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# Gene polymorphisms of SOCS1 and SOCS2 and acute lymphoblastic leukemia

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**Abstract.** – **OBJECTIVE:** Acute lymphoblastic leukemia (ALL) causes the dysfunction of the systemic blood system and immune system. The etiology and predisposing factors of ALL are unknown. The suppressor of cytokine signaling 1 (SOCS1) and SOCS2 are inhibitors of cytokine signal transduction. Gene polymorphisms of SOCS1 and SOCS2 and their expressions may be related to ALL.

**PATIENTS AND METHODS:** A total of 200 ALL patients in our hospital and 200 healthy people were enrolled in ALL group and control group, respectively. Genomic deoxyribonucleic acids (DNAs) and total RNAs were extracted from the peripheral blood of each subject. Gene polymorphisms of SOCS1 at rs33977706, rs243327, and rs33932899 and those of SOCS2 at rs3816997 were amplified by polymerase chain reaction (PCR) and sequenced. Besides, the expression levels of SOCS1 and SOCS2 in ALL patients were detected by real-time fluorescence quantitative PCR.

**RESULTS:** The frequency of the allele C of SOCS1 rs33977706 in ALL group was lower than that in the control group, displaying a significant difference between the two groups ($p$=0.015). The frequency of allele A of SOCS2 rs3816997 was notably higher in ALL group than that of the control group ($p$=0.000). In addition, the frequency of CA genotype of SOCS1 rs33977706 in ALL group was markedly lower than that in the control group, showing a significant difference ($p$=0.000). ALL group had remarkably higher frequencies of AA genotype of SOCS2 rs3816997 ($p$=0.000) and ACC haplotype of SOCS gene ($p$=0.000), and lower frequencies of ATG ($p$=0.026) and CCC ($p$=0.006) haplotypes. The two loci, SOCS1 rs33932899 and SOCS1 rs243327, were linked to each other (D'=0.781). Moreover, the expression level of SOCS1 in ALL group was lower than that in the control group, in which the expression of the CT genotype of SOCS1 rs243327 was relatively higher ($p$=0.021). SOCS2 level was lower in ALL group. Particularly, SOCS2 level in ALL patients carrying AC genotype was lower than those carrying AA and CC genotypes ($p$=0.000). ALL patients carrying CT genotype of SOCS1 rs243327 had shorter period of agranulocytosis ($p$=0.000), a lower ratio of bone marrow primitive/immature cells ($p$=0.001), and a higher hemoglobin (Hb) level in blood ($p$=0.000). The ratio of bone marrow primordial/immature cells was lower in ALL patients with AC genotype of SOCS2 rs3816997 ($p$=0.038).

**CONCLUSIONS:** The expression levels of SOCS1 and SOCS2 are prominently related to ALL, and their polymorphisms are associated with the susceptibility to ALL.

*Key Words:*
SOCS1, SOCS2, Polymorphisms, ALL.

## Introduction

Acute lymphoblastic leukemia (ALL) primarily changes the lymphocyte composition in the blood, leading to the replacement of mature functional lymphocytes with immature lymphocytes[1,2]. Lymphocyte dysfunction results in the hypoimmunity of the body. Hematopoietic dysfunction of the bone marrow results in the plummet of blood cells with normal function in the peripheral blood, thus leading to fatal anemia and scattered bleeding points all over the body. Bone marrow transplantation and targeted drugs at present are preferred for ALL treatment, but they cost enormous economic and human resources[3,4]. Researching the pathogenesis of ALL may contribute to the complete cure of the disease to some extent. The suppressor of cytokine signaling 1 (SOCS1) and SOCS2 play negative regulatory roles in the adaptive immune processes mediated by cytokine receptors and TLRs, especially in the JAK signaling pathway and STAT pathway[5,6]. SOCS1 and SOCS2 influence diverse cellular functions of lymphocytes. For example, they maintain the expressions of FOXP3 and IL-17 in Treg cells[7], as well as the function and differentiation of Th17 cells[8]. It can be concluded



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that SOCS1 and SOCS2 are also likely to affect the function and differentiation of lymphocytes in ALL, thereafter resulting in different clinical outcomes. Notably, gene polymorphisms influence the expressions of SOCS1 and SOCS2, which will cause different susceptibilities to ALL in different populations. Therefore, SOCS1 gene polymorphisms at rs33977706, rs243327, and rs33932899, and SOCS2 gene polymorphism at rs3816997 were analyzed in ALL patients. We aim to explore the pathogenesis and predisposing factors of ALL and to figure out the correlations of the single nucleotide polymorphisms (SNPs) of SOCS1 and SOCS2 genes with the susceptibility to ALL.

