Supplementary Information to:

Genetic predisposition to lung cancer: comprehensive literature integration, meta-analysis, and multiple evidence assessment of candidate-gene association studies

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Information of variants involved in meta-analyses

Our systematic literature search identified 1,018 eligible publications reporting 2,910 genetic variants in 754 unique genes or loci. Main meta-analyses were performed for 246 genetic variants (in 138 genes or loci) with sufficient data (**Supplementary Table S1**). All of these variants are located on autosomes, and chromosome 19 has the highest number of variants (n=47, 19%) (**Supplementary Fig. S1**). According to their population frequency, 235 of the 246 variants are common variants and 11 are rare. These variants were further classified by their potential functional effects: (1) synonymous single nucleotide polymorphisms (sSNPs, n=15); (2) non-synonymous SNPs (nsSNPs, n=90); (3) frameshift polymorphism (n=1); (4) SNPs in 3′ or 5′ untranslated regions (UTRs; n=40); (5) intronic SNPs (n=46); (6) intergenic SNPs (n=38); (7) SNP in a splice site (n=1); (8) one deletion/insertion variant; (9) variants with microsatellite or short tandem repeat (STR) variation (n=4); (10) variants with multi-nucleotide variation (n=2); (11) variants with a specific change in phenotype (n=4); (12) variants with copy number variation (CNV) (n=2); (13) SNPs in microRNA (n=2) (**Supplementary Table S1**).

Supplementary results of main meta-analyses

Strength of association between each genetic variant and lung cancer risk

The strength of association between each genetic variant and lung cancer as measured by ORs had the mean of 1.36 (range 1.08-2.55) for putative "risk" variants and 0.78 (range 0.55-0.90) for putative "protective" variants. Four variants (*HIF1A* rs11549467, *HRAS1* a VNTR [variable number of tandem repeat] variation (loss of heterozygosity in the 15p15.5 region), *UGT1A6* rs6759892, and *WWOX* CNV-67048) showed strong associations (ORs > 2) with risk of lung cancer. Eight variants (*MAPKAPK2* CNV-30450, *SFTPB* variation [a large gene variation within intron 4], *TP53* rs12951053, *BCL2* rs2279115, *CYP2A6* rs1801272 and rs5031016, *ELANE* rs351107 [-903T>G, Rep_a], and *MMP2* rs243865) showed moderate genetic associations ("risk" ORs range 1.5-2.0, or "protective" ORs range 0.50-0.67) with lung cancer. The remaining 44 significant variants showed low associations (ORs range 0.67-1.50) with lung cancer, of note, four variants of them (*CHRNA3* rs6495309, *CYP2E1* rs6413432, *GSTM1* phenotype, and *HYKK* rs931794) showed highly significant associations ($P < 10^{-7}$) with lung cancer risk (**Table 1 and Supplementary Table S2**).

Assessment of heterogeneity across studies

In the 246 main meta-analyses, 86 (34.96%) had little or no heterogeneity ($I^2 <$ 25%) and 122 (49.59%) had high heterogeneity ($I^2 >$ 50%) (**Supplementary Table S1**). And among the 56 main meta-analyses with statistically significant summary ORs, 24 (42.86%) had little or no heterogeneity and 22 (39.29%) had high heterogeneity (**Table 1; Supplementary Table S2**).

Examinations for potential bias in studies enrolled in meta-analyses

Of the 246 main meta-analyses, 21(8.54%) had evidence of substantial publication bias on the basis of the Begg’s test ($P < 0.10$), 11 of which had statistically significant pooled ORs ($P \leq 0.05$) in main meta-analyses (**Supplementary Table S1**). Furthermore, a modified Egger’s test was used to evaluate whether small studies provide different results from larger studies for all main meta-analyses, and 30 (12.20%) had a significant test ($P < 0.10$) including 11 with statistically significant pooled ORs (*BCL2* rs2279115, *CHRNA3* rs938682, *CYP1A1* rs1048943, *ELANE* rs7254054 (-741G>A, Rep_b), *ERCC1* rs11615, *FGFR4* rs351855, *GSTM1* phenotype, *GSTP1* rs1695, *IL10* rs1800896, *MIR146A* rs2910164, and *MMP2* rs243865). To examine whether there were relative excess of formally significant findings in studies due to potential sources of bias, such as selective analyses, selective outcome reporting, and fabricated data, we performed an excess significance test. A total of 40 meta-analyses had evidence of inclusion of many individual studies reporting excess significant results (**Supplementary Table S1**). Among these 40 meta-analyses, seven had statistically significant pooled ORs with small effect sizes (mean pooled ORs 1.18, range 1.08-1.20). When the excess of significance was examined in aggregate across all studies enrolled in all main meta-analyses, there was significant evidence of existing excess significance ($P < 10^{-8}$), indicating potential bias existed in these published studies. A sensitivity analysis was performed to further assess the robustness of these results (**Supplementary Table S2**). Fourteen meta-analyses lost significance after removing the initial study. Of 17 meta-analyses with statistically significant pooled ORs, three became non-significant after removal of studies showing deviations from Hardy-Weinberg equilibrium (HWE).

Supplementary results of subgroup meta-analyses

Subgroup meta-analyses by ethnicity

Subgroup meta-analyses were conducted in Caucasian and Asian population under each of the three genetic models (allelic, dominant, or recessive model), respectively (**Table 3, Supplementary Table S3**). Among those 246 genetic variants investigated in main meta-analyses, there were 86 variants with sufficient available data for subgroup analyses in Caucasian and 71 variants in Asian population (**Supplementary Table S3**). In addition, 29 variants studied only in one specific ethnic population (17 variants in Caucasians and 12 in Asians) have been evaluated previously in the main meta-analyses (**Supplementary Table S1**). Thus, a total of 103 variants were evaluated in Caucasian population and 83 variants in Asian population.

In Caucasian population, 19 (22.1%) variants significantly associated with lung cancer risk. The strength of association between each variant and lung cancer as measured by ORs had the mean of 1.39 (range 1.07-1.99) for putative "risk" variants and 0.73 (range 0.59-0.92) for putative "protective" variants. Of the 19 significant variants, one (*HRAS1* a VNTR variation) showed strong genetic association (OR > 2), five (*CYP1A2* rs762551, *SFTPB* a combination variation [combined deletion and insertion], *CYP2A6* rs1801272, *CYP2E1* rs2031920, and *ELANE* rs351107 [-903T>G, Rep_a]) showed moderate genetic associations ("risk" ORs range 1.5-2.0, or "protective" ORs range 0.50-0.67), and the others showed low associations (ORs range 0.67-1.50) with lung cancer, including one variant (*CHRNA5* rs16969968) showed highly significant association with lung cancer risk with *P*-value at 2.03×10^{-21} (**Supplementary Table S4**). Of the 19 significant variants, 13 were identified from meta-analyses with little or no heterogeneity ($I^2 < 25\%$), four (*CYP1A2* rs762551, *ELANE* rs351107, *ELANE* rs7254054, and *XRCC1* rs1799782) were identified from meta-analyses with moderate heterogeneity ($25\% \leq I^2 \leq 50\%$), and two (*CYP1A1* rs1048943 and *HRAS1* a VNTR variation) were identified from meta-analyses with high heterogeneity. According to the examinations of potential bias (the Begg's test, modified Egger's test, and the excess significance test), significant associations for four variants (*CYP1A1* rs4646903, *SFTPB* variation, *ELANE* rs7254054, and *CYP1A1* rs1048943) had evidence of potential bias (publication bias, small study effects, or excess significance bias) (**Supplementary Table S4**). When the initial study was excluded, the association for four variants (*ELANE* rs351107 and rs7254054, *ERCC2* rs238406, and *HRAS1* a VNTR variation) was no longer statistical significant. When studies with HWE-violating controls were excluded, the association for two variants (*ERCC2* rs238406 and *MTHFR* rs1801131) was no longer statistical significant.

In Asian population, 26 (31.3%) variants showed significant associations with lung cancer. The strength of association between each genetic variant and lung cancer as measured by ORs had the mean of 1.27 (range 1.08-1.50) for putative "risk" variants and 0.76 (range 0.64-0.91) for putative "protective" variants. Of the 26 significant variants, one (*WWOX* CNV-67048) showed strong genetic association (OR > 2), three (*MAPKAPK2* CNV-30450, *CYP2A6* non*4/*4, and *VEGFA* rs833061) showed moderate genetic associations ("risk" ORs range 1.5-2.0, or "protective" ORs range 0.50-0.67), and the other 22 variants showed low genetic associations (ORs range 0.67-1.50) with lung cancer (**Supplementary Table S4**). Of the 26 significant variants, 14 were identified from meta-analyses with little or no heterogeneity ($I^2 <$ 25%), four (*ATM* rs189037, *CHRNA3* rs6495309, *GSTP1* rs1695, and *GSTT1* present/null) were identified from meta-analyses with moderate heterogeneity (25% $\leq I^2 \leq$ 50%), and eight (*CYP1A1* rs4646903, *CYP1A1* rs1048943, *GSTM1* present/null, *IL10* rs1800872, *MAPKAPK2* CNV-30450, *MDM2* rs2279744, *XRCC1* rs25487, and *XRCC1* rs3213245) were identified from meta-analyses with high heterogeneity. Among the 26 significant variants, two (*CYP1A1* rs4646903 and *MDM2* rs2279744) had associations showing evidence of potential bias of small study effects and three (*CYP1A*1 rs1048943, *GSTM1* present/null, and *XRCC1* rs25487) had associations showing evidence of inclusion of studies with excess of significant findings and statistically significant pooled ORs with small effect sizes (mean pooled ORs 1.23, range 1.05-1.43) (**Supplementary Table S4**). When initial study was excluded, the association for seven variants (*AGER* rs1800624, *CYP1A1* rs4646903, *FASLG* rs763110, *IL10* rs1800872, *VEGFA* rs833061, *XRCC1* rs25487 and rs3213245) was no longer significant. When studies with HWE-violating controls were excluded, the association for one variant (*XRCC1* rs25487) was no longer significant.

Subgroup meta-analyses by histological types of lung cancer

Subgroup meta-analyses stratified by histological types of lung cancer were performed under each of the three genetic models (allelic, dominant, or recessive model) (**Supplementary Table S5**). There was sufficient data to evaluate 22 variants in small cell lung cancer [SCLC], 92 in non-small cell lung cancer [NSCLC], 48 in adenocarcinoma [AD], and 46 in squamous cell carcinoma [SCC] group, respectively.

In the SCLC subgroup, statistical significant associations were found for five variants, where three (*CHRNA5* rs16969968, *CYP1A1* rs4646903, and *NQO1* rs1800566) and two (*GSTM1* present/null and *XPC* rs2228001) showed moderate genetic associations (ORs range 1.5-2.0) and low genetic associations (ORs range 0.67-1.50) with lung cancer risk, respectively (**Supplementary Table S6**). Of these significant variants, two (*CYP1A1* rs4646903 and *XPC* rs2228001) were identified from meta-analyses with little or no heterogeneity ($I^2 < 25\%$), one (*GSTM1* present/null) was identified from meta-analysis with moderate heterogeneity (25% ≤

$I^2 \leq 50\%$), and two (*CHRNA5* rs16969968 and *NQO1* rs1800566) were identified from meta-analyses with high heterogeneity. Based on the examinations of potential bias, one variant (*CHRNA5* rs16969968) had association with evidence of potential bias of small study effects. Based on the sensitivity analyses, the association for two variants (*NQO1* rs1800566 and *XPC* rs2228001) was no longer significant after removing the initial study.

In the NSCLC subgroup, 25 (27.2%) variants showed significant associations with lung cancer. The strength of these associations as measured by ORs had the mean of 1.37 (range 1.11-1.73) for putative "risk" variants and 0.77 (range 0.65-0.91) for putative "protective" variants. Of the 25 significant variants, five (*FAS* rs2234767, *IL17A* rs2275913, *TNF* rs1800629, *XRCC1* rs2256507, and *MMP2* rs243865) showed moderate genetic associations ("risk" ORs range 1.5-2.0, or "protective" ORs range 0.50-0.67) and 25 variants showed low genetic associations (ORs range 0.67-1.50) with lung cancer where two variants (*CHRNA5* rs16969968 and *XRCC1* rs3213245) showed highly significant associations ($P < 10^{-7}$) with lung cancer risk (**Supplementary Table S6**). Of the 25 significant variants, 14 were identified from meta-analyses with little or no heterogeneity ($I^2 < 25\%$), four (*ERCC2* rs13181, *IL17A* rs2275913, *OGG1* rs1052133, and *XRCC1* rs1001581) were identified from meta-analyses with moderate heterogeneity ($25\% \leq I^2 \leq 50\%$), and seven (*GSTM1* present/null, *IL1B* rs1143627, *IL6* rs1800796, *MMP2* rs243865, *MPO* rs2333227, *SOD2* rs4880, and *TNF* rs1800629) were identified from meta-analyses with high heterogeneity. Based on the further examinations of potential bias, evidence of publication bias, potential bias of small study effects, inclusion of studies with excess significant findings, was found for one variant (*IL1B* rs1143627), four variants (*IL1B* rs1143627, *IL6* rs1800796, *MMP2* rs243865, and *SOD2* rs4880), and one variant (*OGG1* rs1052133) with association of small effect size (OR 1.16, 95%CI 1.02-1.32), respectively (**Supplementary Table S6**). When initial study was excluded, association for five variants (*FAS* rs2234767, *IL1B* rs1143627, *MMP2* rs243865, *TNF* rs1800629, and *XRCC1* rs1001581) was no longer significant. When sensitivity analyses removing studies with HWE-violating controls, two variants (*ERCC2* rs13181 and *IL1B* rs1143627) became non-significant.

In the AD subgroup, 15 (31.3%) variants significantly associated with lung cancer risk. The strength of associations between each genetic variant and lung cancer as measured by ORs had the mean of 1.37 (range 1.11-1.70) for putative "risk" variants and 0.81 (range 0.71-0.93) for putative "protective" variants. Of the 15 significant variants, three (*BIRC5* rs9904341, *IL17A* rs2275913, and *XRCC1* rs3213245) showed moderate genetic associations (ORs range 1.5-2.0) and 12 variants showed low associations (ORs range 0.67-1.50) with lung cancer where one (*TERT* rs2736098) showed highly significant association ($P = 4.97 \times 10^{-11}$) (**Supplementary Table S6**). Of the 15 significant variants, ten were identified from meta-analyses with little or no heterogeneity ($I^2 < 25\%$), four (*CHRNA5* rs16969968, *GSTM1* present/null, *IL17A* rs2275913, and *MDM2* rs2279744) were identified from meta-analyses with moderate heterogeneity ($25\% \le I^2 \le 50\%$), and one (*BIRC5* rs9904341) was identified from meta-analysis with high heterogeneity. Based on the examinations of potential bias, only one variant (*GSTM1* present/null) had association with evidence of potential bias of small study effect and inclusion of excess significant findings. When the initial study was excluded, the association for three variants (*MIR146A* rs2910164, *SOD2* rs4880, and *XPC* PAT-/+) was no longer significant. When studies included HWE-violating controls were excluded, the association for two variants (*ERCC2* rs238406 and *MTHFR* rs1801131) was no longer significant.

In the SCC subgroup, statistical significant associations were found for eight variants, where three (*SOD2* rs4880, *TNF* rs1800629, and *MMP2* rs243865) and five (*CYP1A1* rs4646903 and rs1048943, *GSTM1* present/null, *TERT* rs2736098, and *CYP2E1* rs6413432) showed moderate genetic associations ("risk" ORs range 1.5-2.0, or "protective" ORs range 0.50-0.67) and low genetic associations (ORs range 0.67-1.50) with lung cancer risk, respectively (**Supplementary Table S6**). Of note, one variant (*CYP1A1* rs4646903) with association showed low strength (OR 1.45, 95%CI 1.26-1.67) but had highly statistical significant ($P = 3.77\times10^{-7}$). Of the eight significant variants, three (*CYP1A1* rs4646903, *CYP2E1* rs6413432, and *TERT* rs2736098) were identified from meta-analyses with little or no heterogeneity ($I^2 <$ 25%) and five (*CYP1A1* rs1048943, *GSTM1* present/null, *MMP2* rs243865, *SOD2* rs4880, and *TNF* rs1800629) were identified from meta-analyses with high heterogeneity. Two variants (*CYP1A1* rs1048943 and *MMP2* rs243865) had associations with evidence of potential bias of small study effects and one variant (*GSTM1* present/null) had association of small effect size (OR 1.23, 95%CI 1.08-1.40) with evidence of potential bias of inclusion of excess significant findings. Based on the sensitivity analyses, three variants (*MMP2* rs243865, *SOD2* rs4880, and *TNF* rs1800629) lost significant associations with lung cancer risk after relative meta-analysis removing the initial study.

Subgroup meta-analyses by smoking status

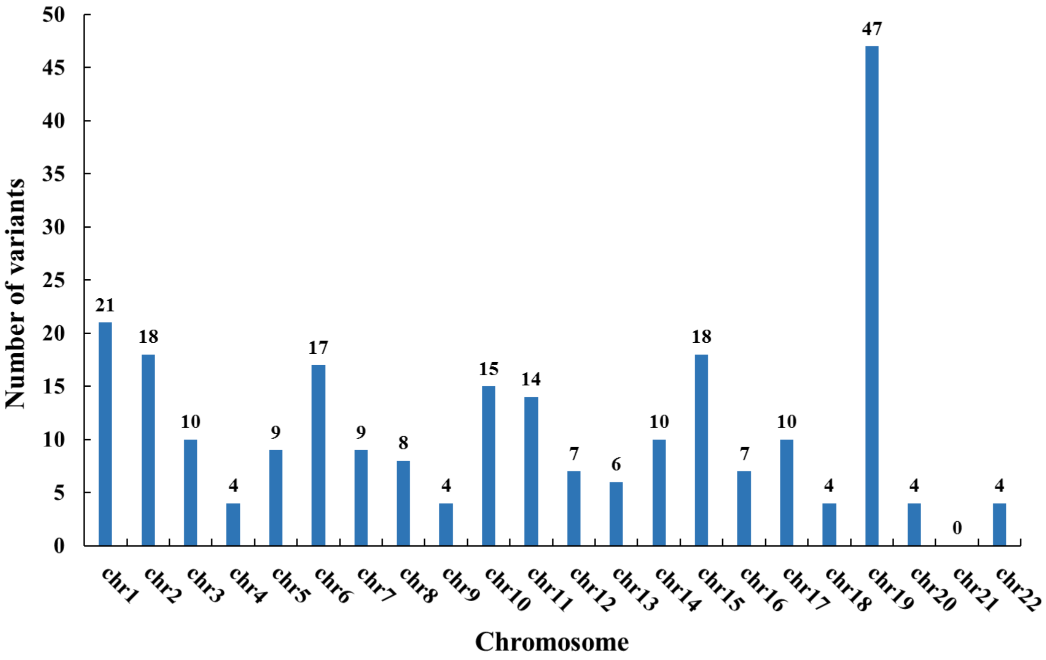
Subgroup meta-analyses by smoking status were conducted separately in smokers and non-smokers under each of the three genetic models (allelic, dominant, or recessive model), if sufficient data were available. Sixty variants were evaluated in smokers and thirty-eight variants in non-smokers (**Supplementary Table S7**).

In smokers, 22 (36.7%) variants significantly associated with lung cancer. The strength of association between each genetic variant and lung cancer as measured by ORs had the mean of 1.32 (range 1.07-1.64) for putative "risk" variants and 0.74 (range 0.58-0.95) for putative "protective" variants (**Supplementary Table S8**). Of the 22 significant variants, two (*GSTP1* rs1138272 and *CYP2A6* rs5031016) showed moderate genetic associations ("risk" ORs range 1.5-2.0, or "protective" ORs range 0.50-0.67) and 20 showed low associations (ORs range 0.67-1.50) with lung cancer, including one variant (*CHRNA5* rs16969968) showed highly significant association ($P = 2.77\times10^{-10}$). Of the 22 significant variants, 12 were identified from meta-analyses with little or no heterogeneity ($I^2 < 25\%$), five (*APEX1* rs1760944, *CYP1A1* rs4646903, *SOD2* rs4880, *XRCC1* rs1799782 and rs25487) were identified from meta-analyses with moderate heterogeneity ($25\% \leq I^2 \leq 50\%$), and five (*CYP1A1* rs1048943, *CYP2A6* rs5031016, *GSTM1* present/null, *GSTP1* rs1695, and *TP53* rs1042522) were identified from meta-analyses with high heterogeneity. Of the 22 significant variants, five (*CHRNA5* rs16969968, *CYP1A1* rs1048943, *GSTM1* present/null, *NAT2* rs1799930, and *XRCC1* rs25489) were identified from meta-analyses showing evidence of potential bias of small study effects and two (*CYP1A1* rs1048943 and *TP53* rs1042522) were identified from meta-analyses showing evidence of inclusion of studies with excess significant findings and having small summary ORs (OR 1.42, 95%CI 1.04-1.93, association for *CYP1A1* rs1048943;

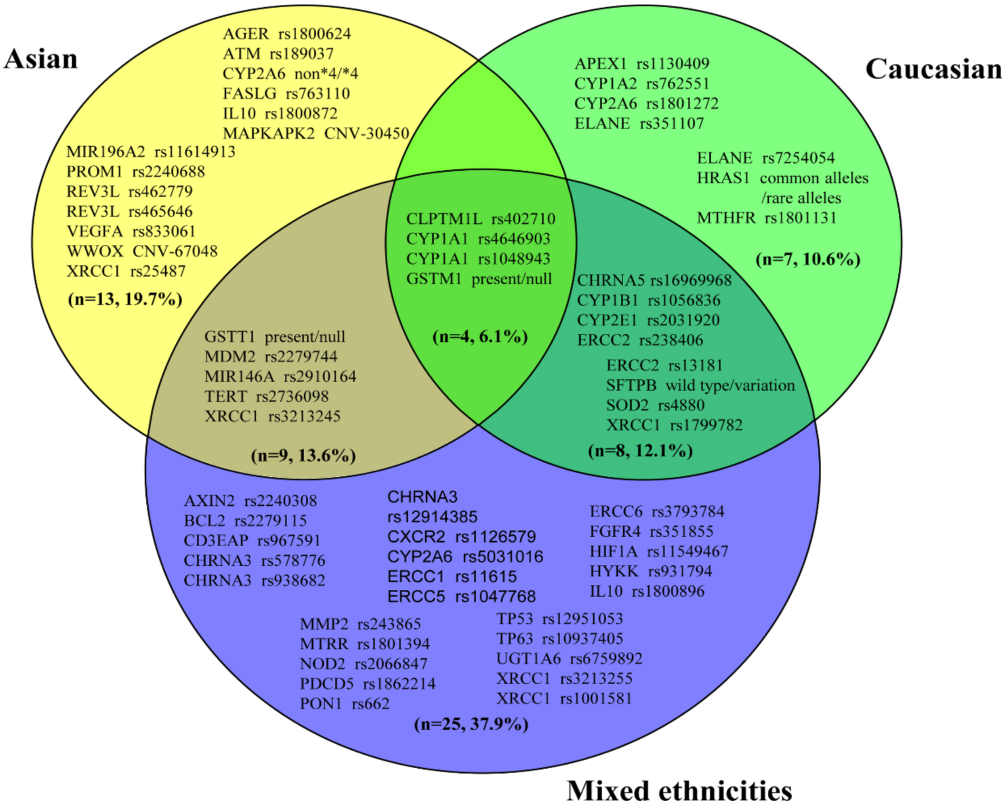
OR 1.23, 95%CI 1.01-1.50, association for *TP53* rs1042522). When sensitivity analyses removing the initial study, 11 (*CYP1A1* rs1048943, *CYP1B1* rs1800440 and rs1056836, *CYP2A6* rs5031016, *EPHX1* rs2234922, *MTHFR* rs1801131, *SOD2* rs4880, *TP53* rs1042522, *XRCC1* rs25489, rs1799782, and rs25487) of 22 significant variants became non-significant. When sensitivity analyses removing studies with HWE-violating controls, four variants (*CYP1A1* rs1048943, *XRCC1* rs25489, rs1799782, and rs25487) became non-significant.

In non-smokers, statistical significant associations were found for ten variants, where two (*CYP1A1* rs1048943 and *ERCC2* rs13181) and eight (*ATM* rs189037, *GSTM1* present/null, *OGG1* rs1052133, *TP53* rs1042522, *XRCC1* rs3213245, *CYP2E1* rs6413432, rs2031920, and *ERCC1* rs11615) showed moderate genetic associations (ORs range 1.5-2.0) and low genetic associations (ORs range 0.67-1.50) with lung cancer risk, respectively (**Supplementary Table S8**). Of the ten significant variants, six (*CYP2E1* rs6413432 and rs2031920, *ERCC1* rs11615, *ERCC2* rs13181, *OGG1* rs1052133, and *XRCC1* rs3213245) and four (*ATM* rs189037, *CYP1A1* rs1048943, *GSTM1* present/null, and *TP53* rs10425220) were identified from meta-analyses with little or no heterogeneity ($I^2 < 25\%$) and moderate heterogeneity ($25\% \leq I^2 \leq 50\%$), respectively. Of the ten significant variants, the variant (*OGG1* rs1052133) and variant (*ATM* rs189037) were identified from meta-analyses showing evidence of potential publication bias and bias of small study effects, respectively (**Supplementary Table S8**). Based on the sensitivity analyses, two variants (*ATM* rs189037 and *CYP1A1* rs1048943) became non-significant associations with lung cancer risk after relative meta-analysis removing the initial study.

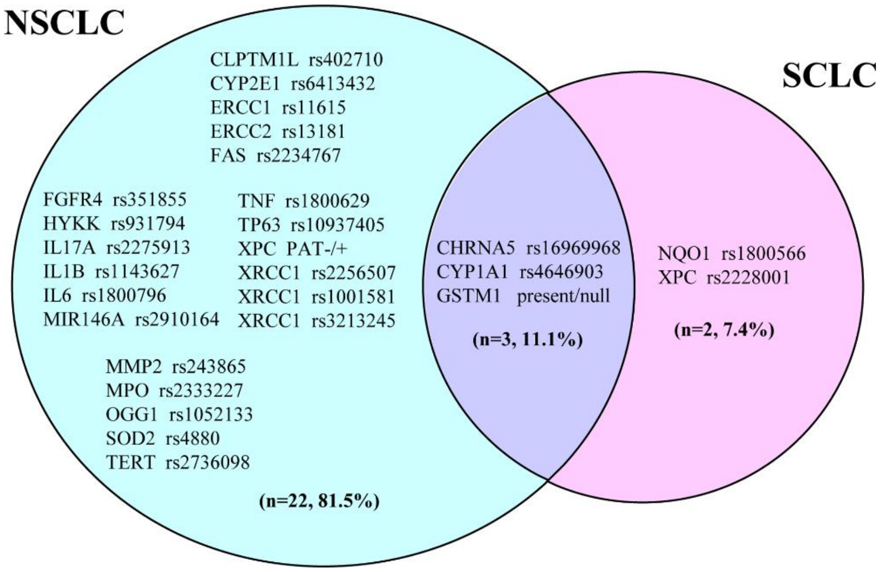
Supplementary Figures



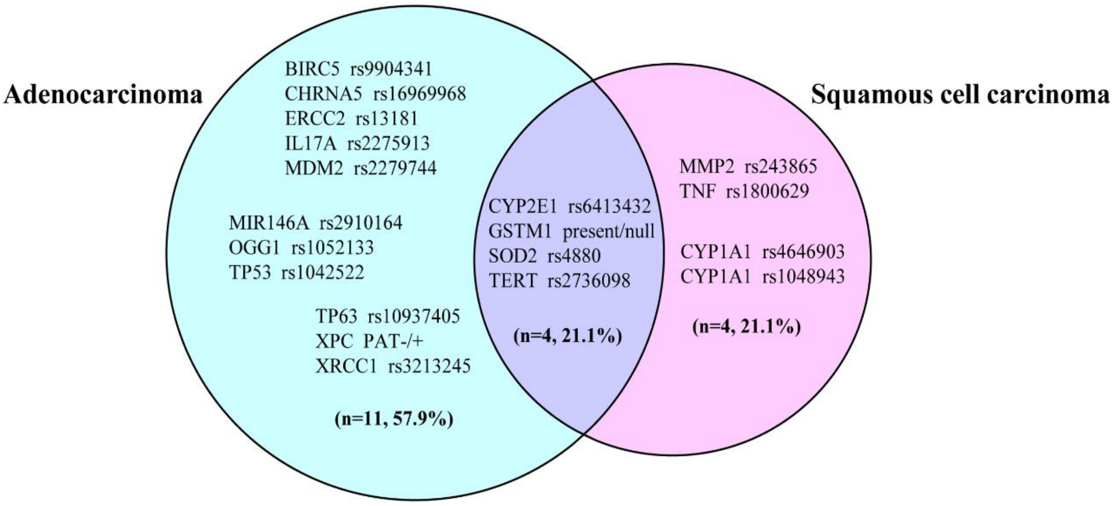
Supplementary Figure S1. Distribution by chromosome of 246 genetic variants available for meta-analyses.



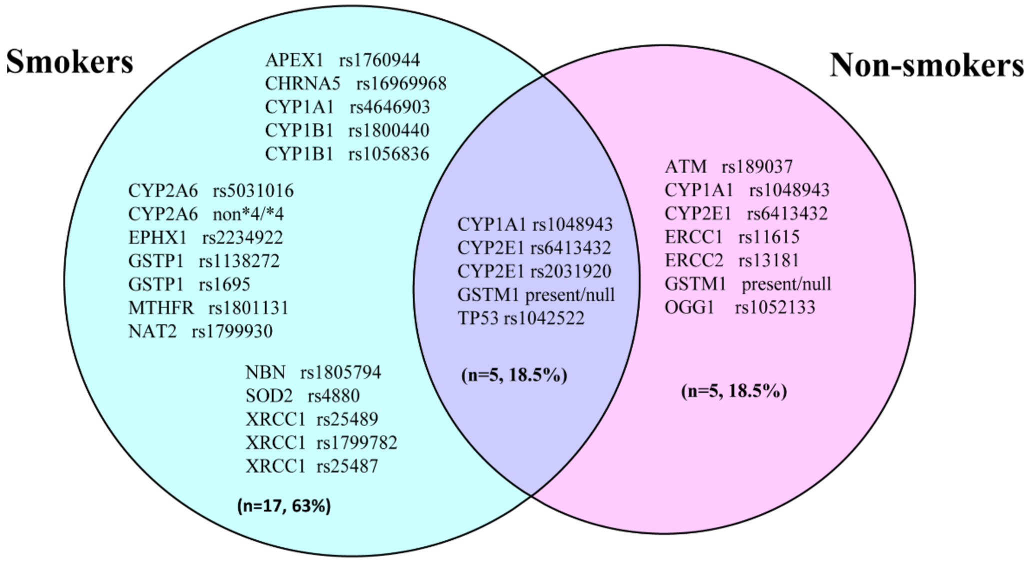
Supplementary Figure S2. Venn diagram of the distributions of genetic variants with significant associations with lung cancer risk in the main meta-analyses and subgroup meta-analyses by ethnicity (Asian and Caucasian).



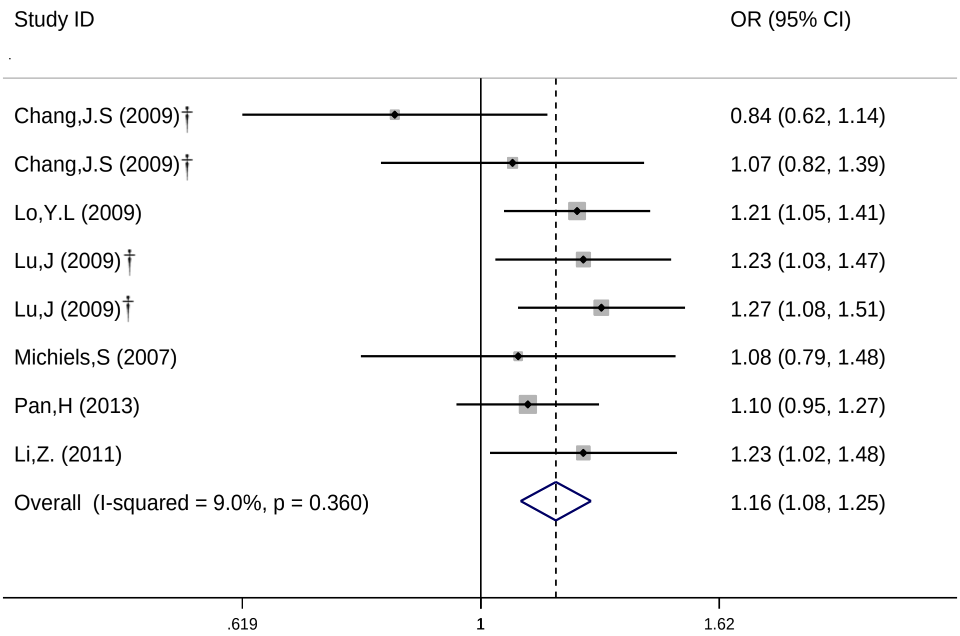
Supplementary Figure S3. Venn diagram of the distributions of genetic variants with significant associations with specific histological types of lung cancer. NSCLC: non-small cell lung cancer; SCLC: small cell lung cancer.



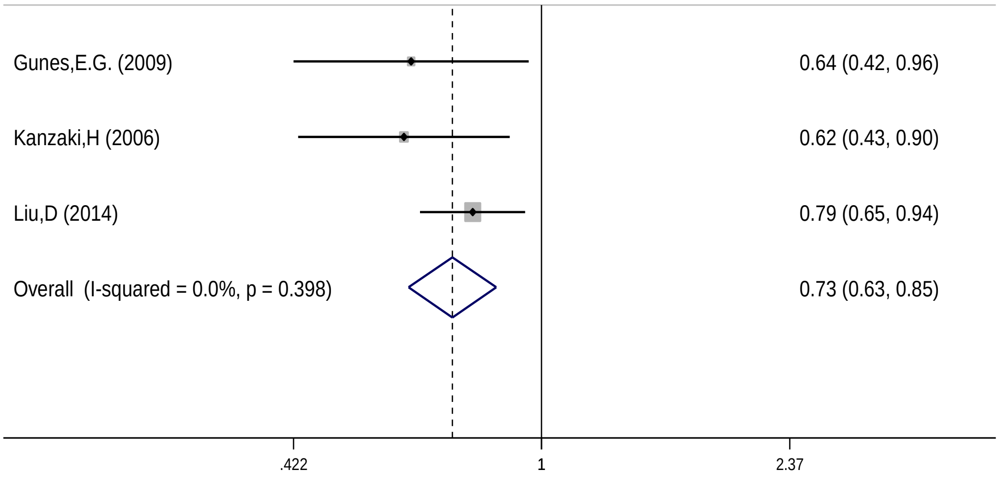
Supplementary Figure S4. Venn diagram of the distributions of genetic variants with significant associations with lung adenocarcinoma and squamous cell carcinoma.



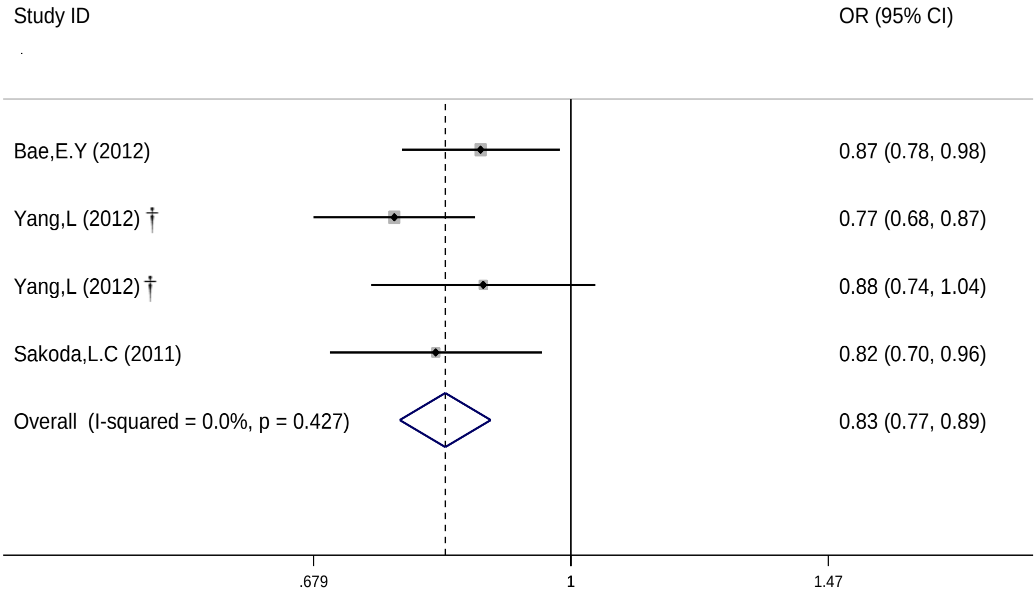
Supplementary Figure S5. Venn diagram of the distributions of genetic variants with significant associations in subgroup meta-analyses of smoker and non-smoker.



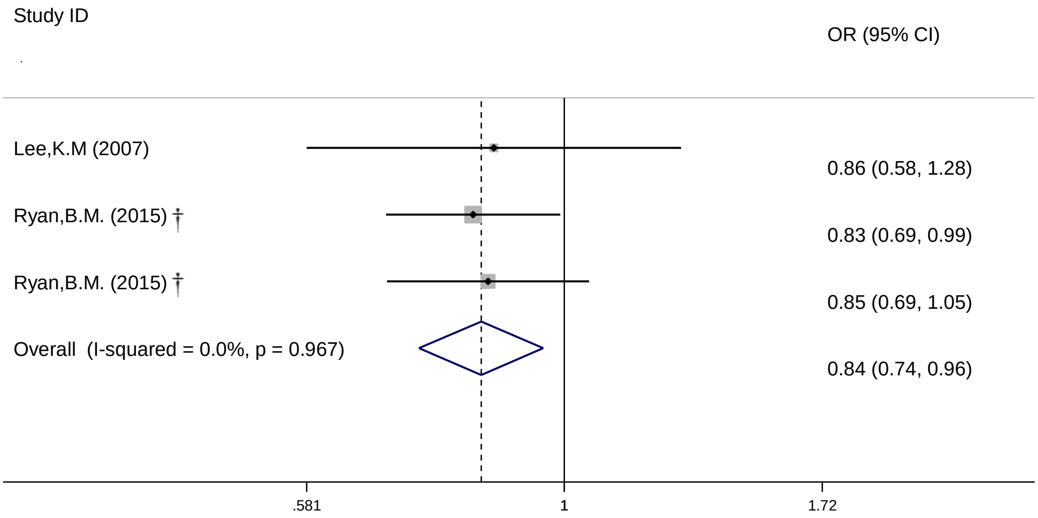
Supplementary Figure S6.1. Main meta-analysis of *APEX1* rs1760944 (allelic contrast: A vs. C).



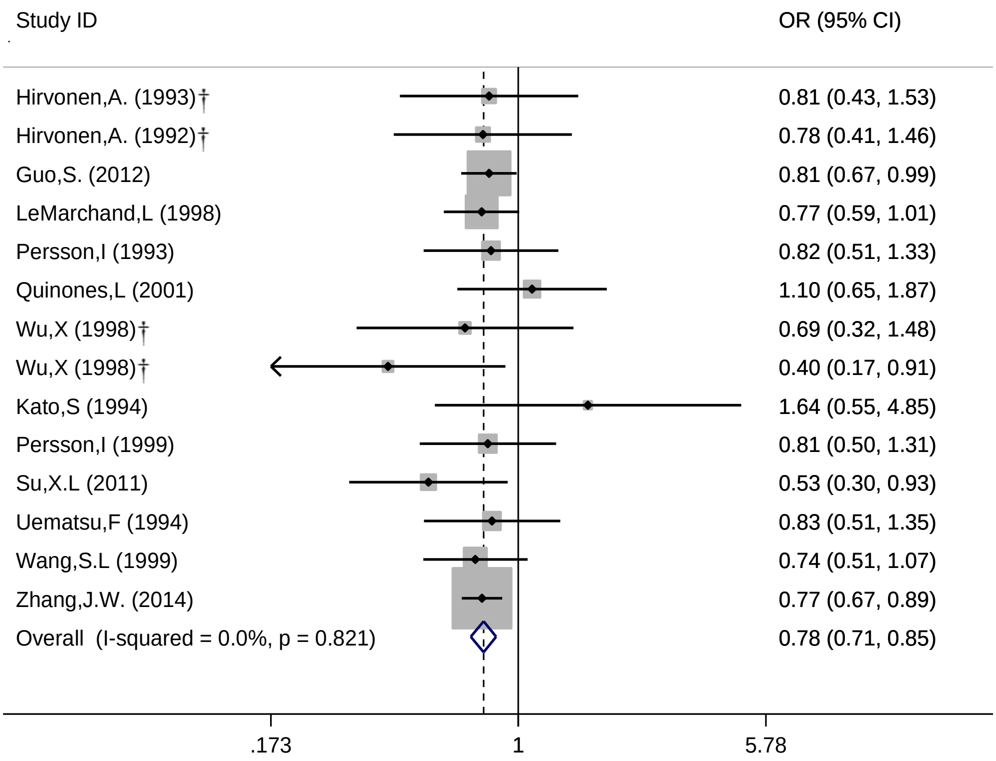
Supplementary Figure S6.2. Main meta-analysis of *AXIN2* rs2240308 (allelic contrast: T vs. C).



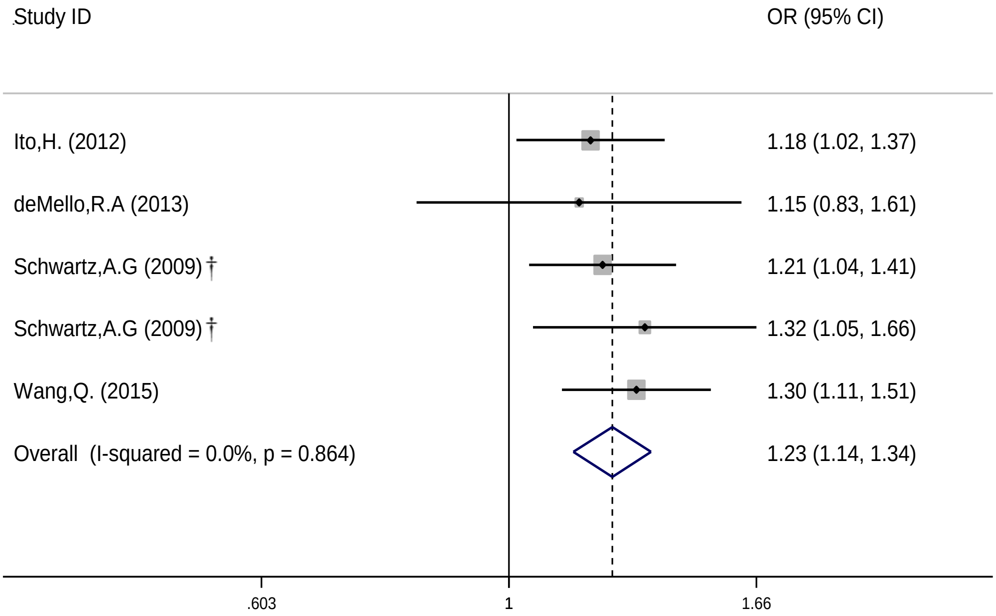
Supplementary Figure S6.3. Main meta-analysis of *CHRNA3* rs6495309 (allelic contrast: T vs. C).



Supplementary Figure S6.4. Main meta-analysis of *CXCR2* rs1126579 (allelic contrast: T vs. C).

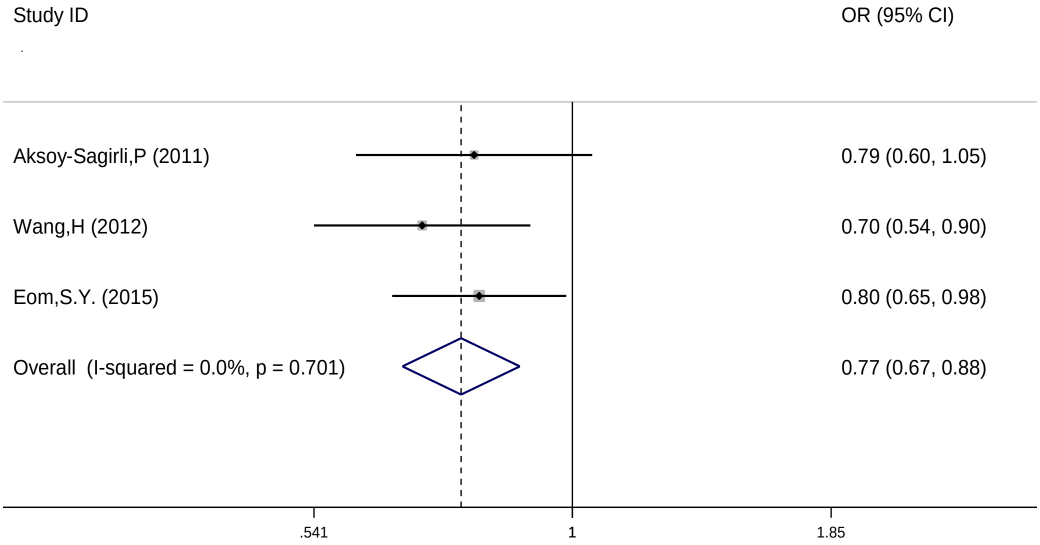


Supplementary Figure S6.5. Main meta-analysis of *CYP2E1* rs6413432 (allelic contrast: A vs. T).

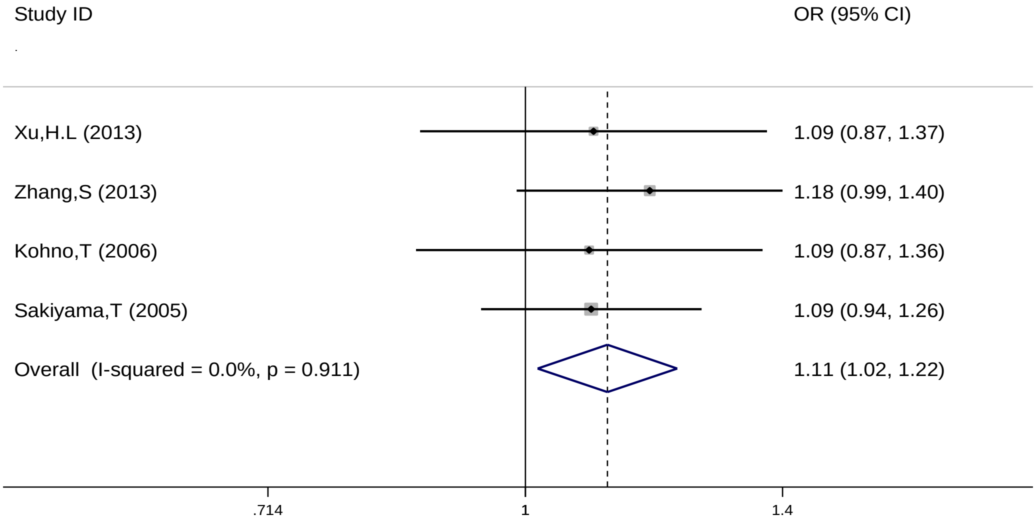


Supplementary Figure S6.6. Main meta-analysis of *HYKK* rs931794 (allelic contrast:

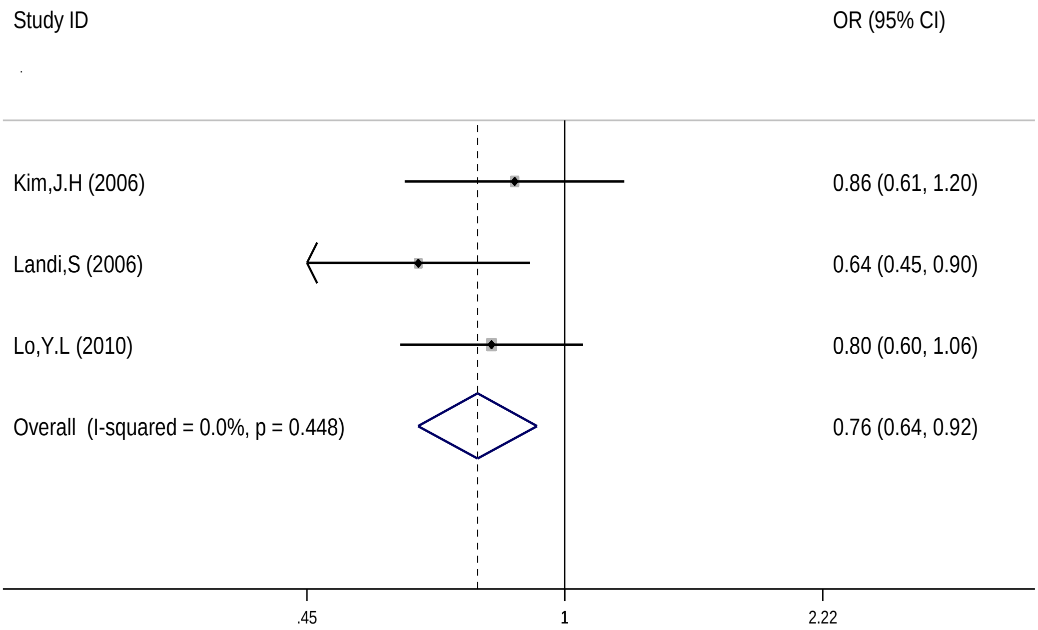
G vs. A).



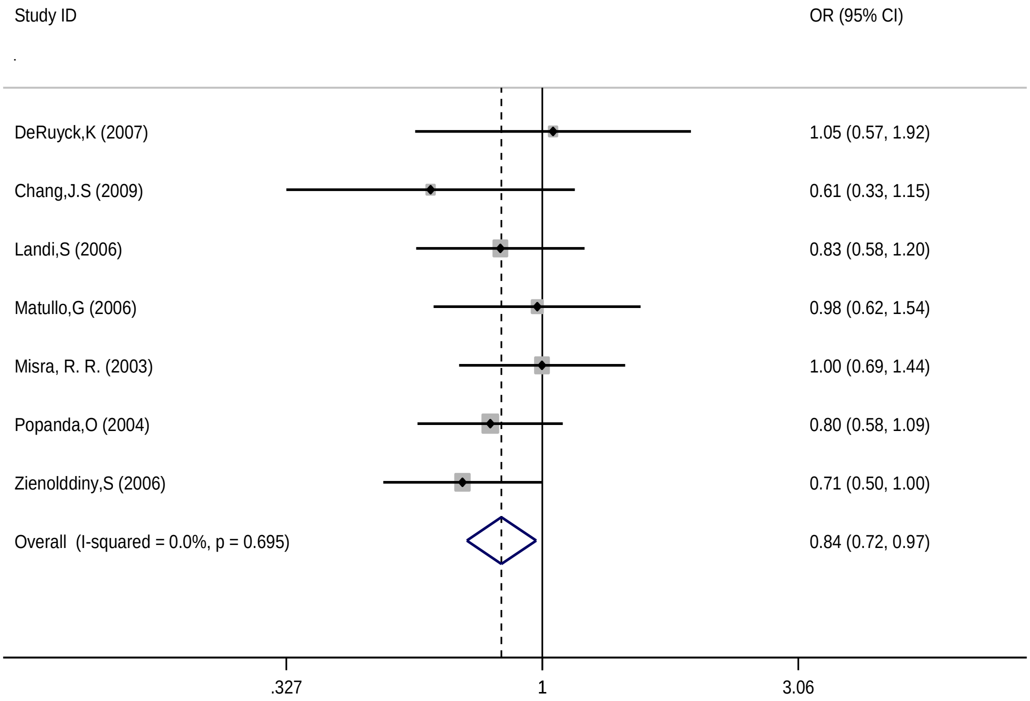
Supplementary Figure S6.7. Main meta-analysis of *PON1* rs662 (allelic contrast: A vs. G).



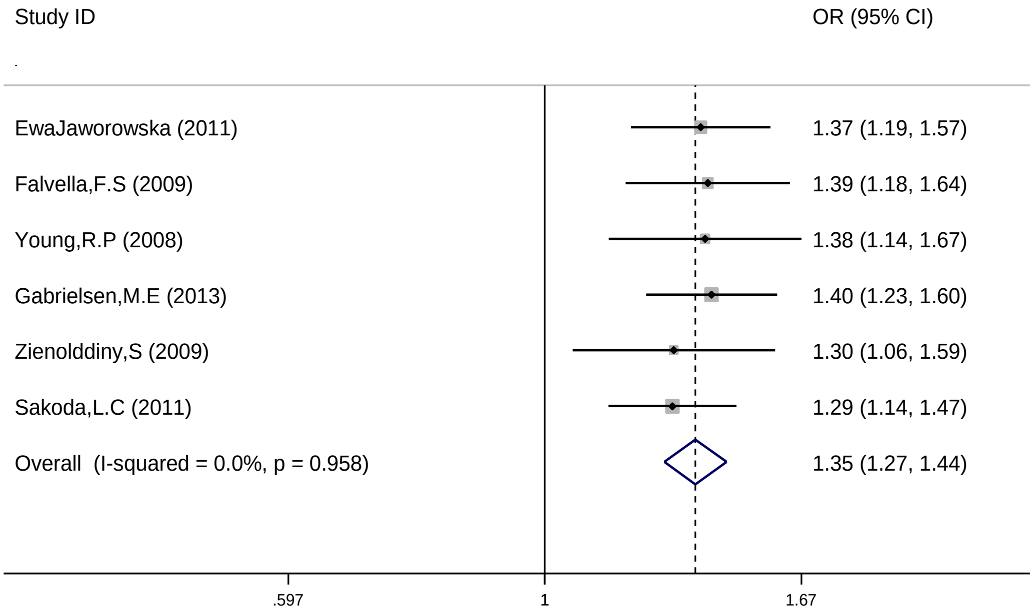
Supplementary Figure S6.8. Main meta-analysis of *REV3L* rs462779 (allelic contrast: T vs. C). (Available data were limited to Asian populations.)



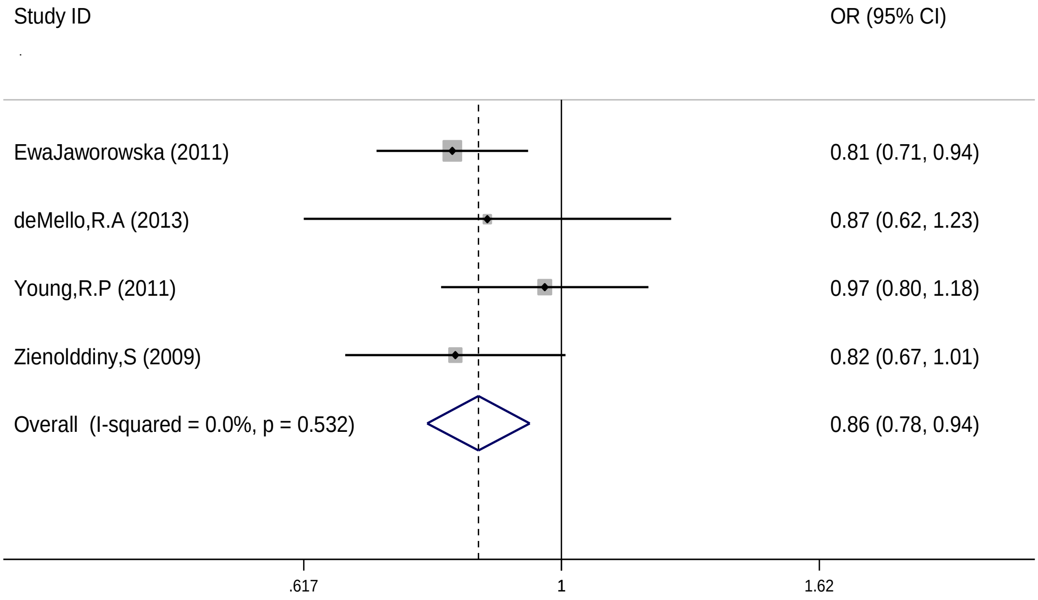
Supplementary Figure S6.9. Meta-analysis of *ATM* rs664677 (Dominant: CC+CT vs. TT).



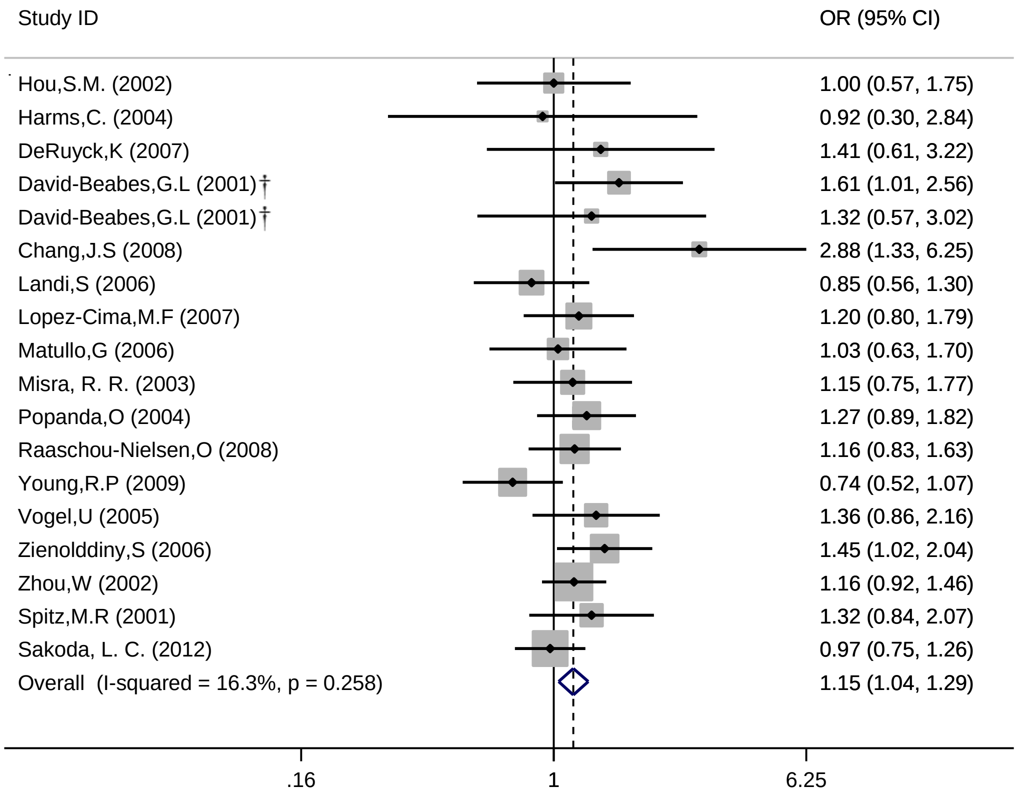
Supplementary Figure S6.10. Subgroup meta-analysis of *APEX1* rs1130409 in Caucasian (Recessive: TT vs. GG+GT).



