

RESEARCH PAPER



Associations between genetic polymorphisms in *interleukin-10* and hematological oncology: evidence from a meta-analysis

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ABSTRACT

Background: Associations between polymorphisms in interleukin-10 (*IL-10*) and hematological oncology were already explored by many genetic association studies, with controversial findings. The aim of this meta-analysis was to more comprehensively analyze associations between polymorphisms in *IL-10* and hematological oncology by combing the results of all relevant studies.

Methods: Eligible articles were searched from Pubmed, Embase, WOS and CNKI. The latest literature searching update was performed on 8 October 2019. We used Review Manager to combine the results of eligible studies.

Results: Forty-one articles were included in this meta-analysis. *IL-10* rs1800890 polymorphism was found to be significantly associated with hematological oncology under AA vs. TT+TA (recessive comparison, OR = 1.12, 95% CI 1.02–1.24), and rs1800896 polymorphism was also found to be significantly associated with hematological oncology under AA vs. AG+GG (dominant comparison, OR = 0.89, 95% CI 0.83–0.95) in overall combined analyses. In subgroup analyses, we observed positive results for rs1800871 (recessive comparison), rs1800872 (dominant, recessive and allele comparisons), and rs1800896 (dominant and allele comparisons) polymorphisms in the non-Hodgkin's lymphoma (NHL) subgroup. Besides, we also detected positive associations between rs1800872 polymorphism and acute leukemia (AL) (dominant and recessive comparisons) and found significant associations between rs1800896 polymorphism and chronic leukemia (CL) (recessive comparison).

Conclusion: In summary, this meta-analysis demonstrated that *IL-10* rs1800890, rs1800896, rs1800871 and rs1800872 polymorphisms may confer susceptibility to hematology oncology, especially for NHL.

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Introduction

Hematological oncology poses a huge threat to public health, and it is one of the leading causes of cancer-related death.¹ Although the exact mechanisms of its pathogenesis are still not fully revealed, accumulating evidence suggests that genetic components play vital roles in the development of hematological oncology. First, the incidences of many types of hematological oncology varied significantly across different populations,^{2,3} and genetic background was probably one of the reasons behind differences in disease prevalence across different populations. Second, previous genetic association studies also identified numerous susceptible genetic loci of hematological oncology.^{4,5} Moreover, using the combination of these susceptible genetic loci to predict the risk of developing hematological oncology in general population was also demonstrated to be effective and cost-saving.⁶

Interleukin-10 (*IL-10*) is a crucial regulator of anti-tumor immune responses.^{7,8} So if a genetic polymorphism could alter transcription activity of *IL-10* or protein structure of *IL-10*, it is biologically plausible that this polymorphism may also confer susceptibility to various kinds of malignancies including hematological oncology.

In the past 20 years, many previous studies explored associations between polymorphisms in *IL-10* and hematological oncology, yet the conclusions of these studies were somehow

inconsistent.^{9–14} To better clarify associations between polymorphisms in *IL-10* and hematological oncology, we designed this study to get a more credible conclusion by combing the results of all relevant studies.

Materials and methods

This meta-analysis was written in accordance with the PRISMA guideline.¹⁵

Literature search and inclusion criteria

To retrieve eligible articles, we searched Pubmed, WOS, Embase and CNKI using key words listed below: 'interleukin-10', 'IL-10', 'interleukin 10', 'IL 10', 'polymorphism', 'variant', 'variation', 'mutation', 'SNP', 'genotype', 'allele', 'leukemia', 'lymphoma' and 'myeloma'. The references of retrieved articles were also screened by us to identify other potentially relevant articles. The latest literature searching update was performed on 8 October 2019.

To be included in this meta-analysis, the following three criteria must be met simultaneously: I. Case-control or cohort studies about associations between polymorphisms in *IL-10* and hematological oncology in humans; II. Offer genotypic or allelic distributions of *IL-10* polymorphisms in patients with

hematological oncology and controls; III. Full manuscript in English or Chinese is retrievable. Articles were considered to be ineligible for inclusion if one of the following conditions was satisfied: I. Not about polymorphisms in *IL-10* polymorphisms and hematological oncology; II. Narrative reviews, systematic reviews or comments; III. Studies only involved patients with hematological oncology or healthy controls. We only included the most up to date study if duplicate reports were found during the literature search.

Data extraction and quality assessment

Two authors extracted the following information from eligible articles: I. Name of the leading author; II. Year of publication; III. Country where the study was conducted; IV. Ethnicity of involved participants; V. Number of patients with hematological oncology and controls in each study; VI. Genotypic distributions of polymorphisms in *IL-10* among patients with hematological oncology and controls. *P* values of Hardy–Weinberg equilibrium (HWE) were also calculated.

