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# Association between genetic polymorphisms in cortactin and susceptibility to gastric cancer

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**Purpose:** Overexpression of cortactin (*CTTN*) in human tumors has been proposed to result in increased cell migration and metastatic potential. Here, we determined the frequencies of *CTTN* g.-9101C>T, g.-8748C>T, and g.72C>T polymorphisms in apparently healthy subjects and gastric cancer patients, respectively, and the influence of the *CTTN* polymorphisms on gastric cancer susceptibility.
**Methods:** Blood samples were collected from 267 patients and 533 controls. *CTTN* g.-8748C>T and g.-9101C>T polymorphisms were determined using polymerase chain reaction-restriction fragment length polymorphism; the g.72C>T polymorphism was determined using the TaqMan method.
**Results:** Genotype frequencies of the *CTTN* g.-9101C>T polymorphism were 97.5% (TT), 2.5% (TC), and 0% (CC) in the patient group, and 98.6% (TT), 1.4% (TC), and 0% (CC) in the control group. Genotype frequencies of the *CTTN* g.-8748C>T polymorphism were 93.3% (TT), 6.8% (TC), and 0% (CC) in the patient group, and 94.2% (TT), 5.8% (TC), and 0% (CC) in the control group. Genotype frequencies of the *CTTN* g.72C>T polymorphism were 82.4% (CC), 17.2% (CT), and 0.4% (TT) in the patient group, and 78.0% (CC), 20.1% (CT), and 1.9% (TT) in the control group. Genotype and allele frequencies of the *CTTN* g.-9101C>T polymorphism differed significantly between the advanced gastric cancer and control groups. Patients with advanced gastric cancer, possessing the TC genotype, had a significantly poorer prognosis than the group with the TT genotype.
**Conclusion:** The *CTTN* g.-9101C>T polymorphism might influence advanced gastric cancer susceptibility. However, the role of the *CTTN* g.-9101C>T, g.-8748C>T, and g.72C>T polymorphisms requires careful interpretation and confirmation through larger studies.
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**Key Words:** Human CTTN protein, Genetic polymorphism, Stomach neoplasms

## INTRODUCTION

Gastric cancer is the most prevalent cancer in Korea, and it ranks as one of the leading causes of cancer death, followed by lung cancer [1,2]. *Helicobacter pylori* infection, diet, bile reflux, excessive cell proliferation, and DNA damage are known to be risk factors for gastric adenocarcinoma [3,4]. Numerous other factors, such as histological features and clinical stage, have also been shown to play important roles in tumor development [5,6].

Cortactin (CTTN) regulates the actin cytoskeleton through its involvement in several processes, including cell motility, adhesion, polarization, contraction, and others [7-9]. The amplification of chromosome 11q13 has been reported in several human carcinomas along with increased expression of *CTTN* [9]. Overexpression of *CTTN* induces cell motility and migration, inhibits cell-cell adhesion, and accelerates tumor

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spreading [10]. *CTTN* is overexpressed in many types of human cancers, including esophageal squamous cell carcinoma, head and neck squamous cell carcinomas (HNSCC), colorectal, gastric, hepatocellular, breast, and ovarian cancers [11-14].

In some studies, overexpression of *CTTN* correlated with histological differentiation, T and N stage in gastric cancer, depth of invasion in colorectal cancer, as well as poor prognosis for patients with lymph node metastasis [15,16]. However, direct evidence is still lacking to establish a relationship between *CTTN* overexpression and tumor progression and metastasis in gastric adenocarcinoma. The relationship between *CTTN* polymorphisms and susceptibility to gastric cancer is also unclear. Therefore, this study was aimed at investigating the association between the *CTTN* g.-9101C>T, g.-8748C>T, and g.72C>T polymorphisms and susceptibility to gastric cancer, to identify specific polymorphisms as potential risk factors.

## METHODS

Peripheral blood samples were collected from 267 consecutive patients who were diagnosed with gastric cancer at Wonkwang University Hospital between June 2001 and August 2007. We collected blood samples from 533 healthy volunteers, which served as controls. Retrospectively, three single nucleotide polymorphisms (SNPs), *CTTN* g.-9101C> T, g.-8748C> T, and g.72C> T, and clinicopathologic data in the corresponding patients and controls, were analyzed to investigate the association of *CTTN* genetic polymorphisms with susceptibility to gastric cancer.

