

Supplementary Material

Genetic variants associated with Osteosarcoma risk: A systematic review and meta-analysis

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Search Terms

Search strategy for MEDLINE/PubMed

1. For Osteosarcoma the following MeSH headings and text words will be used:

osteosarcoma OR osteosarcoma*OR osteogenic sarcoma OR sarcoma, osteogenic OR sarcomas, osteogenic

2. For genetic variation the following MeSH headings and text words will be used:

Disease Susceptibility OR Genetic Variation OR Genetic Association Studies OR Sequence Analysis OR mutation OR Polymorphism, Genetic OR single nucleotide polymorphism OR SNP OR variant OR variation OR risk OR locus

The search thread is as follows:

((((OR "Disease Susceptibility"[Mesh]) OR "Genetic Variation"[Mesh]) OR "Genetic Association Studies"[Mesh] OR "Genotype"[Mesh] OR "Sequence Analysis"[Mesh] OR mutation[Text Word] OR Polymorphism, Genetic[Text Word] OR single nucleotide polymorphism[Text Word] OR SNP[Text Word] OR variant[Text Word] OR variation [Text Word] OR risk[Text Word] OR "Causality"[Mesh] OR locus[Text Word]) AND (((("Neoplasms, Bone Tissue"[Mesh] OR "Osteosarcoma"[Mesh] OR osteosarcoma OR osteosarcoma* OR osteogenic sarcoma OR sarcoma, osteogenic OR sarcomas, osteogenic))))

Search strategy for Ovid/Embase

1. For Osteosarcoma

bone tumors.mp. or bone tumor/ or osteosarcoma/ or osteogenic sarcoma.mp. or osteosarcoma/or osteosarcoma cell/ or osteosarcoma cell/ or osteosarcoma/ or bone sarcoma.mp. or osteosarcoma/

2. for genetic variation

Disease Susceptibility.mp. or disease predisposition/ or Genetic Variation.mp. or genetic variability/ or genetic variation/ or genetics/ or Genetic Association Studies.mp. or genetic association study/ or genotype/ or Genotype.mp. /or Sequence Analysis.mp. or sequence analysis/ or exp mutation/ or Polymorphism, Genetic.mp. or genetic polymorphism/ or DNA polymorphism/ or single nucleotide polymorphism/ or genetic variability/ or genetic association/ or single nucleotide polymorphism/ or variant.mp. or genetic association/ or single nucleotide polymorphism/ or gene locus/

Search strategy for Scopus

KEY (osteosarcoma) AND SUBJAREA (bioc) AND (genetics) OR (disease AND susceptibility) OR (disease AND predisposition) OR (genetic AND variation) OR (genetic AND variability) OR (genotype) OR (genetic AND association AND studies) OR (sequence AND analysis) OR (genetic AND polymorphism) OR (single nucleotide polymorphism) OR (genetic AND association) OR (gene AND locus) OR (variant) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (EXACTKEYWORD , "Human")) OR LIMIT-TO (EXACTKEYWORD , "Humans"))

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4, 5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 5

Section and Topic	Item #	Checklist item	Location where item is reported
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 4,5
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 5,6 Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	5,6,Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary File C1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary File C1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary File C3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 7,8,9,10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 6,7,8,9 Supplementary File C4, Table 1
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 6,7,8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 6,7,8,9
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 10
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 7,8,9,10
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 10, 11
	23b	Discuss any limitations of the evidence included in the review.	Page 11
	23c	Discuss any limitations of the review processes used.	Page 11
	23d	Discuss implications of the results for practice, policy, and future research.	Page 11,12
OTHER INFORMATION			
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 3

Section and Topic	Item #	Checklist item	Location where item is reported
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 12
Competing interests	26	Declare any competing interests of review authors.	Page 12
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 12

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: <http://www.prisma-statement.org/>

Supplementary Table

Table S1: Characteristics of Included Studies

First Author year	Journal	location	Genotyping method	Age cases	Age controls	M/F cases	M/F controls	Source of Controls	Quality Assessment
Mirabello 2010[1]	Carcinogenesis	USA	Custom Infinium BeadChip	means(sd) 26.6 (16)	means(sd) 60.9 (9.9)	56/43	872/493	mixed	moderate
HE 2013[2]	Asian Pac J Cancer Prev	China	taqman (PCR)	21.3±11.1	31.3 ±16.6	35/24	33/30	Hospital based	moderate
Xiao 2017[3]	Sci Rep	China	taqman (PCR)			213/155	355/261	Hospital based	good
Hattinger 2016[4]	Oncotarget.	Italy	PSQ/taqman assay	< 14 years 60 ≥ 14 years 136	median age (16 years)	122/74	285/185	Hospital based	moderate
Zhao 2014[5]	Biomed Res Int.	China	PCR			154/93	265/163	Hospital based	moderate
Cong 2015[6]	Tumour Biol	China	taqman (PCR)	28.0 ± 18.0	27.8 ± 17.2	132/80	226/180	Hospital based	moderate
Wang 2011[7]	DNA and Cell Biology	China	(PCR-RFLP) & sequencing	-	-	119/86	113/103	Hospital based	moderate
Zhang 2019[8]	Med Sci Monit.	China	taqman (PCR)	15.44±3.03	15.96±3.24	97/87	99/86	Hospital based	moderate
He 2014[9]	Tumour Biol.	China	taqman (PCR)	25.5 ± 12.6	28.4 ± 14.0	120/69	105/90	Hospital based	moderate
Guo 2015[10]	Int J Clin Exp Pathol	China	PCR-RFLP	-	-	90/51	208/133	Hospital based	moderate
Bi 2016[11]	Sci.reports	China	Taqman PCR	-	-	139/97	229/189	Hospital based	moderate
Qiao 2016[12]	IJCEM	China	PCR-RFLP	-	-	74/48	79/52	Population based	poor
Liu 2011[13]	DNA Cell Biol	China	PCR-RFLP	-	-	172/95	156/126	Hospital based	moderate
Wang 2011[14]	Genet Test Mol Biomarkers	China	PCR-RFLP	-	-	119/86	113/103	Hospital based	moderate
Bilbao-Aldaiturriaga 2017 [15]	Neoplasma	Spain	PCR-RFLP	-	-	-	-	Hospital based	poor
Jin 2015[16]	Pak J Med Sci	China	PCR-RFLP	17.7±8.2	19.2±5.3	91/57	181/115	Hospital based	moderate
Xu 2017[17]	Mamm Genome	China	taqman (PCR)			208/173	425/340	Hospital based	good
Biason 2011[18]	Pharmacogenomics J	Italy	taqman (PCR)	Median 16 range(4–68)	median age 35 years	79/51	156/101	Hospital based	moderate
Gómez-Díaz [19]	Oncol Lett	México	taqman (PCR)	Median 20.5, range (9-68)	-	12/16	-	Hospital based	poor

Ma 2016[20]	Genet Mol Res	China	PCR-RFLP	>20 total 53 <20 total 88	>20 total 162 <20 total 82	87/54	174/108	Hospital based	moderate
Wang 2015[21]	Tumour Biol.	China	taqman (PCR)	>20 total 48 <20 total 78	>20 total 90 <20 total 78	70/56	88/80	Hospital based	moderate
Jiang 2014[22]	Med Oncol.	China	sequencing	20.09 ± 9.32	20.53 ± 11.79	98/70	134/82	Hospital based	moderate
Barnette 2004[23]	Cancer Epidemiol Biomarkers Prev.	USA	fluorescent, allele- specific PCR	-	-	-	-	Population based	poor
Salinas-Souza 2010[24]	Pharmacogenet Genomics	Brazil	PCR-RFLP	>15 total 40 <15 total 40	>15 total 83 <15 total 77	47/33	94/66	Hospital based	moderate
Lu2011[25]	APJCP	China	TaqMan PCR	13.6±3.2	13.8±2.9	66/44	130/96	Hospital based	moderate
Li 2015[26]	Genetics and molecular research	China	PCR	-	-	-	-	Hospital based	poor
Qu 2016[27]	Genetics and molecular research	China	PCR-RFLP	>20 total 50 <20 total 103	>20 total 150 <20 total 102	61/61	138/114	Hospital based	poor
Moghimi 2018[28]	APJCP	Iran	PCR-RFLP	-	-	-	-	Population based	poor
HE 2017[29]	Eur Rev Med Pharmacol Sci	China	Taqman PCR	>20 total 89 <20 total 104	>20 total 198 <20 total 185	113/80	230/153	Hospital based	moderate
Xin 2015[30]	Int J Clin Exp Pathol.	China	MassARRAY system	Median 19.6 Range(16-53)	Median 20.3 Range(12-51)	53/37	59/41	Hospital based	poor
Zhou 2016[31]	Oncotarget.	China	Sequenom MassARRAY	Meam 23.5±8.5	Mean 23.3±7.1	537/363	533/367	Hospital based	moderate
Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	Taqman PCR	-	-	-	-	Hospital based	moderate
He 2014[33]	Int Orthop.	China	PCR-RFLP	Mean(SD) 23.7(12.8)	Mean(SD) 24.1(13)	68/52	64/56	Hospital based	moderate
Shang 2017[34]	Biomedical Research	China	PCR-RFLP	28.5 ± 13.1	27.3 ± 17.9	150/41	158/49	Hospital based	poor
Qi 2016[35]	Tumour Biol.	China	PCR-RFLP	(mean ± SD) 23.4 (±6.4)	(mean ± SD) 22.5 (±7.9)	118/88	105/101	Hospital based	poor
Oliveira 2007[36]	J Pediatr Hematol Oncol	Brazil	PCR-RFLP	First decade 8 Second decade 61 Third decade 10 Fourth decade		47/33		Hospital based	poor
Tian 2016[37]	Int J Clin Exp Med.	China	PCR-RFLP	>20 total 45 <20 total 64	>20 total 50 <20 total 59	60/49	56/53	Hospital based	moderate

Chen 2016[38]	Tumour Biol	China	PCR-RFLP	>20 total 82 <20 total 108	>20 total 81 <20 total 99	91/99	96/94	Hospital based	moderate
Cui 2016[39]	Tumour Biol	China	PCR-RFLP	23.7 (10.2)	24.9 (11.8)	168/92	143/117	Hospital based	moderate
Wang 2013[40]	DNA Cell Biol	China	PCR-RFLP	>20 total 34 <20 total 72	>20 total 58 <20 total 152	68/38	130/80	Population based	moderate
Tang 2016[41]	Sci Rep	China	PCR-RFLP	Median(range) 18.0 (6.0–58.0)	Median(range) 20.0 (12.0–59.0)	216/142	241/161	Hospital based	moderate
Tang 2014[42]	Medicine	China	PCR-RFLP	Mean 27.5±8.5	Mean 27.9±7.8	105/55	155/95	Population based	moderate
Yang 2014[43]	Med Oncol	China	Taqman PCR	Mean ± SD 21.25 ± 11.04	Mean ± SD 30.99 ± 16.57	70/48	66/60	Hospital based	moderate
Liu 2012[44]	PLoS One	China	PCR-RFLP	>20 total 94 <20 total 232	>20 total 128 <20 total 305	188/138	252/181	Hospital based	moderate
Bilbao-Aldaiturriaga 2016[45]	Pediatr Res	Spain	ARMS and RFLP	-	-	-	-	Hospital based	moderate
Bilbao-Aldaiturriaga 2016[45]	Pediatr Res	Slovenia	ARMS and RFLP	-	-	-	-	Hospital based	moderate
Naumov 2012[46]	Bull Exp Biol Med	Russia	MALDI-TOF minisequencing	16-64 years	-	36/32	-	Not specified	poor
Mirabello 2011[47]	BMC Cancer	USA	Custom Infinium Beadchip	mean age (SD) 26.6(16.5)	mean age (SD) 24.7(15.1)	54/42	34/29		moderate
Toffoli 2009[48]	Clin Cancer Res	Italy	Pyrosequencing	Median 16 years (range, 4-73).	Range 18-40	123/78	-	Population based	moderate
Cui 2016[49]	Biomarkers	China	PCR-RFLP	Mean(±SD) 23.49 (10.23)	Mean(±SD) 24.26 (11.38)	149/102	153/98	Hospital based	moderate
Zhi 2016[50]	J Cancer	China	MALDI-TOF	21.00±4.7	21.02±4.3	146/138	498/483	Hospital based	good
Huang 2015[51]	Onco Targets Ther.	China	Taqman PCR	Mean ± SD 15.90±3.37	Mean ± SD 16.24±3.30	151/109	159/127	Hospital based	moderate
Goricar 2015[52]	J Med Biochem.	Slovenia	PCR-RFLP	Median (range) 19 (15–38)	Median (range) 30 (23–53.5)	40/37	219/153	Population based	poor
Zhang 2014[53]	Tumour Biol	China	TaqMan (PCR)	24.4 ± 8.7	24.3 ± 8.8	365/245	320/300	Population based	good
Lu 2015[54]	Tumour Biol	China	Sequencing	-	-	208/180	193/195	Hospital based	good

Zhi 2014[55]	Tumour Biol	China	Taqman PCR	42.3±12.4	43.1±13.1	121/101	130/110	Hospital based	moderate
Dong 2015[56]	Genet Mol Res.	China	Taqman PCR	32.3 ± 12.1	33.1 ± 12.4	97/88	101/100	Hospital based	poor
Wu 2015[57]	Tumour Biol	China	Taqman PCR	21.25±11.04	30.99±16.57	66/58	78/58	Hospital based	moderate
Xu 2014[58]	DNA Cell Biol	China	PCR-RFLP	>20 total 65 <20 total 137	>20 total 66 <20 total 150	125/77	127/89	Hospital based	moderate
Zhao 2015[59]	Int J Clin Exp Pathol.	China	PCR-RFLP	14.68 (5-22 years)	15.6(12-24)	57/23	54/46	Hospital based	poor
Patino-Garcia 2000[60]	J Medical Genetics	Spain	PCR					Hospital based	good
Savage 2007[61]	Pediatr Blood Cancer	USA	taqman PCR	Mean(SD) 26.4 (16.2)	Mean(SD) 24.9 (14.5)	-	-	Hospital based	good
Ru 2015[62]	Int J Clin Exp Pathol	china	taqman PCR	28.0 ± 18.0	27.9 ± 17.3	130/80	240/180	Hospital based	moderate
Zhang 2018[63]	Cancer Biol Ther.	China	taqman PCR	-	-	690/610	675/625	Not specified	moderate
Zhang 2015[64]	Genet Mol Res.	China	PCR-RFLP	20.6 ± 11.6	21.4 ± 12.1	106/76	106/63	Population based	poor
Zhao 2015[65]	Pak J Med Sci.	China	PCR-RFLP	18.4±11.5	19.5±10.8	109/67	109/67	Hospital based	poor
Tie 2014[66]	Int J Clin Exp Pathol	China	PCR-RFLP	19.1 ± 6.7	19.6 ± 7.2	108/108	215/115	Hospital based	moderate
Liu 2015[67]	Oncol Lett	China	PCR-RFLP	18.5±10.3	19.2±11.8	114/72	114/72	Hospital based	moderate
Wang 2013[68]	Tumour Biol.	China	PCR-RFLP	27.3 ± 13.6	28.2 ± 14.3	188/142	176/166	Population based	moderate
Zhang 2015[69]	Genet Mol Res	China	PCR-RFLP	≤20y 123 >20y 57	≤20y 236 >20y 124	110/70	220/140	Population based	moderate
Li 2017[70]	Biomedical Research	China	MALDI-TOF MS	26.1 ± 16.6	28.1 ± 12.2	118/124	122/131	Hospital based	moderate
Cao 2016[71]	Int J Clin Exp Pathol	China	PCR-RFLP	18.1±10.2	19.3±10.3	231/91	242/101	Hospital based	good
Hu 2015[72]	Genet Mol Res.	China	PCR-RFLP	<20 80 ≥20 50	<20 77 ≥20 53	77/76	76/54	Hospital based	moderate
Guo 2015[73]	Genet Mol Res.	China	PCR-RFLP	17.82 ± 5.40	17.31 ± 5.52	84/52	77/59	Hospital based	poor

Yang 2015[74]	Int J Clin Exp Pathol.	China	PCR-RFLP	<20years 94 ≥ 20 years 58	<20years 182 ≥20 years 122	88/64	176/128	Hospital based	moderate
Koshkina 2007[75]	J Pediatr Hematol Oncol.	USA	PCR-RFLP	13.0±4.0	49.1±11.4	70/35	245/265	Population based	moderate

Table S2: Summary of characteristics of included studies

Total number of studies	75
* Location of study:	
Brazil	1(1.3%)
China	56(74.7%)
Iran	1(1.3%)
Italy	5(6.7 %)
Russia	1(1.3%)
Slovenia	2(2.7%)
Spain	2(2.7%)
USA	6(8%)
Genotyping Methods	
Genotyping method	36(48%)
PCR-RFLP	23(30.7%)
TaqMan PCR	2(2.7%)
PCR	2(2.7%)
Custom Infinium BeadChip	2(2.7%)
MALDI-TOF minisequencing	2(2.7%)
Sequencing	1(1.3%)
(PCR-RFLP) &sequencing	1(1.3%)
ARMS and RFLP	1(1.3%)
fluorescent, allele-specific	1(1.3%)
MALDI-TOF	1(1.3%)
MassARRAY system	1(1.3%)
PSQ/taqman assay	1(1.3%)
Pyrosequencing	1(1.3%)
Sequenom MassARRAY	1(1.3%)
Type of sample	
Blood	74(98.7%)
peripheral blood DNA, mouthwash DNA, or buccal swab DNA collection or Guthrie Card samples	1(1.3%)
Type of controls	
Hospital based	61(81.3%)
Population-based	12(16%)
Not specified	3(34%)
Controls cases ratio	

<1:1	2(2.7%)
1:1	40(53.3%)
2:1	22(29.3%)
>2:1	11(14.7%)
Cases	
Median	168
Minimum	12
Maximum	1300
Controls	
Median	240
Minimum	60
Maximum	1518

Table S3: Summary of all genetic variations

	Gene	chr	Polymorphism	Functional Consequence	First Author year	Journal	location	Cases/ Controls	Genotype frequency cases	Genotype frequency controls	HWE	Genetic Model	P-value
1.	CASC21	8	rs185852	Intron variant	Mirabello 2010[1]	Carcinogenesis	USA	99/1430	GG,AG,AA 60,31,8	GG,AG,AA 934,440,54	0.8	AG vs GG AA vs GG	0.69 0.039
2.	CASC8	8	rs896324	Intron variant, Genic downstream transcript variant	Mirabello 2010[1]	Carcinogenesis	USA	99/1430	AA,AG,GG 76,21,2	AA,AG,GG 1225,191,13	0.1	AG vs AA GG vs AA	0.025 0.19
3.			rs10808555	Intron variant, Genic downstream transcript variant	Mirabello 2010[1]	Carcinogenesis	USA	99/1430	AA,AG,GG 37,52,10	AA,AG,GG 679,595,156	0.1	AG vs AA GG vs AA	0.033 0.67
4.			rs17766217	NA	Mirabello 2010[1]	Carcinogenesis	USA	99/1430	TT,TC,CC 47,42,10	TT,TC,CC 531,692,206	0.4	TC vs TT CC vs TT	0.096 0.1
5.	8q24 region	8	rs12155672	NA	Mirabello 2010[1]	Carcinogenesis	USA	99/1430	GG,AG,AA 23,42,34	GG,AG,AA 366,728,336	0.5	AG vs GG AA vs GG	0.76 0.098
6.			rs7386167	NA	Mirabello 2010[1]	Carcinogenesis	USA	99/1430	GG,AG,AA 37,40,22	GG,AG,AA 618,626,186	0.2	AG vs GG AA vs GG	0.78 0.018
7.	CASC11	8	rs9642880	Intron variant, genic downstream transcript variant	Mirabello 2010[1]	Carcinogenesis	USA	99/1430	GG,GT,TT 39,42,18	GG,GT,TT 416,704,306	0.8	GT vs GG TT vs GG	0.048 0.11
8.	AKT	7	rs6973569	Intron variant, Genic downstream transcript variant	HE 2013[2]	Asian Pac J Cancer Prev	China	59/63	AA,AG,GG 20,21,18	AA,AG,GG 17,24,22	0.06	AG vs AA GG vs AA	0.7
9.	APEX1	14	rs1130409	Synonymous variant, missense variant, coding sequence variant	Xiao 2017[3]	Sci Rep	China	378/616	TT,TG,GG 134,178,66	TT,TG,GG 208,287,121	0.2	TG vs TT GG vs TT TG+GG vs TT G vs T	0.83 0.4 0.63 0.40
10.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TG,GG 31,98,67	TT,TG,GG 94,230,146	0.8	GG GT TT	>0.05
11.			rs1760944	2KB upstream variant, upstream transcript variant	Xiao 2017[3]	Sci Rep	China	378/616	TT,TG,GG 163,163,52	TT,TG,GG 194,299,123	0.7	TG vs TT GG vs TT TG+GG vs TT G vs T	0.003 <0.01 <0.01 <0.01

12.			rs17111750	NA	Xiao 2017[3]	Sci Rep	China	378/616	CC,CT,TT 230,111,37	CC,CT,TT 339,182,41	0.02	CT vs CC TT vs CC CT+TTvs CC T vs C	0.51 0.27 0.89 0.66
13.			rs1130409	Synonymous variant, missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GT,TT 31,98,67	GG,GT,TT 94,230,146	0.8	GG GT TT	>0.05
14.	OSGEP	14	rs2275008	Intron variant	Xiao 2017[3]	Sci Rep	China	378/616	TT,TC,CC 276,94,8	TT,TC,CC 473,128,15	0.08	TC vs TT CC vs TT TC+CC vs TT C vs T	0.16 0.51 0.2 0.28
15.	PIP4P1	14	rs1760941	2KB upstream variant, upstream transcript variant	Xiao 2017[3]	Sci Rep	China	378/616	CC,CA,AA 213,134,31	CC,CA,AA 325,230,61	0.04	CA vs CC AA vs CC CA+AA vs CC A vs C	0.4 0.3 0.29 0.22
16.	ARHGAP3 5	19	rs1052667	3 prime UTR variant, genic downstream transcript variant	Zhao 2014[5]	Biomed Res Int.	China	247/428	CC,CT,TT 133,70,44	CC,CT,TT 341,72,15	<0.01	CT vs CC TT vs CC CT+TTvs CC T vs C	<0.001 <0.001 <0.001 <0.001
17.	BMP2	20	rs3178250	3 prime UTR variant	Cong 2015[6]	Tumour Biol	China	203/406	CC,CT,TT 35,113,54	CC,CT,TT 107,219,80	0.09	CT vs CC TT vs CC CT+TTvs CC	0.006
18.			rs235768	Coding sequence variant,synonymous variant, missense variant	Cong 2015[6]	Tumour Biol	China	203/406	TT, TA, AA 123,71,8	TT, TA, AA 241,148,17	0.3	TA vs TT AA vs TT TA+AA vs TT	0.72
19.			rs1005464	Intron variant	Cong 2015[6]	Tumour Biol	China	203/406	GG,GA,AA 112,77,13	GG,GA,AA 181,177,48	0.6	GA vs GG AA vs GG GA+AA vs GG	0.05
20.			rs235770	NA	Cong 2015[6]	Tumour Biol	China	203/406	CC,CT,TT 82,102,18	CC,CT,TT 169,199,38	0.06	CT vs CC TT vs CC CT+TTvs CC	0.92

