Original Article

Association of DNMT3B -283 T > C and -579 G > T polymorphisms with decreased cancer risk: evidence from a meta-analysis

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Abstract: Numerous studies have explored the association of polymorphisms in the DNA methyltransferase 3b (DNMT3B) gene with the risk of different types of cancer, but yielded controversial results. Therefore, we performed a meta-analysis to derive a more precise estimation of the association between three widely-studied DNMT3B polymorphisms and overall cancer susceptibility. Totally, 4 studies with 1234 cases and 1337 controls were eligible for DNMT3B -283 T > C (rs6087990), 19 studies with 5332 cases and 7407 controls for DNMT3B -149 C > T (rs2424913), and 14 studies with 3933 cases and 4436 controls for DNMT3B -579 G > T (rs1569686). Overall, DNMT3B -283 T > C was associated with a significantly reduced risk of overall cancer (T vs. C: OR = 0.84, 95% CI = 0.71-0.99, P = 0.039). Likewise, the association of DNMT3B -579 G > T with a decreased overall cancer risk was also observed (heterozygous: OR = 0.77, 95% CI = 0.65-0.91, P = 0.003 and dominant: OR = 0.80, 95% CI = 0.66-0.98, P = 0.029); in the subgroup analysis, the protective association was found for lung and colorectal cancer, but not for head and neck cancer. Finally, the pooled analysis showed no significant association between DNMT3B -149 C > T and overall cancer susceptibility, but stratification analysis indicated that this polymorphism decreased the risk of developing head and neck cancer (heterozygous: OR = 0.73, 95% CI = 0.59-0.90, P = 0.003 and dominant: OR = 0.76, 95% CI = 0.61-0.93, P = 0.009). In conclusion, our results suggested that DNMT3B -283 T > C and DNMT3B -579 G > T might confer protection against overall cancer risk. In the future, large and well-designed case-control studies are needed to validate our findings.

Keywords: DNMT3B, polymorphisms, cancer, risk, meta-analysis

Introduction

Cancer is a serious public health problem, with over 12 million new cancer cases diagnosed worldwide each year [1]. Genetic factors play an important role in the development of cancer [2]. DNA methylation, one of the epigenetic markers, can regulate the gene activity and may contribute to the initiation and development of cancer. In human, aberrations of DNA methylation have been found to associate with inactivating of microRNA, which is involved in the maintenance of global gene expression patterns. Moreover, DNA methylation also participates in the modification of histone structure that is commonly disrupted in cancer cells [3-7]. DNA methyltransferases (DNMTs) are the key effectors to establish and maintain proper DNA methylation patterns by converting cytosine residues to 5-methylcytosine (5 mC) within the cytosine-guanine (CpG) dinucleotides [8, 9]. DNMTs family encompasses three active forms, DNMT1, DNMT3A and DNMT3B. DNMT1 has been reported to maintain DNA methylation patterns during replication, whereas DNMT3A and DNMT3B are responsible for de novo DNA methylation during embryogenesis and germ cell development [4, 6, 10]. Overexpression of DNMT3B has been found in several different types of tumors, suggesting that DNMT3B plays a critical role in carcinogenesis [11-13].

Human DNMT3B gene is located on chromosome 20q11.2 and encodes DNA methyltrans-
DNMT3B polymorphisms and cancer risk

DNMT3B ferase 3b (DNMT3B). Single nucleotide polymorphisms (SNPs) in the promoter of DNMT3B gene have been reported to be associated with a wide spectrum of cancer, such as colorectal cancer, head and neck cancer, gastric cancer, lung cancer and acute myeloid leukemia [14-18]. Among them, the following three promoter SNPs may be able to alter the promoter activity: DNMT3B -149 C > T (rs2424913, in the transcription start site), DNMT3B -579 G > T (rs1569686, in the exon 1B transcription start site) and DNMT3B -283 T > C (rs6087990, in the exon 1A transcription start site). The three SNPs and their association with cancer risk have been widely studied. However, the individual studies have appeared to either support or negate the association of these SNPs with cancer susceptibility. Therefore, there is an urgent need to determine whether there is a truly association between them.

