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META-ANALYSIS

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Association of 3 Common Polymorphisms of IL-27 Gene with Susceptibility to Cancer in Chinese: Evidence From an Updated Meta-Analysis of 27 Studies

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Background: Many epidemiology studies have indicated that several functional polymorphisms of the *IL-27* gene may contribute to individual susceptibility to cancer. Nevertheless, the data arising from these studies were inconclusive. Therefore, we conducted the current meta-analysis aiming to elucidate the effects of *IL-27* polymorphisms (rs153109, rs17855750, and rs181206) on cancer susceptibility.

Material/Methods: We searched the CNKI (Chinese National Knowledge Infrastructure), Wanfang database, PubMed, Web of Science, and Google Scholar for all eligible publications. We used odds ratios (ORs) corresponding with 95% confidence intervals (CIs) by using the random/fixed-effects model to evaluate the association. Finally, a total of 12 publications, including 27 case-control studies comprising of 7570 patients and 9839 controls, were enrolled in our meta-analysis.

Results: Our work demonstrates that *IL-27* rs17855750 polymorphism is significantly associated with cancer susceptibility, particularly for bladder cancer. However, no association between *IL-27* rs153109 and rs181206 polymorphisms and cancer susceptibility was identified. When a stratification analysis was performed by cancer type, we identified an increased susceptibility of bladder cancer in rs153109 polymorphism. Moreover, in the stratification analysis by genotyping method, we identified an increased susceptibility for PCR-RFLP group in rs17855750 polymorphism, whereas a decreased susceptibility was identified in rs153109 polymorphism.

Conclusions: Our study shows that *IL-27* rs17855750 polymorphism is significantly associated with increased susceptibility to cancer in Chinese.

MeSH Keywords: Interleukin-27 • Meta-Analysis • Polymorphism, Single-Stranded Conformational

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Background

With the obvious increasing prevalence and mortality rate, cancer has become one of the primary causes of morbidity and mortality [1]. The underlying mechanisms of the tumorigenesis are obscure because of the involvement of multiple risk factors containing complicated gene-gene and gene-environment interactions [2]. Many studies have demonstrated that the occurrence of cancers may be related to inflammation, and that cytokines are associated with individual susceptibility to cancers [3].

Cytokine-mediated immunity plays a critical role in the tumorigenesis [4]. IL-27 is included in the cytokines of IL-12 family. It is located on chromosome 16 (16p11) and comprises 2 subunits-Epstein-Barr virus-induced gene 3 (EBI3) and p28, which is a recently discovered IL-12p35-related polypeptide [5]. IL-27 is mainly secreted by antigen-presenting cells. It was described as a pro-inflammatory cytokine that enhances T helper (Th) 1 responses, cytotoxic T lymphocytes (CTLs) maturation, natural killer (NK) cells stimulation, and secretion of interferon-γ (IFN-γ) [5]. Research shows that IL-27 can impair tumor progression by CD8+ T cells with promoted CTL reaction, regardless of tumor immunogenicity [6]. Additionally, IL-12 inhibits neoangiogenesis in tumors by stimulation of IFN-γ-inducible protein-10 (IP-10) [7].

In view of the association of *IL-27* polymorphisms and susceptibility to cancer, some previous case-control studies were conducted among Chinese population [8–13]. However, the conclusions were inconsistent and inconclusive. In 2014, Hu et al. [14] conducted a meta-analysis of 6 case-control studies and concluded that *IL-27* rs153109 polymorphism was associated with cancer susceptibility in Chinese, a result consistent with another meta-analysis of 8 case-control studies by Xu et al. [15] that *IL-27*-964A/G (rs153109) polymorphism might enhance cancer susceptibility. Using more recent studies, we conducted an updated meta-analysis to obtain a more precise evaluation of the relevance of *IL-27* polymorphisms (rs153109, rs17855750, and rs181206) and cancer susceptibility.

Material and Methods

Literature search strategy

We conducted a comprehensive literature search in PubMed, Web of Science, Google Scholar, CNKI (Chinese National Knowledge Infrastructure), and Wanfang databases to find all eligible case-control studies up to June 11, 2015 on the association between polymorphisms of *IL-27* (rs153109, rs17855750 and rs181206) and cancer susceptibility by applying the searching terms: ("interleukin-27" OR "*IL-27*") and ("mutation" OR "polymorphism" OR "variant") and ("cancer" OR "malignancy" OR "carcinoma" OR "tumour" OR "neoplasm") without language restriction. In addition, we checked the reference lists of all the eligible publications or the relevant reviews for additional studies.