## Patients and Methods

### *Patients*

The peripheral blood samples and clinical data of 200 ALL patients and 200 healthy people from the Physical Examination Center in Yixing People's Hospital since 2017 were collected. There were 112 males and 88 females in ALL groups, with an average age of (37.17±2.96) years old. Control group consisted of 108 males and 92 females, with an average age of (39.19±3.18) years old. There were no statistically significant differences in age, gender, and other general clinical data between the control group and ALL group ($p>0.05$). This study was approved by the Ethics Committee of the Yixing People's Hospital. Signed written informed consents were obtained from all participants before the study. ALL was diagnosed according to WHO criteria (2016) using MICM (morphology, immunology, cytogenetics, molecular biology) diagnostic approach. Based on medical history (fever, anemia, unexplained hemorrhage, etc.), hemogram (triple reduction and occurrence of primitive and immature lymphocytes), and bone marrow images, the patients with the ratio of primitive/immature lymphocytes in the bone marrow ≥20% were diagnosed with ALL.

### Detection Methods

### *Sample Collection*

About 8 mL of peripheral blood was collected from 200 ALL patients and 200 healthy people. Immediately after the collection, the samples were centrifuged at 3000 rpm for 8 min. Then, the nucleated cells in the intermediate layer were separated into new centrifuge tubes, respectively, and used to extract the genomic deoxyribonucleic acids (DNAs) and ribonucleic acids (RNAs).

### *Extraction of Genomic DNAs from Peripheral Blood*

Genomic DNAs in the peripheral blood of ALL patients and healthy controls were extracted using TIANGEN blood genomic extraction kit (Beijing, China). All steps were strictly carried out according to the standard operation of the kit. Briefly, 200 μL of the protein K solution, peripheral blood samples, and 3 mL of buffer GE were added in the centrifuge tube. They were mixed evenly using a vortex oscillator for 30 s and placed at 65°C for 10 min. Then, the samples were added with 2 mL of anhydrous ethanol, mixed well, and transferred to the adsorption column. After that, the adsorption column was added with 2 mL of the buffer for 1-min centrifugation at 4000 rpm. After applying buffer PW, the centrifugation was conducted again. Subsequently, 250 μL of elution buffer (genomic DNAs) was added to the adsorption column. DNA purity was detected using an ultraviolet spectrophotometer, and the optical density $(OD)_{260}/OD_{280}$ of the qualified samples was 1.8-2.

### *Extraction of the Total RNAs From the Peripheral Blood*

The total RNAs were extracted from the peripheral blood of nucleated cells *via* TRIzol method (Invitrogen, Carlsbad, CA, USA): the nucleated cells were separated, incubated in 500 μL of TRIzol, and placed at 15°C for 5 min. Next, 0.2 mL of chloroform was added, shaken vigorously for 15 s, and placed at 15°C for 2-3 min, followed by centrifugation at 12000 g for 15 min. Thereafter, the upper aqueous phase was transferred to a new Eppendorf (EP) tube (Hamburg, Germany), where 0.5 mL of isopropanol was added, followed by letting stand for 10 min and centrifugation at 12000 g for 15 min. 75% ethanol was added to wash RNA precipitates and mixed well for centrifugation at 7500 g for 5 min. Ultimately, RNA precipitates were desiccated, and dissolved in the enzyme-free water. RNA sample was reversely transcribed into cDNAs and stored at -20°C after concentration measurement.

