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Original Article

A case-control study: association of *SMAD7* single nucleotide polymorphisms with colorectal cancer in the Han population

Bin Song[1], Wenhui Zhao[2], Yanbin Long[1], Long Zhou[3], Wen Zhang[4], Ping Wang[5], Tian Feng[3], Tianbo Jin[3], Xianglong Duan[1]

[1]Second Department of General Surgery, Shaanxi Province Hospital, Xi'an 710061, China; [2]Department Anesthesia, Tumor Hospital of Shaanxi Province, Xi'an 710061, China; [3]School of Life Sciences, Northwest University, Xi'an 710069, China; [4]Department of Ear-Nose-Throat, Shaanxi Province Hospital, Xi'an 710061, China; [5]Department of Digestion Internal Medicine, Shaanxi Province Hospital, Xi'an 710061, China

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Abstract: Recent genome-wide studies and analyses of the TGF-β pathway have identified a risk locus among the Caucasian population for colorectal cancer (CRC). This risk locus is located at 18q21, which maps to the SMAD7 gene. As a result, the CRC susceptibility loci identified thus far among Caucasians cannot be used to predict the risk of CRC in Chinese Han population. A Chinese Han population case-control study was conducted to assess genetic associations with CRC risk. Four SNPs in the *SMAD7* gene were genotyped among 276 CRC cases and 385 controls using the Sequenom Mass-ARRAY® platform. The associations of the SNP frequencies with CRC were analyzed by Chi-square (χ^2) tests, SNPStats software, and SHEsis software. Based on χ^2 tests, rs12956924 (P = 0.010), rs11874392 (P = 0.003) and rs4939827 (P = 0.026) correlate with CRC risk. We found that allele "A" of rs12956924 may reduce the risk of CRC (P = 0.048) and rectal cancer (P = 0.03) using the log-additive model genetic analysis. The minor allele "A" of rs11874392 may increase the risk of CRC (P = 0.017), colon (P = 0.038) and rectal (P = 0.03) cancers based on the log-additive model. And we also found the minor allele "T" of rs4939827 was also significantly associated with increase CRC risk (P = 0.026) and colon cancer (P = 0.048) under the dominant model. No significant associations were observed for the rs1873190 SNP evaluated in the *SMAD7* gene. Our data add evidence supporting the genes *SMAD7* is associated with CRC susceptibility and found the differences of susceptibility loci between colon and rectal cancers in Chinese Han population. Collectively, these data suggest that *SMAD7* SNP may be considered as potential diagnostic biomarkers in patients with colorectal cancer in Chinese Han populations.

Keywords: Colorectal cancer (CRC), single nucleotide polymorphism (SNP), case-control study, *SMAD7*, transforming growth factor beta (TGF-β)

Introduction

Colorectal cancer (CRC) is the most common malignant tumor of the digestive tract and the second most common of all gastrointestinal tumors. CRC is the fourth-leading cause of cancer death worldwide [1]. CRC has a high mortality rate because it has no obvious symptoms in the early stages. Both genetic and environmental factors are contribute to the disease etiology of CRC, and about one-third of disease variance is attributed to inherited genetic factors [2]. Recent progress through the application of genome-wide association studies (GWAS) have identified a number of common variants involved in the etiology of CRC. Three GWAS [3-5] identified a risk locus for CRC at 18q21, which maps to *SMAD7*, a functional candidate gene for CRC. *SMAD7* is involved in inflammation-related pathways and has been shown to modulate transforming growth factor-β (TGF-β) and Wnt signaling, which are central to the development of CRC tumors [6]. The TGF-β signaling pathway plays an important role in cancer initiation and progression. This pathway has been reported to correlate with CRC, one recent

Table 1. Characteristics of cases and controls in this study

Characteristic	Case (N = 276)	Control (N = 385)	Total	*P*-value
Sex, No. (%)				0.006*
Male	171 (62)	197 (51.2)	368	
Female	105 (38)	188 (48.8)	293	
Age, No				< 0.001*
< 50	58	191	249	
≥ 50	218	194	412	
Mean age ± SD	58.2 ± 11.6	50.67 ± 8.4		
Histology, No. (%)				
Colon	154 (55.8)		154	
Rectum	106 (5.8)		106	
Others	16 (38.4)		16	

*$P < 0.05$ indicates statistical significance.

study indicates that the *SMAD7*-mediated plastic effect on T-cell phenotype induces protection against colorectal cancer [7, 8]. Although *SMAD7* has been shown to induce hepatic metastasis in colorectal cancer, its role in cancer development has not been fully explored.