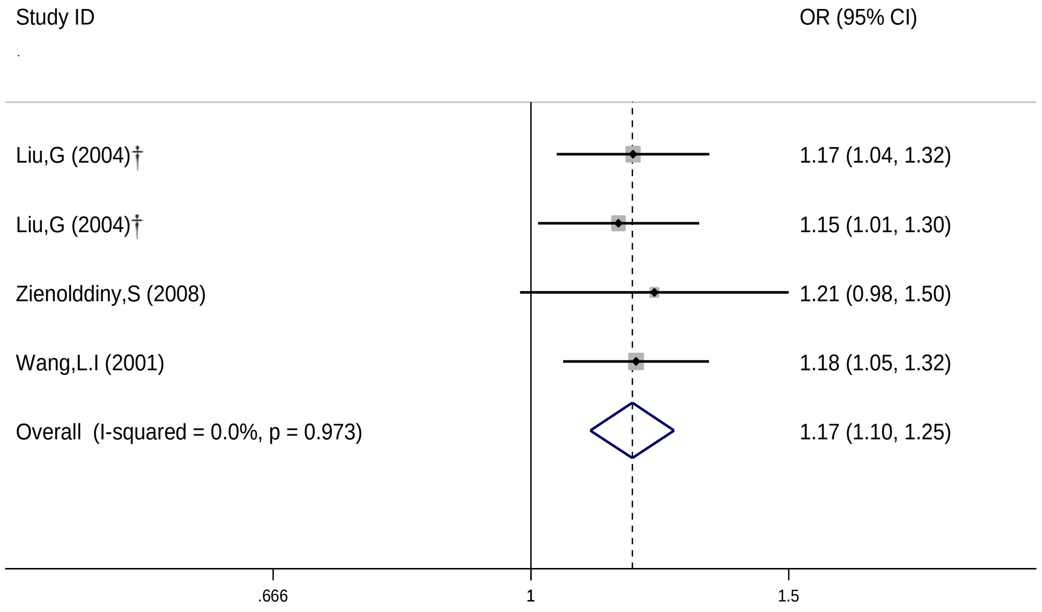
Supplementary Figure S6.11. Subgroup meta-analysis of *CHRNA5* rs16969968 in Caucasian (allelic contrast: A vs. G).



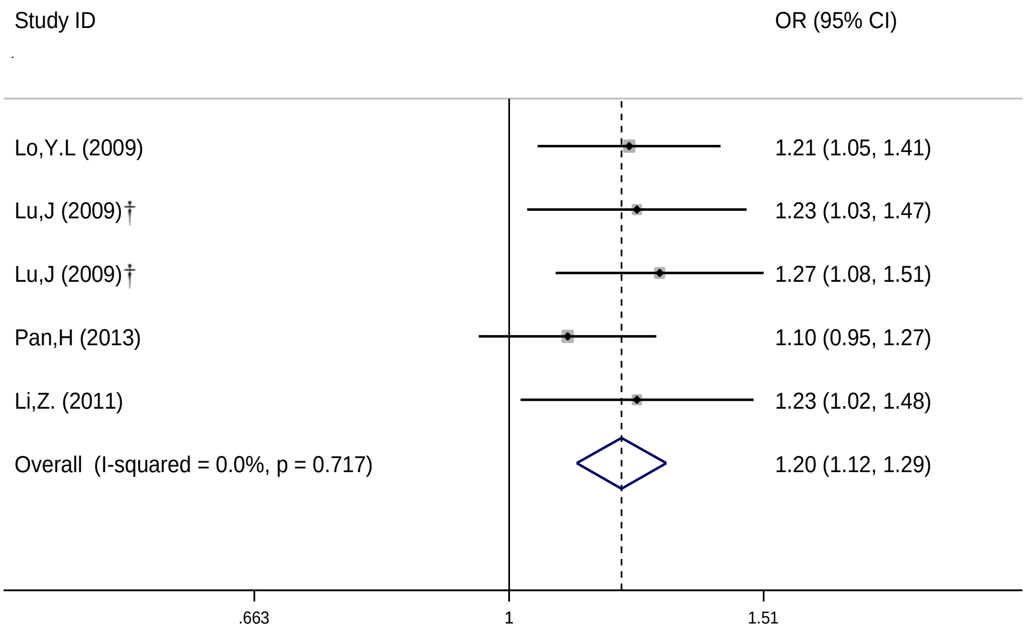
Supplementary Figure S6.12. Subgroup meta-analysis of *CLPTM1L* rs402710 in Caucasian (allelic contrast: T vs. C).



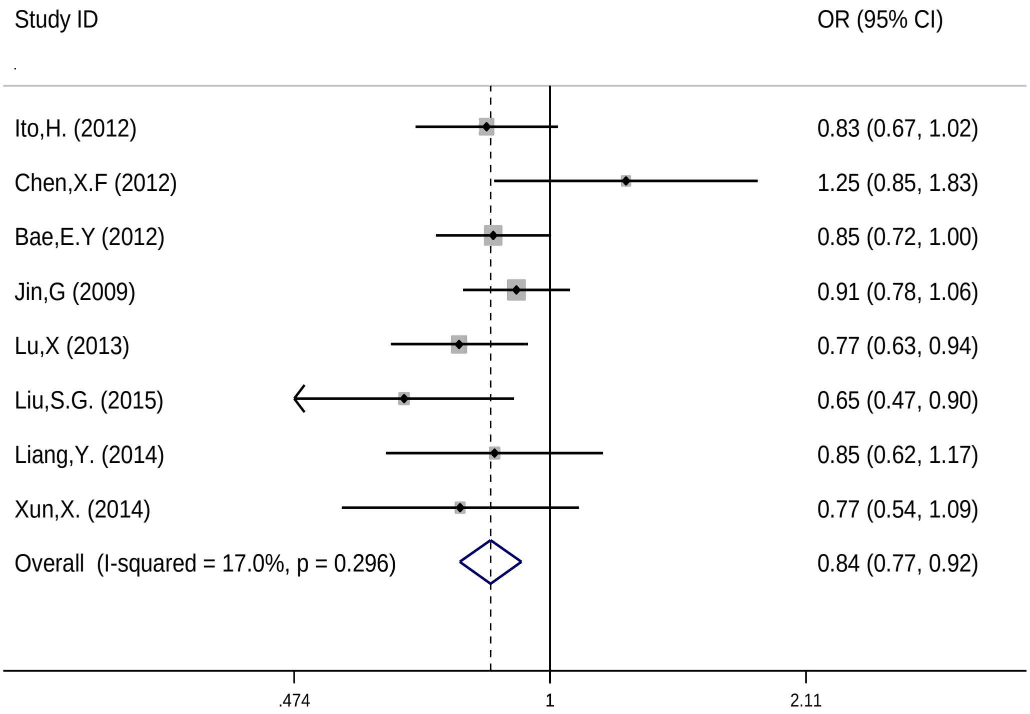
Supplementary Figure S6.13. Subgroup meta-analysis of *ERCC2* rs13181 in Caucasian (Recessive: AA vs. CC+CA).



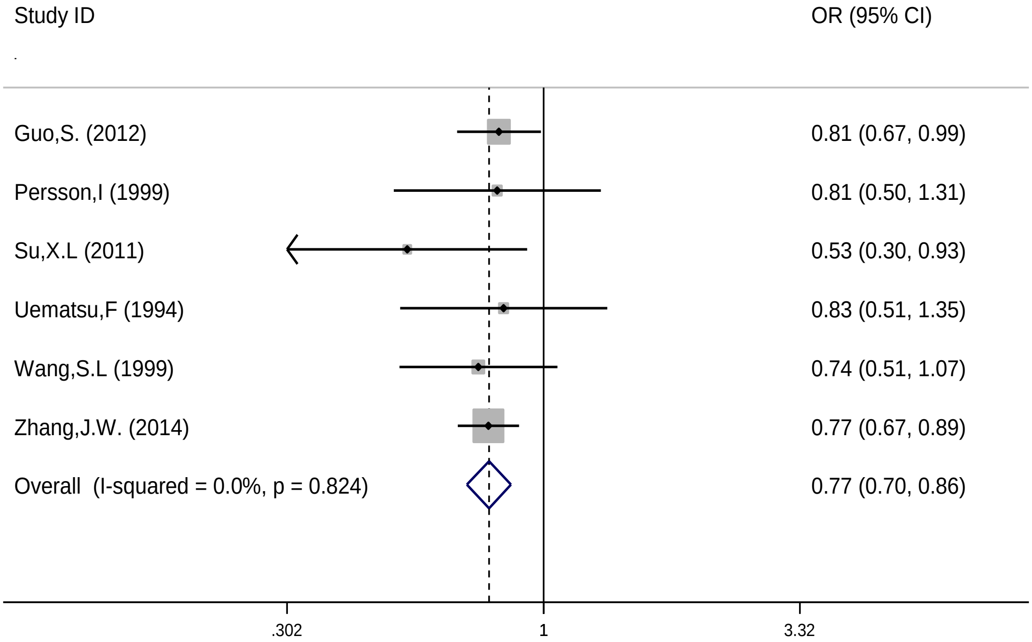
Supplementary Figure S6.14. Subgroup meta-analysis of *SOD2* rs4880 in Caucasian (allelic contrast: T vs. C).



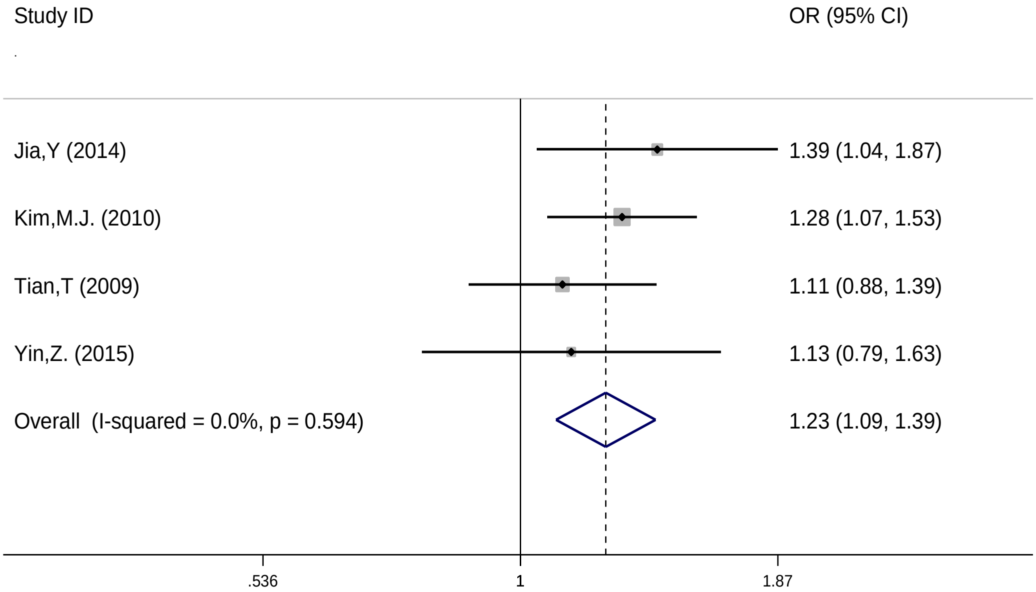
Supplementary Figure S6.15. Subgroup meta-analysis of *APEX1* rs1760944 in Asian (allelic contrast: A vs. C).



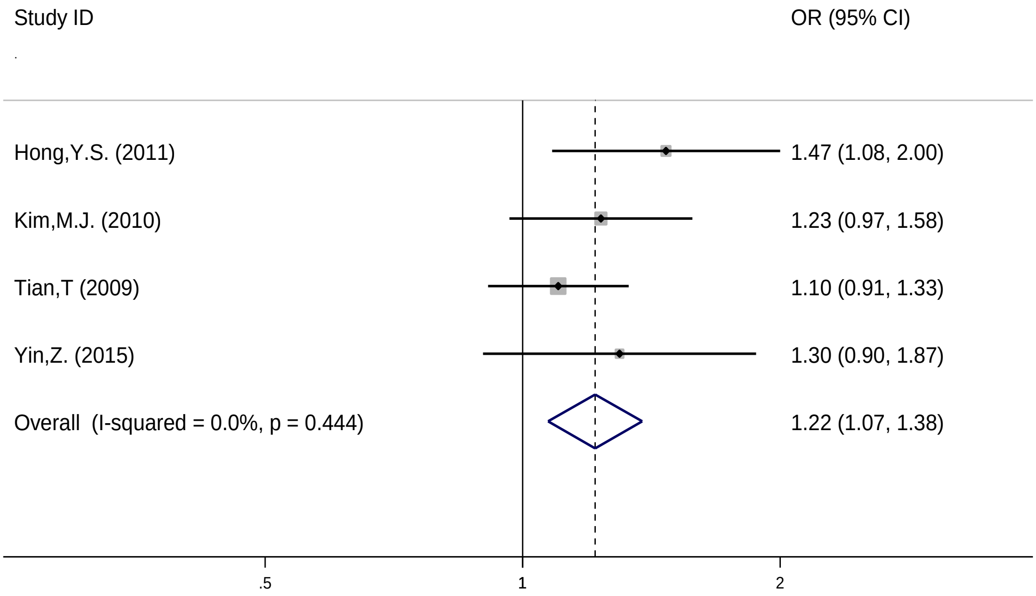
Supplementary Figure S6.16. Subgroup meta-analysis of *CLPTM1L* rs402710 in Asian (Dominant: TT+TC vs. CC).



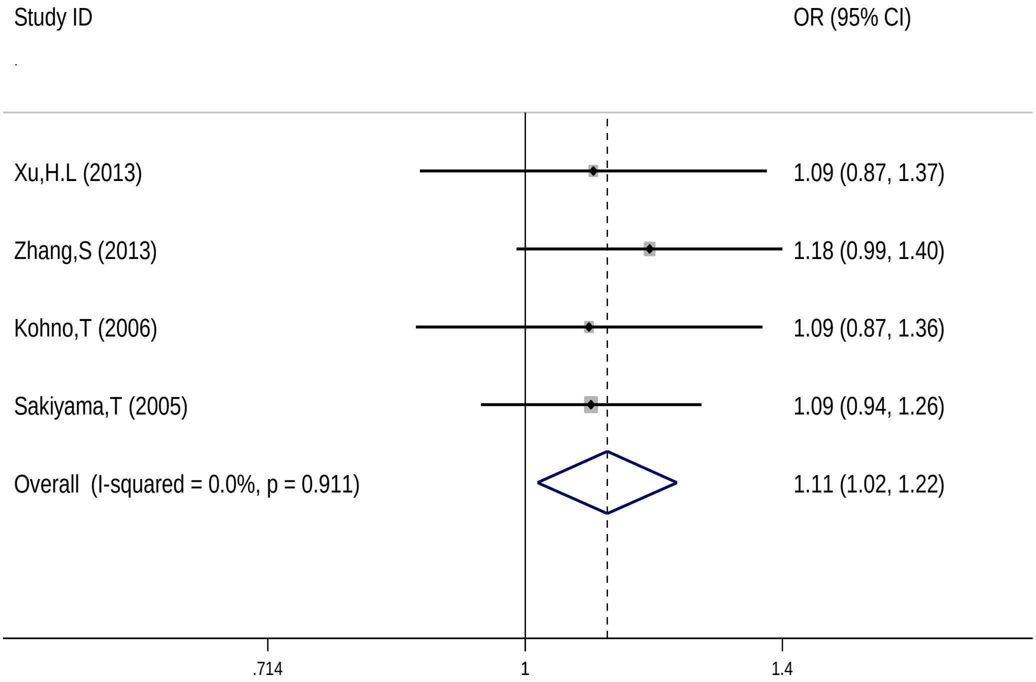
Supplementary Figure S6.17. Subgroup meta-analysis of *CYP2E1* rs6413432 in Asian (allelic contrast: A vs. T).



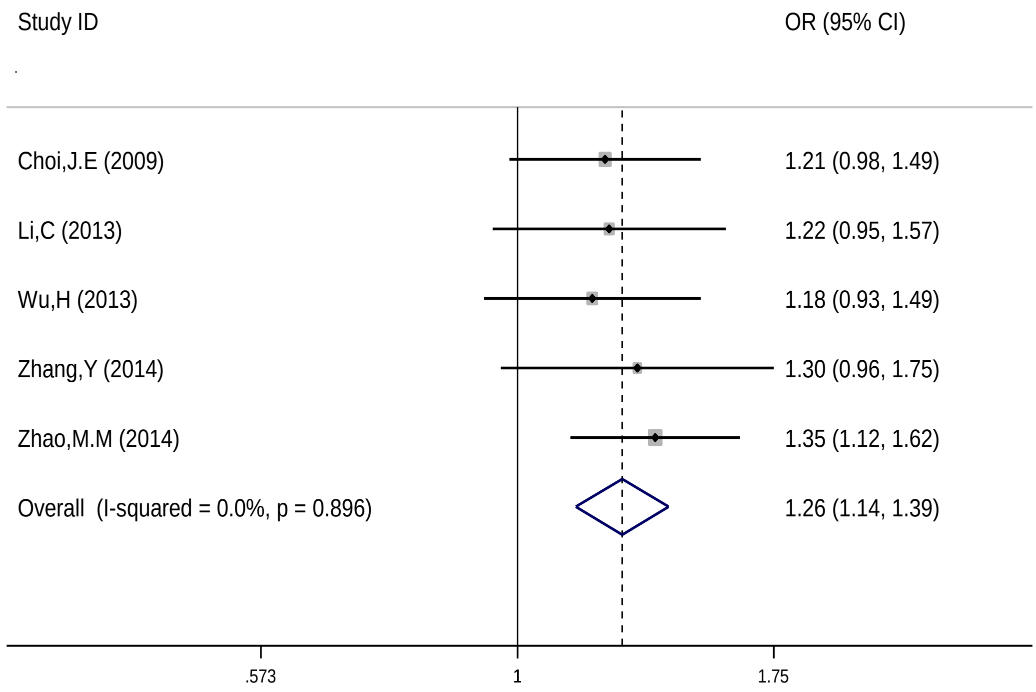
Supplementary Figure S6.18. Subgroup meta-analysis of *MIR146A* rs2910164 in Asian (Recessive: GG vs. CC+CG).



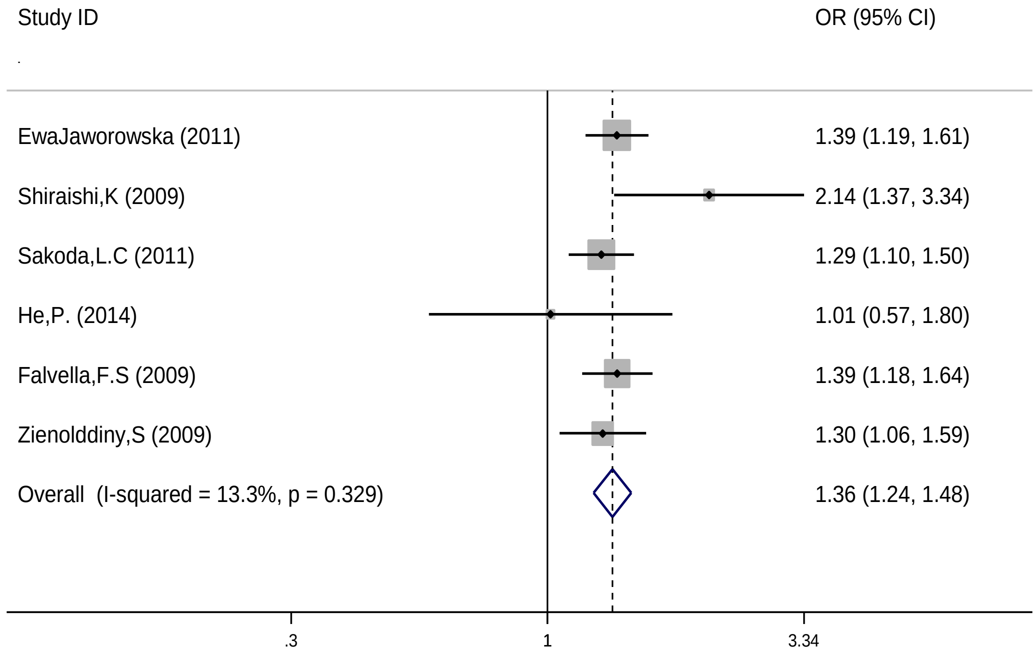
Supplementary Figure S6.19. Subgroup meta-analysis of *MIR196A2* rs11614913 in Asian (Dominant: CC+CT vs. TT).



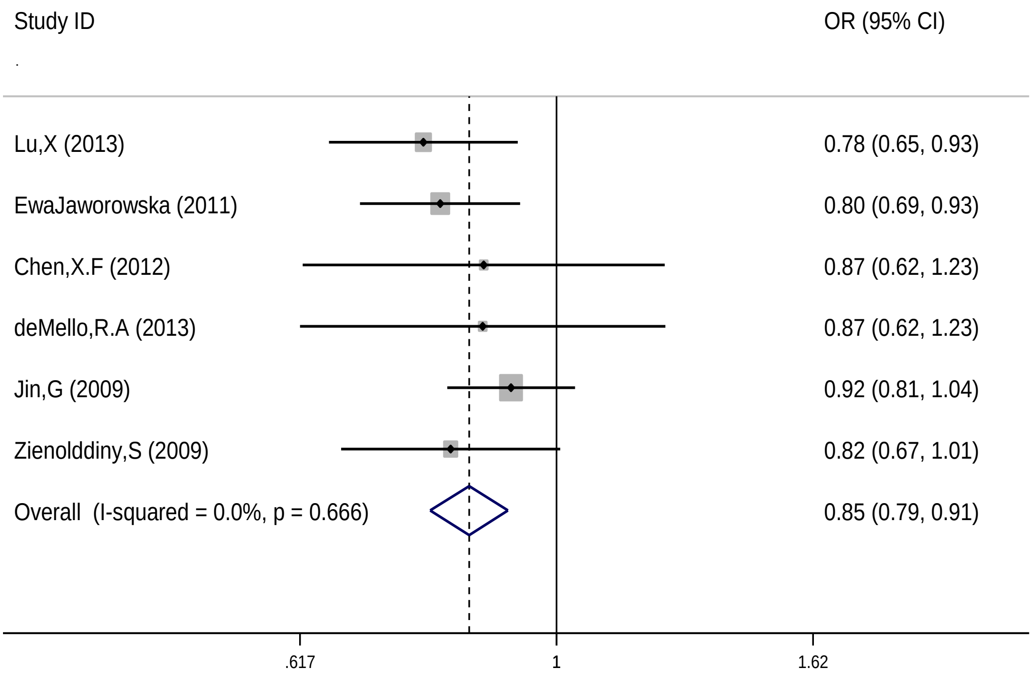
Supplementary Figure S6.20. Subgroup meta-analysis of *REV3L* rs462779 in Asian (allelic contrast: T vs. C).



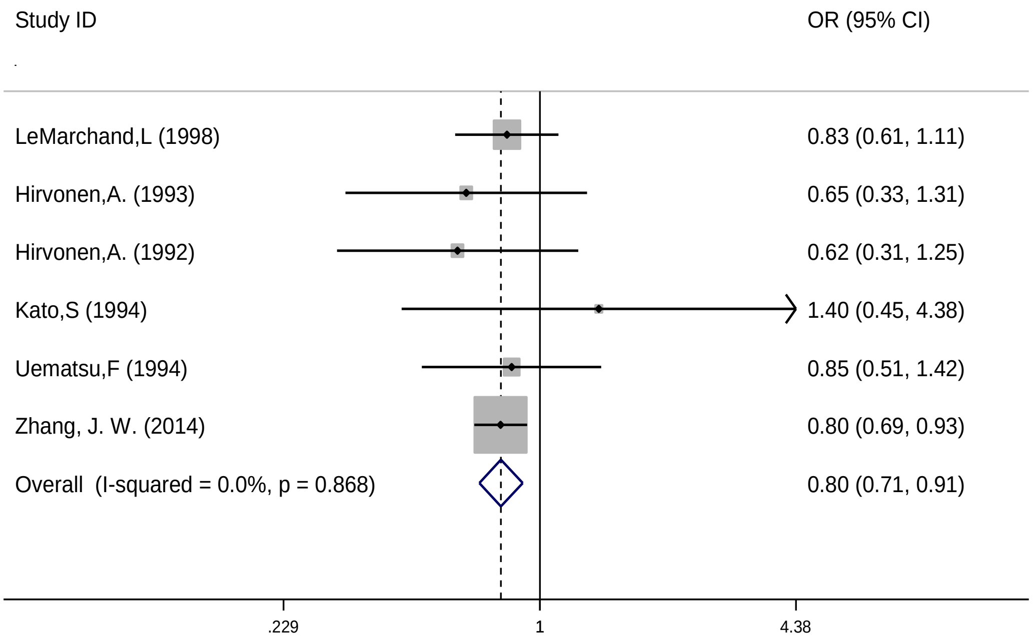
Supplementary Figure S6.21. Subgroup meta-analysis of *TERT* rs2736098 in Asian (Dominant: AA+AG vs. GG).



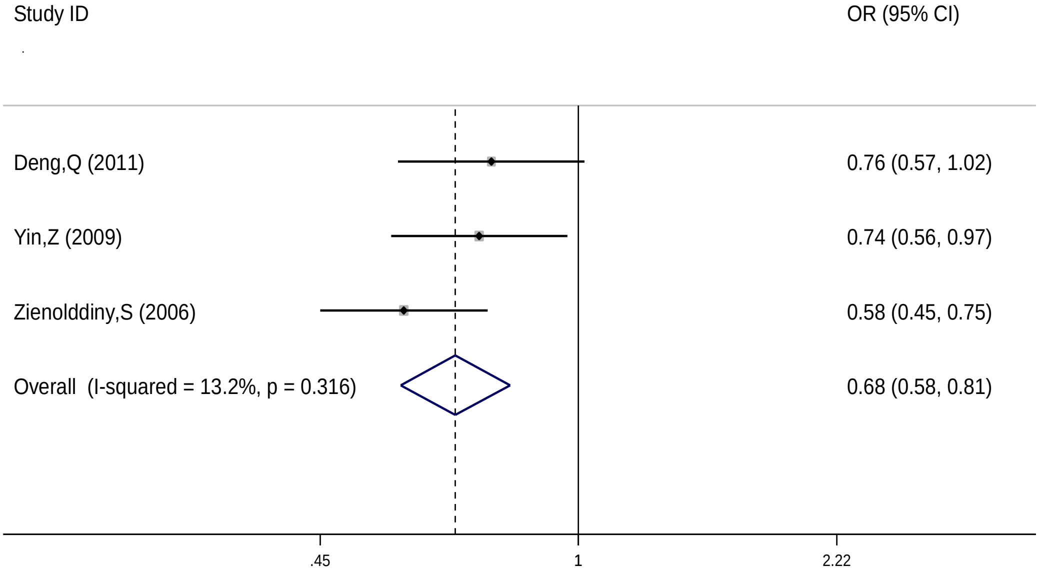
Supplementary Figure S6.22. Subgroup meta-analysis of *CHRNA5* rs16969968 in non-small cell lung cancer population (allelic contrast: A vs. G).



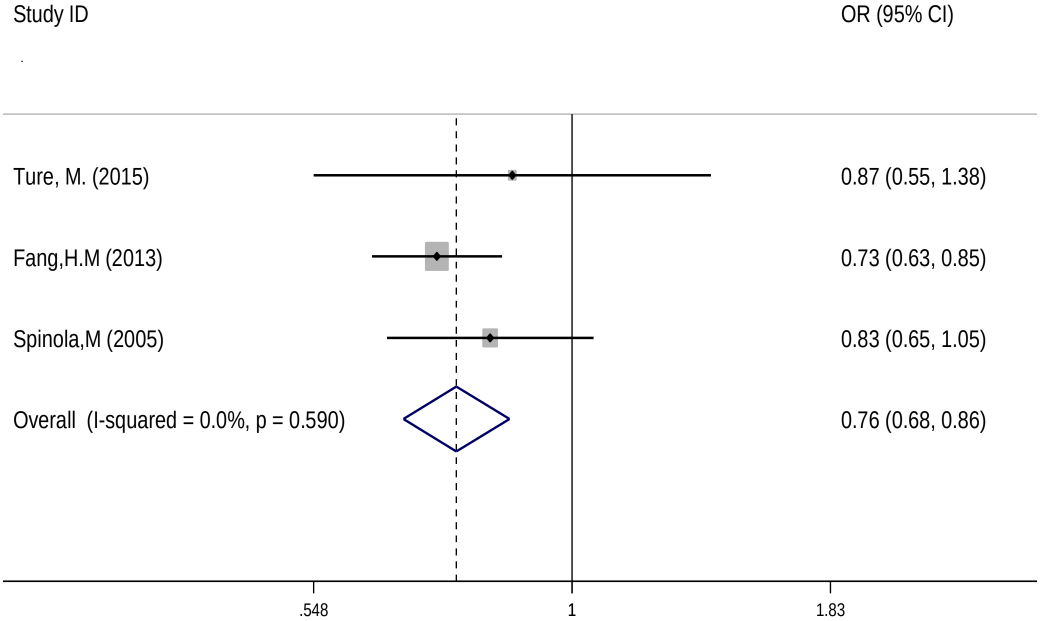
Supplementary Figure S6.23. Subgroup meta-analysis of *CLPTM1L* rs402710 in non-small cell lung cancer population (allelic contrast: T vs. C).



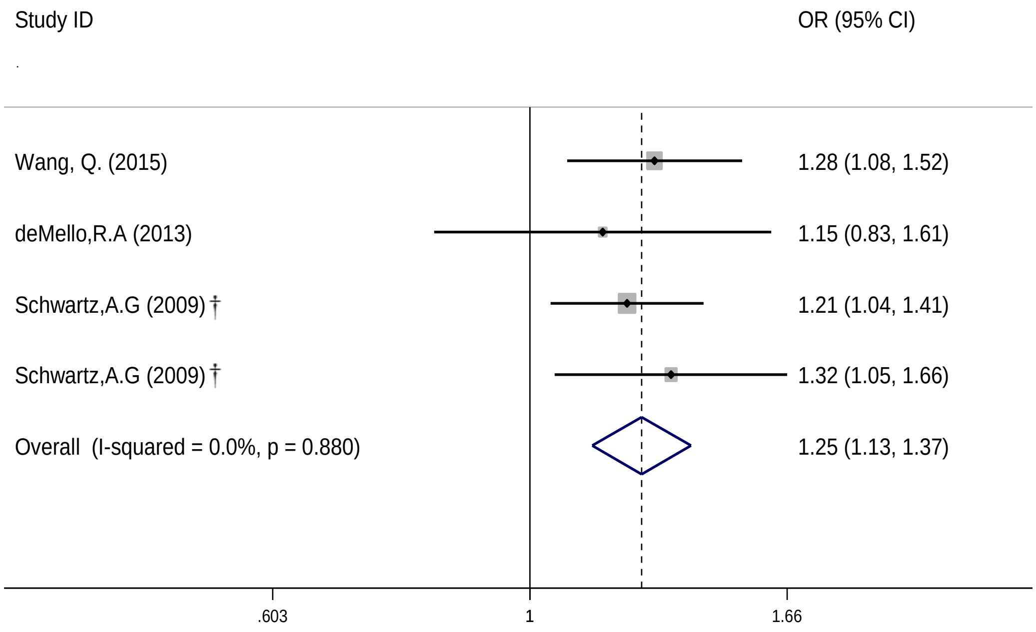
Supplementary Figure S6.24. Subgroup meta-analysis of *CYP2E1* rs6413432 in non-small cell lung cancer population (allelic contrast: A vs. T).



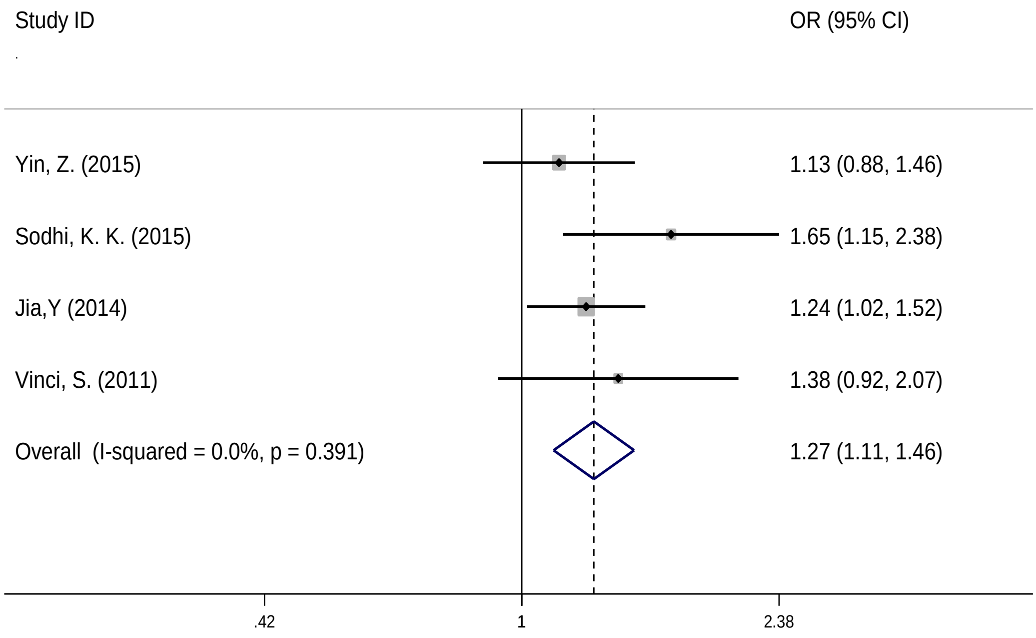
Supplementary Figure S6.25. Subgroup meta-analysis of *ERCC1* rs11615 in non-small cell lung cancer population (allelic contrast: C vs. T).



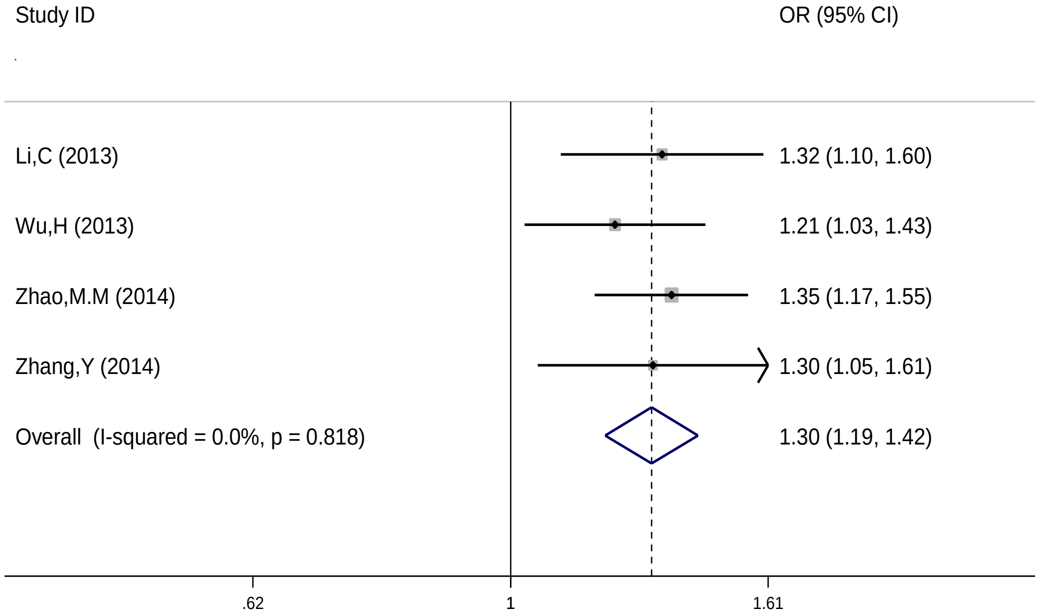
Supplementary Figure S6.26. Subgroup meta-analysis of *FGFR4* rs351855 in non-small cell lung cancer population (allelic contrast: A vs. G).



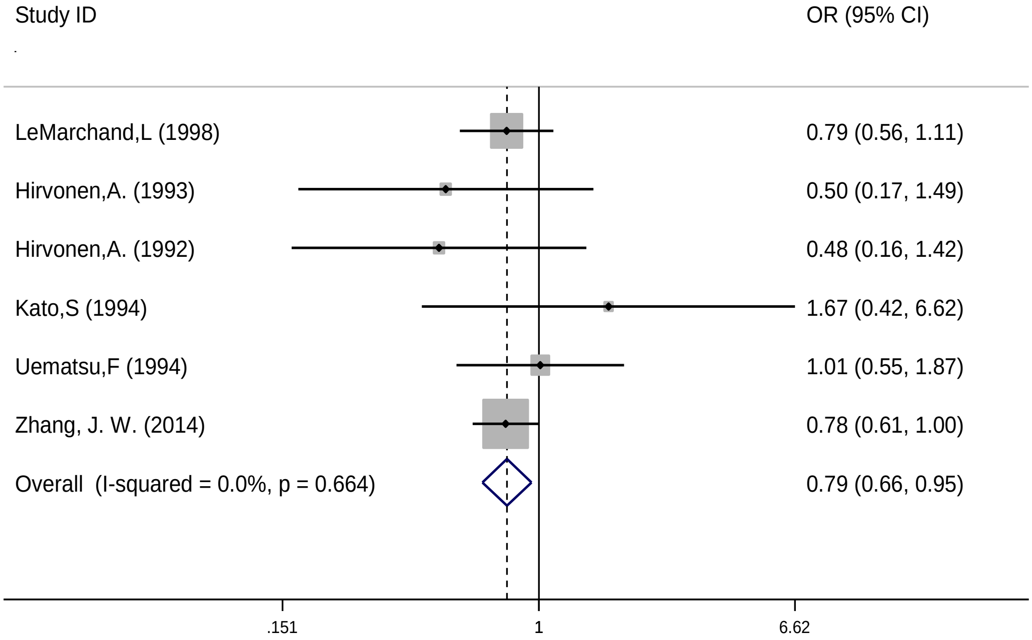
Supplementary Figure S6.27. Subgroup meta-analysis of *HYKK* rs931794 in non-small cell lung cancer population (allelic contrast: G vs. A).



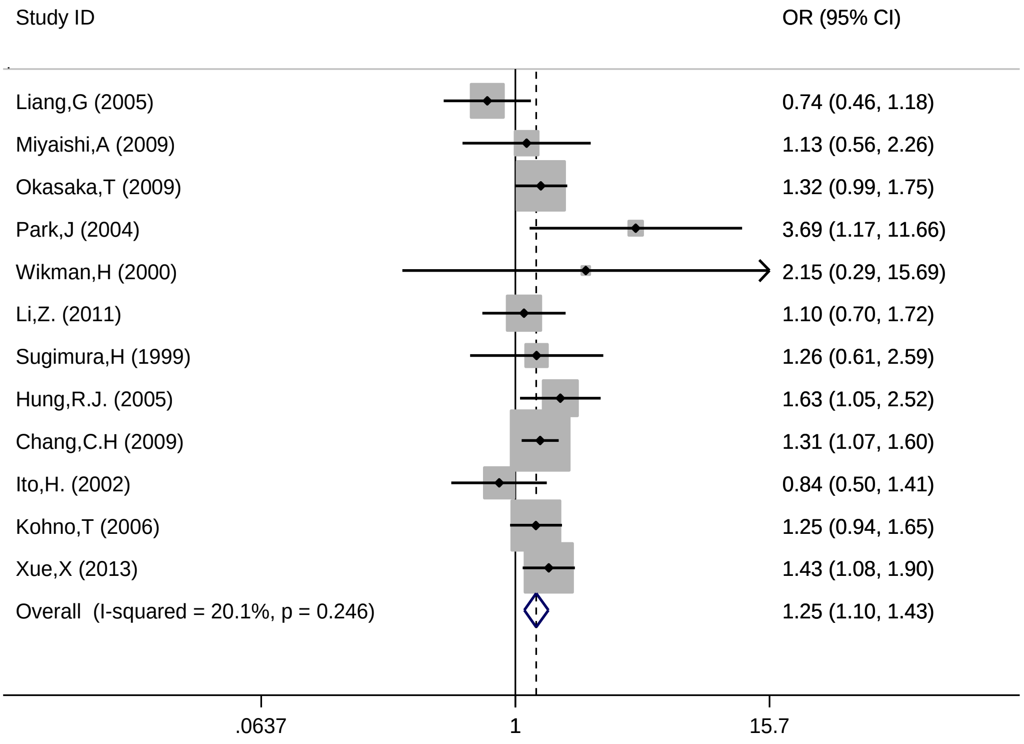
Supplementary Figure S6.28. Subgroup meta-analysis of *MIR146A* rs2910164 in non-small cell lung cancer population (allelic contrast: C vs. G).



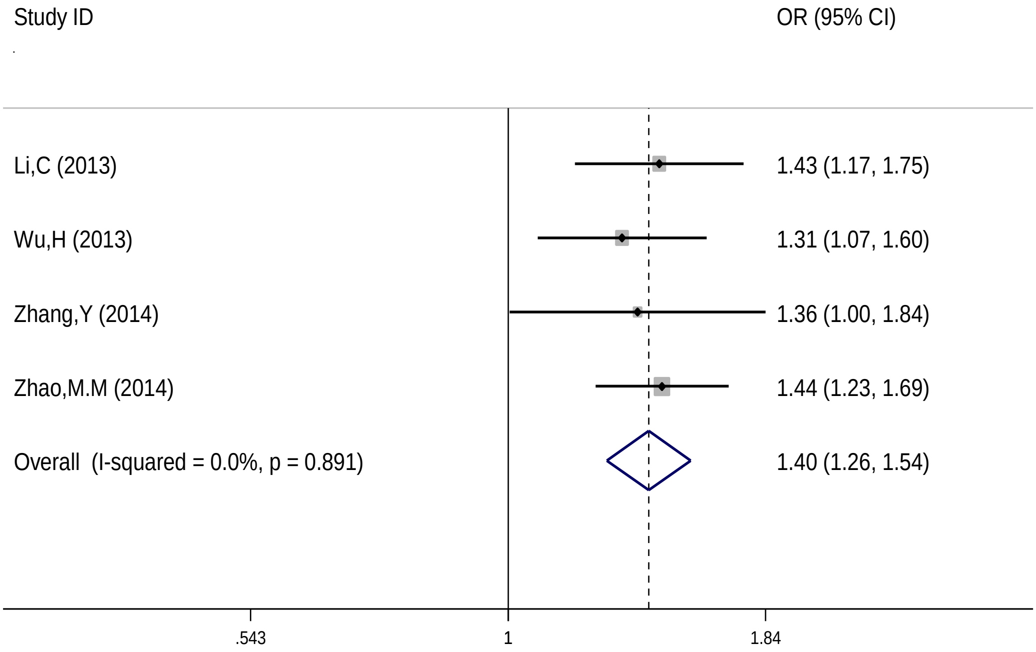
Supplementary Figure S6.29. Subgroup meta-analysis of *TERT* rs2736098 in non-small cell lung cancer population (allelic contrast: A vs. G).



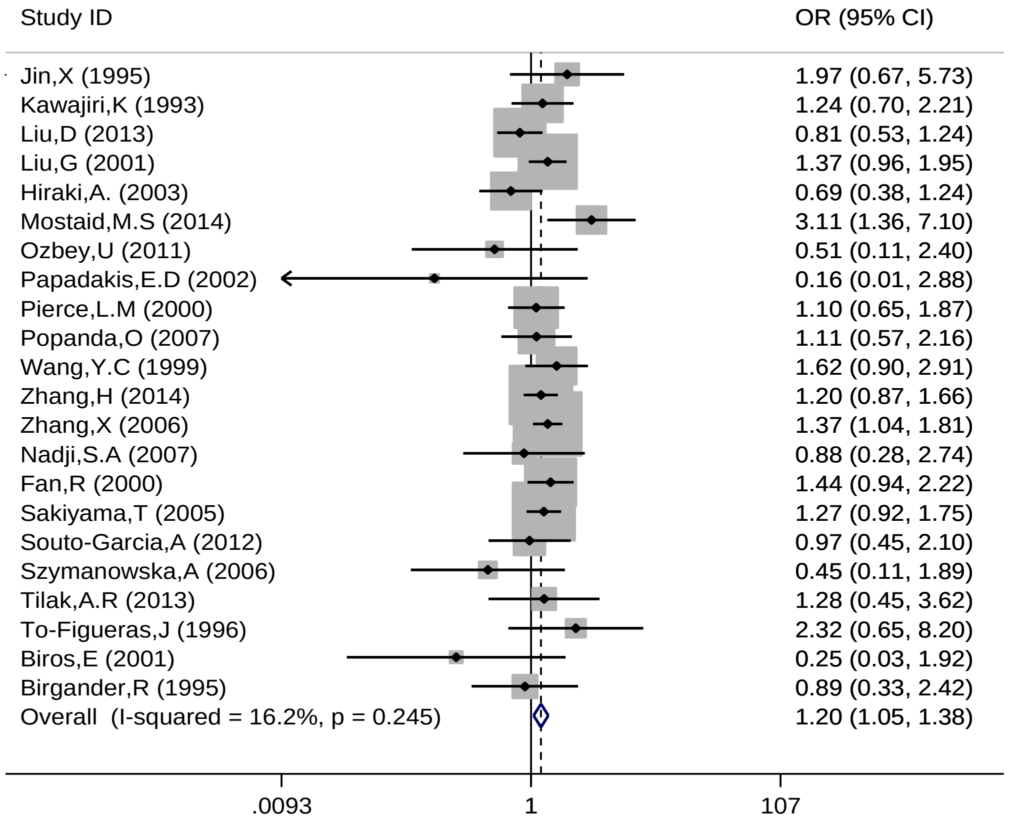
Supplementary Figure S6.30. Subgroup meta-analysis of *CYP2E1* rs6413432 in adenocarcinoma population (allelic contrast: A vs. T).



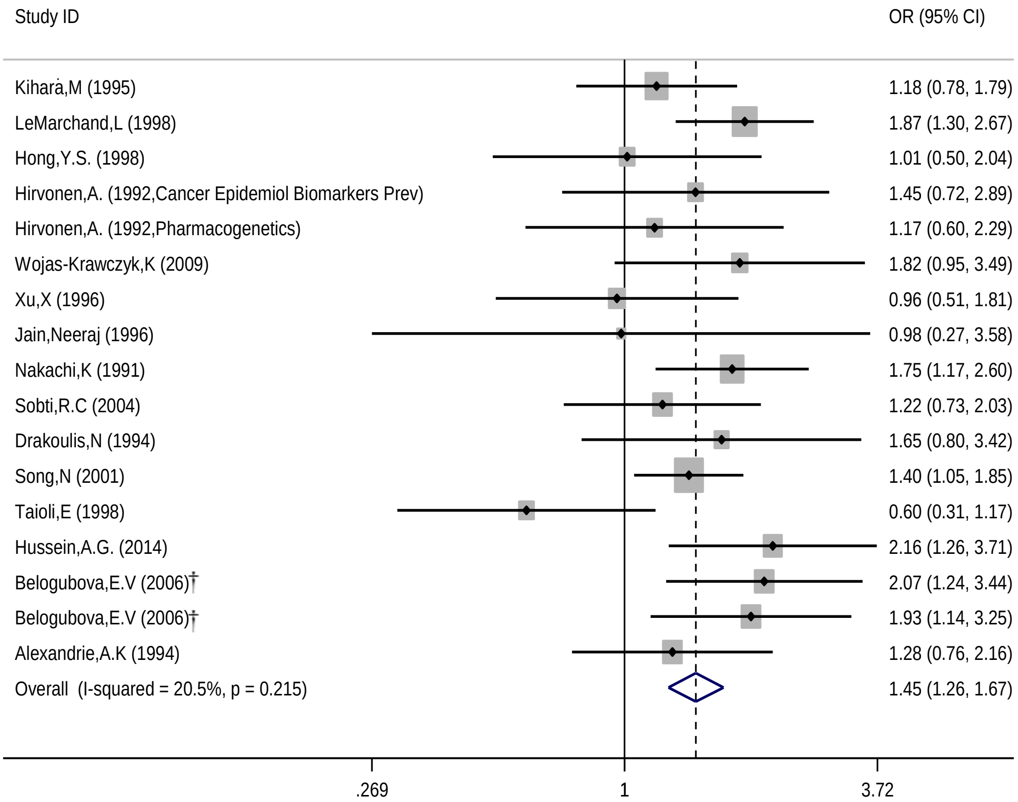
Supplementary Figure S6.31. Subgroup meta-analysis of *OGG1* rs1052133 in adenocarcinoma population (Recessive: CC vs. GG+GC).



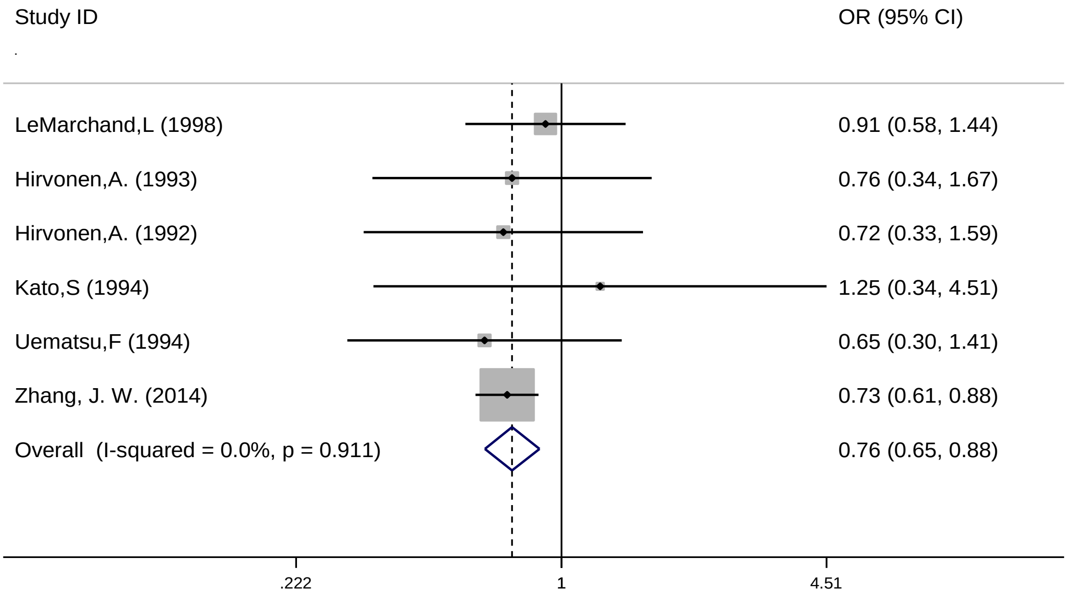
Supplementary Figure S6.32. Subgroup meta-analysis of *TERT* rs2736098 in adenocarcinoma population (allelic contrast: A vs. G).



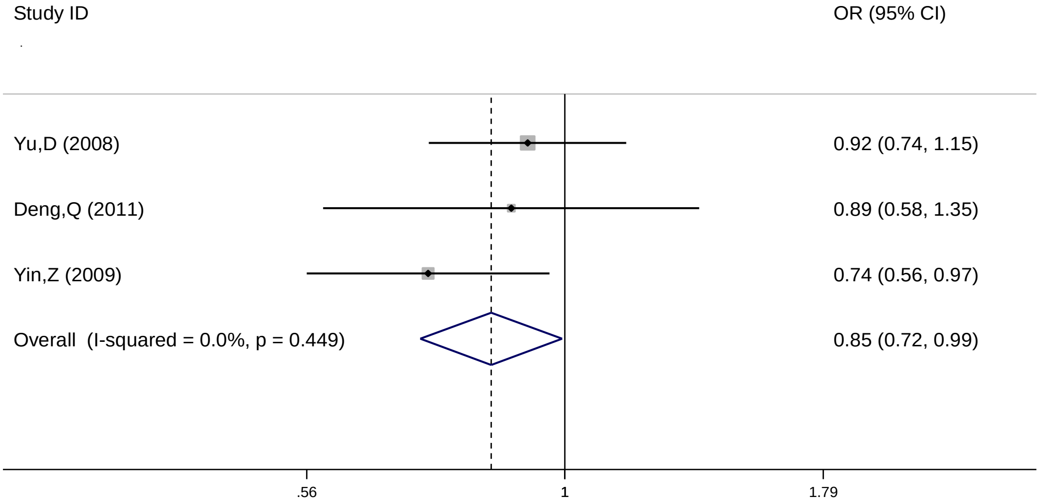
Supplementary Figure S6.33. Subgroup meta-analysis of *TP53* rs1042522 in adenocarcinoma population (Recessive: GG vs. CC+CG).



Supplementary Figure S6.34. Subgroup meta-analysis of *CYP1A1* rs4646903 in squamous cell carcinoma population (allelic contrast: C vs. T).

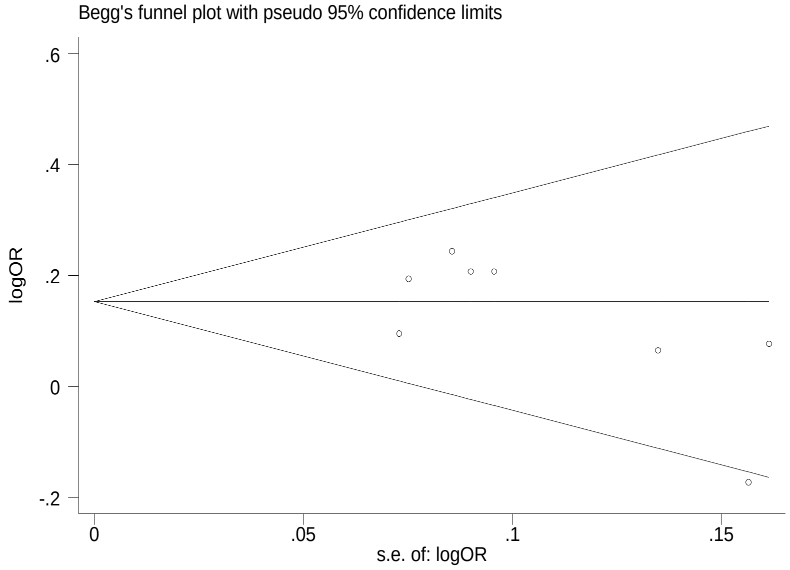


Supplementary Figure S6.35. Subgroup meta-analysis of *CYP2E1* rs6413432 in squamous cell carcinoma population (allelic contrast: A vs. T).

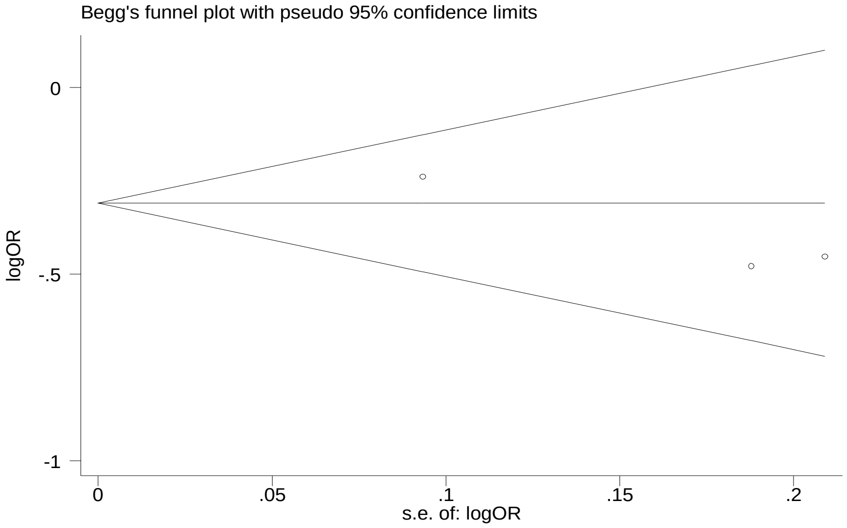


Supplementary Figure S6.36. Subgroup meta-analysis of *ERCC1* rs11615 in non-smokers (allelic contrast: C vs. T).

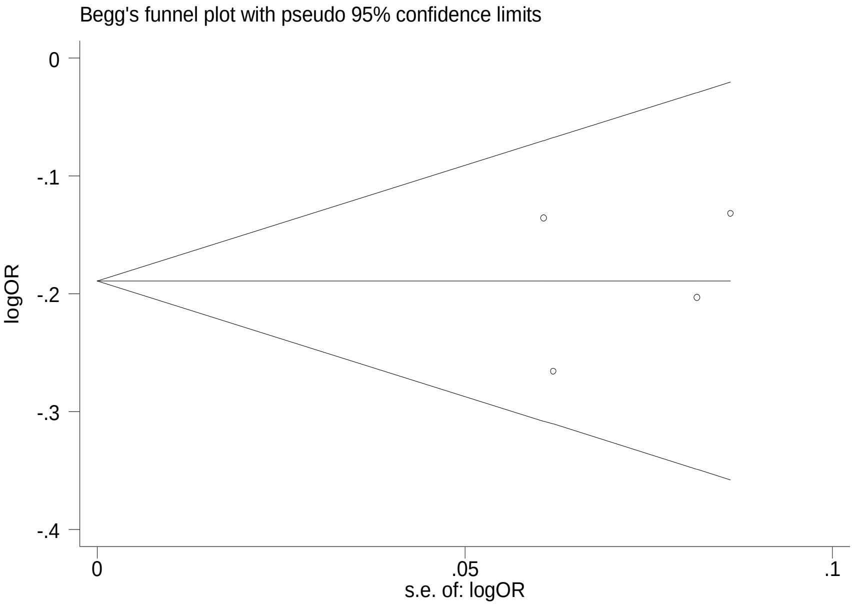
Supplementary Figure S6. Forest plots of main or subgroup meta-analyses for variants showed significant associations to lung cancer susceptibility with strong cumulative evidence. Study-specific allelic odds ratios (ORs, gray squares) and 95% confidence intervals (CIs, lines) were calculated for each included independent dataset. The summary OR and CI was calculated using DerSimonian and Laird random-effects models (white diamond), and genetic model used for meta-analysis was annotated in each single panel. For a complete list of meta-analyses performed for these variants, see **Supplementary Table S2**, **Table S4**, **Table S6**, and **Table S8**. †A report included two independent study populations or different racial groups, and data for each independent population was extracted and analyzed separately.



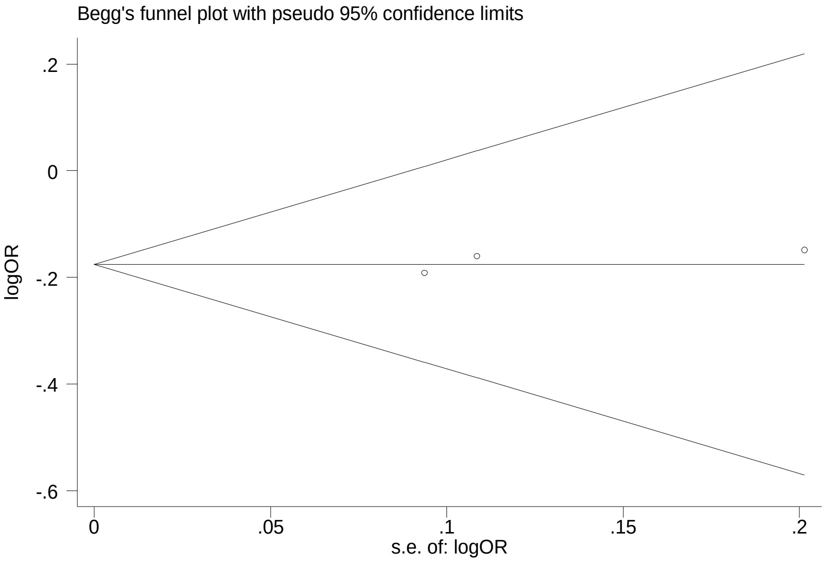
Supplementary Figure S7.1. Main meta-analysis of *APEX1* rs1760944 (allelic contrast: A vs. C).



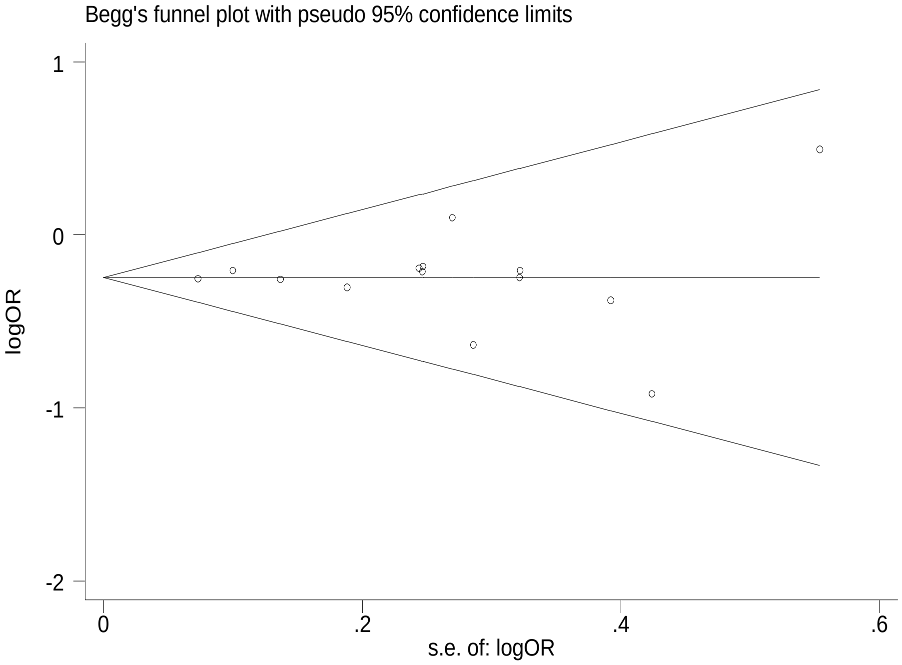
Supplementary Figure S7.2. Main meta-analysis of *AXIN2* rs2240308 (allelic contrast: T vs. C).