### *Polymerase Chain Reaction (PCR) Amplification and Sequencing*

PCR apparatus was utilized to amplify the polymorphisms of SOCS1 gene at rs33977706, rs243327, and rs33932899 and those of SOCS2

gene at rs3816997, respectively. The total PCR system (20 μL) consisted of primers (1 μL each), template DNAs (0.5 μL), Taq enzymes (10 μL) and $dH_2O$ (7.5 μL). PCR reaction conditions: 96°C for 6 min, (96°C for 35 s, 56°C for 40 s, and 72°C for 40 s) × 35 cycles and 72°C for 5 min. The primers at the polymorphic sites: SOCS1 rs33977706: forward: (5'→3')'TTTTCGCCCTTAGGTGAAGA' and reverse: (5'→3')'GAGGAGTCGAAGCTCG', SOCS1 rs243327: forward: (5'→3')'CTGCGGCTTCTATTGGGGAC' and reverse: (5'→3')'AAAAGGCAGTCGAAGGTCTCG', SOCS1 rs33932899: forward: (5'→3')'GACGCCTGCGGCTTCTATT' and reverse: (5'→3')'CAGCTCGAAAAGGCAGTCG', and SOCS2 rs3816997: forward: (5'→3')'CAGATGTGCAAGGATAAGCGG' and reverse: (5'→3')'GCGGTTTGGTCAGATAAAGGTG'. PCR products were sent to Shanghai Biotechnology Co., Ltd. (Shanghai, China) for sequencing to obtain the DNA sequences at each locus, and the SNPs of SOCS1 and SOCS2 genes at each locus were obtained through analysis.

### Detection of the Expressions of SOCS1 and SOCS2 Genes

The expressions of SOCS1 and SOCS2 were examined by real-time fluorescence quantitative PCR. Each gene primer was designed using Premier 5.0 and synthesized by Shanghai Bioengineering Co., Ltd. (Shanghai, China). The primers of SOCS1 gene: forward: (5'→3')'CACGCACTTCCGCACATTC' and reverse: (5'→3')'TAAGGGCGAAAAAGCAGTTCC', and SOCS2 gene: forward: (5'→3')'TTAAAAGAGGCACCAGAAGGAAC' and reverse: (5'→3')'AGTCGATCAGATGAACCACACT'. PCR conditions (25 μL): primers (1 μL each), template cDNAs (0.5 μL), Sybr Premix Taq (12.5 μL), and $dH_2O$ (10 μL). PCR conditions: 94°C for 3 min, (95°C for 30 s, 59°C for 40 s, and 72°C for 35 s) × 40 cycles and 72°C for 5 min.

### Statistical Analysis

The Statistical Product and Service Solutions (SPSS) 22.0 (IBM Corp., Armonk, NY, USA) was adopted for statistical analysis. The count data and measurement data were analyzed by the $\chi^2$-test and the *t*-test, respectively. The Hardy-Weinberg equilibrium analysis was carried out. The haplotype analysis was conducted on-line through the SHEsis website, and $p<0.05$ suggested a statistically significant difference.

## Results

### Allele Distribution of SOCS1 Gene at Rs33977706, Rs243327, Rs33932899, and SOCS2 Gene at Rs3816997

The allele frequencies of SOCS1 gene at rs33977706, rs243327, and rs33932899 and SOCS2 gene at rs3816997 were shown in Table I. It was found that the frequency of the allele C of SOCS1 rs33977706 in ALL group was relatively low, showing a significant difference ($p$=0.015). The frequency of the allele A of SOCS2 rs3816997 in ALL group was remarkably higher than that in the control group, displaying a significant difference ($p$=0.000).

### Genotype Distribution of SOCS1 Gene at Rs33977706, Rs243327 and Rs33932899, and SOCS2 Gene at Rs3816997

The genotype distribution of SOCS1 gene at rs33977706, rs243327, and rs33932899 and SOCS2 gene at rs3816997 were shown in Table II. It was displayed that the frequency of CA genotype of SOCS1 rs33977706 was significantly lower in ALL group ($p$=0.000). Besides, ALL group had a remarkably higher frequency of AA genotype of SOCS2 rs3816997 ($p$=0.000).