So far, there were two previously published meta-analyses conducted in 2012 focusing on the association of DNMT3B polymorphisms with cancer risk. One of them only involved DNMT3B -149 C > T and colorectal cancer, and the other was performed to merely investigate the association between DNMT3B -149 C > T and DNMT3B -579 G > T and cancer risk [19, 20]. Recently, there have been at least 9 newly published studies, concerning the relationship between these two DNMT3B polymorphisms and cancer. In addition, DNMT3B -283 T > C polymorphism was not evaluated in the two previous meta-analyses. Hence, we performed an updated meta-analysis to assess the association between the three most frequently reported DNMT3B SNPs (-149 C > T, -579 G > T and -283 T > C) and overall cancer risk.

Inclusion/exclusion criteria

Studies were eligible for inclusion in this meta-analysis if they met the following criteria: 1) case-control studies; 2) focused on the association of DNMT3B polymorphisms (-149 C > T, -579 G > T and -283 T > C) and cancer risk; 3) studies with sufficient raw data for estimating odds ratios (ORs) and 95% confidence intervals [21]. Exclusion criteria were as follows: 1) reviews; 2) cancer-only studies; 3) publication with overlapped subjects; 4) genotype distribution of control group was not in Hardy-Weinberg equilibrium (HWE). If studies had partly overlapped subjects, only the latest study or the one with largest sample size was chosen.

Data extraction

Using a standardized form, information from all the publications were independently extracted by two of the authors. We recorded the first author, year of publication, cancer type, genotype methods, ethnicity, and numbers of cases and controls with the different genotypes for each of DNMT3B SNPs. In the subgroup analysis by cancer type, if there was only one study regarding a specific type of cancer, we merged the study into “other” group.

Quality assessment

We assessed the quality of each study using the quality assessment criteria [22, 23]. The quality assessment criteria included seven aspects: 1) representativeness of case, 0-2 points; 2) representativeness of control, 0-3 points; 3) ascertainment of cancer case, 0-2 points; 4) control selection, 0-2 points; 5) genotyping examination, 0-2 points; 6) HWE; 0-1 points; and 7) total sample size, 0-3 points. Quality scores ranged from 0 to 15. Studies with scores > 9 were considered as high quality studies; otherwise, studies were considered to have a low quality.

Statistical analysis

We conducted all statistical analysis using STATA software (Version 11.0; Stata Corp LP, College Station, TX). ORs and their corresponding 95% CI were applied to evaluate the strength of association between DNMT3B gene polymorphisms and cancer risk. Heterogeneity between studies was tested by Chi square-
DNMT3B polymorphisms and cancer risk

Based Q-test. A $P > 0.10$ indicated a lack of observed heterogeneity between studies, and then, the fixed-effects model was used to calculate the pooled ORs [24]. Otherwise, the random-effects model was used [25]. Publication bias was checked using Begger's funnel plots and Egger's linear regression test [26].

Results

Study characteristics

As shown in Figure 1, a total of 101 potential relevant articles were found. After initial examination of titles and abstracts, 64 publications were excluded. Of the remaining 37 relevant publications, 11 studies were further removed for the following reasons: one was cancer-only study [27], two did not investigate any of the three DNMT3B polymorphisms [28, 29], one reported on the same population as another included study [30], two failed to provide sufficient genotype distribution data [31, 32], and five were deviated from HWE [33-37]. As a result, 26 eligible studies were included in the final meta-analysis, including 4 articles (1234 cases and 1337 controls) for DNMT3B -283 T > C [17, 18, 38, 39], 19 articles (5332 cases and 7407 controls) for DNMT3B -149 C > T [14-16, 40-55], and 14 articles (3933 cases and 4436 controls) for DNMT3B -579 G > T [15-18, 38-42, 48, 49, 56-58]. The genotype distributions in control groups for the DNMT3B -149 C > T and DNMT3B -579 G > T polymorphism were all in compliance with HWE in all included studies, whereas the genotype distributions of DNMT3B -283 T > C was deviated from HWE in one study [18]. Since the distribution of DNMT3B -579 G > T followed HWE (HWE = 0.27) in this study [18], we decided to include this one in our final meta-analysis.