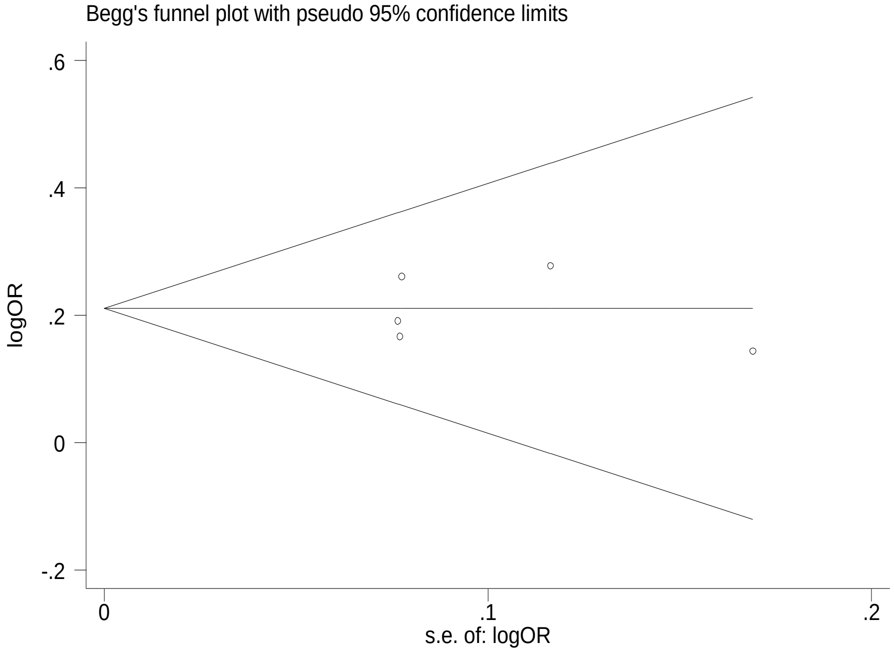
Supplementary Figure S7.3. Main meta-analysis of *CHRNA3* rs6495309 (allelic contrast: T vs. C).



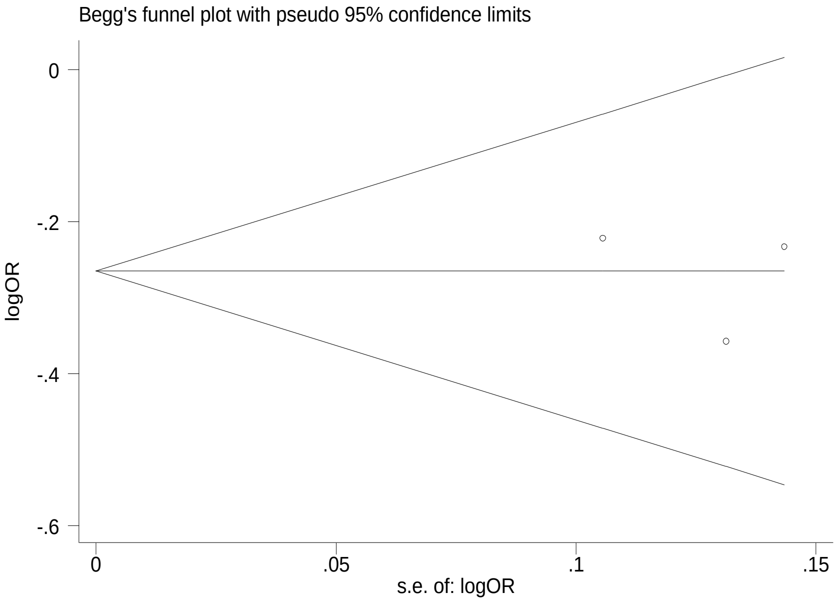
Supplementary Figure S7.4. Main meta-analysis of *CXCR2* rs1126579 (allelic contrast: T vs. C).



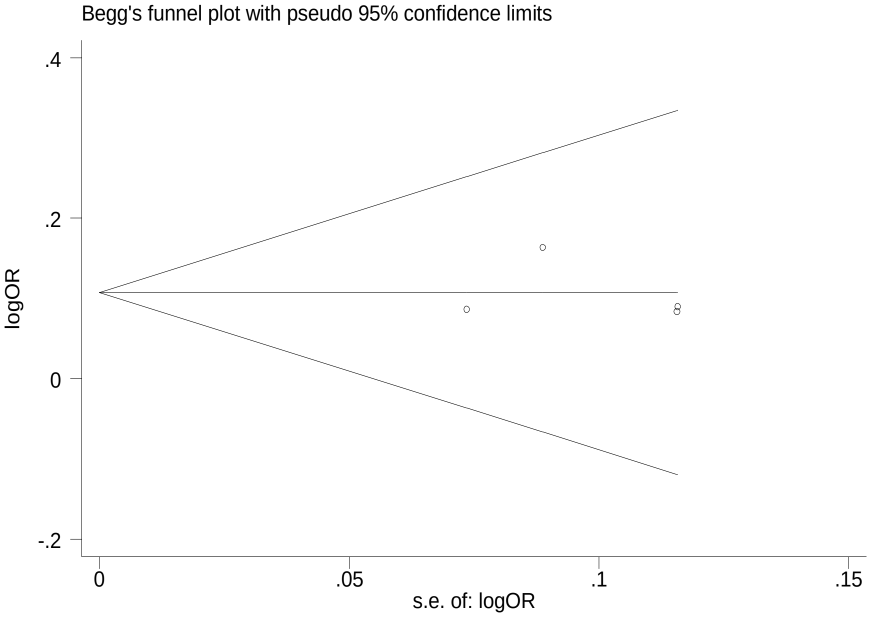
Supplementary Figure S7.5. Main meta-analysis of *CYP2E1* rs6413432 (allelic contrast: A vs. T).



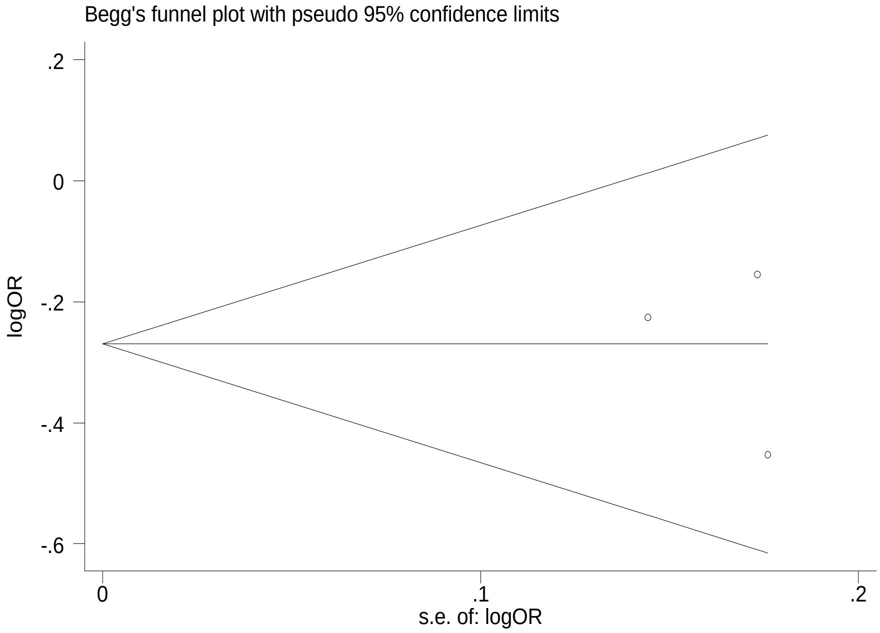
Supplementary Figure S7.6. Main meta-analysis of *HYKK* rs931794 (allelic contrast: G vs. A).



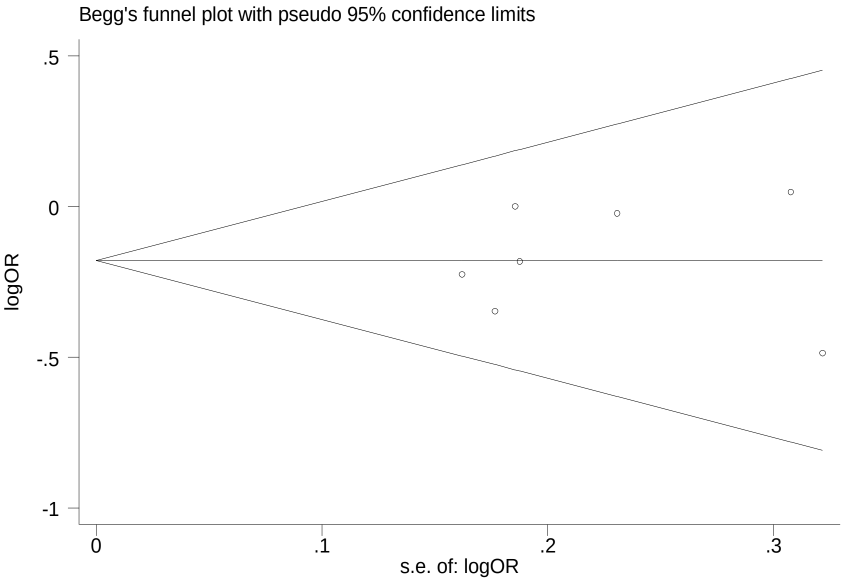
Supplementary Figure S7.7. Main meta-analysis of *PON1* rs662 (allelic contrast: A vs. G).



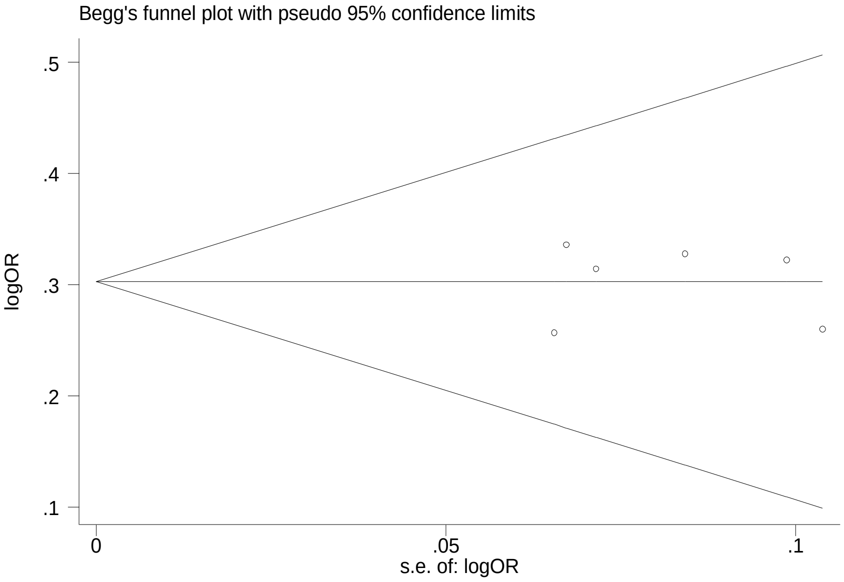
Supplementary Figure S7.8. Main meta-analysis of *REV3L* rs462779 (allelic contrast: T vs. C). (Available data limited to Asian populations.)



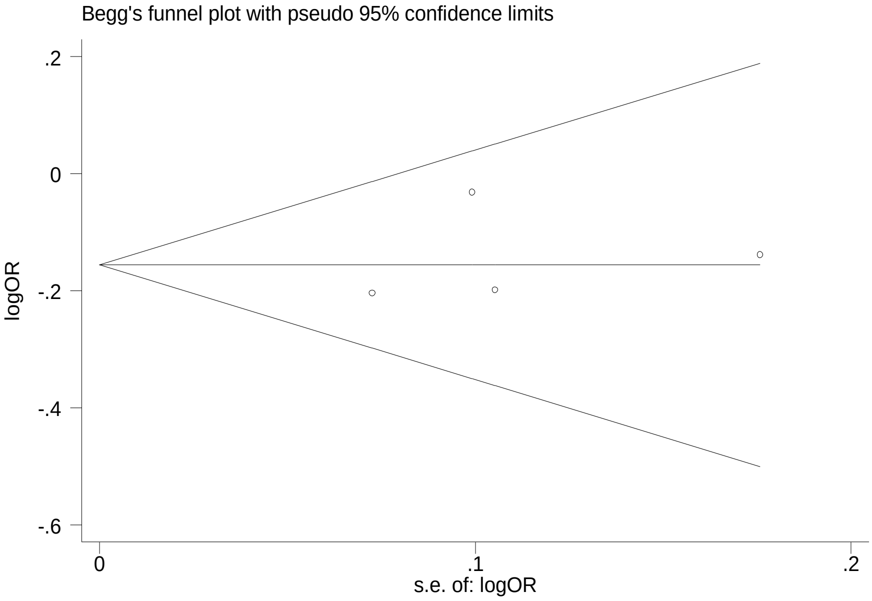
Supplementary Figure S7.9. Meta-analysis of *ATM* rs664677 (Dominant: CC+CT vs. TT).



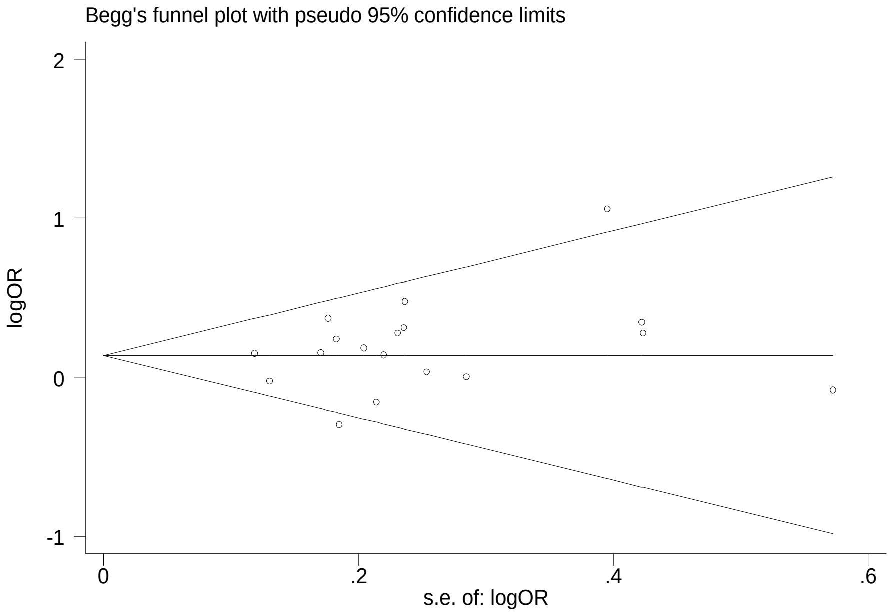
Supplementary Figure S7.10. Subgroup meta-analysis of *APEX1* rs1130409 in Caucasian (Recessive: GG+GT vs. TT).



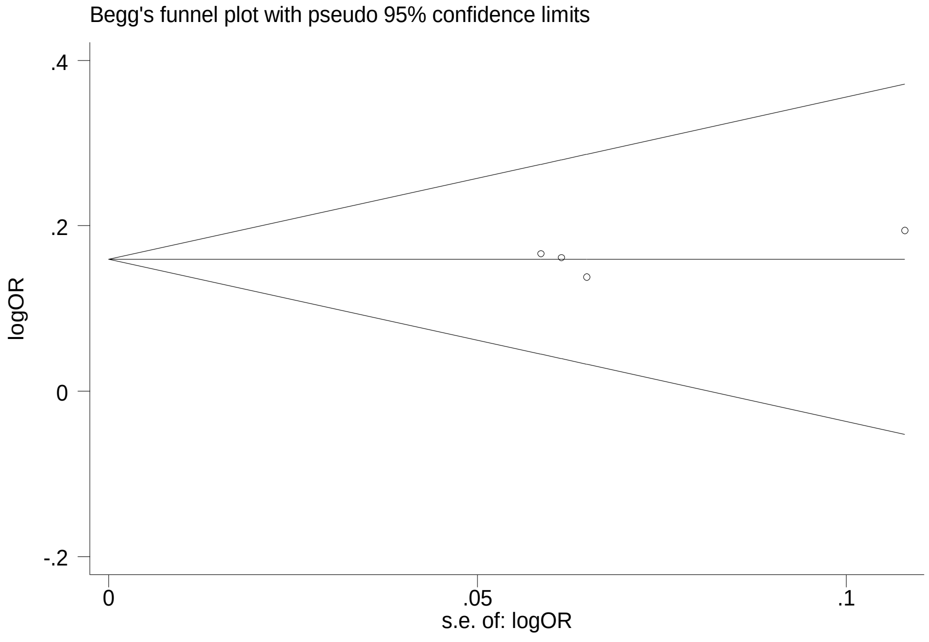
Supplementary Figure S7.11. Subgroup meta-analysis of *CHRNA5* rs16969968 in Caucasian (allelic contrast: A vs. G).



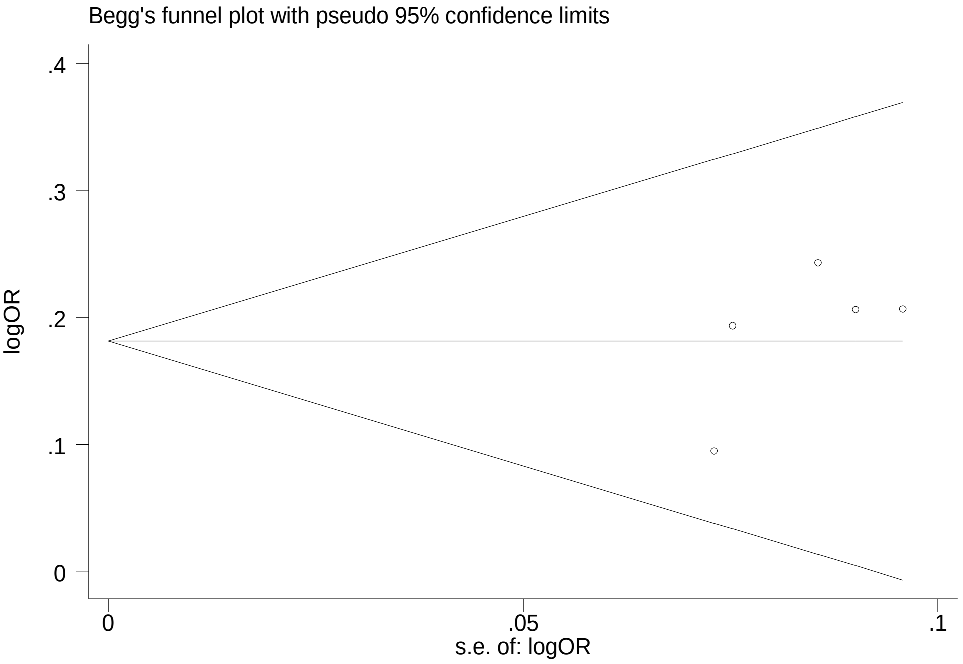
Supplementary Figure S7.12. Subgroup meta-analysis of *CLPTM1L* rs402710 in Caucasian (allelic contrast: T vs. C).



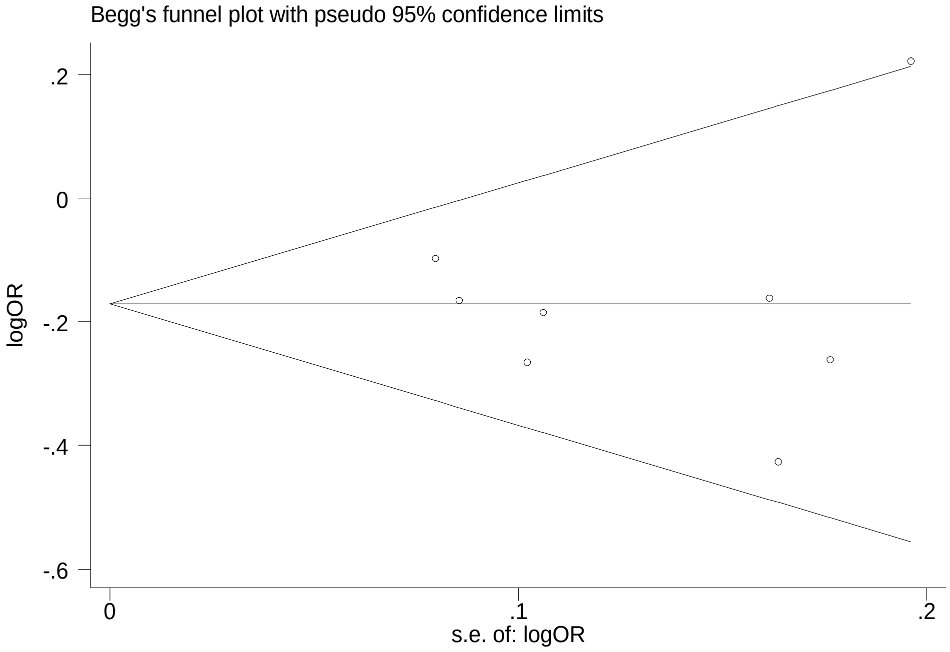
Supplementary Figure S7.13. Subgroup meta-analysis of *ERCC2* rs13181 in Caucasian (Recessive: AA vs. CC+CA).



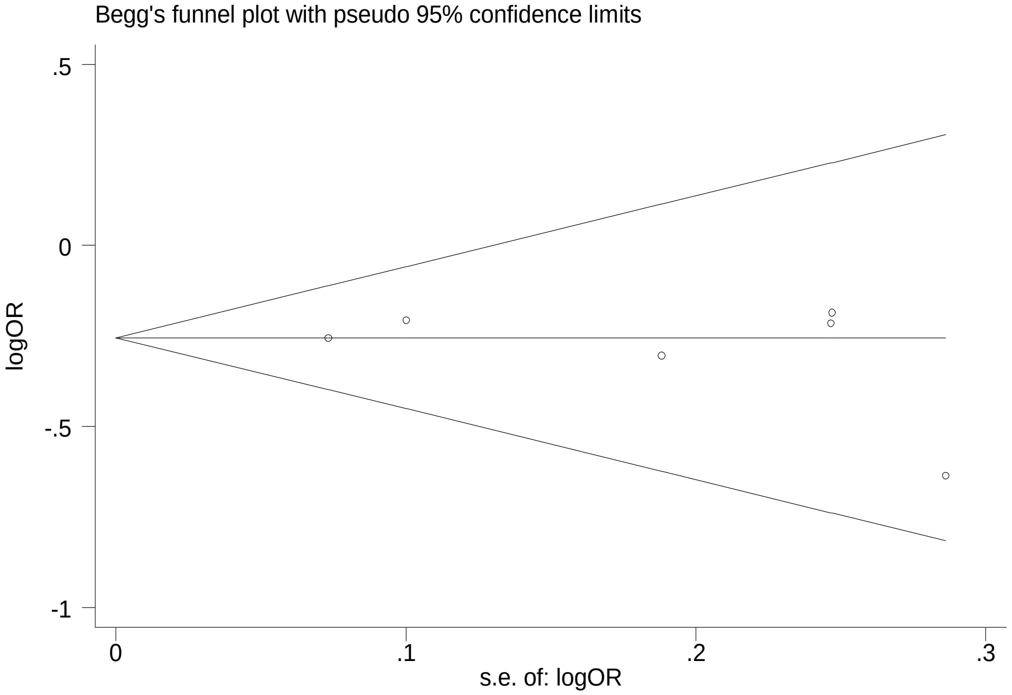
Supplementary Figure S7.14. Subgroup meta-analysis of *SOD2* rs4880 in Caucasian (allelic contrast: T vs. C).



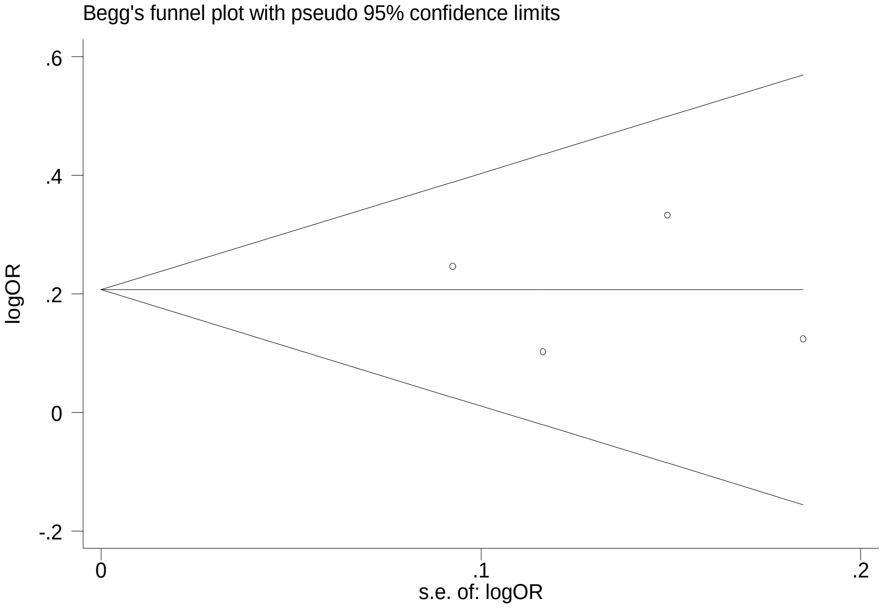
Supplementary Figure S7.15. Subgroup meta-analysis of *APEX1* rs1760944 in Asian (allelic contrast: A vs. C).



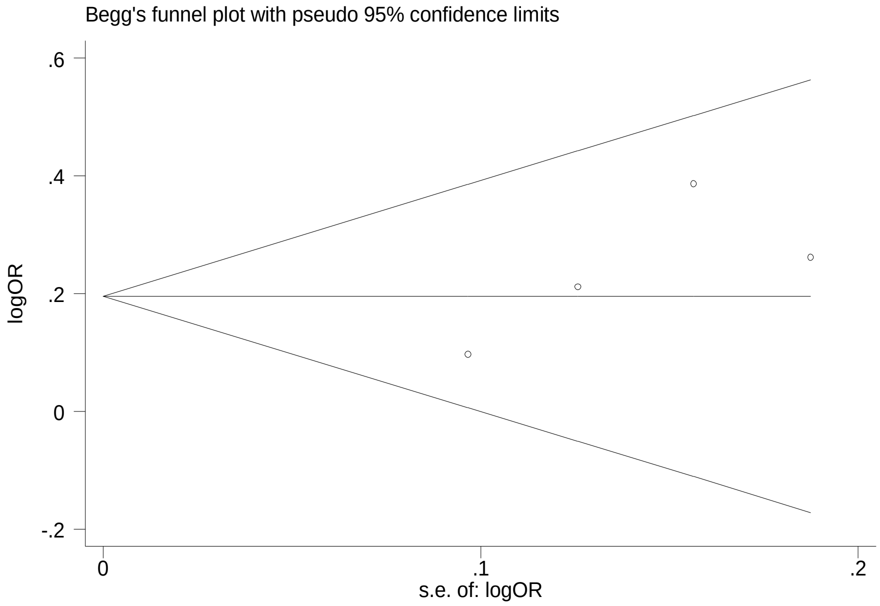
Supplementary Figure S7.16. Subgroup meta-analysis of *CLPTM1L* rs402710 in Asian (Dominant: TT+TC vs. CC).



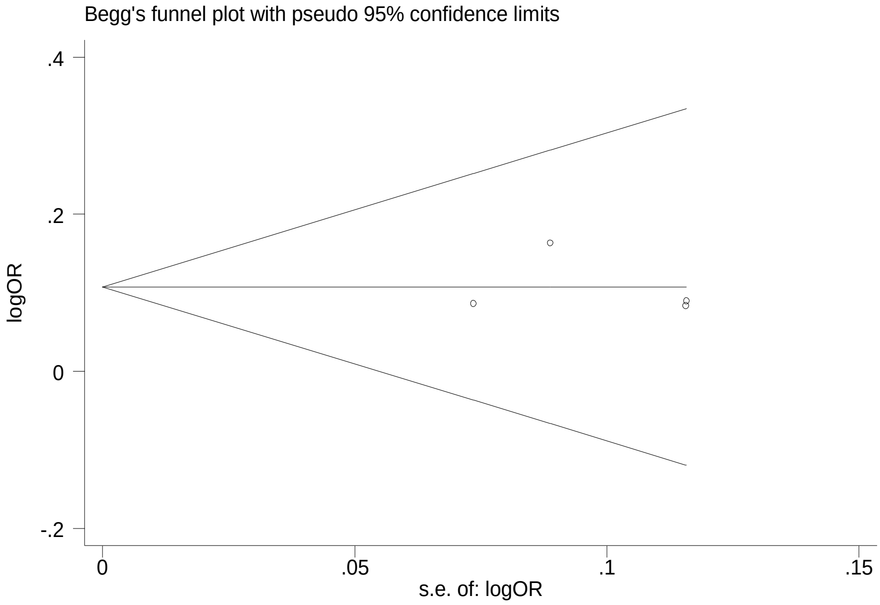
Supplementary Figure S7.17. Subgroup meta-analysis of *CYP2E1* rs6413432 in Asian (allelic contrast: A vs. T).



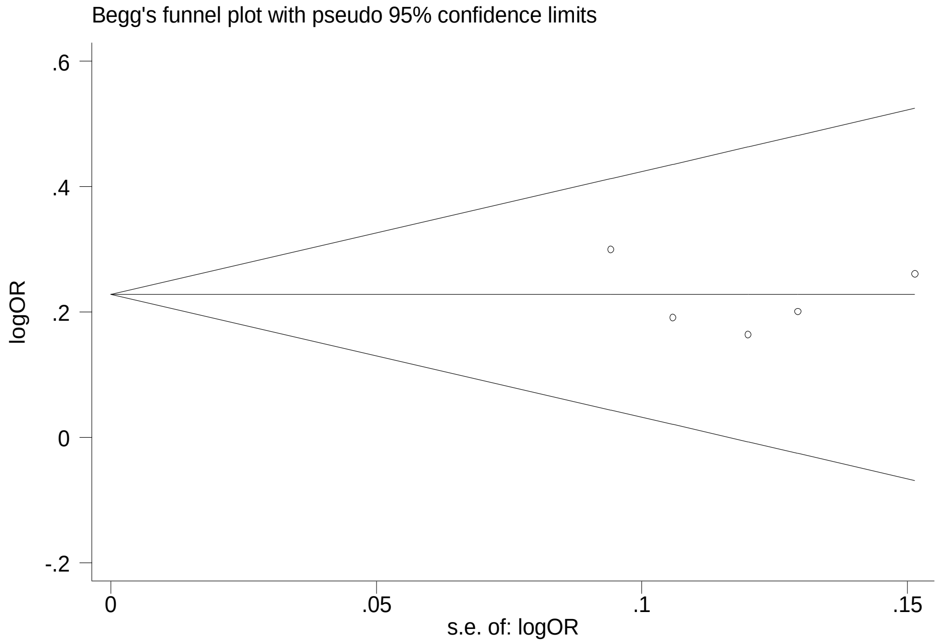
Supplementary Figure S7.18. Subgroup meta-analysis of *MIR146A* rs2910164 in Asian (Recessive: GG vs. CC+CG).



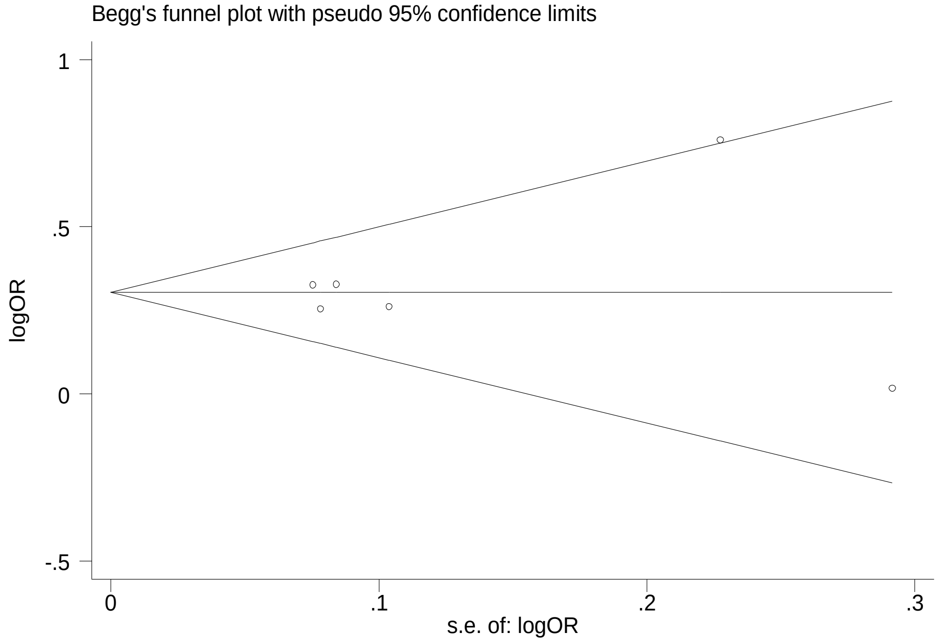
Supplementary Figure S7.19. Subgroup meta-analysis of *MIR196A2* rs11614913 in Asian (Dominant: CC+CT vs. TT).



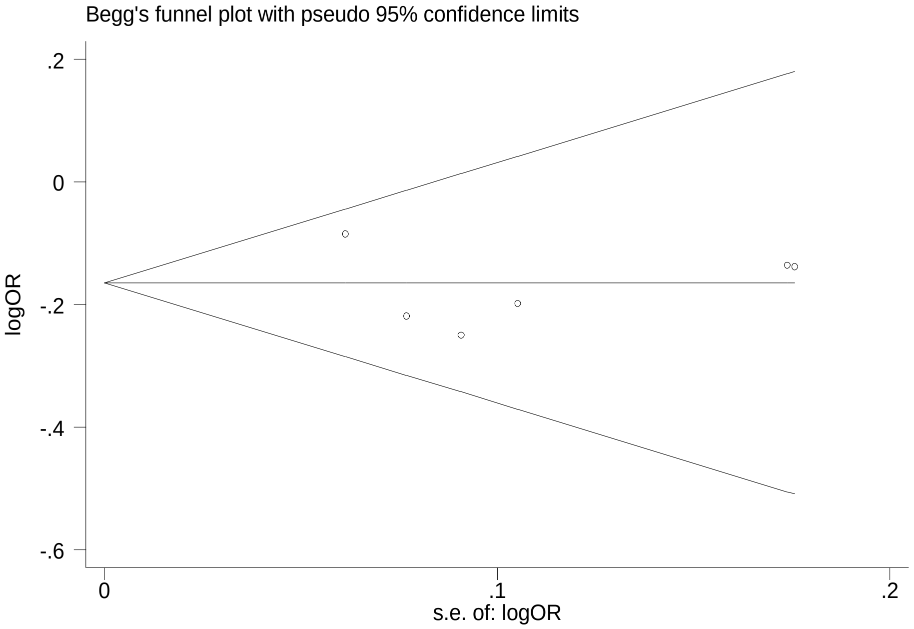
Supplementary Figure S7.20. Subgroup meta-analysis of *REV3L* rs462779 in Asian (allelic contrast: T vs. C).



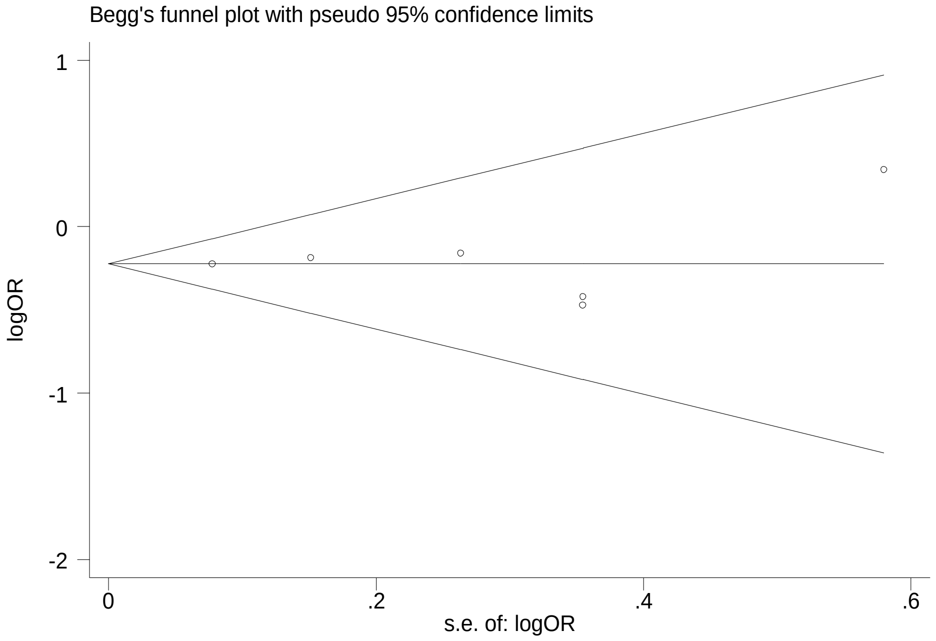
Supplementary Figure S7.21. Subgroup meta-analysis of *TERT* rs2736098 in Asian (Dominant: AA+AG vs. GG).



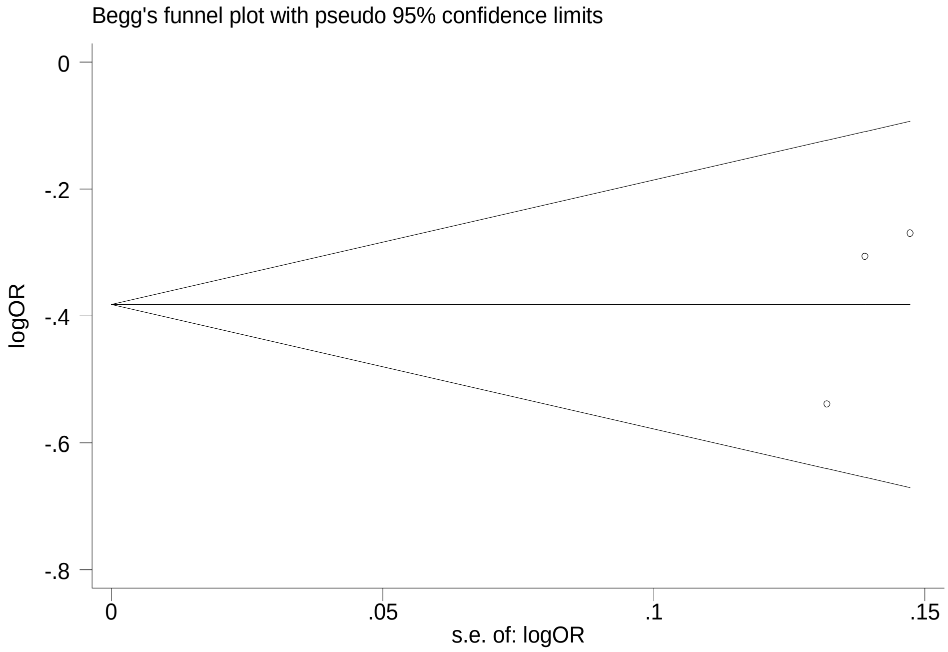
Supplementary Figure S7.22. Subgroup meta-analysis of *CHRNA5* rs16969968 in non-small cell lung cancer population (allelic contrast: A vs. G).



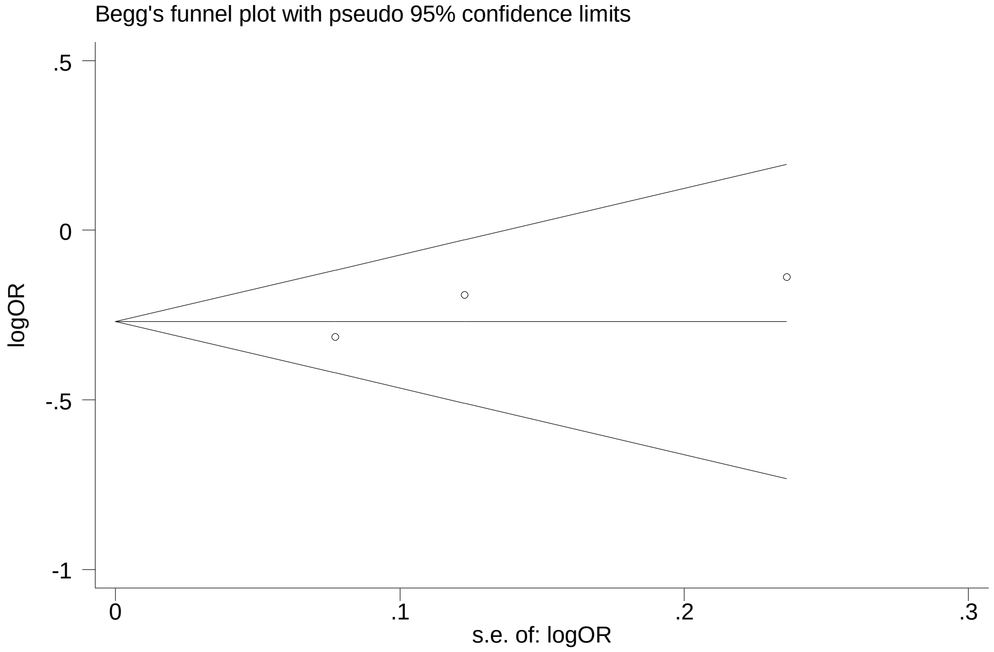
Supplementary Figure S7.23. Subgroup meta-analysis of *CLPTM1L* rs402710 in non-small cell lung cancer population (allelic contrast: T vs. C).



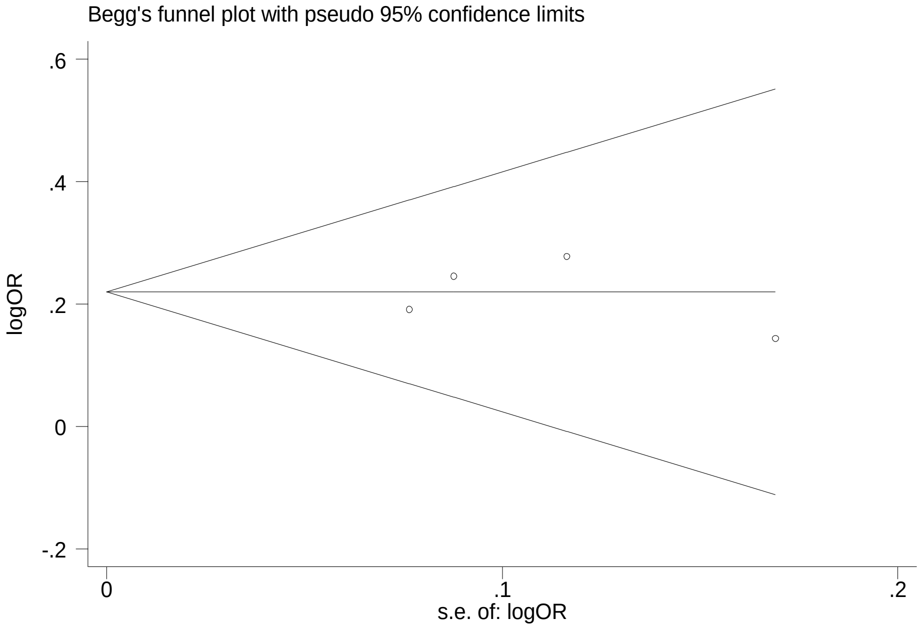
Supplementary Figure S7.24. Subgroup meta-analysis of *CYP2E1* rs6413432 in non-small cell lung cancer population (allelic contrast: A vs. T).



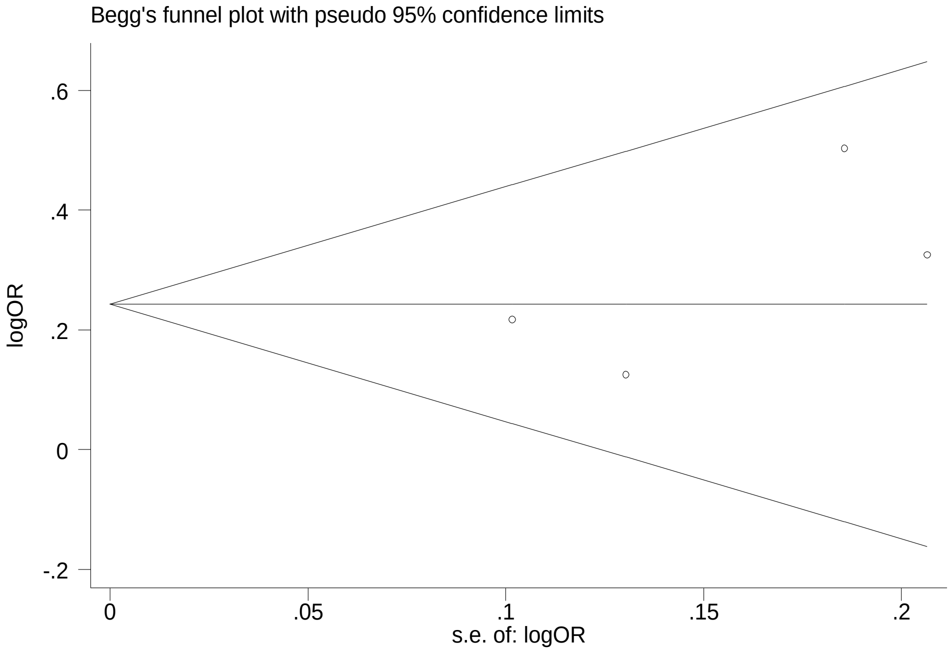
Supplementary Figure S7.25. Subgroup meta-analysis of *ERCC1* rs11615 in non-small cell lung cancer population (allelic contrast: C vs. T).



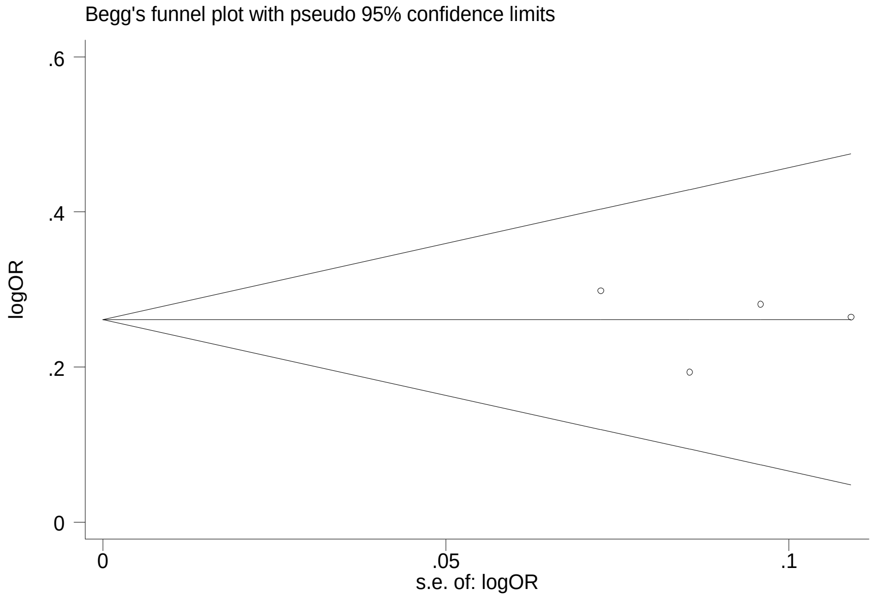
Supplementary Figure S7.26. Subgroup meta-analysis of *FGFR4* rs351855 in non-small cell lung cancer population (allelic contrast: A vs. G).



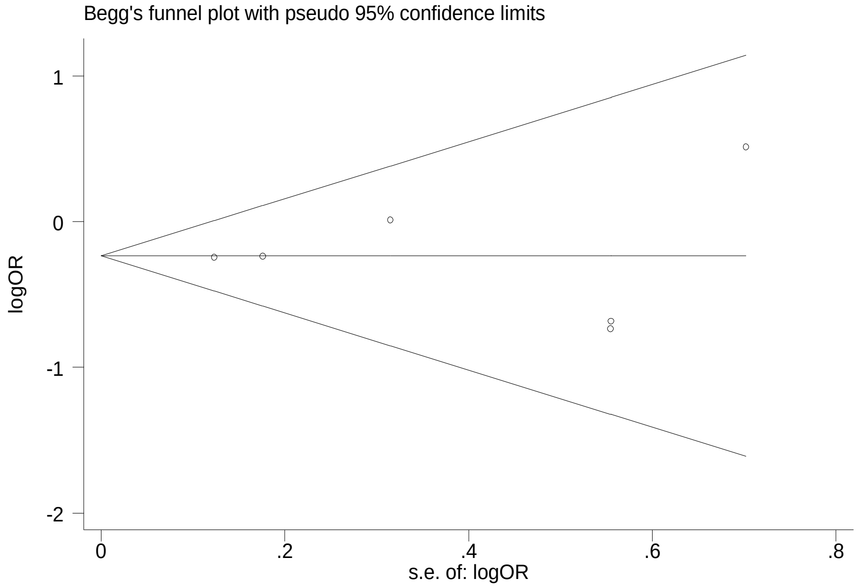
Supplementary Figure S7.27. Subgroup meta-analysis of *HYKK* rs931794 in non-small cell lung cancer population (allelic contrast: G vs. A).



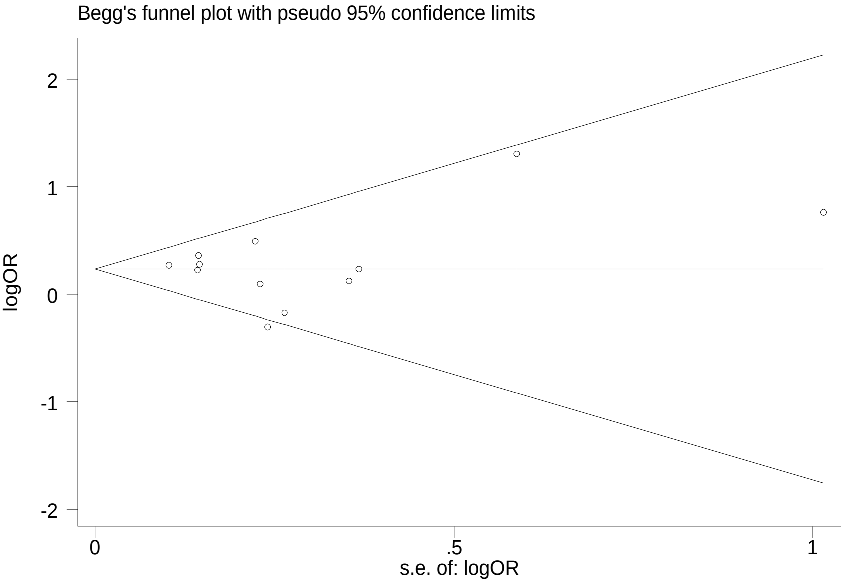
Supplementary Figure S7.28. Subgroup meta-analysis of *MIR146A* rs2910164 in non-small cell lung cancer population (allelic contrast: C vs. G).



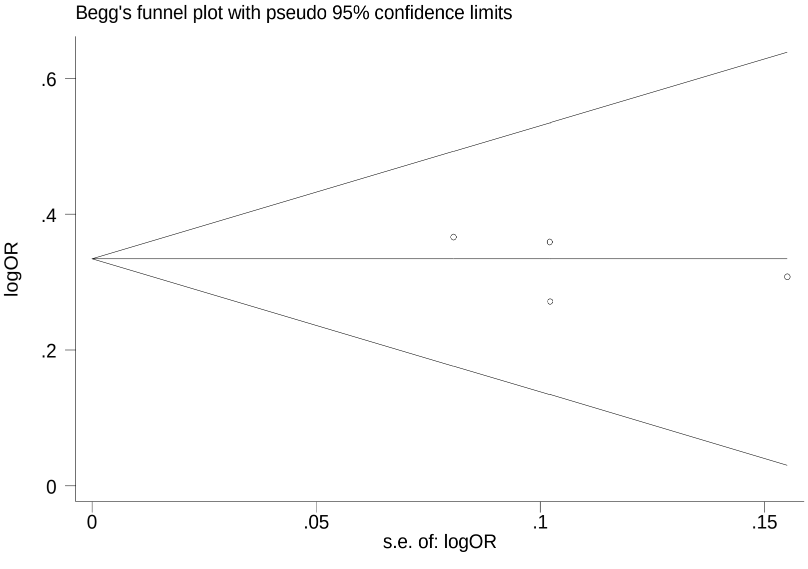
Supplementary Figure S7.29. Subgroup meta-analysis of *TERT* rs2736098 in non-small cell lung cancer population (allelic contrast: A vs. G).



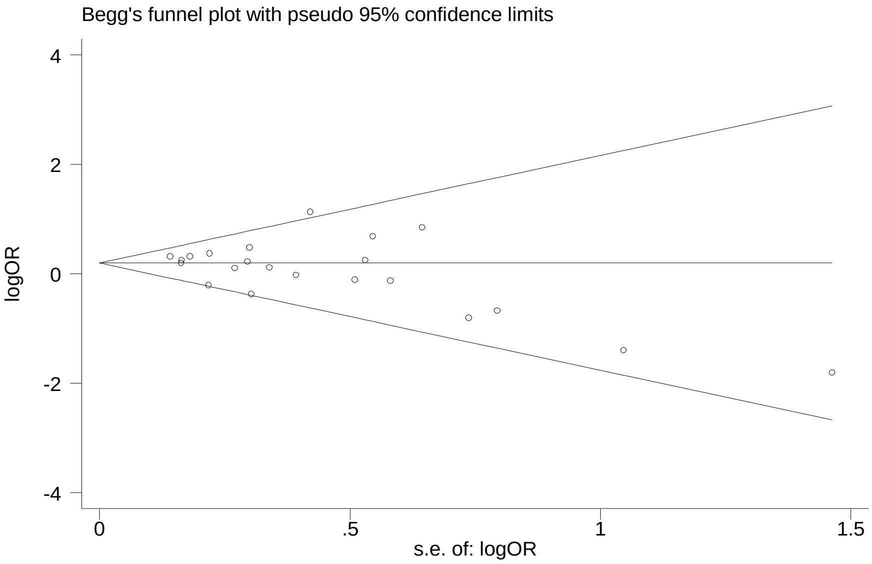
Supplementary Figure S7.30. Subgroup meta-analysis of *CYP2E1* rs6413432 in adenocarcinoma population (allelic contrast: A vs. T).



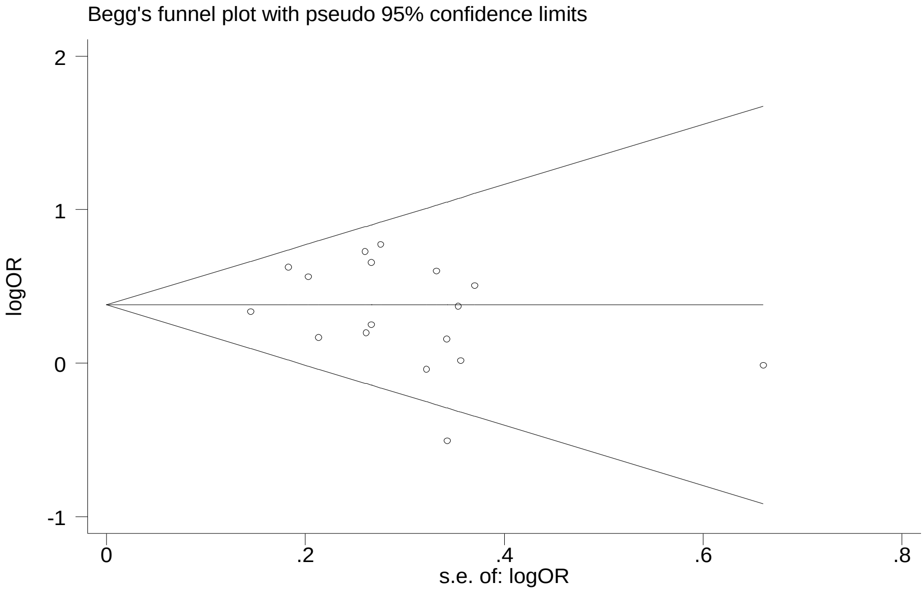
Supplementary Figure S7.31. Subgroup meta-analysis of *OGG1* rs1052133 in adenocarcinoma population (Recessive: CC vs. GG+GC).



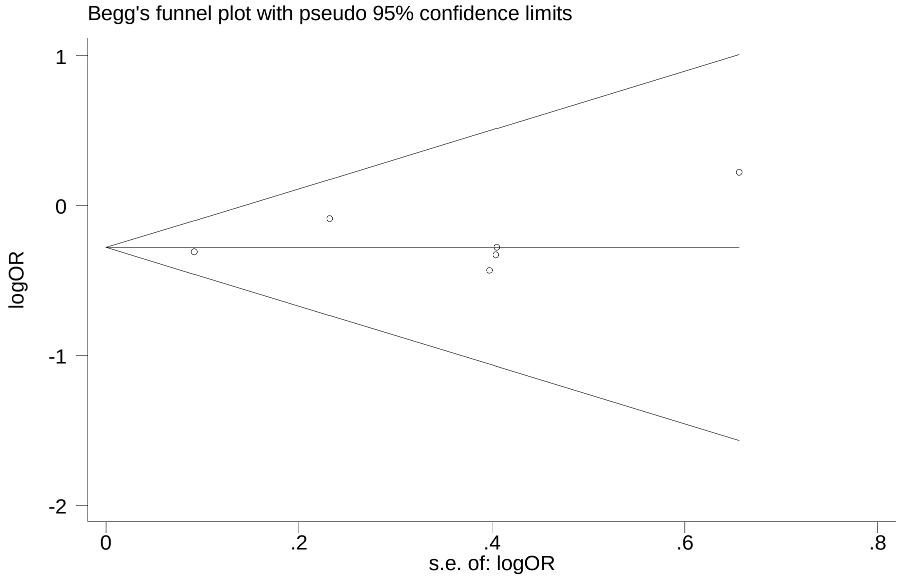
Supplementary Figure S7.32. Subgroup meta-analysis of *TERT* rs2736098 in adenocarcinoma population (allelic contrast: A vs. G).



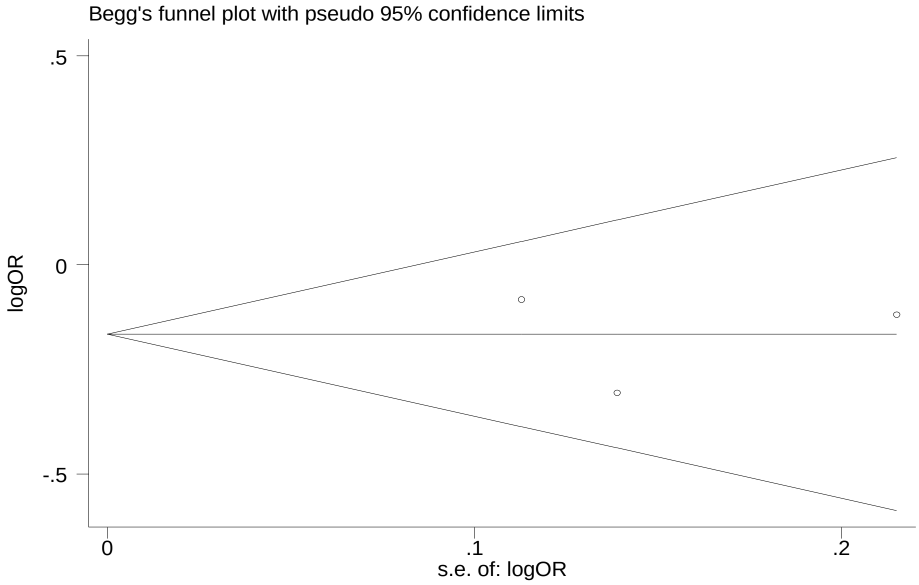
Supplementary Figure S7.33. Subgroup meta-analysis of *TP53* rs1042522 in adenocarcinoma population (Recessive: GG vs. CC+CG).