**Table I.** Allele distribution of SOCS1 gene at rs33977706, rs243327 and rs33932899, and SOCS2 gene at rs3816997.

| Gene | Locus | Allele | Control group | ALL group | OR value | 95% CI | $\chi^2$ | p |
|---|---|---|---|---|---|---|---|---|
| SOCS1 | rs33977706 | C | 234 (0.585) | 166 (0.415) | 1.41 | 1.06-1.86 | 5.82 | 0.015 |
| | | A | 200 (0.500) | 234 (0.585) | | | | |
| | rs243327 | C | 200 (0.500) | 230 (0.575) | 1.35 | 1.02-1.78 | 3.52 | 0.064 |
| | | T | 200 (0.500) | 170 (0.425) | | | | |
| | rs33932899 | G | 208 (0.520) | 185 (0.463) | 1.25 | 0.95-1.66 | 2.64 | 0.103 |
| | | C | 192 (0.480) | 215 (0.537) | | | | |
| SOCS2 | rs3816997 | A | 189 (0.473) | 259 (0.647) | 2.05 | 1.54-2.72 | 24.85 | 0.000 |
| | | C | 211 (0.527) | 141 (0.353) | | | | |

**Table II.** Genotype distribution of SOCS1 gene at rs33977706, rs243327 and rs33932899, and SOCS2 gene at rs3816997.

| Gene | Locus | Allele | Control group | ALL group | OR value | 95% CI | $\chi^2$ | *p* |
|---|---|---|---|---|---|---|---|---|
| SOCS1 | rs33977706 | CC | 41 (0.205) | 50 (0.250) | 1.23 | 1.08-1.41 | 30.37 | 0.000 |
| | | CA | 118 (0.590) | 66 (0.330) | | | | |
| | | AA | 41 (0.205) | 84 (0.420) | | | | |
| | rs243327 | CC | 46 (0.230) | 65 (0.325) | 1.51 | 1.36-1.78 | 5.05 | 0.079 |
| | | CT | 108 (0.540) | 100 (0.500) | | | | |
| | | TT | 46 (0.230) | 35 (0.175) | | | | |
| | rs33932899 | GG | 57 (0.285) | 44 (0.220) | 0.98 | 0.78-1.08 | 2.64 | 0.266 |
| | | GC | 94 (0.470) | 97 (0.485) | | | | |
| | | CC | 49 (0.245) | 59 (0.295) | | | | |
| SOCS2 | rs3816997 | AA | 45 (0.225) | 93 (0.465) | 1.17 | 0.97-1.37 | 26.03 | 0.000 |
| | | AC | 99 (0.495) | 73 (0.365) | | | | |
| | | CC | 56 (0.280) | 34 (0.170) | | | | |

### *Polymorphism Analyses of SOCS1 Gene at Rs33977706, Rs243327 and Rs33932899, and SOCS2 Gene at Rs3816997*

Polymorphisms of SOCS1 gene at rs33977706, rs243327, and rs33932899, and SOCS2 gene at rs3816997 were analyzed (Table III). The proportions of CC genotype (*p*=0.031) in the homozygous model of SOCS1 rs243327 and AA+AC genotype (*p*=0.002) in the dominant model of SOCS2 rs3816997 in ALL group were higher than those in the control group. The