21.			rs235764	Intron variant	Cong 2015[6]	Tumour Biol	China	203/406	GG,GA,AA 120,72,10	GG,GA,AA 248,140,18	0.8	GA vs GG AA vs GG GA+AA vs GG	0.66
22.	CD86	3	rs1129055	Coding sequence variant, missense variant	Wang 2011[7]	DNA and Cell Biology	China	205/216	GG,GA,AA 27,105,73	GG,GA,AA 46,113,57	0.5	GA vs GG AA vs GG A vs G	0.097 0.008 0.011
23.	CDKN2B	9	rs1063192	3 prime UTR variant, intron variant	Zhang 2019[8]	Med Sci Monit.	China	184/185	GG,GA,AA 54,88,42	GG,GA,AA 52,89,44	0.6	GA vs GG AA vs GG GA+AA vs GG	0.329 0.321 0.421
24.			rs3217992	3 prime UTR variant, intron variant	Zhang 2019[8]	Med Sci Monit.	China	184/185	GG,GA,AA 114,63,7	GG,GA,AA 142,42,1	0.3	GA vs GG AA vs GG GA+AA vs GG	0.024 0.006 0.013
25.			r rs3217986	3 prime UTR variant, intron variant	Zhang 2019[8]	Med Sci Monit.	China	184/185	CC,CA,AA 66,90,28	CC,CA,AA 69,86,30	0.7	CA vs CC AA vs CC CA+AA vs CC	0.235 0.22 0.311
26.	CDKN2B-AS1	9	rs3218009	intron variant	Zhang 2019[8]	Med Sci Monit.	China	184/185	CC,CG,GG 78,83,23	CC,CG,GG 86,79,20	0.8	CG vs CC GG vs CC CG+GG vs CC	0.311 0.229 0.32
27.	CDKN2A-DT	9	rs3731257	3 prime UTR variant, intron variant	Zhang 2019[8]	Med Sci Monit.	China	184/185	CC,CT,TT 115,57,12	CC,CT,TT 119,53,13	0.05	CT vs CC TT vs CC CT+TT vs CC	0.521 0.771 0.32
28.	COL1A1	17	rs1061970	3 prime UTR variant	He 2014[9]	Tumour Biol.	China	189/195	TT,CT,CC 72,90,27	TT,CT,CC 114,,57,24	0.0003	TC vs TT CCs TT C vs T	0.02 0.295 0.022
29.			rs2075559	intron variant	He 2014 [9]	Tumour Biol.	China	189/195	CC,CG,GG 27,108,54	CC,CG,GG 60,84,51	0.06	CG vs CC GG vs CC G vs C	0.027 0.103 0.029
30.	COL18A1	21	rs12483377	Intron variant, coding sequence variant, missense variant, genic downstream transcript variant	Guo 2015[10]	Int J Clin Exp Pathol	China	141/341	DD,DN,NN 119,14,8	DD,DN,NN 312,28,1	0.7	DN vs DD NN vs DD	0.43 <0.001

31.			c.4309G> A (p.D104N)		Bi 2016[11]	Sci.reeports	China	236/418	WT,HET,VA R 205,23,8	WT,HET,VA R 376,39,3		WT HET VAR	>0.05
32.	CTLA4	2	rs5742909	Upstream transcript variant, 2KB upstream variant	Qiao 2016[12]	IJCEM	China	122/131	CC,CT,TT 74,40,8	CC,CT,TT 97,30,4	0.38	CT vs CC TT vs CC	0.598 0.115
33.					Liu 2011[13]	DNA Cell Biol	China	267/282	CC,CT,TT 175,77,15	CC,CT,TT 195,80,7	0.38	CT vs CC TT vs CC	0.713 0.057
34.			rs4553808	Upstream transcript variant, 2KB upstream variant	Liu 2011[13]	DNA Cell Biol	China	267/282	AA,AG,GG 177,76,14	AA,AG,GG 197,73,12	0.2	AG vs AA GG vs AA AG+GG vs AA G vs A	0.447 0.52 0.37 0.33
35.					Liu 2011[13]	DNA Cell Biol	China	267/282	GG,GA,AA 176,77,14	GG,GA,AA 188,83,11	0.6	GA vs AA GG vs AA GG+GA vs AA G vs A	0.962 0.459 0.853 0.66
36.			rs231775	Missense variant, coding sequence variant	Liu 2011[13]	DNA Cell Biol	China	267/282	GG,GA,AA 120,140,22	GG,GA,AA 99,128,40	<0.05	GA vs GG AA vs GG	0.574 0.007
37.					Wang 2011[14]	Genet Test Mol Biomarkers	China	205/216	GG,GA,AA 64,106,35	GG,GA,AA 87,108,21	0.16	GA vs GG AA vs GG	0.178 0.01
38.					Qiao 2016[12]	IJCEM	China	122/131	GG,GA,AA 46,58,18	GG,GA,AA 64,56,56	0.92	GA vs GG AA vs GG	0.178 0.01
39.					Bilbao- Aldaiturriaga 2017 [15]	Neoplasma	Spain	99/125	GG,GA,AA 5,83,37	GG,GA,AA 6,28,32	<0.05	AA vs AG, AA vs GG AA vs AG+GG	0.005 0.011
40.	ERCC1	19	rs11615		Jin 2015[16]	Pak J Med Sci	China	148/296	TT,TC+CC 135,46	TT,TC+CC 63,52	-	TC+CC vs TT	0.58

				Coding sequence variant, synonymous variant									
41.					Xu 2017[17]	Mamm Genome	China	381/765	TT,TC,CC 33,149,199	TT,TC,CC 44,275,446	0.91	TC vs TT CC vs TT	
42.					Biason 2011[18]	Pharmacogenomics J	Italy	130/250	TT,TC,CC 37,59,30	TT,TC,CC 86,111,53	0.15	TC vs TT CC vs TT TC+CC vs TT	>0.05 0.37 0.35
43.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TC,CC 67,84,45	TT,TC,CC 164,221,85	0.5	TT TC CC	>0.05
44.					Gómez-Díaz [19]	Oncol Lett	México	28/97	CC,TC,TT 16,9,3	CC,TC,TT 59,32,6	0.6	GA vs GG AA vs GG	0.94 0.42
45.			rs3212981	Genic downstream transcript variant, intron variant	Xu 2017[17]	Mamm Genome	China	381/765	CC,CA,AA 197,145,39	CC,CA,AA 442,272,51	0.3	CA vs CC AA vs CC	
46.			rs3212986	Genic downstream transcript variant ,coding sequence variant,3 prime UTR variant, missense variant	Jin 2015[16]	Pak J Med Sci	China	148/296	GG,GA+AA 79,69	GG,GA+AA 169,129	-	GA+AA vs GG	0.5
47.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GT,TT 121,63,12	GG,GT,TT 254,183,33	0.99	GG GT TT	>0.05
48.	ERCC2	19	rs1799793	Missense variant, coding sequence variant, non-coding transcript variant	Gómez-Díaz [19]	Oncol Lett	México	28/97	CC,CT,TT 74,26,8	CC,CT,TT 81,23,15	<0.001	CT vs CC TT vs CC CC+CT vs CC	0.52 0.24 0.94
49.					Jin 2015[16]	Pak J Med Sci	China	148/296	GG,GA+AA 84,64	GG,GA+AA 201,97	-	GA+AA vs GG	0.03
50.					Ma 2016[20]	Genet Mol Res	China	141/282	AA,AG,GG 60,62,19	AA,AG,GG 134,117,31	0.5	AG vs AA GG vs AA Ag+GG vs AA	0.45 0.34 0.33
51.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 84,79,33	GG,GA,AA 207,193,70	0.03	GG GA	>0.05

												AA	
52.			rs13181	Genic downstream transcript variant, coding sequence variant, missense variant, 500B downstream variant	Gómez-Díaz [19]	Oncol Lett	México	28/97	TT,TG,GG 21,7,0	TT,TG,GG 64,31,2	<0.001	AC vs AA CC vs AA AC+CC vs AA	0.74 0.91 0.79
53.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TG,GG 78,88,30	TT,TG,GG 179,216,75	0.5	TT TG GG	>0.05
54.					Ma 2016[20]	Genet Mol Res	China	141/282	TT,TG,GG 96,32,13	TT,TG,GG 206,58,18	<0.001	TG vs TT GG vs TT TG +GG vs TT	0.5 0.25 0.29
55.					Jin 2015[16]	Pak J Med Sci	China	148/296	TT, TG+GG 117,62	TT, TG+GG 181,86	-	TG+GG vs TT	0.59
56.	ERCC3	19	rs4150441	intron variant	Xu 2017[17]	Mamm Genome	China	381/765	GG,GA,AA 190,152,39	GG,GA,AA 500,231,34	0.32	GA vs GG AA vs GG GA+AA vs GG	
57.					Ma 2016[20]	Genet Mol Res	China	141/282	GG,GA,AA 56,66,19	GG,GA,AA 123,129,30	0.73	GA vs GG AA vs GG GA+AA vs GG	
58.			rs4150506	intron variant	Xu 2017[17]	Mamm Genome	China	381/765	CC,CT,TT 231,133,35	CC,CT,TT 486,238,41	0.12	CT vs CC TT vs CC	
59.					Ma 2016[20]	Genet Mol Res	China	141/282	CC,CT,TT 190,152,39	CC,CT,TT 148,109,29	0.43	CT vs CC TT vs CC	0.34 0.25
60.	GRM4	6	rs1906953	intron variant	Wang 2015[21]	Tumour Biol.	China	126/168	TT, TC, CC 29,65,32	TT, TC, CC 60,80,28	0.12	TT(ref) TC CC	0.034
61.					Jiang 2014[22]	Med Oncol.	China	168/216	TT, TC, CC 45,82,41	TT, TC, CC 39,101,79	0.43	TT(ref) TC CC C vs T	0.010 0.002
62.			rs2229901	3 prime UTR variant	Wang 2015[21]	Tumour Biol.	China	126/168	GG,GA,AA 33,94,31	GG,GA,AA 33,62,41	0.3	GG(ref) GA AA	0.37
63.			rs733457	intron variant	Wang 2015[21]	Tumour Biol.	China	126/168	TT,TG,GG	TT,TG,GG 79,58,31	0.001	TT(ref) TG GG	0.8
64.			rs7591996	NA	Jiang 2014[22]	Med Oncol.	China	168/216	AA,AC,CC 15,70,83	AA,AC,CC 21.94,101	0.9	AA(ref) AC	0.9

												CC	
65.			rs17206779	Intron variant, genic downstream transcript variant	Jiang 2014[22]	Med Oncol.	China	168/216	TT,TC,CC 24,74,70	TT,TC,CC 35,96,85	0.4	TT(ref) TC CC	0.83
66.	GSTM1	1	rs_GSTM1_gen_null	2KB upstream variant, upstream transcript variant(DELINS)	Barnette 2004[23]	Cancer Epidemiol Biomarkers Prev.	USA	12/326	Null ,Present 2,10	Null ,Present 183,143	-	A0 versus 00 B0 versus 00	0.038 0.002
67.					Salinas-Souza 2010[24]	Pharmacogenet Genomics	Brazil	80/160	Null ,Present 35,45	Null ,Present 72,88	-	Null vs present	0.9
68.					Lu2011[25]	APJCP	China	110/226	Null ,Present 61,49	Null ,Present 104,122		Null vs present	>0.05
69.					Li 2015[26]	Genetics and molecular research	China	52/79	Null ,Present 16,36	Null ,Present 37,42		Null vs present	<0.05
70.					Qu 2016[27]	Genetics and molecular research	China	153/252	Null ,Present 65/88	Null ,Present 95/157		Null vs present	0.34
71.					Moghimi 2018[28]	APJCP	Iran	51/60	Null ,Present 22,29	Null ,Present 24,36	-	Null vs present	-
72.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	Null ,Present 112,84	Null ,Present 249,221		WT HET VAR	>0.05
73.	GSTM3	1		Non-coding transcript variant	Barnette 2004[23]	Cancer Epidemiol Biomarkers Prev.	USA	12/326	TT,TC,CC 7,5,0	TT,TC,CC 224,71,5	0.817		-
74.				Non-coding transcript variant	Moghimi 2018[28]	APJCP	Iran	51/60	TT,TC,CC 34,16,1	TT,TC,CC 38,21,1	0.315		-
75.	GSTP1	11	rs1695	Coding sequence variant, missense variant	Moghimi 2018[28]	APJCP	Iran	51/60	AA,AG,GG 32,16,3	AA,AG,GG 39,19,2	0.8		-

76.					Qu 2016[27]	Genetics and molecular research	China	153/252	AA,AG,GG 64,71,19	AA,AG,GG 135,105,12	0.14	AG vs AA GG vs AA AG+GG vs AA	0.09 0.002 0.02
77.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	AA,AG,GG 94,86,16	AA,AG,GG 240,202,28	0.09	AA AG GG	>0.05
78.	GSTT1	22	rs_GSTT1_gen _null	reduced or no protein activity(DELINS)	Barnette 2004[23]	Cancer Epidemiol Biomarkers Prev.	USA	12/326	Null ,Present 2,10	Null ,Present 66.234	-	Null vs Present	-
79.					Salinas-Souza 2010[24]	Pharmacogenet Genomics	Brazil	80/160	Null ,Present 26,54	Null ,Present 42,118	-	Null vs Present	0.3
80.					Qu 2016[27]	Genetics and molecular research	China	153/252	Null ,Present 70,40	Null ,Present 111,115	-	Null vs Present	0.7
81.					Lu2011[25]	APJCP	China	110/226	Null ,Present 68,85	Null ,Present 107,145	-	Null vs Present	<0.05
82.					Moghimi 2018[28]	APJCP	Iran	51/60	Null ,Present 24,26	Null ,Present 27,34	-	Null vs Present	-
83.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	Null ,Present 31,165,	Null ,Present 89,381		WT HET VAR	>0.05
84.	H19	11	rs2735971	Intron variant ,genic downstream transcript variant, genic upstream transcript variant	HE 2017[29]	Eur Rev Med Pharmacol Sci	China	193/383	CC,CT,TT 88,94,11	CC,CT,TT 169,182,32	0.8	CT vs CC TT vs CC	0.816 0.674
85.			rs217727	Intron variant, non-coding transcript variant, genic	HE 2017[29]	Eur Rev Med Pharmacol Sci	China	193/383	GG,GA,AA 79,102,12	GG,GA,AA 195,165,23	0.1	GA vs GG AA vs GG	0.024 0.004

				downstream transcript variant									
86.			rs2839698	upstream transcript variant, noncoding transcript variant, intron variant, 2KB upstream variant, genic downstream	HE 2017[29]	Eur Rev Med Pharmacol Sci	China	193/383	GG,GA,AA 83,98,12	GG,GA,AA 178,175,30	0.15	GA vs GG AA vs GG	0.112 0.892
87.			rs3024270	Intron variant ,genic downstream transcript variant	HE 2017[29]	Eur Rev Med Pharmacol Sci	China	193/383	GG,GC,CC 85,91,17	GG,GC,CC 173,179,31	0.1	GC vs GG CC vs GG	0.882 0.457
88.	ERBB2/HE R2		rs1058808	non-coding transcript variant, coding sequence variant, missense variant, genic downstream transcript variant	Xin 2015[30]	Int J Clin Exp Pathol.	China	90/100	CC,CG ,GG 48,28,14	CC,CG ,GG 69,26,5	0.2	CG vs CC GG vs CC C vs G	0.02 3.00×10 ⁻³
89.			rs1136201	Intron variant ,genic downstream transcript variant, coding sequence variant, missense variant	Xin 2015[30]	Int J Clin Exp Pathol.	China	90/100	AA,AG ,GG 20,47,23	AA ,AG ,GG 38,46,16	0.7	AG vs AA GG vs AA A vs G	0.04 0.01
90.			rs2952156	Genic downstream transcript variant, intron variant	Xin 2015[30]	Int J Clin Exp Pathol.	China	90/100	GG,GA,AA 47,26,17	GG,GA,AA 46,41,13	0.4	GA vs GG AA vs GG G vs A	0.18 0.97
91.			rs1810132	Intron variant	Xin 2015[30]	Int J Clin Exp Pathol.	China	90/100	CC ,CT ,TT 19,39,32	CC ,CT ,TT 31,41,28	0.07	CT vs CC TT vs CC T vs C	0.26 0.09
92.			rs2952155	Intron variant	Xin 2015[30]	Int J Clin Exp Pathol.	China	90/100	CC ,CT ,TT 33,31,26	CC ,CT ,TT 26,41,33	0.08	CT vs CC TT vs CC T vs C	0.28 0.15

93.	HOTAIR	12	rs7958904	Non-coding transcript variant	Zhou 2016[31]	Oncotarget.	China	900/900	GG,GC,CC 524,320,56	GG,GC,CC 466,346,88	>0.05	GC vs GG CC vs GG	6.77×10 ⁻⁴
94.			rs874945	None	Zhou 2016[31]	Oncotarget.	China	400/400	GG,GA,AA 267,106,27	GG,GA,AA 270,108,22	>0.05	GA vs GG AA vs GG	0.614
95.			rs4759314	Intron variant	Zhou 2016[31]	Oncotarget.	China	500/500	AA,AG,GG 423,62,15	AA,AG,GG 425,64,11	>0.05	AG vs AA GG vs AA	0.64
96.	IGF2R	6	rs1570070	Coding sequence variant, synonymous variant	Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	140/74 Orthopedic controls	AA,AG,GG 48,42,14	AA,AG,GG 33,34,7	0.7	Additive dominant	0.6 0.8
97.			rs894817	Coding sequence variant, synonymous variant	Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	140/74 Orthopedic controls	GG,GA,AA 48,45,11	GG,GA,AA 34,32,8	0.9	Additive dominant	0.99 0.98
98.			rs998075	Coding sequence variant, synonymous variant	Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	140/74 Orthopedic controls	GG,GA,AA 18,54,31	GG,GA,AA 24,40,10	0.3	Additive dominant	0.01 0.02
99.			rs998074	Intron variant	Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	140/74 Orthopedic controls	CC,CT,TT 18,53,33	CC,CT,TT 24,40,10	0.3	Additive dominant	0.008 0.019
100.			rs629849	Coding sequence variant, synonymous variant, missense variant	Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	140/74 Orthopedic controls	GG,GA,AA 75,26,2	GG,GA,AA 61,12,1	0.64	Additive dominant	0.33 0.14
101.			rs2282140	Intron variant	Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	140/74 Orthopedic controls	CC,CT,TT 78,17,2	CC,CT,TT 47,21,1	0.4	Additive dominant	0.15 0.07
102.			rs1803989	500B downstream variant, coding sequence variant, downstream transcript variant, synonymous variant	Savage 2007[32]	Cancer Epidemiol Biomarkers	USA	140/74 Orthopedic controls	TT,TC,CC 97,6,0	TT,TC,CC 63,11,0	0.5	Additive dominant	0.04 0.04
103.	IL1B	2	rs1143627	5 prime UTR variant, genic upstream transcript	He 2014[33]	Int Orthop.	China	120/120	TT,TC,CC 60,50,10	TT,TC,CC 50,49,21	0.15	Tc vs TT CC vs TT C vs T	0.56 0.03 0.04

				variant, upstream transcript variant									
104.			rs16944	Upstream transcript variant, 2KB upstream variant	He 2014[33]	Int Orthop.	China	120/120	CC,CT,TT 59,52,9	CC,CT,TT 52,48,20	0.13	CT vs CC TT vs CC T vs C	0.87 0.04 0.08
105.			rs1143634	Synonymous variant, coding sequence variant	He 2014[33]	Int Orthop.	China	120/120	CC,CT,TT 77,30,13	CC,CT,TT 79,32,9	0.04	CT vs CC TT vs CC T vs C	0.9 0.4 0.51
106.	IL6	7	rs1800796	Non-coding transcript variant,upstream transcript variant, intron variant, genic upstream transcript variant	Shang 2017[34]	Biomedical Research	China	191/207	CC,CG,CG 85,88,17	CC,CG,CG 124,68,15	0.2	CG vs CC GG vs CC CG+GG vs CC G vs CC	0.003 0.19 0.002 0.001
107.			rs1800795	Upstream transcript variant, intron variant, genic upstream transcript variant	Qi 2016[35]	Tumour Biol.	China	206/206	GG,GC,CC 94,83,39	GG,GC,CC 130,62,24	0.0003	GC vs GG CC vs GG GC+CC vs GG	0.028 0.022 0.029
108.					Oliveira 2007[36]	J Pediatr Hematol Oncol	Brazil	64/160	GG,GC,CC 9,23,32	GG,GC,CC 10,68,82	0.4	-	-
109.			rs1800796	non_coding transcript variant, upstream transcript variant, intron variant, genic upstream transcript variant	Qi 2016[35]	Tumour Biol.	China	206/206	GG,GC,CC 94,99,23	GG,GC,CC 95,89,32	0.14	GC vs GG CC vs GG GC+CC vs GG C vs G	0.289 0.189 0.193 0.172
110.	IL8	4	rs4073	2KB upstream variant, upstream transcript variant	Tian 2016[37]	Int J Clin Exp Med.	China	109/109	TT,TA,AA 58,32,19	TT,TA,AA 73,24,12	0.0004	TA vs TT AA vs TT	0.014 0.025
111.					Chen 2016[38]	Tumour Biol	China	190/190	TT,TA,AA 99,63,28	TT,TA,AA 122,50,18	0.001	TA vs TT AA vs TT	0.021 0.018

112.			rs2227306	2KB upstream variant, upstream transcript variant	Chen 2016[38]	Tumour Biol	China	190/190	CC,CT,TT 86,90,14	CC,CT,TT 90,88,12	0.11	CT vs CC TT vs CC CT+TT vs CC T vs C	0.271 0.262 0.159 0.105
113.	IL10	1	rs1800896	Genic upstream transcript variant ,intron variant, 2KB upstream variant upstream transcript variant	Cui 2016[39]	Tumour Biol	China	260/260	AA,AG,GG 139,73,48	AA,AG,GG 155,76,29	>0.05	AG vs AA GG vs AA AG+GG vs AA G vs A	0.017 0.01 0.019 0.026
114.					Oliveira 2007[36]	J Pediatr Hematol Oncol	Brazil	80/157	AA,AG,GG 5,44,29	AA,AG,GG 23,76,58	0.8	-	-
115.			rs1800871	Genic upstream transcript variant,intron variant, 2KB upstream variant ,upstream transcript variant	Cui 2016[39]	Tumour Biol	China	260/260	CC,CT,TT 106,120,34	CC,CT,T 99,118,43	0.4	CT vs CC TT vs CC CT+TT vs CC T vs C	0.159 0.137 0.161 0.251
116.			rs1800872	Genic upstream transcript variant,intron variant, 2KB upstream variant ,upstream transcript variant	Cui 2016[39]	Tumour Biol	China	260/260	AA, AC,CC 108,125,27	AA, AC,CC 100,128,32	0.4	AC vs AA CC vs AA AC+CC vs AA C vs A	0.195 0.152 0.204 0.195
117.	IL 12A	3	rs568408	3 prime UTR variant, intron variant	Wang 2013[40]	DNA Cell Biol	China	106/210	GG,GA,AA 66,37,3	GG,GA,AA 156,47,7	0.15	GA vs GG AA vs GG GA+AA vs GG	<0.05 >0.05 <0.05
118.			rs2243115	Intron variant, 2KB_upstream variant ,upstream transcript variant	Wang 2013[40]	DNA Cell Biol	China	106/210	TT,TG,GG 89,16,1	TT,TG,GG 175,31,4	0.07	TG vs GG TT vs GG TG+TT vs GG	>0.05 >0.05 >0.05
119.			rs3212227	3 prime UTR variant	Wang 2013[40]	DNA Cell Biol	China	106/210	AA,AC,CC 27,50,29	AA,AC,CC 78,101,31	0.9	AC vs AA CC vs AA	>0.05 <0.05

