′-CAA-AAG-CCT-TCA-
TAC-ATC-TCA-AGT-3'); 0.2 mmol/L each of dATP,
dGTP, dCTP and dTTP; and 1 μL of Advantage™
cDNA Polymerase Mix (50X; contains KlenTaq-1 and
Deep Vent polymerases). The PCR cycling was as
follows: PCR tubes were preheated at 94°C for 20 s;
then run 30 cycles at 96°C for 6 s (denature); 60°C for
20 s for annealing and 72°C for 1 min for extension,
in a DNA thermal cycle 9600 (PE Biosystems, CA, USA).
PCR products were applied to electrophoresis on 1%
agarose gel analysis; the expected TSPAN1 gene was
a band at 1159 bp. TSPAN1 expression was evaluated by
calculating the average ratios of light density using
symmetry computerized gel imaging system10.

**Immunohistochemistry**

All 88 adenocarcinoma samples were routinely fixed
in 40 g/L formaldehyde solution and embedded in
paraffin. After slicing into 4 μm thick sections,
immunohistochemistry was performed using Dako
Elivision TM Plus Two-step System (PV-6000 kit,
Zymed, Co., USA). To detect the TSPAN1 and PCNA
expressions in colorectal adenocarcinoma tissues,
the sections were dewaxed in xylene and rinsed in alcohol
and graded alcohol/water mixtures. Sections were then
submitted to antigen retrieval treatment in a pressure
cooker. The tissues were boiled in 0.01 mol/L, pH 6.0
citric acid buffer to retrieval antigen for 5 min. They
were then treated with 0.3% hydrogen peroxide in
absolute methanol to inhibit endogenous peroxidase
activity for 15 min at room temperature. After blocking
of background staining with diluted normal calf serum,
sections were incubated overnight at 4°C with polyclonal
antibodies against TSPAN1 (antibody prepared with the
help of American San Francisco gene biotechnology
company) and PCNA (PC10, No. 40780708, DAKO,
USA), respectively. Subsequent reaction proceeded
using a two step assay, immunoreaction was visualized
with peroxidase-3,3′-diaminobenzidine (DAB). Finally,
sections were lightly counterstained with Mayer’s
haematoxylin and mounted. The negative controls were
set by omitting the primary antibodies. The positive
controls were the hepatocellular carcinoma with positive
expressions of TSPAN1. In addition, 10 specimens from
the marginal normal mucosa of tumor were used as
normal controls16.

**Evaluation of immunohistochemical staining**

All sections were blindly analyzed by two experienced
pathologists under light microscope. Based on the
estimated percentages of positive parenchyma cells and/
or the immunostaining intensity, which was determined
by comparing the immunoreactivity of the positive
controls that were included in each experiment, staining
results were divided into four categories: (-) tissues
specimens: positive parenchyma cell with less than 5% of
the cancer tissues and/or weakly stained; (+) tissue
specimens: positive parenchyma cell with less than 25% of
the cancer tissues and/or weakly stained; (+++) tissues
specimens: positive parenchyma cell with less than 50%

**Statistical analysis**

Association between TSPAN1 gene expression and other
clinicopathological factors of the tumor were assessed
by the Fisher’s exact test (two-sided) for categorical
variables and χ² test were used to compare ordinal
variables. The grading-related data was analysed by
Spearman test. Overall survival was defined as the period
from the date of diagnosis to the date of death. Survival
curves were determined according to the Kaplan-Meier
method, and compared using Log-rank test statistical
differences. Multivariate survival analysis was performed
with SPSS version 11.0 Software (Chicago, IL, USA).

**RESULTS**

**RT-PCR detection of TSPAN1 mRNA expression**

Total RNA was extracted from 20 cases of colorectal
adenocarcinoma tissues. RT-PCR analysis of TSPAN1
mRNA expression was then performed. The positive
rate of TSPAN1 mRNA expression was 90% (18/20)
in the colorectal adenocarcinoma (Figure 1), and the
relative amount of TSPAN1 mRNA levels in cancer
tissues was assessed based on the β-actin control. The
relative amounts of TSPAN1 mRNA were 0.89 ± 0.30.