Supplementary Figure S7.34. Subgroup meta-analysis of *CYP1A1* rs4646903 in squamous cell carcinoma population (allelic contrast: C vs. T).



Supplementary Figure S7.35. Subgroup meta-analysis of *CYP2E1* rs6413432 in squamous cell carcinoma population (allelic contrast: A vs. T).



Supplementary Figure S7.36. Subgroup meta-analysis of *ERCC1* rs11615 in non-smokers (allelic contrast: C vs. T).

Supplementary Figure S7. Begg's funnel plots of main or subgroup meta-analyses for variants showed significant associations to lung cancer susceptibility with strong cumulative evidence. Begg's funnel plots were used for publication bias test. Each point represented a separate study. LogOR, natural logarithm of OR. Horizontal line, mean effect size. The degree of asymmetry of the funnel plots were evaluated by the Begg’s test, and all P-value of Begg’s test were displayed on the respective table in the manuscript.

Supplementary Table S1. Genetic associations with lung cancer risk for all 246 variants analyzed in main meta-analyses under different genetic models (Continued on next three pages)

Gene	Variant	Chr	Category	Ethnicity	Comparison[a]	Frequency(%)[b]	Number evaluated		Lung cancer risk meta-analysis in allelic model								Dominant model			Recessive model		
							Studies	Cases/Controls	OR(95% CI)	*P* value	Q	*P* for Q	I^2(%)	Begg *P*	Modified *P*[c]	Excess *P*[d]	OR(95% CI)	*P* value	I^2(%)	OR(95% CI)	*P* valute	I^2(%)
ABCB1	rs1045642(p.Ile1145Ile,c.3435T>C)	7	synonymous	All	T vs C	39.40	4	1025/1080	1.30(0.79-2.16)	0.307	28.98	0.00	90	0.308	0.535	1.000	1.21(0.67-2.19)	0.535	83	1.34(0.72-2.50)	0.353	79
ACE	287-bp repeat(I/D)	17	STR	All	Ins vs del	49.31	8	1730/8359	1.01(0.85-1.21)	0.885	19.95	0.01	65	0.536	0.627	0.019	1.00(0.76-1.32)	0.985	57	1.00(0.76-1.33)	0.998	66
AGER	rs1800624(-374T>A,Mun1)	6	intergenic	Asian	A vs T	34.41	3	1656/1693	1.18(1.04-1.33)	0.010	2.38	0.31	16	1.000	0.480	1.000	1.34(0.97-1.85)	0.077	72	1.18(0.95-1.46)	0.127	0
AGER	rs1800625(-429T>C,Alu1)	6	intergenic	Asian	C vs T	31.19	3	1656/1693	1.16(0.78-1.74)	0.468	20.99	0.00	91	1.000	0.741	0.232	1.12(0.74-1.68)	0.598	85	1.52(0.52-4.42)	0.443	90
AGER	rs2070600(p.Gly82Ser,c.244G>A)	6	non-synonymous	All	A vs G	31.57	4	2104/2178	1.10(0.93-1.31)	0.270	7.15	0.07	58	0.089	0.003	0.110	1.17(0.81-1.70)	0.408	83	1.15(0.77-1.72)	0.502	57
AHR	rs2066853(Arg554Lys,Ex10+501G>A)	7	non-synonymous	All	A vs G	30.44	5	1749/1925	0.96(0.84-1.10)	0.567	5.82	0.21	31	1.000	0.922	1.000	0.95(0.74-1.22)	0.703	63	0.96(0.78-1.18)	0.699	0
ALDH2	rs671(p.Glu487Lys/Glu504Lys,c.1510G>A)	12	non-synonymous	All	A vs G	24.03	3	1555/2079	1.36(0.74-2.50)	0.322	29.62	0.00	93	1.000	0.724	1.000	1.16(0.72-1.88)	0.539	89	1.10(0.53-2.29)	0.793	63
APEX1	rs1760944(c.-468T>G,-141T>G)	14	5'UTR	All	A vs C	47.94	8	3588/3783	1.16(1.08-1.25)	2.85×10^{-5}	7.70	0.36	9	0.386	0.119	0.287	1.21(1.02-1.44)	0.030	55	1.24(1.11-1.38)	1.54×10^{-4}	0
APEX1	rs1048945(p.Gln51His,c.153G>C)	14	non-synonymous	Caucasian	C vs G	4.72	3	745/816	0.93(0.67-1.31)	0.684	0.30	0.86	0	1.000	0.500	1.000						
APEX1	rs1130409(p.Asp148Glu,c.444T>G)	14	non-synonymous	All	G vs T	42.30	21	6479/8565	1.00(0.93-1.09)	0.922	34.22	0.02	45	1.000	0.985	0.023	1.07(0.96-1.19)	0.224	56	0.97(0.84-1.13)	0.731	56
APEX1	rs2307486(p.Ile64Val,c.190A>G)	14	non-synonymous	All	G vs A	6.97	4	2281/2505	0.82(0.63-1.06)	0.121	6.35	0.10	53	0.089	0.119	0.567						
ATM	rs609429(IVS48+238C>G)	11	intron	All	(GG+GC) vs CC	54.72	3	1490/1501	0.82(0.66-1.03)	0.086	3.02	0.22	34	1.000	0.495	0.515	0.82(0.66-1.03)	0.086	34			
ATM	rs664677(IVS21T-77C)	11	intron	All	C vs T	58.90	3	1627/1641	0.91(0.82-1.00)	0.056	1.82	0.40	0	1.000	0.427	1.000	0.76(0.64-0.92)	0.004	0	0.97(0.85-1.11)	0.680	0
ATM	rs189037(c.-111G>A,−4519G>A)	11	5'UTR	Asian	A vs G	42.68	5	3036/3415	1.09(1.00-1.18)	0.050	5.65	0.23	29	0.806	0.195	1.000	1.10(0.98-1.23)	0.105	9	1.16(1.01-1.33)	0.043	20
ATM	rs664143(IVS34G+60A)	11	intron	All	(GG+GA) vs AA	45.53	3	1465/1465	0.93(0.79-1.10)	0.392	1.61	0.45	0	0.296	0.083	1.000	0.93(0.79-1.10)	0.392	0			
AURKA	rs2273535(p.Phe31Ile,c.91T>A)	20	non-synonymous	Caucasian	A vs T	48.28	3	2301/2069	0.96(0.86-1.06)	0.421	0.63	0.73	0	0.296	0.338	1.000	0.97(0.83-1.14)	0.723	0	0.88(0.57-1.34)	0.547	61
AURKA	rs1047972(p.Ile57Val,c.169A>G)	20	non-synonymous	Caucasian	A vs G	15.75	3	2463/2283	0.96(0.86-1.07)	0.425	1.65	0.44	0	0.296	0.167	1.000	0.97(0.86-1.11)	0.681	0	0.77(0.53-1.11)	0.156	0
AXIN2	rs2240308(p.Pro50Ser,c.148C>T)	17	non-synonymous	All	T vs C	37.40	3	758/742	0.73(0.63-0.85)	6.39×10^{-5}	1.84	0.40	0	1.000	0.120	0.251	0.69(0.56-0.85)	3.98×10^{-4}	0	0.55(0.34-0.89)	0.015	32
BCL2	rs2279115(c.-938C>A)	18	5'UTR	All	A vs C	43.37	5	1847/2367	0.65(0.46-0.91)	0.011	45.33	0.00	91	0.624	0.035	0.481	0.59(0.39-0.90)	0.014	88	0.59(0.41-0.84)	0.004	80
BIRC5	rs9904341(c.-31G>C）	17	5'UTR	All	C vs G	43.56	5	1008/963	1.23(0.80-1.88)	0.352	27.16	0.00	85	0.806	0.925	0.091	1.07(0.65-1.77)	0.783	78	1.75(0.99-3.12)	0.056	70
BRCA2	rs144848(p.Asn372His,c.1114A>C)	13	non-synonymous	All	C vs A	23.94	4	1586/2513	1.00(0.82-1.21)	0.959	6.90	0.08	57	0.734	0.734	1.000						
CASC8	rs1447295(C>A)	8	intron	All	A vs C	14.41	3	1541/2057	1.00(0.88-1.14)	0.991	1.52	0.47	0	1.000	0.441	1.000	0.96(0.80-1.15)	0.658	33	1.43(0.90-2.26)	0.129	0
CASC8	rs6983267(T>G)	8	intron	All	G vs T	44.77	3	1539/1989	1.14(0.95-1.38)	0.166	7.70	0.02	74	0.296	0.223	0.263	1.16(0.81-1.66)	0.409	83	1.22(1.04-1.44)	0.013	0
CASP5	rs523104(p.Leu318Val,c.748C>G)	11	non-synonymous	All	C vs G	36.90	3	758/943	1.12(0.98-1.29)	0.105	1.18	0.55	0	1.000	0.371	1.000	1.09(0.90-1.33)	0.378	0	1.32(0.94-1.86)	0.113	33
CASP8	rs3834129(-652 6N del,-/CTTACT)	2	intergenic	All	Del vs non-del	27.82	4	2737/2696	0.95(0.77-1.17)	0.631	16.45	0.00	82	0.308	0.167	0.275	0.93(0.73-1.17)	0.526	76	0.98(0.72-1.32)	0.890	52
CASP8	rs1045485(p.Asp302His,c.853G>C)	2	non-synonymous	All	C vs G	10.96	4	1054/1259	1.20(0.97-1.49)	0.101	4.02	0.26	25	1.000	0.186	0.460	1.25(1.00-1.56)	0.056	20	0.90(0.42-1.91)	0.781	0
CCND1	rs678653(G>C)	11	3'UTR	All	C vs G	29.98	3	1323/1901	1.03(0.85-1.24)	0.773	5.03	0.08	60	1.000	0.347	1.000	0.99(0.76-1.27)	0.905	62	1.09(0.87-1.35)	0.464	0
CCND1	rs9344(rs603965,p.Pro241Pro,c.723G>A)	11	synonymous	All	A vs G	48.82	11	6058/7315	1.02(0.92-1.12)	0.696	30.90	0.00	68	0.533	0.992	0.007	0.98(0.85-1.12)	0.745	55	1.07(0.90-1.26)	0.460	69
CD3EAP	rs967591(c.-21G>A)	19	5'UTR	All	A vs G	32.09	3	676/726	1.23(1.01-1.49)	0.036	2.56	0.28	22	1.000	0.988	1.000	1.38(0.92-2.07)	0.119	62	1.30(0.95-1.78)	0.105	0
CDKN1A	rs1801270(p.Ser31Arg, c.93C>A, 6829C>A)	6	non-synonymous	All	A vs C	13.18	9	4039/4804	1.04(0.89-1.21)	0.663	16.82	0.03	52	0.029	0.009	0.280	1.08(0.88-1.32)	0.483	61	0.92(0.73-1.16)	0.489	0
CDKN2A	rs3731249(p.Ala148Thr,c.442G>A)	9	non-synonymous	Caucasian	(AA+AG) vs GG	1.75	3	2875/2707	1.38(0.81-2.35)	0.230	4.56	0.10	56	0.296	0.177	1.000	1.38(0.81-2.35)	0.230	56			
Chr8q24	rs16901979(C>A)	8	intergenic	All	A vs C	19.48	3	1534/1992	1.15(0.99-1.35)	0.065	3.29	0.19	39	1.000	0.259	1.000	1.18(1.02-1.37)	0.025	0	1.22(0.80-1.86)	0.352	51
CHRNA3	rs12914385(2594C>T)	15	intron	All	T vs C	35.09	4	5356/2873	1.20(1.01-1.44)	0.044	12.27	0.01	76	0.734	0.353	1.000	1.26(1.00-1.57)	0.047	70	1.34(1.04-1.71)	0.022	49
CHRNA3	rs3743073(A>C)	15	intron	All	G vs T	43.53	3	1391/1500	1.27(0.89-1.83)	0.191	23.05	0.00	91	0.296	0.088	1.000	1.37(0.95-1.98)	0.094	80	1.32(0.72-2.44)	0.368	91
CHRNA3	rs578776(C>T)	15	intron	All	T vs C	31.98	3	1245/2009	0.87(0.77-0.98)	0.018	0.19	0.91	0	1.000	0.969	0.576	0.84(0.72-0.98)	0.026	0	0.84(0.66-1.07)	0.162	0
CHRNA3	rs938682(T>C,T78896547C)	15	intron	All	C vs T	28.37	3	1240/1986	0.86(0.76-0.96)	0.009	1.08	0.58	0	0.296	0.054	1.000						
CHRNA3	rs6495309(4064C>T)	15	5'UTR	All	T vs C	38.44	4	3381/4244	0.83(0.77-0.89)	6.55×10^{-8}	2.78	0.43	0	1.000	0.727	1.000	0.78(0.71-0.86)	9.82×10^{-7}	0	0.81(0.68-0.95)	0.010	37
CHRNA5	rs142774214(rs3841324,-62ins/del,22bp indel)	15	5'UTR	All	Del vs ins	37.67	3	1431/1606	0.92(0.83-1.03)	0.131	2.02	0.36	1	1.000	0.828	1.000	0.96(0.83-1.11)	0.571	0	0.80(0.65-0.98)	0.032	0
CHRNA5	rs16969968(p.Asp398Asn,c.1192G>A)	15	non-synonymous	All	A vs G	32.51	11	6222/62452	1.23(1.06-1.43)	0.007	48.96	0.00	80	0.119	0.131	0.071	1.26(1.01-1.59)	0.045	85	1.49(1.32-1.68)	5.18×10^{-11}	0
CLPTM1L	rs402710(C>T)	5	intron	All	T vs C	32.92	13	7214/8051	0.89(0.83-0.95)	2.63×10^{-4}	19.48	0.08	38	0.669	0.437	0.335	0.84(0.78-0.90)	2.42×10^{-7}	0	0.81(0.71-0.93)	0.002	24
COMT	rs4680(p.Val158Met,c.472G>A)	22	non-synonymous	All	A vs G	29.90	5	1497/1958	1.09(0.84-1.43)	0.517	21.84	0.00	82	0.806	0.920	0.077	1.13(0.87-1.45)	0.366	63	1.12(0.66-1.90)	0.674	77
CRP	rs2808630(T>C)	1	3'UTR	All	C vs T	27.26	3	826/895	0.82(0.68-1.01)	0.056	2.79	0.25	28	1.000	0.859	1.000	0.81(0.61-1.07)	0.135	44	0.71(0.48-1.04)	0.080	0
CTLA4	rs3087243(g.6230G>A,CT60)	2	3'UTR	All	A vs G	26.64	3	1132/1220	0.99(0.86-1.14)	0.887	1.05	0.59	0	0.296	0.158	1.000	1.05(0.88-1.26)	0.566	0	0.81(0.59-1.11)	0.184	0
CTLA4	rs231775(p.Thr17Ala,c.49A>G)	2	non-synonymous	All	G vs A	61.94	6	2828/2953	0.88(0.64-1.21)	0.445	63.12	0.00	92	0.707	0.894	0.024	0.83(0.50-1.38)	0.477	91	0.93(0.66-1.31)	0.682	82
CTLA4	rs5742909(g.319C>T,-318C>T)	2	intergenic	All	T vs C	15.64	4	1205/1349	0.68(0.30-1.56)	0.364	48.66	0.00	94	0.308	0.581	0.634	0.67(0.30-1.50)	0.331	92	0.78(0.13-4.81)	0.791	82
CXCL12	rs1801157(801G>A)	10	3'UTR	All	A vs G	28.71	3	489/815	1.29(0.76-2.18)	0.351	17.39	0.00	89	1.000	0.954	0.277	1.40(0.75-2.60)	0.296	85	1.38(0.56-3.39)	0.483	81
CXCR2	rs1126579(C>T)	2	3'UTR	All	T vs C	55.45	3	942/964	0.84(0.74-0.96)	0.009	0.07	0.97	0	1.000	0.496	1.000	0.72(0.58-0.90)	0.004	0	0.87(0.71-1.06)	0.171	0
CYP17A1	rs743572(T-34C,A1/A2)	10	intergenic	All	A2 vs A1(G vs A)	56.19	4	1245/1689	1.03(0.89-1.19)	0.701	4.80	0.19	38	0.308	0.114	1.000	1.01(0.75-1.35)	0.961	45	1.04(0.84-1.30)	0.703	34
CYP1A1	rs1799814(m4,Thr461Asn,C>A)	15	non-synonymous	All	A vs C	5.97	5	1712/1967	1.22(0.57-2.62)	0.617	51.87	0.00	92	0.806	0.859	0.122	1.40(0.77-2.54)	0.269	90	1.77(0.19-16.66)	0.617	81
CYP1A1	rs1800031(m3,T5639C)	15	3'UTR	All	(CC+CT) vs TT	4.08	3	500/919	1.32(0.83-2.11)	0.248	0.63	0.73	0	0.296	0.146	1.000	1.32(0.83-2.11)	0.248	0			
CYP1A1	rs2606345(IVS1+606T>G)	15	intron	Caucasian	G vs T	34.44	3	2770/3609	1.00(0.91-1.11)	0.937	3.05	0.22	35	1.000	0.998	1.000	1.02(0.89-1.18)	0.786	38	0.99(0.85-1.15)	0.882	0
CYP1A1	rs4646903(m1,MspI,T3801C)	15	3'UTR	All	C vs T	21.88	57	9844/12410	1.16(1.07-1.25)	1.59×10^{-4}	121.62	0.00	55	0.772	0.256	0.014	1.20(1.10-1.30)	1.92×10^{-5}	46	1.30(1.11-1.52)	0.001	40
CYP1A1	rs1048943(*2C,m2,p.Ile462Val,c.1384A>G)	15	non-synonymous	All	G vs A	17.83	54	9869/12114	1.23(1.11-1.36)	7.64×10^{-5}	159.34	0.00	67	0.649	0.081	0.007	1.27(1.13-1.43)	5.60×10^{-5}	65	1.44(1.18-1.77)	4.16×10^{-4}	46
CYP1A2	rs2069514(CYP1A2*1C,-3860G>A)	15	intron	All	A vs G	4.23	5	925/1383	1.55(0.64-3.74)	0.327	32.99	0.00	88	0.221	0.927	1.000	1.28(0.72-2.26)	0.400	78			
CYP1A2	rs2069526(-739T>G)	15	intron	All	G vs T	8.00	3	396/494	1.70(0.77-3.76)	0.189	11.15	0.00	82	1.000	0.858	1.000	1.63(0.92-2.87)	0.095	54			
CYP1A2	rs35694136(-2467delT)	15	5'UTR	All	Carriers vs non-carriers	18.62	4	811/1254	1.16(0.67-2.02)	0.594	11.94	0.01	75	0.734	0.839	0.002	1.16(0.67-2.02)	0.594	75			
CYP1A2	rs762551(CYP1A2*1F,c.A-164C)	15	intron	All	C vs A	31.14	6	1273/1877	1.07(0.82-1.40)	0.616	27.04	0.00	82	0.452	0.491	0.000	1.01(0.72-1.43)	0.947	78	1.27(0.86-1.85)	0.226	67
CYP1B1	rs10012(p.Arg48Gly,c.142C>G)	2	non-synonymous	All	G vs C	25.98	3	622/666	1.46(0.88-2.40)	0.142	15.51	0.00	87	0.296	0.099	1.000	1.69(1.05-2.72)	0.031	74	1.54(0.52-4.53)	0.436	87
CYP1B1	rs1056827(p.Ala119Ser,c.355G>T,m2)	2	non-synonymous	All	T vs G	26.90	5	1501/2245	1.16(0.90-1.50)	0.253	18.67	0.00	79	1.000	0.789	0.289	1.24(0.91-1.69)	0.170	76	1.18(0.69-2.01)	0.549	73
CYP1B1	rs1800440(p.Asn453Ser,Ex3+315A>G)	2	non-synonymous	All	G vs A	18.97	5	3009/3887	0.99(0.85-1.14)	0.836	6.88	0.14	42	0.462	0.318	1.000	0.95(0.80-1.14)	0.579	47	1.23(0.97-1.56)	0.093	0
CYP1B1	rs1056836(CYP1B1*3,p.Leu432Val,c.1294C>G)	2	non-synonymous	All	G vs C	38.50	12	3033/3866	1.13(1.05-1.22)	0.002	9.77	0.55	0	0.064	0.228	0.387	1.17(1.05-1.30)	0.005	0	1.15(1.00-1.31)	0.043	0
CYP2A13	rs8192789(p.Arg257Cys,3375C>T)	19	non-synonymous	All	(TT+TC) vs CC	9.36	3	1517/2231	0.81(0.57-1.15)	0.238	3.54	0.17	43	1.000	0.482	0.384	0.81(0.57-1.15)	0.238	43			
CYP2A6	non*4/*4(*1/*4,a deletion of the CYP2A6 gene)	19	a deletion of gene	All	Del vs non-del	13.48	8	2867/2630	0.81(0.64-1.02)	0.074	23.21	0.00	70	0.711	0.928	0.015	0.88(0.68-1.14)	0.324	71	0.51(0.35-0.73)	2.93×10^{-4}	0
CYP2A6	rs1801272(p.Leu160His,Ex3-15T>A)	19	non-synonymous	Caucasian	(AA+AT) vs TT	3.99	3	2411/2644	0.66(0.52-0.84)	0.001	0.79	0.67	0	1.000	0.929	1.000	0.66(0.52-0.84)	0.001	0			
CYP2A6	rs5031016(p.Ile471Thr,c1412T>C,wt/*7)	19	non-synonymous	All	C vs T	9.89	3	1527/1138	0.57(0.33-1.00)	0.048	7.38	0.03	73	0.296	0.587	1.000	0.58(0.34-0.98)	0.043	66			
CYP2C9	rs1799853(p.Arg144Cys,c.430C>T)	10	non-synonymous	All	(TT+TC) vs CC	12.23	4	756/1293	1.14(0.85-1.55)	0.381	4.57	0.21	34	1.000	0.660	0.240	1.14(0.85-1.55)	0.381	34			
CYP2D6	phenotype(EM/HEM/PM)	22	phenotype	All	PM vs EM	5.38	9	1627/1970	0.80(0.53-1.22)	0.296	9.90	0.27	19	0.348	0.139	1.000	1.07(0.88-1.30)	0.487	27	0.81(0.55-1.20)	0.300	26
CYP2D6	rs1065852(p.Pro34Ser,188C>T)	22	non-synonymous	All	C vs T	43.08	3	581/636	0.86(0.57-1.30)	0.463	9.94	0.01	80	0.296	0.059	0.041	0.86(0.58-1.27)	0.439	55	0.55(0.17-1.85)	0.337	89
CYP2E1	rs2031920(RsaI,c1>c2,-1053C>T)	10	intergenic	All	T vs C (c2 vs c1)	17.33	23	4983/6628	0.86(0.76-0.97)	0.018	44.31	0.00	50	0.509	0.250	0.309	0.87(0.76-0.99)	0.030	44	0.91(0.60-1.37)	0.638	55
CYP2E1	rs3813867(g.3739G>C,c.-1293G>C)	10	intergenic	All	C vs G (c2 vs c1)	13.17	4	893/1029	0.94(0.56-1.56)	0.803	8.50	0.04	65	0.734	0.480	0.008	0.85(0.61-1.19)	0.348	28	1.06(0.34-3.34)	0.919	59
CYP2E1	rs6413432(c.967+1143T>A,7632T>A)	10	intron	All	A vs T(variation vs wild)	22.17	14	2944/3347	0.78(0.71-0.85)	6.76×10^{-8}	8.34	0.82	0	0.827	0.999	0.541	0.78(0.69-0.88)	3.12×10^{-5}	8	0.65(0.47-0.90)	0.010	16
CYP3A4	rs2740574(-392A>G,*1A/*1B)	7	intergenic	All	G vs A	21.71	4	1283/956	1.20(0.73-1.97)	0.465	9.14	0.03	67	1.000	0.153	0.362	1.13(0.89-1.42)	0.319	0	0.99(0.38-2.59)	0.981	36
CYP3A5	rs776746(A6986G,CYP3A5*3,22892A>G)	7	intron	All	A vs G	25.62	4	1166/929	0.65(0.36-1.16)	0.144	25.41	0.00	88	0.308	0.220	1.000	0.71(0.47-1.07)	0.099	77	0.85(0.28-2.56)	0.773	81
DRD2	rs1079597(G>A,TaqI-)	11	intron	All	A vs G	20.43	3	393/509	1.09(0.86-1.38)	0.499	1.53	0.47	0	0.296	0.436	1.000	1.01(0.78-1.30)	0.957	0	1.35(0.47-3.91)	0.582	56
DRD2	rs1800497(p.Glu714Lys,A2/A1,C>T)	11	non-synonymous	All	A2 vs A1(C vs T)	32.13	3	451/607	1.05(0.85-1.29)	0.667	0.48	0.79	0	1.000	0.611	1.000	1.06(0.79-1.42)	0.691	0	0.97(0.71-1.32)	0.833	0
EGF	rs4444903(+61A>G)	4	5'UTR	All	G vs A	59.28	3	666/690	1.54(0.93-2.57)	0.096	16.52	0.00	88	0.296	0.218	1.000	2.07(1.01-4.24)	0.048	79	1.47(0.84-2.59)	0.180	78
ELANE	rs351107(-903T>G,Rep_a)	19	5'UTR	Caucasian	G vs T	5.31	3	745/762	0.55(0.34-0.87)	0.011	2.80	0.25	29	1.000	0.794	0.565	0.54(0.31-0.94)	0.030	45			

Gene	Variant	Chr	Category	Ethnicity	Comparison[a]	Frequency(%)[b]	Number evaluated		Lung cancer risk meta-analysis in allelic model								Dominant model			Recessive model		
							Studies	Cases/Controls	OR(95% CI)	*P* value	Q	*P* for Q	I^2(%)	Begg *P*	Modified *P*[c]	Excess *P*[d]	OR(95% CI)	*P* value	I^2(%)	OR(95% CI)	*P* valute	I^2(%)
ELANE	rs7254054(-741G>A,REP_b)	19	5'UTR	Caucasian	A vs G	27.20	3	754/750	0.77(0.61-0.97)	0.030	3.72	0.16	46	0.296	0.022	0.567	0.77(0.63-0.95)	0.014	0	0.50(0.18-1.38)	0.183	81
EPHX1	rs1051740(p.Tyr113His,c.337T>C)	1	non-synonymous	All	C vs T	31.81	21	3461/7217	1.05(0.89-1.24)	0.564	106.98	0.00	81	0.057	0.153	0.000	1.05(0.86-1.28)	0.633	77	1.01(0.79-1.28)	0.951	61
EPHX1	rs2234922(p.His139Arg,c.416A>G)	1	non-synonymous	All	G vs A	18.85	23	5582/9556	1.12(0.99-1.28)	0.076	69.15	0.00	68	0.051	0.032	0.289	1.15(1.00-1.33)	0.059	65	1.09(0.88-1.35)	0.428	18
ERCC1	rs11615(rs3177700,p.Asn118Asn,c.354T>C)	19	synonymous	All	C vs T	51.18	12	5731/7058	0.90(0.83-0.99)	0.023	22.97	0.02	52	0.086	0.072	0.434	0.86(0.73-1.00)	0.048	51	0.89(0.80-1.00)	0.051	31
ERCC1	rs16979802(15310G>C)	19	intron	Caucasian	C vs G	21.81	3	1311/2114	0.87(0.74-1.03)	0.102	0.87	0.65	0	1.000	0.444	1.000	0.91(0.73-1.13)	0.399	0	0.75(0.45-1.26)	0.281	15
ERCC1	rs2298881(262G>T,C>A)	19	intron	All	T vs G	29.82	4	3049/3791	0.99(0.91-1.07)	0.723	3.50	0.32	14	0.308	0.727	1.000	0.96(0.86-1.07)	0.439	0	1.02(0.88-1.18)	0.799	0
ERCC1	rs3212948(C>G)	19	intron	All	G vs C	56.25	5	2144/2544	1.04(0.89-1.22)	0.591	10.24	0.04	61	0.462	0.568	0.243	0.95(0.81-1.11)	0.523	3	1.13(0.94-1.36)	0.181	34
ERCC1	rs3212955(A>G)	19	intron	All	G vs A	26.05	4	2271/2845	1.08(0.98-1.18)	0.109	2.42	0.49	0	0.734	0.744	1.000	1.06(0.94-1.20)	0.350	10	1.21(0.96-1.53)	0.107	9
ERCC1	rs3212961(IVS5+33C＞A,17677C>A)	19	intron	All	A vs C	35.50	6	2207/2311	0.94(0.86-1.03)	0.167	4.90	0.43	0	1.000	0.704	1.000	0.93(0.81-1.07)	0.321	0	0.97(0.74-1.28)	0.848	37
ERCC1	rs3212986(8092C>A,14443C>A)	19	3'UTR	All	A vs C	26.25	5	4079/4475	1.00(0.94-1.08)	0.931	1.63	0.80	0	0.806	0.929	1.000	1.01(0.93-1.10)	0.846	0	0.99(0.84-1.17)	0.894	0
ERCC1	rs735482(p.Lys261Thr,A>C)	19	non-synonymous	All	C vs A	19.32	5	1682/2797	1.02(0.91-1.15)	0.709	4.34	0.36	8	0.462	0.490	1.000	1.02(0.85-1.22)	0.830	25	1.14(0.86-1.51)	0.359	0
ERCC2	rs1052555(Asp711Asp,G>A)	19	synonymous	All	A vs G	18.91	3	511/751	1.09(0.85-1.40)	0.493	2.95	0.23	32	0.296	0.145	1.000						
ERCC2	rs171140(A>C)	19	intron	All	C vs A	34.69	3	511/751	1.04(0.87-1.26)	0.645	0.61	0.74	0	1.000	0.716	1.000						
ERCC2	rs13181(p.Lys751Gln,c.2251A>C)	19	non-synonymous	All	C vs A	25.26	40	13111/16749	1.12(1.05-1.19)	4.18×10^{-4}	76.17	0.00	49	0.753	0.272	0.048	1.16(1.08-1.26)	1.26×10^{-4}	40	1.15(1.01-1.30)	0.034	41
ERCC2	rs1799787(IVS19-70C＞T,G>A)	19	intron	All	T vs C	21.34	6	1792/2807	1.03(0.83-1.27)	0.824	10.74	0.06	54	1.000	0.996	0.171	1.02(0.81-1.28)	0.872	49	1.07(0.61-1.88)	0.807	25
ERCC2	rs1799793(p.Asp312Asn,c.981G>A)	19	non-synonymous	All	A vs G	23.17	26	10209/12967	1.02(0.95-1.09)	0.637	43.81	0.01	43	0.628	0.578	0.182	1.02(0.96-1.09)	0.498	1	1.10(0.97-1.25)	0.129	14
ERCC2	rs238406(p.Arg156Arg,C>A)	19	synonymous	All	A vs C	40.05	6	1754/2688	1.12(1.02-1.23)	0.013	3.94	0.56	0	0.260	0.332	0.599	1.08(0.93-1.25)	0.303	11	1.30(1.10-1.52)	0.001	0
ERCC4	rs1799801(p.Ser835Ser,Ex11-247T＞C)	16	synonymous	All	C vs T	27.99	3	1009/1758	1.02(0.88-1.17)	0.835	2.16	0.34	8	1.000	0.786	1.000						
ERCC4	rs1800067(Arg415Gln)	16	non-synonymous	Caucasian	A vs G	6.78	5	1521/2420	1.10(0.92-1.32)	0.286	1.19	0.88	0	0.806	0.952	1.000	1.12(0.92-1.37)	0.261	0	1.63(0.51-5.22)	0.413	20
ERCC5	rs1047768(p.His46His,335C>T)	13	synonymous	All	T vs C	43.99	4	1449/2248	0.86(0.74-1.00)	0.049	5.78	0.12	48	0.734	0.414	1.000	0.92(0.80-1.06)	0.256	0	0.76(0.61-0.94)	0.013	32
ERCC5	rs17655(p.Asp1104His,c.3310G>C)	13	non-synonymous	All	C vs G	39.06	10	3528/4481	0.96(0.84-1.10)	0.525	29.83	0.00	70	1.000	0.952	0.087	0.96(0.77-1.21)	0.754	72	0.90(0.72-1.12)	0.352	53
ERCC6	rs3793784(-6530C>G)	10	5'UTR	All	G vs C	30.82	3	1643/1689	0.75(0.60-0.92)	0.007	6.23	0.04	68	1.000	0.550	0.167						
ERCC6	rs2228528(p.Gly399Asp,G1275A)	10	non-synonymous	All	T vs C	41.74	4	1856/2059	1.05(0.95-1.15)	0.365	2.91	0.41	0	0.734	0.556	1.000						
EXO1	rs1047840(p.Glu589Lys,c.1765G>A)	1	non-synonymous	All	A vs G	21.78	3	1114/1166	1.23(0.96-1.57)	0.099	6.15	0.05	68	1.000	0.981	0.300	1.23(0.85-1.79)	0.274	78	1.33(0.94-1.88)	0.105	0
FANCG	rs2237857(p.Thr297Ile,C1382T)	9	non-synonymous	All	T vs C	8.77	3	1553/1774	0.98(0.68-1.41)	0.903	4.52	0.10	56	1.000	0.330	0.100						
FAS	rs2234767(-1377G/A)	10	5'UTR	All	A vs G	27.07	5	4125/3696	1.09(0.97-1.22)	0.153	7.90	0.10	49	1.000	0.777	0.171	1.05(0.93-1.18)	0.480	24	1.30(0.99-1.73)	0.063	58
FASLG	rs763110(-844C/T)	1	5'UTR	All	T vs C	34.01	4	4004/3639	0.83(0.65-1.07)	0.156	34.08	0.00	91	0.734	0.536	0.630	0.80(0.56-1.14)	0.213	92	0.83(0.70-0.99)	0.038	30
FGFR4	rs351855(p.Gly388Arg,G>A)	5	non-synonymous	All	A vs G	42.47	4	1083/1275	0.82(0.69-0.98)	0.025	4.48	0.21	33	0.089	0.015	1.000	0.73(0.61-0.87)	3.56×10^{-4}	0	0.87(0.58-1.32)	0.521	51
GPC5	rs2352028(C>T)	13	intron	Asian	T vs C	21.65	3	1648/2002	0.97(0.87-1.09)	0.611	1.43	0.49	0	1.000	0.765	1.000						
GPX1	rs1050450(p.Pro200Leu,c.599C>T)	3	non-synonymous	Caucasian	T vs C	34.06	4	976/1339	1.04(0.75-1.44)	0.811	16.02	0.00	81	0.734	0.934	0.157	1.11(0.72-1.71)	0.632	80	0.93(0.54-1.59)	0.785	71
GSTM1	Present/Null(Large gene deletion)	1	phenotype	All	Null vs present	48.85	133	33253/37867	1.18(1.12-1.23)	2.54×10^{-11}	269.09	0.00	52	0.105	0.037	0.011						
GSTM3	rs1799735(c.468+21delAGG,3bp deletion,*A/*B)	1	intron	All	Del vs non-del	17.64	8	1749/2069	0.97(0.86-1.09)	0.608	3.43	0.84	0	0.902	0.668	1.000	0.95(0.84-1.09)	0.483	0	0.90(0.50-1.63)	0.728	54
GSTP1	rs1138272(p.Ala114Val,c.341C>T)	11	non-synonymous	Caucasian	T vs C	7.63	6	1479/1573	1.24(0.93-1.65)	0.149	10.60	0.06	53	1.000	0.529	0.177	1.18(0.90-1.55)	0.236	63	1.56(0.51-4.77)	0.438	39
GSTP1	rs1695(p.Ile105Val,c.313A>G)	11	non-synonymous	All	G vs A	30.41	46	12521/14411	1.08(1.02-1.15)	0.011	100.57	0.00	55	0.075	0.009	0.008	1.08(1.00-1.16)	0.059	55	1.11(1.01-1.22)	0.035	13
GSTT1	Present/Null(Large gene deletion)	22	phenotype	All	Null vs present	26.14	77	23009/25365	1.10(1.02-1.19)	0.011	179.38	0.00	58	0.346	0.345	0.000						
HIF1A	rs11549465(p.Pro582Ser,c.1744C>T)	14	non-synonymous	All	T vs C	13.60	3	509/566	1.19(0.50-2.86)	0.690	18.09	0.00	89	1.000	0.488	0.293	1.19(0.51-2.76)	0.688	86			
HIF1A	rs11549467(p.Ala588Thr,c.1762G>A)	14	non-synonymous	All	A vs G	9.45	3	509/566	2.27(1.74-2.96)	1.62×10^{-9}	1.47	0.48	0	0.296	0.261	0.610	2.15(1.56-2.95)	2.51×10^{-6}	0			
HRAS1	common alleles /rare alleles(HRAS1 VNTR alleles, loss of heterozygosity in the 15p15.5 region)	11	combined variant	Caucasian	rare vs common	7.03	4	746/1174	2.55(1.01-6.45)	0.048	9.56	0.02	69	0.734	0.561	0.346						
HYKK	rs931794(A>G)	15	intron	All	G vs A	32.89	5	2435/3180	1.23(1.14-1.34)	1.85×10^{-7}	1.28	0.86	0	1.000	0.967	0.411	1.29(1.15-1.43)	6.08×10^{-6}	0	1.35(1.16-1.58)	1.58×10^{-4}	0
IFNG	rs2069705 (-1615T>C)	12	intergenic	All	C vs T	38.30	3	2119/2654	1.02(0.93-1.11)	0.727	2.01	0.37	0	1.000	0.662	1.000						
IGFBP3	rs2854744 (C-202A)	7	intergenic	Asian	C vs A	27.71	3	789/960	0.79(0.52-1.20)	0.262	13.99	0.00	86	0.296	0.298	1.000	0.79(0.50-1.26)	0.328	82	0.57(0.26-1.28)	0.175	73
IL10	rs1800871 (c.-854T>C, -819C>T)	1	5'UTR	All	T vs C	30.14	11	3269/4627	0.93(0.76-1.14)	0.488	37.41	0.00	73	0.640	0.656	0.019	0.90(0.64-1.26)	0.525	75	0.92(0.69-1.23)	0.569	60
IL10	rs1800872 (g.4433A>C, -592C>A)	1	intergenic	All	A vs C	35.53	8	3710/4965	0.90(0.81-1.01)	0.075	15.64	0.03	55	0.174	0.165	0.369	0.86(0.71-1.04)	0.122	52	0.84(0.63-1.11)	0.211	61
IL10	rs1800896 (g.3943A>G, -1082A>G)	1	intergenic	All	G vs A	37.18	10	2861/3817	1.29(1.05-1.59)	0.017	35.95	0.00	75	0.074	0.042	1.000	1.49(0.96-2.31)	0.072	80	1.25(1.00-1.56)	0.048	0
IL13	rs1800925 (-1069C>T, -1112C>T)	5	intergenic	All	T vs C	21.93	3	1788/1920	1.02(0.91-1.13)	0.785	0.91	0.64	0	0.296	0.311	1.000						
IL13	rs20541 (Arg130Gln,+2044G>A)	5	non-synonymous	All	A vs G	21.66	3	1877/2020	1.01(0.90-1.12)	0.921	0.93	0.63	0	1.000	0.999	1.000						
IL17A	rs2275913 (-73G>A, -152G>A)	6	5'UTR	All	A vs G	24.90	3	889/998	1.40(1.00-1.96)	0.051	9.72	0.01	79	1.000	0.932	1.000	1.40(0.90-2.17)	0.140	80	1.76(1.21-2.55)	0.003	18
IL1B	rs1143634 (p.Phe105Phe, Ex5+14C>T)	2	synonymous	All	T vs C	21.37	5	4626/4116	1.05(0.95-1.17)	0.317	5.76	0.22	31	0.462	0.304	0.345	1.14(0.92-1.40)	0.229	41	1.14(0.87-1.48)	0.346	0
IL1B	rs1143627 (g.4970C>T, -31T>C)	2	intergenic	All	C vs T	38.81	9	5735/7138	0.93(0.84-1.03)	0.176	27.03	0.00	70	0.029	0.040	0.104	0.95(0.78-1.14)	0.554	74	0.80(0.68-0.95)	0.010	49
IL1B	rs16944 (C-511T)	2	intergenic	All	T vs C	41.62	11	4866/5910	0.94(0.84-1.06)	0.332	36.62	0.00	73	1.000	0.533	0.215	0.94(0.79-1.12)	0.517	68	0.86(0.70-1.06)	0.155	65
IL4	rs2243250 (-509C>T)	5	intergenic	All	T vs C	42.88	5	3496/4037	1.09(0.92-1.31)	0.320	14.46	0.01	72	0.462	0.815	0.542	1.07(0.68-1.68)	0.784	69	1.12(0.82-1.54)	0.470	71
IL6	rs1800795 (G-174C)	7	intergenic	All	C vs G	42.08	10	4619/5490	1.08(0.94-1.24)	0.287	28.73	0.00	69	0.858	0.567	1.000	1.09(0.84-1.42)	0.517	70	1.14(0.88-1.47)	0.326	47
IL6	rs1800796 (-572C>G, 634C>G)	7	intergenic	All	G vs C	22.43	9	2972/3395	0.96(0.75-1.22)	0.717	54.15	0.00	85	0.754	0.818	0.000	0.99(0.75-1.31)	0.927	84	0.94(0.64-1.39)	0.766	54
IL8	rs4073 (T-251A)	4	intergenic	All	T vs A	49.84	7	4787/5310	1.02(0.90-1.15)	0.764	18.80	0.01	68	1.000	0.783	0.233	1.01(0.83-1.23)	0.894	45	1.10(0.88-1.39)	0.398	71
LIG1	rs156641 (G>A)	19	intron	All	A vs G	31.71	4	1255/2220	1.12(0.98-1.28)	0.092	3.57	0.31	16	0.734	0.139	0.513	1.13(0.95-1.33)	0.163	7	1.45(1.14-1.83)	0.002	0
LIG1	rs20579 (-7C>T)	19	5'UTR	All	A vs G	14.40	5	1818/3139	1.12(0.84-1.51)	0.440	23.17	0.00	83	0.806	0.366	0.017	1.11(0.82-1.50)	0.510	78	1.41(0.66-3.01)	0.380	68
LIG1	rs20581 (p.Asp802Asp, G>A)	19	synonymous	All	A vs G	41.09	4	828/1386	1.02(0.90-1.17)	0.726	0.96	0.81	0	0.734	0.506	1.000	0.91(0.74-1.13)	0.400	0	1.09(0.76-1.57)	0.651	33
LIG1	rs3730931 (IVS9-21A>G)	19	intron	All	G vs A	13.56	4	1399/2364	1.05(0.80-1.38)	0.715	9.55	0.02	69	0.308	0.139	0.174	1.05(0.79-1.40)	0.723	63	0.95(0.55-1.64)	0.859	20
LIG1	rs439132 (A>G)	19	intron	All	G vs A	8.36	3	739/1220	1.21(0.74-1.96)	0.444	6.66	0.04	70	1.000	0.339	0.053	1.21(0.70-2.09)	0.507	72	1.82(0.72-4.55)	0.204	20
LIG1	rs20580 (p.Ala170Ala, c.417C>A)	19	synonymous	All	A vs C	52.69	6	2357/3592	0.92(0.77-1.10)	0.370	24.88	0.00	80	0.133	0.151	0.559	0.95(0.75-1.19)	0.643	58	0.96(0.71-1.30)	0.780	82
LIG4	rs1805388 (p.Thr9Ile,Ex2+54C>T)	13	non-synonymous	All	T vs C	17.05	3	515/1246	1.07(0.77-1.50)	0.676	4.84	1.50	59	1.000	0.785	0.140	1.07(0.76-1.52)	0.688	48	1.41(0.72-2.76)	0.313	7
LTA	rs909253 (A+252G)	6	intron	All	G vs A	35.92	7	941/1683	0.93(0.83-1.05)	0.263	4.55	0.60	0	0.035	0.208	1.000	1.00(0.82-1.23)	0.972	18	0.79(0.61-1.01)	0.057	0
MAPKAPK2	CNV-30450(2 copies/3 copies/4 copies)	1	CNV	Asian	4 copies vs 2 copies	9.76	3	2332/2480	1.60(1.04-2.45)	0.031	10.57	0.01	81	1.000	0.947	0.298	1.28(1.05-1.57)	0.016	59	1.58(1.04-2.40)	0.034	81
MBD4	rs140693 (p.Glu346Lys, G1212A)	3	non-synonymous	Asian	A vs G	35.62	4	2295/2469	0.99(0.86-1.13)	0.881	7.04	0.07	57	1.000	0.655	1.000						
MCP1	rs1024611 (-2518A>G, PvuII)	17	5'UTR	All	G vs A	31.47	3	1985/1981	0.76(0.53-1.09)	0.134	13.04	0.00	85	1.000	0.260	1.000						
MDM2	rs117039649 (G>C, SNP285)	12	intron	All	C vs G	3.20	3	1846/4400	1.10(0.89-1.37)	0.374	0.51	0.77	0	1.000	0.743	1.000	1.09(0.87-1.36)	0.445	0			
MDM2	rs2279744 (SNP309,c.14+309T>G)	12	intergenic	All	G vs T	41.05	19	11076/14434	1.10(1.01-1.19)	0.021	71.76	0.00	75	0.700	0.355	0.242	1.12(1.00-1.27)	0.058	75	1.15(1.04-1.27)	0.005	46
MDM2	rs769412 (p.Glu184Glu,2164A>G,SNP354)	12	synonymous	All	G vs A	27.44	4	1691/1915	1.02(0.91-1.14)	0.785	1.58	0.66	0	0.734	0.836	1.000	0.98(0.84-1.14)	0.768	0	1.11(0.89-1.39)	0.338	0
MGMT	rs12268840 (C>T)	10	intron	Caucasian	T vs C	32.82	3	247/355	0.88(0.64-1.19)	0.396	2.64	0.27	24	1.000	0.996	1.000	0.84(0.60-1.16)	0.282	0	0.87(0.39-1.94)	0.730	35
MGMT	rs12917 (p.Leu115Phe, c.343C>T)	10	non-synonymous	All	T vs C	15.64	7	2552/3836	1.05(0.95-1.17)	0.335	5.87	0.44	0	0.548	0.766	1.000	1.05(0.93-1.18)	0.445	0	1.15(0.85-1.56)	0.377	0
MGMT	rs1803965 (Leu53Leu,171C>T, TaqI)	10	synonymous	All	T vs C	12.27	3	1060/1149	0.96(0.80-1.15)	0.671	0.75	0.69	0	0.296	0.416	1.000	0.98(0.81-1.20)	0.870	0	0.69(0.32-1.45)	0.321	0
MGMT	rs2308321 (p.Ile174Val,Ile143Val,c.520A>G)	10	non-synonymous	All	G vs A	12.32	6	2023/2191	1.05(0.86-1.28)	0.649	7.97	0.16	37	0.452	0.643	1.000	1.06(0.82-1.38)	0.665	48	0.86(0.51-1.43)	0.550	0
MGMT	rs2308327 (p.Lys178Arg, c.533A>G)	10	non-synonymous	Caucasian	G vs A	20.45	5	759/880	0.73(0.50-1.07)	0.109	12.48	0.01	68	0.086	0.029	1.000	0.73(0.47-1.12)	0.149	67	0.92(0.59-1.41)	0.687	0
MIR146A	rs2910164 (C>G)	5	non-coding transcript	All	C vs G	45.26	6	3158/3225	1.16(1.06-1.27)	0.001	6.35	0.27	21	0.260	0.076	0.415	1.20(1.04-1.38)	0.012	24	1.23(1.09-1.39)	0.001	0
MIR196A2	rs11614913 (T>C)	12	non-coding transcript	All	C vs T	48.95	6	2727/2797	1.02(0.88-1.18)	0.839	16.57	0.01	70	0.060	0.093	0.014	1.13(0.91-1.41)	0.260	56	0.94(0.73-1.20)	0.618	71
MLH1	rs1799977 (p.Ile219Val, c.655A>G)	3	non-synonymous	All	G vs A	9.64	5	2147/2355	0.92(0.72-1.18)	0.531	7.91	0.10	49	0.806	0.401	1.000						
MLH1	rs1800734 (-93G>A)	3	5'UTR	All	A vs G	48.86	6	2328/2491	0.98(0.86-1.12)	0.780	11.53	0.04	57	0.707	0.479	0.015	0.80(0.68-0.95)	0.009	24	1.27(0.94-1.70)	0.114	75
MLH3	rs175080 (p.Pro844Leu, C2645T)	14	non-synonymous	All	T vs C	20.13	3	1363/1540	1.03(0.79-1.33)	0.837	5.85	0.05	66	0.296	0.611	0.103						
MMP1	rs1799750 (-1607 1G/2G,insG)	11	intergenic	All	2G vs 1G	54.13	10	4787/4446	1.08(0.96-1.22)	0.197	27.39	0.00	67	0.474	0.852	0.331	1.11(0.99-1.25)	0.087	13	1.10(0.91-1.34)	0.341	70
MMP2	rs243865 (-1306C>T)	16	intergenic	All	T vs C	16.77	3	1751/1729	0.63(0.45-0.89)	0.009	9.86	0.01	80	0.296	0.001	0.458	0.60(0.40-0.90)	0.014	82	0.60(0.36-0.99)	0.047	0
MMP3	rs3025058 (-1612 5A/6A, -1171 5A/6A)	11	intergenic	All	5A vs 6A	44.49	5	3043/2422	1.08(0.93-1.27)	0.322	8.27	0.08	52	0.027	0.100	0.489	1.05(0.92-1.18)	0.489	0	1.09(0.88-1.35)	0.448	31