Given the role of *SMAD7* in the TGF-β signaling pathway [12] and the wide variation of association between *SMAD7* SNPs and CRC risk among different studies and populations, we performed a case-control study to comprehensively examine four SNPs (rs12956924, rs11874392, rs4939827, and rs1873190) in the *SMAD7* gene and their associations with CRC in a Han Chinese population.

Materials and methods

Study population

A Chinese Han population-based case-control study comprised of newly diagnosed CRC patients from Xi Jing Hospital and Tang du Hospital, which are both affiliated with the Fourth Military Medical University. Control subjects were randomly recruited from the health centers of the two hospitals during the same period. The control population was matched with the case population based upon age and gender. All cases had histologically confirmed CRC. Cases that underwent radiotherapy or chemotherapy were excluded, as were controls with chronic disease. All participants were at least 18 years old and were in good mental condition. Additionally, all participants were Han Chinese. The 385 controls consisted of 188 females and 197 males with a mean age of 50.7 years. The 276 CRC cases consisted of 105 females and 171 males with a mean age of 58.2 years. Detailed population information is shown in **Table 1**.

Clinical data and demographic information

For each participant, a standard questionnaire was used to collect demographic information, including age, sex, smoking status, alcohol use, education, and family history of cancer. All subjects signed informed consent forms. Blood (5 ml) was collected from each subject according to the study protocol approved by the Clinical Research Ethics Committee of the Fourth Military Medical University.

SNPs selection and genotyping

A total of four SNPs from *SMAD7* gene were selected for our study, including rs12956924, rs11874392, rs4939827 and rs1873190. The four SNPs were associated with CRC risk as reported by GWAS [4, 5] and other studies [9, 10]. These SNPs were involved in the transforming growth factor beta (TGF-β) signaling pathway [11]. Genomic DNA was extracted from the peripheral blood using the GoldMag® Whole Blood Genomic DNA Extraction kit (GoldMag® Co. Ltd. Xi'an, China) according to the manufacturer's instructions. DNA concentrations were measured using a NanoDrop™ 2000 (Thermo Scientific, Waltham, MA, USA). A Sequenom Mass ARRAY® mass spectrometry analyzer (Sequenom, San Diego, CA, USA) was used for genotyping, and data were managed using Sequenom Typer 4.0 Software (Sequenom, San Diego, CA, USA) [12, 13].

Statistical analyses

The association for each of the *SMAD7* genotypes and haplotypes was evaluated using unconditional logistic regression models under unrestricted, additive, dominant, and recessive genetic modes of inheritance. In all analyses, the lower frequency allele was coded as the 'risk' allele. For the additive model, individuals were assigned a 0, 1, or 2 representing the number of risk alleles they possessed for that

Table 2. Basic information of the four SNPs in this study

SNP	Chr (Gene)	Position	Alleles A/B	MAF Case	MAF Control	ORs	95% CI	*P*-value
rs12956924	18 SMAD7	46451146	A/G	0.234	0.299	0.71	0.55-0.92	0.010*
rs11874392	18 SMAD7	46453156	A/T	0.487	0.406	1.39	1.11-1.73	0.003*
rs4939827	18 SMAD7	46453463	T/C	0.293	0.239	1.30	1.03-1.69	0.026*
rs1873190	18 SMAD7	46468356	T/C	0.444	0.441	1.02	0.81-1.27	0.890

A/B stands for minor/major alleles. *$P < 0.05$ indicates statistical significance. Abbreviations: MAF, minor allele frequency; OR odds ratio; CI, confidence interval.