The stages of gastric cancer were sorted using the American Joint Committee on Cancer manual, seventh edition. Patients were divided by tumor depth into an early gastric cancer (EGC) group and an advanced gastric cancer (AGC) group, respectively. Patients were also divided based on the presence or absence of lymph node metastasis, into an LN (+) group and an LN (–) group, respectively. Clinicopathologic characteristics of gastric cancer patients are listed in Table 1.

**Table 1.** Clinicopathologic characteristics of 267 patients with gastric adenocarcinoma

| Variable | Value |
|---|---|
| Age (yr) | 60.2 ± 10.8 |
| Gender | |
| Male | 177 (66.3) |
| Female | 90 (33.7) |
| Histological type | |
| Well-differentiated | 70 (26.2) |
| Moderately differentiated | 75 (28.1) |
| Poorly differentiated | 63 (23.6) |
| Poorly cohesive carcinoma | 42 (15.7) |
| Mixed type | 17 (6.4) |
| Others | 0 (0) |
| Pathologic T stage[a] | |
| T1 | 157 (58.8) |
| T2 | 60 (22.5) |
| T3 | 43 (16.1) |
| T4 | 7 (2.6) |
| Pathologic N stage[a] | |
| N0 | 131 (49.1) |
| N1 | 45 (16.9) |
| N2 | 54 (20.2) |
| N3 | 37 (13.8) |
| Tumor stage[a] | |
| I | 165 (61.8) |
| II | 31 (11.6) |
| III | 63 (23.6) |
| IV | 8 (3.0) |
| Lymphovascular invasion | |
| Absent | 204 (76.4) |
| Present | 63 (23.6) |

Values are presented as mean ± standard deviation or number (%).
[a]TNM classification as per guidelines in American Joint Committee on Cancer 7th edition.

### Analysis of *CTTN* polymorphisms

Genomic DNA extracted from the peripheral blood of members of each group was analyzed using the polymerase chain reaction-restriction fragment length polymorphism method for the *CTTN* g.-9101C> T, g.-8748C> T polymorphisms, and using the TaqMan method for the g.72C> T polymorphism. In gastric cancer patients, *CTTN* SNPs were analyzed using their peripheral blood collected before surgery.

The DNA samples used in the current study were provided by the Biobank of Wonkwang University Hospital, a member of the National Biobank of Korea; this Biobank is supported by the Ministry of Health and Welfare. The current study was approved by the Institutional Review Board of Wonkwang University Hospital (WKUH-1157), and written informed consent was obtained from all participants.

### Polymerase chain reaction-restriction fragment length polymorphism

Each of the *CTTN* sequences containing the -9101C>T or -8748C>T polymorphic sites was partially amplified using the corresponding primer set (CTTN-PF1; 5'-TCCCAGGTGAG TACCCATGTGGT-3' and CTTN-PR1; 5'-TCGCGGCCAGGCGACGCC ACA-3'). An initial polymerase chain reaction (PCR) denaturation step was performed at 95°C for 5 minutes, followed by 30 cycles of denaturation at 98°C for 10 seconds, then annealing at the melting temperature of each primer pair for 15 seconds, and then extension at 72°C for 30 seconds, with a final 10-minute extension step at 72°C. The PCR products of the sequences containing -9101C>T and -8748C>T were digested with 2U of *Eco*52I for 12 hours at 37°C, and with 1U of *Nar*I for 12 hours

at 37°C, respectively, and then separated on a 1.5% agarose gel and visualized under UV light with ethidium bromide. After restriction enzyme digestion, the PCR products of the sequences containing -9101C>T (630bp) and -8748C>T (630bp) took the form of two fragments, of 490 bp and 140 bp in length, respectively.

### Taq-Man analysis

The assay reagents used for analysis of the g.72C>T (rs2298397) polymorphic site in the *CTTN* gene were designed by Applied Biosystems (Applied Biosystems, Foster City, CA, USA). The reagents consist of a 40× mix of unlabeled PCR primer and TaqMan MGB probes (FAM and VIC dye-labeled). The 10-μL reaction mix was optimized to work with 0.125 μL of 40× reagents, 5 μL of 2× TaqMan Genotyping Master mix (Applied Biosystems) and 2 μL of 50-ng genomic DNA. PCR conditions were as follows: one cycle at 95°C for 15 minutes; 50 cycles, each at 95°C for 10 seconds and 60°C for 45 seconds. The PCR was performed in the Rotor-Gene thermal cycler RG6000 (Corbett Research, Sydney, Australia). The samples were read and analyzed using the Rotor-Gene 1.7.40 software (Corbett Research). The reference sequence for the *CTTN* gene was based on sequence 11q13 of human chromosome 11.