Gene	Variant	Chr	Category	Ethnicity	Comparison^a	Frequency(%)^b	Number evaluated		Lung cancer risk meta-analysis in allelic model								Dominant model			Recessive model		
							Studies	Cases/Controls	OR(95% CI)	*P* value	Q	*P* for Q	I^2(%)	Begg *P*	Modified *P*^{c}	Excess *P*^{d}	OR(95% CI)	*P* value	I^2(%)	OR(95% CI)	*P* valute	I^2(%)
MMP9	rs3918242 (g.3430C>T,-1562 C>T)	20	intergenic	All	T vs C	13.28	3	1205/1099	0.89(0.69-1.14)	0.357	3.40	0.18	41	1.000	0.987	1.000	0.92(0.74-1.14)	0.438	15	0.53(0.13-2.08)	0.362	48
MPO	rs2333227 (G-463A)	17	intron	All	A vs G	20.93	27	9595/10754	0.92(0.85-1.00)	0.058	56.29	0.00	54	0.269	0.098	0.048	0.92(0.85-1.00)	0.055	38	0.92(0.74-1.15)	0.471	45
MSH3	rs26279 (p.Ala1045Thr,c.3133G>A)	5	non-synonymous	All	G vs A	27.74	4	1649/1849	0.90(0.75-1.08)	0.251	6.83	0.08	56	0.734	0.688	0.447						
MSH6	rs1042821 (p.Gly39Glu,c.116G>A)	2	non-synonymous	All	A vs G	29.44	3	1454/1620	0.95(0.83-1.08)	0.415	2.30	0.32	13	0.296	0.271	1.000						
MTHFR	rs1801131 (p.Ala429Glu, c.1286A>C, A1298C)	1	non-synonymous	All	C vs A	24.91	11	4125/5131	1.07(1.00-1.14)	0.069	7.93	0.64	0	0.876	0.443	1.000	1.03(0.91-1.16)	0.636	38	1.22(0.99-1.51)	0.067	27
MTHFR	rs1801133 (p.Ala222Val, Ex4+79C＞T)	1	non-synonymous	All	T vs C	37.83	16	8692/8412	1.10(0.98-1.24)	0.125	69.01	0.00	78	0.192	0.101	0.069	1.07(0.92-1.26)	0.365	73	1.15(0.96-1.37)	0.124	62
MTR	rs1805087 (Asp919Gly, A2756G)	1	non-synonymous	All	G vs A	13.88	4	2488/3335	1.06(0.93-1.22)	0.387	4.61	0.20	35	1.000	0.920	0.261	1.07(0.88-1.29)	0.507	55	1.14(0.79-1.63)	0.490	0
MTRR	rs1801394 (Ile49Met, A66G)	5	non-synonymous	All	G vs A	43.28	3	1668/2291	1.13(1.03-1.24)	0.011	1.29	0.53	0	1.000	0.916	1.000	1.19(1.00-1.42)	0.054	23	1.15(0.98-1.34)	0.086	0
MUTYH	rs3219489 (p.Gln324His, c.972G>C)	1	non-synonymous	All	C vs G	31.13	4	1250/1137	1.10(0.86-1.39)	0.455	8.17	0.04	63	1.000	0.778	0.321	1.05(0.82-1.34)	0.690	41	1.25(0.76-2.06)	0.372	54
MYCL	L/S(EcoRI)	1	the restriction site absence	All	S vs L	49.65	9	636/1004	1.05(0.91-1.22)	0.530	3.99	0.86	0	1.000	0.792	1.000	1.10(0.86-1.40)	0.443	0	1.03(0.81-1.31)	0.813	0
NAT2	Rapid/slow(Acetylation Phenotype)	8	phenotype	All	Slow vs rapid	48.33	17	3747/4852	1.06(0.90-1.25)	0.502	38.19	0.00	58	0.064	0.622	0.000						
NAT2	rs1799929 (p.Leu161Leu, 481C>T)	8	synonymous	All	T vs C	36.88	3	576/686	1.11(0.87-1.41)	0.407	4.14	0.13	52	1.000	0.717	0.257	1.36(0.76-2.44)	0.308	80	1.06(0.72-1.57)	0.754	24
NAT2	rs1799930 (p.Arg197Gln, 590G>A,NAT2*6B)	8	non-synonymous	All	A vs G	32.47	4	712/893	1.01(0.81-1.25)	0.964	5.94	0.12	50	0.734	0.903	0.107	0.97(0.74-1.28)	0.831	65	1.20(0.82-1.76)	0.361	21
NBN	rs1805794 (p.Gln185Glu, Ex5-32C>G, 605C>G)	8	non-synonymous	All	G vs C	49.91	8	3578/4688	0.95(0.80-1.13)	0.554	41.58	0.00	83	0.174	0.292	0.001	0.93(0.66-1.30)	0.662	82	0.90(0.72-1.12)	0.334	58
NFKB1	rs28362491 (-94ins/delATTG)	4	intergenic	All	Ins vs del	45.72	3	935/935	1.02(0.72-1.43)	0.919	11.51	0.00	83	0.296	0.355	0.003	1.04(0.59-1.83)	0.892	82	1.01(0.69-1.49)	0.961	64
NOD2	rs2066847 (3020insC, WT/insC, L1007fs)	16	frameshift	All	Carriers vs non-carriers	0.50	3	807/4078	1.42(1.07-1.90)	0.017	1.04	0.59	0	1.000	0.988	0.567	1.42(1.07-1.90)	0.017	0			
NQO1	rs1800566 (p.Pro187Ser,c.648C>T, 609C>T,*2)	16	non-synonymous	All	T vs C	29.63	23	5088/6381	1.02(0.92-1.14)	0.670	54.88	0.00	60	0.398	0.598	0.031	1.03(0.92-1.16)	0.586	56	1.06(0.86-1.31)	0.586	45
OGG1	rs1052133 (p.Ser326Cys,c.977C>G,8055C>G)	3	non-synonymous	All	G vs C	38.90	33	11944/14309	1.04(0.97-1.11)	0.243	76.29	0.00	58	0.914	0.970	0.000	1.06(0.96-1.17)	0.289	54	1.11(1.00-1.24)	0.052	41
PADPRP	A/B (a 193-bp deletion)	13	STR	All	Del vs non-del	34.59	3	288/292	1.13(0.70-1.82)	0.617	6.42	0.04	69	0.296	0.331	0.168	1.24(0.71-2.18)	0.451	59	1.09(0.51-2.31)	0.829	46
PARP1	rs1136410(p.Val762Ala,Ex17+8T＞C)	1	non-synonymous	All	C vs T	41.02	6	3192/2874	1.01(0.89-1.15)	0.842	12.64	0.03	60	1.000	0.313	0.170	1.05(0.88-1.27)	0.572	36	1.11(0.88-1.40)	0.372	43
PCNA	rs25406(2232C>T)	20	intron	All	T vs C	38.63	4	970/1302	0.91(0.77-1.06)	0.231	4.99	0.17	40	0.734	0.345	1.000	0.91(0.76-1.10)	0.322	0	0.91(0.52-1.60)	0.741	77
PDCD5	rs1862214 (G>A)	19	intergenic	All	G vs C	32.06	3	737/683	1.32(1.12-1.56)	0.001	1.86	0.40	0	0.296	0.156	1.000	1.42(1.13-1.77)	0.002	0	1.54(0.83-2.87)	0.173	58
POLD1	rs1726801 (p.Arg119His,c.356G>A)	19	non-synonymous	Asian	A vs G	19.30	3	1263/1420	1.11(0.96-1.28)	0.168	1.61	0.45	0	0.296	0.073	1.000						
POLI	rs3730668 (-78G>T)	18	intergenic	All	T vs G	58.99	3	672/823	0.94(0.80-1.09)	0.397	0.63	0.73	0	1.000	0.688	1.000						
POLI	rs8305 (Thr706Ala, 2180A>G)	18	non-synonymous	All	G vs A	25.24	4	1655/2593	1.09(0.98-1.20)	0.111	2.17	0.54	0	0.734	0.250	0.379						
POLL	rs3730477 (p.Arg438Trp, 1683C>T)	10	non-synonymous	All	T vs C	3.66	3	1356/1542	1.29(0.69-2.40)	0.425	4.07	0.13	51	1.000	0.503	0.347						
PON1	rs662 (p.Gln192Arg,c.575A>G)	7	non-synonymous	All	A vs G	46.70	3	995/834	0.77(0.67-0.88)	2.02×10^{-4}	0.71	0.70	0	1.000	0.704	1.000	0.78(0.63-0.96)	0.018	0	0.61(0.46-0.83)	0.001	30
PPARG	rs1801282 (p.Pro12Ala,c.36C>G)	3	non-synonymous	All	G vs C	15.24	4	2476/3377	1.00(0.88-1.12)	0.956	0.82	0.84	0	0.734	0.887	1.000	0.93(0.93-1.18)	0.542	0	1.17(0.80-1.73)	0.415	0
PPP1R13L	rs6966 (T>A)	19	3'UTR	All	T vs A	46.66	5	1120/1361	1.09(0.92-1.29)	0.302	6.96	0.14	43	0.806	0.755	0.349	1.16(0.95-1.43)	0.145	0	1.11(0.82-1.51)	0.502	54
PPP1R13L	rs1970764 (IVS1-4364A>G)	19	intron	All	G vs A	36.71	3	678/726	1.12(0.90-1.39)	0.313	3.24	0.20	38	1.000	0.918	1.000	1.12(0.89-1.41)	0.349	0	1.07(0.54-2.10)	0.851	69
PROM1	rs2240688 (A>C)	4	3'UTR	Asian	C vs A	27.37	3	2332/2457	0.83(0.76-0.91)	6.92×10^{-5}	0.02	0.99	0	0.296	0.379	0.281	0.80(0.72-0.90)	1.65×10^{-4}	0	0.78(0.63-0.97)	0.026	0
PTGS2	rs20417 (-765G>C)	1	intergenic	All	C vs G	16.15	4	2355/2731	0.96(0.86-1.08)	0.505	1.84	0.61	0	1.000	0.299	1.000	0.80(0.57-1.13)	0.200	42			
PTGS2	rs689466 (g.38139393T>C,-1195A>G)	1	intergenic	All	G vs A	38.07	4	1676/2180	0.82(0.65-1.02)	0.070	13.44	0.00	78	0.734	0.218	0.626	0.78(0.62-0.97)	0.026	56	0.87(0.62-1.20)	0.391	66
PTGS2	rs5275 (c.*427T>C, 8473T>C)	1	3'UTR	All	C vs T	29.41	11	6813/7988	0.95(0.83-1.09)	0.493	58.16	0.00	83	0.755	0.955	0.038	0.93(0.79-1.10)	0.389	74	0.90(0.62-1.30)	0.578	79
RAD23B	rs1805329 (p.Ala249Val,Ex7+65C＞T)	9	non-synonymous	All	T vs C	23.29	4	653/878	1.10(0.80-1.51)	0.572	9.39	0.03	68	0.089	0.059	0.231	1.10(0.67-1.81)	0.703	75	1.04(0.52-2.06)	0.922	49
REV1	rs3087386 (p.Phe257Ser,892T>C)	2	non-synonymous	All	C vs T	40.81	3	1437/1818	1.03(0.92-1.14)	0.658	0.51	0.78	0	1.000	0.366	1.000				0.98(0.74-1.31)	0.909	52
REV3L	rs462779 (p.Thr1146Ile,4259C>T)	6	non-synonymous	Asian	T vs C	39.36	4	1937/2335	1.11(1.02-1.22)	0.021	0.54	0.91	0	0.734	0.921	1.000						
REV3L	rs465646 (460T>C)	6	3'UTR	All	C vs T	18.18	4	1438/1683	0.88(0.73-1.07)	0.197	5.42	0.14	45	0.308	0.058	0.429	0.78(0.67-0.92)	0.003	0	0.93(0.62-1.41)	0.740	0
SFTPB	wild type/variation (deletions or insertions)	2	intron	All	Variation vs wild	5.83	3	157/240	1.92(1.11-3.33)	0.020	0.08	0.96	0	0.296	0.495	1.000	2.09(1.16-3.76)	0.014	0	0.32(0.15-0.68)	0.003	0
SOD2	rs4880 (rs1799725, Ala16Val)	6	non-synonymous	All	T vs C	51.48	9	3738/4467	1.20(1.06-1.36)	0.005	20.34	0.01	61	0.348	0.723	0.733	1.33(1.08-1.64)	0.007	52	1.17(0.98-1.38)	0.082	55
SULT1A1	rs9282861(p.Arg213His,c.638G>A,*1/*2)	16	non-synonymous	All	A vs G	21.68	6	1965/2286	1.20(0.97-1.48)	0.094	18.08	0.00	72	1.000	0.779	1.000	1.24(0.94-1.63)	0.127	74	1.14(0.87-1.50)	0.343	0
TDG	rs4135113(p.Gly199Ser,c.595G>A)	12	non-synonymous	All	A vs G	6.13	3	289/318	0.85(0.51-1.42)	0.531	1.45	0.49	0	1.000	0.497	1.000						
TERT	rs2736098(p.Ala305Ala,c.915G>A)	5	synonymous	All	A vs G	33.01	7	4660/4825	1.20(1.08-1.33)	0.001	17.98	0.01	67	0.548	0.734	0.706	1.23(1.13-1.35)	4.84×10^{-6}	0	1.65(1.43-1.89)	1.87×10^{-12}	0
TGFB1	rs1800469 (C-509T)	19	intergenic	Asian	T vs C	49.31	4	1091/1238	0.95(0.85-1.07)	0.428	3.10	0.38	3	0.089	0.100	1.000	0.96(0.72-1.28)	0.777	56	0.96(0.79-1.17)	0.691	0
TGFB1	rs1800470 (p.Leu10Pro,c.29C>T)	19	non-synonymous	All	C vs T	44.49	7	1398/1553	1.16(0.97-1.39)	0.104	15.61	0.02	62	0.764	0.718	1.000	1.33(0.97-1.82)	0.079	69	1.10(0.92-1.32)	0.285	0
TNF	rs1799724 (-857C>T, -1036C>T)	6	intergenic	All	C vs T	28.19	3	2080/2164	0.98(0.86-1.11)	0.727	1.80	0.41	0	1.000	0.797	1.000						
TNF	rs1800629 (G-308A, *1/*2)	6	intergenic	All	A vs G	15.20	15	3817/4813	1.09(0.85-1.41)	0.488	84.83	0.00	84	0.843	0.839	0.065	1.11(0.79-1.57)	0.538	83	1.28(0.73-2.24)	0.395	41
TNF	rs361525 (A-417G, -238G>A)	6	intergenic	All	A vs G	7.32	6	1047/1099	1.07(0.55-2.08)	0.847	33.99	0.00	85	0.133	0.356	0.001	0.99(0.52-1.88)	0.967	82			
TNFRSF10A	rs2230229 (p.Arg441Lys, c.1322G>A)	8	non-synonymous	All	G vs A	14.57	5	1479/1932	1.06(0.80-1.39)	0.702	11.74	0.02	66	0.806	0.885	1.000	1.10(0.83-1.47)	0.499	61	0.89(0.56-1.41)	0.616	1
TP53	rs1042522 (p.Pro72Arg, c.215C>G)	17	non-synonymous	All	C vs G	33.34	59	23673/25061	1.04(0.98-1.12)	0.221	287.17	0.00	80	0.013	0.011	0.000	1.06(0.98-1.15)	0.176	72	1.08(0.96-1.22)	0.216	73
TP53	rs12951053 (IVS7+92T>G)	17	intron	All	G vs T	9.93	3	475/569	1.57(1.11-2.23)	0.011	3.19	0.20	37	0.296	0.169	0.579	1.80(1.01-3.19)	0.045	67	1.82(0.76-4.32)	0.178	0
TP53	rs1625895 (IVS6+62G>A, A2>A1)	17	intron	All	A vs G	14.33	8	2666/2847	1.10(0.90-1.34)	0.351	17.49	0.01	60	0.386	0.160	0.117	1.09(0.84-1.41)	0.534	68	0.95(0.53-1.70)	0.860	44
TP53	rs1642785 (IVS2+38G>C, 1827G>C)	17	5'UTR	All	C vs G	36.23	5	534/621	1.05(0.88-1.25)	0.614	3.00	0.56	0	0.086	0.011	1.000	1.13(0.88-1.45)	0.322	0	0.94(0.66-1.33)	0.711	0
TP53	rs17878362(IVS3 16bp Del/Ins,a 16-bp duplication)	17	intergenic	Caucasian	Ins vs del	12.97	4	4196/4327	1.13(0.96-1.34)	0.152	8.22	0.04	64	0.734	0.904	1.000	1.14(0.93-1.38)	0.210	67	1.25(0.75-2.08)	0.395	55
TP53BP1	rs560191(p.Asp353Glu, c.1059C>G）	15	non-synonymous	All	G vs C	46.36	3	1393/1373	0.94(0.69-1.30)	0.723	15.68	0.00	87	1.000	0.814	0.219	0.97(0.67-1.40)	0.853	79	0.88(0.51-1.53)	0.655	85
TP63	rs10937405(C>T)	3	intron	All	T vs C	42.62	4	4927/8794	0.87(0.81-0.94)	2.20×10^{-4}	4.56	0.21	34	0.308	0.108	0.636	0.85(0.76-0.94)	0.002	34	0.82(0.75-0.91)	6.83×10^{-5}	0
TP73	G4C14/A4T14	1	Combined variant	All	AT vs GC(mutation vs wild)	22.98	7	3054/3311	1.04(0.88-1.24)	0.647	23.42	0.00	74	0.024	0.053	0.000	1.10(0.93-1.30)	0.289	59	1.00(0.67-1.49)	0.980	68
TYMS	28-bp tandem repeat	18	STR	All	2R vs 3R(2R vs Non-2R)	30.41	4	2052/2861	0.99(0.90-1.08)	0.742	1.79	0.62	0	1.000	0.446	1.000	0.97(0.85-1.09)	0.582	0	1.02(0.85-1.22)	0.857	0
UGT1A6	rs1105879 (p.Arg184Ser,c.552A>C)	2	non-synonymous	All	G vs T	20.40	3	253/250	3.03(0.79-11.62)	0.106	36.84	0.00	95	0.296	0.248	0.151	6.14(0.70-54.11)	0.102	96	2.09(0.56-7.79)	0.272	52
UGT1A6	rs6759892 (p.Ser7Ala, c.19T>G)	2	non-synonymous	All	G vs T	25.10	3	266/261	2.27(1.14-4.53)	0.020	12.15	0.00	84	1.000	0.437	0.338	2.96(1.12-7.83)	0.029	86	3.17(0.69-14.68)	0.139	41
VEGFA	rs2010963 (634G>C)	6	5'UTR	All	C vs G	37.63	5	2989/2522	1.12(0.99-1.27)	0.083	7.23	0.12	45	0.806	0.667	1.000	1.21(0.98-1.49)	0.071	50	1.12(0.88-1.42)	0.377	46
VEGFA	rs3025039 (C936T)	6	3'UTR	All	T vs C	14.90	6	2887/2506	1.01(0.87-1.17)	0.917	7.10	0.21	30	1.000	0.777	1.000	1.02(0.90-1.15)	0.790	0	1.09(0.70-1.69)	0.702	22
VEGFA	rs699947 (C-2578A)	6	intergenic	All	A vs C	26.74	4	879/804	0.97(0.81-1.15)	0.712	3.60	0.31	17	0.308	0.413	1.000	0.89(0.70-1.13)	0.335	26	1.54(0.69-3.45)	0.297	73
VEGFA	rs833061 (-460T>C)	6	intergenic	All	C vs T	40.74	5	3011/2532	0.93(0.82-1.05)	0.245	7.02	0.14	43	0.221	0.222	0.482	0.94(0.78-1.14)	0.527	50	0.87(0.71-1.05)	0.147	15
vWF	rs9295740 (G>A)	6	intergenic	All	A vs G	19.86	3	2221/2334	1.02(0.92-1.13)	0.685	0.59	0.74	0	0.296	0.144	1.000	1.03(0.91-1.16)	0.670	0	1.02(0.76-1.38)	0.896	0
WWOX	CNV-67048(2copies/1copy/0copy)	16	CNV	Asian	0 copy vs 2 copies	2.86	4	2942/3074	2.06(1.58-2.70)	1.20×10^{-7}	0.54	0.91	0	1.000	0.648	1.000	1.38(1.24-1.54)	1.00×10^{-8}	0	1.92(1.47-2.50)	1.59×10^{-6}	0
XPA	rs1800975 (c.-4A>G, 23G>A)	9	5'UTR	All	A vs G	36.74	12	4221/5240	1.09(0.99-1.19)	0.082	22.18	0.02	50	0.411	0.292	0.125	1.04(0.93-1.17)	0.467	37	1.22(1.05-1.42)	0.011	33
XPC	PAT-/+ (24660_24664delGTAAC inspoly(AT))	3	STR	All	Ins vs non-ins	39.34	4	1417/1449	1.06(0.90-1.25)	0.475	6.34	0.10	53	1.000	0.677	0.252	1.02(0.82-1.26)	0.877	43	1.22(0.95-1.57)	0.113	31
XPC	rs2228000 (p.Ala499Val, Ex9-377C>T)	3	non-synonymous	All	T vs C	28.61	6	2981/3537	1.05(0.97-1.14)	0.205	5.17	0.40	3	1.000	0.890	0.347	1.07(0.94-1.21)	0.302	29	1.09(0.91-1.31)	0.342	0
XPC	rs2228001 (p.Gln939Lys, Ex16+211A＞C)	3	non-synonymous	All	C vs A	37.46	16	5920/7337	1.04(0.98-1.10)	0.232	19.01	0.21	21	0.137	0.136	0.538	1.04(0.93-1.16)	0.471	37	1.12(0.99-1.27)	0.074	10
XRCC1	rs1001581 (c.145-216G>A)	19	intron	All	T vs C	34.52	5	851/1166	1.17(1.00-1.37)	0.044	5.59	0.23	28	0.221	0.132	1.000	1.25(0.93-1.69)	0.139	54	1.20(0.91-1.59)	0.200	0
XRCC1	rs1799782 (p.Arg194Trp,c.580C>T,Ex6-22C＞T)	19	non-synonymous	All	T vs C	18.19	30	11096/13772	0.90(0.82-0.98)	0.022	76.74	0.00	62	0.372	0.536	0.121	0.85(0.76-0.96)	0.010	62	1.06(0.87-1.31)	0.563	35
XRCC1	rs2030404 (A>G)	19	3'UTR	All	G vs A	35.55	3	514/751	0.98(0.83-1.17)	0.836	2.05	0.36	2	1.000	0.567	1.000						
XRCC1	rs2256507 (G>A)	19	intron	All	A vs G	25.61	3	565/779	1.13(0.95-1.35)	0.162	1.79	0.41	0	0.296	0.065	1.000	1.12(0.90-1.40)	0.308	0	1.41(0.87-2.28)	0.167	15
XRCC1	rs25486 (A>G)	19	intron	All	G vs A	40.44	3	507/795	0.99(0.74-1.34)	0.955	5.17	0.08	61	1.000	0.885	1.000	1.10(0.85-1.42)	0.482	0	0.97(0.50-1.89)	0.923	69
XRCC1	rs25487 (p.Gln399Arg,c.1196A>G)	19	non-synonymous	All	A vs G	29.70	51	18308/22033	1.03(0.98-1.08)	0.272	109.98	0.00	55	0.465	0.706	0.001	1.01(0.95-1.08)	0.685	45	1.16(1.03-1.30)	0.018	54
XRCC1	rs25489 (p.Arg280His,c.839G>A,Ex9+16G>A)	19	non-synonymous	All	A vs G	7.65	18	7822/8474	0.96(0.81-1.14)	0.650	60.06	0.00	72	0.112	0.592	0.002	0.95(0.76-1.19)	0.640	77	1.09(0.69-1.72)	0.703	0
XRCC1	rs2682562 (A>G)	19	3'UTR	All	G vs A	14.05	3	513/751	1.00(0.79-1.25)	0.974	0.70	0.71	0	1.000	0.989	1.000						
XRCC1	rs2682585 (p.His6Arg,c.17A>G)	19	non-synonymous	All	A vs G	15.75	3	514/749	1.09(0.88-1.35)	0.416	1.91	0.39	0	1.000	0.971	1.000						
XRCC1	rs2854510 (A>G)	19	intron	All	G vs A	17.58	3	513/751	0.97(0.79-1.20)	0.777	0.48	0.79	0	0.296	0.259	1.000						
XRCC1	rs3213255 (A>G)	19	intron	All	G vs A	38.15	3	1089/1506	1.21(1.08-1.35)	0.001	1.57	0.46	0	0.296	0.118	1.000	1.18(1.00-1.39)	0.052	0	1.30(0.89-1.90)	0.173	50

Gene	Variant	Chr	Category	Ethnicity	Comparison[a]	Frequency(%)[b]	Number evaluated		Lung cancer risk meta-analysis in allelic model								Dominant model			Recessive model		
							Studies	Cases/Controls	OR(95% CI)	*P* value	Q	*P* for Q	I^2(%)	Begg *P*	Modified *P*[c]	Excess *P*[d]	OR(95% CI)	*P* value	I^2(%)	OR(95% CI)	*P* valute	I^2(%)
XRCC1	rs3213403 (A>G)	19	3'UTR	All	G vs A	9.52	3	511/751	0.98(0.72-1.33)	0.880	2.19	0.34	9	1.000	0.706	1.000						
XRCC1	rs3547 (p.Gln632Gln,c.1896G>A)	19	synonymous	All	A vs G	23.31	5	881/1201	1.00(0.86-1.17)	0.991	1.17	0.88	0	0.806	0.559	1.000	1.03(0.83-1.27)	0.800	0	1.10(0.71-1.70)	0.671	0
XRCC1	rs3213245 (-77T>C)	19	5'UTR	All	C vs T	11.03	5	2795/2865	1.29(1.04-1.59)	0.020	12.53	0.01	68	0.806	0.539	0.661	1.31(1.04-1.65)	0.021	65	1.58(1.05-2.38)	0.030	0
XRCC2	rs3218536 (p.Arg188His,c.563G>A)	7	non-synonymous	Caucasian	A vs G	8.08	3	645/1373	1.23(0.54-2.77)	0.625	16.79	0.00	88	1.000	0.049	0.317	1.26(0.51-3.11)	0.618	89	1.78(0.58-5.46)	0.315	0
XRCC3	rs1799794 (4541A>G)	14	5'UTR	All	G vs A	41.09	4	1389/1941	0.91(0.76-1.08)	0.266	7.01	0.07	57	1.000	0.614	0.438	0.92(0.72-1.17)	0.495	58	0.82(0.67-0.99)	0.038	0
XRCC3	rs1799796(17893A>G,IVS5-14)	14	intron	All	G vs A	31.99	5	1478/3040	1.02(0.92-1.12)	0.756	3.45	0.49	0	0.806	0.675	1.000	1.00(0.87-1.16)	0.956	16	1.06(0.85-1.32)	0.604	0
XRCC3	rs861539(p.Thr241Met,c.722C>T)	14	non-synonymous	All	T vs C	20.93	18	6407/8356	1.04(0.95-1.13)	0.414	27.73	0.05	39	0.705	0.314	0.142	1.03(0.92-1.16)	0.600	42	1.06(0.90-1.24)	0.489	0

Chr=chromosome; OR=odds ratio, 95%CI = 95% confidence interval; ins=insertion; del=deletion; STR=short tandem repeat ; VNTR=variable number of tandem repeats; UTR=untranslated region; CNV=copy number variation.

[a] Allelic contrast or phenotype trait for common variants; genetic comparison for rare variants or variants only with genotype group data

[b] Frequency of minor allele or effect genotype(s) in controls in main meta-analyses

[c] *P* value for potential small study effect based on the modified Egger's test

[d] *P* value for possible existing an excess of significant findings (the number of observed significant studies more than the number of expected significant studies) based on the excess significance test

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Supplementary Table S2. Credibility assessment for variants with significant associations with lung cancer risk in meta-analyses for all available data (Continued on next page)

Genes	Variants	Alleles[a]	Ethinicity	Number evaluated		Lung-cancer risk meta-analysis					Venice criteria grades[d]	Credibility of evidence[e]	Amount of evidence[f]		Replication[g]	Protection from bias[h]			Sensitivity analysis[i]			Low OR[j]	Modified P[k]	Excess P[l]	Begg P[m]
				Studies	Cases/Controls	Genetic models	OR(95%CI)[b]	P value	I^2 (%)	P_Q[c]			Numbers	Grade		Grade	Reasons for bias	Reason for bias exemption	Initial study influence		Deviation from HWE				
																			OR(95%CI)	P value					
Associations identified by analysis of all available data in main meta-analysis																									
AGER	rs1800624	A/T	Asian	3	1656/1693	Allelic	1.18(1.04-1.33)	0.010	16	0.305	AAC	Weak	2292	A	A	C	First study		1.20(0.90-1.60)	0.215	None	No	0.480	1.000	1.000
APEX1	rs1760944	A/C	All	8	3588/3783	Allelic	1.16(1.08-1.25)	2.85×10^{-5}	9	0.360	AAA	Strong	7338	A	A	A			1.17(1.08-1.26)	0.000	None	No	0.119	0.287	0.386
ATM	rs189037	A/G	Asian	5	3036/3415	Allelic	1.09(1.00-1.18)	0.050	29	0.227	ABC	Moderate	5653	A	B	C	Low OR	Highly consistent OR	1.12(1.02-1.22)	0.016	None	Yes	0.195	1.000	0.806
AXIN2	rs2240308	T/C	All	3	758/742	Allelic	0.73(0.63-0.85)	6.39×10^{-5}	0	0.398	AAA	Strong	1015	A	A	A			0.76(0.64-0.90)	0.001	None	No	0.120	0.251	1.000
BCL2	rs2279115	A/C	All	5	1847/2367	Allelic	0.65(0.46-0.91)	0.011	91	0.000	ACC	Weak	3448	A	C	C	Small study		0.58(0.51-0.66)	0.000	None	No	0.035	0.481	0.624
CD3EAP	rs967591	A/G	All	3	676/726	Allelic	1.23(1.01-1.49)	0.036	22	0.278	BAA	Moderate	956	B	A	A			1.33(1.10-1.61)	0.003	None	No	0.988	1.000	1.000
CHRNA3	rs578776	T/C	All	3	1245/2009	Allelic	0.87(0.77-0.98)	0.018	0	0.908	AAC	Weak	2089	A	A	C	First study		0.86(0.70-1.05)	0.139	None	No	0.969	0.576	1.000
CHRNA3	rs938682	C/T	All	3	1240/1986	Allelic	0.86(0.76-0.96)	0.009	0	0.582	AAC	Weak	1836	A	A	C	First study,small study		0.91(0.77-1.09)	0.307	None	No	0.054	1.000	0.296
CHRNA3	rs12914385	T/C	All	4	5356/2873	Allelic	1.20(1.01-1.44)	0.044	76	0.007	ACA	Weak	6567	A	C	A			1.32(1.19-1.46)	0.000	None	No	0.353	1.000	0.734
CHRNA3	rs6495309	T/C	All	4	3381/4244	Allelic	0.83(0.77-0.89)	6.55×10^{-8}	0	0.427	AAA	Strong	5804	A	A	A			0.83(0.76-0.91)	0.000	None	No	0.727	1.000	1.000
CHRNA5	rs16969968	A/G	All	11	6222/62452	Allelic	1.23(1.06-1.43)	0.007	80	0.000	ACC	Weak	43607	A	C	C	Excess of significant studies		1.20(1.02-1.42)	0.032	NO	No	0.131	0.071	0.119
CLPTM1L	rs402710	T/C	All	13	7214/8051	Allelic	0.89(0.83-0.95)	2.63×10^{-4}	38	0.078	ABC	Weak	9708	A	B	C	Low OR		0.88(0.82-0.95)	0.001	NO	Yes	0.437	0.335	0.669
CXCR2	rs1126579	T/C	All	3	942/964	Allelic	0.84(0.74-0.96)	0.009	0	0.967	AAA	Strong	2037	A	A	A			0.84(0.73-0.96)	0.012	None	No	0.496	1.000	1.000
CYP1A1	rs4646903	C/T	All	56	9789/12307	Allelic	1.16(1.07-1.25)	1.59×10^{-4}	55	0.000	ACC	Weak	9955	A	C	C	Excess of significant studies		1.16(1.07-1.25)	0.000	NO	No	0.256	0.014	0.772
CYP1A1	rs1048943	G/A	All	54	9869/12114	Allelic	1.23(1.11-1.36)	7.64×10^{-5}	67	0.000	ACC	Weak	8169	A	C	C	Small study,excess of significant studies		1.22(1.10-1.35)	0.000	NO	No	0.081	0.007	0.649
CYP1B1	rs1056836	G/C	All	12	3033/3866	Allelic	1.13(1.05-1.22)	0.002	0	0.551	AAC	Weak	5372	A	A	C	Low OR,publication bias		1.13(1.04-1.22)	0.003	None	Yes	0.228	0.387	0.064
CYP2A6	rs5031016	C/T	All	3	1527/1138	Allelic	0.57(0.33-1.00)	0.048	73	0.025	BCC	Weak	465	B	C	C	First study		0.46(0.17-1.24)	0.125	NO	No	0.587	1.000	0.296
CYP2A6	rs1801272	A/T	Caucasian	3	2411/2644	carriers vs non-carriers	0.66(0.52-0.84)	0.001	0	0.674	BAB	Moderate	307	B	A	B	Missing information		0.65(0.51-0.83)	0.001	NA	No	0.929	1.000	1.000
CYP2E1	rs6413432	A/T(C/D)	All	14	2944/3347	Allelic	0.78(0.71-0.85)	6.76×10^{-8}	0	0.821	AAA	Strong	2561	A	A	A			0.78(0.71-0.86)	0.000	NO	No	0.999	0.541	0.827
CYP2E1	rs2031920	T/C(c2/c1)	All	23	4983/6628	Allelic	0.86(0.76-0.97)	0.018	50	0.003	ACA	Weak	4010	A	C	A			0.86(0.76-0.97)	0.015	NO	No	0.250	0.309	0.509
ELANE	rs351107	G/T	Caucasian	3	745/762	Allelic	0.55(0.34-0.87)	0.011	29	0.246	BBC	Weak	126	B	B	C	First study		0.57(0.24-1.38)	0.213	None	No	0.794	0.565	1.000
ELANE	rs7254054	A/G	Caucasian	3	754/750	Allelic	0.77(0.61-0.97)	0.030	46	0.155	BBC	Weak	735	B	B	C	First study,small study		0.84(0.53-1.32)	0.444	NA	No	0.022	0.567	0.296
ERCC1	rs11615	C/T	All	12	5731/7058	Allelic	0.90(0.83-0.99)	0.023	52	0.018	ACC	Weak	13244	A	C	C	Low OR,small study,publication bias	Highly consistent OR	0.90(0.82-0.99)	0.026	NO	Yes	0.072	0.434	0.086
ERCC2	rs238406	A/C	All	6	1754/2688	Allelic	1.12(1.02-1.23)	0.013	0	0.558	AAC	Weak	3611	A	A	C	Low OR		1.10(1.01-1.21)	0.037	NO	Yes	0.332	0.599	0.260
ERCC2	rs13181	C/A	All	40	13111/16749	Allelic	1.12(1.05-1.19)	4.18×10^{-4}	49	0.000	ABC	Weak	14855	A	B	C	Low OR,excess of significant studies		1.12(1.05-1.19)	0.001	NO	Yes	0.272	0.048	0.753
ERCC5	rs1047768	T/C	All	4	1449/2248	Allelic	0.86(0.74-1.00)	0.049	48	0.123	ABC	Weak	3204	A	B	C	First study,HWE		0.86(0.72-1.04)	0.114	Yes	No	0.414	1.000	0.734
ERCC6	rs3793784	G/C	All	3	1643/1689	Allelic	0.75(0.60-0.92)	0.007	68	0.044	ACA	Weak	1834	A	C	A			0.72(0.55-0.95)	0.022	None	No	0.550	0.167	1.000
FGFR4	rs351855	A/G	All	4	1083/1275	Allelic	0.82(0.69-0.98)	0.025	33	0.214	ABC	Weak	1892	A	B	C	First study,small study,publication bias		0.90(0.74-1.09)	0.266	NO	No	0.015	1.000	0.089
GSTM1	Present/Null	NA	All	131	32985/37533	null vs present	1.18(1.12-1.24)	2.54×10^{-11}	52	0.000	ACC	Weak	35699	A	C	C	Small study,excess of significant studies		1.18(1.12-1.24)	0.000	None	No	0.037	0.011	0.105
GSTP1	rs1695	G/A	All	46	12521/14411	Allelic	1.08(1.02-1.15)	0.011	55	0.000	ACC	Weak	16519	A	C	C	Low OR,small study,excess of significant studies,publication bias		1.07(1.01-1.14)	0.024	NO	Yes	0.009	0.008	0.075
GSTT1	Present/Null	NA	All	76	22796/25134	null va present	1.10(1.02-1.19)	0.015	58	0.000	ACC	Weak	13531	A	C	C	Low OR,excess of significant studies		1.10(1.02-1.18)	0.018	None	Yes	0.345	0.000	0.346
HIF1A	rs11549467	A/G	All	3	509/566	Allelic	2.27(1.74-2.96)	1.62×10^{-9}	0	0.481	BAA	Moderate	297	B	A	A			2.31(1.77-3.02)	0.000	None	No	0.261	0.610	0.296
HRAS1	common/rare (HRAS1 VNTR)	NA	Caucasian	4	746/1174	rare vs common	2.55(1.01-6.45)	0.048	69	0.023	BCC	Weak	305	B	C	C	First study		2.02(0.66-6.21)	0.221	None	No	0.561	0.346	0.734
HYKK	rs931794	G/A	All	5	2435/3180	Allelic	1.23(1.14-1.34)	1.85×10^{-7}	0	0.864	AAA	Strong	3927	A	A	A			1.23(1.11-1.36)	0.000	None	No	0.967	0.411	1.000
IL10	rs1800896	G/A	All	10	2861/3817	Allelic	1.29(1.05-1.59)	0.017	75	0.000	ACC	Weak	5175	A	C	C	First study,small study,publication bias		1.13(0.97-1.30)	0.108	NO	No	0.042	1.000	0.074
MAPKAPK2	CNV-30450	NA	Asian	3	2332/2480	4 copies vs 2 copies	1.60(1.04-2.45)	0.031	81	0.005	BCB	Weak	586	B	C	B	Missing information		NA		None	No	0.947	0.298	1.000
MDM2	rs2279744	G/T	All	19	11076/14434	Allelic	1.10(1.01-1.19)	0.021	75	0.000	ACC	Weak	21593	A	C	C	Low OR		1.10(1.01-1.19)	0.031	None	Yes	0.355	0.242	0.700
MIR146A	rs2910164	C/G	All	6	3158/3225	Allelic	1.16(1.06-1.27)	0.001	21	0.274	AAC	Weak	5983	A	A	C	Small study		1.20(1.10-1.31)	0.000	None	No	0.076	0.415	0.260
MMP2	rs243865	T/C	All	3	1751/1729	Allelic	0.63(0.45-0.89)	0.009	80	0.007	BCC	Weak	954	B	C	C	First study,small study		0.74(0.37-1.48)	0.395	None	No	0.001	0.458	0.296
MTRR	rs1801394	G/A	All	3	1668/2291	Allelic	1.13(1.03-1.24)	0.011	0	0.525	AAC	Weak	3616	A	A	C	HWE,low OR		1.12(1.02-1.24)	0.024	Yes	Yes	0.916	1.000	1.000
NOD2	rs2066847	3020insC/-	All	3	807/4078	carriers vs non-carriers	1.42(1.07-1.90)	0.017	0	0.593	×AC	Weak	340	×	A	C	First study		1.23(0.83-1.84)	0.310	NA	No	0.988	0.567	1.000
PDCD5	rs1862214	G/C	All	3	737/683	Allelic	1.32(1.12-1.56)	0.001	0	0.395	BAB	Moderate	971	B	A	B	Missing information		NA		None	No	0.156	1.000	0.296
PON1	rs662	A/G	All	3	995/834	Allelic	0.77(0.67-0.88)	2.02×10^{-4}	0	0.701	AAA	Strong	1569	A	A	A			0.76(0.65-0.89)	0.001	None	No	0.704	1.000	1.000
PROM1	rs2240688	C/A	Asian	3	2332/2457	Allelic	0.83(0.76-0.91)	6.92×10^{-5}	0	0.991	AAB	Moderate	2459	A	A	B	Missing information		NA		None	No	0.379	0.281	0.296
REV3L	rs462779	T/C	Asian	4	1937/2335	Allelic	1.11(1.02-1.22)	0.021	0	0.911	AAC	Strong	3433	A	A	C	Low OR	Highly consistent OR	1.13(1.00-1.27)	0.043	None	Yes	0.921	1.000	0.734
SFTPB	wild type/variation	NA	All	3	157/240	variation vs wild	1.92(1.11-3.33)	0.020	0	0.960	CAB	Weak	59	C	A	B	Missing information		NA		None	No	0.495	1.000	0.296
SOD2	rs4880	T/C	All	9	3738/4467	Allelic	1.20(1.06-1.36)	0.005	61	0.009	ACA	Weak	8801	A	C	A			1.21(1.03-1.43)	0.023	NO	No	0.723	0.733	0.348
TERT	rs2736098	A/G	All	7	4660/4825	Allelic	1.20(1.08-1.33)	0.001	67	0.006	ACB	Weak	6619	A	C	B	Missing information		1.19(1.05-1.35)	0.006	NA	No	0.734	0.706	0.548
TP53	rs12951053	G/T	All	3	475/569	Allelic	1.57(1.11-2.23)	0.011	37	0.203	BBB	Moderate	258	B	B	B	Missing information		NA		None	No	0.169	0.579	0.296
TP63	rs10937405	T/C	All	4	4927/8794	Allelic	0.87(0.81-0.94)	2.20×10^{-4}	34	0.207	ABA	Moderate	11355	A	B	A			0.75(0.62-0.89)	0.001	None	No	0.108	0.636	0.308
UGT1A6	rs6759892	G/T	All	3	266/261	Allelic	2.27(1.14-4.53)	0.020	84	0.002	BCA	Weak	346	B	C	A			3.21(2.21-4.67)	0.000	None	No	0.437	0.338	1.000
WWOX	CNV-67048	NA	Asian	4	2942/3074	0 copy vs 2 copies	2.06(1.58-2.70)	1.20×10^{-7}	0	0.911	BAB	Moderate	247	B	A	B	Missing information		NA		None	No	0.648	1.000	1.000
XRCC1	rs3213255	G/A	All	3	1089/1506	Allelic	1.21(1.08-1.35)	0.001	0	0.457	AAB	Moderate	2110	A	A	B	Missing information		NA		None	No	0.118	1.000	0.296
XRCC1	rs1001581	T/C	All	5	851/1166	Allelic	1.17(1.00-1.37)	0.044	28	0.232	ABC	Weak	1467	A	B	C	First study		1.18(0.97-1.44)	0.094	None	No	0.132	1.000	0.221
XRCC1	rs1799782	T/C	All	30	11096/13772	Allelic	0.90(0.82-0.98)	0.022	62	0.000	ACC	Weak	9151	A	C	C	HWE,low OR		0.90(0.82-0.99)	0.031	Yes	Yes	0.536	0.121	0.372
XRCC1	rs3213245	C/T	All	5	2795/2865	Allelic	1.29(1.04-1.59)	0.020	68	0.014	ACC	Weak	1413	A	C	C	First study		1.23(0.94-1.61)	0.138	None	No	0.539	0.661	0.806
Associations identified from additional analyses under dominant or recessive genetic model																									
ATM	rs664677	C/T	All	3	1627/1641	Dominant	0.76(0.64-0.92)	0.004	0	0.448	AAA	Strong	2692	A	A	A			0.73(0.59-0.91)	0.004	None	No	0.763	1.000	1.000
Chr8q24	rs16901979	A/C	All	3	1534/1992	Dominant	1.18(1.02-1.37)	0.025	0	0.610	AAC	Weak	1306	A	A	C	First study,HWE		1.13(0.95-1.34)	0.167	Yes	No	0.324	0.543	1.000
CYP1B1	rs10012	G/C	All	3	622/666	Dominant	1.69(1.05-2.72)	0.031	74	0.021	BCC	Weak	657	B	C	C	First study		1.47(0.58-3.75)	0.415	No	No	0.460	1.000	1.000
EGF	rs4444903	G/A	All	3	666/690	Dominant	2.07(1.01-4.24)	0.048	79	0.009	ACC	Weak	1141	A	C	C	First study,small study		1.55(0.79-3.05)	0.201	None	No	0.041	1.000	0.296
MLH1	rs1800734	A/G	All	5	2178/2320	Dominant	0.80(0.68-0.95)	0.009	24	0.260	AAC	Weak	3344	A	A	C	HWE		0.78(0.64-0.95)	0.013	Yes	No	0.583	0.605	0.462
PTGS2	rs689466	G/A	All	4	1676/2180	Dominant	0.78(0.62-0.97)	0.026	56	0.076	ACA	Weak	2198	A	C	A			0.72(0.54-0.98)	0.034	No	No	0.336	0.644	0.734
REV3L	rs465646	C/T	All	3	1296/1511	Dominant	0.78(0.67-0.92)	0.003	0	0.437	BAB	Moderate	888	B	A	B	Missing information		NA		None	No	0.423	1.000	1.000
CASC8	rs6983267	G/T	All	3	1539/1989	Recessive	1.22(1.04-1.44)	0.013	0	0.644	BAA	Moderate	802	B	A	A			1.30(1.06-1.59)	0.012	None	No	0.117	0.566	0.296
CHRNA5	rs142774214	ins/-	All	3	1431/1606	Recessive	0.80(0.65-0.98)	0.032	0	0.597	BAA	Moderate	432	B	A	A			0.78(0.62-0.98)	0.031	None	No	0.861	1.000	1.000
CYP2A6	non*4/*4	del/-(*4/non*4)	All	7	2623/2380	Recessive	0.51(0.35-0.73)	2.93×10^{-4}	0	0.539	BAA	Moderate	133	B	A	A			0.52(0.35-0.76)	0.001	No	No	0.826	0.654	1.000
FASLG	rs763110	T/C	All	5	4436/4120	Recessive	0.83(0.70-0.99)	0.038	30	0.221	ABC	Weak	1034	A	B	C	First study		0.86(0.70-1.05)	0.137	None	No	0.205	1.000	0.462

IL17A	rs2275913	A/G	All	3	889/998	Recessive	1.76(1.21-2.55)	0.003	18	0.295	BAB	Moderate	179	B	A	B	Missing information	2.00(1.41-2.83)	<0.001	NA	No	0.492	0.587	0.296
IL1B	rs1143627	C/T	All	8	4201/5431	Recessive	0.80(0.68-0.95)	0.010	49	0.059	ABC	Weak	1588	A	B	C	Small study,publication bias	0.83(0.70-0.98)	0.027	No	No	0.002	0.404	0.019
LIG1	rs156641	A/G	All	3	1112/2048	Recessive	1.45(1.14-1.83)	0.002	0	0.370	BAC	Weak	335	B	A	C	HWE	NA		Yes	No	0.217	1.000	1.000
XPA	rs1800975	A/G	All	12	4221/5240	Recessive	1.22(1.05-1.42)	0.011	33	0.124	ABA	Moderate	1463	A	B	A		1.23(1.04-1.45)	0.015	No	No	0.524	0.397	0.681
XRCC1	rs25487	A/G	All	48	16999/20567	Recessive	1.16(1.03-1.30)	0.018	54	0.000	ACC	Weak	3691	A	C	C	HWE,excess of significant studies	1.15(1.02-1.30)	0.022	Yes	No	0.428	0.006	0.729
XRCC3	rs1799794	G/A	All	4	1389/1941	Recessive	0.82(0.67-0.99)	0.038	0	0.469	BAC	Weak	571	B	A	C	First study	0.83(0.68-1.01)	0.058	No	No	0.712	0.490	1.000

Chr=chromosome; OR=odds ratio, 95%CI = 95% confidence interval; VNTR=variable number of tandem repeats; ins=insertion, del=deletion; NA=Not Applicable.

[a] Minor alleles/major alleles (per Caucasian)

[b] Summary ORs were calculated based on the DerSimonian-Lairs random-effects model

[c] *P*-value of heterogeneity test between studies

[d] Venice criteria grades contained assessments of three aspects: the amount of evidence, extent of replication, and protection from bias, and each assessment was assigned three levels (A, B, or C).

[e] Credibility of evidence was evaluated based on Venice criteria with three aspects (the amount of evidence, extent of replication, and protection from bias), and was categorized as strong (all three aspect grades were A), moderate (any grade was B, but not C) or weak (any grade was C).

[f] Amount of evidence, depending on total sample size of the smallest genetic group among cases and controls in each meta-analysis, was graded as A (sample size>1000), B (sample size between 100 and 1000), or C (sample size <100). One rare variant was not scored for amount of evidence (×), for this variant with frequency less than 0.5% and an A grade was unlikely to obtain.

[g] Extent of replication, depending on between-study heterogeneity, was graded as A ($I^2<25\%$), B (I^2 between 25% and 50%), or C ($I^2>50\%$).

[h] Protection from bias, considering various potential sources of bias in meta-analysis, was graded as A when there was no demonstrable bias and bias was unlikely invalidate the association, was graded as B when there was insufficient information for identifying evidence (i.e. missing information for evaluating Hardy-Weinberg equilibrium (HWE) among controls in an individual study) although there was no obvious bias, and C when the bias was evident and/or was likely to explain the presence of association. For the C grade, it was assigned if a meta-analysis had any of the following potential sources of bias: (1) magnitude of the association was low; (2) sensitivity analysis altered the statistical significance; (3) potential small study effect; (4) possible existence of an excess of significant findings (the number of observed significant studies more than the number of expected significant studies); (5) potential publication bias.

First study=Significance lost excluding the first published or first positive report; Low OR=Low magnitude of the association (i.e. 0.87<OR<1.15); Small study=Possible existence of potential small study effect (modified Egger's test, *p*<0.10); Excess of significant studies=Possible existence of an excess of significant findings (excess significance test, *p*<0.10); Publication bias= Possible existence of potential publication bias (Begg's test, *p*<0.10); Missing information= Insufficient information for bias evaluation; HWE=Significance lost excluding studies with controls violating HWE; Highly consistent OR=A meta-analysis with a low OR was not considered if there is a highly consistent OR across studies enrolled in this meta-analysis.

[i] A sensitivity analysis was performed to examine whether the significant summary ORs were robust after excluding the first published or first positive report (defined as the earliest study reported a significant association), or excluding studies with controls violating HWE. None=A meta-analysis didn't include studies with controls violating HWE or evaluated association for a variant with a phenotype change; NO=Without the influence from studies with controls violating HWE; NA=Insufficient information for evaluation of influence from first published/positive study or studies with controls violating HWE; Yes=Evidence of influence from studies with controls violating HWE.

[j] Low OR (i.e. 0.87<OR<1.15; No=Association without a low OR; Yes=Association with a low OR.)

[k] *P* value for potential small study effect based on the modified Egger's test. (*P*<0.10 is usually considered evidence for significant evidence of small study effect.)

[l] *P* value for possible existing an excess of significant findings based on the excess significance test. (*P*<0.10 is usually considered evidence for significant evidence of an excess of significant findings.)

[m] *P* value for potential publication bias of studies based on the Begg's test. (*P*<0.10 is usually considered evidence for significant evidence of publication bias.)

Supplementary Table S3. Subgroup meta-analyses stratified by ethnicity for genetic variants with available data (Continued on next three pages)

Gene	Variant	Alleles[a]	Meta-analysis performed in Caucasian population							Meta-analysis performed in Asian population						
			Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2(%)	Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2(%)
ABCB1	rs1045642(p.Ile1145Ile,c.3435T>C)	T/C														
ACE	287-bp repeat	287-bp ins/-														
AGER	rs1800624(-374T>A, Mun1)	A/T								3	1656/1693	34.41	Allelic	1.18(1.04-1.33)	0.010	16
AGER	rs1800625(-429T>C, Alu1)	C/T								3	1656/1693	31.19	Allelic	1.16(0.78-1.74)	0.468	91
AGER	rs2070600(p.Gly82Ser,c.244G>A)	A/G								3	1656/1693	38.36	Allelic	1.17(0.99-1.38)	0.067	52
AHR	rs2066853(Arg554Lys,Ex10+501G>A)	A/G								3	1382/1381	37.33	Allelic	0.99(0.86-1.14)	0.901	38
ALDH2	rs671(p.Glu487Lys/Glu504Lys,c.1510G>A)	A/G								3	1610/2059	NA	Dominant	0.88(0.61-1.26)	0.476	83
APEX1	rs1760944(c.-468T>G,-141T>G)	A/C								5	3071/3038	49.95	Allelic	1.20(1.12-1.29)	9.14×10^{-7}	0
APEX1	rs1048945(p.Gln51His,c.153G>C)	C/G	3	745/816	4.72	Allelic	0.93(0.67-1.31)	0.684	0							
APEX1	rs1130409(p.Asp148Glu,c.444T>G)	G/T	8	1807/3065	47.91	Allelic	0.94(0.85-1.04)	0.249	19	10	4220/5054	39.20	Allelic	1.02(0.92-1.12)	0.729	58
APEX1	rs2307486(p.Ile64Val,c.190A>G)	G/A								3	1941/2095	4.89	Allelic	0.90(0.73-1.11)	0.307	0
ATM	rs609429(IVS48+238C>G)	G/C														
ATM	rs664677(IVS21T-77C)	C/T														
ATM	rs189037(c.-111G>A,-4519G>A)	A/G								5	3036/3415	42.68	Allelic	1.09(1.00-1.18)	0.050	29
ATM	rs664143(IVS34G+60A)	G/A														
AURKA	rs2273535(p.Phe31Ile,c.91T>A)	A/T	3	2301/2069	48.28	Allelic	0.96(0.86-1.06)	0.421	0							
AURKA	rs1047972(p.Ile57Val,c.169A>G)	A/G	3	2463/2283	15.75	Allelic	0.96(0.86-1.07)	0.425	0							
AXIN2	rs2240308(p.Pro50Ser,c.148C>T)	T/C														
BCL2	rs2279115(c.-938C>A)	A/C								3	1537/2057	41.15	Allelic	0.76(0.51-1.13)	0.170	93
BIRC5	rs9904341(c.-31G>C）	C/G														
BRCA2	rs144848(p.Asn372His,c.1114A>C)	C/A														
CASC8	rs1447295(C>A)	A/C														
CASC8	rs6983267(T>G)	G/T														
CASP5	rs523104(p.Leu318Val,c.748C>G)	C/G														
CASP8	rs3834129(-652 6N del,-/CTTACT)	-/CTTACT								3	2301/2263	23.84	Allelic	0.88(0.72-1.07)	0.207	73
CASP8	rs1045485(p.Asp302His,c.853G>C)	C/G	3	758/964	10.79	Allelic	1.27(0.94-1.73)	0.125	45							
CCND1	rs678653(G>C)	C/G														
CCND1	rs9344(rs603965,p.Pro241Pro,c.723G>A)	A/G	6	10204/11646	48.88	Allelic	0.97(0.88-1.07)	0.517	62							
CD3EAP	rs967591(c.-21G>A)	A/G														
CDKN1A	rs1801270(p.Ser31Arg,c.93C>A,6829C>A)	A/C	7	3335/4082	7.06	Allelic	1.12(0.89-1.41)	0.340	62							
CDKN2A	rs3731249(p.Ala148Thr,c.442G>A)	A/G	3	2875/2707	1.75	Dominant	1.38(0.81-2.35)	0.230	56							
Chr8q24	rs16901979(C>A)	A/C														
CHRNA3	rs12914385(2594C>T)	T/C	3	4640/2157	37.00	Allelic	1.20(0.91-1.58)	0.195	82							
CHRNA3	rs3743073(A>C)	G/T														
CHRNA3	rs578776(C>T)	T/C														
CHRNA3	rs938682(T>C, T78896547C)	C/T														
CHRNA3	rs6495309(4064C>T)	T/C								3	2635/2767	47.83	Allelic	0.83(0.76-0.91)	6.17×10^{-5}	27
CHRNA5	rs142774214(rs3841324,-62ins/del,22bp indel)	22-bp ins/-														
CHRNA5	rs16969968(p.Asp398Asn, c.1192G>A)	A/G	6	3305/59780	33.76	Allelic	1.35(1.27-1.44)	2.03×10^{-21}	0	4	2811/2556	3.85	Allelic	0.78(0.33-1.85)	0.574	92
CLPTM1L	rs402710(C>T)	T/C	4	1801/1908	38.29	Allelic	0.86(0.78-0.94)	0.002	0	9	5413/6143	31.25	Allelic	0.89(0.82-0.97)	0.010	51
COMT	rs4680(p.Val158Met,c.472G>A)	A/G														
CRP	rs2808630(T>C)	C/T														
CTLA4	rs3087243(g.6230G>A,CT60)	A/G														
CTLA4	rs231775(p.Thr17Ala,c.49A>G)	G/A								3	2426/2403	67.23	Allelic	1.08(0.72-1.63)	0.712	95
CTLA4	rs5742909(g.319C>T,-318C>T)	T/C														
CXCL12	rs1801157(801G>A)	A/G														
CXCR2	rs1126579(C>T)	T/C														
CYP17A1	rs743572(T-34C,A1/A2)	G/A														
CYP1A1	rs1799814(m4,Thr461Asn,C>A)	A/C	4	1522/1585	5.93	Allelic	1.30(0.49-3.41)	0.598	94							
CYP1A1	rs1800031(m3,T5639C)	C/T														
CYP1A1	rs2606345(IVS1+606T>G)	G/T	3	2770/3609	34.44	Allelic	1.00(0.91-1.11)	0.937	35							
CYP1A1	rs4646903(m1,MspI,T3801C)	C/T	21	5083/6022	11.45	Allelic	1.12(1.03-1.21)	0.011	0	15	2418/3107	36.39	Allelic	1.18(1.01-1.38)	0.036	73
CYP1A1	rs1048943(*2C,m2, p.Ile462Val,c.1384A>G)	G/A	15	3375/3871	6.99	Allelic	1.27(1.02-1.59)	0.037	54	21	4265/5242	24.90	Allelic	1.17(1.02-1.33)	0.024	73
CYP1A2	rs2069514(CYP1A2*1C,-3860G>A)	A/G	3	761/1186		Dominant	1.06(0.50-2.25)	0.873	26							
CYP1A2	rs2069526(-739T>G)	G/T														
CYP1A2	rs35694136(-2467delT)	-2467delT/-														
CYP1A2	rs762551(CYP1A2*1F,c.A-164C)	C/A	3	869/1468	26.77	Allelic	1.38(1.12-1.71)	0.002	57							
CYP1B1	rs10012(p.Arg48Gly,c.142C>G)	G/C														
CYP1B1	rs1056827(p.Ala119Ser,c.355G>T, m2)	T/G	3	975/1684	29.42	Allelic	0.99(0.85-1.16)	0.904	21							
CYP1B1	rs1800440(p.Asn453Ser,Ex3+315A>G)	G/A	4	2809/3687	19.01	Allelic	0.95(0.81-1.11)	0.530	47							
CYP1B1	rs1056836(CYP1B1*3,p.Leu432Val,c.1294C>G)	G/C	6	1849/2655	43.71	Allelic	1.12(1.02-1.22)	0.013	0	3	770/764	13.68	Allelic	1.07(0.82-1.39)	0.633	37
CYP2A13	rs8192789(p.Arg257Cys,3375C>T)	T/C														
CYP2A6	non*4/*4(*1/*4, a deletion of the CYP2A6 gene)	del/- (*4/non*4)								6	2517/2264	14.66	Allelic	0.81(0.64-1.03)	0.089	71
CYP2A6	rs1801272(p.Leu160His,Ex3-15T>A)	A/T	3	2411/2644	3.99	Dominant	0.66(0.52-0.84)	0.001	0							
CYP2A6	rs5031016(p.Ile471Thr,c1412T>C,wt/*7)	C/T														
CYP2C9	rs1799853(p.Arg144Cys,c.430C>T)	T/C	3	604/1054		Dominant	1.19(0.85-1.68)	0.319	48							
CYP2D6	phenotype (EM/HEM/PM)	NA	8	1327/1787	5.54	PM vs EM	0.90(0.60-1.34)	0.595	7							
CYP2D6	rs1065852(p.Pro34Ser,188C>T)	C/T														
CYP2E1	rs2031920(RsaI, c1>c2, -1053C>T)	T/C	6	665/1224	4.90	Allelic	0.61(0.42-0.90)	0.013	0	11	3370/3951	23.40	Allelic	0.89(0.77-1.04)	0.152	66
CYP2E1	rs3813867(g.3739G>C,c.-1293G>C)	C/G														
CYP2E1	rs6413432(c.967+1143T>A,7632T>A)	A/T	4	441/538	11.52	Allelic	0.79(0.58-1.06)	0.121	0	6	1964/2085	26.55	Allelic	0.78(0.70-0.86)	1.31×10^{-6}	0
CYP3A4	rs2740574(-392A>G,*1A/*1B)	G/A	3	1665/1979		Dominant	1.08(0.84-1.39)	0.561	6							
CYP3A5	rs776746(A6986G,CYP3A5*3,22892A>G)	A/G														
DRD2	rs1079597(G>A,TaqI-)	A/G	3	461/537		Dominant	1.04(0.79-1.37)	0.781	0							
DRD2	rs1800497(p.Glu714Lys,A2/A1,C>T)	C/T	3	510/621		Recessive	1.00(0.69-1.44)	0.986	0							
EGF	rs4444903(+61A>G)	G/A														
ELANE	rs351107(-903T>G,Rep_a)	G/T	3	745/762	5.31	Allelic	0.55(0.34-0.87)	0.011	29							
ELANE	rs7254054(-741G>A,Rep_b)	A/G	3	754/750	27.20	Allelic	0.77(0.61-0.97)	0.030	46							

Gene	Variant	Alleles[a]	Meta-analysis performed in Caucasian population							Meta-analysis performed in Asian population						
			Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2(%)	Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2(%)
EPHX1	rs1051740(p.Tyr113His,c.337T>C)	C/T	12	2560/5862	31.06	Allelic	0.88(0.74-1.04)	0.123	77							
EPHX1	rs2234922(p.His139Arg,c.416A>G)	G/A	13	4410/7749	18.91	Allelic	1.12(0.94-1.34)	0.195	79							
ERCC1	rs11615(rs3177700, p.Asn118Asn,c.354T>C)	C/T	7	3544/4862	39.68	Allelic	0.89(0.79-1.01)	0.064	60	5	2187/2196	76.66	Allelic	0.91(0.79-1.06)	0.224	49
ERCC1	rs16979802(15310G>C)	C/G	3	1311/2114	21.81	Allelic	0.87(0.74-1.03)	0.102	0							
ERCC1	rs2298881(262G>T, C>A)	T/G								3	2305/2315	42.07	Allelic	1.00(0.90-1.11)	0.986	33
ERCC1	rs3212948(C>G)	G/C	3	1034/1446	42.98	Allelic	1.01(0.84-1.20)	0.960	55							
ERCC1	rs3212955(A>G)	G/A	3	1287/1857	24.21	Allelic	1.05(0.93-1.20)	0.415	9							
ERCC1	rs3212961(IVS5+33C＞A,17677C>A)	A/C	3	771/883	14.84	Allelic	0.93(0.77-1.13)	0.485	0	3	1436/1428	48.28	Allelic	0.96(0.82-1.12)	0.584	37
ERCC1	rs3212986(8092C>A,14443C>A)	A/C	4	3091/3489	25.24	Allelic	1.00(0.92-1.08)	0.986	0							
ERCC1	rs735482(p.Lys261Thr,A>C)	C/A	3	1287/2365	14.63	Allelic	0.94(0.82-1.08)	0.390	0							
ERCC2	rs1052555(Asp711Asp,G>A)	A/G														
ERCC2	rs171140(A>C)	C/A														
ERCC2	rs13181(p.Lys751Gln,c.2251A>C)	C/A	19	5967/8851	36.08	Allelic	1.10(1.03-1.18)	0.003	32	15	5878/6060	7.90	Allelic	1.12(0.95-1.33)	0.170	61
ERCC2	rs1799787(IVS19-70C＞T,G>A)	T/C								3	688/756	7.34	Allelic	0.90(0.51-1.62)	0.733	74
ERCC2	rs1799793(p.Asp312Asn,c.981G>A)	A/G	15	5165/7680	34.91	Allelic	1.02(0.96-1.08)	0.542	11	10	4797/5010	5.76	Allelic	1.00(0.79-1.28)	0.976	68
ERCC2	rs238406(p.Arg156Arg,C>A)	A/C	3	1150/2080	42.76	Allelic	1.13(1.01-1.25)	0.026	0							
ERCC4	rs1799801(p.Ser835Ser,Ex11-247T＞C)	C/T														
ERCC4	rs1800067(Arg415Gln)	A/G	5	1521/2420	6.78	Allelic	1.10(0.92-1.32)	0.286	0							
ERCC5	rs1047768(p.His46His,335C>T)	T/C	3	1331/2136	42.51	Allelic	0.86(0.72-1.04)	0.114	63							
ERCC5	rs17655(p.Asp1104His,c.3310G>C)	C/G	4	1249/2203	22.95	Allelic	0.95(0.78-1.14)	0.570	47	5	2024/2683	56.71	Allelic	0.90(0.75-1.08)	0.248	71
ERCC6	rs3793784(-6530C>G)	G/C														
ERCC6	rs2228528(p.Gly399Asp,G1275A)	T/C								3	1713/1887	43.91	Allelic	1.03(0.92-1.17)	0.591	31
EXO1	rs1047840(p.Glu589Lys,c.1765G>A)	A/G														
FANCG	rs2237857(p.Thr297Ile,C1382T)	T/C														
FAS	rs2234767(-1377G/A)	A/G								3	1857/2149	36.81	Allelic	1.12(0.94-1.35)	0.216	72
FASLG	rs763110(-844C/T)	T/C								3	1857/2149	30.97	Allelic	0.77(0.58-1.01)	0.063	86
FGFR4	rs351855(p.Gly388Arg,G>A)	A/G														
GPC5	rs2352028(C>T)	T/C								3	1648/2002	21.65	Allelic	0.97(0.87-1.09)	0.611	0
GPX1	rs1050450(p.Pro200Leu,c.599C>T)	T/C	4	976/1339	34.06	Allelic	1.04(0.75-1.44)	0.811	81							
GSTM1	Present/Null(Large gene deletion)	NA	58	16976/20622	51.28	Null vs present	1.08(1.03-1.13)	0.001	7	36	11012/9982	50.56	Null vs presrnt	1.27(1.14-1.41)	9.06×10^{-6}	65
GSTM3	rs1799735(c.468+21delAGG,3bp deletion,*A/*B)	delAGG/-	6	1427/1613	15.25	Allelic	1.00(0.87-1.15)	0.956	0							
GSTP1	rs1138272(p.Ala114Val,c.341C>T)	T/C	6	1479/1573	7.63	Allelic	1.24(0.93-1.65)	0.149	53							
GSTP1	rs1695 (p.Ile105Val, c.313A>G)	G/A	26	9151/10531	32.85	Allelic	1.04(0.98-1.09)	0.224	29	11	2307/2430	18.87	Allelic	1.14(1.01-1.29)	0.036	27
GSTT1	Present/Null(Large gene deletion)	NA	38	12560/15525	18.88	Null vs present	1.01(0.92-1.10)	0.910	45	14	7043/5289	49.57	Null vs presrnt	1.15(1.03-1.28)	0.010	34
HIF1A	rs11549465(p.Pro582Ser,c.1744C>T)	T/C														
HIF1A	rs11549467(p.Ala588Thr, c.1762G>A)	A/G														
HRAS1	common/rare (HRAS1 VNTR alleles, loss of heterozygosity in the 15p15.5 region)	NA	4	746/1174	7.03	rare vs common	2.55(1.01-6.45)	0.048	69							
HYKK	rs931794(A>G)	G/A														
IFNG	rs2069705(-1615T>C)	C/T														
IGFBP3	rs2854744(C-202A)	C/A								3	789/960	27.71	Allelic	0.79(0.52-1.20)	0.262	86
IL10	rs1800871(c.-854T>C,-819C>T)	T/C	5	1741/2296	6.82	Allelic	1.03(0.81-1.31)	0.820	0	4	959/1367	69.09	Allelic	0.84(0.54-1.32)	0.447	91
IL10	rs1800872(g.4433A>C,-592C>A)	A/C	3	2368/2869	22.85	Allelic	0.98(0.89-1.08)	0.677	0	3	842/1257	66.31	Allelic	0.76(0.62-0.93)	0.009	56
IL10	rs1800896(g.3943A>G,-1082A>G)	G/A	6	2190/2729	47.62	Allelic	1.08(0.92-1.27)	0.347	49	3	627/1029	10.11	Allelic	1.83(0.75-4.49)	0.188	88
IL13	rs1800925(-1069C>T,-1112C>T)	T/C														
IL13	rs20541(Arg130Gln,+2044G>A)	A/G														
IL17A	rs2275913(-73G>A,-152G>A)	A/G														
IL1B	rs1143634(p.Phe105Phe,Ex5+14C>T)	T/C	3	4045/3627	23.55	Allelic	1.02(0.94-1.10)	0.666	0							
IL1B	rs1143627(g.4970C>T,-31T>C)	C/T	4	3681/4142	33.23	Allelic	0.98(0.87-1.10)	0.757	60	3	1352/1906	48.87	Allelic	0.89(0.71-1.10)	0.277	75
IL1B	rs16944(C-511T)	T/C								7	2391/2858	47.10	Allelic	0.92(0.78-1.09)	0.343	75
IL4	rs2243250(-509C>T)	T/C								3	1691/1737	78.12	Allelic	1.18(0.88-1.59)	0.276	76
IL6	rs1800795(G-174C)	C/G	8	4385/5232	43.43	Allelic	1.01(0.95-1.07)	0.721	0							
IL6	rs1800796(-572C>G,634C>G)	G/C								8	2782/3195	22.35	Allelic	1.04(0.83-1.31)	0.713	82
IL8	rs4073(T-251A)	T/A	4	4308/4773	49.36	Allelic	1.00(0.94-1.06)	0.973	0							
LIG1	rs156641(G>A)	A/G	3	1000/1940	34.48	Allelic	1.09(0.90-1.32)	0.396	44							
LIG1	rs20579(-7C>T)	A/G	3	1140/2079	12.84	Allelic	1.25(0.84-1.86)	0.279	80							
LIG1	rs20581(p.Asp802Asp,G>A)	A/G														
LIG1	rs3730931(IVS9-21A>G)	G/A	3	1145/2084	12.00	Allelic	1.15(0.78-1.70)	0.479	77							
LIG1	rs439132(A>G)	G/A														
LIG1	rs20580(p.Ala170Ala,c.417C>A)	A/C	3	1412/2214	48.85	Allelic	1.01(0.88-1.17)	0.876	47							
LIG4	rs1805388(p.Thr9Ile,Ex2+54C>T)	T/C														
LTA	rs909253(A+252G)	G/A	4	234/596	31.12	Allelic	1.10(0.87-1.41)	0.428	0							
MAPKAPK2	CNV-30450(2copies/3copies/4copies)	NA								3	2332/2480	9.76	4 copies vs 2 copies	1.60(1.04-2.45)	0.031	81
MBD4	rs140693(p.Glu346Lys,G1212A)	A/G								4	2295/2469	35.62	Allelic	0.99(0.86-1.13)	0.881	57
MCP1	rs1024611(-2518A>G,PvuII)	G/A														
MDM2	rs117039649(G>C,SNP285)	C/G														
MDM2	rs2279744(SNP309,c.14+309T>G)	G/T	7	5541/7830	37.31	Allelic	1.00(0.93-1.08)	0.979	45	8	5013/5834	49.07	Allelic	1.13(1.03-1.24)	0.011	64
MDM2	rs769412(p.Glu184Glu,2164A>G,SNP354)	G/A	3	1574/1715	29.53	Allelic	1.01(0.90-1.13)	0.889	0							
MGMT	rs12268840(C>T)	T/C	3	247/355	32.82	Allelic	0.88(0.64-1.19)	0.396	24							
MGMT	rs12917(p.Leu115Phe,c.343C>T)	T/C	5	1930/3022	14.36	Allelic	1.08(0.94-1.24)	0.292	14							
MGMT	rs1803965(Leu53Leu,171C>T,TaqI)	T/C														
MGMT	rs2308321(p.Ile174Val,Ile143Val,c.520A>G)	G/A	5	1942/2110	12.68	Allelic	1.02(0.85-1.23)	0.809	33							
MGMT	rs2308327(p.Lys178Arg,c.533A>G)	G/A	5	759/880	20.45	Allelic	0.73(0.50-1.07)	0.109	68							
MIR146A	rs2910164(C>G)	C/G								4	2807/2841	49.03	Allelic	1.12(1.04-1.21)	0.002	0
MIR196A2	rs11614913(T>C)	C/T								4	2376/2413	45.86	Allelic	1.14(1.05-1.23)	0.002	0
MLH1	rs1799977(p.Ile219Val,c.655A>G)	G/A								3	1713/1874	3.98	Allelic	1.03(0.59-1.79)	0.927	69
MLH1	rs1800734(-93G>A)	A/G								4	1756/1809	57.19	Allelic	1.03(0.86-1.23)	0.745	69
MLH3	rs175080(p.Pro844Leu,C2645T)	T/C														
MMP1	rs1799750(-16071G/2G,insG)	2G/1G	6	3607/3073	49.40	Allelic	1.05(0.89-1.23)	0.580	74							
MMP2	rs243865(-1306C>T)	T/C														
MMP3	rs3025058(-16125A/6A,-11715A/6A)	5A/6A	3	2759/2021	48.74	Allelic	1.02(0.93-1.10)	0.726	0							
MMP9	rs3918242(g.3430C>T,-1562C>T)	T/C														