												AC+CC vs AA	<0.05
120.	IL16	15	rs4778889	Intron variant, genic upstream transcript variant ,upstream transcript variant	Tang 2016[41]	Sci Rep	China	358/402	TT,TC,CC 215,127,16	TT,TC,CC 240,140,22	0.8	TC vs TT CC vs TT C vs T	0.94 0.55 0.76
121.			rs11556218	Coding sequence variant, non-coding transcript variant, missense variant	Tang 2016[41]	Sci Rep	China	358/402	TT,TG,GG 165,174,19	TT,TG,GG 235,151,16	0.17	TG vs TT GG vs GG G vs T	0.001 0.14 0.002
122.			rs4072111	Coding sequence variant,missense variant ,5 prime UTR variant, genic upstream transcript variant, non-coding	Tang 2016[41]	Sci Rep	China	358/402	CC,CT,TT 229,158,15	CC,CT,TT 218,124,16	0.8	CT vs CC TT vs CC T vs C	0.19 0.75 0.45
123.	IL27	16	rs153109	Intron variant, upstream transcript variant, genic upstream transcript variant	Tang 2014[42]	Medicine	China	160/250	AA,AG,GGG 56,85,19	AA,AG,GGG 100,124,26	0.17	AG vs AA GG vs AA G vs A	0.355 0.44 0.347
124.			rs17855750	Missense variant, coding sequence variant	Tang 2014[42]	Medicine	China	160/250	TT,TG,GG 132,28,0	TT,TG,GG 205,45,0	0.12	TG vs TT GG vs TT G vs T	0.897 ... 0.902
125.			rs181206	Missense variant, coding sequence variant	Tang 2014[42]	Medicine	China	160/250	TT,TC,CC 131,29,0	TT,TC,CC 207,43,0	0.14	TC vs TT CC vs TT C vs T	0.81 ... 0.819
126.	ITGA3	17	rs2230392	Missense variant, non-coding transcript variant, coding sequence variant	Yang 2014[43]	Med Oncol	China	118/126	AA,AG,GG 50,44,24	AA,AG,GG 33,54,39	> 0.05	AA AG GG G vs A	0.02 0.003
127.			rs2285524	Synonymous variant, non-coding transcript variant,	Yang 2014[43]	Med Oncol	China	118/126	AA,AG,GG 36,47,35	AA,AG,GG 31,57,38	> 0.05	AA AG GG G vs A	0.55 0.48

				coding sequence variant									
128.			rs16948627	Intron variant	Yang 2014[43]	Med Oncol	China	118/126	AA,AC,CC 37,48,33	AA,AC,CC 47,24,55	< 0.05	AA AC CC C vs A	0.001 0.28
129.	LOX	5	-22 G/C		Liu 2012[44]	PLoS One	China	326/433	GG,GC,CC 306,9,11	GG,GC,CC 425,5,3	>0.05	CG vs GG CC vs GG C vs G	0.093* 0.006 4.18×10 ⁻⁵
130.			225C/G		Liu 2012[44]	PLoS One	China	326/433	CC,CG,GG 315,11,0	CC,CG,GG 416,17,0	>0.05	CG vs CC G vs C	0.69 0.693
131.			rs1800449	Coding sequence variant, genic upstream transcript variant, missense variant ,upstream transcript variant	Liu 2012[44]	PLoS One	China	326/433	GG,GA,AA 209,86,31	GG,GA,AA 301,112,20	>0.05	GA vs GG AA vs GG A vs G	0.552 0.006 0.013
132.	MDM2	12	rs1690916	3 prime UTR variant	Bilbao-Aldaiturriaga 2016[45]	Pediatr Res	Spain	99/125	GG,GA,AA 38,49,12	GG,GA,AA 73,74,20	>0.05	GG GA AA	0.68
133.					Bilbao-Aldaiturriaga 2016[45]	Pediatr Res	Slovenia	27/91	GG,GA,AA 3,17,7	GG,GA,AA 26,51,4	>0.05	GG GA AA	0.11
134.					Naumov 2012[46]	Bull Exp Biol Med	Russia	24/86	GG,GA,AA 12,9,3	GG,GA,AA 23,45,18	>0.05	GG GA AA	0.1
135.					Mirabello 2011[47]	BMC Cancer	USA	96/1416	GG,GA,AA 44,44,8	GG,GA,AA 468,691,257	0.94	GG GA AA	0.006
136.			rs2279744	Intron variant, genic upstream transcript variant, upstream transcript variant	Bilbao-Aldaiturriaga 2016[45]	Pediatr Res	Spain	99/125	TT,TG,GG 44,37,13	TT,TG,GG 65,72,27	>0.05	TT TG GG	0.53
137.					Bilbao-Aldaiturriaga 2016[45]	Pediatr Res	Slovenia	27/91	TT,TG,GG 11,14,1	TT,TG,GG 40,38,14	>0.05	TT TG GG	0.19
138.					Mirabello 2011[47]	BMC Cancer	USA	96/1416	TT,TG,GG 32,46,17	TT,TG,GG 580,662,174	>0.05	TT TG	0.20

												GG	
139.					Toffoli 2009[48]	Clin Cancer Res	Italy	201/250	TT,TG,GG 69,86,46	TT,TG,GG 111,107,32	>0.05	TT TG GG	0.52
140.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TG,GG 67,82,47	TT,TG,GG 221,193,56	0.2	TT TG GG	< 0.001
141.	MMP2	16	rs243865	Upstream transcript variant, 2KB upstream variant	Cui 2016[49]	Biomarkers	China	251/251	CC,CT,TT 148,72,31	CC,CT,TT 179,52,20	>0.05	CT vs CC TT vs CC CT+TT vs CC T vs C	0.014 0.028 0.032 0.018
142.	MMP3	11	rs3025058	Upstream transcript variant ,2KB upstream variant	Cui 2016[49]	Biomarkers	China	251/251	6A/6A,6A/5A ,5A/5A 76,126,,49	6A/6A,6A/5A ,5A/5A 95,104,52	>0.05	6A/5A 5A/5A 6A/5A + 5A/5A 6A vs 5A	0.131 0.228 0.109 0.091
143.	MMP9	20	rs3918242	2KB upstream variant, Upstream transcript variant	Cui 2016[49]	Biomarkers	China	251/251	CC,CT,TT 79,128,45	CC,CT,TT 97,102,52	>0.05	CT vs CC TT vs CC CT+TT vs CC T vs C	0.2 0.18 0.5 0.07
144.	MTAP	9	rs7023329	Intron variant	Zhi 2016[50]	J Cancer	China	Discovery stage 284/981	AA,AG,GG 90,42,52	AA,AG,GG 238,492,251	>0.05	AA AG GG G vs A	0.05 0.05
145.				Intron variant	Zhi 2016[50]	J Cancer	China	Validation Stage 108/597	AA,AG,GG 37,51,20	AA,AG,GG 135,301,161	>0.05	AA AG GG G vs A	0.049 0.047
146.			rs7027989	Intron variant	Zhi 2016[50]	J Cancer	China	108/597	GG,GA,AA 65,38,5	GG,GA,AA 405,38,5	>0.05	AA AG GG G vs A	0.2914 0.1054

147.	NAT2	8	rs1799929	Coding sequence variant synonymous variant	Huang 2015[51]	Onco Targets Ther	China	260/280	CC,CT,TT 236,20,4	CC,CT,TT 254,30,2	0.295	CT vs CC TT vs CC CT+TT vs CC	0.272 0.379 0.452
148.			rs1208	Missense variant, coding sequence variant	Huang 2015[51]	Onco Targets Ther	China	260/280	AA,AG,GG 248,9,3	AA,AG,GG 272,13,1	0.063	AG vs AA GG vs AA AG+GG	0.534 0.304 0.878
149.			rs1041983	Coding sequence variant synonymous variant	Huang 2015[51]	Onco Targets Ther	China	260/280	CC,CT,TT 120,107,33	CC,CT,TT 109,145,32	0.115	CT vs CC TT vs CC CT+TT vs CC	0.029 0.816 0.057
150.			rs1801280	Missense variant, coding sequence variant	Huang 2015[51]	Onco Targets Ther	China	260/280	TT,TC,CC 238,20,2	TT,TC,CC 247,36,3	0.205	TC vs CC TT vs CC TC+TT vs CC	0.06 0.688 0.057
151.			rs1799930	Missense variant, coding sequence variant	Huang 2015[51]	Onco Targets Ther	China	260/280	GG,GA,AA 158,73,29	GG,GA,AA 167,98,21	0.216	GA vs GG AA vs GG AA+GA vs GG	0.209 0.218 0.572
152.			rs1799931	Missense variant, coding sequence variant	Huang 2015[51]	Onco Targets Ther	China	260/280	GG,GA,AA 177,77,6	GG,GA,AA 164,112,10	0.081	GA vs GG AA vs GG AA+GA vs GG	0.014 0.266 0.01
153.			rs1801279	Missense variant, coding sequence variant	Huang 2015[51]	Onco Targets Ther	China	260/280	GG,GA,AA 251,8,1	GG,GA,AA 270,15,1	0.125	GA vs GG AA vs GG AA+GA vs GG	0.213 0.959 0.238

154.	NBN	8	rs709816	Missense variant, coding sequence variant, synonymous variant	Jin 2015[16]	Pak J Med Sci.	China	148/298	GG,GC+CC 55,93	GG,GC+CC 115,183	>0.05	GC+CC vs GG	0.78
155.					Goricar 2015[52]	J Med Biochem.	Slovenia	79/373	CC,CT+TT 29,50	CC,CT+TT 139,234	-	CT+TT vs CC	0.926
156.			rs1805794	Missense variant, 5 prime UTR variant, coding sequence variant, intron variant	Jin 2015[16]	Pak J Med Sci.	China	148/298	GG,GC+CC 52,96	GG,GC+CC 127,171	>0.05	GC+CC vs GG	<0.001
157.					Goricar 2015[52]	J Med Biochem.	Slovenia	79/373	GG,GC+CC 11,68	GG,GC+CC 33,340	-	GC+CC vs GG	0.17
158.			rs1063054	3 prime UTR variant, genic downstream transcript variant	Goricar 2015[52]	J Med Biochem.	Slovenia	79/373	AA,AC+CC 38,38	AA,AC+C 163,210	-	AC+CC vs AA	0.32
159.	PRKCG	19	rs454006	Intron variant	Zhang 2014[53]	Tumour Biol	China	610/1610	CC,CT,TT 90,215,305	CC,CT,TT 52,213,345	VEGF	CC CT TT	0.001
160.					Lu 2015[54]	Tumour Biol	China	388/388	CC,CT,TT 98,123,167	CC,CT,TT 53,162,173	>0.05	TC+CC vs. TT CC vs. TT+TC CC vs. TT C vs T	0.66 0.001 0.001 0.008
161.			rs2242245	Intron variant	Zhang 2014[53]	Tumour Biol	China	610/1610	GG,GA,AA 27,168,415	GG,GA,AA 20,163,427	0.4	AA AG GG	0.52
162.					Lu 2015[54]	Tumour Biol	China	388/388	TT,TC,CC 285,84,19	TT,TC,CC 282,93,13	>0.05	TC+CC vs. TT CC vs. TT+TC CC vs. TT C vs T	0.8 0.3 0.3 0.8
163.			rs8103851	Intron variant	Zhang 2014[53]	Tumour Biol	China	610/1610	GG,GC,CC 113,286,211	GG,GC,CC 137,278,195	0.05	CC CG GG	0.2
164.					Lu 2015[54]	Tumour Biol	China	388/388	GG,GC,CC 87,169,132	GG,GC,C 81,172,135	>0.05	GG+GC vs. CC GG vs. CC+CG GG vs. CC G vs C	0.8 0.6 0.6 0.6
165.			rs2547362	Coding sequence variant, synonymous variant	Lu 2015[54]	Tumour Biol	China	388/388	TT,TC,CC 283,81.24	TT,TC,CC 287,88,13	>0.05	TC+CC vs. TT CC vs. TT+TC CC vs. TT	0.7 0.06 0.07

											C vs T	0.3	
166.			rs3745406	Missense variant, coding sequence variant, synonymous variant	Lu 2015[54]	Tumour Biol	China	388/388	TT,TC,CC 120,196,72	TT,TC,CC 149,176,53	>0.05	TC+CC vs. TT CC vs. TT+TC CC vs. TT C vs T	0.014 0.09 0.016 0.009
167.	RECQL5	17	rs820196	Non coding transcript variant, coding sequence variant, missense variant, 5 prime UTR variant, genic downstream variant	Zhi 2014[55]	Tumour Biol	China	212/240	CC,CT,TT 20,122,98	CC,CT,TT 37,109,66	0.48	CC CT TT	0.005
168.					Dong 2015[56]	Genet Mol Res.	China	185/201	CC,CT,TT 30,96,59	CC,CT,TT 18,102,81	>0.05	CC CT TT C vs T	0.005 0.001
169.			rs820200	Intron variant, genic upstream transcript variant , genic downstream transcript variant, 3 prime UTR variant	Zhi 2014[55]	Tumour Biol	China	212/240	GG,GT,TT	GG,GT,TT 39,132,69	0.07	GG GT TT	0.59
170.			rs4789223	Intron variant, genic upstream transcript variant, genic downstream transcript variant, 2KB upstream variant, upstream transcript variant	Zhi 2014[55]	Tumour Biol	China	212/240	AA,AG,GG 46,128,38	AA,AG,GG 34,114,92	0.9	AA AG GG A vs G	<0.001 <0.001
171.	TGF-β1	19	rs1800470	Missense variant, coding sequence variant	Wu 2015[57]	Tumour Biol	China	124/136	TT,TC,CC 52,45,27	TT,TC,CC 37,59,40	>0.5	TT TC CC T vs C	0.04 0.001
172.					Xu 2014[58]	DNA Cell Biol	China	202/216	TT,TC,CC 42,102,58	TT,TC,CC 66,110,40	0.6	TC vs TT CC vsTT	0.11 0.001
173.			rs180xc0469	Downstream transcript variant ,500B downstream	Wu 2015[57]	Tumour Biol	China	124/136	CC,CT,TT 31,65,40	CC,CT,TT 36,47,41	>0.5	CC CT TT	0.26

				variant, 2KB upstream variant ,upstream transcript variant							C vs T	0.77	
174.					Xu 2014[58]	DNA Cell Biol	China	202/216	CC,CT,TT 60,104,38	CC,CT,TT 69,109,38	0.62	CT vs CC TT vs CC	0.678 0.629
175.			rs1982073	Missense variant ,coding sequence variant	Wu 2015[57]	Tumour Biol	China	124/136	TT,TC,CC 39,50,35	TT,TC,CC 38,56,42	>0.5	TT TC CC T vs C	0.8 0.48
176.	TNF- α	6	rs1800629	2KB upstream variant, upstream transcript varia	Zhao 2015[59]	Int J Clin Exp Pathol.	China	80/99	GG,GA,AA 30,34,16	GG,GA,AA 45,48,6	0.14	GA vs GG AA vs GG G vs A	0.9 0.007 0.031
177.					Oliveira 2007[36]	J Pediatr Hematol Oncol.	Brazil	80/160	GG,GA,AA 55,19,6	GG,GA,AA 130,25,5		-	-
178.					Patino-Garcia 2000[60]	J Medical Genetics	Spain	63/111	GG,GA,AA 49,14,0	GG,GA,AA 83,28,0	0.12	-	-
179.			rs361525	2KB upstream variant, upstream transcript variant	Zhao 2015[59]	Int J Clin Exp Pathol.	China	80/99	GG,GA,AA 62,16,2	GG,GA,AA 74,24,1	0.14	GA vs GG AA vs GG G vs A	0.4 0.5 0.03
180.					Patino-Garcia 2000[60]	J Medical Genetics	Spain	63/111	GG,GA,AA 61,2,0	GG,GA,AA 93,18,0	0.4	-	-
181.	TNF- β	6	rs909253	Intron variant	Oliveira 2007[36]	J Pediatr Hematol Oncol.	Brazil	80/160	GG,GA,AA 34,37,9	GG,GA,AA 77,66,17	0.6		
182.	TP53	17	rs17878362	TP53_PIN3_IVS3 + 16 bp (STR)	Hattinger 2016[4]	Oncotarget.	Italy	196/470	WT,HET,VA R 133,49,14	WT,HET,VA R 324,127,19		WT HET VAR	>0.05
183.			rs8079544	Upstream transcript variant, intron variant, genic upstream transcript variant	Savage 2007[61]	Pediatr Blood Cancer	USA	103/73	GG,GA,AA 97,6,0	GG,GA,AA 66,7,0	>0.05	Additive Dominant Recessive	0.35 0.35 no homozygo te variants.

184.			rs1642785	Upstream transcript variant, intron variant, genic upstream transcript variant, 5 prime UTR variant	Savage 2007[61]	Pediatr Blood Cancer	USA	99/68	CC,CG,GG 47,43,9	CC,CG,GG 31,36,1	>0.05	Additive Dominant Recessive	0.95 0.81 0.041
185.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CG,GG 16,64,116	CC,CG,GG 263,169,38		HET + VAR	< 0.0001
186.			rs1042522	Missense variant, upstream transcript variant, genic upstream transcript variant, coding sequence variant	Savage 2007[61]	Pediatr Blood Cancer	USA	98/67	CC,CG,GG 47,41,10	CC,CG,GG 30,36,1	>0.05	Additive Dominant Recessive	0.054 0.069 0.028
187.					Ru 2015[62]	Int J Clin Exp Pathol	china	210/420	CC,CG,GG 59,106,44	CC,CG,GG 162,194,64	0.64	CC CG GG	0.007
188.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CG,GG 139,41,16	CC,CG,GG 277,160,33	>0.05	Wild type	0.005
189.					Toffoli 2009[48]	Clin Cancer Res	Italy	201/250	CC,CG,GG 16,43,142	CC,CG,GG 17,87,146	>0.05	CG vs GG CC vs GG	0.002 1
190.			rs9895829	Upstream transcript variant, intron variant, genic upstream transcript variant	Savage 2007[61]	Pediatr Blood Cancer	USA	101/71	TT,TC,CC 94,7,0	TT,TC,CC 64,7,0	>0.05	Additive Dominant Recessive	0.49 0.49 NH
191.			rs2909430	Upstream transcript variant, intron variant, genic upstream transcript variant	Savage 2007[61]	Pediatr Blood Cancer	USA	95/66	AA,AG,GG 65,27,3	AA,AG,GG 45,21,0	>0.05	Additive Dominant Recessive	0.33 0.97 0.15
192.			rs1800372	Synonymous variant ,coding sequence variant	Savage 2007[61]	Pediatr Blood Cancer	USA	97/65	AA,AG,GG 94,3,0	AA,AG,GG 60,5,0	>0.05	Additive Dominant Recessive	0.19 0.19 NH
193.			rs1625895	Intron variant	Savage 2007[61]	Pediatr Blood Cancer	USA	98/66	AA,AG,GG 66,30,2	AA,AG,GG 43,22,1	>0.05	Additive Dominant Recessive	0.91 0.77 0.81

194.			E3346_28#		Savage 2007[61]	Pediatr Blood Cancer	USA	99/68	GG,GC,CC 97,2,0	GG,GC,CC 63,5,0	>0.05	Additive Dominant Recessive	0.09 0.09 NH
195.			rs12947788	Intron variant	Savage 2007[61]	Pediatr Blood Cancer	USA	102/72	CC,CT,TT 84,16,2	CC,CT,TT 62,10,0	>0.05	Additive Dominant Recessive	0.46 0.51 0.23
196.			rrs1614984	500B downstream variant ,downstream transcript variant	Savage 2007[61]	Pediatr Blood Cancer	USA	98/66	CC,CT,TT 34,53,11	CC,CT,TT 28,29,9	>0.05	Additive Dominant Recessive	0.44 0.32 0.64
197.			rs9894946	-	Savage 2007[61]	Pediatr Blood Cancer	USA	96/66	TT,TC,CC 65,28,3	TT,TC,CC 40,25,1	>0.05	Additive Dominant Recessive	0.44 0.35 0.52
198.			E3355_424#		Savage 2007[61]	Pediatr Blood Cancer	USA	103/72	AA,AG,GG 87,16,0	AA,AG,GG 62,10,,0	>0.05	Additive Dominant Recessive	0.76 0.76 NH
199.			rs12951053	Intron variant	Ru 2015[62]	Int J Clin Exp Pathol	China	210/420	AA,AC,CC 54,103,53	AA,AC,CC 140,198,82	>0.05	AA AC CC	0.03
200.			rs8064946	2KB upstream variant,upstream transcript variant, intron variant, genic upstream transcript variant	Ru 2015[62]	Int J Clin Exp Pathol	China	210/420	GG,GC,CC 68,100,41	GG,GC,CC 135,189,96	>0.05	GG GC CC	0.56
201.			rs12602273	Genic upstream transcript variant, intron variant	Ru 2015[62]	Int J Clin Exp Pathol	China	210/420	CC,CG,GG	CC,CG,GG	>0.05	CC CG GG	0.15
202.	TP53/VMP 1	17	rs1295925	Intron variant	Zhang 2018[63]	Cancer Biol Ther.	China	1300/1300	TT,TC,CC 476,583,241	TT,TC,CC 399,631,241	>0.05	TC vs TT CC vs TT C vs T	0.004 0.009 0.003
203.	TP53/BCA S1	20	rs3787547	Intron variant ,genic upstream transcript ariant	Zhang 2018[63]	Cancer Biol Ther.	China	1300/1300	GG,AG,AA 654,513,133	GG,AG,AA 570,566,163	>0.05	AG vs GG AA vs GG A vs G	0.003 0.006 4.0×10^{-4}
204.	TP53/BCA S1	20	rs290392	2KB upstream variant, upstream transcript variant	Zhang 2018[63]	Cancer Biol Ther.	China	500/500	AA,AG,GG 164,259,77	AA,AG,GG 176,241,83	>0.05	AG vs AA GG vs AA	0.31 0.982

205.	VEGF	6	rs699947	Intron variant, genic downstream transcript variant, 2KB upstream variant, upstream transcript variant	Zhang 2015[64]	Genet Mol Res.	China	182/182	CC,CA,AA 68,79,35	CC,CA,AA 88,71,23	0.16	CA vs CC AA vs CC CA+AA vs CC	0.11 0.03 0.03
206.					Zhao 2015[65]	Pak J Med Sci.	China	176/176	CC,CA,AA 62,78,36	CC,CA,AA 84,71,21	>0.05	CA vs CC AA vs CC CA+AA vs CC	0.09 <0.05 <0.05
207.					Tie 2014[66]	Int J Clin Exp Pathol	China	165/330	CC,CA,AA 64,72,29	CC,CA,AA 159,136,35	0.46	CA vs CC AA vs CC A vs C	0.19 0.001 0.008
208.					Liu 2015[67]	Oncol Lett	China	186/186	CC,CA,AA 79,75,107	CC,CA,AA 87,73,26	>0.05	CA vs CC AA vs CC	0.59 0.32
209.			rs3025039	3 prime UTR variant, intron variant, genic downstream transcript variant	Zhang 2015[64]	Genet Mol Res.	China	182/182	CC,CT,TT 128,35,19	CC,CT,TT 138,32,12	<0.05	CT vs CC TT vs CC CT+TT vs CC	0.55 0.17 0.24
210.					Zhao 2015[65]	Pak J Med Sci.	China	176/176	CC,CT,TT 85,75,16	CC,CT,TT 92,71,13	>0.05	CT vs CC TT vs CC CT+TT vs CC	0.55 0.41 0.46
211.					Wang 2013[68]	Tumour Biol.	China	330/342	CC,CT,TT 185,116,29	CC,CT,TT 207,123,12	>0.05	CT vs CC TT vs CC CT+TT vs CC	0.74 0.005 0.04
212.					Tie 2014[66]	Int J Clin Exp Pathol	China	165/330	CC,CT,TT 111,39,15	CC,CT,TT 232,74,24	< 0.001	CT vs CC TT vs CC CT+TT vs CC	0.67 0.44 0.33
213.					Zhang 2015[69]	Genet Mol Res	China	180/360	CC,CT,TT 66,92,22	CC,CT,TT 148,175,37	0.16	CT vs CC TT vs CC T vs C	0.4 0.35 0.3
214.					Liu 2015[67]	Oncol Lett.	China	186/186	CC,CT,TT 125,46,16	CC,CT,TT 134,42,10	>0.05	CT vs CC TT vs CC	0.52 0.2
215.					Li 2017[70]	Biomedical Research	China	242/253	CC,CT,TT 131,95,16	CC,CT,TT 159,86,8	0.4	CT vs CC TT vs CC CT+TT vs CC C vs T	0.12 0.004 0.04 0.02

216.					Cao 2016[71]	Int J Clin Exp Pathol	China	322/343	CC,CT,TT 188,103,31	CC,CT,TT 213,108,22	0.1	CT vs CC TT vs CC	0.33 0.13
217.					Hu 2015[72]	Genet Mol Res.	China	130/130	CC,CT,TT 67,47,16	CC,CT,TT 79,44,7	0.79	CT vs CC TT vs CC CT+TT vs CC	0.39 0.03 0.13
218.			rs833061	Intron variant ,genic downstream transcript variant,2KBupstream variant ,upstream transcript variant	Zhang 2015[64]	Genet Mol Res.	China	182/182	TT,TC,CC 65,91,26	TT,TC,CC 77,86,24	0.83	TC vs TT CC vs TT CT+TC vs TT	0.49 0.58 0.45
219.					Zhao 2015[65]	Pak J Med Sci.	China	176/176	TT,TC,CC 48,89,39	TT,TC,CC 66,85,25	>0.05	TC vs TT CC vs TT CT+TC vs TT	0.13 <0.05 <0.05
220.			rs1570360	Intron variant ,genic downstream transcript variant,2KBupstream variant ,upstream transcript variant	Zhao 2015[65]	Pak J Med Sci.	China	176/176	AA,AG,GG 93,73,11	AA,AG,GG 97,71,8	>0.05	AG vs AA GG vs AA GG+GA vs AA	0.75 0.46 0.63
221.					Tie 2014[66]	Int J Clin Exp Pathol	China	165/330	AA,AG,GG 90,45,30	AA,AG,GG 203,81,46	< 0.001	AG vs AA GG vs AA	0.32 0.15
222.					Liu 2015[67]	Oncol Lett.	China	186/186	AA,AG,GG 107,53,27	AA,AG,GG 116,49,21	<0.05	AG vs AA GG vs AA	0.51 0.3
223.			rs2010963	5 prime UTR variant,genicupstream transcript variant, upstream transcript variant ,intron variant, genic downstream transcript variant	Zhao 2015[65]	Pak J Med Sci.	China	176/176	CC,CG,GG 61,85,30	CC,CG,GG 67,81,28	>0.05	CG vs CC GG vs CC	0.55 0.61
224.					Wang 2013[68]	Tumour Biol.	China	330/342	CC,CG,GG 50,165,115	CC,CG,GG 58.166,118	0.84	CC vs. GG GC vs. GG CC/GC vs. GG CC vs. GC/GG C vs. G	0.6 0.9 0.9 0.5
225.					Tie 2014[66]	Int J Clin Exp Pathol	China	165/330	CC,CG,GG 42,80,43	CC,CG,GG 120,151,59	0.34	CG vs CC GG vs CC	0.07 0.006
226.					Zhang 2015[64]	Genet Mol Res.	China	182/182	CC,CG,GG 48,90,42	CC,CG,GG 138,170,53	0.95	CG vs CC GG vs CC	0.05 0.002
227.					Liu 2015[67]	Oncol Lett.	China	186/186	CC,CG,GG 50,91,45	CC,CG,GG 69,86,31	>0.05	CG vs CC	0.11 0.02