Table 3. Single SNP association with colorectal cancer (logistic regression, adjusted by sex, age)

SNP	Model	Genotype	Case	Control	OR (95% CI)	*P*-value
rs12956924	Co-dominant	G/G	156 (59.8%)	192 (51.1%)	1	0.120
		A/G	88 (33.7%)	143 (38%)	0.82 (0.57-1.18)	
		A/A	17 (6.5%)	41 (10.9%)	0.53 (0.28-1.01)	
	Dominant	G/G	156 (59.8%)	192 (51.1%)	1	0.11
		A/G-A/A	105 (40.2%)	184 (48.9%)	0.76 (0.54-1.07)	
	Recessive	G/G-A/G	244 (93.5%)	335 (89.1%)	1	0.078
		A/A	17 (6.5%)	41 (10.9%)	0.57 (0.30-1.08)	
	Log-additive	---	---	---	0.77 (0.59-1.00)	0.048*
rs11874392	Co-dominant	T/T	77 (27.9%)	138 (35.9%)	1	0.057
		T/A	129 (46.7%)	180 (46.9%)	1.30 (0.89-1.91)	
		A/A	70 (25.4%)	66 (17.2%)	1.77 (1.11-2.85)	
	Dominant	T/T	77 (27.9%)	138 (35.9%)	1	0.051
		T/A-A/A	199 (72.1%)	246 (64.1%)	1.43 (1.00-2.05)	
	Recessive	T/T-T/A	206 (74.6%)	318 (82.8%)	1	0.048*
		A/A	70 (25.4%)	66 (17.2%)	1.51 (1.00-2.28)	
	Log-additive	---	---	---	1.33 (1.05-1.68)	0.017*
rs4939827	Co-dominant	C/C	139 (50.4%)	231 (60%)	1	0.081
		T/C	112 (40.6%)	124 (32.2%)	1.49 (1.04-2.12)	
		T/T	25 (9.1%)	30 (7.8%)	1.37 (0.73-2.55)	
	Dominant	C/C	139 (50.4%)	231 (60%)	1	0.026*
		T/C-T/T	137 (49.6%)	154 (40%)	1.46 (1.05-2.05)	
	Recessive	C/C-T/C	251 (90.9%)	355 (92.2%)	1	0.62
		T/T	25 (9.1%)	30 (7.8%)	1.17 (0.64-2.14)	
	Log-additive	---	---	---	1.29 (1.00-1.67)	0.053
rs1873190	Co-dominant	C/C	87 (32.2%)	116 (31.4%)	1	0.71
		T/C	126 (46.7%)	182 (49.2%)	0.89 (0.60-1.31)	
		T/T	57 (21.1%)	72 (19.5%)	1.05 (0.65-1.70)	
	Dominant	C/C	87 (32.2%)	116 (31.4%)	1	0.71
		T/C-T/T	183 (67.8%)	254 (68.7%)	0.93 (0.65-1.34)	
	Recessive	C/C-T/C	213 (78.9%)	298 (80.5%)	1	0.57
		T/T	57 (21.1%)	72 (19.5%)	1.13 (0.74-1.72)	
	Log-additive	---	---	---	1.01 (0.80-1.28)	0.94

*$P < 0.05$ indicates statistical significance. Abbreviations: OR, odds ratio; CI, confidence interval.

SNP. For the dominant model, individuals were coded as 1 if they carried at least 1 risk allele and 0 otherwise. For the recessive model, individuals were coded as 1 if they were homozygous for the risk allele (two copies) and 0 otherwise.