**Immunohistochemistry detection of TSPAN1 protein
expression**

TSPAN1 was mainly presented in cytoplasm and located
at membrane as well. In the normal control epithelium,
3 cases presented a weakly positive staining of
TSPAN1, and only 1 case presented moderately positive
expression (Figure 2A). We observed TSPAN1 protein
expression in 78.41% (69/88) cases of tumors, in which
17.39% (12/69) was displayed as strong expressed
(+++), 44.93% (31/69) as moderately expressed
(++), and 37.68% (26/69) as weakly expressed (+). There
were significant differences between colorectal
adenocarcinoma and normal control epithelium (P <
0.05), (Figures 2B-E).

**Correlation with clinicopathological parameters**

To investigate the role of TSPAN1 expression in
colorectal cancer, we examined the correlation of
TSPAN1 expression with the clinicopathological features (Table 1). We found a positive correlation with histological grade, PCNA expression, nodal metastasis and TNM stages \( (P = 0.001, 0.015, 0.008 \text{ and } 0.002, \text{ respectively}) \). TNM staging of colorectal cancer is more important for patient’s prognosis evaluation. The five-year survival rate of TMN stage I is more than 95\%, while it is less 10\% in patients with TNM stage III-IV. From Table 1, it can be found that the TSPAN1 expression rate and intensity in early TNM stage were lower than in late TNM stage cancer tissues. In addition, TSPAN1 expression was not associated with vascular invasion, perineural invasion and desmoplasia.

**Correlation with patients' survival rate**

Within a period of 60 mo of the follow-up, 24 cancer-related deaths occurred, 3 of the deaths come from 9 patients with TSPAN1 negative tumors, and 21 from 33 patients in the TSPAN1 positive group. In the entire cohort, the overall survival rate of patients with TSPAN1 negative tumors were significantly higher than that of those with TSPAN1 positive tumors (63.64% vs 33.33%; log-rank test: \( \chi^2 = 15.48, P = 0.001 \)). Kaplan-Meier estimated the overall survival rate based on cell TSPAN1 expression in the patients with a follow-up period of 60 mo (Figure 3). To compare with other clinicopathological factors, the effects of histologic grades, node status, PCNA expression, TNM stages, vascular invasion or perineural invasion on the patients’ survival were also analysed with univariate log-rank test. As shown in Table 2, the factors of cellular differentiation, node status, PCNA expression, TNM stages had a significant effect on the overall survival rate \( (P = 0.03, 0.001, 0.0003 \text{ and } 0.002, \text{ respectively}) \). Furthermore, univariate survival analysis was performed to investigate possible prognostic impact of TSPAN1 in
This was also confirmed by a multivariate survival analysis including above factors (Table 3). All of these results suggested that TSPAN1 expression in tumors was an independent prognostic factor for colorectal adenocarcinoma patients (relative risk = 0.755; 95% confidence interval: 0.302-1.208 P = 0.001).

**DISCUSSION**

Many studies reported that TSPAN1 mRNA and protein were expressed in human normal tissues and carcinomas[13-17]. Serru detected TSPAN1 expression in various cell lines by RT-PCR including cervical cancer, lung cancer, squamous carcinoma, colorectal cancer and breast cancer cells[13]. Wollscheid et al[17] detected TSPAN1 mRNA level by RT-PCR and TSPAN1 protein by immunohistochemistry in cervical cancer and found that the gene was expressed in CIN III, cervical squamous cell carcinoma and adenocarcinoma,