The authors used Newcastle–Ottawa scale (NOS) to assess the quality of eligible articles.¹⁶ The score range of NOS is between zero and nine, when a study got a score of seven or more, we considered that the methodology quality of this study was good.

Two authors extracted data and assessed the quality of eligible articles. The authors wrote to the leading authors for additional information if essential information was found to be incomplete.

Statistical analyses

We used Review Manager to combine the results of eligible studies. *Z* test was employed to assess associations between polymorphisms in *IL-10* and susceptibility to hematological oncology. The statistical significant threshold of *p* value was set at 0.05. We used *I*² statistics to assess between-study heterogeneities. We used Random-effect models (DerSimonian–Laird method) to combine the results of eligible studies if *I*² is larger than 50%. Otherwise, fixed-effect models (Mantel–Haenszel method) were used to combine the results of eligible studies. We further carried out subgroup analyses by ethnicity to get ethnic-specific results. We also conducted subgroup analyses by type of disease. We examined the stabilities of combined results by deleting one study each time and combining the results of the remaining studies. We used funnel plots to estimate whether our combined results may be influenced by publication biases.

Results

Characteristics of included studies

We found 933 articles during literature searching. Seventy-one articles were assessed for eligibility after excluding unrelated or duplicate reports. We further excluded 11 reviews and 16 case series, another three articles were excluded because of

missing crucial data. Totally 41 eligible articles were ultimately included in this meta-analysis (Figure 1). Extracted data of eligible articles are summarized in Table 1.

Meta-analyses results

IL-10 rs1800890 polymorphism was found to be significantly associated with hematological oncology under AA vs. TT + TA (recessive comparison, OR 1.12, 95% CI 1.02–1.24, *I*² = 45%), and rs1800896 polymorphism was also found to be significantly associated with hematological oncology under AA vs. AG + GG (dominant comparison, OR 0.89, 95% CI 0.83–0.95, *I*² = 43%) in overall combined analyses. In subgroup analyses, we observed positive results for rs1800871 (recessive comparison), rs1800872 (dominant, recessive and allele comparisons), and rs1800896 (dominant and allele comparisons) polymorphisms in the non-Hodgkin's lymphoma (NHL) subgroup. Besides, we also detected positive associations between rs1800872 polymorphism and acute leukemia (AL) (dominant and recessive comparisons) and found significant associations between rs1800896 polymorphism and chronic leukemia (CL) (recessive comparison) (Table 2).

Sensitivity analyses

We examined the stabilities of combined results by deleting one study each time and combining the results of the remaining studies. The trends of associations remained consistent in sensitivity analyses, which indicated that our combined results were statistically stable.

Publication biases

Funnel plots were employed to estimate whether our combined results may be influenced by publication biases. Funnel plots were overall symmetrical, which indicated that our combined results were unlikely to be seriously impacted by overt publication biases.

Discussion

The combined results of this meta-analysis revealed that *IL-10* rs1800890, rs1800896, rs1800871 and rs1800872 polymorphisms may confer susceptibility to hematological oncology, especially for NHL. The trends of associations remained consistent in sensitivity analyses, which indicated that our combined results were statistically stable.

Several points should be considered when interpreting our combined results. Firstly, past pre-clinical studies revealed that rs1800871 (–819C>T), rs1800872 (–592C>A), rs1800896 (–1082A>G) and rs1800890 (–3575T/A) polymorphisms could alter transcription activity of *IL-10*.^{17,18} So these variations may influence the biological function of *IL-10*, impact anti-tumor immune responses, and ultimately confer susceptibility to hematological oncology. Thus, our meta-analysis may be statistically insufficient to observe the real underlying associations between polymorphisms in *IL-10* and

