Ann Hematol (2011) 90:293–299
DOI 10.1007/s00277-010-1085-z

ORIGINAL ARTICLE

# CYP2B6 gene single nucleotide polymorphisms and leukemia susceptibility

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Received: 19 April 2010 / Accepted: 12 September 2010 / Published online: 28 September 2010


**Abstract** CYP2B6 is a highly variable and polymorphic cytochrome P450 enzyme which plays a vital role in the degradation of some endogenous metabolites, xenobiotics, and harmful compounds. The 516G>T single nucleotide polymorphism (SNP) in exon 4 of CYP2B6 gene may change CYP2B6 enzyme activity and the gene expression in the liver. Carcinogens' failure to be degraded by CYP2B6 may cause DNA injury and cancer. Here, we aimed to evaluate the association between genotype or allele of CYP2B6 516G>T SNP and acute leukemia and myelodysplastic syndrome (MDS). We recruited 300 patients including 164 cases of acute myeloid leukemia (AML), 96 cases of acute lymphoblastic leukemia (ALL, including 17 cases of T-ALL and 79 cases of B-ALL), 40 cases of MDS, as well as 348 unrelated umbilical cord blood as the controls. Karyotype analysis and multiplex reverse transcription-polymerase chain reaction (RT-PCR) was performed to determine different recurrent genetic abnormalities in these cases. Genotype of CYP2B6 516G>T SNP was determined by allele-specific primers PCR, and confirmed by gel electrophoresis and sequencing. The GT and GT+TT genotype frequencies of c.516G>T SNP were higher in ALL (37.5% and 42.7%, respectively, $P<0.01$), and AML (37.2% and 40.9%, respectively, $P<0.01$) than in control (23.9% and 25.9%, respectively). In the subtypes of acute leukemias, the GT+TT genotype frequency was significantly higher in AML with recurrent genetic abnormalities (41.7%, $p<0.05$), in AML-NOS (40.6%, $p<0.01$), in acute monoblastic and monocytic leukemia (48.3%, $p<0.01$), and in T-ALL (70.6%, $p<0.01$) as compared with those in the controls. The frequency of CYP2B6 516 T allele was higher in AML (22.3%, $p<0.01$) and ALL (24.0%, $p<0.01$) compared with cord blood (13.9%). In different types of acute leukemias, CYP2B6 516 T allele frequency was significantly higher in AML with AML1-ETO (19.2%, $p<0.05$), AML-NOS (22.7%, $p<0.01$), acute monoblastic and monocytic leukemia (25.9%, $p<0.01$), and T-ALL (38.2%, $p<0.01$). MDS was unrelated to the genotype and allele frequencies of c.516G>T SNP in CYP2B6. T allele of CYP2B6 516G>T SNP may be one of the risk factors predisposing to the pathogenesis of a majority of ALL and AML, but has no relationship with B-ALL and leukemia with or without chromosome abnormalities.

**Keywords** Cytochrome P450 2B6 · Gene polymorphism · Acute leukemia · Myelodysplastic syndrome

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## Introduction

The interaction between environmental exposure and genetic susceptibility has been postulated to be a possible cause of many types of cancers. The interindividual differences in the disposal of toxic substances resulting from the polymorphisms in the genes encoding detoxification enzymes may contribute to leukemia susceptibility [1].

Cytochrome P450, family 2, subfamily B, polypeptide 6 (CYP2B6) is a member of the cytochrome P450 superfamily and is mainly expressed in the liver [2]. CYP2B6 acts as

the phase I metabolic enzyme, and plays a key role in the biotransformation of many xenobiotics, such as cyclophosphamide, ifosphamide, ketamin, propofol, bupropion, nevirepine, efavirenz, and some carcinogens such as aflotoxin B1 [3–8]. If the xenobiotics as precarcinogens transform to their biologically active forms, they then may irreversibly react with DNA to cause mutations, chromosomal aberrations, and cancer, including hematological malignancies [9]. One of the single nucleotide polymorphisms (SNP) in exon 4 of CYP2B6 gene, 516G>T (rs3745274, Gln172His), is associated with a pronounced decrease of the gene expression and the CYP2B6 activity in the liver [10, 11]. Berköz et al. [12] reported a higher frequency of GT genotype in CYP2B6 G15631T polymorphism loci in acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL), but without detailed subtype information of these patients. In this study, we tried to classify leukemia according to WHO 2008 criteria and we aimed to explore the relationship between the CYP 2B6 516G>T SNP and the risk of acute leukemia, myelodysplastic syndrome (MDS).

