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Association of interleukin-1B (*IL-1B*) gene polymorphisms with risk of gastric cancer in Chinese population

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Abstract

The incidence of gastric cancer (GC) in China is among the highest in the world. In present work, 154 patients with GC and 166 healthy controls in population of north-western China were investigated to evaluate the genetic associations of *IL-1B* gene single nucleotide polymorphisms (SNP) and variable number tandem repeat (VNTR) polymorphisms of *IL-1RN* gene with increased risk of GC. The frequency of IL-1B+3954C/T was significantly higher in GC cases group (25.97%) than that in controls (4.82%) with odds ratio (OR) = 6.93 (95% confidence interval [CI] 3.13–15.36); the frequencies of IL-1B-31C/T, IL-1B-31C/C and IL-1B-511C/T genotypes were also higher in GC cases group (51.95%, 23.38% and 50.65%) than those in controls (46.99%, 19.88% and 42.77%) with OR = 1.48 (95% CI 0.88–2.49), OR = 1.58 (95% CI 0.84–2.95) and OR = 1.39 (95% CI 0.80–2.41), respectively. The results show that these SNPs of *IL-1B* gene are associated with significantly increased risk of GC. This is the first report that IL-1B+3954C/T heterozygote is associated with greatly increased risk of GC. The results of this study did not support the report that IL-1RN*2+ genotypes were associated with increased risk of GC in Chinese population.

Keywords: IL-1B; IL-1RN; Polymorphism; Risk of gastric cancer; SNP

1. Introduction

The mortality of GC in China is among the highest in the world, especially in north-western China [1]. It is considered that GC is a complicated disease of multi-pathogeny including environmental and genetic factors [2].

The IL-1 genes cluster consists of 3 linked genes: IL-1A, IL-1B and IL-1RN, mapping to chromosome 2q13–24 that encodes the glycoproteins IL-1α, IL-1β and IL-1 receptor antagonist (IL-1Ra). IL-1α and IL-1β are pro-inflammatory cytokines, whereas IL-1Ra is an anti-inflammatory cytokine and competes with IL-1α and IL-1β for binding to IL-1 receptors. IL-1β is important in starting and enhancing the inflammatory response to *Helicobacter pylori* infection [3–5] and is also a very powerful inhibitor of gastric acid secretion [6,7], long-time inhibition of gastric acid secretion may lead to gastric mucosa atrophy which is considered as a pre-cancerous lesion. SNPs of *IL-1B* gene have been

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reported, including IL-1B-31 representing T–C base transition, IL-1B-511 and IL-1B+3954 both representing C–T base transitions; and there is an 86 bp VNTR polymorphism consisting of 6 alleles (1–6 repeats) in the second intron of *IL-1RN* gene [8,9]. This work was aimed to evaluate the genetic associations of *IL-1B* gene SNPs (IL-1B-31, IL-1B-511 and IL-1B+3954) and *IL-1RN* gene VNTR polymorphisms with increased risk of GC in population of north-western China.

2. Results

A total of 154 GC cases and 166 healthy controls were evaluated in this study from Oct. 2002 to Jan. 2005.

All the frequencies of tested genotypes were in Hardy–Weinberg equilibrium. There were no statistical differences on genotype frequencies between cancer tissues and para-cancer normal tissues (PCNT) in the cases group (data not shown). The frequency of IL-1B+3954C/T genotype was significantly higher in GC cases group (25.97%) than that in controls (4.82%) with OR = 6.93 (95% CI 3.13–15.36); the frequencies of IL-1B-31C/T, IL-1B-31C/C and IL-1B-511C/T genotypes were also higher in cases group (51.95%, 23.38% and 50.65%) than those in controls (46.99%, 19.88% and 42.77%) with OR = 1.48 (95% CI 0.88–2.49), OR = 1.58 (95% CI 0.84–2.95) and OR = 1.39 (95% CI 0.80–2.41), respectively (Table 1).

Four alleles (allele 1, 2, 3 and 4) of IL-1RN VNTR were found in studied population, and there were no statistical differences on the frequencies of both IL-1RN*1/*2 and IL-1RN *2/*2 genotypes between the 2 groups.

3. Discussion

Since El-Omar et al. [10,11] reported that IL-1B-31C+ and IL-1RN*2/*2 genotypes were associated with a significantly increased risk of GC in Caucasians in 2000, some contradictory results from studies in different countries have been reported [12–16]. In present work, IL-1B+3954C/T heterozygote is associated with significantly increased risk of GC in Chinese population. This is the first report that shows IL-1B+3954C/T heterozygote is associated with greatly increased risk of GC. The results also show that carriers of IL-1B-31C+ and IL-1B-511C/T genotypes have higher susceptibility to GC in Chinese population; this is the same with that in Caucasians, but differs from that in Korean and Japanese populations [11–13]. The study also reveals that alleles of IL-1RN*2+ are not associated with increased risk of GC in Chinese population, this is similar to that in Japanese and Korean populations [12,13] but differs from that in Caucasian populations in which IL-1RN*2+ were associated with greatly increased risk of GC [10,15,16]. No IL-1B+3954T/T homozygote carrier was found in both groups in the study; this differs from the genotype frequencies of 6.76% in Caucasians [10], whether this is a genetic difference between Asian people and Caucasian populations still need to be proved; and this does not seem to support the hypothesis [10] that IL-1B+3954T/T homozygote may protect against GC. In conclusion, IL-1B+3954C/T heterozygote is associated with significantly increased risk of GC, and carriers of IL-1B-31C+ and/or IL-1B-511C/T genotypes also have higher susceptibility to GC; otherwise, IL-1RN*2+ is not associated with the risk of GC in Chinese population.

4. Materials and methods

In a case–control study including 154 patients with GC and 166 healthy controls, samples of GC cases were surgically resected specimens obtained from 4 hospitals in Wuwei city where the incidence of GC (209.8 per 100,000 populations) ranks the first in China [1], Gansu

Table 1
IL-1 genotype frequencies in GC cases and controls in studied Chinese population

Locus	Genotype	GC cases (n = 154) N (%)	Controls (n = 166) N (%)	OR (95% CI)
IL-1B-31	T/T	38 (24.67)	55 (33.13)	1.00
	C/T	80 (51.95)	78 (46.99)	1.48 (0.88–2.49)
	C/C	36 (23.38)	33 (19.88)	1.58 (0.84–2.95)
IL-1B-511	C/C	34 (22.08)	43 (25.90)	1.00
	C/T	78 (50.65)	71 (42.77)	1.39 (0.80–2.41)
	T/T	42 (27.27)	52 (31.33)	1.02 (0.56–1.87)
IL-1B+3954	C/C	114 (74.03)	158 (95.18)	1.00
	C/T	40 (25.97)	8 (4.82)	6.93 (3.13–15.36)
	T/T	0	0	0
IL-1RN	1/1	134 (87.01)	128 (77.11)	1.00
	1/2	19 (12.34)	31 (18.67)	0.59 (0.32–1.08)
	2/2	0	5 (3.01)	0
	1/3	0	2 (1.21)	0
	1/4	1 (0.65)	0	Infinite