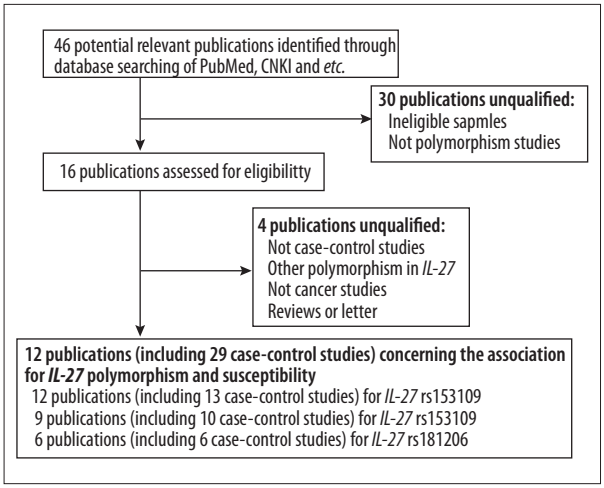

Figure 1. The flow chart presenting the publications selecting procedure.

Selection criteria

The studies enrolled in the current meta-analysis had to satisfy the following criteria: (a) studies that assessed the relevance between the polymorphisms in *IL-27* and cancer susceptibility; (b) studies designed as case-control; (c) we can obtain specific genotype frequency of all the cases and controls or they can be obtained from the available data. We excluded studies which were: (a) case-only studies, reviews, comments, and case reports; (b) studies without the raw statistics of the polymorphisms of *IL-27*; (c) publications that were repetitive; (d) studies focused on animals.

Data extraction

The following details were recorded from each study by 3 investigators (Meng Zhang, Xiuxiu Tan, and Junjie Huang): the name of the first author, year published, ethnicity of the case-control studies, source of controls, genotyping method, the number of cases and controls, and the P value of the HWE in control groups. Any disagreements were discussed by the 3 authors until a consensus was reached.

Statistical analysis

We assessed the association between *IL-27* polymorphisms and cancer susceptibility by OR and 95% CI. A total of 5 different ORs were calculated: allele contrast model (B *vs.* A), dominant model (BB+AB *vs.* AA), recessive model (BB *vs.* AB+AA), heterozygote comparison (AB *vs.* AA), and homozygote comparison

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Table 1. Characteristics of the enrolled studies.