## Materials and methods

### Patients and normal control

The 300 patients included 164 cases AML and related neoplasms, 96 cases ALL, and 40 cases MDS; the data were collected from Peking University First Hospital or Beijing Dao-pei Hospital during the period from March 2007 through July 2009. The 348 DNA samples of umbilical cord blood as controls were consecutively collected from the Department of Obstetrics and Gynecology, Peking University First Hospital. Of the 164 AML cases, 98 cases were males and 66 cases were females; they were 4–62 years old with the mean age of 31.3 years old. Of the 96 ALL cases, 17 cases were T-ALL (males, 12 cases and females, five cases, and 12–40 years old with the mean age of 22.8 years old), and 79 cases were B-ALL (males, 46 cases and females, 33 cases, and 3–60 years old with the mean age of 23.6 years old). Of the 40 MDS cases, 29 cases were males and 11 cases were females; they were 3–53 years old with the mean age 30.4 years old. The stratification of MDS patients is according to the WHO classification (20 cases with refractory anemia (RA), ten cases with refractory anemia with ringed sideroblasts (RARS), eight cases with refractory cytopenia with multilineage dysplasia (RCMD), and two cases with refractory anemia with excess blasts (RAEB). All cases were finally diagnosed by clinical feature, morphology, histochemical stain, as well as immunology. Genetic abnormalities in these cases were detected and analyzed.

This study was approved by the Medical Ethics Committees of Peking University First Hospital and Beijing Dao-pei Hospital, and written consent from patients or parents was obtained before the start of the study.

### Genotyping of CYP2B6 516G>T SNP

All samples from leukemia patients were obtained before treatment. Genomic DNA was extracted from peripheral blood or cord blood by the phenol–chloroform extraction method as described previously [13]. Tetra-primer ARMS-polymerase chain reaction (PCR) primers were designed using BatchPrimer3 software from website (http://batchprimer3.bioinformatics.ucdavis.edu/index.html) based on the allele-specific primer method with some modifications.

The primers for the genotyping G allele of CYP2B6 516G>T SNP were 5′-CTCATGGACCCCACCTTCCTCTTCTAG (forward primer) and 5′-CATCCTTTTCTCGTGTGTTCTGGGTG (reverse primer). The PCR product was 226 bp. Those for the T allele were 5′-AGCCTCTCGGTCTGCCCATCTATAAACT (forward primer) and 5′-AGCAGATGATGTTGGCGGTAATGAAA (reverse primer). The PCR product size was 295 bp.

Two PCRs using the two sets of primers were carried out for every DNA sample. PCR mixture contained 1× SYBR Green buffer, 5 pmol/each primer and 10–20 ng genomic DNA. The amplification was performed in a quantitative real-time PCR (Q-PCR) instrument (7,300, ABI). A typical