												GG vs CC	
228.					Cao 2016[71]	Int J Clin Exp Pathol	China	322/343	CC,CG,GG 93,156,73,	CC,CG,GG 123,165,55	0.97	CG vs CC GG vs CC	0.055 0.031
229.					Hu 2015[72]	Genet Mol Res.	China	130/130	CC,CG,GG 20,68,42	CC,CG,GG 18,65,46	0.51	CG vs CC GG vs CC	0.62 0.61
230.			rs10434	3 prime UTR variant ,intron variant, genic downstream transcript variant	Zhao 2015[65]	Pak J Med Sci.	China	176/176	GG,GA,AA 77,80,19	GG,GA,AA 80,78,18	0.87	GA vs GG AA vs GG	0.78 0.8
231.					Wang 2013[68]	Tumour Biol.	China	330/342	GG,GA,AA 95,157,78	GG,GA,AA 97,172,73	0.84	GA vs GG AA vs GG	0.62 0.7
232.					Tie 2014[66]	Int J Clin Exp Pathol	China	165/330	GG,GA,AA 68,76,20	GG,GA,AA 151,146,33	0.79	CT vs CC TT vs Cc	0.48 0.35
233.					Zhang 2015[64]	Genet Mol Res.	China	182/182	GG,GA,AA 77,80,23	GG,GA,AA 163,155,42	0.58	CT vs CC TT vs Cc	0.65 0.62
234.					Liu 2015[67]	Oncol Lett.	China	186/186	GG,GA,AA 75,86,25	GG,GA,AA 84,83,19	0.82	GA vs GG AA vs GG	0.5 -
235.					Hu 2015[72]	Genet Mol Res.	China	130/130	GG,GA,AA 41,61,28	GG,GA,AA 46,60,24	0.58	GA vs GG AA vs GG	0.64 0.44
236.	XRCC1	19	rs25487	Missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 82,86,28	GG,GA,AA 207,211,52	0.9	GG GA AA	>0.05
237.	XRCC3	14	rs861539	Genic downstream transcript variant, missense variant, intron variant, coding sequence variant	Jin 2015[16]	Pak J Med Sci.	China	148/298	CC,CT+TT 77,71	CC,CT+TT 173,125	-	CT vs CC TT vs Cc	0.17
238.					Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 63,100,33	CC,CT,TT 179,207,84		CC CT TT	>0.05
239.					Guo 2015[73]	Genet Mol Res.	China	136/136	CC,CT,TT 54,55,27	CC,CT,TT 70,52,14	0.36	CT vs CC TT vs Cc	0.23 0.01

240.					Yang 2015[74]	Int J Clin Exp Pathol.	China	152/304	CC,CT,TT 66,63,22	CC,CT,TT 166,117,21	0.95	CT vs CC TT vs Cc	0.15 0.003
241.					Goricar 2015[52]	J Med Biochem.	Sloven ia	79/373	CC,CT+TT 39,40	CC,CT+TT 153,220	-	CT vs CC TT vs Cc	0.23
242.			rs1799794	5 prime UTR variant,downstream transcript variant, intron variant, 500B downstream variant	Goricar 2015[52]	J Med Biochem.	Sloven ia	79/373	AA,AG+GG 47,31	AA,AG+GG 247,126	-	AG+GG vs AA	0.31
243.	ABCB1	7	rs1045642	Synonymous variant, missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TC,CC 51,86,59	TT,TC,CC 113,244,113	0.4	TT TC CC	>0.05
244.			rs1128503	Synonymous variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 63,88,45	CC,CT,TT 155,235,80	0.6	CC CT TT	>0.05
245.			rs2032582	missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 57,94,45	GG,GA,AA 132,249,89	0.14	GG GA AA	>0.05
246.	ABCC2	10	rs2273697	Coding sequence variant, missense variant, non-coding transcript variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 98,90,8	GG,GA,AA 296,160,14	0.17	GG GA AA	0.011
247.			rs717620	Genic upstream transcript variant, 5 prime UTR variant, non-coding transcript variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 118,72,6	GG,GA,AA 310,141,19	0.6	GG GA AA	>0.05
248.			rs3740066	Coding sequence variant, synonymous variant, genic downstream transcript variant, missense variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 90,71,35	GG,GA,AA 221,207,42	0.5	GG GA AA	0.030
249.	ABCG2	4	rs2231137	Missense variant, coding sequence nvariant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 165,31,0	GG,GA,AA 414,52,4	0.11	GG GA AA	>0.05

250.			rs2231142	Missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CA,AA 167,25,4	CC,CA,AA 376,89,5	0.9	CC CA AA	>0.05
251.	RFC	21	rs1051266	Genic upstream transcript variant, 5 prime UTR variant, missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 77,88,31	GG,GA,AA 174,230,66	0.5	GG GA AA	>0.05
252.	hMLH1	3	rs1799977	Coding sequence variant missense variant, 5 prime UTR variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	AA,AG,GG 65,106,25	AA,AG,GG 211,193,66	0.05	AA AG GG	0.010
253.	hMSH2	2	rs2303428	Intron variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TC,CC 167,27,2	TT,TC,CC 404,61,5	0.13	TT TC CC	>0.05
254.	hOGG1	3	rs1052133	Genic downstream transcript variant, 500B downstream variant, missense variant, non-coding transcript variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CG,GG 127,57,12	CC,CG,GG 296,155,19	0.8	CC CG GG	>0.05
255.	ERCC5/XPG	13	rs17655	Missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 112,61,23	GG,GA,AA 254,193,23	0.07	GG GA AA	0.002
256.	DHFR	5	rs70991108	Upstream transcript variant, intron variant, 2KB upstream variant (Ins)^	Hattinger 2016[4]	Oncotarget.	Italy	196/470	Ins/Ins, Ins/del,Del/D el 67,98,31	Ins/Ins, Ins/del,Del/D el 165,258,47	<0.0001	Ins/Ins Ins/Del Del/Del	>0.05
257.	FORLI	11	rs3833748	Genic upstream transcript variant, upstream transcript variant, intron variant (DELINS)#	Hattinger 2016[4]	Oncotarget.	Italy	196/470	Ins/Ins, Ins/del,Del/D el 188,8,0	Ins/Ins, Ins/del,Del/D el 456,14,0	0.7	Ins/Ins Ins/Del Del/Del	>0.05

258.	GGH	8	rs11545078	Coding sequence variant, missense variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 161,29,6	CC,CT,TT 371,94,5	0.7	CC CT TT	>0.05
259.			rs3758149	2KB upstream variant, upstream transcript variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 104,61,31	CC,CT,TT 244,188,38	0.042	CC CT TT	0.042
260.			rs1800909	missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TC,CC 124,43,29	TT,TC,CC 268,164,38	0.07	TT TC CC	0.011
261.	MTHFD1	14	rs2236225	missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 53,104,39	CC,CT,TT 132,235,103	0.9	CC CT TT	>0.05
262.	MTHFR	1	rs1801133	Non-coding transcript variant, missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 59,96,41	CC,CT,TT 150,259,61	<0.001	CC CT TT	>0.05
263.			rs1801131	Non-coding transcript variant, missense variant, coding sequence variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	AA,AC,CC 92,86,18	AA,AC,CC 193,221,56	0.6	AA AC CC	>0.05
264.	SHMT	17	rs2273029	Intron variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 102,74,20	CC,CT,TT 273,160,37	0.05	CC CT TT	>0.05
265.	TYMS	18	rs34743033	Genic upstream transcript variant, intron variant, 5 prime UTR variant STR (3 repeats)	Hattinger 2016[4]	Oncotarget.	Italy	196/470	WT,HET,VA R 86,77,33	WT,HET,VA R 150,212,108	0.05	WT HET VAR	0.012
266.			rs16430	6 bp deletion in micro-RNA binding site(DELINS)	Hattinger 2016[4]	Oncotarget.	Italy	196/470	WT,HET,VA R 59,106,31	WT,HET,VA R 174,221,75	0.7	WT HET VAR	>0.05
267.	ATM	11	rs1800054	5 prime UTR variant, non-coding transcript variant, coding	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CG,GG 192,4,0	CC,CG,GG 451,19,0	0.7	CC CG GG	>0.05

				sequennce variant, missense variant									
268.		11	rs1801516	non-coding transcript variant,coding sequennce variant, missense variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 141,49,6	GG,GA,AA 362,103,5	0.4	GG GA AA	>0.05
269.	CDKN1A/P 21	6	rs1801270	coding sequennce variant, missense variant,geneic downstream transcript variant, synonymous variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	TT,TG,GG 165,29,2	TT,TG,GG 400,66,4	0.5	TT TG GG	>0.05
270.	CYP2C19	10	rs4244285	Coding sequence variant, synonymous	Hattinger 2016[4]	Oncotarget.	Italy	196/470	GG,GA,AA 145,45,6	GG,GA,AA 343,118,9	0.8	GG GA AA	>0.05
271.	CYP2B6*6		rs3745274 and rs2279343	haplotype	Hattinger 2016[4]	Oncotarget.	Italy	196/470	WT,HET,VA R 129,53,14	WT,HET,VA R 273,178,19		WT HET VAR	0.03
272.	CYP2B6*7		rs3745274 and rs2279343 and rs3211371	Haplotype	Hattinger 2016[4]	Oncotarget.	Italy	196/470	WT,HET,VA R 194,2,0	WT,HET,VA R 451,19,0		WT HET VAR	0.032
273.	CYP2C9		rs1799853	Coding sequence variant ,missense variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	CC,CT,TT 147,45,4	CC,CT,TT 338,122,10	0.8	CC CT TT	>0.05
274.			rs1057910	Coding sequence variant ,missense variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	AA,AC,CC 169,23,3	AA,AC,CC 385,80,5	0.9	AA AC CC	>0.05
275.	CYP3A4	10	rs2740574	2KB upstream variant, upstream transcript variant	Hattinger 2016[4]	Oncotarget.	Italy	196/470	AA,AG,GG 178,18,0	AA,AG,GG 446,24,0	0.6	AA AG GG	>0.05
276.	COL18A1	21	c.4309G> A (p.D104N)		Bi 2016[11]	Sci.reeports	China	236/418	WT,HET,VA R 205,23,8	WT,HET,VA R 376,39,3		WT HET VAR	>0.05

277.	RAD51	15	rs1801320	2KB upstream variant,5 prime UTR variant,genic upstream transcript variant,intron variant, upstream transcript	Jin 2015[16]	Pak J Med Sci	China	148/296	GG,GC+CC 101,47	GG,GC+CC 213,85	-	GC+CC vs GG	0.48
278.					Goricar 2015[52]	J Med Biochem.	Slovenia	79/373	GG,GC+CC 69,9	GG,GC+CC 304,69	-	GC+CC vs GG	0.337
279.			rs1801321	2KB upstream variant,5 prime UTR variant,genic upstream transcript variant, intron variant, upstream transcript	Jin 2015[16]	Pak J Med Sci	China	148/296	GG,GT+TT 88,60	GG,GT+TT 187,111		GT+TT vs GG	0.5
280.					Goricar 2015[52]	J Med Biochem.	Slovenia	79/373	GG,GT+TT 25,54	GG,GT+TT 133,240		GT+TT vs GG	0.802
281.			rs12593359	3 prime UTR variant, downstream transcript variant, genic downstream transcript variant	Jin 2015[16]	Pak J Med Sci	China	148/296	TT,TG+GG 49,99	TT,TG+GG 105,193		TG+GG vs TT	0.66
282.					Goricar 2015[52]	J Med Biochem.	Slovenia	79/373	TT,TG+GG 22,57	TT,TG+GG 103,270		TG+GG vs TT	0.702
283.	Fas	10	-1377 G>A		Koshkina 2007[75]	J Pediatr Hematol Oncol.	USA	123/510	GG,GA,AA 99,22,2	GG,GA,AA 400,100,10	0.2	GG GA AA	0.88
284.			rs1800682	Genic upstream transcript variant, upstream transcript variant,intron variant	Koshkina 2007[75]	J Pediatr Hematol Oncol.	USA	123/510	AA,AG,GG 31,21,31	AA,AG,GG 145,251,114	0.8	AA AG GG	0.7
285.			exon 3 18272 A>G		Koshkina 2007[75]	J Pediatr Hematol Oncol.	USA	123/510	AA,AG,GG 99,24,0	AA,AG,GG 449,61,0	0.2	AA AG GG	0.028
286.			exon 7 22628 C>T		Koshkina 2007[75]	J Pediatr Hematol Oncol.	USA	123/510	CC,CTC,TT 67,51,5	CC,CT,TT 288,199,31	0.6	CC CT TT	0.66

*p<0.0167 was considered significant after Bonferroni correction, ^ Ins=Insertion, # DELINS=Deletion/Insertion, WT=wild type, HET=heterozygous, VAR=variant,STR=Short tandem repeats (microsatellite) variation

NH=No homoyzous, SD=Standard Deviation

#Assay identifier from <http://snp500cancer.nci.nih.gov>

Table S4: Genetic variants not associated with osteosarcoma

SNV	chr	Model	OR (95% CI) P-value	I ² %	Q-value	Heterogeneity P-value	Cases vs Controls	#Studies in Asian	Asian OR (95% CI)	#Studies Caucasian	Caucasian OR (95% CI)
APEX1 rs1130409	14	TG vs TT	1.06 [0.18; 6.2] 0.74	9	1.1	0.29	574 vs 1086 (2)	1[3]	0.96 [0.72; 1.28]	1[4]	1.29 [0.81; 2.07]
		GG vs TT	1.05 [0.05; 24.22] 0.87	59	2.46	0.12	574 vs 1086 (2)	1[3]	0.85 [0.58; 1.23]	1[4]	1.39 [0.85; 2.29]
		TG+GG vs TT	1.06 [0.12; 9.75] 0.79	46	1.84	0.17	574 vs 1086 (2)	1[3]	0.93 [0.71; 1.21]	1[4]	1.33 [0.85; 2.08]
		GG vs TT+TG	1.06 [0.12; 9.75] 0.79	25	1.34	0.25	574 vs 1086 (2)	1[3]	0.87 [0.62; 1.21]	1[4]	1.15 [0.81; 1.64]
		G vs T	1.02 [0.24; 4.32] 0.88	55	2.21	0.14	574 vs 1086 (2)	1[3]	0.92 [0.77; 1.11]	1[4]	1.16 [0.91; 1.47]
VEGF rs833061	6	TC vs TT	1.29 [0.35; 4.76] 0.24	0	0.38	0.53	354 vs 358 (2)	2[64, 65]	1.29 [0.35; 4.76]	0	
		CC vs TT	1.61 [0.04; 65.6] 0.34	37	1.39	0.24	354 vs 358 (2)	2[64, 65]	1.61 [0.04; 65.6]	0	
		CC+TC vs TT	1.36 [0.2; 9.42] 0.29	0	0.84	0.36	354 vs 358 (2)	2[64, 65]	1.36 [0.2; 9.42]	0	
		CC vs TT+TC	1.39 [0.08; 24] 0.38	0	0.17	0.27	354 vs 358 (2)	2[64, 65]	1.39 [0.08; 24]	0	
		C vs T	1.27 [0.23; 6.94] 0.3253	35	1.53	0.23	354 vs 358 (2)	2[64, 65]	1.27 [0.23; 6.94]	0	
ERCC1 rs11615	19	TC vs TT	0.92 [0.60; 1.39] 0.56	0	2.65	0.45	735 vs 1582 (4)	1[17]	0.72 [0.44; 1.18]	3[4, 18, 19]	1.01 [0.55; 1.87]
		CC vs TT	0.94 [0.46; 1.95] 0.82	57.7	7.09	0.07	735 vs 1582 (4)	1[17]	0.60 [0.37; 1.0]	3[4, 18, 19]	1.24 [0.67; 2.29]
		TC+CC vs TT	0.97 [0.70; 1.3] 0.80	14.8	4.7	0.32	883 vs 1878 (5)	2[16, 17]	0.90 [0.66; 1.22]	3[4, 18, 19]	1.05 [0.80 1.38]
		TT vs CC+TC	0.99 [0.64; 1.52] 0.92	46.7	5.62	0.13	735 vs 1582 (4)	1[17]	0.78 [0.61; 1.0]	3[4, 18, 19]	1.18 [0.74; 1.9]
		C vs T	0.96 [0.70; 1.30] 0.69	52.4	6.3	0.1	735 vs 1582 (4)	1[17]	0.79 [0.65; 1.0]	3[4, 18, 19]	1.08 [0.81; 1.44]
ERCC2 rs13181	19	TG vs TT	1.02 [0.24; 4.33] 0.89	0	0.57	0.45	365 vs 849 (3)	1[20]	1.18 [0.72; 1.94]	2[4,19]	0.93 [0.65; 1.34]
		GG vs TT	1.07 [0.71; 1.62] 0.74	22.4	1.29	0.26	337 vs 772 (2)	1[20]	1.55 [0.73; 3.29]	1[4]	0.92[0.56; 1.51]
		TG+GG vs TT	1.04 [0.76; 1.43] 0.69	0	2.33	0.51	513 vs 1145(4)	2[20,16]	1.19 [0.89; 1.61]	2[4, 19]	0.89 [0.65; 1.23]
		GG vs TT+TG	1.11 [0.08; 16.16] 0.72	0.6	1.01	0.32	337 vs 772 (2)	1[20]	1.49 [0.71; 3.13]	1[4]	0.95 [0.60; 1.51]
		G vs T	1.02 [0.5; 2.02] 0.92	47.6	1.91	0.17	365 vs 849 (3)	1[20]	1.29 [0.90; 1.86]	2[4,19]	0.95 [0.75; 1.21]
ERCC3 rs4150441	19	GA vs GG	1.31 [0.12; 14.56] 0.40	60	2.48	0.122	522 vs 1047(2)	2[17, 20]	1.31 [0.12; 14.56]	0	
		AA vs GG	2.12 [0.016; 85.55] 0.30	71	3.45	0.06	522 vs 1047(2)	2[17, 20]	2.12 [0.016; 85.55]	0	
		GA+AA vs GG	1.54 [0.07; 31.6] 0.32	74	3.81	0.051	522 vs 1047(2)	2[17, 20]	1.54 [0.07; 31.6]	0	
		AA vs GG+GA	1.85 [0.03; 97.96] 0.30	60	2.51	0.11	522 vs 1047(2)	2[17, 20]	1.85 [0.03; 97.96]	0	
		G vs A	1.46 [0.09; 22.1] 0.33	82	5.48	0.019	522 vs 1047(2)	2[17, 20]	1.46 [0.09; 22.1]	0	
GRM4 rs1906953	6	TC vs TT	1.04 [0.69; 1.82] 0.2	0	0.06	0.81	294 vs 384 (2)	2[21, 22]	1.04 [0.69; 1.82]	0	
		CC vs TT	0.85 [0.60; 1.20] 0.4	99	9.03	0.0027	294 vs 384 (2)	2[21, 22]	0.85 [0.60; 1.20]	0	
		CC+TC vs TT	0.99 [0.70; 1.40] 0.9	91	11.14	0.0008	294 vs 384 (2)	2[21, 22]	0.99 [0.70; 1.40]	0	
		CC vs TT+TC	0.98 [0.02; 2.22] 0.9	66	14.7	0.001	294 vs 384 (2)	2[21, 22]	0.98 [0.02; 2.22]	0	
		C vs T	0.94 [0.75; 1.16] 0.5	94	15.71	0.0001	294 vs 384 (2)	2[21, 22]	0.94 [0.75; 1.16]	0	
MDM2 rs1690916	12	GA vs GG	0.91 [0.28; 2.40] 0.81	67	9.02	0.03	246 vs 1718(4)	0		4[45–47]	0.91 [0.28; 2.40]
		AA vs GG	0.8 [0.12; 5.13] 0.72	75	11.9	0.007	246 vs 1718(4)	0		4[45–47]	0.8 [0.12; 5.13]
		GA +AA vs GG	0.70 [0.18; 2.79] 0.47	62	7.82	0.051	246 vs 1718(4)	0		4[45–47]	0.70 [0.18; 2.79]
		GG+GA vs AA	0.72[0.25; 2.10] 0.40	50	5.9	0.11	246 vs 1718(4)	0		4[45–47]	0.72[0.25; 2.10]
		A vs G	0.77 [0.34; 1.78] 0.40	70	10.11	0.018	246 vs 1718(4)	0		4[45–47]	0.77 [0.34; 1.78]

MDM2 rs2279744	12	GT vs TT	1.20 [0.90; 1.62] 0.15	0	3.5	0.50	440 vs 1919 (5)	0		5[4, 45, 47, 48]	1.20 [0.90; 1.62]
		GG vs TT	1.57[0.62; 4.0] 0.25	68.4	12.7	0.01	619 vs 2352 (5)	0		5[4, 45, 47, 48]	1.57[0.62; 4.0]
		GT +GG vs TT	1.0[0.39; 2.55] 0.99	87.2	31.27	< 0.0001	619 vs 2352 (5)	0		5[4, 45, 47, 48]	1[0.39; 2.55]
		GG vs TT+GT	1.21 [0.42; 3.52] 0.64	74.8	36.72	< 0.0001	619 vs 2352 (5)	0		5[4, 45, 47, 48]	1.21 [0.42; 3.52]
		G vs T	1.057[0.53; 2.10] 0.83	89	36.27	< 0.0001	619 vs 2352 (5)	0		5[4, 45, 47, 48]	1.057[0.53; 2.10]
GSTM1 gen_null	1	Null vs. Present	1.10[0.62; 1.96] 0.7	40.1	10.2	0.12	654 vs 1573 (7)	3[25–27]	1.42 [0.84; 2.40]	4[4, 23, 24, 28]	0.80 [0.22; 2.95]
GSTM3 rs138440339	1	TC vs TT	1.13[0.58; 2.19] 0.7	44	1.8	0.18	63 vs 360 (2)	0		2[23, 28]	1.13[0.58; 2.19]
		CC vs TT	1.01 [0.06; 16.55] 0.96	0	0.03	0.87	63 vs 360 (2)	0		2[23, 28]	1.01 [0.06; 16.55]
		TC+CC vs TT	1.11[0.58; 2.14] 0.75	35	1.53	0.22	63 vs 360 (2)	0		2[23, 28]	1.11[0.58; 2.14]
		CC vs TT+TC	0.97[0.08; 11.33] 0.98	0	0.07	0.80	63 vs 360 (2)	0		2[23, 28]	0.97[0.08; 11.33]
		C vs T	1.007 [0.13; 7.57] 0.97	0	0.3	0.59	63 vs 360 (2)	0		2[23, 28]	1.007 [0.13; 7.57]
GSTT1 gen_null	22	Null vs present	1.16 [0.83; 1.62] 0.32	27.1	6.68	0.23	602 vs 1468 (6)	2[25]	1.38 [0.05; 36.06]	4[4, 23, 24, 28]	0.99 [0.64; 1.53]
PRKCG rs8103851	19	CG vs CC	0.97[0.69; 1.40] 0.48	0	0.07	0.79	998 vs 998 (2)	2[53, 54]	0.97[0.69; 1.40]	0	
		GG vs CC	0.90 [0.09; 9.06] 0.66	51	2.06	0.15	998 vs 998 (2)	2[53, 54]	0.90 [0.09; 9.06]	0	
		CG+GG vs CC	0.94 [0.37; 2.42] 0.58	0	0.62	0.43	998 vs 998 (2)	2[53, 54]	0.94 [0.37; 2.42]	0	
		GG v s CC+CG	0.91[0.11; 7.52] 0.68	54	2.19	0.14	998 vs 998 (2)	2[53, 54]	0.91[0.11; 7.52]	0	
		G vs C	0.95 [0.30; 2.96] 0.66	41	1.9	0.17	998 vs 998 (2)	2[53, 54]	0.95 [0.30; 2.96]	0	
TGF-β1 rs1800470	19	TC vs TT	0.98 [0.68; 1.4] 0.90	85	6.81	0.009	326vs 352 (2)	2[57,58]	0.98 [0.68; 1.4]	0	
		CC vs TT	1.16 [0.77; 1.75] 0.47	92.2	13	0.0003	326vs 352 (2)	2[57,58]	1.16 [0.77; 1.75]	0	
		TC+CC vs TT	1.02 [0.73; 1.42] 0.91	91.2	11.31	0.0008	326vs 352 (2)	2[57,58]	1.02 [0.73; 1.42]	0	
		CC vs TT+TC	1.20 [0.84; 1.70] 0.31	85.5	6.9	0.0085	326vs 352 (2)	2[57,58]	1.20 [0.84; 1.70]	0	
		C vs T	1.10 [0.87; 1.33] 0.49	93	14.32	0.0002	326vs 352 (2)	2[57,58]	1.10 [0.87; 1.33]	0	
TGF-β1 rs1800469	19	CT vs CC	0.86 [0.03; 30.30] 0.69	54	2.19	0.14	326 vs 352 (2)	2[57,58]	0.86 [0.03; 30.30]	0	
		TT vs CC	1.03 [0.2; 5.43] 0.88	0	0.36	0.55	326 vs 352 (2)	2[57,58]	1.03 [0.20; 5.43]	0	
		CT+TT vs CC	0.94 [0.06; 13.73] 0.80	32	1.48	0.22	326 vs 352 (2)	2[57,58]	0.94 [0.06; 13.73]	0	
		TT vs CT+CC	1.13 [0.65; 1.98] 0.22	0	0.06	0.81	326 vs 352 (2)	2[57,58]	1.13 [0.65; 1.98]	0	
		T vs C	1.02 [0.48; 2.18] 0.80	0	0.3	0.60	326 vs 352 (2)	2[57,58]	1.02 [0.48; 2.18]	0	
TP53 rs1642785	17	CG vs CC	2.24 [0; 124.85] 0.58	95.6	22.57	< 0.0001	295 vs 538 (2)	0		2[61,4]	2.24 [0; 124.85]
		GG vs CC	22.07 [0; 110.80] 0.21	72	3.57	0.06	295 vs 538 (2)	0		2[61,4]	22.07 [0; 110.80]
		CG+ GG vs CC	14.72 [0.48; 452.29] 0.06	0	0.95	0.42	295 vs 538 (2)	0		2[61,4]	14.72 [0.48; 452.29]
		GG vs CC+CG	3.66[0; 129.08] 0.52	97.6	42.41	< 0.0001	295 vs 538 (2)	0		2[61,4]	3.66[0; 129.08]
		G vs C	3.18 [0; 116.50] 0.46	98	51.2	< 0.0001	295 vs 538 (2)	0		2[61,4]	3.18 [0; 116.50]
NBN rs1805794	8	GC vs GG	NA								
		GG vs GG	NA								
		GC+CC vs GG	1.15[0.80; 1.64] 0.50	73	3.76	0.04	227 vs 671 (2)	1[16]	1.37 [0.91; 2.06]	1[52]	0.60 [0.29; 1.25]