**Table III.** Polymorphism analysis of SOCS1 gene at rs33977706, rs243327 and rs33932899, and SOCS2 gene at rs3816997.

| | Locus | Genotype | Control group | ALL group | OR value | 95% CI | $\chi^2$ | *p* |
|---|---|---|---|---|---|---|---|---|
| Dominant model | rs33977706 | CC+CA | 159 (0.795) | 116 (0.580) | 1.35 | 1.21-1.45 | 2.51 | 0.132 |
| | AA | 41 (0.205) | 84 (0.420) | | | | | |
| | rs243327 | CC+CT | 154 (0.770) | 165 (0.825) | 1.89 | 1.35-1.97 | 1.14 | 0.256 |
| | | TT | 46 (0.230) | 35 (0.175) | | | | |
| | rs33932899 | GG+GC | 151 (0.755) | 141 (0.795) | 1.17 | 0.98-1.26 | 1.36 | 0.278 |
| | | CC | 49 (0.245) | 59 (0.295) | | | | |
| | rs3816997 | AA+AC | 144 (0.720) | 166 (0.830) | 0.81 | 0.73-1.37 | 7.89 | 0.002 |
| | | CC | 56 (0.280) | 34 (0.170) | | | | |
| Recessive model | rs33977706 | CC | 41 (0.205) | 50 (0.250) | 1.08 | 0.94-1.42 | 1.19 | 0.351 |
| | CA+AA | 159 (0.795) | 150 (0.750) | | | | | |
| | rs243327 | CC | 46 (0.230) | 65 (0.325) | 1.63 | 1.24-1.51 | 4.56 | 0.037 |
| | | CT+TT | 154 (0.770) | 135 (0.675) | | | | |
| | rs33932899 | GG | 57 (0.285) | 44 (0.220) | 0.85 | 0.74-0.98 | 0.98 | 0.761 |
| | | GC+CC | 143 (0.715) | 156 (0.780) | | | | |
| | rs3816997 | AA | 45 (0.225) | 93 (0.465) | 1.73 | 1.24-1.97 | 35.15 | 0.000 |
| | | AC+CC | 155 (0.775) | 103 (0.535) | | | | |
| Hybrid model | rs33977706 | CC | 41 (0.205) | 50 (0.250) | 1.05 | 0.76-1.32 | 1.87 | 0.148 |
| | | CA | 118 (0.590) | 66 (0.330) | | | | |
| | rs243327 | CC | 46 (0.230) | 65 (0.325) | 1.02 | 0.78-1.34 | 5.15 | 0.041 |
| | | CT | 108 (0.540) | 100 (0.500) | | | | |
| | rs33932899 | GG | 57 (0.285) | 44 (0.220) | 0.98 | 0.76-1.1.21 | 1.67 | 0.173 |
| | | GC | 94 (0.470) | 97 (0.485) | | | | |
| | rs3816997 | AA | 45 (0.225) | 93 (0.465) | 0.93 | 0.83-1.01 | 2.01 | 0.161 |
| | | AC | 99 (0.495) | 73 (0.365) | | | | |
| Homozygous model | rs33977706 | CC | 41 (0.205) | 50 (0.250) | 1.24 | 1.02-1.34 | 1.84 | 0.153 |
| | | AA | 41 (0.205) | 84 (0.420) | | | | |
| | rs243327 | CC | 46 (0.230) | 65 (0.325) | 1.08 | 0.71-1.24 | 6.15 | 0.031 |
| | | TT | 46 (0.230) | 35 (0.175) | | | | |
| | rs33932899 | GG | 57 (0.285) | 44 (0.220) | 0.75 | 0.46-1.01 | 1.37 | 0.203 |
| | | CC | 49 (0.245) | 59 (0.295) | | | | |
| | rs3816997 | AA | 45 (0.225) | 93 (0.465) | 1.09 | 0.93-1.23 | 1.41 | 0.222 |
| | | CC | 56 (0.280) | 34 (0.170) | | | | |

**Table IV.** Haplotype analysis of SOCS1 gene at rs33977706, rs243327, and rs33932899.

| Haplotype | Control group | ALL group | OR value | 95% CI | $\chi^2$ | p |
|---|---|---|---|---|---|---|
| ACC | 37.33 (0.093) | 86.17 (0.215) | 2.667 | 1.765-4.030 | 22.84 | 0.000 |
| ACG | 59.28 (0.148) | 76.94 (0.192) | 1.369 | 0.944-1.984 | 2.76 | 0.097 |
| ATC | 56.64 (0.142) | 42.56 (0.106) | 0.722 | 0.472-1.103 | 2.28 | 0.131 |
| ATG | 46.75 (0.117) | 28.32 (0.071) | 0.576 | 0.353-0.939 | 4.99 | 0.026 |
| CCC | 52.00 (0.130) | 28.59 (0.071) | 0.515 | 0.319-0.832 | 7.56 | 0.006 |
| CCG | 51.39 (0.128) | 38.30 (0.096) | 0.718 | 0.461-1.119 | 2.15 | 0.143 |
| CTC | 46.03 (0.115) | 57.68 (0.144) | 1.296 | 0.856-1.962 | 1.50 | 0.220 |
| ATG | 50.58 (0.126) | 41.43 (0.104) | 0.798 | 0.516-1.235 | 1.03 | 0.310 |

control group had higher proportions of CT+TT genotype ($p$=0.037) in the recessive model and CT genotype ($p$=0.041) in the hybrid model of SOCS1 rs243327. Besides, AC+CC genotype ($p$=0.000) in the recessive model of SOCS2 rs3816997 was higher in the control group than ALL group.