Gene	Variant	Alleles[a]	Meta-analysis performed in Caucasian population							Meta-analysis performed in Asian population						
			Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2(%)	Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2 (%)
MPO	rs2333227(G-463A)	A/G	16	7248/8119	23.27	Allelic	0.93(0.85-1.03)	0.152	60	8	2030/2185	11.95	Allelic	0.85(0.69-1.04)	0.112	50
MSH3	rs26279(p.Ala1045Thr,c.3133G>A)	G/A														
MSH6	rs1042821(p.Gly39Glu,c.116G>A)	A/G														
MTHFR	rs1801131(p.Ala429Glu,c.1286A>C,A1298C)	C/A	5	2127/2179	31.30	Allelic	1.10(1.00-1.20)	0.043	0	5	1946/2740	19.20	Allelic	1.04(0.94-1.16)	0.442	0
MTHFR	rs1801133(p.Ala222Val,Ex4+79C＞T)	T/C	7	2219/3028	31.46	Allelic	0.99(0.81-1.23)	0.953	72	8	6421/5172	42.56	Allelic	1.10(0.96-1.25)	0.186	77
MTR	rs1805087(Asp919Gly,A2756G)	G/A								3	1453/2187	13.33	Allelic	1.13(0.97-1.32)	0.128	16
MTRR	rs1801394(Ile49Met,A66G)	G/A														
MUTYH	rs3219489(p.Gln324His,c.972G>C)	C/G														
MYCL	L/S(EcoRI)	NA	4	202/548	49.36	S vs L	1.03(0.81-1.30)	0.821	0							
NAT2	Rapid/slow (Acetylation Phenotype)	NA	11	2148/2887	64.39	Slow vs rapid	1.06(0.91-1.23)	0.482	28	6	1599/1965	24.73	Slow vs rapid	0.98(0.66-1.46)	0.915	79
NAT2	rs1799929(p.Leu161Leu,481C>T)	T/C														
NAT2	rs1799930(p.Arg197Gln,590G>A,NAT2*6B)	A/G	4	964/936		Dominant	0.88(0.64-1.21)	0.422	61							
NBN	rs1805794(p.Gln185Glu,Ex5-32C>G,605C>G)	G/C	3	688/1528	39.95	Allelic	1.00(0.86-1.16)	0.989	0	5	2890/3160	54.73	Allelic	0.93(0.73-1.19)	0.556	90
NFKB1	rs28362491(-94ins/delATTG)	-94insATTG/-														
NOD2	rs2066847(3020insC,WT/insC,L1007fs)	3020insC/-														
NQO1	rs1800566(p.Pro187Ser,c.648C>T,609C>T,*2)	T/C	10	3181/3582	22.79	Allelic	1.06(0.97-1.15)	0.231	0	8	1482/2325	42.37	Allelic	0.92(0.73-1.16)	0.492	81
OGG1	rs1052133(p.Ser326Cys,c.977C>G,8055C>G)	G/C	11	4089/5931	22.05	Allelic	0.98(0.85-1.14)	0.827	69	18	7311/7683	53.05	Allelic	1.06(0.99-1.13)	0.080	42
PADPRP	A/B(a193-bp deletion)	193-bp del/-	3	217/213		Dominant	1.02(0.41-2.53)	0.965	75							
PARP1	rs1136410(p.Val762Ala,Ex17+8T＞C)	C/T								5	2900/2567	43.83	Allelic	1.03(0.89-1.19)	0.724	66
PCNA	rs25406(2232C>T)	T/C	3	746/854	40.11	Allelic	0.95(0.80-1.14)	0.597	35							
PDCD5	rs1862214(G>A)	G/C														
POLD1	rs1726801(p.Arg119His,c.356G>A)	A/G								3	1263/1420	19.30	Allelic	1.11(0.96-1.28)	0.168	0
POLI	rs3730668(-78G>T)	T/G														
POLI	rs8305(Thr706Ala,2180A>G)	G/A														
POLL	rs3730477(p.Arg438Trp,1683C>T)	T/C														
PON1	rs662(p.Gln192Arg,c.575A>G)	A/G														
PPARG	rs1801282(p.Pro12Ala,c.36C>G)	G/C	3	2178/2659	18.11	Allelic	1.00(0.89-1.14)	0.961	0							
PPP1R13L	rs6966(T>A)	T/A														
PPP1R13L	rs1970764(IVS1-4364A>G)	G/A														
PROM1	rs2240688(A>C)	C/A								3	2332/2457	27.37	Allelic	0.83(0.76-0.91)	6.92×10^{-5}	0
PTGS2	rs20417(-765G>C)	C/G														
PTGS2	rs689466(g.38139393T>C,-1195A>G)	G/A														
PTGS2	rs5275(c.*427T>C,8473T>C)	C/T	5	4378/4847	35.47	Allelic	1.06(0.85-1.33)	0.590	91	5	2245/2941	20.10	Allelic	0.87(0.74-1.03)	0.097	60
RAD23B	rs1805329(p.Ala249Val,Ex7+65C＞T)	T/C	3	535/767	23.79	Allelic	0.97(0.73-1.28)	0.815	51							
REV1	rs3087386(p.Phe257Ser,892T>C)	C/T								3	1437/2503	33.72	Allelic	1.03(0.93-1.14)	0.544	0
REV3L	rs462779(p.Thr1146Ile,4259C>T)	T/C								4	1937/2335	39.36	Allelic	1.11(1.02-1.22)	0.021	0
REV3L	rs465646(460T>C)	C/T								3	1296/1511	18.73	Allelic	0.83(0.71-0.97)	0.016	14
SFTPB	wildtype/variation(deletions or insertions)	NA	3	157/240	5.83	Variation vs wild	1.92(1.11-3.33)	0.020	0							
SOD2	rs4880(rs1799725,Ala16Val)	T/C	4	3185/3966	48.20	Allelic	1.17(1.10-1.25)	2.24×10^{-6}	0	3	551/683	NA	Recessive	1.06(0.82-1.37)	0.671	0
SULT1A1	rs9282861(p.Arg213His,c.638G>A,*1/*2)	A/G	3	865/1152	29.95	Allelic	1.11(0.92-1.35)	0.275	44							
TDG	rs4135113(p.Gly199Ser,c.595G>A)	A/G														
TERT	rs2736098(p.Ala305Ala,c.915G>A)	A/G								6	3829/3992	35.11	Allelic	1.20(1.06-1.37)	0.004	72
TGFB1	rs1800469(C-509T)	T/C								4	1091/1238	49.31	Allelic	0.95(0.85-1.07)	0.428	3
TGFB1	rs1800470(p.Leu10Pro,c.29C>T)	C/T								4	935/1031	49.13	Allelic	1.03(0.91-1.17)	0.668	0
TNF	rs1799724(-857C>T,-1036C>T)	C/T														
TNF	rs1800629(G-308A,*1/*2)	A/G	8	2576/3091	16.68	Allelic	0.97(0.86-1.10)	0.668	10							
TNF	rs361525(A-417G,-238G>A)	A/G	3	575/584	3.94	Allelic	1.05(0.67-1.65)	0.834	0							
TNFRSF10A	rs2230229(p.Arg441Lys,c.1322G>A)	G/A	4	1183/1637	14.87	Allelic	1.01(0.71-1.44)	0.948	72							
TP53	rs1042522(p.Pro72Arg,c.215C>G)	C/G	23	10470/12364	26.37	Allelic	1.06(0.98-1.14)	0.178	63	18	10520/9977	40.03	Allelic	1.08(0.99-1.17)	0.068	69
TP53	rs12951053(IVS7+92T>G)	G/T														
TP53	rs1625895(IVS6+62G>A,A2>A1)	A/G	5	2382/2504	12.68	Allelic	1.17(0.93-1.49)	0.185	67							
TP53	rs1642785(IVS2+38G>C,1827G>C)	C/G								3	132/107	53.74	Allelic	0.82(0.57-1.17)	0.272	0
TP53	rs17878362(IVS3 16bp Del/Ins)	16-bp ins/-	4	4196/4327	12.97	Allelic	1.13(0.96-1.34)	0.152	64							
TP53BP1	rs560191(p.Asp353Glu,c.1059C>G）	G/C														
TP63	rs10937405(C>T)	T/C														
TP73	G4C14/A4T14	A4T14/G4C14								6	2000/2172	24.19	Allelic	0.99(0.81-1.21)	0.942	73
TYMS	28-bp tandem repeat	NA														
UGT1A6	rs1105879(p.Arg184Ser,c.552A>C)	G/T														
UGT1A6	rs6759892(p.Ser7Ala,c.19T>G)	G/T														
VEGFA	rs2010963(634G>C)	C/G														
VEGFA	rs3025039(C936T)	T/C								3	753/754	17.31	Allelic	1.10(0.84-1.45)	0.487	43
VEGFA	rs699947(C-2578A)	A/C								3	735/660	22.95	Allelic	0.97(0.75-1.25)	0.829	43
VEGFA	rs833061(-460T>C)	C/T								3	967/930	29.62	Allelic	0.85(0.68-1.05)	0.123	52
vWF	rs9295740(G>A)	A/G														
WWOX	CNV-67048(2copies/1copy/0copy)	NA								4	2942/3074	2.86	0 copy vs 2 copies	2.06(1.58-2.70)	1.20×10^{-7}	0
XPA	rs1800975(c.-4A>G,23G>A)	A/G	9	3294/4385	35.01	Allelic	1.05(0.94-1.16)	0.404	53							
XPC	PAT-/+(24660_24664delGTAAC, inspoly(AT))	inspoly(AT)/-														
XPC	rs2228000(p.Ala499Val,Ex9-377C>T)	T/C								5	2238/2062	31.13	Allelic	1.06(0.95-1.18)	0.310	23
XPC	rs2228001(p.Gln939Lys,Ex16+211A＞C)	C/A	6	1919/3265	37.81	Allelic	1.05(0.97-1.15)	0.236	7	8	3696/3729	37.92	Allelic	1.03(0.96-1.10)	0.401	0
XRCC1	rs1001581(c.145-216G>A)	T/C														
XRCC1	rs1799782(p.Arg194Trp,c.580C>T,Ex6-22C＞T)	T/C	12	4740/6868	6.96	Allelic	0.84(0.72-0.98)	0.028	28	15	5844/6259	31.07	Allelic	0.92(0.81-1.03)	0.152	74
XRCC1	rs2030404(A>G)	G/A														
XRCC1	rs2256507(G>A)	A/G														
XRCC1	rs25486(A>G)	G/A														
XRCC1	rs25487(p.Gln399Arg,c.1196A>G)	A/G	18	7846/10215	34.51	Allelic	1.00(0.95-1.05)	0.958	11	22	8845/9585	25.49	Allelic	1.04(0.96-1.14)	0.344	65
XRCC1	rs25489(p.Arg280His,c.839G>A,Ex9+16G>A)	A/G	9	4038/4481	5.27	Allelic	1.06(0.87-1.29)	0.594	36	9	3784/3993	10.32	Allelic	0.92(0.70-1.19)	0.513	81
XRCC1	rs2682562(A>G)	G/A														
XRCC1	rs2682585(p.His6Arg,c.17A>G)	A/G														
XRCC1	rs2854510(A>G)	G/A														
XRCC1	rs3213255(A>G)	G/A														
XRCC1	rs3213403(A>G)	G/A														

Gene	Variant	Alleles[a]	Meta-analysis performed in Caucasian population							Meta-analysis performed in Asian population						
			Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2(%)	Studies	Cases/Controls	Frequency(%)[b]	Genetic models	OR (95% CI)	*P* value	I^2 (%)
XRCC1	rs3547(p.Gln632Gln,c.1896G>A)	A/G														
XRCC1	rs3213245(-77T>C)	C/T								4	2686/2755	9.87	Allelic	1.33(1.04-1.69)	0.021	74
XRCC2	rs3218536(p.Arg188His,c.563G>A)	A/G	3	645/1373	8.08	Allelic	1.23(0.54-2.77)	0.625	88							
XRCC3	rs1799794(4541A>G)	G/A														
XRCC3	rs1799796(17893A>G,IVS5-14)	G/A	3	665/1672	31.19	Allelic	0.98(0.85-1.14)	0.827	0							
XRCC3	rs861539(p.Thr241Met,c.722C>T)	T/C	9	2271/3339	36.63	Allelic	0.97(0.90-1.06)	0.541	0	7	3805/4330	6.91	Allelic	1.20(0.98-1.47)	0.072	63

Chr=chromosome; OR=odds ratio, 95%CI = 95% confidence interval; bp=base pair; VNTR=variable number of tandem repeats; ins=insertion; NA = Not Applicable.

[a] Minor alleles/major alleles (per Caucasian).

[b] Frequency of minor allele or effect genotype(s) in controls in specific ethnicity.

Supplementary Table S4. Credibility assessment for variants with significant associations with lung cancer risk in subgroup meta-analyses by ethnicity

Genes	Variants	Alleles[a]	Sub-group	Number evaluated		Lung cancer risk meta-analysis					Venice criteria grades[d]	Credibility of evidence[e]	Amount of evidence[f]		Replication[g]	Protection from bias[h]			Sensitivity analysis[i]			Low OR[j]	Modified P[k]	Excess P[l]	Begg's P[m]
																			Initial study influence		Deviation from HWE				
				Studies	Cases/Controls	Genetic models	OR(95%CI)[b]	P value	I^2 (%)	P_Q[c]			Numbers	Grade		Grade	Reasons for bias	Reason for bias exemption	OR(95%CI)	P value					
APEX1	rs1130409	G/T	Caucasian	7	1807/3065	Recessive	0.84(0.72-0.97)	0.021	0	0.695	AAA	Strong	1119	A	A	A			0.81(0.68-0.95)	0.011	No	No	0.719	0.573	0.764
CHRNA5	rs16969968	A/G	Caucasian	6	3305/59780	Allelic	1.35(1.27-1.44)	2.03×10^{-21}	0	0.958	AAA	Strong	43126	A	A	A			1.35(1.26-1.44)	0.000	None	No	0.963	1.000	0.990
CLPTM1L	rs402710	T/C	Caucasian	4	1801/1908	Allelic	0.86(0.78-0.94)	0.002	0	0.532	AAA	Strong	2717	A	A	A			0.87(0.78-0.97)	0.010	None	No	0.678	1.000	0.734
CYP1A1	rs4646903	C/T	Caucasian	21	5083/6022	Allelic	1.12(1.03-1.21)	0.011	0	0.779	AAC	Weak	2633	A	A	C	Low OR,small study,publication bias		1.12(1.03-1.22)	0.011	None	Yes	0.002	1.000	0.002
CYP1A1	rs1048943	G/A	Caucasian	15	3375/3871	Allelic	1.27(1.02-1.59)	0.037	54	0.006	ACC	Weak	1088	A	C	C	Excess of significant studies		1.27(1.00-1.60)	0.050	None	No	0.264	0.091	0.295
CYP1A2	rs762551	C/A	Caucasian	3	869/1468	Recessive	1.69(1.20-2.36)	0.002	30	0.232	BBA	Moderate	237	B	B	A			1.84(1.13-3.00)	0.015	None	No	0.504	1.000	1.000
CYP1B1	rs1056836	G/C	Caucasian	6	1849/2655	Dominant	1.18(1.04-1.34)	0.010	0	0.856	AAB	Moderate	3408	A	A	B	Missing information		1.16(1.02-1.33)	0.026	NA	No	0.822	0.607	0.711
CYP2A6	rs1801272	A/T	Caucasian	3	2411/2644	carriers vs non-carriers	0.66(0.52-0.84)	0.001	0	0.674	BAB	Moderate	307	B	A	B	Missing information		0.65(0.51-0.83)	0.001	NA	No	0.929	1.000	1.000
CYP2E1	rs2031920	T/C	Caucasian	6	665/1224	Allelic	0.61(0.42-0.90)	0.013	0	0.456	BAB	Moderate	160	B	A	B	Missing information		0.57(0.39-0.85)	0.006	NA	No	0.767	0.588	0.837
ELANE	rs351107	G/T	Caucasian	3	745/762	Allelic	0.55(0.34-0.87)	0.011	29	0.246	BBC	Weak	126	B	B	C	First study		0.57(0.24-1.38)	0.213	None	No	0.794	0.565	1.000
ELANE	rs7254054	A/G	Caucasian	3	754/750	Allelic	0.77(0.61-0.97)	0.030	46	0.155	BBC	Weak	735	B	B	C	First study,small study		0.84(0.53-1.32)	0.444	NA	No	0.022	0.567	0.296
ERCC2	rs238406	A/C	Caucasian	3	1150/2080	Allelic	1.13(1.01-1.25)	0.026	0	0.457	AAC	Weak	2826	A	A	C	First study,HWE,low OR		1.10(0.98-1.24)	0.110	Yes	Yes	0.158	1.000	0.157
ERCC2	rs13181	C/A	Caucasian	18	5967/8851	Recessive	1.15(1.04-1.29)	0.009	16	0.258	AAA	Strong	2209	A	A	A			1.15(1.03-1.29)	0.017	No	No	0.191	0.206	0.495
GSTM1	Present/Null	NA	Caucasian	58	16976/20622	Allelic	1.08(1.03-1.13)	0.001	7	0.332	AAC	Weak	19614	A	A	C	Low OR		1.08(1.03-1.13)	0.001	None	Yes	0.452	0.383	0.448
HRAS1	common/rare (HRAS1 VNTR)	NA	Caucasian	4	746/1174	rare vs common	2.55(1.01-6.45)	0.048	69	0.023	BCC	Weak	305	B	C	C	First study		2.02(0.66-6.21)	0.221	None	No	0.561	0.346	0.734
MTHFR	rs1801131	C/A	Caucasian	5	2127/2179	Allelic	1.10(1.00-1.20)	0.043	0	0.862	AAC	Weak	2814	A	A	C	HWE,low OR	Highly consistent OR	1.13(1.01-1.25)	0.029	Yes	Yes	0.800	1.000	0.797
SFTPB	wild type/variation	NA	Caucasian	3	157/240	Allelic	1.92(1.11-3.33)	0.020	0	0.960	CAC	Weak	59	C	A	C	Publication bias		NA		None	No	0.495	1.000	0.049
SOD2	rs4880	T/C	Caucasian	4	3185/3966	Allelic	1.17(1.10-1.25)	2.24×10^{-6}	0	0.973	AAA	Strong	7146	A	A	A			1.17(1.08-1.27)	0.000	None	No	0.407	1.000	0.406
XRCC1	rs1799782	T/C	Caucasian	12	4740/6868	Allelic	0.84(0.72-0.98)	0.028	28	0.172	ABA	Moderate	1510	A	B	A			0.84(0.72-0.99)	0.039	No	No	0.927	0.636	0.790
AGER	rs1800624	A/T	Asian	3	1656/1693	Additive	1.18(1.04-1.33)	0.010	16	0.305	AAC	Weak	2292	A	A	C	First study		1.20(0.90-1.60)	0.215	None	No	0.480	1.000	1.000
APEX1	rs1760944	A/C	Asian	5	3071/3038	Allelic	1.20(1.12-1.29)	9.14×10^{-7}	0	0.717	AAA	Strong	5851	A	A	A			1.17(1.07-1.28)	0.001	None	No	0.223	0.401	0.462
ATM	rs189037	A/G	Asian	5	3036/3415	Additive	1.09(1.00-1.18)	0.050	29	0.227	ABC	Moderate	5653	A	B	C	Low OR	Highly consistent OR	1.12(1.02-1.22)	0.016	None	Yes	0.195	1.000	0.806
CHRNA3	rs6495309	T/C	Asian	3	2635/2767	Allelic	0.83(0.76-0.91)	6.17×10^{-5}	27	0.254	ABA	Moderate	4924	A	B	A			0.83(0.76-0.91)	0.000	None	No	0.758	1.000	1.000
CLPTM1L	rs402710	T/C	Asian	8	5413/6143	Dominant	0.84(0.77-0.92)	1.53×10^{-4}	17	0.296	AAA	Strong	5150	A	A	A			0.82(0.74-0.91)	0.000	No	No	0.934	1.000	0.711
CYP1A1	rs4646903	C/T	Asian	15	2418/3107	Allelic	1.18(1.01-1.38)	0.036	73	0.000	ACC	Weak	4263	A	C	C	First study,small study		1.17(0.99-1.38)	0.073	No	No	0.037	0.156	0.113
CYP1A1	rs1048943	G/A	Asian	21	4265/5242	Allelic	1.17(1.02-1.33)	0.024	73	0.000	ACC	Weak	5007	A	C	C	Excess of significant studies		1.15(1.00-1.32)	0.048	No	No	0.213	0.025	0.740
CYP2A6	non*4/*4	del/-(*4/non*4)	Asian	6	2517/2264	Recessive	0.52(0.36-0.75)	0.001	0	0.454	BAA	Moderate	128	B	A	A			0.53(0.34-0.83)	0.006	No	No	0.961	0.636	0.707
CYP2E1	rs6413432	A/T	Asian	6	1964/2085	Allelic	0.78(0.70-0.86)	1.31×10^{-6}	0	0.824	AAA	Strong	1956	A	A	A			0.77(0.70-0.86)	0.000	No	No	0.440	0.680	0.707
FASLG	rs763110	T/C	Asian	3	1857/2149	Recessive	0.77(0.60-0.99)	0.039	16	0.303	BAC	Weak	351	B	A	C	First study		0.80(0.50-1.27)	0.344	None	No	0.959	0.543	1.000
GSTM1	Present/Null	NA	Asian	36	11012/9982	Allelic	1.27(1.14-1.41)	9.06×10^{-6}	65	0.000	ACC	Weak	11195	A	C	C	Excess of significant studies		1.26(1.13-1.41)	0.000	None	No	0.543	0.023	0.967
GSTP1	rs1695	G/A	Asian	11	2307/2430	Allelic	1.14(1.01-1.29)	0.036	27	0.187	ABC	Weak	1860	A	B	C	Low OR		1.16(1.01-1.35)	0.038	No	Yes	0.914	0.293	0.755
GSTT1	Present/Null	NA	Asian	14	7043/5289	Allelic	1.15(1.03-1.28)	0.010	34	0.105	ABA	Moderate	6305	A	B	A			1.15(1.03-1.29)	0.014	None	No	0.805	0.431	0.827
IL10	rs1800872	A/C	Asian	3	842/1257	Allelic	0.76(0.62-0.93)	0.009	56	0.106	ACC	Weak	2644	A	C	C	First study		0.81(0.64-1.02)	0.068	None	No	0.420	1.000	0.296
MAPKAPK2	CNV-30450	NA	Asian	3	2332/2480	4 copies vs 2 copies	1.60(1.04-2.45)	0.031	81	0.005	BCB	Weak	586	B	C	B	Missing information		NA		None	No	0.947	0.298	1.000
MDM2	rs2279744	G/T	Asian	8	5013/5834	Allelic	1.13(1.03-1.24)	0.011	64	0.006	ACC	Weak	11054	A	C	C	Low OR,small study		1.15(1.03-1.27)	0.010	None	Yes	0.097	0.724	0.458
MIR146A	rs2910164	C/G	Asian	4	2807/2841	Recessive	1.23(1.09-1.39)	0.001	0	0.594	AAA	Strong	1481	A	A	A			1.28(1.11-1.48)	0.001	None	No	0.861	0.622	1.000
MIR196A2	rs11614913	C/T	Asian	4	2376/2413	Dominant	1.22(1.07-1.38)	0.002	0	0.444	AAA	Strong	3448	A	A	A			1.32(1.11-1.56)	0.002	None	No	0.173	1.000	0.308
PROM1	rs2240688	C/A	Asian	3	2332/2457	Additive	0.83(0.76-0.91)	6.92×10^{-5}	0	0.991	AAB	Moderate	2459	A	A	B	Missing information		NA		None	No	0.379	0.281	0.296
REV3L	rs462779	T/C	Asian	4	1937/2335	Additive	1.11(1.02-1.22)	0.021	0	0.911	AAC	Strong	3433	A	A	C	Low OR	Highly consistent OR	1.13(1.00-1.27)	0.043	None	Yes	0.921	1.000	0.734
REV3L	rs465646	C/T	Asian	3	1296/1511	Allelic	0.83(0.71-0.97)	0.016	14	0.311	BAB	Moderate	982	B	A	B	Missing information		NA		None	No	0.288	1.000	1.000
TERT	rs2736098	A/G	Asian	5	3829/3992	Dominant	1.26(1.14-1.39)	1.03×10^{-5}	0	0.896	AAA	Strong	3696	A	A	A			1.27(1.13-1.43)	0.000	None	No	0.550	0.379	1.000
VEGFA	rs833061	C/T	Asian	3	967/930	Recessive	0.65(0.46-0.93)	0.018	0	0.800	BAC	Weak	146	B	A	C	First study		0.70(0.46-1.07)	0.104	None	No	0.709	1.000	1.000
WWOX	CNV-67048	NA	Asian	4	2942/3074	0 copy vs 2 copies	2.06(1.58-2.70)	1.20×10^{-7}	0	0.911	BAB	Moderate	247	B	A	B	Missing information		NA		None	No	0.648	1.000	1.000
XRCC1	rs25487	A/G	Asian	22	8845/9585	Recessive	1.25(1.00-1.56)	0.049	60	0.000	ACC	Weak	1128	A	C	C	First study,HWE, excess of significant studies		1.24(0.99-1.57)	0.063	Yes	No	0.795	0.046	0.721
XRCC1	rs3213245	C/T	Asian	4	2686/2755	Allelic	1.33(1.04-1.69)	0.021	74	0.010	ACC	Weak	1234	A	C	C	First study		1.27(0.91-1.78)	0.167	None	No	0.773	0.651	0.734

NA=Not Applicable; VNTR=variable number of tandem repeats.

[a] Minor alleles/major alleles (per Caucasian)

[b] Summary ORs were calculated based on the DerSimonian-Lairs random-effects model

[c] *P*-value of heterogeneity between studies

[d] Venice criteria grades contained assessments of three aspects: the amount of evidence, extent of replication, and protection from bias, and each assessment was assigned three levels (A, B, or C).

[e] Credibility of evidence was evaluated based on Venice criteria with three aspects (the amount of evidence, extent of replication, and protection from bias), and was categorized as strong (all three aspect grades were A), moderate (any grade was B, but not C) or weak (any grade was C).

[f] Amount of evidence, depending on total sample size of the smallest genetic group among cases and controls in each meta-analysis, was graded as A (sample size>1000), B (sample size between 100 and 1000), or C (sample size <100).

[g] Extent of replication, depending on between-study heterogeneity, was graded as A (I^2<25%), B (I^2 between 25% and 50%), or C (I^2>50%).

[h] Protection from bias, considering various potential sources of bias in meta-analysis, was graded as A when there was no demonstrable bias and bias was unlikely invalidate the association, was graded as B when there was insufficient information for identifying evidence (i.e. missing information for evaluating Hardy-Weinberg equilibrium (HWE) among controls in an individual study) although there was no obvious bias, and C when the bias was evident and/or was likely to explain the presence of association. For the C grade, it was assigned if a meta-analysis had any of the following potential sources of bias: (1) magnitude of the association was low; (2) sensitivity analysis altered the statistical significance; (3) potential small study effect; (4) possible existence of an excess of significant findings (the number of observed significant studies more than the number of expected significant studies); (5) potential publication bias.

First study=Significance lost excluding the first published or first positive report; Low OR=Low magnitude of the association (i.e. 0.87<OR<1.15); Small study=Possible existence of potential small study effect (modified Egger's test, *p*<0.10); Excess of significant studies=Possible existence of an excess of significant findings (excess significance test, *p*<0.10); Publication bias= Possible existence of potential publication bias (Begg's test, *p*<0.10); Missing information= Insufficient information for bias evaluation; HWE=Significance lost excluding studies with controls violating HWE; Highly consistent OR=A meta-analysis with a low OR was not considered if there is a highly consistent OR across studies enrolled in this meta-analysis

[i] A sensitivity analysis was performed to examine whether the significant summary ORs were robust after excluding the first published or first positive report (defined as the earliest study reported a significant association), or excluding studies with controls violating HWE. None=A meta-analysis didn't include studies with controls violating HWE or evaluated association for a variant with a phenotype change; NO=Without the influence from studies with controls violating HWE; NA=Insufficient information for evaluation of influence from first published or first reported positive study; Yes=Evidence of influence from studies with controls violating HWE.

[j] Low OR (i.e. 0.87<OR<1.15; No=Association without a low OR;Yes=Association with a low OR)

[k] *P* value for potential small study effect based on the modified Egger's test. (*P*<0.10 is usually considered evidence for significant evidence of small study effect.)

[l] *P* value for possible existing an excess of significant findings based on the excess significance test. (*P*<0.10 is usually considered evidence for significant evidence of an excess of significant findings.)

[m] *P* value for potential publication bias of studies based on the Begg's test. (*P*<0.10 is usually considered evidence for significant evidence of publication bias).

Supplementary Table S5. Subgroup meta-analyses stratified by different histological types of lung cancer for variants with sufficient data under different genetic models

(Continued on next two pages)

Genes	Sub-group	Variants	Comparison[a]	Results of meta-analysis using allelic model						Results of meta-analysis using dominant model						Results of meta-analysis using recessive model					
				Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]
CHRNA5	SCLC	rs16969968(p.Asp398Asn,c.1192G>A)	A vs G	3	513/3253	1.55(1.15-2.10)	0.004	55	0.109												
CYP1A1	SCLC	rs4646903(m1,MspI,T3801C)	C vs T	14	325/2955	1.05(0.84-1.32)	0.650	0	0.879	17	494/3409	1.00(0.79-1.28)	0.979	0	0.77	12	273/2545	1.71(1.08-2.71)	0.021	0	0.90
CYP1A1	SCLC	rs1048943(*2C,m2,p.Ile462Val,c.1384A>G)	G vs A	11	402/2172	1.06(0.74-1.53)	0.752	46	0.050	11	422/2218	0.83(0.53-1.29)	0.403	40	0.08	7	285/1143	1.93(0.79-4.72)	0.149	47	0.08
CYP2D6	SCLC	phenotype(EM/HEM/PM)	PM vs EM	4	93/433	1.01(0.31-3.27)	0.986	0	0.438	5	117/509	0.80(0.50-1.28)	0.349	0	0.73	4	16/228	1.12(0.35-3.58)	0.849	0	0.44
CYP2E1	SCLC	rs6413432(c.967+1143T>A,7632T>A)	A vs T	6	254/1809	0.91(0.54-1.52)	0.714	56	0.044	6	254/1809	1.05(0.56-1.97)	0.886	61	0.03	5	250/1771	0.70(0.23-2.07)	0.514	24	0.26
CYP2E1	SCLC	rs2031920(RsaI,c1>c2,-1053C>T)	T vs C	6	390/3110	0.80(0.56-1.14)	0.215	57	0.041	6	390/3110	0.70(0.46-1.07)	0.102	56	0.05	5	346/2404	1.45(0.47-4.53)	0.521	69	0.01
ERCC2	SCLC	rs1799793(p.Asp312Asn,c.981G>A)	A vs G	3	303/1321	1.20(0.90-1.60)	0.221	0	0.571												
GSTM1	SCLC	Present/Null(Large gene deletion)	Null vs present	26	1224/7255	1.30(1.09-1.56)	0.004	43	0.010												
GSTP1	SCLC	rs1695(p.Ile105Val,c.313A>G)	G vs A	8	533/3555	1.12(0.97-1.29)	0.122	0	0.847	10	678/3932	1.02(0.86-1.22)	0.811	0	0.45	8	533/3555	1.34(1.00-1.79)	0.054	0	0.62
GSTT1	SCLC	Present/Null(Large gene deletion)	Null vs present	16	762/4200	1.07(0.86-1.32)	0.561	0	0.952												
MDM2	SCLC	rs2279744(SNP309,c.14+309T>G)	G vs T	3	265/2309	0.85(0.70-1.04)	0.117	13	0.318	3	265/2309	0.77(0.58-1.03)	0.078	0	0.92	3	265/2309	0.81(0.46-1.42)	0.453	59	0.09
MPO	SCLC	rs2333227(G-463A)	A vs G	3	392/2783	0.90(0.70-1.16)	0.420	30	0.242	3	392/2783	0.91(0.66-1.26)	0.570	40	0.19	3	392/2783	0.74(0.43-1.29)	0.289	0	0.81
NAT2	SCLC	Rapid/slow(Acetylation Phenotype)	Slow vs rapid	4	234/1993	1.26(0.89-1.77)	0.195	0	0.867												
NQO1	SCLC	rs1800566(p.Pro187Ser,c.648C>T,609C>T,*2)	T vs C	3	205/792	1.68(1.05-2.68)	0.029	56	0.102	4	264/1152	1.58(0.98-2.58)	0.063	59	0.06	3	205/792	2.32(0.93-5.78)	0.071	0	0.80
OGG1	SCLC	rs1052133(p.Ser326Cys,c.977C>G,8055C>G)	G vs C	4	376/2129	0.88(0.71-1.08)	0.225	26	0.254	3	165/1444	0.71(0.43-1.18)	0.192	37	0.20	4	220/2474	1.14(0.65-1.99)	0.66	53	0.09
PADPRP	SCLC	A/B (a 193-bp deletion)	Del vs non-del							3	30/339	0.81(0.34-1.95)	0.641	0	0.66						
TNF	SCLC	rs1800629(G-308A,*1/*2)	A vs G	3	107/512	0.87(0.55-1.38)	0.555	0	0.913	3	107/512	0.89(0.53-1.49)	0.659	0	0.75	3	107/512	0.83(0.18-3.84)	0.813	0	0.74
TP53	SCLC	rs1042522(p.Pro72Arg,c.215C>G)	C vs G	15	835/4556	0.97(0.72-1.29)	0.814	80	0.000	15	714/4453	0.93(0.64-1.35)	0.706	73	0.00	14	624/3871	1.18(0.72-1.91)	0.515	65	0.00
XPC	SCLC	PAT-/+ (24660_24664delGTAAC, inspoly(AT))	Ins vs non-ins	3	208/1340	0.86(0.58-1.27)	0.443	69	0.040	3	208/1340	0.72(0.48-1.09)	0.122	46	0.16	3	208/1340	1.05(0.56-1.95)	0.882	52	0.13
XPC	SCLC	rs2228001(p.Gln939Lys,Ex16+211A＞C)	C vs A	3	347/2108	0.84(0.71-1.00)	0.046	0	0.457												
XRCC1	SCLC	rs1799782(p.Arg194Trp,c.580C>T,Ex6-22C＞T)	T vs C	3	289/1429	0.91(0.73-1.12)	0.364	0	0.519												
XRCC1	SCLC	rs25487(p.Gln399Arg,c.1196A>G)	A vs G	5	470/2097	0.61(0.33-1.12)	0.109	91	0.000	4	259/1412	0.43(0.12-1.56)	0.197	94	0.00	4	259/1412	0.60(0.29-1.24)	0.167	42	0.16
ABCB1	NSCLC	rs1045642(p.Ile1145Ile,c.3435T>C)	T vs C	3	312/331	1.48(0.57-3.82)	0.421	93	0.000	3	312/331	1.29(0.43-3.86)	0.651	89	0.00	3	312/331	1.66(0.54-5.12)	0.38	85.60	0.00
ACE	NSCLC	287-bp repeat (I/D)	Ins vs del	3	450/603	0.97(0.72-1.32)	0.859	59	0.086	3	450/603	0.97(0.74-1.27)	0.823	2	0.36	3	450/603	0.86(0.43-1.72)	0.66	71.00	0.03
APEX1	NSCLC	rs1760944(c.-468T>G,-141T>G)	A vs C	3	330/1017	1.07(0.81-1.41)	0.636	53	0.120	3	330/1017	1.11(0.61-2.03)	0.738	73	0.02	3	330/1017	1.16(0.84-1.60)	0.37	0.00	0.38
APEX1	NSCLC	rs1130409(p.Asp148Glu,c.444T>G)	G vs T	9	2902/3665	0.92(0.82-1.03)	0.151	57	0.018	9	1999/3100	0.94(0.77-1.14)	0.506	58	0.01	8	1900/2980	0.85(0.69-1.05)	0.14	44.50	0.08
BIRC5	NSCLC	rs9904341(c.-31G>C）	C vs G	4	857/916	1.15(0.71-1.85)	0.576	89	0.000	4	857/916	1.04(0.58-1.86)	0.887	83	0.00	4	857/916	1.60(0.88-2.93)	0.13	76.10	0.01
CCND1	NSCLC	rs9344(rs603965,p.Pro241Pro,c.723G>A,c.870G>A)	A vs G	3	724/1264	1.00(0.76-1.32)	0.991	73	0.026	3	724/1264	0.94(0.59-1.52)	0.815	76	0.02	3	724/1264	1.04(0.69-1.56)	0.86	64.60	0.06
CDKN1A	NSCLC	rs1801270(p.Ser31Arg,c.93C>A,6829C>A)	A vs C	5	1163/2043	1.15(0.86-1.54)	0.344	50	0.090	5	1163/2043	1.26(0.93-1.72)	0.140	42	0.14	4	1054/1948	0.71(0.44-1.15)	0.17	0.00	0.97
CHRNA5	NSCLC	rs16969968(p.Asp398Asn,c.1192G>A)	A vs G	6	3201/4736	1.36(1.24-1.48)	1.48×10^{-11}	13	0.329	4	2225/3577	1.50(1.28-1.75)	4.03×10^{-7}	18	0.30	4	2225/3577	1.49(1.24-1.79)	1.71×10^{-5}	0.00	0.80
CLPTM1L	NSCLC	rs402710(C>T)	T vs C	6	2940/4040	0.85(0.79-0.91)	1.13×10^{-5}	0	0.666	5	2257/3195	0.84(0.72-0.97)	0.018	30	0.22	5	2257/3195	0.78(0.62-0.99)	0.04	30.70	0.22
CTLA4	NSCLC	rs5742909(g.319C>T,-318C>T)	T vs C	3	361/549	0.50(0.11-2.31)	0.376	95	0.000	3	361/549	0.48(0.10-2.21)	0.343	94	0.00	3	361/549	0.58(0.04-8.50)	0.69	77.90	0.01
CTLA4	NSCLC	rs231775(p.Thr17Ala,c.49A>G)	G vs A	4	590/800	0.92(0.45-1.87)	0.814	94	0.000	4	590/800	1.01(0.44-2.33)	0.985	92	0.00	4	590/800	0.92(0.36-2.37)	0.86	87.60	0.00
CXCL12	NSCLC	rs1801157(801G>A)	A vs G	3	467/815	1.33(0.75-2.37)	0.325	89	0.000	3	467/815	1.47(0.74-2.94)	0.275	86	0.00	3	467/815	1.43(0.56-3.65)	0.46	81.60	0.00
CYP1A1	NSCLC	rs4646903(m1,MspI,T3801C)	C vs T	24	3032/5165	1.11(1.03-1.21)	0.009	0	0.458	34	4465/6895	1.17(1.06-1.30)	0.003	28	0.07	22	2789/4778	1.18(0.95-1.46)	0.14	16.60	0.24
CYP1A1	NSCLC	rs1048943(*2C,m2,p.Ile462Val,c.1384A>G)	G vs A	22	4672/6125	1.10(0.92-1.32)	0.284	79	0.000	26	5123/6735	1.11(0.90-1.36)	0.322	78	0.00	19	4264/5386	1.24(0.88-1.76)	0.23	55.10	0.00
CYP1A2	NSCLC	rs2069526(-739T>G)	G vs T							3	495/537	1.73(0.79-3.80)	0.173	69	0.04						
CYP1A2	NSCLC	rs35694136(-2467delT)	Del vs non-del							3	390/494	1.30(0.62-2.73)	0.481	76	0.02						
CYP1A2	NSCLC	rs2069514(CYP1A2*1C,-3860G>A)	A vs G							3	440/425	1.39(0.30-6.44)	0.677	92	0.00						
CYP1A2	NSCLC	rs762551(CYP1A2*1F,c.A-164C)	C vs A	3	636/691	0.88(0.58-1.34)	0.550	84	0.002	4	729/802	0.78(0.48-1.29)	0.334	79	0.00	4	718/887	0.99(0.64-1.53)	0.95	55.90	0.08
CYP1B1	NSCLC	rs1056836(CYP1B1*3,p.Leu432Val,c.1294C>G)	G vs C	3	640/737	1.14(0.95-1.37)	0.164	0	0.695	3	640/737	1.20(0.95-1.52)	0.131	0	0.64	3	640/737	1.10(0.74-1.62)	0.65	0.00	0.92
CYP2A6	NSCLC	non*4/*4(*1/*4, a deletion of the CYP2A6 gene)	Del vs non-del							4	979/1432	1.07(0.67-1.69)	0.784	75	0.01						
CYP2C9	NSCLC	rs1799853(p.Arg144Cys,c.430C>T)	T vs C							3	518/1096	1.06(0.54-2.07)	0.871	73	0.03						
CYP2D6	NSCLC	rs1065852(p.Pro34Ser,188C>T)	C vs T							3	571/636	0.83(0.58-1.18)	0.299	45	0.16						
CYP2D6	NSCLC	phenotype(EM/HEM/PM)	PM vs EM	6	611/1424	0.84(0.38-1.88)	0.676	50	0.076	7	682/1500	0.98(0.80-1.20)	0.825	0	0.52	7	661/1474	0.76(0.35-1.65)	0.48	55.60	0.04
CYP2E1	NSCLC	rs3813867(g.3739G>C,c.-1293G>C)	C vs G							4	900/971	0.97(0.58-1.64)	0.921	59	0.06						
CYP2E1	NSCLC	rs6413432(c.967+1143T>A,7632T>A)	A vs T	6	1290/1809	0.80(0.71-0.91)	4.90×10^{-4}	0	0.868	7	1372/1890	0.84(0.72-0.98)	0.022	0	0.44	5	1240/1771	0.51(0.25-1.04)	0.06	40.30	0.15
CYP2E1	NSCLC	rs2031920(RsaI,c1>c2,-1053C>T)	T vs C	9	2512/4101	0.92(0.78-1.08)	0.301	61	0.009	10	2648/4280	0.90(0.77-1.04)	0.151	34	0.14	8	2309/3395	1.04(0.56-1.94)	0.89	71.30	0.00
CYP3A4	NSCLC	rs2740574(–392A>G,*1A/*1B)	G vs A	3	923/845	0.94(0.64-1.39)	0.756	37	0.203	3	923/845	1.03(0.74-1.44)	0.868	0	0.55						
EPHX1	NSCLC	rs1051740(p.Tyr113His,c.337T>C)	C vs T	5	742/1343	1.48(0.94-2.33)	0.094	89	0.000	5	742/1343	1.74(0.92-3.29)	0.087	89	0.00	5	742/1343	1.67(0.91-3.08)	0.10	73.10	0.01
EPHX1	NSCLC	rs2234922(p.His139Arg,c.416A>G)	G vs A	4	1710/2512	1.18(0.77-1.79)	0.454	86	0.000	4	1710/2512	1.28(0.76-2.14)	0.354	86	0.00	4	1710/2512	0.99(0.49-1.98)	0.98	65.60	0.03
ERCC1	NSCLC	rs11615(rs3177700,p.Asn118Asn,c.354T>C)	C vs T	3	780/811	0.68(0.58-0.81)	1.01×10^{-5}	13	0.316	3	780/811	0.49(0.36-0.68)	1.73×10^{-5}	0	0.63	3	780/811	0.69(0.56-0.85)	0.00	0.00	0.50
ERCC2	NSCLC	rs1799793(p.Asp312Asn,c.981G>A)	A vs G	8	2884/2833	1.03(0.80-1.33)	0.832	81	0.000	7	1882/2148	1.11(0.91-1.36)	0.294	44	0.10	6	2643/3168	1.52(0.95-2.45)	0.08	63.30	0.01
ERCC2	NSCLC	rs13181(p.Lys751Gln,c.2251A>C)	C vs A	8	2770/2856	1.19(1.04-1.36)	0.014	39	0.116	6	1672/2075	1.32(1.14-1.53)	1.80×10^{-4}	0	0.85	7	2438/3112	1.37(1.12-1.68)	0.00	0.00	0.74
ERCC5	NSCLC	rs17655(p.Asp1104His,c.3310G>C)	C vs G							3	1641/1204	0.95(0.54-1.67)	0.851	87	0.00						
FAS	NSCLC	rs2234767(-1377G/A)	A vs G	3	2482/1844	1.12(0.88-1.42)	0.354	58	0.092	3	2482/1844	1.12(0.84-1.49)	0.460	50	0.14	3	3194/3064	1.51(1.23-1.87)	1.26×10^{-4}	0.00	0.45
FASLG	NSCLC	rs763110(-844C/T)	T vs C							3	3167/3057	0.74(0.47-1.17)	0.202	94	0.00						
FGFR4	NSCLC	rs351855(p.Gly388Arg,G>A)	A vs G	3	985/1230	0.76(0.68-0.86)	1.97×10^{-5}	0	0.590	3	985/1230	0.70(0.58-0.84)	1.14×10^{-4}	0	0.62	3	985/1230	0.75(0.51-1.10)	0.14	36.60	0.21
GSTM1	NSCLC	Present/Null (Large gene deletion)	Null vs present	60	11551/15673	1.18(1.08-1.29)	1.56×10^{-4}	62	0.000												
GSTM3	NSCLC	rs1799735(c.468+21delAGG,3bp deletion,*A/*B)	Del vs non-del	4	760/1174	1.00(0.84-1.20)	0.976	0	0.878	4	760/1174	0.89(0.72-1.10)	0.278	0	0.46	4	760/1174	1.88(0.94-3.76)	0.07	37.70	0.19
GSTP1	NSCLC	rs1695(p.Ile105Val,c.313A>G)	G vs A	21	5642/7022	1.07(0.99-1.16)	0.086	38	0.043	27	6767/8503	1.05(0.96-1.14)	0.281	32	0.06	21	5642/7022	1.16(1.00-1.35)	0.05	17.40	0.23
GSTT1	NSCLC	Present/Null(Large gene deletion)	Null vs present	31	6368/9045	1.00(0.89-1.13)	0.979	45	0.004												
HYKK	NSCLC	rs931794(A>G)	G vs A	4	1548/2464	1.25(1.13-1.37)	9.08×10^{-6}	0	0.880	4	1548/2464	1.30(1.14-1.48)	1.09×10^{-4}	0	0.90	4	1548/2464	1.37(1.13-1.65)	0.00	0.00	0.49
IL10	NSCLC	rs1800871(c.-854T>C,-819C>T)	T vs C	4	753/1428	0.95(0.71-1.28)	0.753	68	0.024	4	753/1428	0.87(0.54-1.41)	0.576	75	0.01	4	753/1428	0.99(0.63-1.56)	0.98	51.60	0.10
IL10	NSCLC	rs1800896(g.3943A>G,-1082A>G)	G vs A	3	306/523	1.74(0.75-4.04)	0.202	89	0.000	3	306/523	1.61(0.46-5.64)	0.459	91	0.00						
IL17A	NSCLC	rs2275913(-73G>A,-152G>A)	A vs G	3	780/998	1.37(0.95-1.98)	0.093	81	0.005	3	780/998	1.36(0.84-2.20)	0.206	82	0.00	3	780/998	1.72(1.12-2.65)	0.01	31.00	0.24
IL1B	NSCLC	rs1143627(g.4970C>T,-31T>C)	C vs T	5	1915/2551	0.82(0.67-0.99)	0.043	78	0.001	5	1915/2551	0.79(0.58-1.08)	0.146	78	0.00	5	1915/2551	0.70(0.52-0.92)	0.01	65.50	0.02
IL1B	NSCLC	rs16944(C-511T)	T vs C	6	2147/2798	0.89(0.74-1.09)	0.257	80	0.000	6	2147/2798	0.92(0.69-1.21)	0.542	77	0.00	6	2147/2798	0.78(0.57-1.07)	0.12	74.40	0.00
IL4	NSCLC	rs2243250(-509C>T)	T vs C	3	1892/2295	1.10(0.84-1.44)	0.477	82	0.004	3	1892/2295	1.16(0.75-1.80)	0.502	73	0.03	3	1892/2295	1.04(0.72-1.50)	0.86	78.80	0.01
IL6	NSCLC	rs1800795(G-174C)	C vs G	4	567/725	1.35(0.87-2.08)	0.184	81	0.001	4	567/725	1.20(0.68-2.12)	0.523	79	0.00	4	567/725	1.82(0.98-3.37)	0.06	59.40	0.06
IL6	NSCLC	rs1800796(-572C>G,634C>G)	G vs C	3	1333/1452	0.75(0.57-0.99)	0.039	77	0.013	4	1416/1614	0.82(0.65-1.04)	0.095	54	0.09	3	1333/1452	0.67(0.36-1.24)	0.20	62.80	0.07
IL8	NSCLC	rs4073(T-251A)	T vs A	4	1997/2751	1.07(0.83-1.39)	0.593	81	0.001	4	1997/2751	1.04(0.78-1.38)	0.789	57	0.07	4	1997/2751	1.11(0.78-1.57)	0.56	75.80	0.01
LTA	NSCLC	rs909253(A+252G)	G vs A	4	663/1297	0.92(0.80-1.06)	0.235	0	0.573	4	663/1297	0.95(0.74-1.22)	0.702	28	0.24	4	663/1297	0.78(0.57-1.05)	0.10	0.00	0.86
MDM2	NSCLC	rs2279744(SNP309,c.14+309T>G)	G vs T	10	4170/5502	1.08(0.88-1.33)	0.472	91	0.000	10	4170/5502	1.10(0.80-1.51)	0.559	90	0.00	10	4170/5502	1.19(0.93-1.51)	0.16	77.40	0.00
MIR146A	NSCLC	rs2910164(C>G)	C vs G	4	880/1094	1.28(1.11-1.46)	4.63×10^{-4}	0	0.391	4	880/1094	1.41(1.13-1.74)	0.002	0	0.45	5	1832/2190	1.28(1.11-1.48)	0.00	0.00	0.72