SNP	First author	Year	Source of Control	Country	Genotyping method	Cancer type	Case			Control			
							AA	AB	BB	AA	AB	BB	P (HWE)
RS153109	Wei et al.	2009	HB	Chinese	PCR-RFLP	NPC	119	150	33	113	161	36	0.060
	Zhao et al.	2009	HB	Chinese	PCR-RFLP	Glioma	79	101	30	81	112	27	0.215
	Peng et al.	2013	HB	Chinese	PCR-RFLP	HCC	38	48	21	40	46	19	0.371
	Zhang et al.	2015	HB	Chinese	PCR-RFLP	PTC	287	309	68	332	399	96	0.147
	Pan et al.	2012	HB	Chinese	PCR-RFLP	NPC	90	78	22	85	87	28	0.453
	Tao et al.	2012	HB	Chinese	PCR-RFLP	ESC	163	205	58	162	219	51	0.075
	Zhang et al.	2014	HB	Chinese	PCR-RFLP	EOC	85	103	41	161	124	35	0.139
	Guo et al.	2012	HB	Chinese	PCR-RFLP	CRC	53	84	33	75	66	19	0.449
	Huang et al.	2012	HB	Chinese	PCR-RFLP	CRC	151	213	46	183	222	45	0.059
	Zhang et al.	2014	HB	Chinese	PCR-RFLP	BRC	143	156	27	185	223	52	0.213
	Tang et al.	2014	HB	Chinese	PCR	Osteosarcoma	56	85	19	100	124	26	0.167
	Zhou et al.	2015	HB	Chinese	PCR	BC	66	87	23	229	204	66	0.058
	Zhou et al.	2015	HB	Chinese	PCR	BC	61	73	22	229	204	66	0.058
RS17855750	Wei et al.	2009	HB	Chinese	PCR-RFLP	NPC	247	55	0	259	51	0	0.115
	Zhao et al.	2009	HB	Chinese	PCR-RFLP	Glioma	169	41	0	185	35	0	0.200
	Peng et al.	2013	HB	Chinese	PCR-RFLP	HCC	83	21	3	72	28	5	0.304
	Zhang et al.	2014	HB	Chinese	PCR-RFLP	OC	170	51	8	267	53	0	0.106
	Tao et al.	2012	HB	Chinese	PCR-RFLP	ESC	345	81	0	355	77	0	**0.042**
	Huang et al.	2012	HB	Chinese	PCR-RFLP	CRC	341	69	0	382	68	0	0.083
	Guo et al.	2012	HB	Chinese	PCR-RFLP	CRC	120	41	9	122	33	5	0.151
	Tang et al.	2014	HB	Chinese	PCR	Osteosarcoma	132	28	0	205	45	0	0.118
	Zhou et al.	2015	HB	Chinese	PCR	BC	149	26	1	421	78	0	0.058
	Zhou et al.	2015	HB	Chinese	PCR	BC	126	27	3	421	78	0	0.058
RS181206	Wei et al.	2009	HB	Chinese	PCR-RFLP	NPC	241	61	0	253	57	0	0.075
	Zhao et al.	2009	HB	Chinese	PCR-RFLP	Glioma	166	44	0	182	38	0	0.161
	Pan et al.	2012	HB	Chinese	PCR-RFLP	NPC	157	33	0	158	42	0	0.097
	Tao et al.	2012	HB	Chinese	PCR-RFLP	ESC	335	91	0	354	78	0	**0.039**
	Huang et al.	2012	HB	Chinese	PCR-RFLP	CRC	331	79	0	373	77	0	**0.047**
	Tang et al.	2014	HB	Chinese	PCR	Osteosarcoma	131	29	0	207	43	0	0.137

NPC – nasopharyngeal carcinoma; HCC – hepatocellular carcinoma; PTC – papillary thyroid cancer; CRC – colorectal cancer; BC – bladder cancer; ESC – esophageal cancer; EOC – epithelial ovarian cancer; BRC – breast cancer; PCR-RFLP – polymerase chain reaction-restriction fragment length polymorphism; HWE – Hardy-Weinberg equilibrium; H-B: hospital based.

(BB *vs.* AB) (AA, homozygotes for the common allele; AB, heterozygotes; BB, homozygotes for the rare allele). We conducted a χ^2-test-based Q statistic test to evaluate the heterogeneity within the case-control studies [16]. If the Q test (P>0.1) suggested homogeneity across studies, we selected the fixed-effects model [17]; otherwise, the random-effects model was used [18]. In addition, we further quantified the heterogeneity effect by I^2 test (I^2<25%: no heterogeneity; I^2=25–50%: moderate heterogeneity; I^2=50–75%: high heterogeneity, I^2>75%: extreme high heterogeneity) [19]. P values of the HWE for control groups were tested by χ^2 test. Stratification analyses on tumor type and genotyping method were conducted. If any cancer type totals no more than 2 studies, we included it into the "other cancers" group. Sensitivity analyses were used to calculate the stability of the results by removing a single case-control study from the enrolled pooled data to detect the influence of that data set on the pooled ORs. Finally, we used Begg's funnel plot and Egger's regression test to evaluate the potential

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Table 2. Results of meta-analysis for the polymorphisms in *IL-27* and cancer risk.