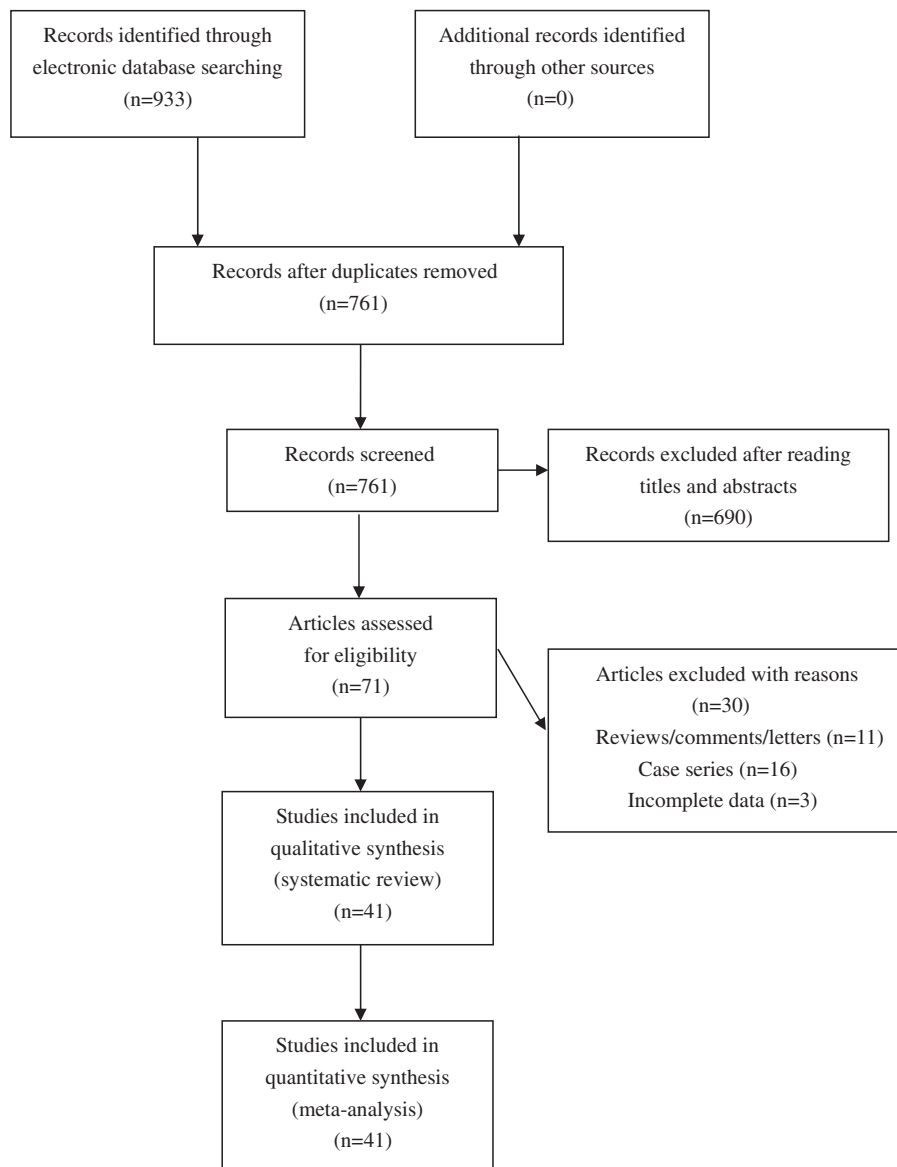


Figure 1. Flowchart of study selection for the present study. Systematic literature search of the present meta-analysis.

hematological oncology in certain comparisons. Secondly, the trends of associations for *IL-10* polymorphisms in different subgroups were somehow opposite, which suggested that genotypic distributions of *IL-10* polymorphisms vary significantly from population to population, and the effects of *IL-10* polymorphisms on different types of hematological oncology may also vary. Therefore, we should not generalize positive findings observed in certain subgroups to a broader population. Thirdly, the etiologies of hematological oncology are very complicated, so we highly recommend further genetic association studies to explore the effects of haplotypes and gene-gene interactions on disease susceptibility.¹⁹ Fourthly, according to our searching strategy, most of the relevant studies only focused on NHL, yet studies concerning other types of hematological oncology were relatively scarce, so

future studies should continue to explore associations between polymorphisms in *IL-10* and hematology oncology, especially for leukemia and myeloma.

Some limitations of this meta-analysis should also be mentioned. Firstly, the results regarding associations between polymorphisms in *IL-10* and hematology oncology were based on combining unadjusted findings of eligible articles due to lack of raw data.²⁰ Secondly, the relationship between polymorphisms in *IL-10* and hematology oncology may also be affected by environmental factors. Unfortunately, the majority of eligible articles only focused on genetic associations between polymorphisms in *IL-10* and hematology oncology, so we could not explore genetic-environmental interactions in this meta-analysis.²¹ Thirdly, gray literatures were not searched. So although funnel plots

Table 1. The characteristics of included studies.