As summarized in Table 1, all the four studies for DNMT3B -283 T > C were conducted among Asians. In term of DNMT3B -149 C > T, there were two head and neck cancer, two gastric cancer, three hepatocellular cancer, and seven colorectal cancer studies, as well as five studies on “other” cancer. Eleven studies focused on Caucasians, seven on Asians and one on mixed ethnicity. For DNMT3B -579 G > T, there were 2 lung cancer, 2 gastric cancer and 2 head and neck cancer studies identified. Moreover, 8 studies were merged into “other” group. Among these studies, 3 studies were conducted on Caucasians and 11 on Asians. All 4 studies were classified as high quality studies for DNMT3B -283 T > C, while 7 and 3 studies were classified as low quality studies for DNMT3B -149 C > T and -579 G > T, respectively.

Meta-analysis results

First of all, individuals with rs6087990 (-283 T > C) TT or CT genotype were not significantly association with cancer risk compared with carriers of wild type CC genotype (TT vs. CC: OR = 0.71, 95% CI = 0.45-1.14, $P = 0.161$) and CT vs. CC: OR = 0.87, 95% CI = 0.72-1.06, $P = 0.170$). Similarly, no significantly association were found under the recessive and dominant
DNMT3B polymorphisms and cancer risk

Table 1. Characteristics of eligible studies in this meta-analysis

<table>
<thead>
<tr>
<th>Surname</th>
<th>Year</th>
<th>Ethnicity</th>
<th>Cancer type</th>
<th>Genotype method</th>
<th>Case</th>
<th>Control</th>
<th>HWE</th>
<th>Score</th>
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<td>Acute myeloid leukemia</td>
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<tr>
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<td>Asian</td>
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-283 T > C
-149 C > T

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-579 G > T

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HRM, high-resolution melting method; MALDI-TOF, matrix-assisted laser desorption/ionization time-of-flight; PCR-RFLP, polymerase chain reaction restriction fragment length polymorphisms; SBE, single base extension; SSCP, single-strand conformational polymorphism; HWE, Hardy-Weinberg equilibrium.

model (recessive: OR = 0.71, 95% CI = 0.44-1.12, P = 0.140 and dominant: OR = 0.85, 95% CI = 0.70-1.02, P = 0.080). Interestingly, comparison of allele frequency revealed that T allele was associated with significantly decreased risk of cancer compared with C allele (T vs. C: OR = 0.84, 95% CI = 0.71-0.99, P = 0.039) (Table 2 and Figure 2).
## Table 2. Meta-analysis of the association between studied DNMT3B polymorphisms and cancer risk