Variables (rs17855750)	Case/ Control	G *vs.* T			GG *vs.* TT			GT *vs.* TT		
		OR (95% CI)	P[a]	I^2 (%)	OR (95% CI)	P[a]	I^2 (%)	OR (95% CI)	P[a]	I^2 (%)
Total		1.177 (1.034–1.341)*	0.156	31.5	3.529 (0.803–15.515)	0.036	61.2	1.120 (0.972–1.290)	0.747	0.0
Bladder cancer		1.196 (0.877–1.630)	0.322	0.0	14.600 (1.653–128.994)*	0.647	0.0	1.042 (0.742–1.464)		
Colorectal cancer		1.211 (0.925–1.586)	0.511	0.0	1.830 (0.596–5.619)	–	–	1.177 (0.872–1.588)	0.746	0.0
Genotyping method			0.554	0.0						
PCR-RFLP		1.194 (1.028–1.387)*	0.074	47.9	2.035 (0.356–11.628)	0.037	69.6	1.155 (0.981–1.361)	0.550	0.0
PCR		1.125 (0.865–1.464)	0.472	0.0	14.600 (1.653–128.994)*	0.647	0.0	1.019 (0.766–1.354)	0.815	0.0
	Case/ control	GG+GT *vs.* TT			GG *vs.* GT+TT					
		OR (95% CI)	P[a]	I^2 (%)	OR (95% CI)	P[a]	I^2 (%)			
Total		1.156 (1.005–1.329)*	0.410	3.3	3.413 (0.818–14.250)	0.046	58.7			
Bladder cancer		1.121 (0.804–1.563)	0.421	0.0	14.480 (1.640–127.836)*	0.658	0.0			
Colorectal cancer		1.205 (0.899–1.615)	0.602	0.0	1.733 (0.568–5.286)	–	–			
Genotyping method										
PCR-RFLP		1.185 (1.008–1.392)*	0.232	25.7%	1.974 (0.380–10.249)	0.051	66.4			
PCR		1.073 (0.811–1.420)	0.645	0.0%	14.480 (1.640–127.8360)*	0.658	0.0			
Variables (rs181206)	Case/ control	C *vs.* T			CC *vs.* TT			CT *vs.* TT		
		OR (95% CI)	P[a]	I^2 (%)	OR (95% CI)	P[a]	I^2 (%)	OR (95% CI)	P[a]	I^2 (%)
Total		1.110 (0.947–1.302)	0.823	0.0%	–	–	–	1.124 (0.950–1.330)	0.784	0.0
NPC		0.983 (0.730–1.322)	0.314	1.2%	–	–	–	0.981 (0.716–1.342)	0.287	11.8
Genotyping method										
PCR-RFLP		1.116 (0.943–1.321)	0.709	0.0%	–	–	–	1.131 (0.946–1.351)	0.662	0.0
	Case/ control	CC+CT *vs.* TT			CC *vs.* CT+TT					
		OR (95% CI)	Pa	I2	OR (95% CI)	Pa	I2			
Total		1.124 (0.950–1.330)	0.784	0.0	–	–	–			
NPC		0.981 (0.716–1.342)	0.287	11.8	–	–	–			
Genotyping method										
PCR–RFLP		1.131 (0.946–1.351)	0.662	0.0	–	–	–			

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Table 2 continued. Results of meta-analysis for the polymorphisms in *IL-27* and cancer risk.

Variables (rs153109)	Case/ control	G *vs.* A			GG *vs.* AA			GG *vs.* AA		
		OR (95% CI)	P^a	I^2 (%)	OR (95% CI)	P^a	I^2 (%)	OR (95% CI)	P^a	I^2 (%)
Total	3526/4732	1.080 (0.972–1.201)	0.003	35.5	1.137 (0.929–1.391)	0.038	20.4	1.095 (0.961–1.249)	0.047	18.8
Cancer type										
NPC	492/510	0.895 (0.746–1.075)	0.661	0.0	0.814 (0.540–1.226)	0.706	0.0	0.870 (0.667–1.134)	0.875	0.0
Colorectal cancer	580/610	1.325 (0.911–1.927)	0.044	57.0	1.671 (0.859–3.253)	0.098	40.3	1.386 (0.910–2.110)	0.123	33.5
Bladder cancer	332/998	1.190 (0.991–1.428)	0.948	0.0	1.230 (0.831–1.819)	0.932	0.0	1.413 (1.080–1.848)*	0.725	0.0
Genotyping method										
PCR–RFLP	3034/3484	1.057 (0.928–1.205)	0.001	44.9	0.943 (0.890–1.000)*	0.094	27.9	1.035 (0.896–1.195)	0.077	17.8
PCR	492/1248	1.178 (1.009–1.375)*	0.979	0.0	1.144 (0.899–1.456)	0.792	0.0	1.357 (1.081–1.703)*	0.805	0.0
	Case/ control	GG+GA *vs.* AA			GG *vs.* GA+AA					
		OR (95% CI)	P^a	I^2 (%)	OR (95% CI)	P^a	I^2 (%)			
Total	3526/4732	1.112 (0.963–1.283)	0.006	32.6	1.064 (0.930–1.218)	0.038	4.9			
Cancer type										
NPC	664/827	0.857 (0.666–1.104)	0.786	0.0	0.878 (0.598–1.289)	0.708	0.0			
Colorectal cancer	160/250	1.465 (0.897–2.393)	0.786	51.4	1.328 (0.934–1.889)	0.237	8.0			
Bladder cancer	492/510	1.368 (1.061–1.764)	0.794	0.0	1.029 (0.715–1.481)	0.812	0.0			
Genotyping method	210/220									
PCR–RFLP	426/432	1.061 (0.898–1.253)	0.006	37.2	1.065 (0.917–1.237)	0.175	8.6			
PCR	229/320	1.331 (1.072–1.652)*	0.890	0.0	1.061 (0.775–1.453)	0.923	0.0			