### Statistical analysis

We determined whether the allelic distribution of the SNPs was consistent with the Hardy-Weinberg equilibrium using the chi-square test. The allele and genotype frequencies of these SNPs were compared between the patients and controls using the chi-square test or the Fisher exact test. Survival rates were calculated using the Kaplan-Meier method. P-values less than 0.05 were considered to indicate statistical significance.

## RESULTS

### Genotype and allele frequencies of the *CTTN* polymorphisms

The genotype frequencies of the *CTTN* g.-9101C>T polymorphism were 97.5% (TT), 2.5% (TC), and 0% (CC) in the patient group, and were 98.6% (TT), 1.4% (TC), and 0% (CC) in the control group. The genotype frequencies of the *CTTN* g.-8748C>T polymorphism were 93.2% (TT), 6.8% (TC), and 0% (CC) in the patient group, and were 94.2% (TT), 5.8% (TC), and 0% (CC) in the control group. The genotype frequencies of the *CTTN* g.72C>T polymorphism were 82.4% (CC), 17.2% (CT), and 0.4% (TT) in the patient group, and were 78.0% (CC), 20.1% (CT), and 1.9% (TT) in the control group. The genotype and allele

**Table 2.** Genotype and allele frequencies of the *CTTN* polymorphisms in gastric cancer patients and controls with susceptibility to gastric cancer

| Position[a] | Genotype/allele | Total | | P-value[b] |
|---|---|---|---|---|
| | | Control | Gastric cancer | |
| g.-9101C>T (rs12576561) | TT | 430 (98.6) | 153 (97.5) | |
| | TC | 6 (1.4) | 4 (2.5) | |
| | CC | 0 (0) | 0 (0) | |
| | TT *vs.* TC *vs.* CC | | | 0.618 |
| | T | 866 (99.3) | 310 (98.7) | |
| | C | 6 (0.7) | 4 (1.3) | |
| | T *vs.* C | | | 0.141 |
| g.-8748C>T (rs11825736) | TT | 404 (94.2) | 124 (93.2) | |
| | TC | 25 (5.8) | 9 (6.8) | |
| | CC | 0 (0) | 0 (0) | |
| | TT *vs.* TC *vs.* CC | | | 0.923 |
| | T | 833 (97.1) | 257 (96.6) | |
| | C | 25 (2.9) | 9 (3.4) | |
| | T *vs.* C | | | 0.684 |
| g.72C>T (rs2298397) | CC | 416 (78.0) | 220 (82.4) | |
| | CT | 107 (20.1) | 46 (17.2) | |
| | TT | 10 (1.9) | 1 (0.4) | |
| | CC *vs.* CT *vs.* TT | | | 0.129 |
| | C | 939 (88.1) | 486 (91.0) | |
| | T | 127 (11.9) | 48 (9.0) | |
| | C *vs.* T | | | 0.089 |

Values are presented as number (%).
CTTN, cortactin.
[a]Calculated from the translation start site. [b]Fisher exact test or chi-square test from a 2 × 3 contingency table.

**Table 3.** Comparison of genotype and allele frequencies of the *CTTN* polymorphisms among patients in the EGC group, the AGC group, and controls susceptible to gastric cancer