### Haplotype Analyses of SOCS1 Gene at Rs33977706, Rs243327, and Rs33932899

Haplotypes of SOCS1 gene at rs33977706, rs243327, and rs33932899 were analyzed (Table IV). ALL group had a higher frequency of ACC haplotype ($p$=0.000) and lower frequencies of ATG ($p$=0.026) and CCC ($p$=0.006) haplotypes of SOCS gene. SOCS1 rs33932899 was closely linked to SOCS1 rs243327 (D'=0.781) (Table V).

### Correlations of the Expression Levels of SOCS1 and SOCS2 with ALL

The correlations of the expression levels of SOCS1 gene with the genotypes at rs33977706, rs243327, and rs33932899 were manifested in Figures 1-3, respectively. In general, the expression of SOCS1 in ALL group was lower than that in the control group, in which the expression of CT genotype of SOCS1 rs243327 was higher ($p$=0.021). The relationship between the expression level of SOCS2 gene and the genotype at rs3816997 was shown in Figure 4. SOCS2 level in ALL group was lower than that in the control group, among which the SOCS2 level in ALL patients carrying AC genotype was lower than that in those carrying AA and CC genotypes ($p$=0.000).

### Correlation Analyses of Genotypes of SOCS1 Gene at Rs33977706, Rs243327 and Rs33932899, and SOCS2 Gene at Rs3816997 with ALL Clinical Indicators

The correlations of the genotypes of SOCS1 gene at rs33977706, rs243327, and rs33932899, and SOCS2 gene at rs3816997 with clinical indicators of ALL patients were assessed (Table VI). ALL patients carrying CT genotype of SOCS1 rs243327 had shorter period of agranulocytosis ($p$=0.000), a lower ratio of bone marrow primitive/immature cells ($p$=0.001), and a higher hemoglobin (Hb) level in the blood ($p$=0.000). The ratio of bone marrow primordial/immature cells was lower in ALL patients carrying AC genotype of SOCS2 rs3816997 ($p$=0.038).

## Discussion

Leukemia is a highly malignant disease leading to a great harm to patients and their families. ALL mainly arises in adolescents, causing a huge damage to the systemic blood system and immune function, so that minor infection can threaten the patient's life[9]. The ratio of bone marrow primitive/immature cells in ALL patients often increases, and immature blood cells

**Table V.** Linkage disequilibrium analysis of SOCS1 gene at rs33977706, rs243327, and rs33932899.

| | rs33977706 | rs243327 | rs33932899 |
|---|---|---|---|
| rs33977706 | – | 0.186 | 0.072 |
| rs243327 | 0.186 | – | 0.781 |
| rs33932899 | 0.072 | 0.781 | – |

**Table VI.** Correlation analysis of genotypes of SOCS1 gene at rs33977706, rs243327 and rs33932899, and SOCS2 gene at rs3816997 with ALL clinical indicators.

| | | Time of agranulocytosis (d) | | | Ratio of bone marrow primitive/ immature cells | | | WBC ($10^9$/L) | | | Hb (g/L) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Genotype | Control group | ALL group | *p* | Control group | ALL group | *p* | Control group | ALL group | *p* | Control group | ALL group | *p* |
| rs33977706 | CC | 0 | 23.14 | 0.146 | 0.02 | 0.78 | 0.265 | 6.15 | 56.16 | 0.074 | 145.14 | 84.24 | 0.127 |
| | CA | 0 | 24.15 | | 0.03 | 0.74 | | 7.61 | 51.56 | | 136.87 | 82.15 | |
| | AA | 0 | 21.67 | | 0.02 | 0.81 | | 6.15 | 53.89 | | 146.15 | 79.53 | |
| rs243327 | CC | 0 | 25.56 | 0.000 | 0.02 | 0.82 | 0.001 | 7.45 | 53.68 | 0.108 | 152.35 | 78.14 | 0.000 |
| | CT | 0 | 19.14 | | 0.03 | 0.65 | | 5.68 | 54.17 | | 133.28 | 92.18 | |
| | TT | 0 | 24.47 | | 0.01 | 0.83 | | 7.45 | 58.18 | | 151.87 | 62.85 | |
| rs33932899 | GG | 0 | 23.14 | 0.256 | 0.03 | 0.76 | 0.417 | 6.45 | 52.87 | 0.098 | 145.18 | 67.35 | 0.094 |
| | GC | 0 | 22.71 | | 0.02 | 0.83 | | 5.16 | 52.91 | | 143.85 | 73.15 | |
| | CC | 0 | 22.85 | | 0.02 | 0.78 | | 7.63 | 61.08 | | 153.75 | 74.18 | |
| rs3816997 | AA | 0 | 25.87 | 0.079 | 0.01 | 0.82 | 0.038 | 5.46 | 53.87 | 0.087 | 159.41 | 82.15 | 0.103 |
| | AC | 0 | 22.56 | | 0.01 | 0.75 | | 6.91 | 57.51 | | 123.75 | 72.75 | |
| | CC | 0 | 24.67 | | 0.04 | 0.85 | | 6.49 | 49.87 | | 146.42 | 81.45 | |