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<th>N (Case/Control)</th>
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<th>OR (95% Cl)</th>
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<th>OR (95% Cl)</th>
<th>Phet</th>
<th>OR (95% Cl)</th>
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<td>TT vs. CC</td>
<td>CT vs. CC</td>
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<td>(CT + TT) vs. CC</td>
<td>T vs. C</td>
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<td>0.71 (0.44-1.12)</td>
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<td>1.18 (0.45-3.04)</td>
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<td>1.06 (0.90-1.25)</td>
<td>0.370</td>
<td>1.08 (0.93-1.26)</td>
<td>0.685</td>
<td>1.00 (0.88-1.13)</td>
<td>0.047</td>
<td>1.07 (0.93-1.23)</td>
<td>0.799</td>
<td>1.01 (0.91-1.11)</td>
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<tr>
<td>Gastric</td>
<td>2 (471/556)</td>
<td>-</td>
<td>-</td>
<td>0.64 (0.28-1.45)</td>
<td>0.956</td>
<td>-</td>
<td>-</td>
<td>0.64 (0.28-1.45)</td>
<td>0.956</td>
<td>0.65 (0.29-1.45)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (822/920)</td>
<td>1.19 (0.85-1.67)</td>
<td>0.147</td>
<td>1.65 (0.92-2.97)</td>
<td>0.003</td>
<td>0.99 (0.77-1.28)</td>
<td>0.300</td>
<td>1.59 (0.89-2.82)</td>
<td>0.002</td>
<td>1.23 (0.87-1.75)</td>
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<tr>
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<tr>
<td>Caucasian</td>
<td>11 (3738/5342)</td>
<td>1.01 (0.89-1.14)</td>
<td>0.199</td>
<td>1.08 (0.86-1.34)</td>
<td>0.001</td>
<td>1.02 (0.92-1.12)</td>
<td>0.909</td>
<td>1.06 (0.87-1.30)</td>
<td>0.002</td>
<td>1.02 (0.95-1.09)</td>
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<tr>
<td>Asian</td>
<td>7 (1520/1993)</td>
<td>4.94 (0.20-122.01)</td>
<td>-</td>
<td>1.06 (0.46-2.47)</td>
<td>0.015</td>
<td>4.52 (0.18-111.74)</td>
<td>-</td>
<td>1.07 (0.45-2.55)</td>
<td>0.011</td>
<td>1.08 (0.45-2.57)</td>
</tr>
<tr>
<td>Mixed</td>
<td>1 (74/72)</td>
<td>0.43 (0.17-1.11)</td>
<td>-</td>
<td>1.67 (0.73-3.80)</td>
<td>-</td>
<td>0.30 (0.14-0.66)</td>
<td>-</td>
<td>1.04 (0.48-2.23)</td>
<td>-</td>
<td>0.64 (0.40-1.02)</td>
</tr>
<tr>
<td>-579 G &gt; T</td>
<td></td>
<td>GG vs. TT</td>
<td>GT vs. TT</td>
<td>GG vs. (GT + TT)</td>
<td>(GT + GG) vs. TT</td>
<td>G vs. T</td>
<td></td>
<td></td>
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<tr>
<td>All</td>
<td>14 (3933/4436)</td>
<td>1.16 (0.73-1.87)</td>
<td>0.006</td>
<td>0.77 (0.65-0.91)</td>
<td>0.021</td>
<td>1.26 (0.85-1.87)</td>
<td>0.014</td>
<td>0.80 (0.66-0.98)</td>
<td>&lt; 0.001</td>
<td>0.86 (0.71-1.04)</td>
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<tr>
<td>Cancer type</td>
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<tr>
<td>Lung</td>
<td>2 (613/567)</td>
<td>0.63 (0.20-2.01)</td>
<td>0.442</td>
<td>0.70 (0.52-0.93)</td>
<td>0.323</td>
<td>0.68 (0.21-1.25)</td>
<td>0.431</td>
<td>0.69 (0.52-0.92)</td>
<td>0.416</td>
<td>0.72 (0.56-0.93)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>2 (681/841)</td>
<td>0.69 (0.06-7.75)</td>
<td>0.139</td>
<td>0.51 (0.37-0.69)</td>
<td>0.410</td>
<td>0.75 (0.07-8.63)</td>
<td>0.136</td>
<td>0.51 (0.38-0.70)</td>
<td>0.698</td>
<td>0.55 (0.41-0.73)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>2 (1058/1092)</td>
<td>0.86 (0.65-1.13)</td>
<td>-</td>
<td>0.82 (0.64-1.04)</td>
<td>0.950</td>
<td>0.99 (0.81-1.21)</td>
<td>-</td>
<td>0.83 (0.66-1.04)</td>
<td>0.898</td>
<td>0.93 (0.82-1.07)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (1581/1936)</td>
<td>1.39 (0.71-2.73)</td>
<td>0.014</td>
<td>0.88 (0.69-1.11)</td>
<td>0.073</td>
<td>1.47 (0.81-2.68)</td>
<td>0.014</td>
<td>0.93 (0.69-1.24)</td>
<td>0.004</td>
<td>0.99 (0.74-1.32)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>3 (1061/1223)</td>
<td>0.89 (0.70-1.14)</td>
<td>0.813</td>
<td>0.81 (0.65-1.02)</td>
<td>0.925</td>
<td>1.02 (0.85-1.22)</td>
<td>0.803</td>
<td>0.84 (0.70-1.04)</td>
<td>0.906</td>
<td>0.95 (0.84-1.08)</td>
</tr>
<tr>
<td>Asian</td>
<td>11 (2872/3213)</td>
<td>1.19 (0.55-2.59)</td>
<td>0.014</td>
<td>0.76 (0.61-0.94)</td>
<td>0.005</td>
<td>1.25 (0.59-2.64)</td>
<td>0.020</td>
<td>0.78 (0.60-1.02)</td>
<td>&lt; 0.001</td>
<td>0.82 (0.62-1.08)</td>
</tr>
</tbody>
</table>
For rs2424913 (-149 C > T), its null association with risk of overall cancer was found (homozygous: OR = 1.00, 95% CI = 0.88-1.13, P = 0.973; heterozygous: OR = 1.10, 95% CI = 0.89-1.36, P = 0.392; recessive: OR = 1.00, 95% CI = 0.91-1.10, P = 0.963; dominant: OR = 1.07, 95% CI = 0.88-1.30, P = 0.513, and comparison of allele frequency: OR = 1.01, 95% CI = 0.91-1.12, P = 0.210). In the stratified analysis by ethnicity, we did not detect significant association between DNMT3B -149 C > T polymorphism and cancer susceptibility in Asian or in Caucasian populations. While data was stratified by cancer type, this polymorphism was shown to significantly decreased the risk of head and neck cancer (heterozygous: OR = 0.73, 95% CI = 0.59-0.90, P = 0.003 and dominant: OR = 0.76, 95% CI = 0.61-0.93, P = 0.009), but not the risk of hepatocellular cancer, gastric cancer, colorectal cancer and others (Table 2).