Table 4. Single SNP association with colon cancer (crude)

SNP	Model	Genotype	Case	Control	OR (95% CI)	*P*-value
rs12956924	Co-dominant	G/G	85 (57.8%)	192 (51.1%)	1	0.34
		A/G	50 (34%)	143 (38%)	0.79 (0.52-1.19)	
		A/A	12 (8.2%)	41 (10.9%)	0.66 (0.33-1.32)	
	Dominant	G/G	85 (57.8%)	192 (51.1%)	1	0.16
		A/G-A/A	62 (42.2%)	184 (48.9%)	0.76 (0.52-1.12)	
	Recessive	G/G-A/G	135 (91.8%)	335 (89.1%)	1	0.34
		A/A	12 (8.2%)	41 (10.9%)	0.73 (0.37-1.42)	
	Log-additive	---	---	---	0.80 (0.60-1.08)	0.14
rs11874392	Co-dominant	T/T	45 (29.2%)	138 (35.9%)	1	0.1
		T/A	71 (46.1%)	180 (46.9%)	1.21 (0.78-1.87)	
		A/A	38 (24.7%)	66 (17.2%)	1.77 (1.05-2.98)	
	Dominant	T/T	45 (29.2%)	138 (35.9%)	1	0.13
		T/A-A/A	109 (70.8%)	246 (64.1%)	1.36 (0.91-2.04)	
	Recessive	T/T-T/A	116 (75.3%)	318 (82.8%)	1	0.051
		A/A	38 (24.7%)	66 (17.2%)	1.58 (1.00-2.48)	
	Log-additive	---	---	---	1.32 (1.02-1.71)	0.038*
rs4939827	Co-dominant	C/C	78 (50.6%)	231 (60%)	1	0.13
		T/C	63 (40.9%)	124 (32.2%)	1.50 (1.01-2.24)	
		T/T	13 (8.4%)	30 (7.8%)	1.28 (0.64-2.58)	
	Dominant	C/C	78 (50.6%)	231 (60%)	1	0.048*
		T/C-T/T	76 (49.4%)	154 (40%)	1.46 (1.00-2.13)	
	Recessive	C/C-T/C	141 (91.6%)	355 (92.2%)	1	0.8
		T/T	13 (8.4%)	30 (7.8%)	1.09 (0.55-2.15)	
	Log-additive	---	---	---	1.27 (0.95-1.69)	0.1
rs1873190	Co-dominant	C/C	53 (35.1%)	116 (31.4%)	1	0.71
		T/C	70 (46.4%)	182 (49.2%)	0.84 (0.55-1.29)	
		T/T	28 (18.5%)	72 (19.5%)	0.85 (0.49-1.47)	
	Dominant	C/C	53 (35.1%)	116 (31.4%)	1	0.41
		T/C-T/T	98 (64.9%)	254 (68.7%)	0.84 (0.57-1.26)	
	Recessive	C/C-T/C	123 (81.5%)	298 (80.5%)	1	0.81
		T/T	28 (18.5%)	72 (19.5%)	0.94 (0.58-1.53)	
	Log-additive	---	---	---	0.91 (0.70-1.19)	0.49

*$P < 0.05$ indicates statistical significance. Abbreviation: OR, odds ratio; CI, confidence interval.

In controls, each SNP was tested to determine whether it fit with the Hardy-Weinberg equilibrium (HWE). Chi-squared (χ^2) tests [14] and SNPStats, a web-based software from http://bioinfo.iconcologia.net/snpstats/start.htm [15], were used to test the association between genetic polymorphisms and CRC. Odds ratios (OR) and 95% confidence intervals (CI) were calculated using unconditional logistic regression analyses adjusted for age and gender [16], and the most common control homozygote was used as reference. Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to choose the best model for each SNP. LD of the candidate SNPs was analyzed using Haploview v4.2 [17]. All *P*-values reported in this study were two-tailed and *p*-values less than 0.05 were considered statistically significant. Pairwise linkage disequilibrium and haplotype constructions were performed using the SHEsis software (http://analysis.bio-x.cn/myAnalysis.php) [18].

Results

The distributions of demographic and behavioral characteristics among subjects included in the primary analysis are shown in **Table 1**.