RAD51 rs1801320	15	CC vs GG+GC	NA									
		G vs C	NA									
		GC vs GG	NA									
		GG vs GG	NA									
		GC+CC vs GG	0.87 [0.01; 7.9] 0.76	64	2.75	0.097	227 vs 671 (2)	1[16]	1.17 [0.76; 1.79]	1[52]	0.57 [0.27; 1.19]	
		CC vs GG+GC	NA									
RAD51 rs1801321	15	G vs C	NA									
		GT vs GG	NA									
		TT vs GG	NA									
		GT+TT vs GG	0.17 [0.9; 1.5] 0.08	0	0.02	0.90	227 vs 671 (2)	1[16]	1.15 [0.77; 1.72]	1[52]	1.20 [0.71; 2.01]	
		TT vs GG+GT	NA									
		G vs T	NA									
RAD51 rs12593359	15	TG vs TT	NA									
		GG vs TT	NA									
		TG+GG vs TT	1.06 [0.55; 2.03] 0.45	0	0.09	0.76	227 vs 671 (2)	1[16]	1.10 [0.72; 1.67]	1[52]	0.99 [0.58; 1.70]	
		GG vs TT+TG	NA									
		G vs T	NA									

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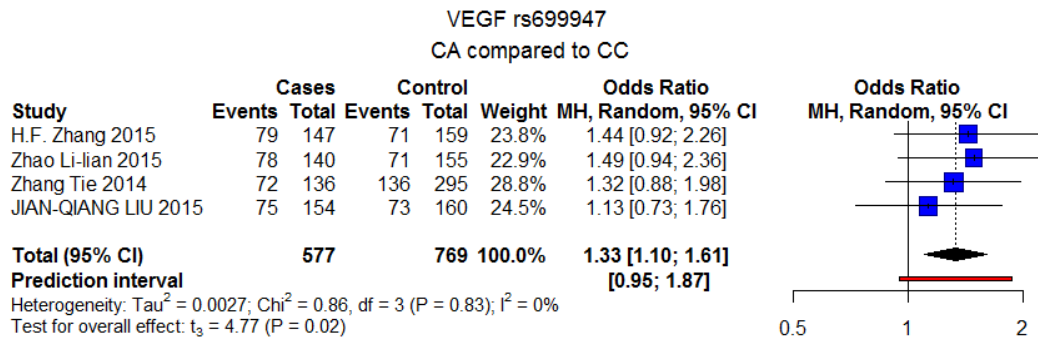
Supplementary Figures

Supplementary Figure 1:

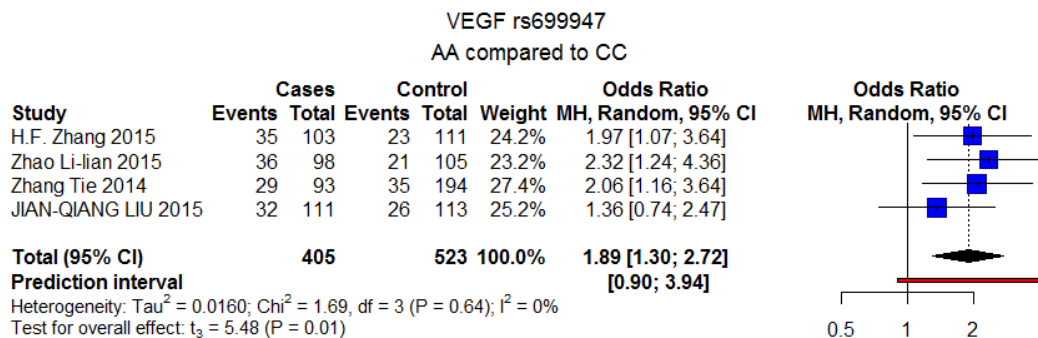
Graphical display of random-effects meta-analyses results

VEGF rs699947

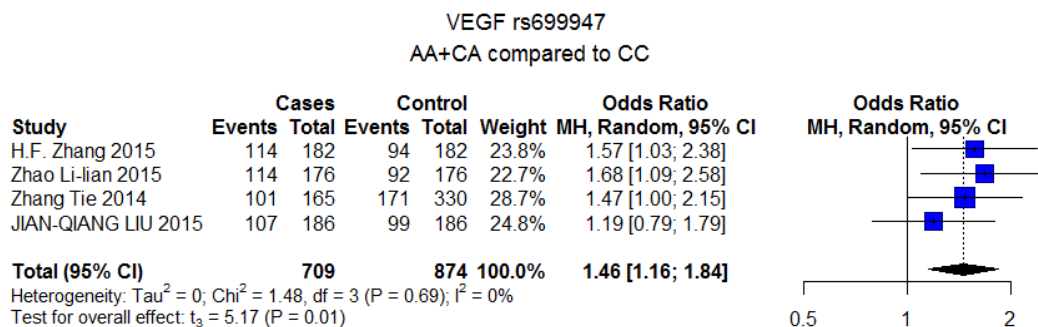
1)



2)



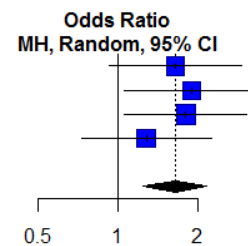
3)



4)

VEGF rs2279744 AA compared to CA+CC

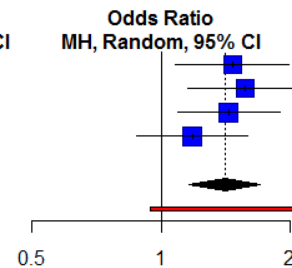
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
H.F. Zhang 2015	35	182	23	182	24.2%	1.65 [0.93; 2.92]
Zhao Li-lian 2015	36	176	21	176	23.2%	1.90 [1.06; 3.41]
Zhang Tie 2014	29	165	35	330	27.6%	1.80 [1.06; 3.06]
JIAN-QIANG LIU 2015	32	186	26	186	24.9%	1.28 [0.73; 2.24]
Total (95% CI)		709		874	100.0%	1.64 [1.24; 2.16]
Heterogeneity: $\tau^2 = 0.0066$; $\chi^2 = 1.10$, $df = 3$ ($P = 0.78$); $I^2 = 0\%$						
Test for overall effect: $t_3 = 5.66$ ($P = 0.01$)						



5)

VEGF rs699947 C compared to A

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
H.F. Zhang 2015	149	364	117	364	24.0%	1.46 [1.08; 1.98]
Zhao Li-lian 2015	150	352	113	352	23.5%	1.57 [1.15; 2.14]
Zhang Tie 2014	130	330	206	660	28.1%	1.43 [1.09; 1.89]
JIAN-QIANG LIU 2015	139	372	125	372	24.4%	1.18 [0.87; 1.59]
Total (95% CI)		1418		1748	100.0%	1.40 [1.16; 1.70]
Prediction interval						[0.94; 2.09]
Heterogeneity: $\tau^2 = 0.0049$; $\chi^2 = 1.90$, $df = 3$ ($P = 0.59$); $I^2 = 0\%$						
Test for overall effect: $t_3 = 5.61$ ($P = 0.01$)						

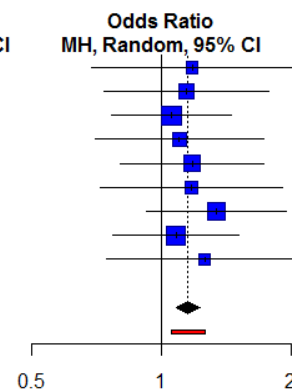


VEGF rs3025039

1)

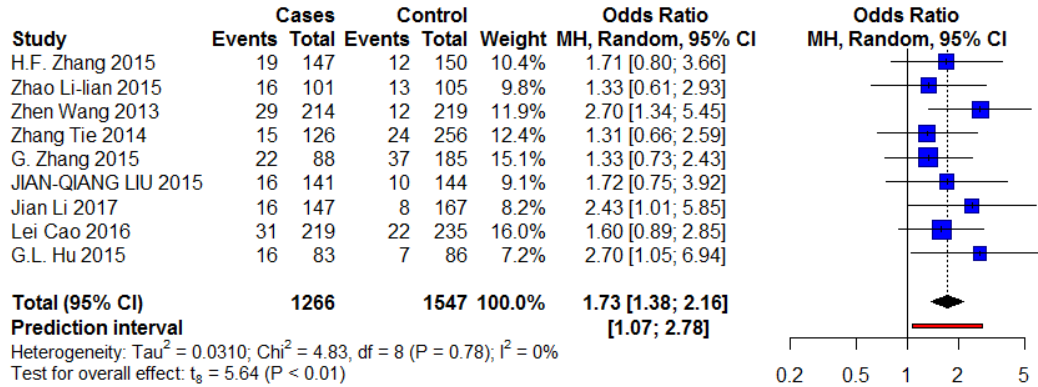
VEGF rs3025039 CT compared to CC

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
H.F. Zhang 2015	35	163	32	170	6.5%	1.18 [0.69; 2.02]
Zhao Li-lian 2015	75	160	71	163	9.6%	1.14 [0.74; 1.77]
Zhen Wang 2013	116	301	123	330	17.7%	1.06 [0.76; 1.46]
Zhang Tie 2014	39	150	74	306	9.2%	1.10 [0.70; 1.73]
G. Zhang 2015	92	158	175	323	12.5%	1.18 [0.80; 1.73]
JIAN-QIANG LIU 2015	46	171	42	176	7.9%	1.17 [0.72; 1.91]
Jian Li 2017	95	226	86	245	13.3%	1.34 [0.92; 1.95]
Lei Cao 2016	103	291	108	321	16.5%	1.08 [0.77; 1.51]
G.L. Hu 2015	47	114	44	123	6.8%	1.26 [0.75; 2.13]
Total (95% CI)		1734		2157	100.0%	1.15 [1.08; 1.23]
Prediction interval						[1.05; 1.26]
Heterogeneity: $\tau^2 = 0.0007$; $\chi^2 = 1.24$, $df = 8$ ($P = 1.00$); $I^2 = 0\%$						
Test for overall effect: $t_8 = 5.23$ ($P < 0.01$)						



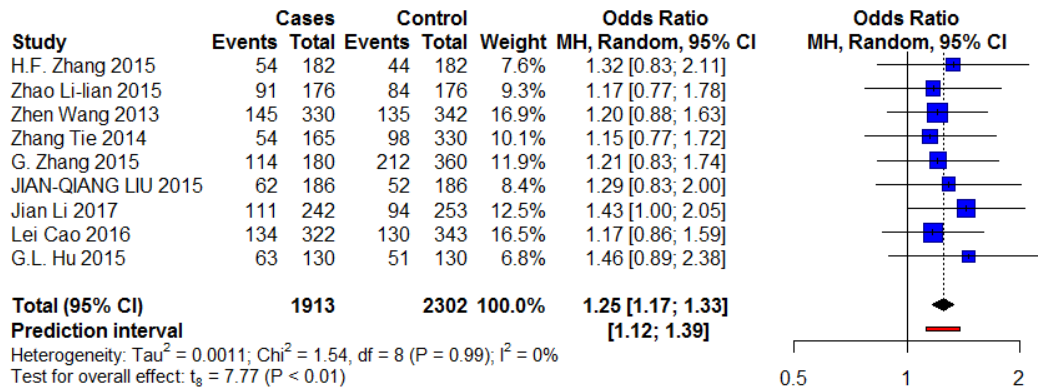
2)

VEGF rs3025039 TT compared to CC

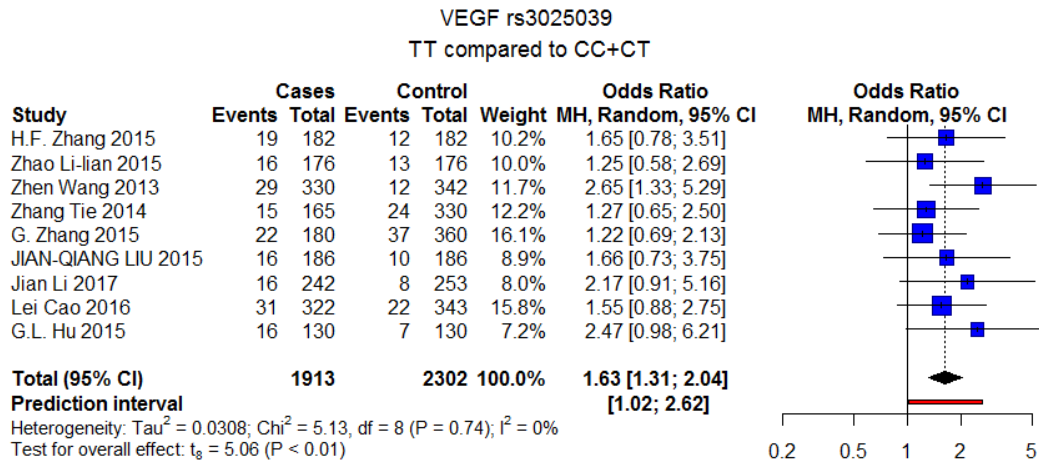


3)

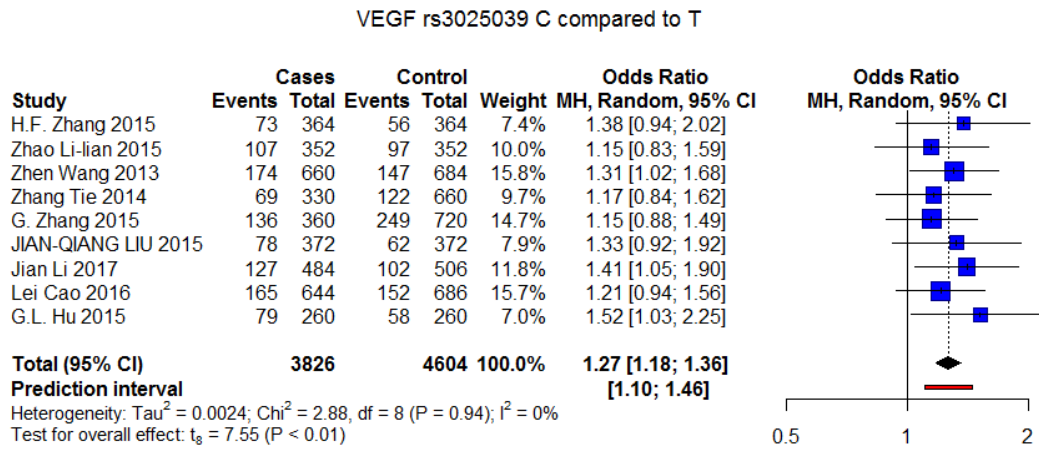
VEGF rs3025039 TT+CT compared to CC



4)



5)



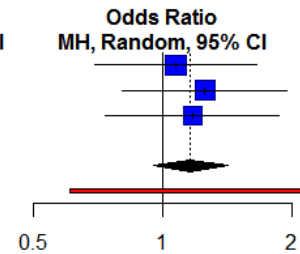
1)

VEGF rs1570360 AG compared to AA

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	73	166	71	168	35.5%	1.07 [0.70; 1.65]
Zhang Tie 2014	45	135	81	284	34.2%	1.25 [0.81; 1.95]
JIAN-QIANG LIU 2015	53	160	49	165	30.3%	1.17 [0.73; 1.87]

Total (95% CI) 461 617 100.0% **1.16 [0.95; 1.42]**
Prediction interval [0.61; 2.22]

Heterogeneity: $\tau^2 = 0.0005$; $\chi^2 = 0.25$, $df = 2$ ($P = 0.88$); $I^2 = 0\%$
 Test for overall effect: $t_2 = 3.26$ ($P = 0.08$)



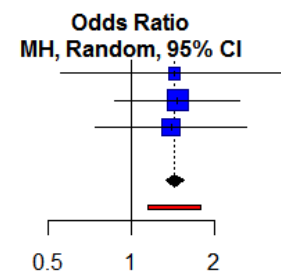
2)

VEGF rs1570360 GG compared to AA

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	11	104	8	105	15.1%	1.43 [0.55; 3.72]
Zhang Tie 2014	30	120	46	249	50.2%	1.47 [0.87; 2.48]
JIAN-QIANG LIU 2015	27	134	21	137	34.8%	1.39 [0.74; 2.61]

Total (95% CI) 358 491 100.0% **1.44 [1.34; 1.55]**
Prediction interval [1.15; 1.79]

Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.02$, $df = 2$ ($P = 0.99$); $I^2 = 0\%$
 Test for overall effect: $t_2 = 21.02$ ($P < 0.01$)



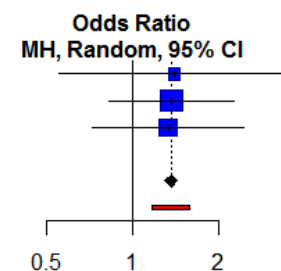
3)

VEGF rs1570360 GG compared to AA+AG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	11	176	8	176	14.7%	1.40 [0.55; 3.57]
Zhang Tie 2014	30	165	46	330	50.8%	1.37 [0.83; 2.27]
JIAN-QIANG LIU 2015	27	186	21	186	34.5%	1.33 [0.72; 2.46]

Total (95% CI) 527 692 100.0% **1.36 [1.29; 1.43]**
Prediction interval [1.17; 1.59]

Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.01$, $df = 2$ ($P = 1.00$); $I^2 = 0\%$
 Test for overall effect: $t_2 = 25.96$ ($P < 0.01$)

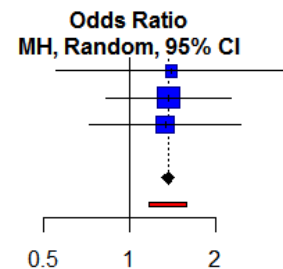


4)

VEGF rs1570360 GG compared to AA+AG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	11	176	8	176	14.7%	1.40 [0.55; 3.57]
Zhang Tie 2014	30	165	46	330	50.8%	1.37 [0.83; 2.27]
JIAN-QIANG LIU 2015	27	186	21	186	34.5%	1.33 [0.72; 2.46]
Total (95% CI)		527		692	100.0%	1.36 [1.29; 1.43]
Prediction interval						[1.17; 1.59]

Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.01$, $df = 2$ ($P = 1.00$); $I^2 = 0\%$
 Test for overall effect: $t_2 = 25.96$ ($P < 0.01$)

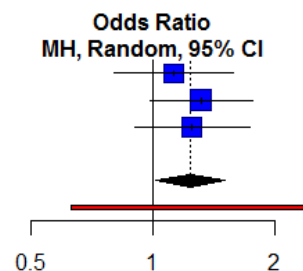


5)

VEGF_rs1570360 G compared to A

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	95	352	87	352	29.2%	1.13 [0.80; 1.58]
Zhang Tie 2014	105	330	173	660	39.4%	1.31 [0.98; 1.75]
JIAN-QIANG LIU 2015	107	372	91	372	31.3%	1.25 [0.90; 1.73]
Total (95% CI)		1054		1384	100.0%	1.24 [1.02; 1.50]
Prediction interval						[0.63; 2.43]

Heterogeneity: $\tau^2 = 0.0008$; $\chi^2 = 0.47$, $df = 2$ ($P = 0.79$); $I^2 = 0\%$
 Test for overall effect: $t_2 = 4.71$ ($P = 0.04$)



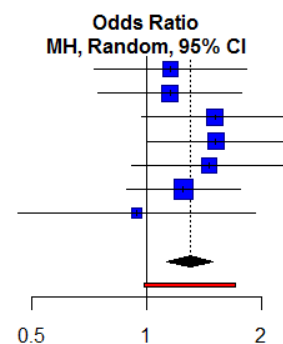
VEGF rs2010963

1)

VEGF rs2010963 CG compared to CC

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	85	146	81	148	13.5%	1.15 [0.73; 1.83]
Zhang Tie 2014	165	215	166	224	15.0%	1.15 [0.75; 1.78]
G. Zhang 2015	80	122	151	271	14.5%	1.51 [0.97; 2.36]
JIAN-QIANG LIU 2015	90	138	170	308	16.1%	1.52 [1.00; 2.31]
Lei Cao 2016	91	141	86	155	13.2%	1.46 [0.91; 2.33]
G.L. Hu 2015	156	249	165	288	21.7%	1.25 [0.88; 1.77]
Zhen Wang 2013	68	88	65	83	6.0%	0.94 [0.46; 1.94]
Total (95% CI)		1099		1477	100.0%	1.30 [1.13; 1.50]
Prediction interval						[0.99; 1.72]

Heterogeneity: $\tau^2 = 0.0083$; $\chi^2 = 2.61$, $df = 6$ ($P = 0.86$); $I^2 = 0\%$
 Test for overall effect: $t_6 = 4.58$ ($P < 0.01$)



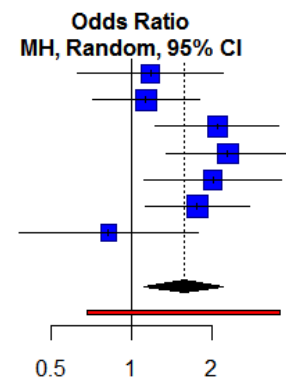
2)

VEGF rs2010963 GG compared to CC

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	30	91	28	95	12.6%	1.18 [0.63; 2.19]
Zhang Tie 2014	115	165	118	176	16.8%	1.13 [0.72; 1.79]
G. Zhang 2015	43	85	59	179	14.9%	2.08 [1.23; 3.53]
JIAN-QIANG LIU 2015	42	90	53	191	15.0%	2.28 [1.35; 3.84]
Lei Cao 2016	45	95	31	100	13.4%	2.00 [1.12; 3.59]
G.L. Hu 2015	73	166	55	178	17.3%	1.76 [1.13; 2.73]
Zhen Wang 2013	42	62	46	64	9.9%	0.82 [0.38; 1.76]

Total (95% CI) **754** **983** **100.0%** **1.56 [1.12; 2.18]**
Prediction interval **[0.69; 3.54]**

Heterogeneity: $\tau^2 = 0.0828$; $\chi^2 = 9.55$, $df = 6$ ($P = 0.14$); $I^2 = 37\%$
 Test for overall effect: $t_0 = 3.25$ ($P = 0.02$)