appear in the peripheral blood. These cells barely have functions and greatly destroy the immune ability of patients[10]. The etiology of ALL may be associated with genetic changes, formaldehyde, and other chemical factors[11]. Therefore, studying the pathogenesis and predisposing factors of ALL is meaningful. SOCS1 and SOCS2 are the inhibitors of the cytokine signal transduction and control the transmission and transfer of cell information. Studies in China and foreign countries discovered that SOCS1 and SOCS2 are related to many diseases. For example, SOCS1 methylation is related to Behcet's disease[12]. The knockdown of SOCS1 can suppress the systemic infection with candida albicans[13]. In addition, SOCS1 is associated with the prognosis of triple negative breast cancer[14]. SOCS2 has a correlation with the occurrence of the inflammatory bowel disease[15]. The knockdown of SOCS2 is able to prevent the metastasis of hepatocellular carcinoma[16]. SNPs are vital components of gene mutations. This genetic information transmits the susceptibility and tolerance to diseases during the alternation of the human generations. SOCS1 and SOCS2 gene polymorphisms have correlations with various diseases. For example, SOCS1 gene polymorphism is related to acute coronary syndrome[17] and biliary cirrhosis[18], while SOCS2 gene polymorphism is associated with type 2 diabetes mellitus[19] and adolescent idiopathic scoliosis[20]. In this study, it was found that the frequency of allele C of SOCS1 rs33977706 in ALL group was lower than that in the control group. The frequency of allele A of SOCS2 rs3816997 in ALL group was remarkably higher than that in the control group. The frequency of CA genotype of SOCS1 rs33977706 was significantly lower in ALL group. Besides, ALL group had a remarkably higher frequency of AA genotype of SOCS2 rs3816997. The above results indicated that the population carrying allele A and genotype AA of SOCS2 rs3816997 were more susceptible to ALL. In contrast, the population carrying allele C and genotype CA of SOCS1 rs33977706 were less susceptible to ALL. Meanwhile, the proportions of the CC genotype in the homozygous model of SOCS1 rs243327 and AA+AC genotype in the dominant model of SOCS2 rs3816997 in ALL group were higher than those in the control group. The control group had higher proportions of CT+TT genotype in the recessive model and CT genotype in the hybrid model of SOCS1 rs243327. AC+CC genotype in the recessive model of SOCS2 rs3816997 was higher in the control group than ALL group. It can be seen that the population carrying AA and AC genotypes in the dominant model of SOCS2 rs3816997 were more prone to being attacked by ALL. These highly risk population should receive gene screening, blood, and bone marrow examination to monitor the susceptibility to ALL. Also, it was found that the population carrying ACC haplotype of SOCS1 gene had a high incidence rate of ALL, to which should be paid attention, clinically. The expressions of SOCS1 and SOCS2 in the ALL group were lower than those in the control group (Figures 1-4), suggesting that SOCS1 and SOCS2 genes can inhibit the occurrence of ALL. SOCS2 expression in the population carrying AC genotype of SOCS2 rs3816997 was lower than those