First author, year	Country	Ethnicity	Type of disease	Sample size Case/Control	Genotypes (wtwt/wtmt/mtmt)		P-value for HWE	NOS score
					Cases	Controls		
rs1800871 – 819 C/T								
Amirzargar 2005	Iran	Mixed	CML	30/40	11/14/5	21/19/0	0.049	7
Cheng 2015	China	Asian	NHL	125/300	57/59/9	136/125/39	0.230	8
Fei 2015	China	Asian	AML	167/328	57/72/38	137/137/54	0.052	8
Haydaroglu 2017	Turkey	Caucasian	MM	113/113	60/46/7	56/47/10	0.975	7
Hellmig 2008	Germany	Caucasian	Lymphoma	84/351	45/32/7	210/124/17	0.811	7
Kube 2007	Germany	Caucasian	NHL	409/193	225/164/20	106/77/10	0.403	8
Lech-Maranda 2004	France	Caucasian	NHL	199/112	107/81/11	53/46/13	0.536	8
Lech-Maranda 2007	Poland	Caucasian	NHL	175/112	92/68/15	53/46/13	0.536	8
Lim 2015	Malaysia	Mixed	NHL	317/330	NA	NA	NA	7
Lo 2016	Taiwan	Asian	ALL	266/266	170/85/11	142/96/28	0.059	7
Mazur 2005	Poland	Caucasian	MM	54/50	35/16/3	27/17/6	0.218	7
Mimicelli 2012	Brazil	Mixed	NHL	61/205	33/24/4	90/92/23	0.944	7
Nielsen 2015	Denmark	Caucasian	NHL	172/304	NA	NA	NA	7
Nursal 2016	Turkey	Caucasian	AML	42/85	15/21/6	49/32/4	0.670	8
Oduor 2014	USA	Mixed	NHL	117/88	32/61/24	28/39/21	0.311	7
Pehlivan 2014	Turkey	Caucasian	CML	60/74	25/32/3	37/33/4	0.330	8
Persico 2006	Italy	Caucasian	NHL	108/110	60/44/4	53/51/6	0.159	8
Rashed 2018	Turkey	Caucasian	AML	80/85	26/23/31	40/36/9	0.832	7
Yao 2013	China	Asian	AML	115/137	68/38/9	56/63/18	0.966	9
rs1800872 – 592 C/A								
Amirzargar 2005	Iran	Mixed	CML	30/40	11/14/5	21/19/0	0.049	7
Bănescu 2019	Romania	Mixed	AML	226/406	117/99/10	222/158/26	0.765	8
Banu 2011	Romania	Caucasian	MM	80/100	NA	NA	NA	7
Breen 2003	USA	Mixed	NHL	138/1019	91/44/3	550/398/71	0.931	7
Cheng 2015	China	Asian	NHL	125/300	57/59/9	138/124/38	0.225	8
Fei 2015	China	Asian	AML	167/327	54/74/39	126/142/59	0.091	8
Haydaroglu 2017	Turkey	Caucasian	MM	113/113	60/46/7	56/47/10	0.975	7
Kasamatsu 2017	Japan	Asian	MM	128/202	11/66/51	16/95/91	0.196	8
Kube 2007	Germany	Caucasian	NHL	409/193	225/164/20	106/77/10	0.403	8
Lech-Maranda 2004	France	Caucasian	NHL	199/112	107/81/11	53/46/13	0.536	8
Lech-Maranda 2007	Poland	Caucasian	NHL	175/112	92/68/15	53/46/13	0.536	8
Lo 2016	Taiwan	Asian	ALL	266/266	117/101/48	170/85/11	0.927	7
Mazur 2005	Poland	Caucasian	MM	54/50	35/16/3	27/17/6	0.218	7
Munro 2003	Brazil	Mixed	NHL	61/205	33/24/4	90/92/23	0.944	7
Mimicelli 2012	UK	Caucasian	HL	147/110	88/55/4	66/42/2	0.105	7
Nielsen 2015	Denmark	Caucasian	NHL	208/304	NA	NA	NA	7
Nursal 2016	Turkey	Caucasian	AML	42/85	15/21/6	49/32/4	0.670	8
Oduor 2014	USA	Mixed	NHL	117/88	32/61/24	28/39/21	0.311	7
Pehlivan 2014	Turkey	Caucasian	CML	60/74	25/32/3	37/33/4	0.330	8
Persico 2006	Italy	Caucasian	NHL	108/110	60/44/4	53/51/6	0.159	8
Yao 2013	China	Asian	AML	115/137	9/38/68	18/63/56	0.966	9
Zhang 2012	China	Asian	NHL	514/557	226/228/60	269/235/53	0.872	7
rs1800890 – 3575 T/A								
Cheng 2015	China	Asian	NHL	125/300	117/8/0	278/22/0	0.510	8
Deng 2013	China	Asian	NHL	510/597	NA	NA	NA	7
Fernberg 2010	Sweden	Caucasian	NHL	2312/1838	847/1092/373	695/865/278	0.742	8
Kube 2007	Germany	Caucasian	NHL	409/193	184/180/45	66/100/27	0.264	8
Lech-Maranda 2013	Poland	Caucasian	CLL	290/192	112/132/46	69/85/38	0.208	8
Liang 2009	USA	Mixed	CLL	39/102	19/16/4	33/48/21	0.645	7
Nieters 2006	Germany	Caucasian	Lymphoma	670/661	268/302/100	262/306/93	0.810	8
Rothman 2006	USA	Mixed	NHL	2049/3921	745/982/322	1593/1816/512	0.876	8
Yri 2012	Norway	Caucasian	HL	223/1048	81/104/38	390/528/130	0.017	8
rs1800896 – 1082 G/A								
Abdel Rahman 2018	Turkey	Caucasian	NHL	100/100	26/51/23	28/59/13	0.038	7