Table 5. Single SNP association with rectal cancer (adjusted by sex, age)

SNP	Model	Genotype	Case	Control	OR (95% CI)	*P*-value
rs12956924	Co-dominant	G/G	64 (64.7%)	192 (51.1%)	1	0.093
		A/G	30 (30.3%)	143 (38.0%)	0.69 (0.42-1.15)	
		A/A	5 (5%)	41 (10.9%)	0.40 (0.15-1.11)	
	Dominant	G/G	64 (64.7%)	192 (51.1%)	1	0.056
		A/G-A/A	35 (35.4%)	184 (48.9%)	0.63 (0.39-1.02)	
	Recessive	G/G-A/G	94 (95%)	335 (89.1%)	1	0.1
		A/A	5 (5%)	41 (10.9%)	0.46 (0.17-1.25)	
	Log-additive	---	---	---	0.66 (0.45-0.97)	0.03*
rs11874392	Co-dominant	T/T	26 (24.5%)	138 (35.9%)	1	0.083
		T/A	51 (48.1%)	180 (46.9%)	1.60 (0.92-2.76)	
		A/A	29 (27.4%)	66 (17.2%)	2.00 (1.05-3.81)	
	Dominant	T/T	26 (24.5%)	138 (35.9%)	1	0.035*
		T/A-A/A	80 (75.5%)	246 (64.1%)	1.71 (1.03-2.86)	
	Recessive	T/T-T/A	77 (72.6%)	318 (82.8%)	1	0.15
		A/A	29 (27.4%)	66 (17.2%)	1.50 (0.87-2.59)	
	Log-additive	---	---	---	1.42 (1.03-1.95)	0.03*
rs4939827	Co-dominant	C/C	52 (49.1%)	231 (60%)	1	0.19
		T/C	44 (41.5%)	124 (32.2%)	1.52 (0.94-2.47)	
		T/T	10 (9.4%)	30 (7.8%)	1.56 (0.68-3.59)	
	Dominant	C/C	52 (49.1%)	231 (60%)	1	0.07
		T/C-T/T	54 (50.9%)	154 (40%)	1.53 (0.97-2.42)	
	Recessive	C/C-T/C	96 (90.6%)	355 (92.2%)	1	0.51
		T/T	10 (9.4%)	30 (7.8%)	1.31 (0.58-2.95)	
	Log-additive	---	---	---	1.35 (0.95-1.91)	0.095
rs1873190	Co-dominant	C/C	31 (29.5%)	116 (31.4%)	1	0.76
		T/C	50 (47.6%)	182 (49.2%)	1.07 (0.62-1.82)	
		T/T	24 (22.9%)	72 (19.5%)	1.28 (0.66-2.45)	
	Dominant	C/C	31 (29.5%)	116 (31.4%)	1	0.65
		T/C-T/T	74 (70.5%)	254 (68.7%)	1.12 (0.68-1.86)	
	Recessive	C/C-T/C	81 (77.1%)	298 (80.5%)	1	0.48
		T/T	24 (22.9%)	72 (19.5%)	1.23 (0.70-2.15)	
	Log-additive	---	---	---	1.12 (0.81-1.56)	0.48

*$P < 0.05$ indicates statistical significance. Abbreviations: OR, odds ratio; CI confidence interval.

CRC cases were older (mean age 58.2 ± 11.6) and more likely to be male 171 (62%) relative to controls (mean age 50.67 ± 8.4, 197 (51.2%) male).

In our initial analyses, we sought to determine whether the four SNPs we tested fit the Hardy-Weinberg Equilibrium. We found that all four SNPs conformed to Hardy-Weinberg proportions in the controls ($P > 0.05$). Based on χ^2 tests, rs12956924 ($P = 0.010$), rs11874392 ($P = 0.003$) and rs4939827 ($P = 0.026$) correlated with CRC risk (**Table 2**).