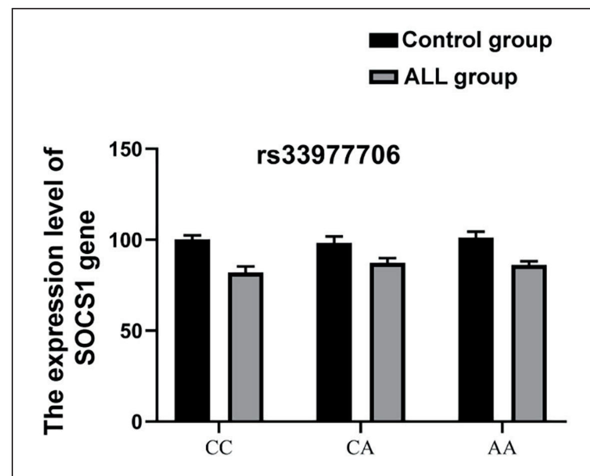


**Figure 1.** Relationship between the expression level of SOCS1 gene and the genotype at rs33977706.

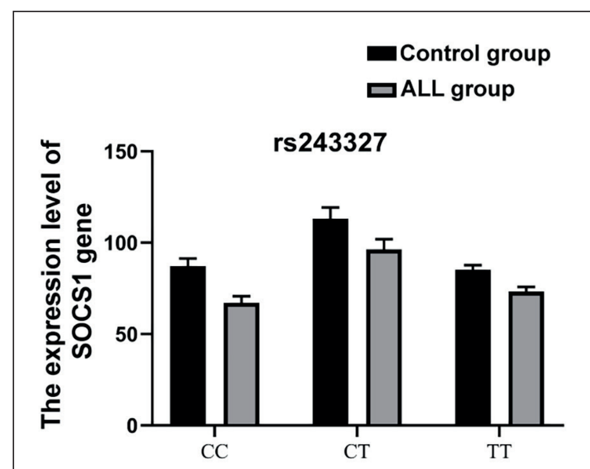


**Figure 2.** Relationship between the expression level of SOCS1 gene and the genotype at rs243327.

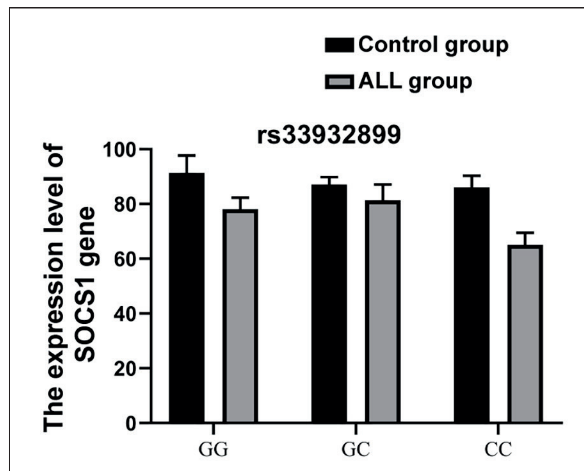


**Figure 3.** Relationship between the expression level of SOCS1 gene and the genotype at rs33932899.

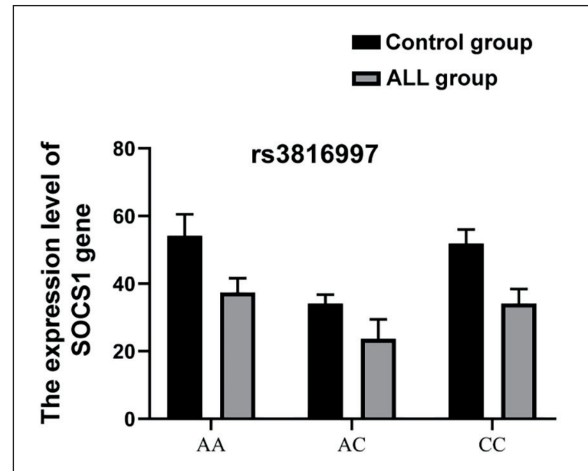


**Figure 4.** Relationship between the expression level of SOCS2 gene and the genotype at rs3816997.

carrying AA and CC genotypes. Ultimately, it was discovered that ALL patients carrying CT genotype of SOCS1 rs243327 had shorter period of agranulocytosis, a lower ratio of bone marrow primitive/immature cells, and a higher Hb level in the blood. The ratio of the bone marrow primordial/immature cells was lower in ALL patients with AC genotype of SOCS2 gene at rs3816997. The above results clearly proved that ALL patients carrying CT genotype of SOCS1 rs243327 and AC genotype of SOCS2 rs3816997 had a better prognosis.

## Conclusions

We discovered that the expression levels of SOCS1 and SOCS2 are prominently related to ALL, and their polymorphisms are associated with the susceptibility to ALL.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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