(Continued)

Table 1. (Continued).

First author, year	Country	Ethnicity	Type of disease	Sample size Case/Control	Genotypes (wtwt/wtmt/mtmt)		P-value for HWE	NOS score
					Cases	Controls		
Amirzargar 2005	Iran	Mixed	CML	30/40	17/13/0	34/6/0	0.609	7
Bănescu 2019	Romania	Mixed	AML	226/406	74/109/43	144/188/74	0.359	8
Banu 2011	Romania	Caucasian	MM	80/100	NA	NA	NA	7
Berglund 2005	Sweden	Caucasian	NHL	244/195	70/136/38	60/89/46	0.250	7
Cheng 2015	China	Asian	NHL	125/300	101/24/0	237/60/3	0.710	8
Cunningham 2003	Australia	Caucasian	NHL	63/164	26/25/12	41/82/41	1.000	7
Deng 2013	China	Asian	NHL	510/587	NA	NA	NA	7
Fei 2015	China	Asian	AML	167/328	75/70/22	159/134/35	0.398	8
Haydaroglu 2017	Turkey	Caucasian	MM	113/113	34/66/13	43/52/18	0.731	7
Hiroki 2015	Brazil	Mixed	ALL	67/75	23/31/13	33/32/10	0.615	7
Hosgood 2013	USA	Mixed	NHL	2459/4079	2107/312/40	3598/452/29	<0.001	7
kube 2007	Germany	Caucasian	NHL	409/193	111/210/88	55/90/48	0.358	8
Lech-Maranda 2013	Poland	Caucasian	CLL	292/192	82/152/58	48/94/50	0.774	8
Lech-Maranda 2004	France	Caucasian	NHL	199/112	55/100/44	45/47/20	0.217	8
Lech-Maranda 2007	Poland	Caucasian	NHL	175/112	56/87/32	45/47/20	0.217	8
Lim 2015	Malaysia	Mixed	NHL	317/330	NA	NA	NA	7
Lo 2016	Taiwan	Asian	ALL	266/266	205/50/11	202/52/12	0.001	7
Mazur 2005	Poland	Caucasian	MM	54/50	20/23/11	16/23/11	0.617	7
Minnicelli 2012	Brazil	Mixed	NHL	61/216	21/26/14	102/92/22	0.852	7
Munro 2003	UK	Caucasian	HL	147/111	30/69/48	24/55/32	0.968	7
Nedoszytko 2016	Poland	Caucasian	NHL	43/173	8/30/5	36/90/47	0.557	8
Nielsen 2015	Denmark	Caucasian	NHL	206/301	NA	NA	NA	7
Nieters 2006	Germany	Caucasian	Lymphoma	664/660	211/298/155	208/302/150	0.046	8
Nursal 2016	Turkey	Caucasian	AML	42/85	22/17/3	32/36/17	0.246	8
Oduor 2014	USA	Mixed	NHL	117/88	53/53/11	39/39/10	0.958	7
Ovsepyan 2015	Russia	Caucasian	CLL	231/314	85/106/40	91/142/81	0.094	7
Pehlivan 2014	Turkey	Caucasian	CML	60/74	31/22/7	28/36/10	0.769	8
Persico 2006	Italy	Caucasian	NHL	108/110	22/38/48	36/56/18	0.628	8
Rothman 2006	USA	Mixed	NHL	1893/3565	521/925/447	1089/1734/742	0.285	7
Sharif 2019	Sudan	Mixed	AML	30/30	11/13/6	11/16/3	0.417	7
Zheng 2001	Sweden	Caucasian	MM	72/107	15/36/21	23/56/28	0.612	7