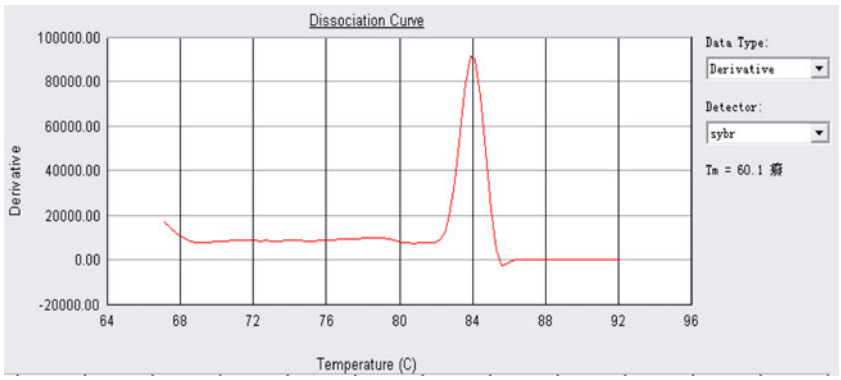


**Fig. 1** A typical dissociation curve of G allele

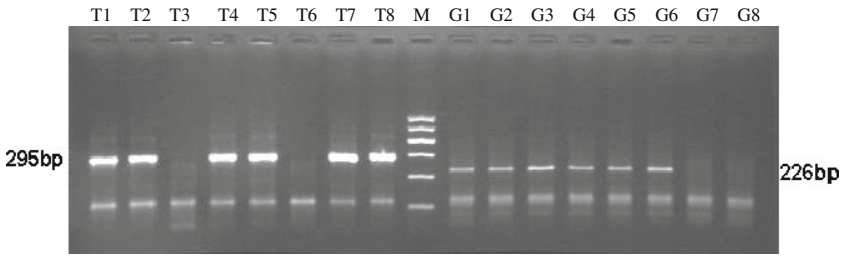


**Fig. 2** PCR product of CYP 2B6 c.516G>T gene region on 2% agarose gel electrophoresis. Samples 1–8 were amplified using T allele-specific primer (*T1–8*) and G allele-specific primer (*G1–8*). The results demonstrate that samples 1, 2, 4, and 5 were heterozygote GT genotype, samples 3 and 6 were homozygote GG genotype, and samples 7 and 8 were homozygote TT genotype

PCR product curve with a typical dissociation curve was recognized as positive, and no PCR product curve as negative. Only a typical dissociation curve of G allele was GG genotype (Fig. 1). Only a typical dissociation curve of T allele was TT genotype. Both typical dissociation curves of G and T allele were GT genotype. The genotypes of GG, TT, and GT were then identified.

PCR products were also visualized on a 2% agarose gel containing ethidium bromide. Homozygote genotype GG produced a band at 226 bp, homozygote TT produced a band at 295 bp, and heterozygote GT produced two bands of 226 and 295 bp (Fig. 2). Sequencing was also done for some samples to confirm the Q-PCR results.

### Detection of genetic abnormalities in leukemia and MDS

Chromosome G-banding karyotype analysis was manipulated according to the clinical routine. The 32 types of fusion gene resulting from chromosomal aberrations in leukemia were detected by multiplex reverse transcription-PCR (RT-PCR) as described previously [14]. These fusion genes include AML1–EAP, AML1–ETO, AML1–MDS1, BCR–ABL, CBFβ–MYH11, DEK–CAN, dupMLL, E2A–HLF, E2A–PBX1, FIP1L1–PDGFRα, MLL–AF10, MLL–AF17, MLL–AF1p, MLL–AF1q, MLL–AF4, MLL–AF6, MLL–AF9, MLL–AFX, MLL–ELL, MLL–ENL, NPM1–ALK, NPM1–MLF1, NPM1–RARα, PLZF–RARα, PML–RARα, SET–CAN, SIL–TAL1, TEL–ABL, TEL–AML1, TEL–PDGFR, TLS–ERG, and HOX11. These fusion genes include all the genetic abnormalities involved in WHO 2008 classification and common genetic abnormalities in clinic. Chromosome abnormalities can lead to the forming of fusion genes, the corresponding relationships between them are shown in Table 1.

### Statistical analysis

Differences in genotype and allele frequencies between acute leukemia and MDS patients and controls were determined by Chi-square test. $P<0.05$ was considered to be statistically significant.