I^2: 0–25, means no heterogeneity; 25–50, means modest heterogeneity; >50, means high heterogeneity; P^a: P value of Q test for heterogeneity test; * means statistically significant (P<0.05).

publication bias [20, 21]. P<0.05 was considered as statistically significant. We used STATA 12.0 (Stata Corporation, College Station, Texas) to conduct all statistical analyses.

Results

Study characteristics

As presented in Figure 1, after a systematic literature search in the databases, 46 potential relevant studies on the association between *IL-27* polymorphisms and cancer were identified. Nevertheless, of them, 34 were unqualified in that some were based on case-only design, some were not polymorphism studies and the others were not concerning the susceptibility of cancer. In the end, a total of 12 publications with 27 independent case-control studies comprising of 7,570 cases and 9,839 controls were concerning the associations of *IL-27* polymorphisms and cancer susceptibility. The characteristics of enrolled studies were presented in Table 1 [8–13,22–27]. The genotype distributions of the three polymorphisms and the genotyping method of the enrolled studies were retrieved scrupulously, and the controls were selected from non-cancer populations. Additionally, there were three case-control studies deviated from HWE [13,23].

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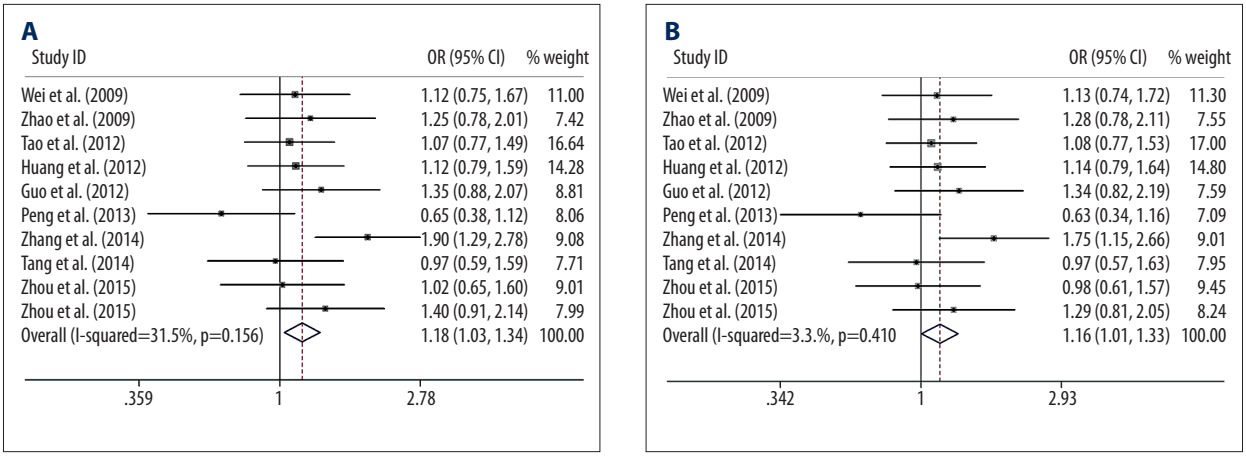
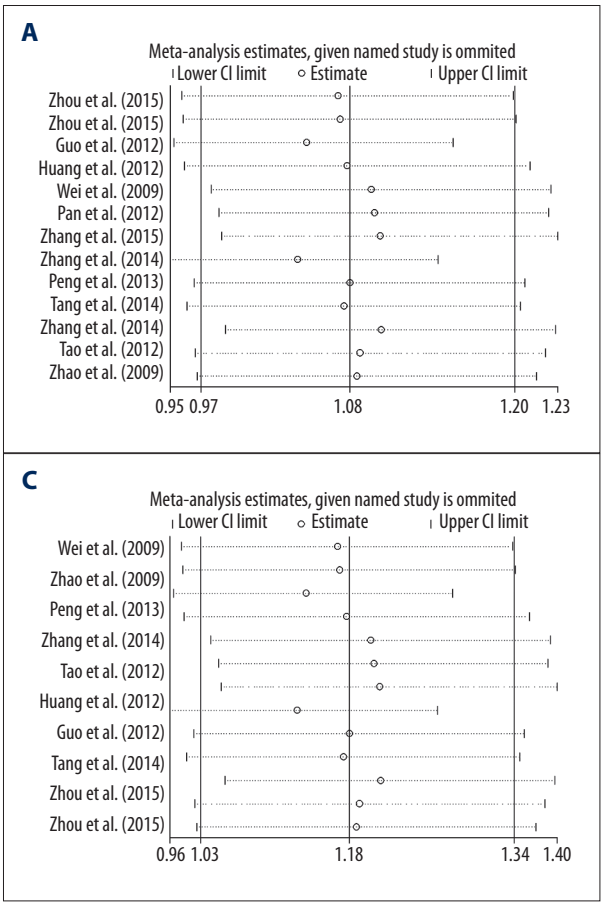