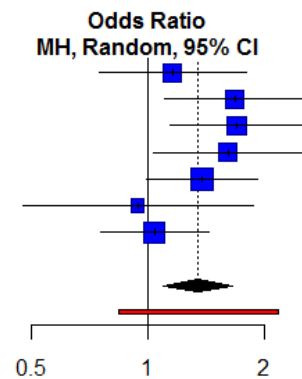
3)

VEGF rs2010963 GG+CG compared to CC

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	115	176	109	176	13.3%	1.16 [0.75; 1.79]
Zhang Tie 2014	123	165	210	330	14.1%	1.67 [1.10; 2.54]
G. Zhang 2015	132	180	223	360	15.1%	1.69 [1.14; 2.50]
JIAN-QIANG LIU 2015	136	186	117	186	13.1%	1.60 [1.03; 2.49]
Lei Cao 2016	229	322	220	343	18.6%	1.38 [0.99; 1.91]
G.L. Hu 2015	110	130	111	130	6.9%	0.94 [0.48; 1.86]
Zhen Wang 2013	110	330	111	342	18.9%	1.04 [0.75; 1.44]

Total (95% CI) **1489** **1867** **100.0%** **1.35 [1.09; 1.65]**
Prediction interval **[0.84; 2.16]**

Heterogeneity: $\tau^2 = 0.0266$; $\chi^2 = 6.93$, $df = 6$ ($P = 0.33$); $I^2 = 13\%$
 Test for overall effect: $t_0 = 3.51$ ($P = 0.01$)



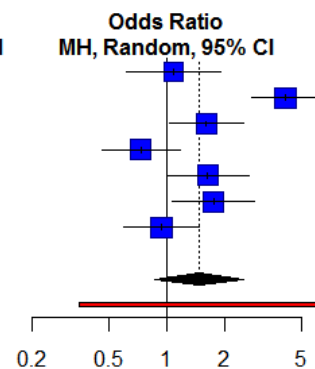
4)

VEGF rs2010963 GG compared to CC+CG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	30	176	28	176	13.3%	1.09 [0.62; 1.91]
Zhang Tie 2014	115	165	118	330	15.0%	4.13 [2.77; 6.17]
G. Zhang 2015	43	180	59	360	14.6%	1.60 [1.03; 2.49]
JIAN-QIANG LIU 2015	42	186	53	186	14.3%	0.73 [0.46; 1.17]
Lei Cao 2016	45	322	31	343	14.1%	1.64 [1.01; 2.66]
G.L. Hu 2015	73	130	55	130	14.1%	1.75 [1.07; 2.85]
Zhen Wang 2013	42	330	46	342	14.5%	0.94 [0.60; 1.47]

Total (95% CI) **1489** **1867** **100.0%** **1.47 [0.87; 2.49]**
Prediction interval **[0.35; 6.22]**

Heterogeneity: $\tau^2 = 0.2675$; $\chi^2 = 39.44$, $df = 6$ ($P < 0.01$); $I^2 = 85\%$
 Test for overall effect: $t_0 = 1.80$ ($P = 0.12$)



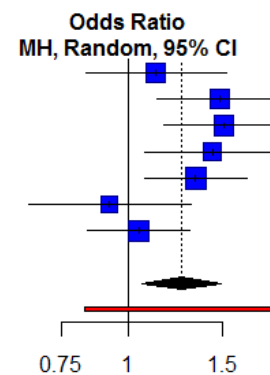
5)

VEGF rs2010963 C compared to G

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhao Li-lian 2015	147	352	137	352	12.7%	1.13 [0.83; 1.52]
Zhang Tie 2014	167	330	270	660	14.4%	1.48 [1.13; 1.93]
G. Zhang 2015	174	360	276	720	14.9%	1.50 [1.17; 1.94]
JIAN-QIANG LIU 2015	181	372	148	372	13.2%	1.43 [1.07; 1.92]
Lei Cao 2016	302	644	273	686	17.0%	1.34 [1.07; 1.66]
G.L. Hu 2015	152	260	157	260	10.8%	0.92 [0.65; 1.31]
Zhen Wang 2013	395	660	402	684	17.0%	1.05 [0.84; 1.30]

Total (95% CI) 2978 3734 100.0% 1.26 [1.06; 1.49]
Prediction interval [0.83; 1.91]

Heterogeneity: $\tau^2 = 0.0216$; $\chi^2 = 10.69$, $df = 6$ ($P = 0.10$); $I^2 = 44\%$
 Test for overall effect: $t_6 = 3.28$ ($P = 0.02$)



VEGF rs10434

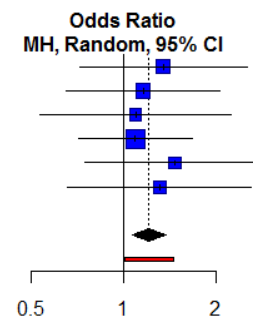
1)

VEGF rs10434 AA compared to GG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhang Tie 2014	20	88	33	184	14.9%	1.35 [0.72; 2.51]
G. Zhang 2015	23	100	42	205	17.4%	1.16 [0.65; 2.06]
Zhao Li-lian 2015	19	96	18	98	11.3%	1.10 [0.54; 2.25]
Zhen Wang 2015	78	173	73	170	31.3%	1.09 [0.71; 1.67]
JIAN-QIANG LIU 2015	25	100	19	103	12.8%	1.47 [0.75; 2.89]
G.L. Hu 2015	28	69	24	70	12.3%	1.31 [0.66; 2.61]

Total (95% CI) 626 830 100.0% 1.21 [1.07; 1.37]
Prediction interval [1.01; 1.45]

Heterogeneity: $\tau^2 = 0.0018$; $\chi^2 = 0.81$, $df = 5$ ($P = 0.98$); $I^2 = 0\%$
 Test for overall effect: $t_5 = 3.85$ ($P = 0.01$)



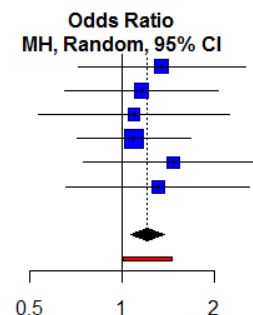
2)

VEGF rs10434 AA compared to GG

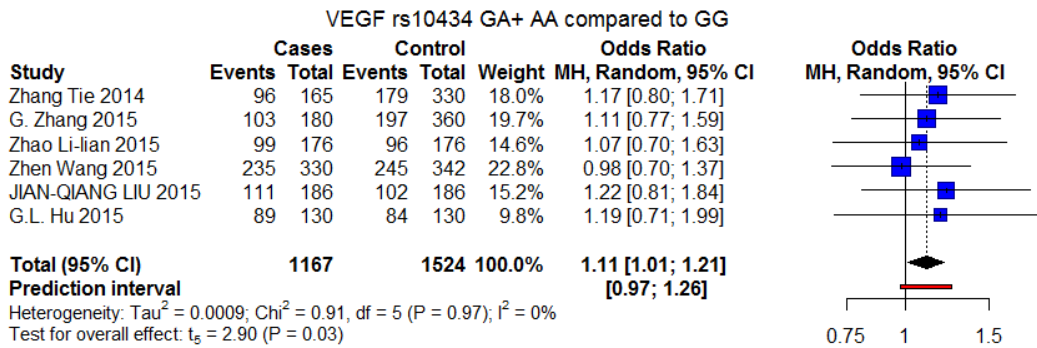
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Zhang Tie 2014	20	88	33	184	14.9%	1.35 [0.72; 2.51]
G. Zhang 2015	23	100	42	205	17.4%	1.16 [0.65; 2.06]
Zhao Li-lian 2015	19	96	18	98	11.3%	1.10 [0.54; 2.25]
Zhen Wang 2015	78	173	73	170	31.3%	1.09 [0.71; 1.67]
JIAN-QIANG LIU 2015	25	100	19	103	12.8%	1.47 [0.75; 2.89]
G.L. Hu 2015	28	69	24	70	12.3%	1.31 [0.66; 2.61]

Total (95% CI) 626 830 100.0% 1.21 [1.07; 1.37]
Prediction interval [1.01; 1.45]

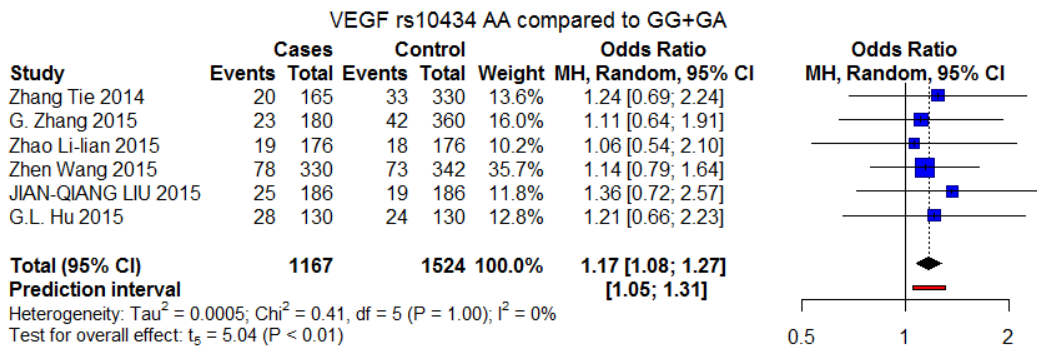
Heterogeneity: $\tau^2 = 0.0018$; $\chi^2 = 0.81$, $df = 5$ ($P = 0.98$); $I^2 = 0\%$
 Test for overall effect: $t_5 = 3.85$ ($P = 0.01$)



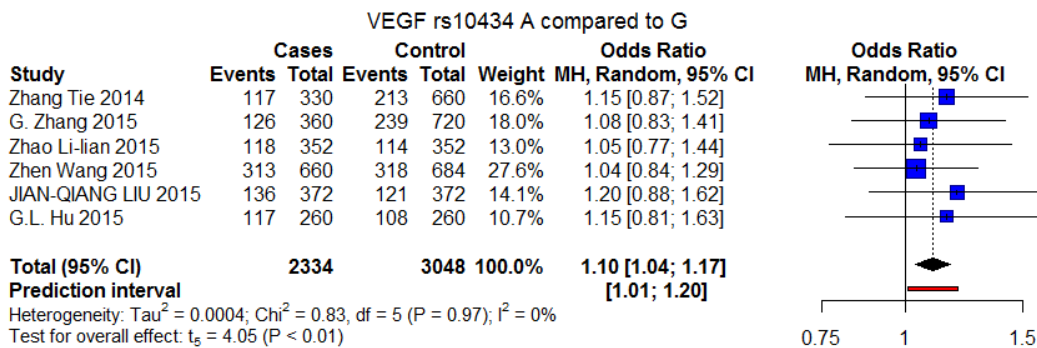
3)



4)



5)

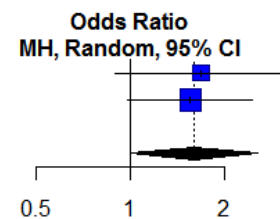


IL-8 rs4073

1)

IL-8 rs4073 TA compared to TT

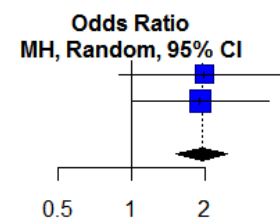
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Xu Tian 2016	32	90	24	97	34.3%	1.68 [0.89; 3.16]
Yang Chen 2015	63	162	50	172	65.7%	1.55 [0.98; 2.45]
Total (95% CI)		252		269	100.0%	1.59 [1.00; 2.55]
Heterogeneity: $\tau^2 < 0.0001$; $\text{Chi}^2 = 0.04$, $\text{df} = 1$ ($P = 0.85$); $I^2 = 0\%$						
Test for overall effect: $t_1 = 12.65$ ($P = 0.05$)						



2)

IL-8 rs4073 AA compared to TT

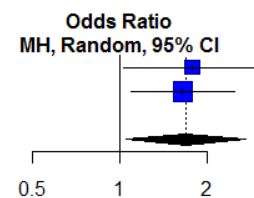
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Xu Tian 2016	19	77	12	85	39.6%	1.99 [0.89; 4.44]
Yang Chen 2015	28	127	18	140	60.4%	1.92 [1.00; 3.67]
Total (95% CI)		204		225	100.0%	1.95 [1.53; 2.48]
Heterogeneity: $\tau^2 < 0.0001$; $\text{Chi}^2 = 0.01$, $\text{df} = 1$ ($P = 0.94$); $I^2 = 0\%$						
Test for overall effect: $t_1 = 35.09$ ($P = 0.02$)						



3)

IL-8 rs4073 TA+ AA compared to TT

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Xu Tian 2016	51	109	36	109	36.0%	1.78 [1.03; 3.09]
Yang Chen 2015	91	190	68	190	64.0%	1.65 [1.09; 2.49]
Total (95% CI)		299		299	100.0%	1.70 [1.05; 2.73]
Heterogeneity: $\tau^2 < 0.0001$; $\text{Chi}^2 = 0.05$, $\text{df} = 1$ ($P = 0.82$); $I^2 = 0\%$						
Test for overall effect: $t_1 = 14.10$ ($P = 0.05$)						

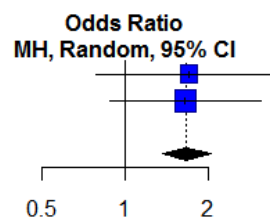


4)

IL-8 rs4073 AA compared to TT+TA

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Xu Tian 2016	19	109	12	109	39.6%	1.71 [0.78; 3.71]
Yang Chen 2015	28	190	18	190	60.4%	1.65 [0.88; 3.10]
Total (95% CI)	299	299	100.0%	299		1.67 [1.37; 2.05]

Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.00$, $df = 1$ ($P = 0.95$); $I^2 = 0\%$
 Test for overall effect: $t_1 = 32.18$ ($P = 0.02$)

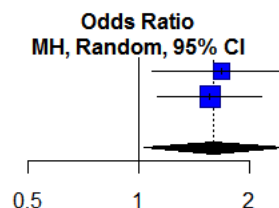


5)

IL-8 rs4073 A compared to T

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Xu Tian 2016	70	218	48	218	36.4%	1.68 [1.09; 2.57]
Yang Chen 2015	119	380	86	380	63.6%	1.56 [1.13; 2.15]
Total (95% CI)	598	598	100.0%	598		1.60 [1.03; 2.49]

Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.07$, $df = 1$ ($P = 0.79$); $I^2 = 0\%$
 Test for overall effect: $t_1 = 13.56$ ($P = 0.05$)



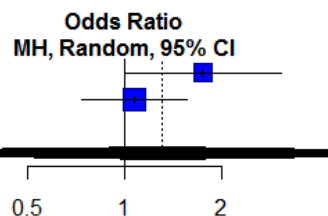
CTLA-4 rs5742909

1)

CTLA-4 rs5742909 CT compared to CC

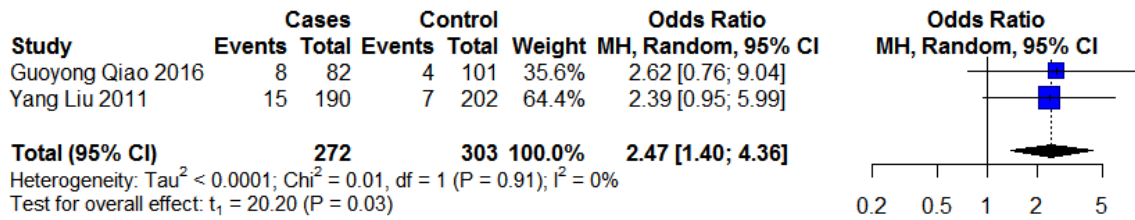
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Guoyong Qiao 2016	40	114	30	127	40.4%	1.75 [1.00; 3.07]
Yang Liu 2011	77	252	80	275	59.6%	1.07 [0.74; 1.56]
Total (95% CI)	366	402	100.0%	402		1.31 [0.00; 27.43]

Heterogeneity: $\tau^2 = 0.0598$; $\chi^2 = 2.01$, $df = 1$ ($P = 0.16$); $I^2 = 50\%$
 Test for overall effect: $t_1 = 1.12$ ($P = 0.47$)



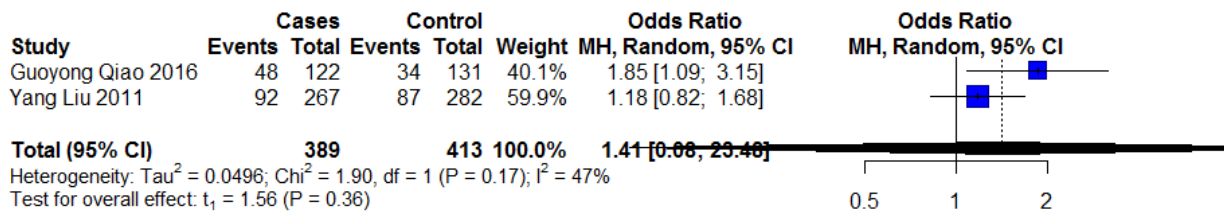
2)

CTLA-4 rs5742909 TT compared to CC



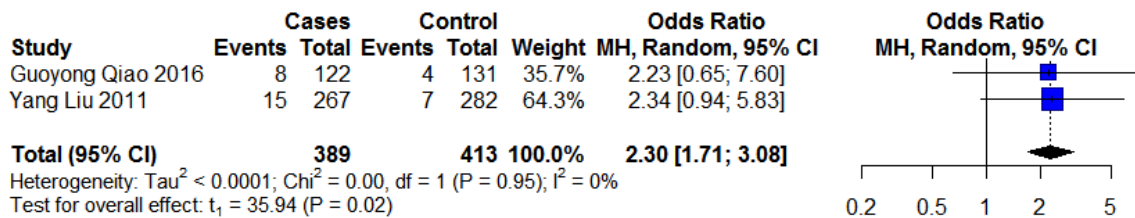
3)

CTLA-4 rs5742909 TT+CT compared to CC



4)

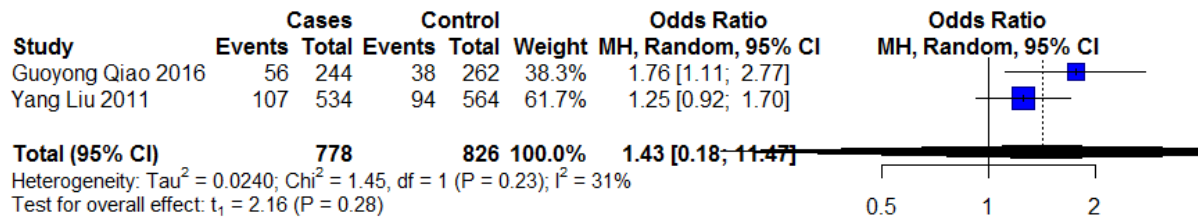
CTLA-4 rs5742909 TT compared to CC+ CT



5)

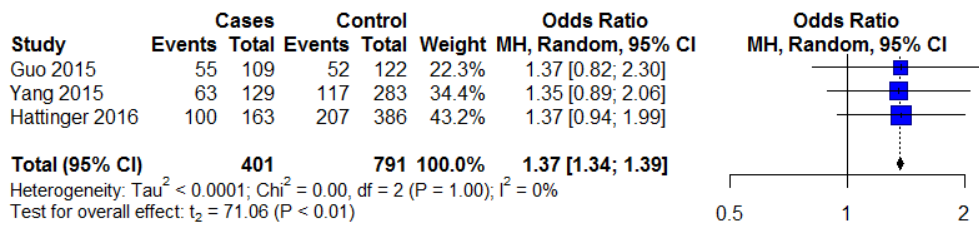
CTLA-4_rs5742909

C compared to T



XRCC3 rs861539

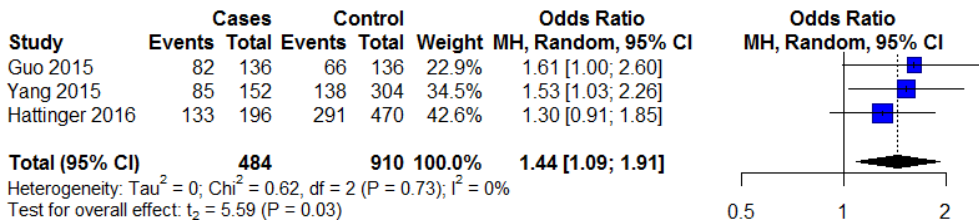
XRCC3 rs861539 CT compared to CC



XRCC3 rs861539 CT+TT compared to CC



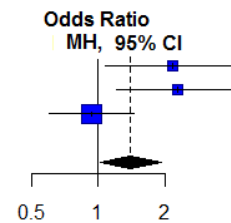
XRCC3 rs861539 CT+TT compared to CC



XRCC3 rs861539 TT compared to CT+CC

Study	Cases		Control		Weight	Odds Ratio MH, Fixed, 95% CI
	Events	Total	Events	Total		
Guo 2015	27	136	14	136	17.4%	2.16 [1.08; 4.33]
Yang 2015	22	152	21	304	18.6%	2.28 [1.21; 4.29]
Hattinger 2016	33	196	84	470	63.9%	0.93 [0.60; 1.45]
Total (95% CI)	484	910	100.0%	1.40 [1.02; 1.91]		

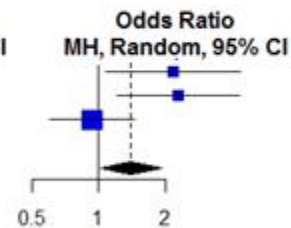
Heterogeneity: $\tau^2 = 0.1771$; $\chi^2 = 7.05$, $df = 2$ ($P = 0.03$); $I^2 = 72\%$
Test for overall effect: $z = 2.08$ ($P = 0.04$)



XRCC3 rs861539 TT compared to CT+CC

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Guo 2015	27	136	14	136	17.4%	2.16 [1.08; 4.33]
Yang 2015	22	152	21	304	18.6%	2.28 [1.21; 4.29]
Hattinger 2016	33	196	84	470	63.9%	0.93 [0.60; 1.45]
Total (95% CI)	484	910	100.0%	1.40 [1.02; 1.91]		

Heterogeneity: $\tau^2 = 0.1771$; $\chi^2 = 7.05$, $df = 2$ ($P = 0.03$); $I^2 = 72\%$
Test for overall effect: $z = 2.08$ ($P = 0.04$)



MDM2

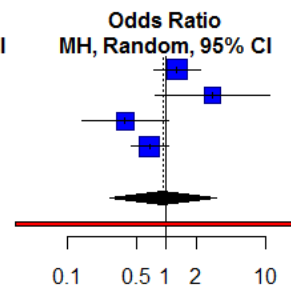
MDM2 rs1690916

MDM2 rs1690916 GA compared to GG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Bilbao-Aldaiturriaga 2016	49	87	74	147	29.5%	1.27 [0.75; 2.17]
Bilbao-Aldaiturriaga 2016	17	20	51	77	17.5%	2.89 [0.78; 10.76]
Naumov 2012	9	21	45	68	22.1%	0.38 [0.14; 1.04]
Mirabello 2011	44	88	691	1159	30.9%	0.68 [0.44; 1.05]
Total (95% CI)	216	1451	100.0%	0.93 [0.27; 3.22]		

Prediction interval
[0.03; 28.21]

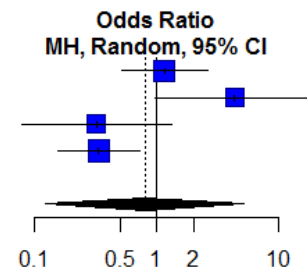
Heterogeneity: $\tau^2 = 0.4769$; $\chi^2 = 9.01$, $df = 3$ ($P = 0.03$); $I^2 = 67\%$
Test for overall effect: $t_3 = -0.19$ ($P = 0.86$)



MDM2 rs1690916 AA compared to GG

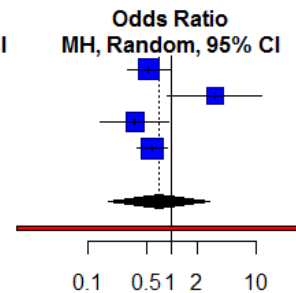
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Bilbao-Aldaiturriaga 2016	12	50	20	93	28.8%	1.15 [0.51; 2.61]
Bilbao-Aldaiturriaga 2016	7	10	14	40	20.4%	4.33 [0.97; 19.43]
Naumov 2012	3	15	18	41	21.5%	0.32 [0.08; 1.31]
Mirabello 2011	8	52	257	725	29.3%	0.33 [0.15; 0.71]
Total (95% CI)	127	899	100.0%	0.80 [0.12; 5.13]		

Heterogeneity: $\tau^2 = 0.8360$; $\chi^2 = 11.99$, $df = 3$ ($P < 0.01$); $I^2 = 75\%$
Test for overall effect: $t_3 = -0.39$ ($P = 0.72$)