## Results

### Analysis of genetic abnormalities in leukemia and MDS

Because of the one-to-one relationship between chromosome abnormalities and fusion genes, here, we only mentioned fusion genes to represent genetic abnormalities. According to WHO 2008 classification of 164 cases acute myeloid leukemia (AML), 36 cases were identified as AML with recurrent genetic abnormalities or fusion gene, including 13 cases with AML1–ETO, six cases with CBFβ–MYH11, seven cases acute promyelocytic leukemia (APL) with PML–RARα, seven cases with MLL–AF9, and three cases with DEK–CAN. One hundred and twenty eight cases were identified as acute myeloid leukemia not otherwise specified (AML-NOS), including two cases with

**Table 1** The corresponding relationships between chromosome abnormalities and fusion genes

| Chromosome abnormalities | Fusion genes |
|---|---|
| t(8;21)(q22;q22) | AML1–ETO |
| t(9;22)(q34;q11) | BCR–ABL |
| t(15;17)(q22;q11–22) | PML–RARα |
| inv(16)(p13;q22) | CBFβ–MYH11 |
| t(6;9)(p23;q34) | DEK–CAN |
| Del4q | FIP1L1–PDGFRα |
| dupMLL(11q23) | dupMLL |
| t(1;11)(p32;q23) | MLL–AF1p |
| t(6;11)(q27;q23) | MLL–AF6 |
| t(9;11)(p22;q23) | MLL–AF9 |
| t(10;11)(p12;q23) | MLL–AF10 |
| t(11;17)(q23;q21) | MLL–AF17 |
| t(X;11)(q13;q23) | MLL–AFX |
| t(11;19)(q23;p13.1) | MLL–ELL |
| t(11;19)(q23;p13.3) | MLL–ENL |
| TAL1D | SIL–TAL1 |
| t(16;21)(p11;q22) | TLS–ERG |

**Table 2** Genotype and allele frequencies of c.516G>T SNP in *CYP 2B6* in ALL

| Genotype and allele frequencies | GG*n* (%) | GT*n* (%) | TT*n* (%) | GT+TT*n* (%) | G allele*n* (%) | T allele*n* (%) |
|---|---|---|---|---|---|---|
| Control (*n*=348) | 258 (74.1) | 83 (23.9) | 7 (2.0) | 90 (25.9) | 599 (86.1) | 97 (13.9) |
| ALL (*n*=96) | 55 (57.3) | 36 (37.5)* | 5 (5.2) | 41 (42.7)* | 146 (76.0) | 46 (24.0)* |
| T-ALL (*n*=17) | 5 (29.4) | 11 (64.7)*,a | 1 (5.9) | 12 (70.6)*,a | 21 (61.8) | 13 (38.2)* |
| B-ALL (*n*=79) | 50 (63.3) | 25 (31.7) | 4 (5.1) | 29 (36.7) | 125 (79.1) | 33 (20.9)** |
| ALL with fusion gene (*n*=18) | 8 (44.4) | 10 (55.6)**,a | | 10(55.6)**,a | 26 (72.2) | 10 (27.8)** |
| ALL without fusion gene (*n*=78) | 47 (60.3) | 26 (33.3)** | 5 (6.4) | 31 (39.7)** | 120 (76.9) | 36 (23.1)* |
| T-ALL with fusion gene (*n*=3) | 0 (0.0) | 3 (100.0) | | | 3(50.0) | 3 (50.0)**,a |
| T-ALL without fusion gene (*n*=14) | 5 (35.7) | 8 (57.1)*,a | 1 (7.1) | 9 (64.3)*,a | 18 (64.3) | 10 (35.7)*,a |
| B-ALL with fusion gene (*n*=15) | 8 (53.3) | 7 (46.7) | | | 23 (76.7) | 7 (23.3) |
| B-ALL without fusion gene (*n*=64) | 42 (65.6) | 18 (28.1) | 4 (6.3) | 22 (34.4) | 102 (79.7) | 26 (20.3) |

* $P<0.01$, ** $P<0.05$, compared with that of controls

[a] Fisher's exact test

AML with minimal differentiation, nine cases with AML without maturation, 58 cases with AML with maturation, 18 cases with acute myelomonocytic leukemia, 29 cases with acute monoblastic and monocytic leukemia, and 12 cases with acute erythroid leukemia. Other types of AML and related neoplasms were not found.