| Position[a] | Genotype/allele | Tumor depth, n (%) | | | | | P-value[b] | |
|---|---|---|---|---|---|---|---|---|
| | | Control | T1 | T2 | T3 | T4 | *vs.* EGC | *vs.* AGC |
| g.-9101C>T (rs12576561) | TT | 430 (98.6) | 97 (61.8) | 26 (16.5) | 22 (14.0) | 2 (1.3) | | |
| | TC | 6 (1.4) | 0 (0) | 4 (2.6) | 3 (2.0) | 1 (0.6) | | |
| | CC | 0 (0) | 0 (0) | 0 (0) | 1 (0.6) | 1 (0.6) | | |
| | TT *vs.* TC *vs.* CC | | | | | | 0.677 | 0.036 |
| | T | 866 (99.3) | 194 (61.8) | 56 (17.8) | 47 (15.0) | 5 (1.6) | | |
| | C | 6 (0.70) | 0 (0.0) | 4 (1.3) | 5 (1.6) | 3 (0.9) | | |
| | T *vs.* C | | | | | | 0.517 | 0.040 |
| g.-8748C>T (rs11825736) | TT | 404 (94.2) | 73 (55.0) | 32 (24.1) | 22 (16.5) | 4 (3.0) | | |
| | TC | 25 (5.8) | 0 (0) | 1 (0.7) | 1 (0.7) | 0 (0) | | |
| | CC | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | |
| | TT *vs.* TC *vs.* CC | | | | | | 0.208 | 0.970 |
| | T | 833 (97.1) | 146 (54.9) | 65 (24.4) | 45 (16.9) | 8 (3.0) | | |
| | C | 25 (2.9) | 0 (0) | 1 (0.4) | 1 (0.4) | 0 (0) | | |
| | T *vs.* C | | | | | | 0.399 | 0.450 |
| g.72C>T (rs2298397) | CC | 416 (78.0) | 127 (47.6) | 54 (20.2) | 29 (10.7) | 4 (1.5) | | |
| | CT | 107 (20.1) | 30 (11.2) | 5 (1.9) | 14 (5.2) | 3 (1.1) | | |
| | TT | 10 (1.9) | 0 (0.4) | 1 (0.3) | 0 (0) | 0 (0) | | |
| | CC *vs.* CT *vs.* TT | | | | | | 0.304 | 0.835 |
| | C | 939 (88.1) | 284 (53.2) | 113 (21.2) | 72 (13.4) | 11 (2.1) | | |
| | T | 127 (11.9) | 30 (5.6) | 7 (1.3) | 14 (2.6) | 3 (0.6) | | |
| | C *vs.* T | | | | | | 0.739 | 0.904 |

CTTN, cortactin; EGC, early gastric cancer; AGC, advanced gastric cancer.
[a]Calculated from the translation start site. [b]Fisher exact test or chi-square test from a 2 × 3 contingency table.

**Table 4.** Comparison of genotype and allele frequencies of the *CTTN* polymorphisms among the LN (–) and LN (+) gastric cancer groups, and controls susceptible to gastric cancer

| Position[a] | Genotype/allele | LN (–) *vs.* LN (+), n (%) | | | P-value[b] | |
|---|---|---|---|---|---|---|
| | | Control | LN (–) | LN (+) | *vs.* LN (–) | *vs.* LN (+) |
| g.-9101C>T (rs12576561) | TT | 430 (98.6) | 53 (100) | 94 (97.0) | | |
| | TC | 6 (1.4) | 0 (0) | 3 (3.0) | | |
| | CC | 0 (0) | 0 (0) | 0 (0) | | |
| | TT *vs.* TC *vs.* CC | | | | 0.852 | 0.300 |
| | T | 866 (99.3) | 106 (100) | 191 (98.5) | | |
| | C | 6 (0.7) | 0 (0) | 3 (1.5) | | |
| | T *vs.* C | | | | 0.266 | 0.140 |
| g.-8748C>T (rs11825736) | TT | 404 (94.2) | 40 (100) | 91 (97.8) | | |
| | TC | 25 (5.8) | 0 (0) | 2 (2.2) | | |
| | CC | 0 (0) | 0 (0) | 0 (0) | | |
| | TT *vs.* TC *vs.* CC | | | | 0.541 | 0.557 |
| | T | 833 (97.1) | 80 (100) | 184 (98.9) | | |
| | C | 25 (2.9) | 0 (0) | 2 (1.1) | | |
| | T *vs.* C | | | | 0.622 | 0.410 |
| g.72C>T (rs2298397) | CC | 416 (78.0) | 117 (89.3) | 124 (91.1) | | |
| | CT | 107 (20.1) | 14 (11.7) | 11 (8.1) | | |
| | TT | 10 (1.9) | 0 (0) | 1 (0.8) | | |
| | CC *vs.* CT *vs.* TT | | | | 0.101 | 0.250 |
| | C | 939 (88.1) | 248 (94.7) | 259 (92.2) | | |
| | T | 127 (11.9) | 14 (5.3) | 13 (7.8) | | |
| | C *vs.* T | | | | 0.033 | 0.631 |

CTTN, cortactin; LN (–), lymph node-negative gastric cancer; LN (+), lymph node-positive gastric cancer.
[a]Calculated from the translation start site. [b]Fisher exact test or chi-square test from a 2 × 3 contingency table.