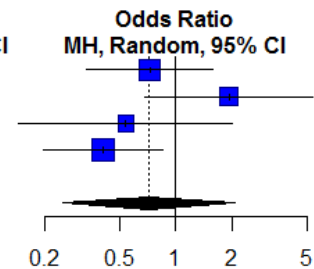
MDM2 rs1690916
GA + AA compared to GG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Bilbao-Aldaiturriaga 2016	61	99	94	125	28.0%	0.53 [0.30; 0.94]
Bilbao-Aldaiturriaga 2016	24	27	65	91	18.8%	3.20 [0.89; 11.55]
Naumov 2012	12	24	63	86	23.4%	0.37 [0.14; 0.93]
Mirabello 2011	52	96	948	1416	29.7%	0.58 [0.38; 0.88]
Total (95% CI)	246	1718	100.0%			0.70 [0.18; 2.79]
Prediction interval						[0.01; 33.43]
Heterogeneity: $\tau^2 = 0.6179$; $\chi^2 = 7.82$, $df = 3$ ($P = 0.05$); $I^2 = 62\%$						
Test for overall effect: $t_3 = -0.82$ ($P = 0.47$)						



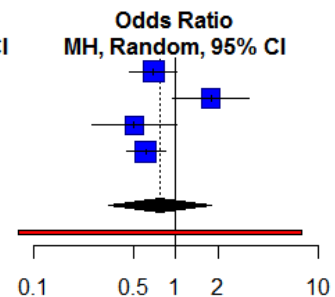
MDM2 rs1690916 AA compared to GG+GA

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Bilbao-Aldaiturriaga 2016	12	99	20	125	29.9%	0.72 [0.34; 1.56]
Bilbao-Aldaiturriaga 2016	7	27	14	91	22.5%	1.93 [0.69; 5.40]
Naumov 2012	3	24	18	86	16.6%	0.54 [0.14; 2.01]
Mirabello 2011	8	96	257	1416	31.0%	0.41 [0.20; 0.86]
Total (95% CI)	246	1718	100.0%			0.72 [0.25; 2.07]
Heterogeneity: $\tau^2 = 0.2155$; $\chi^2 = 5.95$, $df = 3$ ($P = 0.11$); $I^2 = 50\%$						
Test for overall effect: $t_3 = -0.99$ ($P = 0.39$)						



MDM2 rs1690916
A compared to G

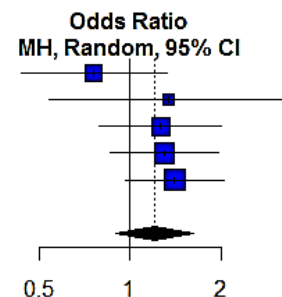
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Bilbao-Aldaiturriaga 2016	73	198	114	250	27.7%	0.70 [0.48; 1.02]
Bilbao-Aldaiturriaga 2016	31	54	79	182	22.3%	1.76 [0.95; 3.25]
Naumov 2012	15	48	81	172	20.9%	0.51 [0.26; 1.01]
Mirabello 2011	60	192	1205	2832	29.1%	0.61 [0.45; 0.84]
Total (95% CI)	492	3436	100.0%			0.77 [0.34; 1.78]
Prediction interval						[0.08; 7.60]
Heterogeneity: $\tau^2 = 0.2135$; $\chi^2 = 10.11$, $df = 3$ ($P = 0.02$); $I^2 = 70\%$						
Test for overall effect: $t_3 = -0.98$ ($P = 0.40$)						



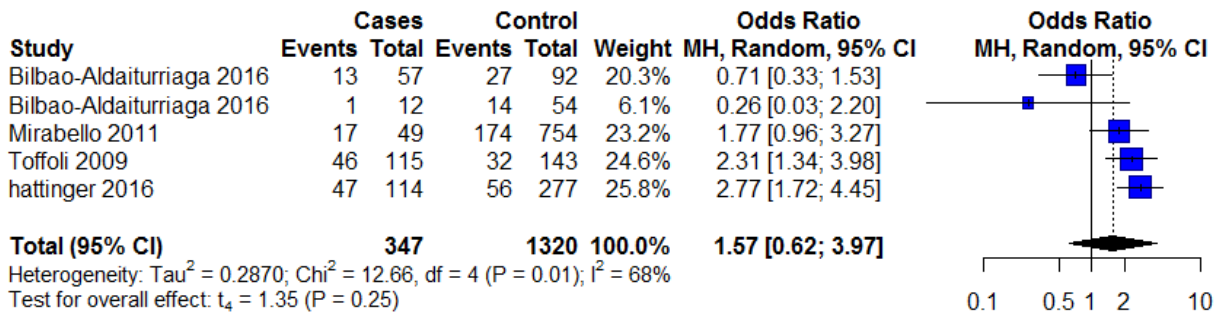
MDM2 rs2279744

MDM2 rs2279744 GT compared to TT

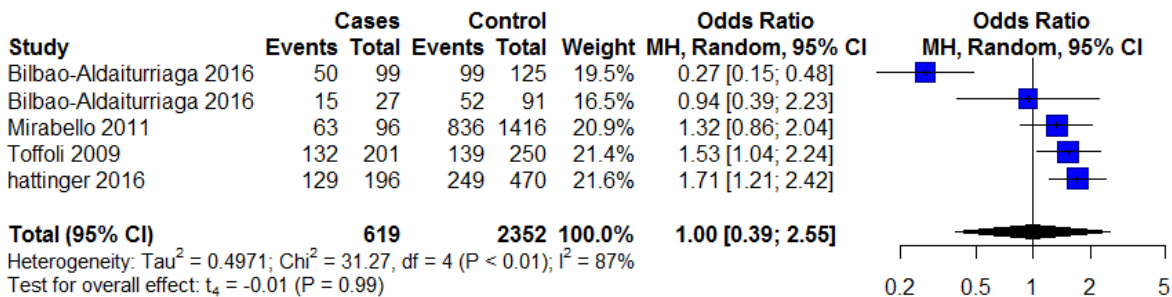
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Bilbao-Aldaiturriaga 2016	37	81	72	137	17.0%	0.76 [0.44; 1.32]
Bilbao-Aldaiturriaga 2016	14	25	38	78	7.4%	1.34 [0.54; 3.31]
Mirabello 2011	46	78	662	1242	21.7%	1.26 [0.79; 2.00]
Toffoli 2009	86	155	107	218	25.4%	1.29 [0.86; 1.95]
hattinger 2016	82	149	193	414	28.5%	1.40 [0.96; 2.04]
Total (95% CI)	488	2089	100.0%			1.20 [0.90; 1.62]
Heterogeneity: $\tau^2 = 0.0255$; $\chi^2 = 3.50$, $df = 4$ ($P = 0.48$); $I^2 = 0\%$						
Test for overall effect: $t_4 = 1.75$ ($P = 0.15$)						



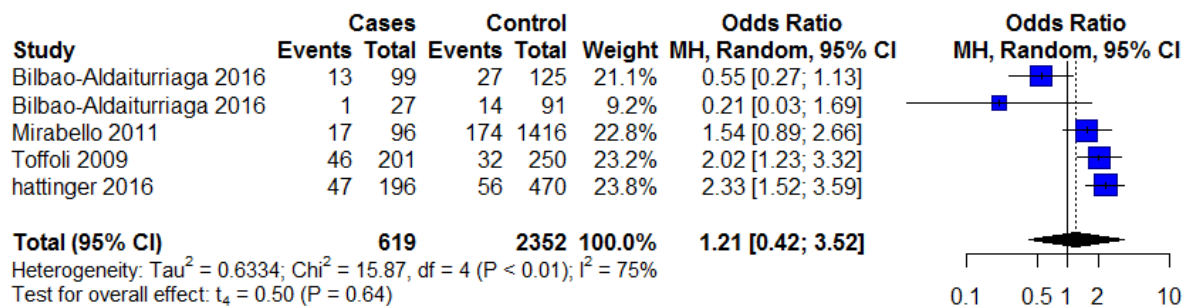
MDM2 rs2279744 GG compared to TT



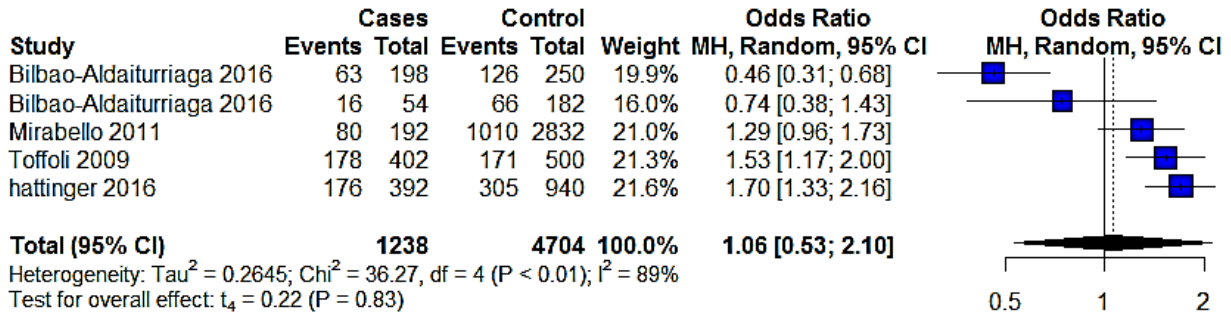
MDM2 rs2279744 GT+GG compared to TT



MDM2 rs2279744 GG compared to GT+TT

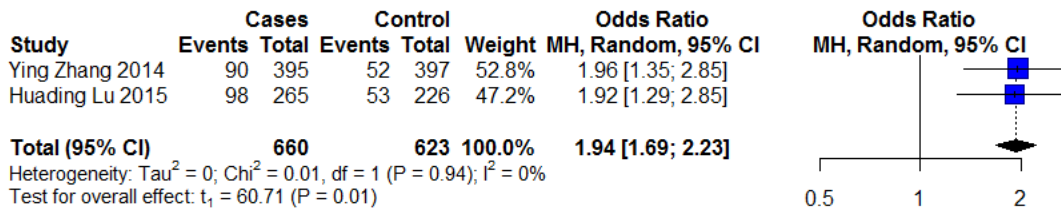


MDM2 rs2279744 G compared to T

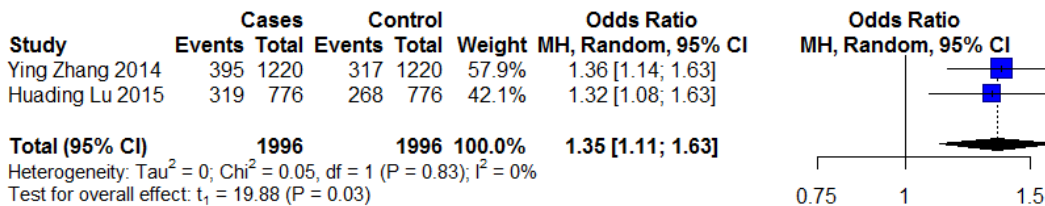


PRKCG rs454006

PRKCG rs454006 CC compared to TT

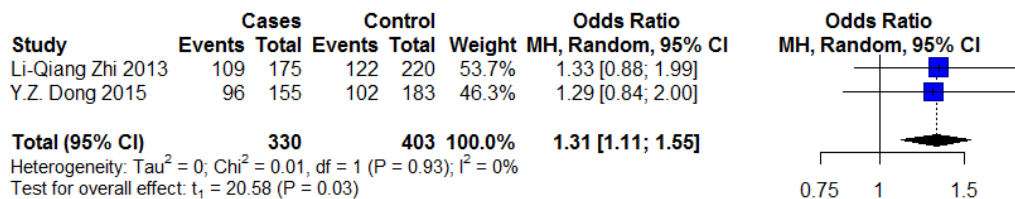


PRKCG rs454006 T compared to C

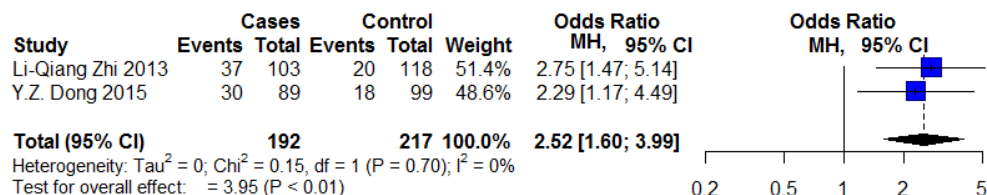


RECQL5 rs820196

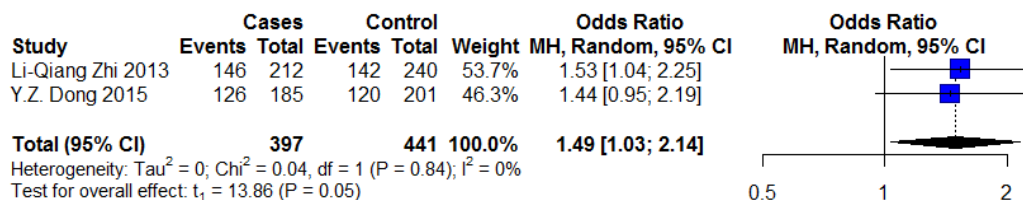
RECQL5 rs820196 TC compared to TT



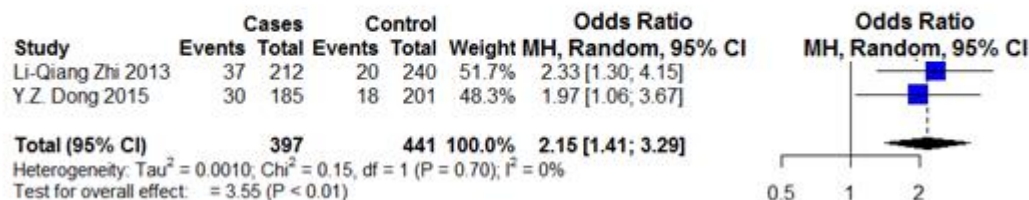
RECQL5 rs820196 CC compared to TT



RECQL5 rs820196 CC+TC compared to TT

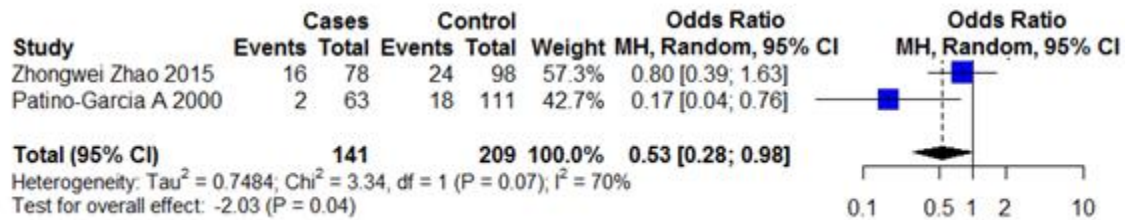


RECQL5 rs820196 CC compared to TC+TT

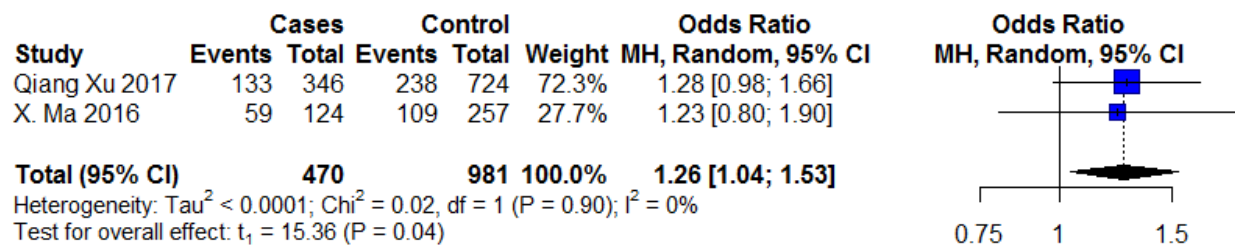


RECQL5 rs820196 C compared to T



TNF- α rs 361525 GA compared to GG

ERCC3 rs4150506 CT compared to CC



ERCC3 rs4150506 TT compared to CC



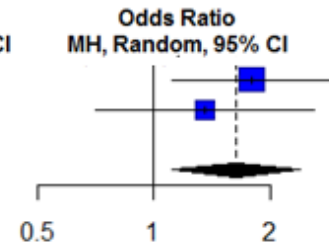
ERCC3 rs4150506 CT+TT compared to CC



ERCC3 rs4150506 TT compared to CT+CC

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Qiang Xu 2017	35	381	41	765	61.9%	1.79 [1.12; 2.85]
X. Ma 2016	17	141	26	282	38.1%	1.35 [0.71; 2.58]
Total (95% CI)		522		1047	100.0%	1.62 [1.11; 2.37]

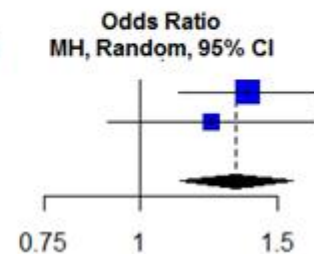
Heterogeneity: $\tau^2 = 0.0075$; $\chi^2 = 0.47$, $df = 1$ ($P = 0.49$); $I^2 = 0\%$
Test for overall effect: $Z = 2.49$ ($P = 0.01$)



ERCC3 rs4150506 T compared to C

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Qiang Xu 2017	203	762	320	1530	68.5%	1.37 [1.12; 1.68]
X. Ma 2016	93	282	161	564	31.5%	1.23 [0.90; 1.68]
Total (95% CI)		1044		2094	100.0%	1.33 [1.12; 1.57]

Heterogeneity: $\tau^2 = 0.0008$; $\chi^2 = 0.33$, $df = 1$ ($P = 0.56$); $I^2 = 0\%$
Test for overall effect: $Z = 3.29$ ($P < 0.01$)



Supplementary Figure S2

Sensitivity Analyses.

VEGF rs699947

leave-one-out- Analysis

CA vs CC

	Effect	LLCI	ULCI	I2
Omitting H.F. Zhang 2015	1.301	0.935	1.809	0
Omitting Zhao Li-lian 2015	1.289	0.961	1.730	0
Omitting Zhang Tie 2014	1.340	0.922	1.947	0
Omitting JIAN-QIANG LIU 2015	1.405	1.194	1.653	0

AA vs CC

	Effect	LLCI	ULCI	I2
Omitting H.F. Zhang 2015	1.859	0.928	3.727	0
Omitting Zhao Li-lian 2015	1.770	1.001	3.129	0
Omitting Zhang Tie 2014	1.825	0.917	3.631	0
Omitting JIAN-QIANG LIU 2015	2.106	1.714	2.587	0

AA +AC vs CC

	Effect	LLCI	ULCI	I2
Omitting JIAN-QIANG LIU 2015	1.558	1.314	1.846	0.000
Omitting Zhao Li-lian 2015	1.335	0.774	2.301	0.090
Omitting H.F. Zhang 2015	1.360	0.742	2.494	0.248
Omitting Zhang Tie 2014	1.385	0.719	2.665	0.312

AA vs AC+CC

	Effect	LLCI	ULCI	I2
Omitting H.F. Zhang 2015	1.634	0.965	2.767	0
Omitting Zhao Li-lian 2015	1.565	1.008	2.431	0
Omitting Zhang Tie 2014	1.580	0.960	2.599	0
Omitting JIAN-QIANG LIU 2015	1.777	1.493	2.114	0

A vs C

	Effect	LLCI	ULCI	I2
Omitting H.F. Zhang 2015	1.859	0.928	3.727	0
Omitting Zhao Li-lian 2015	1.770	1.001	3.129	0
Omitting Zhang Tie 2014	1.825	0.917	3.631	0
Omitting JIAN-QIANG LIU 2015	2.106	1.714	2.587	0

rs1570360

Leave-one-out Analysis

AG vs AA

	Effect	LLCI	ULCI	I2
Omitting Zhao Li-lian 2015	1.215	0.797	1.850	0
Omitting Zhang Tie 2014	1.117	0.635	1.968	0
Omitting JIAN-QIANG LIU 2015	1.158	0.431	3.113	0

GG vs AA

	Effect	LLCI	ULCI	I2
Omitting Zhao Li-lian 2015	1.439	1.028	2.015	0
Omitting Zhang Tie 2014	1.406	1.191	1.660	0
Omitting JIAN-QIANG LIU 2015	1.462	1.277	1.675	0

GA+GG vs AA

	Effect	LLCI	ULCI	I2
Omitting Zhao Li-lian 2015	1.211	0.921	1.592	0
Omitting Zhang Tie 2014	1.130	0.649	1.969	0
Omitting JIAN-QIANG LIU 2015	1.162	0.508	2.660	0

GG vs AA+GA

	Effect	LLCI	ULCI	I2
Omitting Zhao Li-lian 2015	1.357	1.140	1.614	0
Omitting Zhang Tie 2014	1.354	1.023	1.791	0
Omitting JIAN-QIANG LIU 2015	1.378	1.238	1.534	0

G vs A

	Effect	LLCI	ULCI	I2
Omitting Zhao Li-lian 2015	1.284	0.923	1.785	0
Omitting Zhang Tie 2014	1.187	0.621	2.268	0
Omitting JIAN-QIANG LIU 2015	1.229	0.466	3.243	0

VEGF rs10434

leave-one-out- Analysis

	Effect	LLCI	ULCI	I2
Omitting Zhang Tie 2014	1.058	0.943	1.188	0
Omitting G. Zhang 2015	1.071	0.943	1.217	0
Omitting Zhao Li-lian 2015	1.077	0.951	1.220	0
Omitting Zhen wang 2015	1.121	1.069	1.175	0
Omitting JIAN-QIANG LIU 2015	1.061	0.945	1.190	0
Omitting G.L. Hu 2015	1.069	0.950	1.202	0

AA vs GG

	Effect	LLCI	ULCI	I2
Omitting Zhang Tie 2014	1.188	1.020	1.383	0
Omitting G. Zhang 2015	1.221	1.034	1.442	0
Omitting Zhao Li-lian 2015	1.225	1.050	1.430	0
Omitting Zhen wang 2015	1.268	1.098	1.464	0
Omitting JIAN-QIANG LIU 2015	1.175	1.042	1.324	0
Omitting G.L. Hu 2015	1.197	1.022	1.401	0

GA+AA vs GG

	Effect	LLCI	ULCI	I2
Omitting Zhang Tie 2014	1.092	0.977	1.221	0
Omitting G. Zhang 2015	1.106	0.981	1.249	0
Omitting Zhao Li-lian 2015	1.113	0.991	1.249	0
Omitting Zhen Wang 2015	1.147	1.074	1.224	0
Omitting JIAN-QIANG LIU 2015	1.087	0.984	1.202	0
Omitting G.L. Hu 2015	1.098	0.985	1.224	0

AA s GA+GG

	Effect	LLCI	ULCI	I2
Omitting Zhang Tie 2014	1.092	0.977	1.221	0
Omitting G. Zhang 2015	1.106	0.981	1.249	0
Omitting Zhao Li-lian 2015	1.113	0.991	1.249	0
Omitting Zhen Wang 2015	1.147	1.074	1.224	0
Omitting JIAN-QIANG LIU 2015	1.087	0.984	1.202	0
Omitting G.L. Hu 2015	1.098	0.985	1.224	0

A vs G

	Effect	LLCI	ULCI	I2
Omitting Zhang Tie 2014	1.090	1.013	1.173	0
Omitting G. Zhang 2015	1.104	1.019	1.196	0
Omitting Zhao Li-lian 2015	1.107	1.028	1.193	0
Omitting Zhen Wang 2015	1.124	1.056	1.198	0
Omitting JIAN-QIANG LIU 2015	1.085	1.021	1.153	0
Omitting G.L. Hu 2015	1.094	1.016	1.178	0

[XRCC3 rs861539](#)

CT vs CC

	Effect	LLCI	ULCI	I2
Omitting Guo 2015	1.364	1.254	1.485	0
Omitting Yang 2015	1.372	1.363	1.381	0
Omitting Hattinger 2016	1.361	1.261	1.469	0

TT vs CC

	Effect	LLCI	ULCI	I2
Omitting Hattinger 2016	2.571	1.570	4.210	0.000
Omitting Yang 2015	1.444	0.965	2.162	0.685
Omitting Guo 2015	1.503	1.016	2.225	0.759

CT+TT vs CC

	Effect	LLCI	ULCI	I2
Omitting Jin 2015	2.647	0.379	18.488	0.922
Omitting Goricar 2015	0.806	0.118	5.529	0.966
Omitting Guo 2015	1.440	0.060	34.324	0.979
Omitting Yang 2015	1.460	0.061	34.901	0.979
Omitting Hattinger 2016	1.521	0.064	36.291	0.979

TT vs CC+CT

	Effect	LLCI	ULCI	I2
Omitting Hattinger 2016	2.224	1.571	3.150	0.000
Omitting Yang 2015	1.350	0.007	273.588	0.750
Omitting Guo 2015	1.410	0.005	413.674	0.807