Figure 2. (**A**) OR estimates with the corresponding 95% CI for the association of *IL-27* rs17855750 polymorphism with overall cancer risk (G *vs.* T). The sizes of the squares represent the weighting of included studies; OR: odds ratio; CI: confidence interval. (**B**) OR estimates with the corresponding 95% CI for the association of *IL-27* rs17855750 polymorphism with overall cancer risk (GG+GT *vs.* TT). The sizes of the squares represent the weighting of included studies; OR: odds ratio; CI: confidence interval.



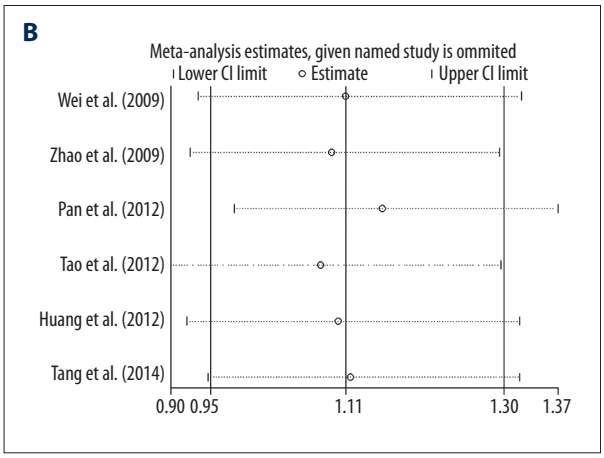


Figure 3. (**A**) Sensitivity analysis of overall OR coefficients for *IL-27* rs153109 polymorphism (G *vs.* A). Results were calculated by omitting each study in turn. The 2 ends of the dotted lines represent the 95%CI. (**B**) Sensitivity analysis of overall OR coefficients for *IL-27* rs181206 polymorphism (C *vs.* T). Results were calculated by omitting each study in turn. The 2 ends of the dotted lines represent the 95%CI. (**C**) Sensitivity analysis of overall OR coefficients for *IL-27* rs17855750 polymorphism (G *vs.* T). Results were calculated by omitting each study in turn. The 2 ends of the dotted lines represent the 95%CI.