For rs1569686 (-579 G > T), interestingly, the DNMT3B -579 G > T polymorphism seemed to confer decreased overall cancer risk (heterozygous: OR = 0.77, 95% CI = 0.65-0.91, P = 0.003; dominant: OR = 0.80, 95% CI = 0.66-0.98, P = 0.029, Table 2 and Figure 3). The protective association remained significant for lung cancer (heterozygous: OR = 0.70, 95% CI = 0.52-0.93, P = 0.013; dominant: OR = 0.69, 95% CI = 0.52-0.92, P = 0.011 and allele: OR = 0.72, 95% CI = 0.56-0.93, P = 0.013), colorectal cancer (heterozygous: OR = 0.51, 95% CI = 0.37-0.69, P < 0.001; dominant: OR = 0.51, 95% CI = 0.38-0.70, P < 0.001 and comparison of allele frequency: OR = 0.55, 95% CI = 0.41-0.73, P < 0.001), and Asians (heterozygous: OR = 0.76, 95% CI = 0.61-0.94, P = 0.014).

Heterogeneity and sensitivity analyses

There were substantial between-studies heterogeneities observed for DNMT3B -149 C > T while calculating pooled risk estimates under the heterozygous model (P < 0.001), dominant model (P = 0.001), and comparison of allele frequency (P = 0.015), but not homozygous model (P = 0.132) and recessive model (P = 0.258). The leave-one-out sensitivity analysis showed that six studies changed the pooled ORs. After excluding the six studies [42, 44, 46, 48, 54, 55], the degree of heterogeneity dramatically decreased (homozygous model, P = 0.426; recessive model, P = 0.163; heterozygous model, P = 0.440; dominant model, P = 0.577 and comparison of allele frequency, P = 0.466), without qualitatively altering the overall estimates (homozygous: OR = 0.92, 95% CI = 0.73-1.17; heterozygous: OR = 0.94, 95% CI = 0.77-
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1.15; recessive: OR = 0.91, 95% CI = 0.76-1.10; dominant: OR = 0.92, 95% CI = 0.76-1.11; and comparison of allele frequency: OR = 0.94, 95% CI = 0.83-1.05). For DNMT3B -283 T > C, no significant heterogeneity was found (homozygous model, \( P = 0.969 \); recessive model, \( P = 0.976 \); heterozygous model, \( P = 0.370 \); dominant model, \( P = 0.540 \) and comparison of allele frequency, \( P = 0.717 \)). On the contrary, there is obvious heterogeneity under all the modes of inheritance for DNMT3B -579 G > T (homozygous model, \( P = 0.006 \); recessive model, \( P = 0.625 \); heterozygous model, \( P = 0.297 \); dominant model, \( P = 0.254 \) and comparison of allele frequency, \( P = 0.079 \)), without qualitatively altering the overall estimates (homozygous: OR = 0.81, 95% CI = 0.63-1.04; heterozygous: OR = 0.77, 95% CI = 0.67-0.89; recessive: OR = 0.95, 95% CI = 0.79-1.15; dominant: OR = 0.77, 95% CI = 0.67-0.88), except for comparison of allele frequency (OR = 0.85, 95% CI = 0.77-0.94).

Publication bias

There was no obvious asymmetry in Begger’s funnel plots and no significant publication bias detected by Egger’s linear regression test in the current meta-analysis, DNMT3B -283 T > C (\( P = 0.546 \) for homozygous model; \( P = 0.724 \) for recessive model; \( P = 0.684 \) for heterozygous model; \( P = 0.611 \) for dominant model, and \( P = 0.488 \) for comparison of allele frequency), DNMT3B -149 C > T (\( P = 0.535 \) for homozygous model; \( P = 0.103 \) for recessive model; \( P = 0.516 \) for heterozygous model; \( P = 0.668 \) for dominant model and \( P = 0.879 \) for comparison of allele frequency) and DNMT3B -579 G > T (\( P = 0.860 \) for homozygous model; \( P = 0.772 \) for recessive model; \( P = 0.706 \) for heterozygous model; \( P = 0.505 \) for dominant model and \( P = 0.274 \) for comparison of allele frequency).