Abbreviations: AML, acute myeloid leukemia; CML, chronic myelogenous leukemia; NHL, non-Hodgkin's lymphoma; HL, Hodgkin's lymphoma; MM, multiple myeloma; ALL, acute lymphoblastic leukemia; CLL, chronic lymphoblastic leukemia; wt, wild type; mt, mutant type; HWE, Hardy-Weinberg equilibrium; NOS, Newcastle-Ottawa scale; NA, not available.

Table 2. Meta-analyses results of IL-10 polymorphisms and hematological oncology.

Variables	Sample size	Dominant comparison			Recessive comparison			Over-dominant comparison			Allele comparison		
		p value	OR (95%CI)	I ² statistic	p value	(95%CI)	I ² statistic	p value	OR (95%CI)	I ² statistic	p value	OR (95%CI)	I ² statistic
rs1800871 – 819 C/T													
Overall	2694/3283	0.81	1.02 (0.84–1.26)	68%	1.00	1.00 (0.68–1.47)	73%	0.56	0.96 (0.85–1.09)	0%	0.67	1.04 (0.88–1.22)	77%
Asian	673/1031	0.83	0.95 (0.62–1.46)	71%	0.83	0.92 (0.42–2.00)	85%	0.46	0.93 (0.76–1.13)	50%	0.81	0.95 (0.61–1.46)	87%
Caucasian	1496/1589	0.40	1.14 (0.84–1.53)	66%	0.07	0.76 (0.57–1.03)	25%	0.76	0.97 (0.83–1.15)	0%	0.35	1.11 (0.90–1.37)	66%
AL	670/901	0.87	1.06 (0.53–2.14)	87%	0.80	1.10 (0.54–2.24)	84%	0.30	0.84 (0.61–1.16)	51%	0.89	0.96 (0.56–1.66)	91%
CL	90/144	0.12	0.64 (0.37–1.13)	0%	0.45	3.11 (0.16–60.15)	70%	0.44	1.24 (0.72–2.17)	0%	0.08	0.68 (0.44–1.04)	35%
NHL	1683/1754	0.18	1.13 (0.95–1.34)	0%	0.009	0.66 (0.49–0.90)	0%	0.85	1.02 (0.85–1.22)	0%	0.50	1.06 (0.89–1.28)	62%
rs1800872 – 592 C/A													
Overall	3256/4504	0.93	0.99 (0.81–1.21)	68%	0.94	1.01 (0.73–1.40)	67%	0.69	1.02 (0.92–1.13)	0%	0.63	0.96 (0.82–1.13)	76%
Asian	1315/1789	0.31	0.83 (0.57–1.20)	76%	0.35	1.42 (0.68–2.97)	88%	0.25	1.09 (0.94–1.26)	33%	0.87	0.97 (0.68–1.40)	90%
Caucasian	1595/1363	0.29	1.15 (0.89–1.48)	54%	0.17	0.78 (0.55–1.11)	1%	0.98	1.00 (0.84–1.19)	0%	0.23	1.08 (0.95–1.22)	34%