Of the 96 ALL cases, positive of fusion gene had 17 cases, including two cases with SIL–TAL1(T-ALL), eight cases with BCR–ABL(one case T-ALL, seven cases B-ALL), four cases with E2A–PBX1(B-ALL), one case with MLL–AF4(B-ALL), one case with EVI1(B-ALL), and one case with HOX11(B-ALL).

Of the 40 MDS cases, 20 cases were classified as RA, ten cases as RARS, eight cases as RCMD, and two cases as RAEB. Fusion gene of the rearrangement involving EVI1 was found in two RAEB cases.

## The distribution of CYP2B6 516G>T SNP in control population

We used the umbilical cord blood DNA consecutively collected from Beijing area to represent the healthy population. The genotype types of the 348 cord blood DNA were GG 258 (74.1%), GT 83 (23.9%), and TT 7 (2.0%).

**Table 3** Genotype and allele frequencies of c.516G>T SNP *CYP 2B6* in AML

| Genotype and allele frequencies | GG*n* (%) | GT*n* (%) | TT*n* (%) | GT+TT*n* (%) | G allele*n* (%) | T allele*n* (%) |
|---|---|---|---|---|---|---|
| Control (*n*=348) | 258 (74.1) | 83 (23.9) | 7 (2.0) | 90 (25.9) | 599 (86.1) | 97 (13.9) |
| AML (*n*=164) | 97 (59.2) | 61 (37.2)* | 6 (3.7) | 67 (40.9)* | 255 (77.7) | 73 (22.3)* |
| AML with fusion genes (*n*=36) | 21 (58.3) | 15 (41.7)# | | 15 (41.7)** | 57 (79.2) | 15 (20.8) |
| With AML1-ETO(*n*=13) | 8 (61.5) | 5 (38.5) | | | 21 (80.8) | 5(19.2)**,a |
| With CBFB-MYH11 (*n*=6) | 4 (66.7) | 2 (33.3) | | | 10 (83.3) | 2 (16.7) |
| With PML-RARα (APL; *n*=7) | 3 (42.9) | 4 (57.1) | | | 10(71.4) | 4(28.6) |
| With MLLT3-MLL (*n*=7) | 4 (57.1) | 3 (42.9) | | | 11 (78.6) | 3 (21.4) |
| With DEK-NUP214 (*n*=3) | 2 (66.7) | 1 (33.3) | | | 5(83.3) | 1(16.7) |
| AML-NOS (*n*=128) | 76 (59.4) | 46 (35.9)* | 6 (4.7) | 52 (40.6)* | 198 (77.3) | 58 (22.7)* |
| With minimal differentiation (M0; *n*=2) | 2 (100.0) | 0 | | | 4 (100.0) | 0 |
| Without maturation (M1; *n*=9) | 4 (44.4) | 4 (44.4) | 1 (11.2) | 5 (55.6) | 12 (66.7) | 6 (33.3)**,a |
| With maturation (M2; *n*=58) | 36 (62.1) | 19 (32.8) | 3 (5.1) | 22 (37.9) | 91 (78.4) | 25 (21.6)** |
| Acute myelomonocytic leukemia (M4; *n*=18) | 11 (61.1) | 6 (33.3) | 1 (5.6) | 7 (38.9) | 28 (77.8) | 8 (22.2) |
| Acute monoblastic and monocytic leukemia (M5; *n*=29) | 15 (51.7) | 13 (44.8)** | 1 (3.5) | 14 (48.3)* | 43 (74.1) | 15 (25.9)** |
| Acute erythroid leukemia (M6; *n*=12) | 8 (66.7) | 4 (33.3) | | | 20 (83.3) | 4 (16.7) |

* $P<0.01$, ** $P<0.05$, compared with that of controls

[a] Fisher's exact test

**Table 4** Genotype and allele frequencies of CYP 2B6 516G>T SNP in MDS patients and controls

| Genotype/allele type | Control ($n$=348) $n$ (%) | MDS ($n$=40) $n$ (%) | $P$ |
|---|---|---|---|
| GG | 258 (74.1) | 31 (77.5) | |
| GT | 83 (23.9) | 9 (22.5) | 0.797 |
| TT | 7 (2.0) | 0 (0) | 1.000 |
| G | 599 (86.1) | 71 (88.8) | |
| T | 97 (13.9) | 9 (11.3) | 0.508 |