Discussion

DNA methyltransferase 3b is necessary for the establishment and maintenance of genomic methylation patterns and facilitate proper embryonic development [59]. It was demonstrated that some polymorphisms in the DNMT3B gene could significantly increase the promoter activity in lung cancer in 2002 [35]. Since then, a number of epidemiological studies have assessed the association between DNMT3B gene polymorphisms and the risk of different types of cancer, but the findings are inconclusive. In order to resolve this conflict, this meta-analysis with 26 studies was performed to provide an updated, more precise estimation of the associations of three DNMT3B polymorphisms (-283 T > C, -149 C > T and -579 G > T) with cancer risk.

To the best of our knowledge, no previous meta-analysis has comprehensively assessed the association between the three DNMT3B polymorphisms and overall cancer risk. To data, there were only two meta-analyses investigating the association between DNMT3B polymorphisms and cancer risk [19, 20]. Fang et al. attempted to evaluate the association of the DNMT3B -149 C > T polymorphism with the risk of colorectal cancer. They pooled together seven eligible studies, comprising 2666 cases and 4022 controls, and failed to provide the evidence of such association [19]. Zhu et al. performed a meta-analyses including 5229 cases/6910 controls from 17 case-control studies for DNMT3B -149 C > T and 3513 cases/3714 controls from 11 case-control studies for DNMT3B -579 G > T in 2012 [20]. The results indicated that there was no significant association between DNMT3B -149 C > T and cancer risk under all genetic model, even in the stratified analysis by cancer type. However, a significant association of DNMT3B -579 G > T with decreased cancer risk, particularly for colorectal cancer, were found while using heterozygous model, dominant model and comparison of allele frequency. It was worth noting that Zhu et al. included some publications that were deviated from HWE [20]. In contrast, in the current meta-analysis, we excluded all publications deviate from HWE [34, 35, 37]. Moreover, we included several extra case-control studies about these two polymorphisms that were published since 2012 [14, 18, 40-42, 56]. As results, some findings in the present meta-analysis were different from those in the previous meta-analysis: 1) Unlike the previous meta-analysis, we found that DNMT3B -149 C > T was associated with a decreased risk of head...
DNMT3B polymorphisms and cancer risk

and neck cancer under the heterozygous model and dominant model; 2) We failed to replicate the significant association between DNMT3B -579 G > T and overall cancer risk under the comparison of allele frequency; 3) We found a significant association between DNMT3B -579 G > T and lung cancer under the heterozygous, dominant, and allele comparison model for the first time. The exclusion of the publication deviated from HWE and the inclusion of several additional eligible studies might reduce the chance of false positive results and increase the statistical power to evaluate the association of interest. Taken together, this meta-analysis provided some new insight into the mechanisms of the development of cancer, especially for head and neck cancer, lung cancer and colorectal cancer.

There were several limitations inherited from the published studies in this meta-analysis. First, the sample size was not large enough to draw a convincing conclusion for DNMT3B -283 T > C and the sample size in some subgroup analysis was also relatively small for DNMT3B -149 C > T and DNMT3B -579 G > T. Second, significant heterogeneities were observed under a few genetic models, thus we chose the random-effects to calculate ORs and 95% CIs. Third, due to lacking other important original data, our conclusions were based on unadjusted estimates of ORs without adjustment for environment factors such as smoking or drinking habits.

In conclusion, our meta-analysis suggests that DNMT3B -283 T > C and DNMT3B -579 G > T may play a protective role against cancer. Moreover, in the subgroup analysis, DNMT3B -579 G > T appeared to contribute to decreased risk of lung cancer and colorectal cancer as well as decreased cancer risk among Asians; meanwhile, DNMT3B -149 C > T was associated with a reduced risk of head and neck cancer. Future large-scale case-control designed prospective studies are warranted to confirm our finding in different ethnicities and in different cancer types.

Disclosure of conflict of interest

None.

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References

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