In the genetic model analyses, we found the minor allele "A" of rs12956924 was associated with reduced risk of colorectal cancer, based on results from the log-additive model (OR = 0.77; 95% CI = 0.59-1.00, $P = 0.048$). In contrast, the minor allele "A" of rs11874392 was associated with increased risk of colorectal cancer as revealed by the log-additive model (OR = 1.33, 95% CI = 1.05-1.68, $P = 0.017$) and the genotype "AA" may significantly increase CRC risk in the recessive model ($P = 0.048$). Additionally, we found the minor allele "T" of rs4939827 was significantly associated with

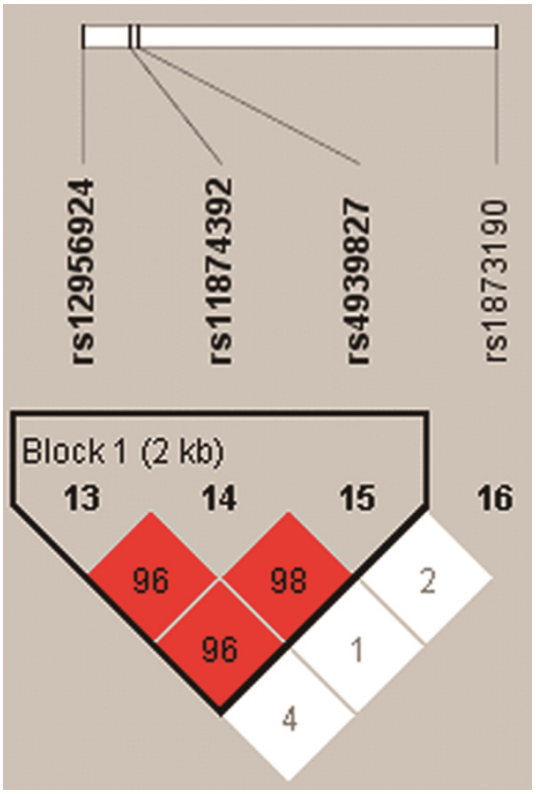

Figure 1. Haplotype block map for four SNPs in the *SMAD7* gene (D'). Linkage disequilibrium analysis of *SMAD7* in Chinese Li controls. LD is indicated using standard color schemes with bright red signifying very strong LD (LOD ≥ 2, D' = 1), pink red (LOD ≥ 2, D' < 1).

increased CRC risk, with an OR = 1.46, 95% CI = 1.05-2.05, *P* = 0.026 under the dominant model (**Table 3**).

We examined the cancer risk of these SNPs by dividing the populations into subgroups of colon and rectal cancers. Within the subgroups of colon and rectal cancers, we found the minor allele "A" of rs11874392 may increase the risk of colon cancer in the log-additive model (OR = 1.32, 95% CI = 1.02-1.71, *P* = 0.038). The rs4939827 allele was also significantly associated with increased colon cancer risk, with an OR = 1.46, 95% CI = 1.05-2.13, and *P* = 0.048 under the dominant model (**Table 4**). However, when adjusted by sex and age, this SNP was not found to be significantly associated with colon cancer risk. In the rectal cancer subgroup, we found the minor allele "A" of rs12956924 may reduce the risk of rectal cancer in the log-additive model (OR = 0.66, 95% CI = 0.45-0.97, *P* = 0.03), and the minor allele "A" of rs11874392 may increase the risk of rectal cancer in the log-additive model (OR = 1.42, 95% CI = 1.03-1.95, *P* = 0.03) (**Table 5**).

Finally, we looked for interactions of the four SNPs with patient age and patient gender. We found that none of these SNPs showed evidence of interaction with age or gender of colorectal cancer patients (data not shown). One block was detected in *SMAD7* SNPs by haplotype analyses. The three SNPs (rs12956924, rs11874392 and rs4939827) construct four haplotypes "GAT" "GTC" "ATC", and "GAC". The linkage disequilibrium (LD) between three SNPs is standardized D' (red schemes) showed in **Figure 1**. No haplotype was observed to significant associate with CRC.

Discussion

Four SNPs were selected in *SMAD7* in this study, we found that allele "A" of rs12956924 may reduce the risk of CRC (*P* = 0.048) and rectal cancer (*P* = 0.03) using the log-additive model genetic analysis. The minor allele "A" of rs11874392 may increase the risk of CRC (*P* = 0.017), colon (*P* = 0.038) and rectal (*P* = 0.03) cancers based on the log-additive model. And we also found the minor allele "T" of rs4939827 was also significantly associated with increase CRC risk (*P* = 0.026) and colon cancer (*P* = 0.048) under the dominant model. No significant associations were observed for the rs1873190 SNP evaluated in the *SMAD7* gene.