Table 1 Correlation of clinicopathological parameters with TSPAN1 expression

| Parameters          | Cases | TSPAN1 expression intensity | P     |
|---------------------|-------|-----------------------------|-------|
| Gender              |       | -                           | +     |+++ |++++ |
| Male                | 50    | 19                          | 21    | 6   | 0.472 |
| Female              | 38    | 10                          | 12    | 10  | 6   |
| Tumor size (cm)     |       | -                           | +     |+++ |++++ |
| < 4.0               | 35    | 10                          | 10    | 5   | 0.469 |
| > 4.0               | 53    | 9                           | 16    | 21  | 7   |
| Type                |       | -                           | +     |+++ |++++ |
| Cauliflower/polypl  | 48    | 9                           | 14    | 16  | 9   | 0.595 |
| Ulcer/infiltration  | 40    | 10                          | 12    | 15  | 3   |
| Location            |       | -                           | +     |+++ |++++ |
| Rectum              | 41    | 9                           | 11    | 17  | 4   | 0.595 |
| Colon               | 47    | 10                          | 15    | 14  | 8   |
| Grade               |       | -                           | +     |+++ |++++ |
| Well                | 14    | 6                           | 6     | 2   | 0   | 0.001 |
| Moderate            | 39    | 9                           | 14    | 14  | 2   |
| Poor                | 35    | 4                           | 6     | 15  | 10  |
| PCNA                |       | +                           | ++++  |     |
| +                   | 43    | 14                          | 14    | 13  | 2   | 0.015 |
| ++++                | 45    | 5                           | 12    | 18  | 10  |
| Lymph node metastasis| No   | 55                          | 16    | 20  | 14  | 5   | 0.008 |
| Yes                 | 33    | 3                           | 6     | 17  | 7   |
| TNM stage           |       | -                           | +     |+++ |++++ |
| I                   | 29    | 11                          | 9     | 7   | 2   | 0.002 |
| II                  | 26    | 5                           | 11    | 7   | 3   |
| III-IV              | 33    | 3                           | 6     | 17  | 7   |
| Vascular invasion   |       | -                           | +     |+++ |++++ |
| No                  | 62    | 14                          | 21    | 20  | 7   | 0.424 |
| Yes                 | 26    | 5                           | 5     | 11  | 5   |
| Perineural invasion |       | -                           | +     |+++ |++++ |
| No                  | 67    | 16                          | 22    | 22  | 7   | 0.235 |
| Yes                 | 21    | 3                           | 4     | 9   | 5   |
| Desmoplasia         |       | -                           | +     |+++ |++++ |
| No                  | 55    | 10                          | 16    | 20  | 9   | 0.647 |
| Yes                 | 33    | 9                           | 10    | 11  | 3   |

Figure 3 Overall 5-year survival curve of colorectal adenocarcinoma patients with TSPAN1 negative (-) and TSPAN1 positive (+, ++, ++++) for the entire cohort (P = 0.001) was estimated by Kaplan-Meier test. Survival rate in TSPAN1 expression groups (+++, +++) were obviously lower than that of weak expression (+) or negative (-) group, respectively (P < 0.05). There was no significant difference of survival rates between TSPAN1 negative group (-) and TSPAN1 weak expression group (+).

colorectal cancer. As shown in Table 2, the expression of TSPAN1 correlated with a worsening of the survival probability, which was statistically significant. This was also confirmed by a multivariate survival analysis including above factors (Table 3). All of these results suggested that TSPAN1 expression in tumors was an independent prognostic factor for colorectal adenocarcinoma patients (relative risk = 0.755; 95% confidence interval: 0.302-1.208 P = 0.001).

Table 2 Univariate analysis by Log-rank test

| Parameters                          | 5-yr survival rate (%) | Log-rank test |
|-------------------------------------|------------------------|---------------|
| TSPAN1 expression                   |                        |               |
| -                                   | 66.67 (6/9)            | 15.48 0.0015  |
| +                                   | 71.4 (5/7)             |               |
| ++                                  | 35.3 (6/17)            |               |
| +++                                 | 11.1 (1/9)             |               |
| Grade                              |                        |               |
| Well                               | 87.5 (7/8)             | 6.91 0.0316   |
| Moderate                           | 37.5 (6/16)            |               |
| Poor                               | 27.8 (5/18)            |               |
| Node status                        |                        |               |
| No                                 | 71.6 (12/17)           | 15.67 0.0001  |
| Yes                                | 24.0 (6/25)            |               |
| PCNA expression                    |                        |               |
| +                                  | 63.1 (12/19)           | 9.05 0.0026   |
| +++                                 | 26.1 (6/23)            |               |
| TNM stages                         |                        |               |
| I                                  | 83.3 (10/12)           | 16.20 0.0030  |
| II                                 | 62.5 (5/8)             |               |
| III-IV                             | 13.6 (3/22)            |               |
| Vascular invasion                  |                        |               |
| No                                 | 46.4 (13/28)           | 1.39 0.2377   |
| Yes                                | 37.7 (5/14)            |               |
| Perineural invasion                |                        |               |
| No                                 | 44.7 (14/32)           | 0.77 0.3795   |
| Yes                                | 40.0 (4/10)            |               |
| Desmoplasia                        |                        |               |
| No                                 | 33.3 (3/9)             | 0.02 0.8829   |
| Yes                                | 42.4 (15/33)           |               |