Meta-analysis

The results of the meta-analysis for the association of *IL-27* polymorphisms (rs17855750, rs181206 and rs153109) with susceptibility to cancer are presented in Table 2. Obvious heterogeneity was identified in *IL-27* rs17855750 polymorphism (GG *vs.* TT: $P_{heterogeneity}$=0.036, I^2=61.2% and GG *vs.*

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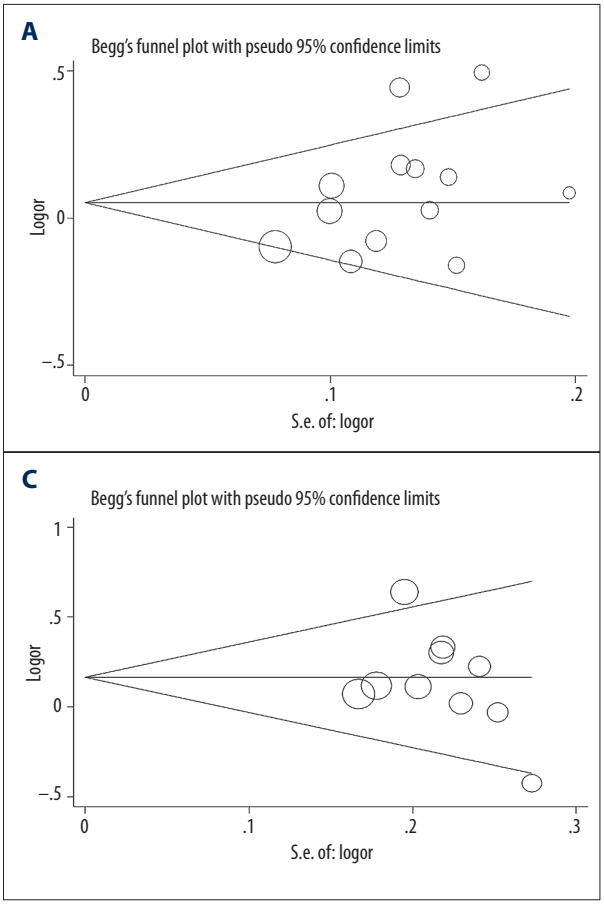

Figure 4. (**A**) Publication bias in studies of the association between the *IL-27* rs153109 polymorphism and cancer susceptibility assessed by Begg's funnel plot and Egger's test (G *vs.* A). Log (OR): the natural logarithm of the odds ratio. (**B**) Publication bias in studies of the association between the *IL-27* rs181206 polymorphism and cancer risk assessed by Begg's funnel plot and Egger's test (C *vs.* T). Log (OR): the natural logarithm of the odds ratio. (**C**) Publication bias in studies of the association between the *IL-27* rs17855750 polymorphism and cancer susceptibility assessed by Begg's funnel plot and Egger's test (G *vs.* T). Log (OR): the natural logarithm of the odds ratio.

GT+TT: $P_{heterogeneity}$=0.046, I^2=58.7%) and rs153109 polymorphism under all 5 genetic models (G *vs.* A: $P_{heterogeneity}$=0.003, I^2=35.5%; GG *vs.* AA: $P_{heterogeneity}$=0.038, I^2=20.4%; GA *vs.* AA: $P_{heterogeneity}$=0.047, I^2=18.8%; GG+GA *vs.* AA: $P_{heterogeneity}$=0.006, I^2=32.6%; GG *vs.* GA+AA: $P_{heterogeneity}$=0.038, I^2=4.9%) (Table 2). Therefore, we chose the random-effects model to generate wider CIs in these genetic models.

The present work identified that rs17855750 polymorphism of *IL-27* was significantly associated with cancer susceptibility (G *vs.* T: OR=1.177, 95%CI=1.304–1.341, $P_{heterogeneity}$=0.156, Figure 2A; GG+GT *vs.* TT: OR=1.156, 95%CI=1.005–1.329, $P_{heterogeneity}$=0.410, Figure 2B), particularly for bladder cancer (GG *vs.* TT: OR=14.600, 95%CI=1.653–128.994, $P_{heterogeneity}$=0.647; GG *vs.* GT+TT: OR=14.480, 95%CI=1.640-127.836, $P_{heterogeneity}$=0.658). Nevertheless, no association was identified between *IL-27* rs153109 and rs181206 polymorphisms and cancer susceptibility. When a stratification analysis was performed by cancer type, we identified an increased susceptibility of bladder cancer in rs153109 polymorphism (GA *vs.* AA: OR=1.413, 95%CI=1.080–1.848, $P_{heterogeneit}$y=0.725). Moreover, in the stratification analysis by genotyping method, we identified an increased susceptibility for PCR-RFLP group in rs17855750 polymorphism (G *vs.* T: OR=1.194, 95%CI=1.028–1.387, $P_{heterogeneity}$=0.074; GG+GT *vs.* TT: OR=1.185, 95%CI=1.008–1.392, $P_{heterogeneity}$=0.232), whereas a decreased susceptibility was identified in rs153109 polymorphism (GG *vs.* AA: OR=0.943, 95%CI=0.890–1.000, $P_{heterogeneity}$=0.094) (Table 2).