**Table 5.** Clinicopathologic characteristics of 60 patients with advanced gastric adenocarcinoma based on the genotypes of *CTTN* g.-9101C>T polymorphism

| Variable | Genotypes of *CTTN* g.-9101C>T polymorphism | | | P-value |
|---|---|---|---|---|
| | TT (n = 50) | TC (n = 8) | CC (n = 2) | |
| Pathologic T stage[a] | | | | 0.267 |
| T2 | 26 (52) | 4 (50) | 0 (0) | |
| T3 | 22 (44) | 3 (37.5) | 1 (50) | |
| T4 | 2 (4) | 1 (12.5) | 1 (50) | |
| Pathologic N stage[a] | | | | 0.154 |
| N0 | 4 (8) | 1 (12.5) | 1 (50) | |
| N1 | 27 (54) | 5 (62.5) | 0 (0) | |
| N2 | 14 (28) | 1 (12.5) | 0 (0) | |
| N3 | 5 (10) | 1 (12.5) | 1 (50) | |
| Tumor stage[a] | | | | 0.210 |
| I | 3 (6) | 1 (12.5) | 0 (0) | |
| II | 29 (58) | 3 (37.5) | 1 (50) | |
| III | 16 (32) | 3 (37.5) | 1 (50) | |
| IV | 2 (4) | 1 (12.5) | 0 (0) | |
| Operation | | | | 0.613 |
| Curative | 48 (96) | 7 (87.5) | 2 (100) | |
| Palliative | 2 (4) | 1 (12.5) | 0 (0) | |
| Chemotherapy | | | | 0.585 |
| Yes | 47 (94) | 7 (87.5) | 2 (100) | |
| No | 3 (6) | 1 (12.5) | 0 (0) | |

Values are presented as number (%).
CTTN, cortactin.
[a]TNM classification as per guidelines in American Joint Committee on Cancer 7th edition.

frequencies of the *CTTN* g.-9101C>T, g.-8748C>T, and g.72C>T polymorphisms were not significantly different between the patient group and the control group (Table 2).

## Genotype and allele frequencies of the *CTTN* polymorphisms, compared among the EGC group, AGC group, and controls susceptible to gastric cancer

The genotype and allele frequencies of the *CTTN* g.-8748C>T, and g.72C>T polymorphisms were not different among the EGC, AGC, and control groups. However, the genotype and allele frequencies of the *CTTN* g.-9101C>T polymorphism were significantly different between the AGC group and the control group (P = 0.036 and P = 0.040, respectively) (Table 3).

## Genotype and allele frequencies of the *CTTN* polymorphisms among the LN (–) and LN (+) gastric cancer groups, and controls susceptible to gastric cancer

The genotype and allele frequencies of the *CTTN* g.-9101C>T, g.-8748C>T, and g.72C>T polymorphisms were not different among lymph node-negative, lymph node-positive, and control groups (Table 4).

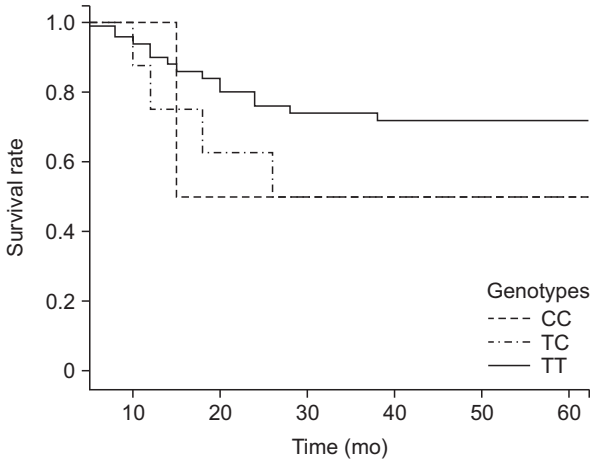


**Fig. 1.** Overall survival of 60 patients with advanced gastric cancer, based on the CTTN g.-9101C>T polymorphism. The group with the TC genotype had a significantly poorer prognosis than the group with the TT genotype (P = 0.020). CTTN, cortactin.

## Relationship between the genotypes in the *CTTN* g.-9101C>T polymorphism and the survival time in patients with AGC

Clinicopathologic characteristics of 60 patients with advanced gastric adenocarcinoma based on the genotypes of *CTTN* g.-9101C>T polymorphism are listed in Table 5 and there was no different between the genotypes (Table 5).

The 60 patients with AGC in the *CTTN* g.-9101C>T polymorphism were followed up for 5 years, and were divided into 3 groups based on the *CTTN* genotype. The group with a TC genotype had a significantly poorer prognosis than the group with a TT genotype (P = 0.020) (Fig. 1).

# DISCUSSION

The development of gastric cancer appears to be the result of a complex interaction between environmental and genetic factors. In particular, the frequency and the variety of genetic polymorphisms in gastric cancer patients seem to vary according to contributing factors, including genetic background and personal factors, which usually go together [3-7,17-19].

