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# Clinical study on gastric cancer susceptibility genes *IL-10-1082* and *TNF-α*

**T. Yu, Q. Lu, X.L. Ou, D.Z. Cao and Q. Yu**

Department of Gastroenterology,
Affiliated Zhongda Hospital of Southeast University, Nanjing, Jiangsu, China

Corresponding author: Q. Lu
E-mail: yuting686868@foxmail.com

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**ABSTRACT.** TNF 308 gene polymorphism and IL-10 polymorphism provided evidence in diagnosing some types of cancer. We aimed to explore the relation of gene polymorphism with gastric cancer. A total of 360 cases of gastric cancer patients were included in the study. The genotypes GG, GA, and AA of the interleukin-10-1082 gene (*IL-10-1082*) and the tumor necrosis factor-alpha gene (*TNF-α*) 308 polymorphism were examined by chromogenic detection. Three hundred healthy individuals' gene as control group were also examined. The GA 308 genotype of *TNF-α* differed significantly between the control group and the gastric cancer group ($\chi^2$ = 9.32, P < 0.05). Genotype frequencies of A/A (17.2%), A/G (26.2%), and G/G (9.1%) of the *IL-10-1082* gene polymorphism in the gastric cancer group differed significantly compared to those of the control group ($\chi^2$ = 20.32, P < 0.05). The *IL-10-1082* gene and the GA 308 genotype of the *TNF-α* gene were found to be susceptibility genes for gastric cancer.

**Key words:** Chromogenic detection; Gastric cancer; *Helicobacter pylori*; Stomach cancer; Susceptibility gene; TNF-α

 

## INTRODUCTION

*Helicobacter pylori* (Hp) is a pathogenic bacterium that causes gastritis, gastric ulcer, duodenal ulcer, gastric cancer, and other diseases (Blanchard et al., 2013). A recent study showed that long-term infection with Hp in patients is an important risk factor for gastric cancer (Adamsson et al., 2013). In 1994, the World Health Organization Cancer Center categorized Hp into the first class of carcinogens (Shin et al., 2013). The incidence of gastric cancer has been steadily increasing. In addition, many younger patients have begun to develop gastric cancer, making this disease a serious threat to public health. Therefore, detecting the cause of stomach cancer, establishing effective prevention, and finding treatment is urgently needed to address this problem (Gotoda et al., 2000; Ma et al., 2012; Leake et al., 2012).

Stomach cancer is a complex disease caused by multiple factors such as environmental factors, genetic factors, and their combination. Identifying genetic factors can help to explain the causes of stomach cancer. However, studies examining the genetic basis of gastric cancer are limited. Thus, we attempted to identify a gastric cancer susceptibility gene. With similar exposure to hazardous environmental factors, some individuals develop stomach cancer, while others do not. This suggests that different individuals react differently in various environments. Some susceptibility genes for gastric cancer have been identified (Lu et al., 2005; Santos et al., 2012; Liang et al., 2013). For example, the interleukin-1B (*IL-1B*) gene polymorphism has been associated with gastric cancer (Shigematsu et al., 2013). So we suspected TNF 308 gene polymorphism and IL-10 polymorphism might be associated with gastric cancer. In this study, polymerase chain reaction-single strand conformation polymorphism was used to study the association between *IL-1* gene polymorphisms and susceptibility to gastric cancer in a Han population to improve early diagnosis and treatment of gastric cancer.

## MATERIAL AND METHODS

From January 2007 to January 2013, 360 gastric cancer patients were selected from our hospital as the gastric cancer group. Through endoscopy and biopsy, these patients were diagnosed with stomach cancer. A total of 124 cases were male, and 136 cases were female. They were aged 25-73 years, with a mean age of 49 ± 3 years. The median age was 50 years.

Among the 360 cases of patients, diffuse gastric cancer was present in 120 cases. There were 110 cases of atrophic gastric cancer and 130 cases had intestinal gastric cancer. Gastric cancer patients were from families that had lived in the region for the last 3 generations of paternal and maternal residents. The control group included 300 healthy patients (162 male, 138 female). They were aged 28-74 years, with a mean age of 56 ± 3 years. The median age was 55 years. Patients in the control group were all of Han Chinese descent. Patients with benign and malignant disease in other systems, pernicious anemia, and immune system disorders were excluded. Gender and other factors in the 2 groups of patients with gastric cancer were not significantly different ($P > 0.05$). This study was approval by the Ethics Committee in our hospital. The patients signed an informed consent form. The polymerase chain reaction Thermal Cycler, high-speed centrifuge, human chromosome *IL-1B-31* and *IL-1B-511* allele mutation detection chip, Baio e-Hyb BSE automated hybridization instrument, biochips reading device, and gene chip detector were used in this study. (Shanghai Bio Technology Co., Ltd.). Patients were tested using the [$^{13}$C] urea breath test kit according to the manufacturer instructions. A delta value over baseline values ≥4.0% indicated that a patient was Hp-positive.

Venous blood samples were collected (4 mL) and subjected to Western blot analysis with Hp antibodies. A 2-mL venous blood sample was collected in an anticoagulant tube containing ethylenediaminetetraacetic acid, mixed, stored at -80°C, and subjected to polymerase chain reaction amplification, hybridization, and chromogenic detection. The GG, GA, and AA genotypes for the *IL-10-1082* and *TNF-α* 308 polymorphisms were detected.

Using the SPSS16.0 software for data processing and analysis (SPSS, Inc.; Chicago, IL, USA), measurement data (± SD) were compared using the Student *t*-test, and counting data were compared using the $\chi^2$ test. $P < 0.05$ was considered to indicate a statistically significant difference.

## RESULTS

### Relationship between the *IL-10-1082* gene polymorphism and gastric cancer

The frequencies of the A/A (17.2%), A/G (26.2%), and G/G (9.1%) genotypes of the *IL-10-1082* polymorphism in the gastric cancer group were significantly different from those of the control group ($\chi^2 = 20.32$, $P < 0.05$).

### Relationship between *TNF-α* gene polymorphism and gastric cancer

The frequencies of the G/G, G/A, A/A genotypes of the *TNF-α* 308 polymorphism in the gastric cancer group and control group were 90.2, 1.6, and 7.2% and 83.6, 12.4, and 3.5%, respectively. The frequency of allele G and A in the gastric cancer and control groups were 90.5 and 8.2% and were 84.5 and 12.4%, respectively. Compared with the control group, *TNF-α* 308 genotype G/G and A/A frequencies of the gastric cancer group showed no significant difference ($\chi^2 = 1.63$, 3.17, $P > 0.05$). Compared with the control group, the *TNF-α* 308 genotype G/A frequency of the cancer group showed a statistical difference ($\chi^2 = 9.32$, $P < 0.05$).

## DISCUSSION

The incidence of gastric cancer is one of the most frequent types of tumors, comprising 1/3 of all malignant tumors in the digestive tract. The incidence of stomach cancer continues to increase. In this study, we detected the *IL-10-1082* and *TNF-α* 308 polymorphisms for genotypes G/G, G/A, and A/A. We found that the *IL-10-1082* gene and *TNF-α* 308 G/A genotype were susceptibility genes for gastric cancer.

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