It is known that the contribution of risk alleles to CRC risk may vary between populations. This phenomenon may be due to differences in allelic frequencies or specific linkage disequilibrium (LD) structures, or because of additional genetic factors or environmental backgrounds may influence the effect of these genetic variants [19, 20]. rs4939827 located at 18q21 was revealed to be associated with CRC risk by two GWA studies, but inconsistent results have been reported by multiple following replication studies [21]. Consistent with the GWAS by Broderick and colleagues [4] which carrying the rs4939827 homozygote variant genotype showed a 27% reduced risk of CRC (95% CI = 0.66-0.80), we observed a statistically significant association with the genotype at the rs4939827 allele of *SMAD7* and CRC. Another GWAS conducted among individuals with a family history of CRC showed that the rs4939827

SMAD7 SNP was inversely associated with CRC [4]. In contrast to other studies, the study by Tenesa and colleagues [5] found a statistically consistent 20% increased risk of CRC with the rs4939827 *SMAD7* variant allele, rather than a 27% reduction in risk reported by others. It is possible that these results reflect different variant alleles in the populations studied, given that the minor allele frequency was close to 0.5 (and two GWAS did not report the actual genotypes, but rather instead OR_{hom} or OR_{het}). In this study, the minor allele frequency for rs4939827 was 0.239 in control group, this date was different with previous studies which closed to 0.5 [22]. Data from HapMap Chinese Han Beijing population showed that the minor allele frequency at this SNP (rs4939827) was 0.214, very closed to the frequency in our study. So this study has the guiding significance to illustrate the relationship between the loci rs4939827 in *SMAD7* and CRC diseases in Chinese Han people. In our study, we found the minor allele "T" of rs4939827 was also significantly associated with increased CRC risk (P = 0.026) and colon cancer risk (P = 0.048) under the dominant model. Our findings corroborate those of the GWAS in colon cancer that pointed to variants in *SMAD7* and reinforces interest in SNPs in this gene. Interestingly, the minor allele gene "C" was reported to be associated with reduced risk in previous studies of other populations [4-6, 22].

TGF-β pathway regulates growth inhibition and apoptosis and plays an important role in cancer initiation and progressions [23, 24], the two study highlights the potential importance of the TGF-β genetic polymorphisms was associated with colorectal carcinogenesis. Our data provide further evidence that common genetic variants in *SMAD7* may confer susceptibility to CRC, particularly in the Chinese Han population. More research is warranted to confirm these findings and functionally characterize the *SMAD7* variants. In our study we found a significant association between *SMAD7* variants and risk of colorectal cancer in Chinese Han population. However, the Chinese population has 56 diverse ethnicities, making it the biggest in the world. Due to the demographics vary widely across the nation this association analysis cannot be used on all Chinese people and must be restricted to Chinese Han people. More research is warranted to confirm our findings whether confirmed in other ethnic groups.

None of these four SNPs showed evidence of interaction with gender in the Han population. Alternatively, our sample size could be too small to detect such an association. Moreover, we did not conduct a pathological classification within our sample population. Thus, we need to increase the sample size and further investigate whether these genes are involved in CRC in the Han population. CRC is a very complex disease related to several environmental and genetic factors. The mechanism by which these SNPs may influence colorectal cancer implicates an inhibitory role for the *SMAD7* protein in the TGF-β signaling pathway [11, 25], but more research is necessary to uncover the precise mechanism. We recommend that persons who carry increased risk alleles should concentrate on developing healthy eating habits and receive regular colonoscopy testing.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xianglong Duan, Second Department of General Surgery, Shaanxi Province Hospital, Xi'an 710061, China. E-mail: xianglduan@163.com; Dr. Tianbo Jin, School of Life Sciences, Northwest University, 386, #229 North Taibai Road, Xi'an 710069, Shaanxi, China. Tel: +86-29-88302831; Fax: +86-29-88302831; E-mail: tianbojinprofessor@163.com

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