The genotype of CYP2B6 516G>T SNP in ALL

*The genotype of 516G>T SNP in CYP2B6 in ALL*

The genotype and allele frequencies of the SNP were compared between ALL and the controls (Table 2). More GT and GT+TT genotypes were found in ALL ($P$<0.01) compared with those in controls. These tendencies were significant ($P$<0.01) in T-ALL, but not found in B-ALL. In the subtypes of ALL, GT and GT+TT genotypes were statistically higher in ALL with fusion genes ($P$<0.05) as well as without fusion genes ($P$<0.05), and in T-ALL without fusion genes ($P$<0.01).

T allele frequency was significantly higher in ALL ($P$<0.01), including in T-ALL ($P$<0.01), in T-ALL with fusion genes ($P$<0.05), in ALL with fusion genes ($P$<0.05) as well as without fusion genes ($P$<0.01). However, the preponderance of T allele was not found in B-ALL.

*The genotype of CYP2B6 516G>T SNP in AML*

The genotype and allele frequencies of the SNP were compared between AML patients and controls (Table 3). More GT and GT+TT genotypes were found in AML ($P$<0.01), and in AML with fusion genes ($P$<0.05) and without fusion genes ($P$<0.01). In the subtype of AML-NOS patients, GT and GT+TT genotypes were statistically higher in acute monoblastic and monocytic leukemia.

T allele frequency was higher in AML than in controls ($P$<0.01). In the subtypes of AML with fusion genes, T allele frequency was significantly higher in AML with AML1–ETO ($P$<0.05). In the subtype of AML-NOS ($P$<0.01), T allele frequency was significantly higher in AML without maturation ($P$<0.05), in AML with maturation ($P$<0.05), and in acute monoblastic and monocytic leukemia ($P$<0.05).

*The genotype of CYP2B6 516G>T SNP in MDS*

Genotype and allele frequencies of the SNP were compared between MDS and controls (Table 4). The genotype frequencies of GT and TT had no differences in MDS ($P$>0.05), nor in the subtypes of MDS ($P$>0.05). In addition, T allele frequency was statistically insignificant between MDS and controls ($P$>0.05).

## Discussion

Acute leukemia is a heterogeneous disease with various biological characteristics [15]. We analyzed the relationship of CYP2B6 516G>T SNP with leukemia susceptibility. The etiology of acute leukemia is largely unknown. Environmental factors causing acute leukemia include radiation, aromatic hydrocarbons, pesticides, viral and bacterial infections, alcohol, cigarette and narcotics [1, 16–22]. Genetic etiologies of acute leukemia include mutations, single nucleotide polymorphisms, and chromosomal aberrances, especially translocations [18–20, 23, 24]. Several polymorphisms in CYP1A1, CYP2D6, CYP2E1, GSTM1, GSTT1, MTHFR, and NQO1 genes have been known to be risk factors for acute leukemia [1, 20, 21, 23, 24]. These genes encode the enzymes taking part in the catabolism of many carcinogenic and precarcinogenic xenobiotics [23, 24]. Xenobiotics such as dibenzanthracene [3], 6-aminochryse [9], styrene [25], nicotine [26], and vinyl chloride [27] can be degraded by the CYP2B6 enzyme. Genetic polymorphisms in these enzymes may result in different capabilities to dispose of carcinogens [28]. Therefore, polymorphisms in the genes encoding detoxification enzymes may be the factors contributing to the interindividual differences in leukemia susceptibility [1]. Acute leukemia originated from different transformed hematologic progenitor cells, lymphoid, or myeloid stem cells determines the diverse characteristics of ALL and AML.