AL	590/815	< 0.0001	0.57 (0.45–0.71)	44%	0.0005	3.23 (1.44–7.25)	79%	0.83	1.04 (0.71–1.53)	62%	0.31	0.73 (0.40–1.34)	92%
CL	90/114	0.12	0.64 (0.37–1.13)	0%	0.45	3.11 (0.16–60.15)	70%	0.44	1.24 (0.72–2.17)	0%	0.08	0.68 (0.44–1.04)	35%
NHL	2054/3000	0.005	1.23 (1.06–1.42)	0%	0.0004	0.60 (0.46–0.80)	0%	0.95	1.00 (0.87–1.14)	0%	0.0004	1.19 (1.08–1.31)	0%
MM	321/415	0.17	1.55 (0.83–2.92)	66%	0.25	0.78 (0.52–1.18)	0%	0.60	1.10 (0.78–1.54)	0%	0.28	1.15 (0.89–1.49)	0%
rs1800890 – 3575 T/A													
Overall	6627/8852	0.87	0.99 (0.86–1.13)	62%	0.02	1.12 (1.02–1.24)	45%	0.97	1.00 (0.93–1.07)	0%	0.86	1.01 (0.90–1.13)	66%
Asian	635/897	0.03	0.78 (0.62–0.98)	0%	NA	NA 0%	NA NA	0%	NA	NA 0%	0%	0%	NA 0%
Caucasian	3904/3932	0.82	1.01 (0.92–1.11)	45%	0.38	1.06 (0.93–1.20)	33%	0.39	0.96 (0.88–1.05)	0%	0.71	1.02 (0.91–1.15)	54%
CL	329/294	0.19	1.26 (0.90–1.76)	43%	0.10	0.70 (0.45–1.07)	0%	0.96	0.99 (0.71–1.38)	0%	0.07	1.25 (0.98–1.58)	49%
NHL	5405/6849	0.54	0.94 (0.79–1.13)	72%	0.25	1.11 (0.93–1.33)	50%	0.62	1.02 (0.94–1.10)	33%	0.91	0.99 (0.85–1.16)	76%
rs1800896 – 1082 G/A													
Overall	9314/13140	0.0005	0.89 (0.83–0.95)	43%	0.48	1.07 (0.89–1.29)	65%	0.09	1.06 (0.99–1.13)	31%	0.25	0.95 (0.86–1.04)	64%
Asian	1068/1481	0.24	0.90 (0.75–1.07)	0%	0.71	1.09 (0.69–1.74)	0%	0.93	1.01 (0.80–1.28)	0%	0.82	0.98 (0.80–1.19)	0%
Caucasian	3302/3266	0.98	1.00 (0.89–1.12)	44%	0.72	0.96 (0.75–1.21)	65%	0.34	1.05 (0.95–1.17)	42%	0.82	1.02 (0.89–1.15)	64%
AL	542/754	0.83	0.97 (0.77–1.24)	33%	0.97	1.01 (0.59–1.72)	38%	0.91	1.01 (0.79–1.30)	0%	0.94	1.01 (0.74–1.39)	59%
CL	613/620	0.72	1.10 (0.66–1.84)	70%	0.005	0.66 (0.50–0.89)	0%	0.61	1.12 (0.72–1.75)	65%	0.36	1.17 (0.84–1.63)	65%
NHL	7029/10625	< 0.0001	0.84 (0.78–0.91)	28%	0.24	2.0 (0.89–1.63)	75%	0.08	1.07 (0.99–1.16)	48%	0.04	0.88 (0.78–0.99)	65%
MM	319/370	0.49	0.87 (0.59–1.29)	0%	0.80	0.6 (0.70–1.58)	10%	0.36	1.18 (0.83–1.67)	30%	0.81	0.97 (0.76–1.25)	0%