Sensitivity analyses and publication bias

We performed sensitivity analysis by omitting each study sequentially, suggesting that the results for the overall population were statistically robust and reliable (Figure 3A–3C). Egger's test and Begg's funnel plot were performed to examine the publication bias risk in our research. No publication bias was identified (rs153109: G *vs.* A: P=0.300 for Begg's test, P=0.112 for Egger's test, Figure 4A; rs181206: C *vs.* T: P=0.133 for Begg's test, P=0.252 for Egger's test; Figure 4B; rs17855750: G *vs.* T: P=0.283 for Begg's test, P=0.322 for Egger's test; Figure 4C).

Discussion

Interleukin-27 is a newly discovered member of the IL-12 family, which is regarded as a mediator of naive T cell proliferation, and an inducer of IFN-g secretion, specifically in synergy with IL-12 [28]. Recently, Chiyo et al. [29] investigated the antitumor ability of IL-27 against a murine tumour model and observed that IL-27 could induce tumour-specific antitumor

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activity. The relationship between *IL-27* polymorphisms and cancer susceptibility had been investigated in recently published case-control studies, but conflicting results were reported. Meta-analysis is regarded as a crucial method to accurately define the influence of specific genetic polymorphisms on cancer susceptibility. After searching the databases, 2 meta-analyses were found focussing on the relevance of the *IL-27* polymorphisms and cancer susceptibility [14,15]. In 2014, Hu et al. [14] conducted a meta-analysis and concluded that *IL-27* rs153109 polymorphism was associated with cancer susceptibility in Chinese, whereas the rs17855750 and rs181206 polymorphisms were not. The results were consistent with another meta-analysis conducted by Xu et al. [15], which reported that *IL-27* rs153109 polymorphism might enhance cancer susceptibility. Additionally, their results also demonstrated that *IL-27* rs153109 polymorphism increased colorectal cancer susceptibility. However, several limitations in both analyses were obvious. First, the number of eligible published studies used was limited to a total of 6, with 1684 patients and 1837 controls. Second, there were 8 case-control studies, including 2044 cancer cases and 2197 controls focussing only on a single *IL-27* polymorphism. Therefore, we performed the current meta-analysis to comprehensively elucidate the effects of *IL-27* polymorphisms (rs153109, rs17855750 and rs181206) in a total of 12 publications, including 27 case-control studies comprising 7570 patients and 9839 controls. Interestingly, the results were inconsistent with previous studies. Except for *IL-27* rs17855750 polymorphism, there was no evident relationship between the *IL-27* rs153109 and rs17855750 polymorphisms and cancer susceptibility. In addition, when we performed a stratification analysis by cancer type, an increased susceptibility to bladder cancer in rs153109 polymorphism was identified.

Nevertheless, there exist several drawbacks in our meta-analysis. Stratifications may be introduced by the combination of genetic studies on various cancers in the meta-analysis. The results of *IL-27* polymorphisms on cancer susceptibility might be affected by several complicated factors, such as age, sex, ethnicity, source of controls, and matching criteria when we lack the original data. Additionally, only papers published in a limited number of databases were searched, and some studies might have been missed; therefore, the eligible case-control samples included into the current meta-analysis were insufficient. Thirdly, all the studies were conducted in Chinese, and no research in whites or Africans was identified.

Conclusions

This meta-analysis illustrated that *IL-27* rs17855750 polymorphism enhanced cancer susceptibility in a Chinese population, and an increased susceptibility of bladder cancer was identified in rs153109 polymorphism when a stratification analysis was performed by cancer type. Further well-planned studies on these variants are warranted to discover the mechanisms of *IL-27* polymorphisms in the tumorigenesis of these cancers.

Competing interests

The authors have declared that no competing interests exist.

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