T vs C

	Effect	LLCI	ULCI	I2
Omitting Hattinger 2016	1.563	1.244	1.963	0.000
Omitting Guo 2015	1.256	1.043	1.513	0.645
Omitting Yang 2015	1.243	1.020	1.515	0.653

CTLA-4 rs231775

GA vs GG

	Effect	LLCI	ULCI	I2
Omitting N. Bilbao-Aldaiturriaga 2016	1.249	0.891	1.750	0.000
Omitting Guoyong Qiao 2016	0.879	0.136	5.671	0.621
Omitting Wen wang 2011	0.890	0.126	6.271	0.636
Omitting Yang Liu 2011	0.944	0.118	7.533	0.652

AA vs GG

	Effect	LLCI	ULCI	I2
Omitting N. Bilbao-Aldaiturriaga 2016	2.241	2.144	2.343	0.000
Omitting Wen wang 2011	1.765	0.435	7.154	0.239
Omitting Yang Liu 2011	1.775	0.423	7.443	0.254
Omitting Guoyong Qiao 2016	1.797	0.463	6.978	0.261

GA +AA vs GG

	Effect	LLCI	ULCI	I2
Omitting N. Bilbao-Aldaiturriaga 2016	1.397	1.038	1.879	0.000
Omitting Wen wang 2011	0.526	0.007	42.359	0.942
Omitting Guoyong Qiao 2016	0.517	0.007	39.609	0.943
Omitting Yang Liu 2011	0.555	0.006	50.139	0.945

AA vs GG+GA

	Effect	LLCI	ULCI	I2
Omitting Guoyong Qiao 2016	0.793	0.384	1.637	0
Omitting Yang Liu 2011	0.734	0.301	1.792	0
Omitting Wen wang 2011	0.789	0.349	1.782	0
Omitting N. Bilbao-Aldaiturriaga 2016	0.716	0.532	0.963	0

G vs A

	Effect	LLCI	ULCI	I2
Omitting N. Bilbao-Aldaiturriaga 2016	1.383	1.202	1.590	0.000
Omitting Wen wang 2011	1.008	0.242	4.202	0.900
Omitting Guoyong Qiao 2016	0.999	0.249	4.002	0.903
Omitting Yang Liu 2011	1.031	0.236	4.510	0.905

MDM2 rs1690916

GA +AA vs GG

	Effect	LLCI	ULCI	I2
Omitting Bilbao-Aldaiturriaga 2016.1	0.531	0.334	0.847	0.000
Omitting Naumov 2012	0.867	0.085	8.810	0.699
Omitting Bilbao-Aldaiturriaga 2016	0.806	0.055	11.844	0.737
Omitting Mirabello 2011	0.782	0.050	12.306	0.744

A vs G

	Effect	LLCI	ULCI	I2
Omitting Bilbao-Aldaiturriaga 2016.1	0.628	0.467	0.845	0.000
Omitting Mirabello 2011	0.853	0.179	4.051	0.764
Omitting Naumov 2012	0.868	0.220	3.426	0.780
Omitting Bilbao-Aldaiturriaga 2016	0.811	0.160	4.101	0.802

MDM2 rs2279744

GT vs TT

	Effect	LLCI	ULCI	I2
Omitting Bilbao-Aldaiturriaga 2016	1.327	1.222	1.441	0.000
Omitting hattinger 2016	1.134	0.749	1.716	0.000
Omitting Toffoli 2009	1.172	0.749	1.832	0.119
Omitting Bilbao-Aldaiturriaga 2016.1	1.190	0.792	1.787	0.133
Omitting Mirabello 2011	1.185	0.760	1.847	0.139

GG vs TT

	Effect	LLCI	ULCI	I2
Omitting Bilbao-Aldaiturriaga 2016	2.230	1.157	4.296	0.429
Omitting hattinger 2016	1.273	0.365	4.442	0.665
Omitting Bilbao-Aldaiturriaga 2016.1	1.780	0.712	4.452	0.676
Omitting Toffoli 2009	1.308	0.323	5.295	0.750
Omitting Mirabello 2011	1.398	0.315	6.205	0.762

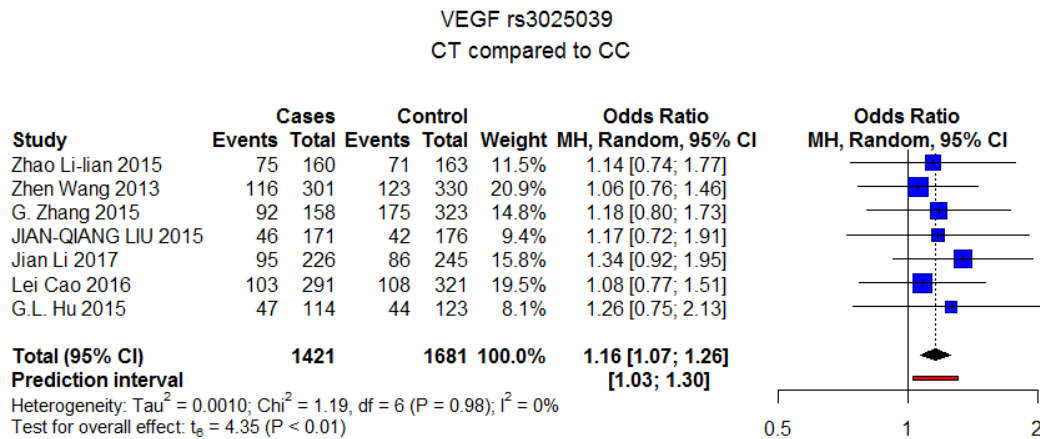
GT+GG vs TT

	Effect	LLCI	ULCI	I2
Omitting Bilbao-Aldaiturriaga 2016	1.495	1.125	1.986	0.000
Omitting hattinger 2016	0.858	0.240	3.062	0.884
Omitting Toffoli 2009	0.885	0.236	3.312	0.898
Omitting Bilbao-Aldaiturriaga 2016.1	1.004	0.257	3.925	0.903
Omitting Mirabello 2011	0.919	0.236	3.587	0.904

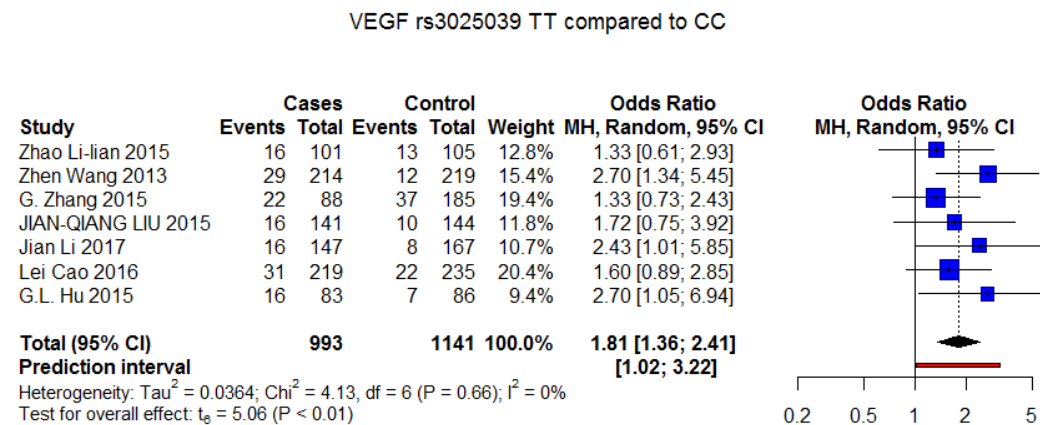
Supplementary Figure S3: Sensitivity analysis: Studies not in HWE removed

VEGF rs3025039

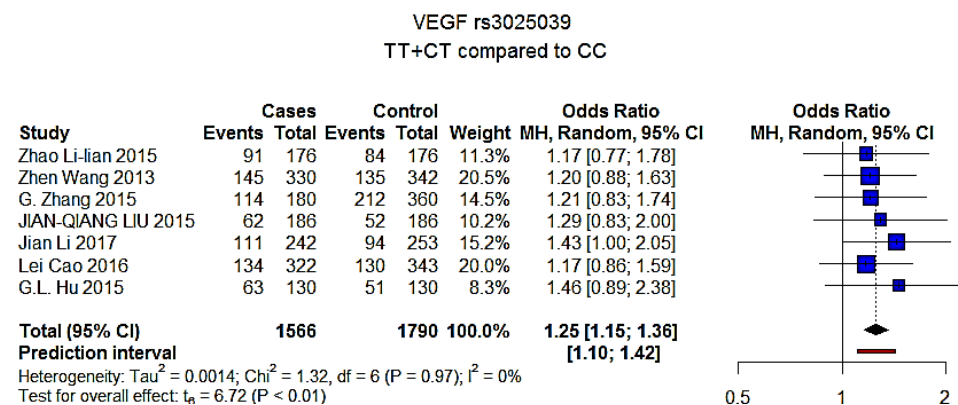
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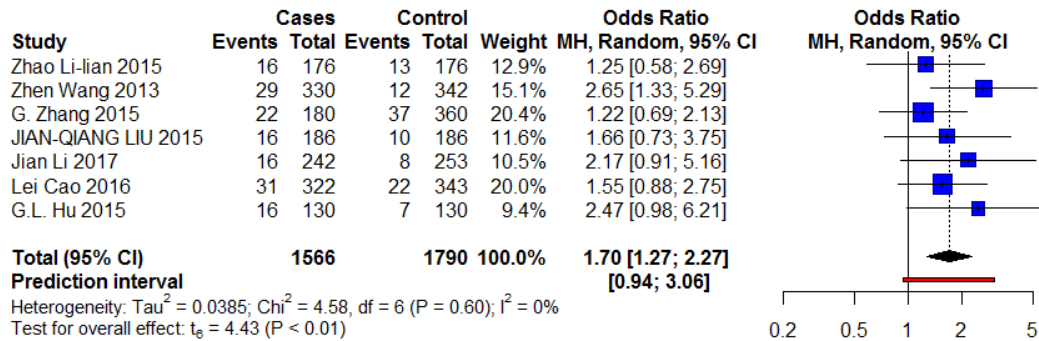
2)



3)

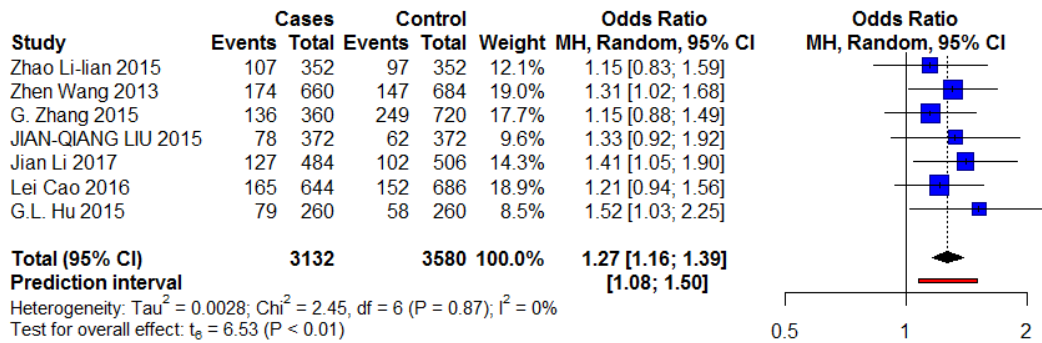


VEGF rs3025039
TT compared to CC+CT



5)

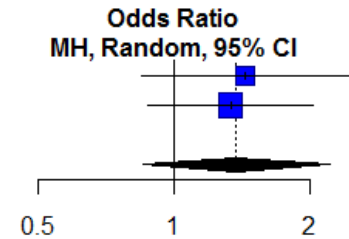
VEGF rs3025039 C compared to T



CTLA-4 rs231775 GA compared to GG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Guoyong Qiao 2016	58	104	56	120	38.7%	1.44 [0.85; 2.44]
Wen Wang 2011	106	170	108	195	61.3%	1.33 [0.88; 2.03]
Total (95% CI)		274		315	100.0%	1.37 [0.85; 2.21]

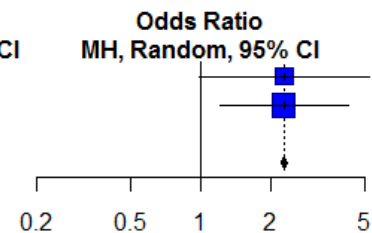
Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.05$, $df = 1$ ($P = 0.82$); $I^2 = 0\%$
 Test for overall effect: $t_1 = 8.48$ ($P = 0.07$)



CTLA-4 rs231775 AA compared to GG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Guoyong Qiao 2016	18	64	11	75	36.0%	2.28 [0.98; 5.28]
Wen Wang 2011	35	99	21	108	64.0%	2.27 [1.21; 4.25]
Total (95% CI)		163		183	100.0%	2.27 [2.20; 2.34]

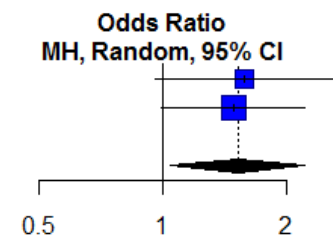
Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.00$, $df = 1$ ($P = 0.99$); $I^2 = 0\%$
 Test for overall effect: $t_1 = 350.84$ ($P < 0.01$)



CTLA-4 rs231775 GA+ AA compared to GG

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Guoyong Qiao 2016	76	122	67	131	39.1%	1.58 [0.96; 2.61]
Wen Wang 2011	141	205	129	216	60.9%	1.49 [0.99; 2.22]
Total (95% CI)		327		347	100.0%	1.52 [1.05; 2.21]

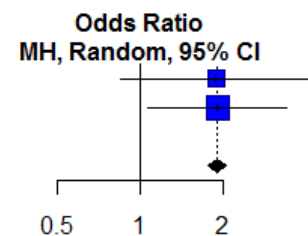
Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.03$, $df = 1$ ($P = 0.85$); $I^2 = 0\%$
 Test for overall effect: $t_1 = 14.26$ ($P = 0.04$)



CTLA-4 rs231775 AA compared to GG+GA

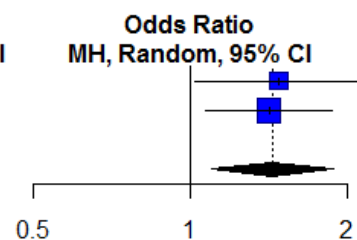
Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Guoyong Qiao 2016	18	122	11	131	34.7%	1.89 [0.85; 4.18]
Wen Wang 2011	35	205	21	216	65.3%	1.91 [1.07; 3.41]
Total (95% CI)		327		347	100.0%	1.90 [1.77; 2.05]

Heterogeneity: $\tau^2 < 0.0001$; $\chi^2 = 0.00$, $df = 1$ ($P = 0.98$); $I^2 = 0\%$
 Test for overall effect: $t_1 = 108.65$ ($P < 0.01$)



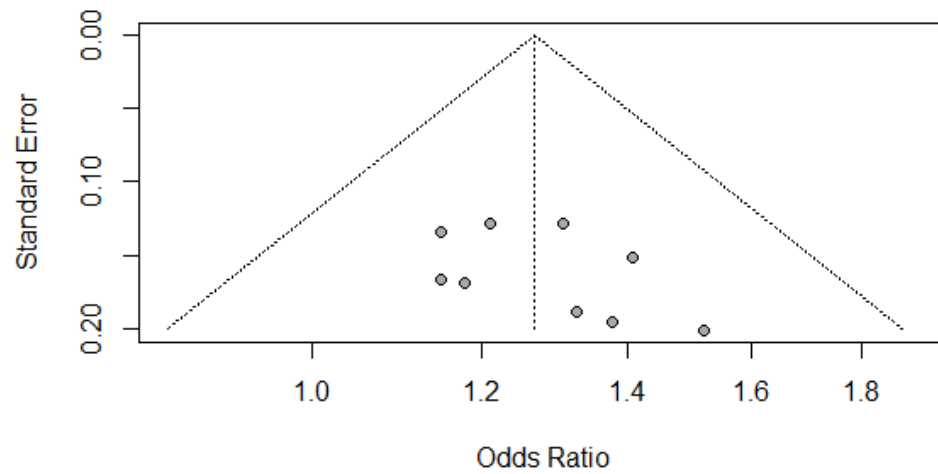
CTLA-4 rs231775 A compared to G

Study	Cases		Control		Weight	Odds Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Guoyong Qiao 2016	94	244	78	262	36.2%	1.48 [1.02; 2.14]
Wen Wang 2011	176	410	150	432	63.8%	1.41 [1.07; 1.87]
Total (95% CI)		654		694	100.0%	1.44 [1.10; 1.89]
Heterogeneity: $\text{Tau}^2 < 0.0001$; $\text{Chi}^2 = 0.04$, $\text{df} = 1$ ($P = 0.85$); $I^2 = 0\%$						
Test for overall effect: $t_1 = 16.97$ ($P = 0.04$)						



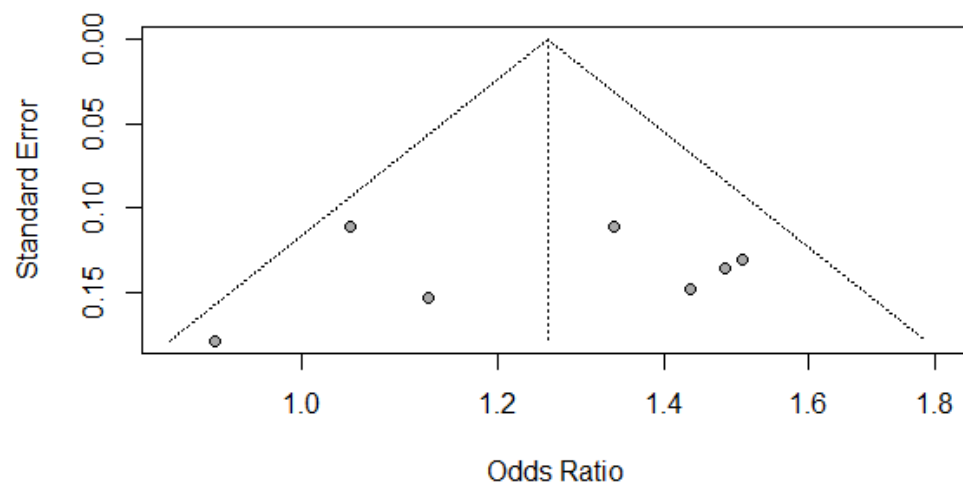
Supplementary Figure S4: Publication Bias

VEGF rs3025039

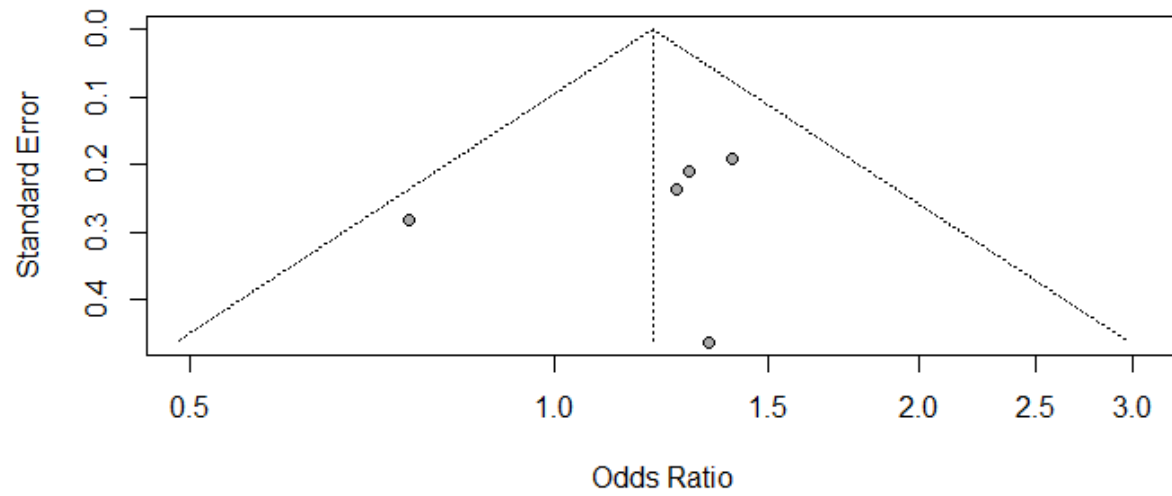


Linear regression test of funnel plot asymmetry Test result: $t = 1.25$, $df = 7$, $p\text{-value} = 0.2511$

VEGF rs2010963

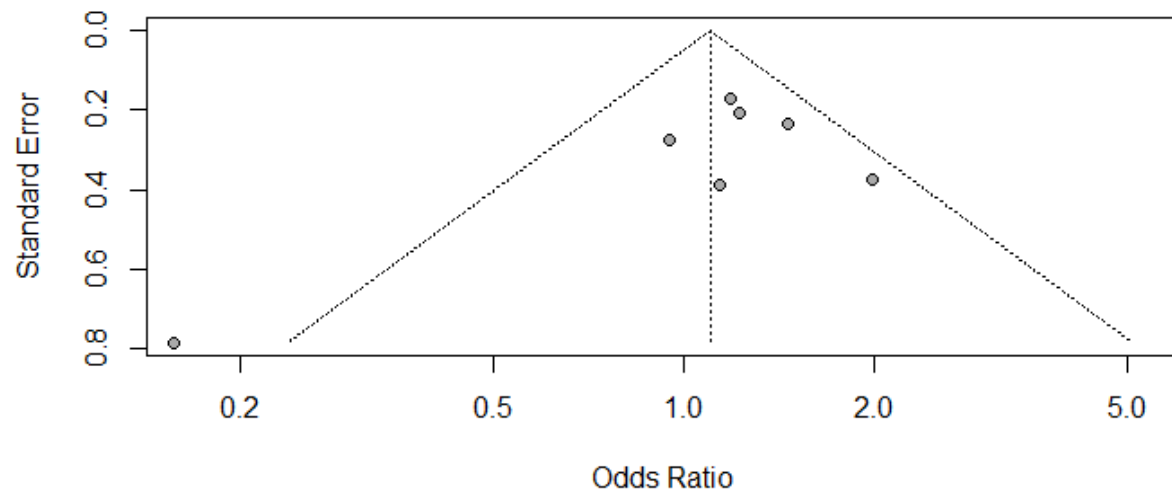


Linear regression test of funnel plot asymmetry Test result: $t = -0.38$, $df = 5$, $p\text{-value} = 0.7196$



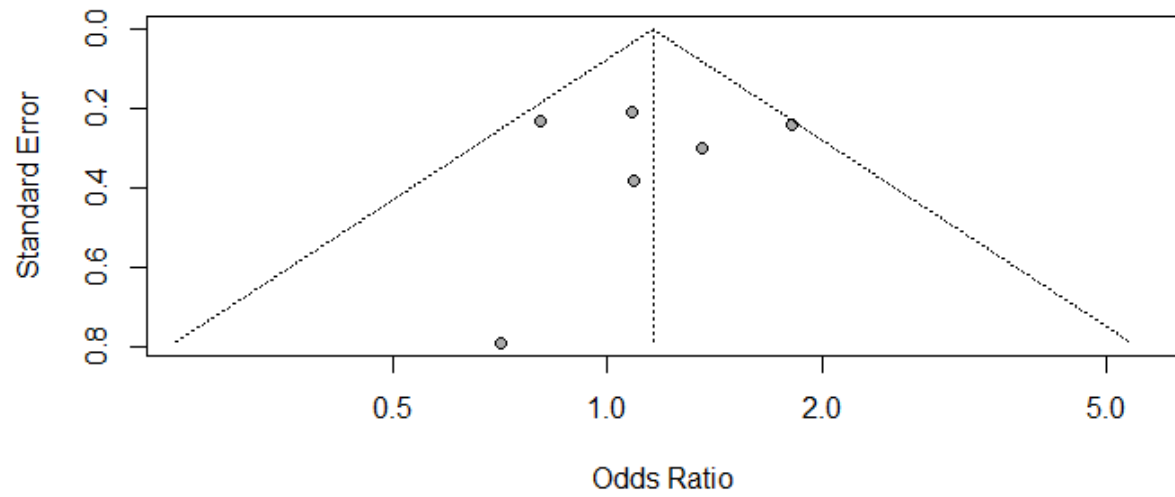
Linear regression test of funnel plot asymmetry Test result: $t = -0.64$, $df = 3$, $p\text{-value} = 0.5661$

GSTM1



Linear regression test of funnel plot asymmetry Test result: $t = -1.21$, $df = 5$, $p\text{-value} = 0.2806$

GSTT1



Linear regression test of funnel plot asymmetry. Test result: $t = -0.23$, $df = 4$, $p\text{-value} = 0.8290$