Table 3 Multivariate analysis in Cox proportional hazard model

| Variable                              | Multivariate analysis | P value |
|---------------------------------------|-----------------------|---------|
|                                      | HR                    | SD      | Z      | 95% CI |
| TSPAN1 expression                     | 0.755                 | 0.231   | 3.27   | 0.302-1.208 | 0.001 |
| Grade                                | 0.798                 | 0.318   | 2.51   | 0.175-1.421 | 0.012 |
| Node status                          | 1.779                 | 0.509   | 3.49   | 0.781-2.778 | 0.000 |
| PCNA expression                      | 1.325                 | 0.475   | 2.79   | 0.394-2.256 | 0.005 |
| TNM stages                           | 1.159                 | 0.341   | 3.39   | 0.490-1.829 | 0.001 |
| Vascular invasion                    | 0.491                 | 0.423   | 1.16   | 0.338-1.320 | 0.246 |
| Perineural invasion                  | 0.409                 | 0.473   | 0.87   | 0.517-1.336 | 0.386 |
| Desmoplasia                          | 0.061                 | 0.415   | 0.15   | 0.752-0.873 | 0.884 |
especially in all undifferentiated cervical carcinoma and adenocarcinoma. They thought TSPAN1 gene expression correlated to cell proliferation and may be used as a marker for cervical cancer prognosis. However, TSPAN1 gene expression in human colorectal cancer tissues has not been reported so far. In this study, we for the first time demonstrated that TSPAN1 mRNA and protein were extensively expressed in 90% and 78% human colorectal cancer tissues, respectively. Our results revealed that epithelial cells of the normal colon or rectum displayed a slight expression of TSPAN1 antigen (Figure 2A). There was significant difference between cancer tissues and normal control. The results are consistent with most other reported data\textsuperscript{[12-14]} and suggest that the TSPAN1 expression is a specific marker for malignant transformation.

In colorectal cancer, the presence of many tumor-associated antigens and their relationship with clinical pathological parameters have been described\textsuperscript{[15-17]} PCNA, a major marker for cell proliferation, is highly expressed in most tumors\textsuperscript{[18]}. In this study, the finding of a significant positive correlation between TSPAN1 and PCNA expression provided further evidence to support a potential role of TSPAN1 in tumor proliferation process (Table 1). The colorectal cancer development may hence relate to the accumulation of TSPAN1 protein in tumor cells. Similarly, our previous study found that TSPAN1 expression correlated with tumor proliferation marker Ki67 expression in human gastric carcinomas\textsuperscript{[19]}

Currently, the TNM stage represents the main tool for identifying prognostic differences among patients with colorectal cancer. The reported 5-year survival rate is 95% for stage I patients, 67% for stages II, and 4.4% for stage III and IV patients\textsuperscript{[20]}. In our prospective 5-year follow-up study, the overall survival rate was 83.3% for stage I patients, 62.5% for stage II patients, and 13.6% for stage III and stage IV patients (Table 2). Similarly, we showed that there was a significant correlation between the overall survival rate and the disease stages. Our study revealed that there was a statistically significant association between TSPAN1 expression and the various stages of colorectal cancer, in which TSPAN1 positive staining was seen in 63.64% patients with shorter survival time (Table 3). The univariate and multivariate analyses suggested that TSPAN1 status, PCNA expression, tumor stages and nodal status were strong predictors for the final clinical outcome (Table 3). Likewise, another study in our lab also showed that TSPAN1 expression was significantly correlated with the metastasis and poor prognosis of gastric carcinoma\textsuperscript{[21]}. Increasing TSPAN1 protein expression was found associated with more advanced stages of cervical carcinoma\textsuperscript{[22]}. All these findings suggest that TSPAN1 over-expression status might yield unfavorable prognosis for some types of cancers. Identifying those patients with high-risk colorectal cancers by TSPAN1 expression detection would be of great benefit for improving the treatment strategies. By the way, other reports displayed that vascular invasion and perineural invasion were correlated with a poor prognosis\textsuperscript{[19-21]}, but in this study we found no direct effect on tumor prognosis.

Colorectal carcinoma is one of the most common cancers in western world and in China, however its molecular mechanism is still unclear. To understand the specific regulation of gene expressions between colorectal cancer and non-cancer tissues and know the genes or proteins characteristics will delineate the molecular changes and obtain useful diagnostic marker. We have demonstrated that TSPAN1 was expressed in majority of human colorectal carcinomas in the current study. TSPAN1 expression, measured by immunohistochemistry in the tumor tissues, may be a candidate gene for diagnosis and prognosis of colorectal carcinoma. The overexpression of TSPAN1 in cytoplasm is associated with higher tumor grade, metastasis, proliferation, and more advanced stages and poor prognosis in colorectal adenocarcinoma patients, suggesting a tumor-related gene role of TSPAN1 in human colorectal cancer development.

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