CYP2B6 is located in a cluster containing six subfamilies on human chromosome 19 [10], which mediates the metabolic activation and inactivation of various drugs such as anticancer drugs [4], antidepressants [6], and antimalarials [29]. This enzyme is also involved in metabolizing many endogenous and exogenous substances, such as testosterone [30] and nicotine [31], in cooperation with other cytochromes. CYP2B6 516G>T SNP changes the amino acid residue of glutamine to histidine [32–34], and this amino acid substitution may cause the decrease of CYP2B6 enzyme activity in the liver [11]. The lower

transformation efficiency from carcinogen substrates to harmless metabolites caused by the lower CYP2B6 activity may become a risk factor for the pathogenesis of acute leukemia, in view of the fact that acute leukemia may be related to the exposure of exogenous chemicals [7, 32].

Although the correlation of the polymorphism in CYP2B6 gene to CYP2B6 enzyme activity has been reported previously, its correlation to the susceptibility of acute leukemia has been rarely found [2, 3, 9, 35] except that Berköz et al. [12] reported a higher frequency of GT genotype in CYP2B6 G15631T SNP loci in acute leukemia recently, namely the GT genotype of CYP2B6 G15631T, which may be an important genetic determinant for acute leukemias. In the present study, we investigated the relationship between CYP2B6 516G>T polymorphism and ALL, AML, and MDS as well as their subtypes diagnosed according to WHO 2008 classification. Our cases mainly included T-ALL, B-ALL, AML with recurrent genetic abnormalities, acute myeloid leukemia, NOS, etc. The RT-PCR method in detecting fusion gene resulting from chromosomal aberrations in leukemia was more sensitive than chromosome karyotype analysis. So, we adopted the results to statistics and analysis. We found that both GT and TT genotypes were related to ALL and AML, which can better demonstrate the important role of T allele in the susceptibility of ALL and AML among people. In this study, we investigated the relationship between the c.516G>T polymorphism and ALL, AML, and MDS as well as their subtypes. The frequency of T allele was higher in ALL (24.0%, odds ratio (OR)=1.946, $P<0.01$) and in AML (22.3%, OR=1.768, $P<0.01$) than in controls (13.9%). This indicated that T allele had an estimated 1.946-fold and 1.768-fold increased risk of ALL and AML, respectively, similar to the results reported by Berköz et al. [12]. T allele frequency was higher in ALL with fusion genes (27.8%, $P<0.05$) and without fusion genes (23.1%, $P<0.01$), as well as in AML with fusion genes (20.8%, $P>0.05$) and without fusion genes (22.7%, $P<0.01$). Consequently, T allele in c.516G>T SNP in CYP2B6 is a risk factor for acute leukemia, and this risk factor is unrelated to the presence or absence of fusion genes in acute leukemia. In the subtype of ALL and AML, frequencies of GT and GT+TT genotypes, and/or T allele were found to be statistically higher in T-ALL without fusion genes, T-ALL with fusion genes, AML with AML1–ETO fusion gene, and acute monoblastic and monocytic leukemia. However, their significance is undetermined due to the insufficient number of cases.

There are many studies about different alleles and genotype frequencies of CYP2B6 516G>T SNP in different ethnic populations [34, 36–38]. Genotype of CYP2B6 516G>T SNP was found to be related to the plasma efavirenz and nevirapine concentrations in adults and children treated with these drugs [39–43]. Here, we show the relationship between the genotype of CYP2B6 516G>T SNP and the subtypes of AML and ALL, which was not mentioned previously. SNPs in CYP1A1, CYP2D6, GSTT1, and GSTM1 genes as the risk factors of acute leukemia were reported in the literature [22, 44]. However, Lemos et al. [45] debated the relationship between the SNPs in GSTT1 and GSTM1 genes and hematological malignancies. Therefore, it is worth to conduct further studies to confirm the suspected genes in the pathogenesis of acute leukemia.

In conclusion, this study demonstrated that the T allele of CYP2B6 516G>T SNP may be one of the factors predisposing to the pathogenesis of ALL and AML, especially to T-ALL, AML with AML1–ETO, AML-NOS as well as acute monoblastic and monocytic leukemia.

**Acknowledgments** This work was funded by the National 863 High-Tech Research and Development Program of China (2008AA02503).

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