Genes	Sub-group	Variants	Comparison[a]	Results of meta-analysis using allelic model						Results of meta-analysis using dominant model						Results of meta-analysis using recessive model					
				Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]
MIR196A2	NSCLC	rs11614913(T>C)	C vs T	5	1320/1762	1.02(0.85-1.22)	0.869	62	0.032	5	1320/1762	1.18(0.88-1.59)	0.274	54	0.07	5	1320/1762	0.91(0.69-1.19)	0.47	55.10	0.06
MMP1	NSCLC	rs1799750(-16071G/2G,insG)	2G vs 1G	3	485/688	0.97(0.75-1.26)	0.832	50	0.134	4	569/770	1.10(0.74-1.63)	0.642	45	0.14	3	485/688	0.94(0.63-1.41)	0.77	50.90	0.13
MMP2	NSCLC	rs243865(-1306C>T)	T vs C	3	1216/1729	0.61(0.40-0.92)	0.019	83	0.003	3	1216/1729	0.57(0.36-0.92)	0.021	83	0.00	3	1216/1729	0.54(0.30-0.99)	0.05	0.00	0.72
MPO	NSCLC	rs2333227(G-463A)	A vs G	10	5036/6646	1.06(0.95-1.18)	0.294	54	0.020	11	5124/6727	1.03(0.93-1.14)	0.633	32	0.14	10	5036/6646	1.38(1.03-1.86)	0.03	51.20	0.03
MTHFR	NSCLC	rs1801131(p.Ala429Glu,c.1286A>C,A1298C)	C vs A	4	785/1111	1.09(0.94-1.27)	0.240	0	0.654	4	785/1111	1.10(0.90-1.33)	0.363	0	0.69	4	785/1111	1.16(0.85-1.57)	0.35	0.00	0.59
MTHFR	NSCLC	rs1801133(p.Ala222Val,Ex4+79C＞T)	T vs C	6	1273/1813	1.09(0.83-1.42)	0.543	78	0.000	6	1273/1813	1.07(0.72-1.59)	0.740	78	0.00	6	1273/1813	1.23(0.84-1.79)	0.29	57.70	0.04
NAT2	NSCLC	Rapid/slow	Slow vs rapid	11	2041/3282	0.94(0.75-1.17)	0.572	58	0.008												
NQO1	NSCLC	rs1800566(p.Pro187Ser,c.648C>T,609C>T,*2)	T vs C	6	1511/2708	1.10(0.87-1.38)	0.442	74	0.002	8	1914/3400	1.08(0.91-1.28)	0.402	41	0.10	6	1511/2708	1.13(0.72-1.77)	0.60	60.60	0.03
OGG1	NSCLC	rs1052133(p.Ser326Cys,c.977C>G,8055C>G)	G vs C	17	6874/7869	1.07(0.98-1.17)	0.141	60	0.001	17	5948/7259	1.08(0.95-1.24)	0.248	54	0.01	17	6279/8214	1.16(1.02-1.32)	0.02	35.70	0.07
PADPRP	NSCLC	A/B(a 193-bp deletion)	Del vs non-del							4	258/339	1.22(0.78-1.90)	0.382	35	0.20						
PARP1	NSCLC	rs1136410(p.Val762Ala,Ex17+8T＞C)	C vs T	3	2157/2095	1.08(0.89-1.32)	0.416	79	0.009												
PTGS2	NSCLC	rs5275(c.*427T>C,8473T>C)	C vs T	4	1143/1319	1.04(0.61-1.76)	0.889	93	0.000	4	1143/1319	1.07(0.62-1.87)	0.800	89	0.00	4	1143/1319	1.02(0.40-2.62)	0.97	83.40	0.00
SOD2	NSCLC	rs4880(rs1799725,Ala16Val)	T vs C	6	3133/4255	1.25(1.08-1.45)	0.002	72	0.003	6	3133/4255	1.32(1.12-1.55)	0.001	38	0.15	7	3321/4587	1.24(1.00-1.53)	0.05	69.70	0.00
SULT1A1	NSCLC	rs9282861(p.Arg213His,c.638G>A,*1/*2)	A vs G							3	977/1476	1.44(0.87-2.41)	0.159	84	0.00						
TERT	NSCLC	rs2736098(p.Ala305Ala,c.915G>A)	A vs G	4	2002/2490	1.30(1.19-1.42)	2.59×10^{-9}	0	0.818	4	2002/2490	1.27(1.12-1.43)	1.18×10^{-4}	0	0.90	4	2002/2490	1.69(1.43-1.99)	7.97×10^{-10}	0.00	0.78
TNF	NSCLC	rs1800629(G-308A,*1/*2)	A vs G	6	1052/1767	1.67(1.01-2.76)	0.044	89	0.000	6	1052/1767	1.75(0.99-3.09)	0.055	89	0.00	6	1052/1767	2.29(1.21-4.33)	0.01	22.80	0.26
TNF	NSCLC	rs361525(A-417G,-238G>A)	A vs G	4	641/779	1.13(0.48-2.68)	0.778	91	0.000	4	641/779	1.04(0.43-2.49)	0.933	89	0.00						
TP53	NSCLC	rs1625895(IVS6+62G>A,A2>A1)	A vs G	3	263/495	0.94(0.64-1.38)	0.754	42	0.178	3	263/495	0.87(0.48-1.55)	0.629	64	0.06	3	263/495	1.19(0.09-16.66)	0.90	72.50	0.03
TP53	NSCLC	rs1042522(p.Pro72Arg,c.215C>G)	C vs G	28	8459/11237	0.98(0.88-1.10)	0.780	83	0.000	30	8908/11898	1.00(0.88-1.13)	0.986	75	0.00	28	8459/11237	1.02(0.83-1.24)	0.87	78.50	0.00
TP63	NSCLC	rs10937405(C>T)	T vs C	3	3587/8484	0.87(0.82-0.92)	9.91×10^{-7}	0	0.595	3	3587/8484	0.84(0.78-0.92)	6.93×10^{-5}	0	0.51	3	3587/8484	0.80(0.72-0.89)	6.49×10^{-5}	0.00	0.62
TP73	NSCLC	G4C14/A4T14	AT vs GC	4	1012/1210	0.90(0.70-1.15)	0.382	66	0.032	5	1946/2349	1.04(0.85-1.27)	0.735	56	0.06	4	1012/1210	0.75(0.35-1.59)	0.45	77.20	0.00
TYMS	NSCLC	28-bp tandem repeat	2R vs 3R (2R vs Non-2R)	3	808/1326	0.89(0.75-1.04)	0.142	0	0.391	3	808/1326	0.84(0.69-1.01)	0.065	0	0.52	3	808/1326	1.07(0.67-1.72)	0.78	0.00	0.53
VEGFA	NSCLC	rs2010963(634G>C)	C vs G	4	2728/2372	1.10(0.93-1.29)	0.264	62	0.047	4	2728/2372	1.12(0.92-1.37)	0.267	49	0.12	5	2828/2522	1.11(0.87-1.42)	0.42	45.40	0.12
VEGFA	NSCLC	rs833061(-460T>C)	C vs T	4	2727/2372	1.00(0.92-1.08)	0.987	0	0.847	4	2727/2372	1.04(0.92-1.17)	0.519	0	0.62	4	2727/2372	0.94(0.81-1.09)	0.42	0.00	0.54
VEGFA	NSCLC	rs3025039(C936T)	T vs C	3	2403/2034	1.04(0.92-1.17)	0.556	0	0.591	5	2640/2356	1.04(0.91-1.18)	0.563	0	0.45	3	2403/2034	1.12(0.73-1.71)	0.60	0.00	0.47
XPA	NSCLC	rs1800975(c.-4A>G,23G>A)	A vs G	4	1637/1793	1.01(0.86-1.19)	0.902	63	0.042	5	1851/1978	0.99(0.79-1.23)	0.910	60	0.04	5	1851/1978	1.11(0.87-1.41)	0.40	41.30	0.15
XPC	NSCLC	PAT-/+ (24660_24664delGTAAC, inspoly(AT))	Ins vs non-ins	3	967/1340	1.17(0.98-1.39)	0.092	55	0.110	3	967/1340	1.10(0.86-1.42)	0.455	51	0.13	3	967/1340	1.46(1.17-1.81)	0.00	0.00	0.48
XPC	NSCLC	rs2228000(p.Ala499Val,Ex9-377C>T)	T vs C	3	1492/1630	1.04(0.93-1.16)	0.514	0	0.567	3	1492/1630	1.03(0.89-1.19)	0.678	0	0.72	3	1492/1630	1.10(0.86-1.39)	0.45	0.00	0.40
XPC	NSCLC	rs2228001(p.Gln939Lys,Ex16+211A＞C)	C vs A	4	2491/2316	1.05(0.96-1.14)	0.303	0	0.744	3	1489/1631	1.05(0.91-1.22)	0.481	0	0.39	3	1489/1631	1.18(0.96-1.45)	0.12	0.00	0.69
XRCC1	NSCLC	rs2256507(G>A)	A vs G	3	431/779	1.23(0.93-1.62)	0.143	50	0.134	3	431/779	1.20(0.89-1.63)	0.236	34	0.22	3	431/779	1.68(1.03-2.74)	0.04	7.80	0.34
XRCC1	NSCLC	rs25486(A>G)	G vs A	3	373/795	1.06(0.69-1.61)	0.795	77	0.013	3	373/795	1.19(0.84-1.69)	0.334	21	0.28	3	373/795	1.13(0.49-2.58)	0.78	77.60	0.01
XRCC1	NSCLC	rs1001581(c.145–216G>A)	T vs C	4	574/994	1.27(1.04-1.56)	0.018	40	0.172	4	574/994	1.35(0.98-1.88)	0.069	55	0.08	4	574/994	1.36(1.02-1.83)	0.04	0.00	0.71
XRCC1	NSCLC	rs3547(p.Gln632Gln,c.1896G>A)	A vs G	3	374/794	1.06(0.85-1.32)	0.592	0	0.850	3	374/794	1.02(0.78-1.34)	0.868	0	0.99						
XRCC1	NSCLC	rs25489(p.Arg280His,c.839G>A,Ex9+16G>A)	A vs G	8	3183/3560	0.93(0.70-1.23)	0.607	74	0.000	7	3441/4871	0.94(0.69-1.28)	0.683	78	0.00	6	2085/2779	0.87(0.45-1.71)	0.69	0.00	0.47
XRCC1	NSCLC	rs1799782(p.Arg194Trp,c.580C>T,Ex6-22C＞T)	T vs C	11	3418/4189	0.93(0.81-1.06)	0.285	40	0.081	10	3717/5540	0.92(0.81-1.05)	0.223	19	0.27	9	2320/3408	1.15(0.90-1.47)	0.25	0.00	0.48
XRCC1	NSCLC	rs25487(p.Gln399Arg,c.1196A>G)	A vs G	19	7715/10261	1.04(0.96-1.14)	0.330	62	0.000	18	6716/9600	1.06(0.95-1.18)	0.284	52	0.01	17	6617/9480	1.08(0.92-1.27)	0.35	47.60	0.02
XRCC1	NSCLC	rs3213245(-77T>C)	C vs T							3	1744/2178	1.50(1.29-1.75)	1.89×10^{-7}	0	0.68						
XRCC3	NSCLC	rs861539(p.Thr241Met,c.722C>T)	T vs C	5	2287/2150	1.02(0.91-1.15)	0.760	0	0.531	4	1288/1489	0.90(0.75-1.08)	0.266	0	0.43	3	1189/1369	1.12(0.75-1.68)	0.57	19.90	0.29
APEX1	AD	rs1130409(p.Asp148Glu,c.444T>G)	G vs T	5	1561/2309	0.96(0.81-1.14)	0.637	64	0.026	5	877/1744	0.97(0.69-1.36)	0.850	70	0.01	4	809/1624	0.96(0.66-1.39)	0.813	58	0.07
BIRC5	AD	rs9904341(c.-31G>C）	C vs G	3	312/818	1.70(1.22-2.37)	0.002	57	0.097	3	312/818	1.86(1.09-3.18)	0.024	50	0.14	3	312/818	2.07(1.38-3.10)	4.41×10^{-4}	32	0.23
CDKN1A	AD	rs1801270(p.Ser31Arg,c.93C>A,6829C>A)	A vs C	5	523/2043	1.18(0.86-1.62)	0.306	36	0.180	5	523/2043	1.32(0.99-1.77)	0.063	7	0.37	4	465/1948	0.66(0.35-1.23)	0.190	0	0.80
CHRNA5	AD	rs16969968(p.Asp398Asn,c.1192G>A)	A vs G	4	1507/2834	1.37(1.14-1.64)	0.001	33	0.214												
CXCL12	AD	rs1801157(801G>A)	A vs G	3	251/815	1.16(0.68-1.99)	0.579	74	0.021	3	251/815	1.29(0.76-2.19)	0.339	55	0.11	3	251/815	1.16(0.37-3.60)	0.802	71	0.03
CYP1A1	AD	rs4646903(m1,MspI,T3801C)	C vs T	17	1001/3991	0.95(0.83-1.08)	0.417	0	0.543	23	1496/4974	0.98(0.85-1.12)	0.735	0	0.86	16	1012/3754	0.95(0.72-1.25)	0.691	0	0.87
CYP1A1	AD	rs1048943(*2C,m2,p.Ile462Val,c.1384A>G)	G vs A	15	1225/4175	1.01(0.80-1.27)	0.926	63	0.001	18	1813/5085	1.06(0.81-1.39)	0.672	68	0.00	11	1043/3146	1.26(0.75-2.11)	0.385	45	0.05
CYP2A6	AD	non*4/*4(*1/*4,a deletion of the CYP2A6 gene)	Del vs non-del (*4 vs non*4)							3	454/1300	1.07(0.80-1.45)	0.639	0	0.57						
CYP2D6	AD	phenotype(EM/HEM/PM)	PM vs EM	5	234/1317	1.42(0.75-2.69)	0.288	0	0.463	5	234/1317	0.93(0.69-1.25)	0.624	0	0.95	6	261/1367	1.20(0.59-2.44)	0.613	23	0.26
CYP2E1	AD	rs6413432(c.967+1143T>A,7632T>A)	A vs T	6	500/1809	0.79(0.66-0.95)	0.011	0	0.664	6	500/1809	0.85(0.63-1.16)	0.304	26	0.24	5	481/1771	0.51(0.20-1.32)	0.166	37	0.17
CYP2E1	AD	rs2031920(RsaI,c1>c2,-1053C>T)	T vs C	8	1250/3903	0.83(0.67-1.04)	0.109	62	0.011	8	1250/3903	0.82(0.65-1.03)	0.091	51	0.05	7	1129/3197	0.78(0.34-1.82)	0.572	63	0.01
EPHX1	AD	rs1051740(p.Tyr113His,c.337T>C)	C vs T							3	209/902	1.00(0.53-1.91)	0.990	66	0.05						
ERCC2	AD	rs1799793(p.Asp312Asn,c.981G>A)	A vs G	6	1568/2449	1.12(0.68-1.85)	0.659	90	0.000	5	816/1764	1.40(0.98-2.02)	0.067	62	0.03	5	1013/2401	1.89(0.65-5.50)	0.243	79	0.00
ERCC2	AD	rs13181(p.Lys751Gln,c.2251A>C)	C vs A	5	1416/1915	1.14(0.89-1.46)	0.294	46	0.118	4	664/1230	1.35(1.06-1.70)	0.013	0	0.64	5	960/2267	1.26(0.86-1.85)	0.242	0	0.61
GSTM1	AD	Present/Null (Large gene deletion)	Null vs present	42	4199/12206	1.17(1.05-1.31)	0.005	45	0.001												
GSTP1	AD	rs1695 (p.Ile105Val, c.313A>G)	G vs A	13	2509/5211	0.96(0.89-1.04)	0.362	2	0.430	18	3060/6381	0.93(0.85-1.02)	0.104	0	0.66	13	2509/5211	1.05(0.85-1.31)	0.642	18	0.26
GSTT1	AD	Present/Null (Large gene deletion)	Null vs present	24	2906/7999	1.08(0.91-1.28)	0.404	51	0.002												
IL10	AD	rs1800871(c.-854T>C,-819C>T)	T vs C	3	317/1172	0.84(0.48-1.48)	0.550	58	0.091	3	317/1172	1.00(0.77-1.28)	0.968	0	0.38	3	317/1172	0.83(0.19-3.56)	0.801	41	0.18
IL17A	AD	rs2275913(-73G>A,-152G>A)	A vs G	3	469/998	1.43(0.85-2.41)	0.184	88	0.000	3	469/998	1.40(0.70-2.82)	0.340	89	0.00	3	469/998	1.84(1.11-3.06)	0.018	36	0.21
IL6	AD	rs1800795(G-174C)	C vs G	3	128/475	0.97(0.72-1.29)	0.810	0	0.701	3	128/475	0.79(0.51-1.22)	0.291	0	0.89	3	128/475	1.21(0.58-2.52)	0.613	29	0.25
IL6	AD	rs1800796(-572C>G,634C>G)	G vs C							3	678/1414	0.83(0.68-1.00)	0.055	6	0.35						
LTA	AD	rs909253(A+252G)	G vs A	4	360/1247	0.92(0.73-1.16)	0.468	21	0.285	4	360/1247	0.93(0.67-1.29)	0.644	26	0.25	4	360/1247	0.80(0.55-1.18)	0.263	0	0.62
MDM2	AD	rs2279744(SNP309,c.14+309T>G)	G vs T	6	1714/4083	1.20(1.00-1.44)	0.052	76	0.001	6	1714/4083	1.28(0.95-1.72)	0.111	76	0.00	6	1714/4083	1.28(1.04-1.56)	0.018	46	0.10
MIR146A	AD	rs2910164(C>G)	C vs G	3	442/965	1.26(1.04-1.51)	0.018	15	0.309	3	442/965	1.42(1.06-1.90)	0.018	4	0.35	4	907/2061	1.33(1.12-1.59)	0.001	0	0.94
MIR196A2	AD	rs11614913(T>C)	C vs T	3	516/1205	1.00(0.79-1.26)	0.999	56	0.104	3	516/1205	1.06(0.66-1.72)	0.804	63	0.07	3	516/1205	0.92(0.67-1.26)	0.591	38	0.20
MMP2	AD	rs243865(-1306C>T)	T vs C	3	476/1729	0.69(0.41-1.16)	0.161	79	0.008	3	476/1729	0.67(0.36-1.27)	0.223	83	0.00	3	476/1729	0.62(0.28-1.40)	0.247	0	1.00
MPO	AD	rs2333227(G-463A)	A vs G	7	2191/5068	1.04(0.96-1.14)	0.337	0	0.514	7	2191/5068	1.02(0.92-1.13)	0.746	0	0.74	7	2191/5068	1.25(0.99-1.56)	0.059	0	0.56
MTHFR	AD	rs1801133(p.Ala222Val,Ex4+79C＞T)	T vs C	3	629/1326	0.84(0.56-1.27)	0.405	85	0.001	3	629/1326	0.79(0.35-1.79)	0.575	90	0.00	3	629/1326	0.94(0.74-1.19)	0.591	0	0.40
NAT2	AD	Rapid/slow (Acetylation Phenotype)	Slow vs rapid	9	851/2963	0.95(0.71-1.26)	0.704	51	0.038												
NQO1	AD	rs1800566(p.Pro187Ser,c.648C>T,609C>T,*2)	T vs C	3	544/1798	0.94(0.77-1.16)	0.571	11	0.325	5	707/2490	0.91(0.76-1.09)	0.287	0	0.77	3	544/1798	1.14(0.34-3.85)	0.836	58	0.09
OGG1	AD	rs1052133(p.Ser326Cys,c.977C>G,8055C>G)	G vs C	12	4039/6332	1.10(0.99-1.22)	0.077	53	0.015	11	3287/5647	1.12(0.93-1.34)	0.230	52	0.02	12	3603/6677	1.25(1.10-1.43)	0.001	20	0.25
PADPRP	AD	A/B (a 193-bp deletion)	Del vs non-del							4	129/339	1.65(0.81-3.35)	0.165	51	0.10						
PARP1	AD	rs1136410(p.Val762Ala,Ex17+8T＞C)	C vs T	3	1459/2095	1.09(0.89-1.33)	0.408	74	0.022												
SOD2	AD	rs4880(rs1799725,Ala16Val)	T vs C	4	1219/2761	1.20(1.08-1.32)	3.80×10^{-4}	0	0.405	4	1219/2761	1.23(1.04-1.45)	0.017	0	0.47	5	1324/3093	1.26(1.00-1.58)	0.052	44	0.13
TERT	AD	rs2736098(p.Ala305Ala,c.915G>A)	A vs G	4	1214/2490	1.40(1.26-1.54)	4.97×10^{-11}	0	0.891	4	1214/2490	1.37(1.19-1.58)	1.78×10^{-5}	0	0.96	4	1214/2490	1.89(1.57-2.28)	2.10×10^{-11}	0	0.78
TNF	AD	rs1800629(G-308A,*1/*2)	A vs G	5	484/1486	1.81(0.83-3.93)	0.133	90	0.000	5	484/1486	1.95(0.81-4.68)	0.135	90	0.00	4	458/1460	2.71(0.99-7.43)	0.054	39	0.18
TP53	AD	rs1625895(IVS6+62G>A,A2>A1)	A vs G	3	89/495	0.92(0.43-2.00)	0.840	63	0.068	3	89/495	0.90(0.31-2.58)	0.839	71	0.03	3	89/495	1.69(0.22-13.20)	0.619	41	0.18
TP53	AD	rs1042522(p.Pro72Arg,c.215C>G)	C vs G	21	3367/8584	1.08(0.98-1.20)	0.130	54	0.002	22	3523/9166	1.06(0.93-1.22)	0.369	51	0.00	22	3504/8822	1.20(1.05-1.38)	0.008	16	0.25
TP63	AD	rs10937405(C>T)	T vs C	3	1158/8484	0.82(0.75-0.90)	2.91×10^{-5}	0	0.898	3	1158/8484	0.79(0.69-0.90)	3.34×10^{-4}	0	0.69	3	1158/8484	0.75(0.62-0.90)	0.002	0	0.58
TP73	AD	G4C14/A4T14	AT vs GC							3	617/1532	1.06(0.82-1.38)	0.659	21	0.28						
XPA	AD	rs1800975(c.-4A>G,23G>A)	A vs G	3	637/1517	1.07(0.93-1.22)	0.334	0	0.990	4	715/1702	1.03(0.86-1.24)	0.743	0	0.66	4	715/1702	1.17(0.86-1.58)	0.324	36	0.20

Genes	Sub-group	Variants	Comparison[a]	Results of meta-analysis using allelic model						Results of meta-analysis using dominant model						Results of meta-analysis using recessive model					
				Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]
XPC	AD	PAT-/+ (24660_24664delGTAAC, inspoly(AT))	Ins vs non-ins	3	398/1340	1.21(1.03-1.42)	0.020	0	0.442	3	398/1340	1.23(0.88-1.72)	0.218	47	0.15	3	398/1340	1.40(1.05-1.88)	0.024	0	0.99
XPC	AD	rs2228001(p.Gln939Lys,Ex16+211A＞C)	C vs A	3	1318/2108	1.06(0.96-1.17)	0.273	0	0.577												
XRCC1	AD	rs25489(p.Arg280His,c.839G>A,Ex9+16G>A)	A vs G	3	1067/1457	0.75(0.42-1.36)	0.343	83	0.002	3	795/2864	0.70(0.34-1.43)	0.322	86	0.00						
XRCC1	AD	rs1799782(p.Arg194Trp,c.580C>T,Ex6-22C＞T)	T vs C	5	1142/1829	0.95(0.80-1.14)	0.594	23	0.265	5	880/3276	0.97(0.80-1.19)	0.784	0	0.63	4	390/1144	1.40(0.82-2.38)	0.213	0	0.59
XRCC1	AD	rs25487(p.Gln399Arg,c.1196A>G)	A vs G	10	2359/6365	1.01(0.89-1.14)	0.917	58	0.011	10	1675/5800	1.04(0.88-1.24)	0.642	49	0.04	9	1607/5680	1.06(0.85-1.31)	0.599	22	0.25
XRCC1	AD	rs3213245(-77T>C)	C vs T							3	860/2178	1.55(1.29-1.87)	4.72×10^{-6}	0	0.76						
XRCC3	AD	rs861539(p.Thr241Met,c.722C>T)	T vs C	3	1108/1578	1.07(0.89-1.28)	0.494	33	0.227	3	424/1013	0.87(0.65-1.18)	0.377	27	0.26						
BIRC5	SCC	rs9904341(c.-31G>C）	C vs G	3	399/818	1.31(0.89-1.95)	0.175	73	0.024	3	399/818	1.03(0.78-1.35)	0.850	0	0.43	3	399/818	1.93(0.88-4.25)	0.102	82	0.00
CCND1	SCC	rs9344(rs603965,p.Pro241Pro,c.723G>A,c.870G>A)	A vs G	3	359/1264	1.05(0.70-1.57)	0.825	78	0.010	3	359/1264	0.96(0.55-1.69)	0.899	70	0.04	3	359/1264	1.11(0.58-2.10)	0.758	77	0.01
CDKN1A	SCC	rs1801270(p.Ser31Arg,c.93C>A,6829C>A)	A vs C	5	597/2043	1.12(0.78-1.60)	0.536	46	0.117	5	597/2043	1.20(0.80-1.81)	0.387	45	0.12	4	546/1948	0.88(0.48-1.60)	0.667	0	0.88
CXCL12	SCC	rs1801157(801G>A)	A vs G	3	198/815	1.30(0.65-2.60)	0.460	88	0.000	3	198/815	1.40(0.59-3.30)	0.444	85	0.00	3	198/815	1.51(0.52-4.35)	0.448	76	0.02
CYP1A1	SCC	rs4646903(m1,MspI,T3801C)	C vs T	17	1021/3959	1.45(1.26-1.67)	3.77×10^{-7}	21	0.215	24	1739/5212	1.51(1.27-1.79)	3.13×10^{-6}	39	0.03	16	976/3722	1.68(1.15-2.47)	0.008	34	0.09
CYP1A1	SCC	rs1048943(*2C,m2,p.Ile462Val,c.1384A>G)	G vs A	16	1572/3981	1.24(1.04-1.49)	0.020	58	0.002	20	2336/5091	1.23(0.98-1.56)	0.078	66	0.00	13	1365/3242	1.65(1.05-2.60)	0.030	53	0.01
CYP1A2	SCC	rs35694136(-2467delT)	Del vs non-del							3	309/494	1.58(0.97-2.56)	0.065	39	0.20						
CYP1A2	SCC	rs2069514(CYP1A2*1C,-3860G>A)	A vs G							3	292/411	1.13(0.39-3.27)	0.818	84	0.00						
CYP1A2	SCC	rs762551(CYP1A2*1F,c.A-164C)	C vs A							3	291/409	0.61(0.32-1.16)	0.132	66	0.06	3	305/494	1.05(0.53-2.10)	0.884	68	0.04
CYP2A6	SCC	non*4/*4(*1/*4,a deletion of the CYP2A6 gene)	Del vs non-del							4	516/1432	1.07(0.59-1.93)	0.826	79	0.00						
CYP2D6	SCC	phenotype (EM/HEM/PM)	PM vs EM	5	341/1153	0.63(0.30-1.31)	0.216	0	0.500	6	412/1229	1.04(0.81-1.34)	0.765	0	0.43	6	364/1203	0.57(0.29-1.14)	0.111	0	0.53
CYP2E1	SCC	rs6413432(c.967+1143T>A,7632T>A)	A vs T	6	715/1809	0.76(0.65-0.88)	3.98×10^{-4}	0	0.911	6	715/1809	0.77(0.64-0.92)	0.005	0	0.89	5	684/1771	0.52(0.34-0.82)	0.004	0	0.47
CYP2E1	SCC	rs2031920(RsaI,c1>c2,-1053C>T)	T vs C	7	962/3722	0.93(0.82-1.06)	0.287	0	0.661	7	962/3722	0.94(0.80-1.10)	0.414	0	0.55	6	880/3016	1.09(0.53-2.22)	0.818	57	0.04
ERCC2	SCC	rs1799793(p.Asp312Asn,c.981G>A)	A vs G	4	684/1704	1.00(0.57-1.77)	0.999	81	0.001	3	434/1019	1.20(0.69-2.07)	0.525	67	0.05	4	895/2039	4.62(0.7-30.53)	0.112	72	0.01
ERCC2	SCC	rs13181(p.Lys751Gln,c.2251A>C)	C vs A	3	476/1171	1.19(0.72-1.98)	0.496	57	0.098							3	698/1523	1.84(0.65-5.23)	0.250	48	0.14
GSTM1	SCC	Present/Null(Large gene deletion)	Null vs present	42	4704/12325	1.23(1.08-1.40)	0.002	66	0.000												
GSTP1	SCC	rs1695(p.Ile105Val, c.313A>G)	G vs A	12	1951/5051	1.01(0.93-1.09)	0.899	0	0.550	17	2502/6290	1.03(0.91-1.15)	0.658	23	0.19	12	1951/5051	1.14(0.92-1.41)	0.233	21	0.24
GSTT1	SCC	Present/Null(Large gene deletion)	Null vs present	23	2823/7727	1.07(0.93-1.24)	0.354	36	0.047												
IL10	SCC	rs1800871(c.-854T>C,-819C>T)	T vs C	3	165/1187	1.37(0.89-2.11)	0.149	55	0.106	3	165/1187	1.56(0.81-3.00)	0.183	66	0.05	3	165/1187	1.30(0.75-2.28)	0.350	0	0.81
IL1B	SCC	rs1143627(g.4970C>T,-31T>C)	C vs T	3	527/2067	0.90(0.78-1.04)	0.154	0	0.371	3	527/2067	0.92(0.67-1.28)	0.634	43	0.17	3	527/2067	0.77(0.54-1.10)	0.154	38	0.20
IL1B	SCC	rs16944(C-511T)	T vs C	3	544/2091	1.03(0.90-1.19)	0.663	0	0.583	3	544/2091	1.15(0.87-1.52)	0.311	31	0.23	3	544/2091	0.97(0.76-1.23)	0.770	0	0.40
IL6	SCC	rs1800795(G-174C)	C vs G	4	297/689	1.41(0.76-2.60)	0.277	85	0.000	4	297/689	1.48(0.75-2.91)	0.260	76	0.01	4	297/689	1.53(0.60-3.90)	0.373	69	0.02
IL6	SCC	rs1800796(-572C>G,634C>G)	G vs C							3	491/1452	0.71(0.49-1.03)	0.072	66	0.05						
IL8	SCC	rs4073(T-251A)	T vs A	3	1090/2541	1.05(0.79-1.38)	0.742	65	0.056	3	1090/2541	1.05(0.73-1.53)	0.790	51	0.13	3	1090/2541	1.01(0.72-1.43)	0.942	50	0.14
LTA	SCC	rs909253(A+252G)	G vs A	4	186/1260	0.97(0.77-1.23)	0.812	0	0.774	4	186/1260	1.07(0.73-1.58)	0.730	24	0.27	4	186/1260	0.74(0.42-1.29)	0.282	0	0.71
MDM2	SCC	rs2279744(SNP309,c.14+309T>G)	G vs T	7	1708/4408	1.11(0.94-1.30)	0.229	71	0.002	7	1708/4408	1.15(0.89-1.49)	0.283	70	0.00	7	1708/4408	1.15(0.94-1.39)	0.169	42	0.11
MIR146A	SCC	rs2910164(C>G)	C vs G													3	796/1751	1.32(0.93-1.86)	0.116	50	0.13
MMP2	SCC	rs243865(-1306C>T)	T vs C	3	740/1729	0.56(0.37-0.84)	0.005	73	0.023	3	740/1729	0.51(0.33-0.79)	0.002	71	0.03	3	740/1729	0.51(0.24-1.11)	0.089	0	0.50
MPO	SCC	rs2333227(G-463A)	A vs G	6	1572/4855	0.98(0.83-1.15)	0.791	53	0.061	6	1572/4855	0.95(0.79-1.14)	0.559	49	0.08	6	1572/4855	1.17(0.81-1.70)	0.396	34	0.18
NAT2	SCC	Rapid/slow(Acetylation Phenotype)	Slow vs rapid	10	1063/3136	0.94(0.72-1.24)	0.677	47	0.049												
NQO1	SCC	rs1800566(p.Pro187Ser,c.648C>T,609C>T,*2)	T vs C	3	408/1798	1.16(0.96-1.41)	0.125	0	0.707	5	648/2490	1.16(0.96-1.39)	0.127	0	0.82	3	408/1798	1.19(0.65-2.20)	0.578	0	0.94
OGG1	SCC	rs1052133(p.Ser326Cys,c.977C>G,8055C>G)	G vs C	9	2108/5170	1.03(0.95-1.11)	0.544	0	0.515	8	1858/4485	1.02(0.87-1.19)	0.843	15	0.31	9	1949/5515	1.09(0.92-1.28)	0.332	0	0.48
PADPRP	SCC	A/B(a 193-bp deletion)	Del vs non-del							4	103/339	0.87(0.53-1.41)	0.561	0	0.47						
PTGS2	SCC	rs5275(c.*427T>C,8473T>C)	C vs T							3	540/1105	0.91(0.74-1.13)	0.401	0	0.56						
SOD2	SCC	rs4880(rs1799725,Ala16Val)	T vs C	4	574/2761	1.54(1.03-2.31)	0.035	83	0.001	4	574/2761	1.44(1.13-1.84)	0.003	3	0.38	5	657/3093	1.50(0.89-2.52)	0.128	80	0.00
TERT	SCC	rs2736098(p.Ala305Ala,c.915G>A)	A vs G	4	788/2490	1.14(1.01-1.29)	0.031	0	0.597	4	788/2490	1.12(0.95-1.33)	0.179	0	0.76	4	788/2490	1.33(1.05-1.69)	0.019	0	0.61
TNF	SCC	rs1800629(G-308A,*1/*2)	A vs G	5	273/1500	1.85(1.17-2.93)	0.009	66	0.019	5	273/1500	1.98(1.24-3.16)	0.004	57	0.06	5	273/1500	2.38(0.82-6.91)	0.112	22	0.28
TP53	SCC	rs1042522(p.Pro72Arg,c.215C>G)	C vs G	21	3135/8809	0.99(0.84-1.17)	0.941	84	0.000	22	3350/9391	1.04(0.88-1.22)	0.654	69	0.00	22	3173/9047	0.95(0.70-1.30)	0.744	82	0.00
TP73	SCC	G4C14/A4T14	AT vs GC							3	438/1532	1.05(0.59-1.85)	0.881	83	0.00						
VEGFA	SCC	rs2010963(634G>C)	C vs G													3	381/920	0.84(0.58-1.21)	0.356	16	0.31
VEGFA	SCC	rs3025039(C936T)	T vs C							3	322/754	0.96(0.69-1.35)	0.812	24	0.27						
XPA	SCC	rs1800975(c.-4A>G,23G>A)	A vs G							3	631/1245	1.15(0.93-1.42)	0.211	0	0.38	3	631/1245	1.11(0.70-1.77)	0.650	68	0.05
XPC	SCC	PAT-/+ (24660_24664delGTAAC, inspoly(AT))	Ins vs non-ins	3	561/1340	1.12(0.88-1.42)	0.369	65	0.059	3	561/1340	1.00(0.80-1.24)	0.970	11	0.32	3	561/1340	1.43(0.94-2.19)	0.095	61	0.08
XPC	SCC	rs2228001(p.Gln939Lys,Ex16+211A＞C)	C vs A	3	789/2108	1.00(0.89-1.13)	0.995	0	0.427												
XRCC1	SCC	rs1799782(p.Arg194Trp,c.580C>T,Ex6-22C＞T)	T vs C	3	490/1429	0.88(0.73-1.06)	0.185	0	0.551	3	1147/2876	0.86(0.70-1.05)	0.136	0	0.85						
XRCC1	SCC	rs25487(p.Gln399Arg,c.1196A>G)	A vs G	7	2142/5112	0.99(0.86-1.13)	0.833	60	0.021	7	1923/4547	0.96(0.78-1.18)	0.713	60	0.02	6	1892/4427	1.03(0.82-1.28)	0.824	28	0.23

SCLC=small cell lung cancer; NSCLC=non-small cell lung cancer; AD=adenocarcinoma; SCC=squamous cell carcinoma; Del=deletion; Ins=insertion.

[a] Allelic contrast or phenotype trait for common variants; genetic comparison for rare variants or variants only with genotype group data

[b] *P* value of the test for between-study heterogeneity

Supplementary Table S6. Credibility assessment for variants with significant associations with lung cancer risk in subgroup meta-analyses by histological types

Genes	Sub-group	Variants	Alleles[a]	Number evaluated		Lung cancer risk meta-analysis					Venice criteria grades[d]	Credibility of evidence[e]	Amount of evidence[f]		Replication[g]	Protection from bias[h]			Sensitivity analysis[i]			Low OR[j]	Modified P^k	Excess P^l	Begg's P^m
																			Initial study influence		Deviation from HWE				
				Studies	Cases/Controls	Genetic models	OR(95% CI)[b]	*P* value	I^2 (%)	P_Q[c]			Numbers	Grade		Grade	Reasons for bias	Reason for bias exemption	OR(95%CI)	*P* value					
CHRNA5	SCLC	rs16969968	A/G	3	513/3253	Allelic	1.55(1.15-2.10)	0.004	55	0.109	ACC	Weak	1813	A	C	C	Small study		1.37(1.12-1.67)	0.002	None	No	0.001	0.558	0.296
CYP1A1	SCLC	rs4646903	C/T	12	273/2545	Recessive	1.71(1.08-2.71)	0.021	0	0.904	BAA	Moderate	176	B	A	A			1.69(1.06-2.68)	0.026	NO	No	0.523	1.000	0.244
GSTM1	SCLC	Present/Null	NA	26	1224/7255	Null vs present	1.30(1.09-1.56)	0.004	43	0.01	ABA	Moderate	4063	A	B	A			1.28(1.06-1.54)	0.01	None	No	0.976	0.311	1.000
NQO1	SCLC	rs1800566	T/C	3	205/792	Allelic	1.68(1.05-2.68)	0.029	56	0.102	BCC	Weak	342	B	C	C	First study		1.44(0.95-2.17)	0.085	None	No	0.259	0.613	0.296
XPC	SCLC	rs2228001	C/A	3	347/2108	Allelic	0.84(0.71-1.00)	0.046	0	0.457	AAC	Weak	1843	A	A	C	First study		0.88(0.72-1.07)	0.192	None	No	0.218	1.000	1.000
CHRNA5	NSCLC	rs16969968	A/G	6	3201/4736	Allelic	1.36(1.24-1.48)	1.48×10^{-11}	13	0.329	AAA	Strong	4303	A	A	A			1.34(1.23-1.45)	2.90×10^{-12}	None	No	0.736	0.672	0.707
CLPTM1L	NSCLC	rs402710	T/C	6	2940/4040	Allelic	0.85(0.79-0.91)	1.13×10^{-5}	0	0.666	AAA	Strong	4634	A	A	A			0.81(0.74-0.89)	7.73×10^{-6}	NO	No	0.650	1.000	1.000
CYP1A1	NSCLC	rs4646903	C/T	24	3032/5165	Allelic	1.11(1.03-1.21)	0.009	0	0.458	AAC	Weak	3650	A	A	C	Low OR		1.09(1.01-1.19)	0.038	NO	Yes	0.986	0.194	0.785
CYP2E1	NSCLC	rs6413432	A/T	6	1290/1809	Allelic	0.80(0.71-0.91)	4.90×10^{-4}	0	0.868	AAA	Strong	1372	A	A	A			0.81(0.71-0.92)	0.001	NO	No	0.880	1.000	1.000
ERCC1	NSCLC	rs11615	C/T	3	780/811	Allelic	0.68(0.58-0.81)	1.01×10^{-5}	13	0.316	AAA	Strong	2162	A	A	A			0.75(0.61-0.91)	0.004	None	No	0.311	0.547	0.296
ERCC2	NSCLC	rs13181	C/A	8	2770/2856	Allelic	1.19(1.04-1.36)	0.014	39	0.116	ABC	Weak	2381	A	B	C	HWE		1.22(1.06-1.40)	0.006	Yes	No	0.776	0.665	1.000
FAS	NSCLC	rs2234767	A/G	3	3194/3064	Recessive	1.51(1.23-1.87)	1.26×10^{-4}	0	0.447	BAC	Weak	396	B	A	C	First study		1.38(0.95-2.00)	0.093	None	No	0.478	1.000	0.296
FGFR4	NSCLC	rs351855	A/G	3	985/1230	Allelic	0.76(0.68-0.86)	1.97×10^{-5}	0	0.59	AAA	Strong	1779	A	A	A			0.74(0.64-0.86)	5.19×10^{-5}	None	No	0.323	0.590	1.000
GSTM1	NSCLC	Present/Null	NA	60	11551/15673	Null vs present	1.18(1.08-1.29)	1.56×10^{-4}	62	0	ACA	Weak	13759	A	C	A			1.17(1.08-1.28)	3.23×10^{-4}	None	No	0.119	0.213	0.448
HYKK	NSCLC	rs931794	G/A	4	1548/2464	Allelic	1.25(1.13-1.37)	9.08×10^{-6}	0	0.88	AAA	Strong	2718	A	A	A			1.25(1.07-1.46)	0.004	None	No	0.902	0.630	0.734
IL17A	NSCLC	rs2275913	A/G	3	780/998	Recessive	1.72(1.12-2.65)	0.013	31	0.235	BBB	Moderate	164	B	B	B	Missing information		2.01(1.40-2.87)	1.41×10^{-4}	NA	No	0.405	0.566	0.296
IL1B	NSCLC	rs1143627	C/T	5	1915/2551	Allelic	0.82(0.67-0.99)	0.043	78	0.001	ACC	Weak	4019	A	C	C	First study, HWE ,small study, publication bias		0.83(0.66-1.05)	0.117	Yes	No	0.019	0.676	0.027
IL6	NSCLC	rs1800796	G/C	3	1333/1452	Allelic	0.75(0.57-0.99)	0.039	77	0.013	ACC	Weak	1473	A	C	C	Small study		0.75(0.57-0.99)	0.039	None	No	0.036	0.227	0.296
MIR146A	NSCLC	rs2910164	C/G	4	880/1094	Allelic	1.28(1.11-1.46)	4.63×10^{-4}	0	0.391	AAA	Strong	1765	A	A	A			1.28(1.11-1.46)	4.63×10^{-4}	None	No	0.327	0.629	0.734
MMP2	NSCLC	rs243865	T/C	3	1216/1729	Allelic	0.61(0.40-0.92)	0.019	83	0.003	BCC	Weak	829	B	C	C	First study, small study		0.72(0.33-1.59)	0.419	None	No	0.025	0.456	0.296
MPO	NSCLC	rs2333227	A/G	10	5036/6646	Recessive	1.38(1.03-1.86)	0.033	51	0.031	BCA	Weak	576	B	C	A			1.41(1.03-1.94)	0.035	None	No	0.881	0.700	0.858
OGG1	NSCLC	rs1052133	G/C	17	6279/8214	Recessive	1.16(1.02-1.32)	0.02	36	0.072	ABC	Weak	2814	A	B	C	Excess of significant studies		1.15(1.01-1.32)	0.039	NO	No	0.920	0.084	0.967
SOD2	NSCLC	rs4880	T/C	6	3133/4255	Allelic	1.25(1.08-1.45)	0.002	72	0.003	ACC	Weak	7713	A	C	C	Small study		1.31(1.07-1.60)	0.008	NO	No	0.090	1.000	0.133
TERT	NSCLC	rs2736098	A/G	4	2002/2490	Allelic	1.30(1.19-1.42)	2.59×10^{-9}	0	0.818	AAA	Strong	3368	A	A	A			1.29(1.17-1.42)	2.09×10^{-7}	None	No	0.775	1.000	0.734
TNF	NSCLC	rs1800629	A/G	6	1052/1767	Allelic	1.67(1.01-2.76)	0.044	89	0	BCC	Weak	829	B	C	C	First study		1.82(0.91-3.65)	0.091	None	No	0.432	0.209	0.452
TP63	NSCLC	rs10937405	T/C	3	3587/8484	Allelic	0.87(0.82-0.92)	9.91×10^{-7}	0	0.595	AAB	Moderate	10101	A	A	B	Missing information		NA		None	No	0.402	1.000	1.000
XPC	NSCLC	PAT-/+	Ins/non-ins	3	967/1340	Recessive	1.46(1.17-1.81)	0.001	0	0.483	BAA	Moderate	383	B	A	A			1.36(1.05-1.76)	0.020	None	No	0.888	0.591	1.000
XRCC1	NSCLC	rs2256507	A/G	3	431/779	Recessive	1.68(1.03-2.74)	0.038	8	0.338	CAB	Weak	80	C	A	B	Missing information		NA		None	No	0.281	0.499	1.000
XRCC1	NSCLC	rs1001581	T/C	4	574/994	Allelic	1.27(1.04-1.56)	0.018	40	0.172	ABC	Weak	1134	A	B	C	First study		1.28(0.87-1.89)	0.218	None	No	0.187	0.592	0.734
XRCC1	NSCLC	rs3213245	C/T	3	1744/2178	Dominant	1.50(1.29-1.75)	1.89×10^{-7}	0	0.683	BAA	Moderate	847	B	A	A			1.53(1.26-1.84)	1.14×10^{-5}	None	No	0.228	0.575	0.296
BIRC5	AD	rs9904341	C/G	3	312/818	Allelic	1.70(1.22-2.37)	0.002	57	0.097	ACA	Weak	1142	A	C	A			2.03(1.46-2.83)	2.33×10^{-5}	None	No	0.189	0.562	0.296
CHRNA5	AD	rs16969968	A/G	4	1507/2834	Allelic	1.37(1.14-1.64)	0.001	33	0.214	ABA	Moderate	1867	A	B	A			1.32(1.16-1.51)	3.06×10^{-5}	None	No	0.861	1.000	0.734
CYP2E1	AD	rs6413432	A/T	6	500/1809	Allelic	0.79(0.66-0.95)	0.011	0	0.664	AAA	Strong	1040	A	A	A			0.80(0.67-0.97)	0.019	NO	No	0.882	1.000	0.707
ERCC2	AD	rs13181	C/A	4	664/1230	Dominant	1.35(1.06-1.70)	0.013	0	0.635	BAA	Moderate	607	B	A	A			1.39(1.08-1.80)	0.010	None	No	0.489	1.000	0.734
GSTM1	AD	Present/Null	NA	42	4199/12206	Null vs present	1.17(1.05-1.31)	0.005	45	0.001	ABC	Weak	8165	A	B	C	Small study,excess of significant studies		1.14(1.03-1.26)	0.011	None	No	0.075	0.039	0.146
IL17A	AD	rs2275913	A/G	3	469/998	Recessive	1.84(1.11-3.06)	0.018	36	0.211	BBB	Moderate	132	B	B	B	Missing information		2.19(1.47-3.26)	1.21×10^{-4}	NA	No	0.570	0.567	1.000
MDM2	AD	rs2279744	G/T	6	1714/4083	Recessive	1.28(1.04-1.56)	0.018	46	0.098	ABA	Moderate	1296	A	B	A			1.34(1.06-1.70)	0.015	None	No	0.792	0.668	0.707
MIR146A	AD	rs2910164	C/G	3	442/965	Allelic	1.26(1.04-1.51)	0.018	15	0.309	AAC	Weak	1311	A	A	C	First study		1.33(0.89-1.99)	0.161	None	No	0.202	1.000	0.296
OGG1	AD	rs1052133	G/C	12	3603/6677	Recessive	1.25(1.10-1.43)	0.001	20	0.246	AAA	Strong	2238	A	A	A			1.25(1.09-1.44)	0.002	None	No	0.777	0.263	0.945
SOD2	AD	rs4880	T/C	4	1219/2761	Allelic	1.20(1.08-1.32)	3.80×10^{-4}	0	0.405	AAC	Weak	4235	A	A	C	First study		1.28(0.98-1.68)	0.075	NO	No	0.104	0.150	0.308
TERT	AD	rs2736098	A/G	4	1214/2490	Allelic	1.40(1.26-1.54)	4.97×10^{-11}	0	0.891	AAA	Strong	2771	A	A	A			1.39(1.24-1.55)	2.68×10^{-8}	None	No	0.533	1.000	0.308
TP53	AD	rs1042522	C/G	22	3504/8822	Recessive	1.20(1.05-1.38)	0.008	16	0.245	AAA	Strong	1835	A	A	A			1.20(1.04-1.39)	0.015	NO	No	0.210	1.000	0.143
TP63	AD	rs10937405	T/C	3	1158/8484	Allelic	0.82(0.75-0.90)	2.91×10^{-5}	0	0.898	AAB	Moderate	8115	A	A	B	Missing information		NA		None	No	0.168	1.000	0.296
XPC	AD	PAT-/+	Ins/non-ins	3	398/1340	Allelic	1.21(1.03-1.42)	0.02	0	0.442	AAC	Weak	1391	A	A	C	First study		1.18(0.94-1.47)	0.149	None	No	0.999	0.575	1.000
XRCC1	AD	rs3213245	C/T	3	860/2178	Dominant	1.55(1.29-1.87)	4.72×10^{-6}	0	0.758	BAA	Moderate	630	B	A	A			1.58(1.25-2.00)	1.25×10^{-4}	None	No	0.192	0.557	0.296
CYP1A1	SCC	rs4646903	C/T	17	1021/3959	Allelic	1.45(1.26-1.67)	3.77×10^{-7}	21	0.215	AAA	Strong	2102	A	A	A			1.42(1.22-1.65)	6.56×10^{-6}	NO	No	0.571	0.415	0.232
CYP1A1	SCC	rs1048943	G/A	16	1572/3981	Allelic	1.24(1.04-1.49)	0.02	58	0.002	ACC	Weak	2328	A	C	C	Small study		1.23(1.01-1.49)	0.038	NO	No	0.073	0.282	0.444
CYP2E1	SCC	rs6413432	A/T	6	715/1809	Allelic	0.76(0.65-0.88)	3.98×10^{-4}	0	0.911	AAA	Strong	1133	A	A	A			0.76(0.65-0.89)	0.001	NO	No	0.389	1.000	0.260
GSTM1	SCC	Present/Null	NA	42	4704/12325	Null vs present	1.23(1.08-1.40)	0.002	66	0	ACC	Weak	8383	A	C	C	Excess of significant studies		1.23(1.08-1.41)	0.003	None	No	0.291	0.025	0.965
MMP2	SCC	rs243865	T/C	3	740/1729	Allelic	0.56(0.37-0.84)	0.005	73	0.023	BCC	Weak	723	B	C	C	First study, small study		0.66(0.32-1.33)	0.242	None	No	0.046	0.448	1.000
SOD2	SCC	rs4880	T/C	4	574/2761	Allelic	1.54(1.03-2.31)	0.035	83	0.001	ACC	Weak	3495	A	C	C	First study		1.93(0.75-4.99)	0.174	NO	No	0.319	0.314	0.734
TERT	SCC	rs2736098	A/G	4	788/2490	Allelic	1.14(1.01-1.29)	0.031	0	0.597	AAC	Weak	2329	A	A	C	Low OR		1.17(1.03-1.33)	0.017	None	Yes	0.389	0.535	1.000
TNF	SCC	rs1800629	A/G	5	273/1500	Allelic	1.85(1.17-2.93)	0.009	66	0.019	BCC	Weak	488	B	C	C	First study		1.98(0.95-4.16)	0.070	None	No	0.720	1.000	1.000

SCLC=small cell lung cancer; NSCLC=non-small cell lung cancer; AD=adenocarcinoma; SCC=squamous cell carcinoma; Ins=insertion; NA=Not Applicable.

[a] Minor alleles/major alleles (per Caucasian)

[b] Summary ORs were calculated based on the DerSimonian-Lairs random-effects model

[c] *P*-value of heterogeneity between studies

[d] Venice criteria grades contained assessments of three aspects: the amount of evidence, extent of replication, and protection from bias, and each assessment was assigned three levels (A, B, or C).

[e] Credibility of evidence was evaluated based on Venice criteria with three aspects (the amount of evidence, extent of replication, and protection from bias), and was categorized as strong (all three aspect grades were A), moderate (any grade was B, but not C) or weak (any grade was C).

[f] Amount of evidence, depending on total sample size of the smallest genetic group among cases and controls in each meta-analysis, was graded as A (sample size>1000), B (sample size between 100 and 1000), or C (sample size <100).

[g] Extent of replication, depending on between-study heterogeneity, was graded as A (I^2<25%), B (I^2 between 25% and 50%), or C (I^2>50%).

[h] Protection from bias, considering various potential sources of bias in meta-analysis, was graded as A when there was no demonstrable bias and bias was unlikely invalidate the association, was graded as B when there was insufficient information for identifying evidence (i.e. missing information for evaluating Hardy-Weinberg equilibrium (HWE) among controls in an individual study) although there was no obvious bias, and C when the bias was evident and/or was likely to explain the presence of association. For the C grade, it was assigned if a meta-analysis had any of the following potential sources of bias: (1) magnitude of the association was low; (2) sensitivity analysis altered the statistical significance; (3) potential small study effect; (4) possible existence of an excess of significant findings (the number of observed significant studies more than the number of expected significant studies); (5) potential publication bias.

Small study=Possible existence of potential small study effect (modified Egger's test, *p*<0.10); First study=Significance lost excluding the first published or first positive report; Low OR=Low magnitude of the association (i.e. 0.87<OR<1.15); HWE=Significance lost excluding studies with controls violating HWE; Missing information= Insufficient information for bias evaluation; Publication bias= Possible existence of potential publication bias (Begg's test, *p*<0.10); Excess of significant studies=Possible existence of an excess of significant findings (excess significance test, *p*<0.10).

[i] A sensitivity analysis was performed to examine whether the significant summary ORs were robust after excluding the first published or first positive report (defined as the earliest study reported a significant association), or excluding studies with controls violating HWE. None=A meta-analysis didn't include studies with controls violating HWE or evaluated association for a variant with a phenotype change; NO=Without the influence from studies with controls violating HWE; Yes=Evidence of influence from studies with controls violating HWE; NA=Insufficient information for evaluation of influence from first published/positive study or studies with controls violating HWE.

[j] Low OR (i.e. 0.87<OR<1.15; No=Association without a low OR; Yes=Association with a low OR)

[k] *P* value for potential small study effect based on the modified Egger's test. (*P*<0.10 is usually considered evidence for significant evidence of small study effect.)

[l] *P* value for possible existing an excess of significant findings based on the excess significance test. (*P*<0.10 is usually considered evidence for significant evidence of an excess of significant findings.)

[m] *P* value for potential publication bias of studies based on the Begg's test. (*P*<0.10 is usually considered evidence for significant evidence of publication bias.)

Supplementary Table S7. Subgroup meta-analyses stratified by smoking status for variants with sufficient data under different genetic models (Continued on next page)

Genes	Sub-group	Variants	Comparison[a]	Results of meta-analysis using allelic model						Results of meta-analysis using dominant model						Results of meta-analysis using recessive model					
				Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]	Studies	Cases/Controls	OR(95% CI)	*P* value	I^2(%)	P_Q[b]
APEX1	Smokers	rs1760944(c.-468T>G,-141T>G)	A vs C	3	655/647	1.37(1.11-1.69)	0.003	43	0.174												
APEX1	Smokers	rs1130409(p.Asp148Glu,c.444T>G)	G vs T	7	1604/1983	0.97(0.86-1.10)	0.678	39	0.133	11	4074/3854	1.15(0.97-1.36)	0.100	64	0.002	6	1462/1811	1.03(0.79-1.34)	0.827	54	0.054
CCND1	Smokers	rs9344(rs603965,p.Pro241Pro,c.870G>A)	A vs G	4	1250/1709	1.14(0.86-1.53)	0.368	82	0.001	4	1250/1709	1.17(0.74-1.86)	0.511	78	0.004	4	1250/1709	1.21(0.78-1.86)	0.393	81	0.002
CHRNA5	Smokers	rs16969968(p.Asp398Asn,c.1192G>A)	A vs G	4	2828/3738	1.30(1.20-1.42)	2.77×10^{-10}	0	0.626	4	2828/3738	1.42(1.26-1.59)	4.52×10^{-9}	0	0.611	4	2828/3738	1.43(1.21-1.69)	2.08×10^{-5}	0	0.842
CYP1A1	Smokers	rs4646903(m1,MspI,T3801C)	C vs T	7	1034/1087	1.30(1.02-1.64)	0.033	46	0.088	21	3225/3067	1.38(1.14-1.67)	0.001	58	0.000	9	1154/1218	1.57(1.03-2.38)	0.034	18	0.285
CYP1A1	Smokers	rs1048943(*2C,m2,p.Ile462Val,c.1384A>G)	G vs A	8	1166/1586	1.25(0.97-1.62)	0.081	62	0.010	14	1888/2413	1.42(1.04-1.93)	0.028	78	0.000	8	1166/1586	1.51(0.75-3.03)	0.251	45	0.077
CYP1A2	Smokers	rs2069526(-739T>G)	G vs T							3	412/401	1.89(0.96-3.71)	0.065	46	0.155						
CYP1A2	Smokers	rs2069514(CYP1A2*1C,-3860G>A)	A vs G							4	534/435	1.40(0.47-4.16)	0.547	85	0.000						
CYP1A2	Smokers	rs762551(CYP1A2*1F,c.A-164C)	C vs A							3	507/544	0.90(0.42-1.94)	0.783	83	0.003	3	553/555	0.80(0.37-1.73)	0.573	75	0.018
CYP1B1	Smokers	rs10012(p.Arg48Gly,c.142C>G)	G vs C							3	542/528	1.86(0.94-3.68)	0.075	81	0.005						
CYP1B1	Smokers	rs1056827(p.Ala119Ser,c.355G>T,m2)	T vs G							3	495/491	1.48(0.72-3.04)	0.286	83	0.003						
CYP1B1	Smokers	rs1800440(p.Asn453Ser,Ex3+315A>G)	G vs A							3	447/449	0.70(0.51-0.95)	0.024	0	0.481						
CYP1B1	Smokers	rs1056836(CYP1B1*3,p.Leu432Val,c.1294C>G)	G vs C							5	622/684	1.28(1.01-1.62)	0.045	0	0.616						
CYP2A6	Smokers	rs5031016(p.Ile471Thr,c1412T>C,wt/*7)	C vs T	3	1527/1138	0.57(0.33-1.00)	0.048	73	0.025	3	1527/1138	0.58(0.34-0.98)	0.043	66	0.055						
CYP2A6	Smokers	non*4/*4(*1/*4,a deletion of the CYP2A6 gene)	*4 vs non*4	3	1339/848	0.71(0.59-0.85)	2.30×10^{-4}	13	0.319	4	1449/1022	0.80(0.54-1.20)	0.281	70	0.019	3	1339/848	0.44(0.28-0.71)	0.001	0	0.768
CYP2C9	Smokers	rs1799853(p.Arg144Cys,c.430C>T)	T vs C							3	637/858	1.22(0.87-1.69)	0.249	24	0.266						
CYP2E1	Smokers	rs3813867(g.3739G>C,c.-1293G>C)	C vs G							4	595/639	1.07(0.67-1.70)	0.788	24	0.267						
CYP2E1	Smokers	rs6413432(c.967+1143T>A,7632T>A)	A vs T	3	796/791	0.75(0.63-0.90)	0.002	2	0.360	6	960/944	0.57(0.37-0.87)	0.010	55	0.047						
CYP2E1	Smokers	rs2031920(RsaI,c1>c2,-1053C>T)	T vs C	3	1064/1220	0.76(0.65-0.90)	0.001	0	0.727	10	1880/1949	0.76(0.63-0.91)	0.003	15	0.304						
EPHX1	Smokers	rs1051740(p.Tyr113His,c.337T>C)	C vs T	5	840/1270	0.87(0.57-1.33)	0.526	88	0.000	6	885/1315	0.98(0.56-1.75)	0.956	88	0.000	6	1074/1364	0.99(0.60-1.63)	0.971	66	0.011
EPHX1	Smokers	rs2234922(p.His139Arg,c.416A>G)	G vs A	5	817/1230	1.26(0.89-1.78)	0.200	76	0.002	6	862/1275	1.34(0.87-2.05)	0.182	77	0.001	5	909/845	1.42(1.02-1.97)	0.039	0	0.535
ERCC1	Smokers	rs2298881(262G>T,C>A)	T vs G							3	1600/2132	0.98(0.74-1.30)	0.878	65	0.059						
ERCC1	Smokers	rs3212986(8092C>A,14443C>A)	A vs C	3	1701/2361	1.01(0.92-1.12)	0.801	0	0.479	3	1701/2361	1.03(0.91-1.17)	0.614	0	0.844	3	1701/2361	1.00(0.70-1.43)	0.982	46	0.155
ERCC1	Smokers	rs3212961(IVS5+33C＞A,17677C>A)	A vs C	3	1125/1074	0.93(0.81-1.07)	0.305	0	0.658	3	1190/1067	0.93(0.77-1.13)	0.478	0	0.465						
ERCC1	Smokers	rs11615(rs3177700,p.Asn118Asn,c.354T>C)	C vs T	5	2011/2486	0.84(0.69-1.04)	0.112	76	0.003	4	1861/2316	0.77(0.47-1.25)	0.290	80	0.002	4	1861/2316	0.77(0.58-1.03)	0.083	68	0.024
ERCC2	Smokers	rs1799793(p.Asp312Asn,c.981G>A)	A vs G	5	1877/2526	0.98(0.88-1.10)	0.712	24	0.261	6	1973/2609	0.91(0.79-1.05)	0.178	16	0.314	5	1877/2526	1.10(0.91-1.32)	0.323	0	0.577
ERCC2	Smokers	rs13181(p.Lys751Gln,c.2251A>C)	C vs A	5	1629/2452	1.07(0.93-1.24)	0.341	49	0.101	5	1576/2363	1.03(0.85-1.25)	0.772	39	0.159	5	1551/2341	1.12(0.93-1.34)	0.232	0	0.491
ERCC4	Smokers	rs1800067(Arg415Gln)	A vs G	3	1110/1807	1.09(0.89-1.34)	0.404	0	0.650												
ERCC5	Smokers	rs17655(p.Asp1104His,c.3310G>C)	C vs G	3	1092/1743	0.98(0.77-1.26)	0.886	57	0.096												
EXO1	Smokers	rs1047840(p.Glu589Lys,c.1765G>A)	A vs G							3	884/840	1.23(0.80-1.90)	0.342	79	0.008						
GSTM1	Smokers	Present/Null(Large gene deletion)	Null vs present	45	9276/9005	1.20(1.09-1.32)	2.16×10^{-4}	51	0.000												
GSTM3	Smokers	rs1799735(c.468+21delAGG,3bp deletion,*A/*B)	Del vs non-del							3	645/624	0.93(0.66-1.31)	0.686	41	0.183						
GSTP1	Smokers	rs1138272(p.Ala114Val,c.341C>T)	T vs C							3	924/1026	1.63(1.28-2.08)	9.17×10^{-5}	0	0.459						
GSTP1	Smokers	rs1695(p.Ile105Val,c.313A>G)	G vs A	8	2830/2178	1.29(1.09-1.53)	0.003	59	0.017	20	5159/4713	1.22(1.07-1.38)	0.003	46	0.014	8	2830/2178	1.37(1.07-1.77)	0.014	23	0.250
GSTT1	Smokers	Present/Null (Large gene deletion)	Null vs present	27	7032/6386	1.08(0.95-1.22)	0.263	41	0.014												
IL1B	Smokers	rs1143627(g.4970C>T,-31T>C)	C vs T							3	2180/1934	1.12(0.99-1.27)	0.086	0	0.408						
IL6	Smokers	rs1800795(G-174C)	C vs G							3	2471/2002	0.93(0.82-1.06)	0.295	0	0.462						
IL8	Smokers	rs4073(T-251A)	T vs A													3	2605/2081	1.00(0.88-1.14)	0.983	0	0.615
LIG1	Smokers	rs20580(p.Ala170Ala,c.417C>A)	A vs C	4	1367/2175	1.06(0.96-1.18)	0.256	6	0.364	3	1225/2004	1.11(0.94-1.31)	0.228	0	0.516	3	1225/2004	1.15(0.98-1.37)	0.095	0	0.898
MDM2	Smokers	rs2279744(SNP309,c.14+309T>G)	G vs T	4	2941/4189	1.01(0.80-1.28)	0.932	90	0.000	4	2941/4189	0.96(0.71-1.31)	0.790	88	0.000	4	2941/4189	1.12(0.83-1.51)	0.466	78	0.004
MMP1	Smokers	rs1799750(-16071G/2G,insG)	2G vs 1G													3	2400/1389	1.32(0.85-2.04)	0.211	84	0.002
MPO	Smokers	rs2333227(G-463A)	A vs G	9	2987/2720	0.99(0.86-1.14)	0.893	50	0.045	9	2987/2720	1.00(0.87-1.13)	0.946	21	0.254	10	3190/2887	1.06(0.68-1.65)	0.814	70	0.001
MTHFR	Smokers	rs1801131(p.Ala429Glu,c.1286A>C,A1298C)	C vs A	3	1245/1383	1.14(1.01-1.27)	0.031	0	0.871	3	1245/1383	1.16(0.99-1.35)	0.060	0	0.999	4	1423/1587	1.18(0.94-1.48)	0.164	0	0.559
MTHFR	Smokers	rs1801133(p.Ala222Val,Ex4+79C＞T)	T vs C	4	1531/1947	0.93(0.79-1.08)	0.324	40	0.171	4	1531/1947	0.87(0.74-1.03)	0.100	23	0.274	5	1840/2117	1.27(0.82-1.97)	0.287	70	0.011
NAT2	Smokers	rs1799930(p.Arg197Gln,590G>A,NAT2*6B)	A vs G	3	428/476	0.81(0.66-0.99)	0.044	0	0.453	4	662/570	0.91(0.63-1.32)	0.621	59	0.064	3	428/476	0.82(0.52-1.30)	0.402	0	0.402
NAT2	Smokers	Rapid/slow (Acetylation Phenotype)	Slow vs rapid	7	1290/1379	1.08(0.80-1.44)	0.623	55	0.037												
NBN	Smokers	rs1805794(p.Gln185Glu,Ex5-32C>G,605C>G)	G vs C													3	1226/1220	0.83(0.71-0.98)	0.030	0	0.554
NQO1	Smokers	rs1800566(p.Pro187Ser,c.648C>T,609C>T,*2)	T vs C	5	1687/1677	1.10(0.90-1.36)	0.355	58	0.049	13	3231/3021	1.04(0.90-1.20)	0.586	33	0.118	5	1687/1677	1.17(0.72-1.93)	0.527	42	0.140
OGG1	Smokers	rs1052133(p.Ser326Cys,c.977C>G,8055C>G)	G vs C	13	4847/3994	0.99(0.86-1.15)	0.900	73	0.000	13	4829/3926	0.99(0.83-1.17)	0.901	55	0.009	12	4704/3834	1.06(0.82-1.37)	0.668	67	0.000
PADPRP	Smokers	A/B(a 193-bp deletion)	Del vs non-del							3	265/202	1.30(0.65-2.58)	0.458	63	0.069						
PTGS2	Smokers	rs5275(c.*427T>C,8473T>C)	C vs T							4	2629/2077	1.06(0.65-1.70)	0.826	90	0.000						
SOD2	Smokers	rs4880(rs1799725,Ala16Val)	T vs C	3	1444/1188	1.25(1.06-1.48)	0.007	33	0.224	3	1444/1188	1.58(1.00-2.48)	0.049	70	0.037	5	1681/1456	1.23(1.04-1.46)	0.013	0	0.438
SULT1A1	Smokers	rs9282861(p.Arg213His,c.638G>A,*1/*2)	A vs G							5	1381/1377	1.23(0.81-1.89)	0.335	83	0.000						
TP53	Smokers	rs1042522(p.Pro72Arg,c.215C>G)	C vs G	7	1887/1830	1.15(0.90-1.48)	0.271	81	0.000	9	2747/2426	1.23(1.01-1.50)	0.035	57	0.017	10	2771/2299	1.07(0.75-1.55)	0.701	76	0.000
XPA	Smokers	rs1800975(c.-4A>G,23G>A)	A vs G	3	1459/2213	0.96(0.78-1.18)	0.674	74	0.021	4	1678/2350	0.98(0.74-1.29)	0.865	71	0.017	3	1459/2213	1.04(0.69-1.57)	0.851	76	0.016
XPC	Smokers	rs2228001(p.Gln939Lys,Ex16+211A＞C)	C vs A	3	1092/1742	0.98(0.87-1.09)	0.689	0	0.582												
XRCC1	Smokers	rs25489(p.Arg280His,c.839G>A,Ex9+16G>A)	A vs G	3	724/762	1.35(1.00-1.81)	0.048	0	0.589	6	3197/2724	1.09(0.91-1.31)	0.356	8	0.366	3	724/762	1.45(0.36-5.85)	0.600	0	0.518
XRCC1	Smokers	rs1799782(p.Arg194Trp,c.580C>T,Ex6-22C＞T)	T vs C	6	1597/1987	0.73(0.55-0.97)	0.028	40	0.137	7	3832/3699	0.77(0.60-0.99)	0.038	49	0.066	5	1310/1554	0.74(0.37-1.45)	0.375	0	0.904
XRCC1	Smokers	rs25487(p.Gln399Arg,c.1196A>G)	A vs G	12	4087/3678	0.93(0.84-1.02)	0.138	33	0.124	15	4650/4287	0.98(0.90-1.06)	0.582	0	0.692	12	4087/3678	0.79(0.63-1.00)	0.050	41	0.068
XRCC3	Smokers	rs861539(p.Thr241Met,c.722C>T)	T vs C	3	1312/1557	1.05(0.81-1.36)	0.710	73	0.005	7	1475/1698	1.13(0.83-1.54)	0.451	71	0.002	5	1312/1557	1.09(0.72-1.64)	0.686	44	0.127
APEX1	Non-smokers	rs1130409(p.Asp148Glu,c.444T>G)	G vs T	5	789/1103	1.04(0.91-1.19)	0.545	0	0.443	10	1544/2531	1.02(0.89-1.17)	0.770	0	0.664	5	789/1103	1.16(0.91-1.48)	0.222	0	0.457
ATM	Non-smokers	rs189037(c.-111G>A,−4519G>A)	A vs G	3	1323/1550	1.18(1.03-1.36)	0.018	42	0.178	3	1323/1550	1.15(0.95-1.38)	0.147	25	0.262	3	1323/1550	1.40(1.16-1.69)	3.87×10^{-4}	0	0.369
CCND1	Non-smokers	rs9344(rs603965,p.Pro241Pro,c.723G>A)	A vs G	3	161/262	1.21(0.79-1.84)	0.384	51	0.131	3	161/262	1.16(0.60-2.22	0.657	28	0.248	4	371/433	1.37(0.85-2.19)	0.197	44	0.149
CYP1A1	Non-smokers	rs4646903(m1,MspI,T3801C)	C vs T	6	412/869	0.94(0.75-1.19)	0.611	18	0.295	19	998/2214	0.95(0.78-1.15)	0.586	20	0.208	8	508/1081	1.07(0.74-1.55)	0.716	0	0.461
CYP1A1	Non-smokers	rs1048943(*2C,m2,p.Ile462Val,c.1384A>G)	G vs A	4	446/561	1.16(0.86-1.56)	0.339	43	0.152	10	926/1327	1.01(0.76-1.35)	0.927	51	0.032	4	446/561	1.93(1.03-3.63)	0.042	32	0.218
CYP1B1	Non-smokers	rs1056836(CYP1B1*3,p.Leu432Val,c.1294C>G)	G vs C							4	396/536	1.03(0.67-1.57)	0.908	37	0.189						
CYP2E1	Non-smokers	rs6413432(c.967+1143T>A,7632T>A)	A vs T							5	315/560	0.72(0.54-0.97)	0.028	0	0.959						
CYP2E1	Non-smokers	rs2031920(RsaI,c1>c2,-1053C>T)	T vs C	3	304/695	0.70(0.54-0.90)	0.005	0	0.863	9	593/1181	0.71(0.55-0.91)	0.008	12	0.336						
ERCC1	Non-smokers	rs11615(rs3177700,p.Asn118Asn,c.354T>C)	C vs T	3	731/958	0.85(0.72-0.99)	0.042	0	0.449	3	731/958	0.68(0.47-1.00)	0.051	0	0.422	3	731/958	0.86(0.71-1.05)	0.136	0	0.585
ERCC2	Non-smokers	rs1799793(p.Asp312Asn,c.981G>A)	A vs G							3	404/399	1.31(0.82-2.09)	0.263	32	0.231						
ERCC2	Non-smokers	rs13181(p.Lys751Gln,c.2251A>C)	C vs A							3	478/469	1.88(1.36-2.58)	1.11×10^{-4}	0	0.550	3	421/444	0.95(0.33-2.70)	0.916	0	0.441
GSTM1	Non-smokers	Present/Null (Large gene deletion)	Null vs present	32	1924/4718	1.37(1.16-1.61)	1.60×10^{-4}	41	0.009												
GSTP1	Non-smokers	rs1695(p.Ile105Val,c.313A>G)	G vs A	3	380/763	0.96(0.78-1.18)	0.690	0	0.861	14	836/1890	1.06(0.81-1.39)	0.666	45	0.034	3	380/763	1.03(0.62-1.74)	0.899	0	0.540
GSTT1	Non-smokers	Present/Null (Large gene deletion)	Null vs present	18	965/2958	1.26(0.95-1.67)	0.105	40	0.041												
IL10	Non-smokers	rs1800872(g.4433A>C,-592C>A)	A vs C							3	424/959	1.08(0.41-2.84)	0.874	88	0.000						
IL10	Non-smokers	rs1800871(c.-854T>C,-819C>T)	T vs C	3	506/909	1.22(0.54-2.77)	0.630	95	0.000	3	506/909	0.90(0.37-2.22)	0.823	88	0.000	3	506/909	1.76(0.51-6.12)	0.373	95	0.000