Various associations of polymorphisms with disease have been shown in many studies, enabled by the sequencing of the entire human genome and by recent developments in genetics. There has also been an explosion of information concerning natural genetic variations in the human genome, and their functional and clinical significance. This scientific progress allows us to delineate the complex role that genetic factors play in the onset and progression of common multifactorial diseases [20,21].

CTTN was initially identified as a tyrosine-phosphorylated protein in v-Src-infected chicken embryofibroblasts [22]. Subsequent cloning of the cDNA encoding CTTN revealed a novel protein with a unique domain structure. Structural predictions based on the amino acid sequence indicated that CTTN is comprised of several domains. At that time, little was known about its function, except that it binds to actin filaments, it has an Src homology (SH) 3 domain, and is phosphorylated in its C-terminus by an Src kinase [7-9,23].

CTTN contains a proline-rich region with c-Src tyrosine phosphorylation sites and a SH3 domain at the COOH terminus. It also contains an N-terminal acidic region that binds to the Arp2/3 complex. Phosphorylation binding sites and the SH3 domain are necessary for both the activation and the regulation of Arp2/3-complex-mediated branched actin assembly [7-9,24].

Resent research suggests that CTTN may regulate endocytosis of integrins and growth factor receptors, or secretion of proteases and extracellular matrix. These regulations have effects on cell motility, which is dependent on the cell context [25,26].

The *CTTN* gene was found to be identical to *Ems1*, a gene that is frequently overexpressed in breast and head and neck cancers, due to its presence in the 11q13 amplicon. 11q13 amplification has been frequently tied to a poor prognosis, with outcomes including associations with a higher pathological stage, lymph node and distant metastases, and a decreased survival rate [9-16].

Although many other genes are present within this amplicon, the consistent overexpression of *CTTN* in 11q13-amplified tumors, along with its ubiquitous presence in structures involved in cell motility, such as lamellipodia and invadopodia, have generated a great deal of interest in the role of *CTTN* in tumor invasion [9-16,27].

In HNSCC patients, 30%–40% of tumors contain the 11q13 amplicon, and its presence clearly correlates with poor patient prognosis, including decreased survival [13].

Of the many interesting genes, which are present in this amplicon, cyclinD1 and *CTTN* have been considered the best candidates for promoting tumor aggressiveness since, unlike many of the other genes in the amplicon, they are consistently overexpressed upon amplification [28].

Chuma et al. [14] reported that overexpression of *CTTN* may play a role in the metastasis of hepatocellular carcinomas (HCC) by influencing cell motility, and that *CTTN* could be a sensitive marker for HCC with intrahepatic metastasis. Recent research has also shown that overexpression of *CTTN* is closely associated with a poor prognosis in patients affected by HCC caused by cancer embolus and metastasis [29].

In colorectal cancer, Lee et al. [30] reported that the genotype and allele frequencies of the *CTTN* g.-8748C>T and g. 72C>T polymorphisms were not different between the colorectal cancer patient group and the control group, but that the genotype and allele frequencies of the *CTTN* g.-9101C>T polymorphism were significantly different between the lymph node-positive colorectal cancer group and the control group. These results show that the *CTTN* g.-9101C>T polymorphism may have an influence on lymph node-positive colorectal cancer.

At present, direct evidence is still lacking to establish a relationship among *CTTN* overexpression, tumor progression, and metastasis in gastric adenocarcinoma, and the relationship between *CTTN* polymorphisms and susceptibility to gastric cancer is unclear.

In our study, we successfully demonstrated that the genotype and allele frequencies of the *CTTN* g.-9101C>T polymorphism were significantly different between the AGC group and the control group, and that advanced gastric patients in the group with the TC genotype in the *CTTN* g.-9101C>T polymorphism had a significantly poorer prognosis than those in the group with the TT genotype.

These results show that there is an association between the specific *CTTN* polymorphism and the depth of invasion of the tumor in gastric cancer. Moreover, there is the possibility that the specific *CTTN* g.-9101C>T polymorphism present influences the susceptibility to AGC.

To our knowledge, this is the first report to evaluate the association between *CTTN* polymorphisms and the susceptibility to gastric cancer.

However, additional studies with large populations and many ethnic groups are needed to clarify the associations between the respective *CTTN* g.-9101C>T, g.-8748C>T, and g.72C>T polymorphisms and susceptibility to gastric cancer.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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