Abbreviations: AL, acute leukemia; CL, chronic leukemia; NHL, non-Hodgkin's lymphoma; HL, Hodgkin's lymphoma; MM, multiple myeloma; OR, odds ratio; CI, confidence interval; NA, not available. The values in bold represent there are statistically significant differences between cases and controls.

were overall symmetrical, we still could not rule out the possibility that our combined results may be affected by potential publication biases.²²

In summary, this meta-analysis demonstrated that *IL-10* rs1800890, rs1800896, rs1800871 and rs1800872 polymorphisms may confer susceptibility to hematology oncology, especially for NHL. However, the combined results of this meta-analysis should still be verified by further studies with larger sample sizes.

Authors' contributions

Pan Hong and Jia-ping Fu conceived and designed the study. Pan Hong and Wei-ying Feng searched literatures. Lei-hua Fu and Jing Jin analyzed data. Pan Hong and Jia-ping Fu drafted the manuscript. All authors approved the final manuscript as submitted.

Disclosure of Potential Conflicts of Interest

The authors declare that they have no conflict of interest.

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Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors, thus ethical approval and informed consent are not required.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136:E359–386.
2. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin*. 2017;67:7–30.
3. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends – an update. *Cancer Epidemiol Biomarkers Prev*. 2016;25:16–27. doi:10.1158/1055-9965.EPI-15-0578.
4. Navin NE. Cancer genomics: one cell at a time. *Genome Biol*. 2014;15:452. doi:10.1186/s13059-014-0452-9.
5. Garraway LA. Genomics-driven oncology: framework for an emerging paradigm. *J Clin Oncol*. 2013;31:1806–1814. doi:10.1200/JCO.2012.46.8934.
6. Gordon BL, Finnerty BM, Aronova A, Fahey TJ 3rd. Genomic medicine for cancer diagnosis. *J Surg Oncol*. 2015;111:24–30. doi:10.1002/jso.23778.
7. Mocellin S, Marincola FM, Young HA. Interleukin-10 and the immune response against cancer: a counterpoint. *J Leukoc Biol*. 2005;78:1043–1051. doi:10.1189/jlb.0705358.
8. Oft M. IL-10: master switch from tumor-promoting inflammation to antitumor immunity. *Cancer Immunol Res*. 2014;2:194–199. doi:10.1158/2326-6066.CIR-13-0214.
9. Abdel Rahman HA, Khorshied MM, Reda Khorshid OM, Mourad HM. Association of interleukin-2-330T/G and interleukin-10-1082A/G genetic polymorphisms with B-cell non-hodgkin lymphoma in a cohort of Egyptians. *Turk J Haematol*. 2018;35:99–108. doi:10.4274/tjh.
10. Amirzargar AA, Bagheri M, Ghavamzadeh A, Alimoghadam K, Khosravi F, Rezaei N, Moheydin M, Ansari-pour B, Moradi B, Nikbin B, et al. Cytokine gene polymorphism in Iranian patients with chronic myelogenous leukaemia. *Int J Immunogenet*. 2005;32:167–171. doi:10.1111/eji.2005.32.issue-3.
11. Banu C, Moise A, Arion CV, Coriu D, Tănase A, Constantinescu I. Cytokine gene polymorphisms support diagnostic monitoring of Romanian multiple myeloma patients. *J Med Life*. 2011;4:264–268.
12. Breen EC, Boscardin WJ, Detels R, Jacobson LP, Smith MW, O'Brien SJ, Chmiel JS, Rinaldo CR, Lai S, Martínez-Maza O, et al. Non-Hodgkin's B cell lymphoma in persons with acquired immunodeficiency syndrome is associated with increased serum levels of IL10, or the IL10 promoter –592 C/C genotype. *Clin Immunol*. 2003;109:119–129. doi:10.1016/S1521-6616(03)00214-6.
13. Cunningham LM, Chapman C, Dunstan R, Bell MC, Joske DJ. Polymorphisms in the interleukin 10 gene promoter are associated with susceptibility to aggressive non-Hodgkin's lymphoma. *Leuk Lymphoma*. 2003;44:251–255. doi:10.1080/1042819021000035590.
14. Deng Q, Zheng T, Lan Q, Lan Y, Holford T, Chen Y, Dai M, Leaderer B, Boyle P, Chanock SJ, et al. Occupational solvent exposure, genetic variation in immune genes, and the risk for non-Hodgkin lymphoma. *Eur J Cancer Prev*. 2013;22:77–82. doi:10.1097/CEJ.0b013e328354d2c1.
15. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151:264–269. doi:10.7326/0003-4819-151-4-200908180-00135.
16. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603–605. doi:10.1007/s10654-010-9491-z.
17. Turner DM, Williams DM, Sankaran D, Lazarus M, Sinnott PJ, Hutchinson IV. An investigation of polymorphism in the interleukin-10 gene promoter. *Eur J Immunogenet*. 1997;24:1–8. doi:10.1111/j.1365-2370.1997.tb00001.x.
18. de Oliveira JG, Rossi AF, Nizato DM, Cadamuro AC, Jorge YC, Valsechi MC, Venâncio LPR, Rahal P, Pavarino EC, Goloni-Bertollo EM, et al. Influence of functional polymorphisms in TNF- α , IL-8, and IL-10 cytokine genes on mRNA expression levels and risk of gastric cancer. *Tumour Biol*. 2015;36:9159–9170. doi:10.1007/s13277-015-3593-x.
19. Nishi A, Milner DA Jr, Giovannucci EL, Nishihara R, Tan AS, Kawachi I, Ogino S. Integration of molecular pathology, epidemiology and social science for global precision medicine. *Expert Rev Mol Diagn*. 2016;16:11–23.
20. Chen R, Zheng Y, Zhuo L, Wang S. The association between miR-423 rs6505162 polymorphism and cancer susceptibility: a systematic review and meta-analysis. *Oncotarget*. 2017;8:40204–40213.
21. Wang BS, Liu Z, Xu WX, Sun SL. CYP3A5*3 polymorphism and cancer risk: a meta-analysis and meta-regression. *Tumour Biol*. 2013;34:2357–2366. doi:10.1007/s13277-013-0783-2.
22. Jia J, Ren J, Yan D, Xiao L, Sun R. Association between the XRCC6 polymorphisms and cancer risks: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2015;94:e283. doi:10.1097/MD.0000000000000283.