Genes	Sub-group	Variants	Comparison[a]	Results of meta-analysis using allelic model						Results of meta-analysis using dominant model						Results of meta-analysis using recessive model					
				Studies	**Cases/Controls**	**OR(95% CI)**	***P* value**	**I^2(%)**	**P_Q[b]**	**Studies**	**Cases/Controls**	**OR(95% CI)**	***P* value**	**I^2(%)**	**P_Q[b]**	**Studies**	**Cases/Controls**	**OR(95% CI)**	***P* value**	**I^2(%)**	**P_Q[b]**
IL1B	Non-smokers	rs1143627(g.4970C>T,-31T>C)	C vs T	3	509/1568	1.20(0.91-1.59)	0.204	70	0.036	4	523/1827	1.27(0.93-1.75)	0.139	43	0.151	3	509/1568	1.15(0.82-1.62)	0.423	34	0.218
IL6	Non-smokers	rs1800796(-572C>G,634C>G)	G vs C	5	1234/2035	0.88(0.66-1.16)	0.360	75	0.003	3	1234/2035	0.88(0.62-1.26)	0.499	78	0.001	5	1234/2035	0.78(0.56-1.09)	0.145	0	0.722
MDM2	Non-smokers	rs2279744(SNP309,c.14+309T>G)	G vs T	6	1642/3277	1.13(0.94-1.35)	0.188	66	0.012	6	1642/3277	1.22(0.95-1.58)	0.124	61	0.025	6	1642/3277	1.17(0.92-1.48)	0.200	39	0.146
MIR146A	Non-smokers	rs2910164(C>G)	C vs G													3	538/717	1.29(0.99-1.67)	0.062	3	0.355
MIR196A2	Non-smokers	rs11614913(T>C)	C vs T	3	369/529	0.79(0.45-1.39)	0.407	84	0.002	3	369/529	1.28(0.93-1.75)	0.129	0	0.903	3	369/529	0.54(0.21-1.41)	0.208	85	0.001
MMP1	Non-smokers	rs1799750(-16071G/2G,insG)	2G vs 1G													3	304/665	0.95(0.70-1.28)	0.718	0	0.774
MPO	Non-smokers	rs2333227(G-463A)	A vs G	4	384/848	0.84(0.63-1.12)	0.233	0	0.986	4	384/848	0.83(0.61-1.15)	0.265	0	0.980	5	495/1001	1.14(0.70-1.86)	0.591	0	0.868
MTHFR	Non-smokers	rs1801131(p.Ala429Glu,c.1286A>C,A1298C)	C vs A													3	339/407	1.46(0.83-2.57)	0.187	0	0.594
MTHFR	Non-smokers	rs1801133(p.Ala222Val,Ex4+79C＞T)	T vs C	3	251/353	1.05(0.81-1.35)	0.730	0	0.843	3	251/353	1.08(0.77-1.50)	0.664	0	0.635	4	404/562	1.19(0.79-1.81)	0.412	0	0.884
NAT2	Non-smokers	Rapid/slow (Acetylation Phenotype)	Slow vs rapid	7	673/1108	1.12(0.72-1.74)	0.603	70	0.003												
NQO1	Non-smokers	rs1800566(p.Pro187Ser,c.648C>T,609C>T,*2)	T vs C	3	243/563	1.05(0.63-1.76)	0.850	67	0.049	9	461/1293	1.08(0.84-1.39)	0.562	4	0.399	3	243/563	1.03(0.35-3.01)	0.957	33	0.224
OGG1	Non-smokers	rs1052133(p.Ser326Cys,c.977C>G,8055C>G)	G vs C	10	1966/2674	1.14(1.04-1.24)	0.007	0	0.785	11	2068/2809	1.19(1.02-1.39)	0.025	0	0.867	10	1966/2674	1.13(0.93-1.38)	0.232	35	0.129
PADPRP	Non-smokers	A/B(a 193-bp deletion)	Del vs non-del							3	23/90	0.80(0.23-2.72)	0.717	0	0.517						
PTGS2	Non-smokers	rs5275(c.*427T>C,8473T>C)	C vs T							4	604/1846	1.01(0.68-1.49)	0.969	65	0.037						
SOD2	Non-smokers	rs4880(rs1799725,Ala16Val)	T vs C													4	271/765	1.00(0.60-1.68)	0.993	48	0.125
SULT1A1	Non-smokers	rs9282861(p.Arg213His,c.638G>A,*1/*2)	A vs G							4	370/675	1.35(1.00-1.83)	0.051	0	0.609						
TP53	Non-smokers	rs1042522(p.Pro72Arg,c.215C>G)	C vs G	9	1526/2415	0.93(0.73-1.18)	0.538	75	0.000	11	1717/2780	0.87(0.66-1.14)	0.316	63	0.002	11	1882/2887	1.28(1.01-1.61)	0.040	39	0.088
XRCC1	Non-smokers	rs25489(p.Arg280His,c.839G>A,Ex9+16G>A)	A vs G							5	666/1266	0.68(0.34-1.37)	0.279	81	0.000						
XRCC1	Non-smokers	rs1799782(p.Arg194Trp,c.580C>T,Ex6-22C＞T)	T vs C							4	552/1313	1.16(0.92-1.48)	0.218	0	0.624	3	395/468	1.39(0.48-4.05)	0.547	42	0.180
XRCC1	Non-smokers	rs25487(p.Gln399Arg,c.1196A>G)	A vs G	7	823/1644	1.01(0.76-1.34)	0.956	72	0.002	10	956/1923	1.04(0.74-1.46)	0.839	69	0.001	7	823/1644	1.04(0.63-1.70)	0.892	57	0.031
XRCC1	Non-smokers	rs3213245(-77T>C)	C vs T							3	977/1310	1.43(1.17-1.75)	4.56×10^{-4}	0	0.530						
XRCC3	Non-smokers	rs861539(p.Thr241Met,c.722C>T)	T vs C							3	180/281	0.87(0.42-1.82)	0.713	48	0.145						

Del=deletion.

[a] Allelic contrast or phenotype trait for common variants; genetic comparison for rare variants or variants only with genotype group data

[b] *P*-value of heterogeneity between studies

Supplementary Table S8. Credibility assessment for variants with significant associations with lung cancer risk in subgroup meta-analyses by smoking status

Genes	Sub-group	Variants	Alleles[a]	Number evaluated		Lung cancer risk meta-analysis					Venice criteria grades[d]	Credibility of evidence[e]	Amount of evidence[f]		Replication[g]	Protection from bias[h]			Sensitivity analysis[i]			Low OR[j]	Modified P[k]	Excess P[l]	Begg's P[m]
																			Initial study influence		Deviation from HWE				
				Studies	Cases/Controls	Genetic models	OR(95% CI)[b]	P value	I^2 (%)	P_Q[c]			Numbers	Grade		Grade	Reasons for bias	Reason for bias exemption	OR(95%CI)	P value					
APEX1	Smokers	rs1760944	A/C	3	655/647	Allelic	1.37(1.11-1.69)	0.003	43	0.174	ABA	Moderate	1391	A	B	A			1.50(1.25-1.80)	9.90×10^{-6}	None	No	0.215	1.000	1.000
CHRNA5	Smokers	rs16969968	A/G	4	2828/3738	Allelic	1.30(1.20-1.42)	2.77×10^{-10}	0	0.626	AAC	Weak	3925	A	A	C	Small study		1.29(1.19-1.41)	1.27×10^{-9}	None	No	0.093	0.317	0.174
CYP1A1	Smokers	rs4646903	C/T	7	1034/1087	Allelic	1.30(1.02-1.64)	0.033	46	0.088	BBA	Moderate	749	B	B	A			1.35(1.01-1.81)	0.043	NO	No	0.145	0.355	0.230
CYP1A1	Smokers	rs1048943	G/A	14	1888/2413	Dominant	1.42(1.04-1.93)	0.028	78	0	ACC	Weak	1493	A	C	C	First study,HWE,small study, excess of significant studies		1.38(1.00-1.92)	0.052	Yes	No	0.060	0.098	0.189
CYP1B1	Smokers	rs1800440	G/A	3	447/449	Dominant	0.70(0.51-0.95)	0.024	0	0.481	BAC	Weak	252	B	A	C	First study		0.82(0.53-1.28)	0.388	None	No	0.364	0.523	1.000
CYP1B1	Smokers	rs1056836	G/C	5	622/684	Dominant	1.28(1.01-1.62)	0.045	0	0.616	BAC	Weak	773	B	A	C	First study		1.28(0.99-1.66)	0.064	NO	No	0.881	1.000	0.806
CYP2A6	Smokers	rs5031016	C/T	3	1527/1138	Allelic	0.57(0.33-1.00)	0.048	73	0.025	BCC	Weak	465	B	C	C	First study		0.46(0.17-1.24)	0.125	NO	No	0.587	1.000	0.296
CYP2A6	Smokers	non*4/*4	*4/non*4	3	1339/848	Allelic	0.71(0.59-0.85)	2.30×10^{-4}	13	0.319	BAA	Moderate	809	B	A	A			0.59(0.43-0.80)	0.001	NO	No	0.150	0.253	1.000
CYP2E1	Smokers	rs6413432	A/T	3	796/791	Allelic	0.75(0.63-0.90)	0.002	2	0.36	BAA	Moderate	691	B	A	A			0.74(0.62-0.88)	0.001	None	No	0.433	1.000	0.296
CYP2E1	Smokers	rs2031920	T/C	3	1064/1220	Allelic	0.76(0.65-0.90)	0.001	0	0.727	BAA	Moderate	770	B	A	A			0.78(0.66-0.92)	0.003	None	No	0.638	1.000	0.296
EPHX1	Smokers	rs2234922	G/A	5	909/845	Recessive	1.42(1.02-1.97)	0.039	0	0.535	BAC	Weak	195	B	A	C	First study		1.41(0.99-1.99)	0.055	NO	No	0.835	0.455	0.806
GSTM1	Smokers	Present/Null	NA	45	9276/9005	Null vs present	1.20(1.09-1.32)	2.16×10^{-4}	51	0	ACC	Weak	9092	A	C	C	Small study		1.19(1.08-1.31)	4.79×10^{-4}	None	No	0.070	0.354	0.304
GSTP1	Smokers	rs1138272	T/C	3	924/1026	Dominant	1.63(1.28-2.08)	9.17×10^{-5}	0	0.459	BAA	Moderate	315	B	A	A			1.64(1.01-2.68)	0.046	None	No	0.600	1.000	1.000
GSTP1	Smokers	rs1695	G/A	8	2830/2178	Allelic	1.29(1.09-1.53)	0.003	59	0.017	ACA	Weak	3118	A	C	A			1.25(1.05-1.50)	0.015	NO	No	0.298	0.474	0.536
MTHFR	Smokers	rs1801131	C/A	3	1245/1383	Allelic	1.14(1.01-1.27)	0.031	0	0.871	AAC	Weak	1728	A	A	C	First study,low OR		1.09(0.89-1.34)	0.423	NO	Yes	0.773	0.519	1.000
NAT2	Smokers	rs1799930	A/G	3	428/476	Allelic	0.81(0.66-0.99)	0.044	0	0.453	BAC	Weak	514	B	A	C	Small study		0.76(0.61-0.96)	0.020	None	No	0.067	0.460	0.296
NBN	Smokers	rs1805794	G/C	3	1226/1220	Recessive	0.83(0.71-0.98)	0.03	0	0.554	BAA	Moderate	930	B	A	A			0.81(0.66-0.98)	0.030	None	No	0.240	0.519	0.296
SOD2	Smokers	rs4880	T/C	3	1444/1188	Allelic	1.25(1.06-1.48)	0.007	33	0.224	ABC	Weak	2650	A	B	C	First study		1.60(0.76-3.39)	0.215	NO	No	0.263	1.000	0.296
TP53	Smokers	rs1042522	C/G	9	2747/2426	Dominant	1.23(1.01-1.50)	0.035	57	0.017	ACC	Weak	2971	A	C	C	First study, excess of significant studies		1.21(0.98-1.49)	0.084	NO	No	0.884	0.016	0.677
XRCC1	Smokers	rs25489	A/G	3	724/762	Allelic	1.35(1.00-1.81)	0.048	0	0.589	BAC	Weak	192	B	A	C	First study,HWE,small study		1.50(0.99-2.27)	0.054	Yes	No	0.012	1.000	0.296
XRCC1	Smokers	rs1799782	T/C	6	1597/1987	Allelic	0.73(0.55-0.97)	0.028	40	0.137	BBC	Weak	445	B	B	C	First study,HWE		0.75(0.54-1.04)	0.087	Yes	No	0.410	0.321	1.000
XRCC1	Smokers	rs25487	A/G	12	4087/3678	Recessive	0.79(0.63-1.00)	0.05	41	0.068	BBC	Weak	885	B	B	C	First study,HWE		0.80(0.61-1.04)	0.100	Yes	No	0.345	1.000	0.451
ATM	Non-smokers	rs189037	A/G	3	1323/1550	Allelic	1.18(1.03-1.36)	0.018	42	0.178	ABC	Weak	2565	A	B	C	First study,small study		1.15(0.93-1.43)	0.203	None	No	0.077	0.576	1.000
CYP1A1	Non-smokers	rs1048943	G/A	4	446/561	Recessive	1.93(1.03-3.63)	0.042	32	0.218	CBC	Weak	68	C	B	C	First study		2.08(0.94-4.60)	0.069	None	No	0.684	0.199	0.734
CYP2E1	Non-smokers	rs6413432	A/T	5	315/560	Dominant	0.72(0.54-0.97)	0.028	0	0.959	BAA	Moderate	378	B	A	A			0.72(0.53-0.96)	0.026	NO	No	0.837	0.489	0.806
CYP2E1	Non-smokers	rs2031920	T/C	3	304/695	Allelic	0.70(0.54-0.90)	0.005	0	0.863	BAA	Moderate	375	B	A	A			0.70(0.54-0.90)	0.005	None	No	0.145	1.000	1.000
ERCC1	Non-smokers	rs11615	C/T	3	731/958	Allelic	0.85(0.72-0.99)	0.042	0	0.449	AAA	Strong	2550	A	A	A			0.78(0.62-0.98)	0.031	None	No	0.898	0.483	1.000
ERCC2	Non-smokers	rs13181	C/A	3	478/469	Dominant	1.88(1.36-2.58)	1.11×10^{-4}	0	0.55	BAA	Moderate	249	B	A	A			1.91(1.25-2.92)	0.003	None	No	0.295	0.251	0.296
GSTM1	Non-smokers	Present/Null	NA	32	1924/4718	Null vs present	1.37(1.16-1.61)	1.60×10^{-4}	41	0.009	ABA	Moderate	3345	A	B	A			1.40(1.18-1.65)	1.18×10^{-4}	None	No	0.408	0.116	0.212
OGG1	Non-smokers	rs1052133	G/C	10	1966/2674	Allelic	1.14(1.04-1.24)	0.007	0	0.785	AAC	Weak	4670	A	A	C	Low OR,publication bias		1.15(1.04-1.26)	0.004	NO	Yes	0.169	1.000	0.074
TP53	Non-smokers	rs1042522	C/G	11	1882/2887	Recessive	1.28(1.01-1.61)	0.04	39	0.088	ABA	Moderate	1006	A	B	A			1.29(1.00-1.65)	0.049	NO	No	0.355	0.215	0.586
XRCC1	Non-smokers	rs3213245	C/T	3	977/1310	Dominant	1.43(1.17-1.75)	4.56×10^{-4}	0	0.53	BAA	Moderate	506	B	A	A			1.39(1.09-1.77)	0.009	None	No	0.107	0.618	0.296

NA=Not Applicable.

[a] Minor alleles/major alleles (per Caucasian)

[b] Summary ORs were calculated based on the DerSimonian-Lairs random-effects model

[c] P-value of heterogeneity between studies

[d] Venice criteria grades contained assessments of three aspects: the amount of evidence, extent of replication, and protection from bias, and each assessment was assigned three levels (A, B, or C).

[e] Credibility of evidence was evaluated based on Venice criteria with three aspects (the amount of evidence, extent of replication, and protection from bias), and was categorized as strong (all three aspect grades were A), moderate (any grade was B, but not C) or weak (any grade was C).

[f] Amount of evidence, depending on total sample size of the smallest genetic group among cases and controls in each meta-analysis, was graded as A (sample size>1000), B (sample size between 100 and 1000), or C (sample size <100).

[g] Extent of replication, depending on between-study heterogeneity, was graded as A (I^2<25%), B (I^2 between 25% and 50%), or C (I^2>50%)

[h] Protection from bias, considering various potential sources of bias in meta-analysis, was graded as A when there was no demonstrable bias and bias was unlikely invalidate the association, was graded as B when there was insufficient information for identifying evidence (i.e. missing information for evaluating Hardy-Weinberg equilibrium (HWE) among controls in an individual study) although there was no obvious bias, and C when the bias was evident and/or was likely to explain the presence of association. For the C grade, it was assigned if a meta-analysis had any of the following potential sources of bias: (1) magnitude of the association was low; (2) sensitivity analysis altered the statistical significance; (3) potential small study effect; (4) possible existence of an excess of significant findings (the number of observed significant studies more than the number of expected significant studies); (5) potential publication bias.

Small study=Possible existence of potential small study effect (modified Egger's test, p<0.10); First study=Significance lost excluding the first published or first positive report; HWE=Significance lost excluding studies with controls violating HWE; Excess of significant studies=Possible existence of an excess of significant findings (excess significance test, p<0.10); Low OR=Low magnitude of the association (i.e. 0.87<OR<1.15); Publication bias= Possible existence of potential publication bias (Begg's test, p<0.10).

[i] A sensitivity analysis was performed to examine whether the significant summary ORs were robust after excluding the first published or first positive report (defined as the earliest study reported a significant association), or excluding studies with controls violating HWE. None=A meta-analysis didn't include studies with controls violating HWE or evaluated association for a variant with a phenotype change; NO=Without the influence from studies with controls violating HWE; Yes=Evidence of influence from studies with controls violating HWE.

[j] Low OR (i.e. 0.87<OR<1.15; No=Association without a low OR;Yes=Association with a low OR)

[k] P value for potential small study effect based on the modified Egger's test. (P<0.10 is usually considered evidence for significant evidence of small study effect.)

[l] P value for possible existing an excess of significant findings based on the excess significance test. (P<0.10 is usually considered evidence for significant evidence of an excess of significant findings.)

[m] P value for potential publication bias of studies based on the Begg's test. (P<0.10 is usually considered evidence for significant evidence of publication bias.)

Supplementary Table S9. Credibility assessment for variants with non-significant associations with lung cancer risk in meta-analyses for all available data (Continued on next page)

Gene	Variant	Ethnicity	Comparison[a]	Number evaluated		Lung cancer risk meta-analysis					Begg P	Evaluation of the evidence[d]			Grade of evidence[e]	Credibility of evidence[f]
				Studies	Cases/Controls	OR(95% CI)[b]	*P* value	Q	P_Q[c]	I^2(%)		Power	Replication	Bias		
ERCC1	rs16979802(15310G>C)	Caucasian	C vs G	3	1311/2114	0.87(0.74-1.03)	0.102	0.87	0.647	0	1.000	A	A	A	AAA	Strong
ERCC1	rs2298881(262G>T,C>A)	All	T vs G	4	3049/3791	0.99(0.91-1.07)	0.723	3.50	0.320	14	0.308	A	A	A	AAA	Strong
ERCC1	rs735482(p.Lys261Thr,A>C)	All	C vs A	5	1682/2797	1.02(0.91-1.15)	0.709	4.34	0.362	8	0.462	A	A	A	AAA	Strong
POLI	rs3730668(-78G>T)	All	T vs G	3	672/823	0.94(0.80-1.09)	0.397	0.63	0.731	0	1.000	A	A	A	AAA	Strong
PPARG	rs1801282(p.Pro12Ala,c.36C>G)	All	G vs C	4	2476/3377	1.00(0.88-1.12)	0.956	0.82	0.844	0	0.734	A	A	A	AAA	Strong
PTGS2	rs20417(-765G>C)	All	C vs G	4	2355/2731	0.96(0.86-1.08)	0.505	1.84	0.606	0	1.000	A	A	A	AAA	Strong
TNF	rs1799724(-857C>T,-1036C>T)	All	C vs T	3	2080/2164	0.98(0.86-1.11)	0.727	1.80	0.406	0	1.000	A	A	A	AAA	Strong
ERCC2	rs1799793(p.Asp312Asn,c.981G>A)	All	A vs G	26	10209/12967	1.02(0.95-1.09)	0.637	43.81	0.011	43	0.628	A	B	A	ABA	Moderate
TYMS	28-bp tandem repeat	All	2R vs 3R (2R vs Non-2R)	4	2052/2861	0.99(0.90-1.08)	0.742	1.79	0.618	0	1.000	A	A	B	AAB	Moderate
XPC	rs2228000(p.Ala499Val,Ex9-377C>T)	All	T vs C	6	2981/3537	1.05(0.97-1.14)	0.205	5.17	0.395	3	1.000	B	A	A	BAA	Moderate
XRCC3	rs861539(p.Thr241Met,c.722C>T)	All	T vs C	18	6407/8356	1.04(0.95-1.13)	0.414	27.73	0.048	39	0.705	A	B	A	ABA	Moderate
ABCB1	rs1045642(p.Ile1145Ile,c.3435T>C)	All	T vs C	4	1025/1080	1.30(0.79-2.16)	0.307	28.98	0.000	90	0.308	C	C	A	CCA	Weak
ACE	287-bp repeat(I/D)	All	Ins vs del	8	1730/8359	1.01(0.85-1.21)	0.885	19.95	0.006	65	0.536	A	C	C	ACC	Weak
AGER	rs1800625(-429T>C,Alu1)	Asian	C vs T	3	1656/1693	1.16(0.78-1.74)	0.468	20.99	0.000	91	1.000	C	C	A	CCA	Weak
AGER	rs2070600(p.Gly82Ser,c.244G>A)	All	A vs G	4	2104/2178	1.10(0.93-1.31)	0.270	7.15	0.067	58	0.089	C	C	C	CCC	Weak
AHR	rs2066853(Arg554Lys,Ex10+501G>A)	All	A vs G	5	1749/1925	0.96(0.84-1.10)	0.567	5.82	0.213	31	1.000	C	B	A	CBA	Weak
ALDH2	rs671(p.Glu487Lys/Glu504Lys,c.1510G>A)	All	A vs G	3	1555/2079	1.36(0.74-2.50)	0.322	29.62	0.000	93	1.000	C	C	A	CCA	Weak
APEX1	rs1048945(p.Gln51His,c.153G>C)	Caucasian	C vs G	3	745/816	0.93(0.67-1.31)	0.684	0.30	0.859	0	1.000	C	A	A	CAA	Weak
APEX1	rs2307486(p.Ile64Val,c.190A>G)	All	G vs A	4	2281/2505	0.82(0.63-1.06)	0.121	6.35	0.096	53	0.089	C	C	C	CCC	Weak
ATM	rs609429(IVS48+238C>G)	All	(GG+GC) vs CC	3	1490/1501	0.82(0.66-1.03)	0.086	3.02	0.221	34	1.000	C	B	A	CBA	Weak
ATM	rs664143(IVS34G+60A)	All	(GG+GA) vs AA	3	1465/1465	0.93(0.79-1.10)	0.392	1.61	0.447	0	0.296	C	A	C	CAC	Weak
AURKA	rs2273535(p.Phe31Ile,c.91T>A)	Caucasian	A vs T	3	2301/2069	0.96(0.86-1.06)	0.421	0.63	0.730	0	0.296	C	A	A	CAA	Weak
AURKA	rs1047972(p.Ile57Val,c.169A>G)	Caucasian	A vs G	3	2463/2283	0.96(0.86-1.07)	0.425	1.65	0.437	0	0.296	C	A	A	CAA	Weak
BRCA2	rs144848(p.Asn372His,c.1114A>C)	All	C vs A	4	1586/2513	1.00(0.82-1.21)	0.959	6.90	0.075	57	0.734	C	C	A	CCA	Weak
CASC8	rs1447295(C>A)	All	A vs C	3	1541/2057	1.00(0.88-1.14)	0.991	1.52	0.469	0	1.000	C	A	A	CAA	Weak
CASP5	rs523104(p.Leu318Val,c.748C>G)	All	C vs G	3	758/943	1.12(0.98-1.29)	0.105	1.18	0.554	0	1.000	C	A	A	CAA	Weak
CASP8	rs3834129(-6526Ndel,-/CTTACT)	All	Del vs non-del	4	2737/2696	0.95(0.77-1.17)	0.631	16.45	0.001	82	0.308	C	C	A	CCA	Weak
CASP8	rs1045485(p.Asp302His,c.853G>C)	All	C vs G	4	1054/1259	1.20(0.97-1.49)	0.101	4.02	0.260	25	1.000	C	B	A	CBA	Weak
CCND1	rs678653(G>C)	All	C vs G	3	1323/1901	1.03(0.85-1.24)	0.773	5.03	0.081	60	1.000	C	C	A	CCA	Weak
CCND1	rs9344(rs603965,p.Pro241Pro,c.723G>A)	All	A vs G	11	6058/7315	1.02(0.92-1.12)	0.696	30.90	0.001	68	0.533	C	C	C	CCC	Weak
CDKN1A	rs1801270(p.Ser31Arg,c.93C>A,6829C>A)	All	A vs C	9	4039/4804	1.04(0.89-1.21)	0.663	16.82	0.032	52	0.029	C	C	C	CCC	Weak
CDKN2A	rs3731249(p.Ala148Thr,c.442G>A)	Caucasian	(AA+AG) vs GG	3	2875/2707	1.38(0.81-2.35)	0.230	4.56	0.102	56	0.296	C	C	A	CCA	Weak
CHRNA3	rs3743073(A>C)	All	G vs T	3	1391/1500	1.27(0.89-1.83)	0.191	23.05	0.000	91	0.296	A	C	C	ACC	Weak
COMT	rs4680(p.Val158Met,c.472G>A)	All	A vs G	5	1497/1958	1.09(0.84-1.43)	0.517	21.84	0.000	82	0.806	B	C	C	BCC	Weak
CRP	rs2808630(T>C)	All	C vs T	3	826/895	0.82(0.68-1.01)	0.056	2.79	0.248	28	1.000	C	B	A	CBA	Weak
CTLA4	rs3087243(g.6230G>A,CT60)	All	A vs G	3	1132/1220	0.99(0.86-1.14)	0.887	1.05	0.591	0	0.296	C	A	A	CAA	Weak
CTLA4	rs231775(p.Thr17Ala,c.49A>G)	All	G vs A	6	2828/2953	0.88(0.64-1.21)	0.445	63.12	0.000	92	0.707	C	C	C	CCC	Weak
CTLA4	rs5742909(g.319C>T,-318C>T)	All	T vs C	4	1205/1349	0.68(0.30-1.56)	0.364	48.66	0.000	94	0.308	C	C	A	CCA	Weak
CXCL12	rs1801157(801G>A)	All	A vs G	3	489/815	1.29(0.76-2.18)	0.351	17.39	0.000	89	1.000	B	C	A	BCA	Weak
CYP17A1	rs743572(T-34C,A1/A2)	All	A2 vs A1 (G vs A)	4	1245/1689	1.03(0.89-1.19)	0.701	4.80	0.187	38	0.308	C	B	A	CBA	Weak
CYP1A1	rs1799814(m4,Thr461Asn,C>A)	All	A vs C	5	1712/1967	1.22(0.57-2.62)	0.617	51.87	0.000	92	0.806	B	C	A	BCA	Weak
CYP1A1	rs1800031(m3,T5639C)	All	(CC+CT) vs TT	3	500/919	1.32(0.83-2.11)	0.248	0.63	0.730	0	0.296	C	A	B	CAB	Weak
CYP1A1	rs2606345(IVS1+606T>G)	Caucasian	G vs T	3	2770/3609	1.00(0.91-1.11)	0.937	3.05	0.217	35	1.000	C	B	A	CBA	Weak
CYP1A2	rs2069514(CYP1A2*1C,-3860G>A)	All	A vs G	5	925/1383	1.55(0.64-3.74)	0.327	32.99	0.000	88	0.221	A	C	A	ACA	Weak
CYP1A2	rs2069526(-739T>G)	All	G vs T	3	396/494	1.70(0.77-3.76)	0.189	11.15	0.004	82	1.000	A	C	A	ACA	Weak
CYP1A2	rs35694136(-2467delT)	All	Carriers vs non-carriers	4	811/1254	1.16(0.67-2.02)	0.594	11.94	0.008	75	0.734	A	C	C	ACC	Weak
CYP1B1	rs1056827(p.Ala119Ser,c.355G>T,m2)	All	T vs G	5	1501/2245	1.16(0.90-1.50)	0.253	18.67	0.001	79	1.000	C	C	A	CCA	Weak
CYP2A13	rs8192789(p.Arg257Cys,3375C>T)	All	(TT+TC) vs CC	3	1517/2231	0.81(0.57-1.15)	0.238	3.54	0.171	43	1.000	C	B	B	CBB	Weak
CYP2C9	rs1799853(p.Arg144Cys,c.430C>T)	All	(TT+TC) vs CC	4	756/1293	1.14(0.85-1.55)	0.381	4.57	0.206	34	1.000	C	B	A	CBA	Weak
CYP2D6	Phenotype (EM/HEM/PM)	All	PM vs EM	9	1627/1970	0.80(0.53-1.22)	0.296	9.90	0.272	19	0.348	C	A	A	CAA	Weak
CYP2D6	rs1065852(p.Pro34Ser,188C>T)	All	C vs T	3	581/636	0.86(0.57-1.30)	0.463	9.94	0.007	80	0.296	C	C	C	CCC	Weak
CYP2E1	rs3813867(g.3739G>C,c.-1293G>C)	All	C vs G	4	893/1029	0.94(0.56-1.56)	0.803	8.50	0.037	65	0.734	C	C	C	CCC	Weak
CYP3A4	rs2740574(–392A>G,*1A/*1B)	All	G vs A	4	1283/956	1.20(0.73-1.97)	0.465	9.14	0.028	67	1.000	A	C	C	ACC	Weak
CYP3A5	rs776746(A6986G,CYP3A5*3,22892A>G)	All	A vs G	4	1166/929	0.65(0.36-1.16)	0.144	25.41	0.000	88	0.308	A	C	A	ACA	Weak
DRD2	rs1079597(G>A,TaqI-)	All	A vs G	3	393/509	1.09(0.86-1.38)	0.499	1.53	0.465	0	0.296	C	A	A	CAA	Weak
DRD2	rs1800497(p.Glu714Lys,A2/A1,C>T)	All	C vs T	3	451/607	1.05(0.85-1.29)	0.667	0.48	0.786	0	1.000	C	A	A	CAA	Weak
EPHX1	rs1051740(p.Tyr113His,c.337T>C)	All	C vs T	21	3461/7217	1.05(0.89-1.24)	0.564	106.98	0.000	81	0.057	C	C	C	CCC	Weak
ERCC1	rs3212948(C>G)	All	G vs C	5	2144/2544	1.04(0.89-1.22)	0.591	10.24	0.037	61	0.462	A	C	A	ACA	Weak
ERCC1	rs3212955(A>G)	All	G vs A	4	2271/2845	1.08(0.98-1.18)	0.109	2.42	0.490	0	0.734	C	A	A	CAA	Weak
ERCC1	rs3212961(IVS5+33C＞A,17677C>A)	All	A vs C	6	2207/2311	0.94(0.86-1.03)	0.167	4.90	0.428	0	1.000	C	A	A	CAA	Weak
ERCC1	rs3212986(8092C>A,14443C>A)	All	A vs C	5	4079/4475	1.00(0.94-1.08)	0.931	1.63	0.804	0	0.806	C	A	A	CAA	Weak
ERCC2	rs1052555(Asp711Asp,G>A)	All	A vs G	3	511/751	1.09(0.85-1.40)	0.493	2.95	0.228	32	0.296	C	B	A	CBA	Weak
ERCC2	rs171140(A>C)	All	C vs A	3	511/751	1.04(0.87-1.26)	0.645	0.61	0.736	0	1.000	C	A	A	CAA	Weak
ERCC2	rs1799787(IVS19-70C＞T,G>A)	All	T vs C	6	1792/2807	1.03(0.83-1.27)	0.824	10.74	0.057	54	1.000	A	C	A	ACA	Weak
ERCC4	rs1799801(p.Ser835Ser,Ex11-247T＞C)	All	C vs T	3	1009/1758	1.02(0.88-1.17)	0.835	2.16	0.339	8	1.000	C	A	A	CAA	Weak
ERCC4	rs1800067(Arg415Gln)	Caucasian	A vs G	5	1521/2420	1.10(0.92-1.32)	0.286	1.19	0.880	0	0.806	C	A	A	CAA	Weak
ERCC5	rs17655(p.Asp1104His,c.3310G>C)	All	C vs G	10	3528/4481	0.96(0.84-1.10)	0.525	29.83	0.000	70	1.000	A	C	C	ACC	Weak
ERCC6	rs2228528(p.Gly399Asp,G1275A)	All	T vs C	4	1856/2059	1.05(0.95-1.15)	0.365	2.91	0.406	0	0.734	C	A	A	CAA	Weak
EXO1	rs1047840(p.Glu589Lys,c.1765G>A)	All	A vs G	3	1114/1166	1.23(0.96-1.57)	0.099	6.15	0.046	68	1.000	C	C	A	CCA	Weak
FANCG	rs2237857(p.Thr297Ile,C1382T)	All	T vs C	3	1553/1774	0.98(0.68-1.41)	0.903	4.52	0.104	56	1.000	C	C	A	CCA	Weak
GPC5	rs2352028(C>T)	Asian	T vs C	3	1648/2002	0.97(0.87-1.09)	0.611	1.43	0.490	0	1.000	C	A	A	CAA	Weak
GPX1	rs1050450(p.Pro200Leu,c.599C>T)	Caucasian	T vs C	4	976/1339	1.04(0.75-1.44)	0.811	16.02	0.001	81	0.734	C	C	A	CCA	Weak
GSTM3	rs1799735(c.468+21delAGG,3bp deletion,*A/*B)	All	Del vs non-del	8	1749/2069	0.97(0.86-1.09)	0.608	3.43	0.842	0	0.902	C	A	A	CAA	Weak
HIF1A	rs11549465(p.Pro582Ser,c.1744C>T)	All	T vs C	3	509/566	1.19(0.50-2.86)	0.690	18.09	0.000	89	1.000	A	C	A	ACA	Weak
IFNG	rs2069705(-1615T>C)	All	C vs T	3	2119/2654	1.02(0.93-1.11)	0.727	2.01	0.366	0	1.000	C	A	A	CAA	Weak
IGFBP3	rs2854744(C-202A)	Asian	C vs A	3	789/960	0.79(0.52-1.20)	0.262	13.99	0.001	86	0.296	C	C	A	CCA	Weak
IL10	rs1800871(c.-854T>C,-819C>T)	All	T vs C	11	3269/4627	0.93(0.76-1.14)	0.488	37.41	0.000	73	0.640	A	C	C	ACC	Weak
IL13	rs1800925(-1069C>T,-1112C>T)	All	T vs C	3	1788/1920	1.02(0.91-1.13)	0.785	0.91	0.635	0	0.296	C	A	A	CAA	Weak
IL13	rs20541(Arg130Gln,+2044G>A)	All	A vs G	3	1877/2020	1.01(0.90-1.12)	0.921	0.93	0.628	0	1.000	C	A	A	CAA	Weak
IL1B	rs1143634(p.Phe105Phe,Ex5+14C>T)	All	T vs C	5	4626/4116	1.05(0.95-1.17)	0.317	5.76	0.218	31	0.462	C	B	A	CBA	Weak
IL1B	rs16944(C-511T)	All	T vs C	11	4866/5910	0.94(0.84-1.06)	0.332	36.62	0.000	73	1.000	C	C	A	CCA	Weak
IL4	rs2243250(-509C>T)	All	T vs C	5	3496/4037	1.09(0.92-1.31)	0.320	14.46	0.006	72	0.462	A	C	A	ACA	Weak
IL6	rs1800795(G-174C)	All	C vs G	10	4619/5490	1.08(0.94-1.24)	0.287	28.73	0.001	69	0.858	C	C	A	CCA	Weak
IL8	rs4073(T-251A)	All	T vs A	7	4787/5310	1.02(0.90-1.15)	0.764	18.80	0.005	68	1.000	C	C	A	CCA	Weak
LIG1	rs20579(-7C>T)	All	A vs G	5	1818/3139	1.12(0.84-1.51)	0.440	23.17	0.000	83	0.806	C	C	C	CCC	Weak
LIG1	rs20581(p.Asp802Asp,G>A)	All	A vs G	4	828/1386	1.02(0.90-1.17)	0.726	0.96	0.810	0	0.734	C	A	A	CAA	Weak
LIG1	rs3730931(IVS9-21A>G)	All	G vs A	4	1399/2364	1.05(0.80-1.38)	0.715	9.55	0.023	69	0.308	C	C	A	CCA	Weak
LIG1	rs439132(A>G)	All	G vs A	3	739/1220	1.21(0.74-1.96)	0.444	6.66	0.036	70	1.000	A	C	C	ACC	Weak
LIG1	rs20580(p.Ala170Ala,c.417C>A)	All	A vs C	6	2357/3592	0.92(0.77-1.10)	0.370	24.88	0.000	80	0.133	C	C	A	CCA	Weak
LIG4	rs1805388(p.Thr9Ile,Ex2+54C>T)	All	T vs C	3	515/1246	1.07(0.77-1.50)	0.676	4.84	1.499	59	1.000	C	C	A	CCA	Weak
LTA	rs909253(A+252G)	All	G vs A	7	941/1683	0.93(0.83-1.05)	0.263	4.55	0.603	0	0.035	C	A	C	CAC	Weak
MBD4	rs140693(p.Glu346Lys,G1212A)	Asian	A vs G	4	2295/2469	0.99(0.86-1.13)	0.881	7.04	0.071	57	1.000	C	C	A	CCA	Weak
MCP1	rs1024611(-2518A>G,PvuII)	All	G vs A	3	1985/1981	0.76(0.53-1.09)	0.134	13.04	0.001	85	1.000	C	C	A	CCA	Weak
MDM2	rs117039649(G>C,SNP285)	All	C vs G	3	1846/4400	1.10(0.89-1.37)	0.374	0.51	0.773	0	1.000	C	A	A	CAA	Weak
MDM2	rs769412(p.Glu184Glu,2164A>G,SNP354)	All	G vs A	4	1691/1915	1.02(0.91-1.14)	0.785	1.58	0.663	0	0.734	C	A	A	CAA	Weak
MGMT	rs12268840(C>T)	Caucasian	T vs C	3	247/355	0.88(0.64-1.19)	0.396	2.64	0.267	24	1.000	C	A	A	CAA	Weak
MGMT	rs12917(p.Leu115Phe,c.343C>T)	All	T vs C	7	2552/3836	1.05(0.95-1.17)	0.335	5.87	0.438	0	0.548	C	A	A	CAA	Weak
MGMT	rs1803965(Leu53Leu,171C>T,TaqI)	All	T vs C	3	1060/1149	0.96(0.80-1.15)	0.671	0.75	0.686	0	0.296	C	A	A	CAA	Weak
MGMT	rs2308321(p.Ile174Val,Ile143Val,c.520A>G)	All	G vs A	6	2023/2191	1.05(0.86-1.28)	0.649	7.97	0.158	37	0.452	C	B	A	CBA	Weak
MGMT	rs2308327(p.Lys178Arg,c.533A>G)	Caucasian	G vs A	5	759/880	0.73(0.50-1.07)	0.109	12.48	0.014	68	0.086	C	C	C	CCC	Weak
MLH1	rs1799977(p.Ile219Val,c.655A>G)	All	G vs A	5	2147/2355	0.92(0.72-1.18)	0.531	7.91	0.095	49	0.806	C	B	A	CBA	Weak
MLH3	rs175080(p.Pro844Leu,C2645T)	All	T vs C	3	1363/1540	1.03(0.79-1.33)	0.837	5.85	0.054	66	0.296	C	C	A	CCA	Weak
MMP1	rs1799750(-16071G/2G,insG)	All	2G vs 1G	10	4787/4446	1.08(0.96-1.22)	0.197	27.39	0.001	67	0.474	C	C	A	CCA	Weak
MMP3	rs3025058(-16125A/6A,-11715A/6A)	All	5A vs 6A	5	3043/2422	1.08(0.93-1.27)	0.322	8.27	0.082	52	0.027	C	C	C	CCC	Weak
MMP9	rs3918242(g.3430C>T,-1562C>T)	All	T vs C	3	1205/1099	0.89(0.69-1.14)	0.357	3.40	0.182	41	1.000	C	B	C	CBC	Weak
MSH3	rs26279(p.Ala1045Thr,c.3133G>A)	All	G vs A	4	1649/1849	0.90(0.75-1.08)	0.251	6.83	0.077	56	0.734	C	C	A	CCA	Weak
MSH6	rs1042821(p.Gly39Glu,c.116G>A)	All	A vs G	3	1454/1620	0.95(0.83-1.08)	0.415	2.30	0.317	13	0.296	C	A	A	CAA	Weak
MTHFR	rs1801133(p.Ala222Val,Ex4+79C＞T)	All	T vs C	16	8692/8412	1.10(0.98-1.24)	0.125	69.01	0.000	78	0.192	A	C	C	ACC	Weak
MTR	rs1805087(Asp919Gly,A2756G)	All	G vs A	4	2488/3335	1.06(0.93-1.22)	0.387	4.61	0.202	35	1.000	C	B	A	CBA	Weak
MUTYH	rs3219489(p.Gln324His,c.972G>C)	All	C vs G	4	1250/1137	1.10(0.86-1.39)	0.455	8.17	0.043	63	1.000	C	C	A	CCA	Weak
MYCL	L/S(EcoRI)	All	S vs L	9	636/1004	1.05(0.91-1.22)	0.530	3.99	0.858	0	1.000	C	A	A	CAA	Weak
NAT2	Rapid/slow(Acetylation Phenotype)	All	Slow vs rapid	17	3747/4852	1.06(0.90-1.25)	0.502	38.19	0.001	58	0.064	C	C	C	CCC	Weak
NAT2	rs1799929(p.Leu161Leu,481C>T)	All	T vs C	3	576/686	1.11(0.87-1.41)	0.407	4.14	0.126	52	1.000	C	C	A	CCA	Weak
NFKB1	rs28362491(-94ins/delATTG)	All	Ins vs del	3	935/935	1.02(0.72-1.43)	0.919	11.51	0.003	83	0.296	C	C	C	CCC	Weak

Gene	Variant	Ethnicity	Comparison[a]	Number evaluated		Lung cancer risk meta-analysis					Begg P	Evaluation of the evidence[d]			Grade of evidence[e]	Credibility of evidence[f]
				Studies	Cases/Controls	OR(95% CI)[b]	*P* value	Q	P_Q[c]	I^2(%)		Power	Replication	Bias		
PADPRP	A/B(a 193-bp deletion)	All	Del vs non-del	3	288/292	1.13(0.70-1.82)	0.617	6.42	0.040	69	0.296	C	C	A	CCA	Weak
PARP1	rs1136410(p.Val762Ala,Ex17+8T＞C)	All	C vs T	6	3192/2874	1.01(0.89-1.15)	0.842	12.64	0.027	60	1.000	C	C	A	CCA	Weak
PCNA	rs25406(2232C>T)	All	T vs C	4	970/1302	0.91(0.77-1.06)	0.231	4.99	0.172	40	0.734	C	B	A	CBA	Weak
POLD1	rs1726801(p.Arg119His,c.356G>A)	Asian	A vs G	3	1263/1420	1.11(0.96-1.28)	0.168	1.61	0.448	0	0.296	C	A	C	CAC	Weak
POLI	rs8305(Thr706Ala,2180A>G)	All	G vs A	4	1655/2593	1.09(0.98-1.20)	0.111	2.17	0.537	0	0.734	C	A	A	CAA	Weak
POLL	rs3730477(p.Arg438Trp,1683C>T)	All	T vs C	3	1356/1542	1.29(0.69-2.40)	0.425	4.07	0.131	51	1.000	C	C	A	CCA	Weak
PPP1R13L	rs6966(T>A)	All	T vs A	5	1120/1361	1.09(0.92-1.29)	0.302	6.96	0.138	43	0.806	C	B	A	CBA	Weak
PPP1R13L	rs1970764(IVS1-4364A>G)	All	G vs A	3	678/726	1.12(0.90-1.39)	0.313	3.24	0.198	38	1.000	C	B	A	CBA	Weak
PTGS2	rs5275(c.*427T>C,8473T>C)	All	C vs T	11	6813/7988	0.95(0.83-1.09)	0.493	58.16	0.000	83	0.755	C	C	C	CCC	Weak
RAD23B	rs1805329(p.Ala249Val,Ex7+65C＞T)	All	T vs C	4	653/878	1.10(0.80-1.51)	0.572	9.39	0.025	68	0.089	C	C	C	CCC	Weak
REV1	rs3087386(p.Phe257Ser,892T>C)	All	C vs T	3	1437/1818	1.03(0.92-1.14)	0.658	0.51	0.775	0	1.000	C	A	A	CAA	Weak
SULT1A1	rs9282861(p.Arg213His,c.638G>A,*1/*2)	All	A vs G	6	1965/2286	1.20(0.97-1.48)	0.094	18.08	0.003	72	1.000	C	C	A	CCA	Weak
TDG	rs4135113(p.Gly199Ser,c.595G>A)	All	A vs G	3	289/318	0.85(0.51-1.42)	0.531	1.45	0.485	0	1.000	C	A	A	CAA	Weak
TGFB1	rs1800469(C-509T)	Asian	T vs C	4	1091/1238	0.95(0.85-1.07)	0.428	3.10	0.377	3	0.089	C	A	C	CAC	Weak
TGFB1	rs1800470(p.Leu10Pro,c.29C>T)	All	C vs T	7	1398/1553	1.16(0.97-1.39)	0.104	15.61	0.016	62	0.764	C	C	A	CCA	Weak
TNF	rs361525(A-417G,-238G>A)	All	A vs G	6	1047/1099	1.07(0.55-2.08)	0.847	33.99	0.000	85	0.133	C	C	C	CCC	Weak
TNFRSF10A	rs2230229(p.Arg441Lys,c.1322G>A)	All	G vs A	5	1479/1932	1.06(0.80-1.39)	0.702	11.74	0.019	66	0.806	C	C	A	CCA	Weak
TP53	rs1625895(IVS6+62G>A,A2>A1)	All	A vs G	8	2666/2847	1.10(0.90-1.34)	0.351	17.49	0.014	60	0.386	C	C	A	CCA	Weak
TP53	rs1642785(IVS2+38G>C,1827G>C)	All	C vs G	5	534/621	1.05(0.88-1.25)	0.614	3.00	0.559	0	0.086	C	A	C	CAC	Weak
TP53	rs17878362(IVS316bpDel/Ins)	Caucasian	Ins vs del	4	4196/4327	1.13(0.96-1.34)	0.152	8.22	0.042	64	0.734	C	C	A	CCA	Weak
TP53BP1	rs560191(p.Asp353Glu,c.1059C>G）	All	G vs C	3	1393/1373	0.94(0.69-1.30)	0.723	15.68	0.000	87	1.000	C	C	A	CCA	Weak
TP73	G4C14/A4T14	All	AT vs GC	7	3054/3311	1.04(0.88-1.24)	0.647	23.42	0.001	74	0.024	C	C	C	CCC	Weak
UGT1A6	rs1105879(p.Arg184Ser,c.552A>C)	All	G vs T	3	253/250	3.03(0.79-11.62)	0.106	36.84	0.000	95	0.296	A	C	A	ACA	Weak
VEGFA	rs2010963(634G>C)	All	C vs G	5	2989/2522	1.12(0.99-1.27)	0.083	7.23	0.124	45	0.806	C	B	A	CBA	Weak
VEGFA	rs3025039(C936T)	All	T vs C	6	2887/2506	1.01(0.87-1.17)	0.917	7.10	0.213	30	1.000	C	B	A	CBA	Weak
VEGFA	rs699947(C-2578A)	All	A vs C	4	879/804	0.97(0.81-1.15)	0.712	3.60	0.308	17	0.308	C	A	A	CAA	Weak
vWF	rs9295740(G>A)	All	A vs G	3	2221/2334	1.02(0.92-1.13)	0.685	0.59	0.744	0	0.296	C	A	A	CAA	Weak
XRCC1	rs2030404(A>G)	All	G vs A	3	514/751	0.98(0.83-1.17)	0.836	2.05	0.359	2	1.000	C	A	A	CAA	Weak
XRCC1	rs25486(A>G)	All	G vs A	3	507/795	0.99(0.74-1.34)	0.955	5.17	0.076	61	1.000	C	C	A	CCA	Weak
XRCC1	rs2682562(A>G)	All	G vs A	3	513/751	1.00(0.79-1.25)	0.974	0.70	0.705	0	1.000	C	A	A	CAA	Weak
XRCC1	rs2682585(p.His6Arg,c.17A>G)	All	A vs G	3	514/749	1.09(0.88-1.35)	0.416	1.91	0.385	0	1.000	C	A	A	CAA	Weak
XRCC1	rs2854510(A>G)	All	G vs A	3	513/751	0.97(0.79-1.20)	0.777	0.48	0.785	0	0.296	C	A	A	CAA	Weak
XRCC1	rs3213403(A>G)	All	G vs A	3	511/751	0.98(0.72-1.33)	0.880	2.19	0.335	9	1.000	C	A	A	CAA	Weak
XRCC1	rs3547(p.Gln632Gln,c.1896G>A)	All	A vs G	5	881/1201	1.00(0.86-1.17)	0.991	1.17	0.884	0	0.806	C	A	A	CAA	Weak
XRCC2	rs3218536(p.Arg188His,c.563G>A)	Caucasian	A vs G	3	645/1373	1.23(0.54-2.77)	0.625	16.79	0.000	88	1.000	A	C	C	ACC	Weak
XRCC3	rs1799796(17893A>G,IVS5-14)	All	G vs A	5	1478/3040	1.02(0.92-1.12)	0.756	3.45	0.486	0	0.806	C	A	A	CAA	Weak

Ins=insertion; Del=deletion; NA=Not Applicable.

[a] Allelic contrast (minor alleles vs major alleles) used in meta-analysis

[b] Summary ORs were calculated based on the DerSimonian-Lairs random-effects model

[c] *P*-value of heterogeneity between studies based on the Q statistic across crudes OR calculated for each enrolled study

[d] Evaluation of the evidence for the non-significant associations based on three aspects: statistical power, the degree of heterogeneity across studies, and potential bias assessment. Assessment of each aspect was assigned three levels (A, B, or C).

Statistical power, calculated by using SNP tools (see Methods in manuscript), was graded as A (Power≥90%), B (Power between 80% and 90%), or C (Power<80%). Replication, depending on the degree of heterogeneity across studies, was graded as A (I^2<25%), B (I^2 between 25% and 50%), or C (I^2>50%). Bias, considering various potential sources of bias in meta-analysis, was graded as A when there was no demonstrable bias and bias was unlikely alter the direction of summary ORs of non-significant associations, was graded as B when there was insufficient information for identifying evidence (i.e. missing information for evaluating Hardy-Weinberg equilibrium (HWE) among controls in an individual study) although there was no obvious bias, and graded as C when the bias was evident and/or was likely to explain the presence of non-significant association. For the C grade of assessment for potential bias, it was assigned if a meta-analysis had any of the following potential sources of bias: (1) the association became statistical significant after excluding studies that showed HWE deviation in controls; (2) potential small study effect (modified Egger's test, p<0.10); (3) possible existence of an excess of significant findings (excess significance test, p<0.10); (4) potential publication bias (Begg's test, p<0.10).

[e] Grade of evidence based on three aspects, including the evaluations of statistical power, replication of evidence, and potential bias.

[f] Credibility of evidence for non-significant association based on the ratings of evidence with three aspects, and was categorized as strong (all three aspect grades were A), moderate (any grade was B, but not C) or weak (any grade was C).

Supplementary literatures

Lists of 1,018 eligible studies enrolled in this comprehensive research synopsis (pp 77-133)

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