Associations of Human Leukocyte Antigen-DRB1 Alleles with Nasopharyngeal Carcinoma and Its Clinical Significance in Xinjiang Uyghur Autonomous Region of China

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Abstract

Background: Genetic susceptibility is one of the major etiological factors for nasopharyngeal carcinoma (NPC). Among the genetic predisposing factors, human leukocyte antigen (HLA) genes have been reported to be associated with NPC. This study aimed to investigate the associations of HLA-DRB1 alleles with NPC and the clinical significance of HLA-DRB1 alleles in NPC.

Methods: From January 2009 to December 2013, 140 NPC patients (118 Han patients and 22 Uyghur patients) and 158 healthy controls (81 Han individuals and 77 Uyghur individuals) from Xinjiang Province were genotyped for HLA-DRB1 using the polymerase chain reaction-sequence specific primer technique. Chi-square analysis was used when comparing allele frequencies between groups. The clinical outcomes were evaluated by Kaplan-Meier method and Cox regression model.

Results: Compared with healthy controls, the allele frequency of HLA-DRB1*0701 was increased in the Uyghur patients (P = 0.008) but not in the Han patients (P = 0.869). HLA-DRB1*0101 allele was presented with higher frequency in clinical Stage I + II group compared with clinical Stage III + IV group in the Han patients (P = 0.015) but not in the Uyghur patients (P = 1.000). Higher frequency of HLA-DRB1*1501 allele was observed in patients aged <45 years compared with those in patients aged ≥45 years (P = 0.002). Neither HLA-DRB1*0701 nor HLA-DRB1*0101 had a statistically significant association with 3-year survival.

Conclusions: This study found HLA-DRB1*0701 in Uyghur population was associated with an increased risk of developing NPC. In Han population, we found HLA-DRB1*0101 was associated with protection from disease progression, and HLA-DRB1*1501 was associated with early age of onset. HLA-DRB1 could not be identified as a prognostic indicator for NPC in either Han or Uyghur patients.

Key words: Human Leukocyte Antigen-DRB1 Allele; Nasopharyngeal Carcinoma; Prognosis

Introduction

Nasopharyngeal carcinoma (NPC) is a malignant epithelial disease, characterized by its distinctive racial and geographic distribution.[1] It is rare in most parts of the world, but endemic in Southern China with an incidence rate of 20/100,000.[2,3] The major etiological factors include genetic susceptibility, environment factors, and Epstein-Barr virus (EBV) infection.[4] Among all genetic factors, human leukocyte antigen (HLA) genes have been shown to have a strong and consistent association with NPC risk.[5] HLA polymorphism can alter disease susceptibility and progression in some tumors. The HLA molecules present antigenic peptides to T lymphocyte and modulate the host-tumor immune response.[6] Except for NPC, HLA polymorphism has a role in malignant diseases such as breast cancer,[7] hepatocellular carcinoma,[8] lymphoma,[9] and cervical cancer.[10] Different HLA-Class I alleles have been reported to be associated with NPC in Southern China. For instance, HLA-A*02, -B*46, and -B*58 increased the susceptibility to NPC, while HLA-A*11 and -B*13 showed protections on this disease.[11-13] However,
few studies focused on the associations of HLA-Class II alleles with NPC. In this study, with the support of clinical data, we were able to investigate the HLA-DRB1 allele frequencies in NPC patients and healthy controls, as well as in several clinical and pathological subgroups of NPC in Han and Uyghur subjects. Our purpose was to determine whether HLA-DRB1 alleles are associated with risk of NPC and the role of the HLA-DRB1 alleles in progress and prognosis of NPC.

**Methods**

**Patients**

From January 2009 to December 2013, 140 NPC patients were enrolled in this study from the Affiliated Tumor Hospital of Xinjiang Medical University. All patients’ diagnoses were confirmed by clinical pathology. Among these patients, 118 were Han and 22 were Uyghur, and their clinicopathological characteristics are listed in Table 1. The clinical stage of these patients was classified according to the Chinese 2008 staging system. All NPC patients received treatment in compliance with the NCCN Practice Guidelines for Head and Neck Cancer. All 158 healthy controls were recruited from volunteers without a family history of NPC. Among the healthy controls, 81 were Han and 77 were Uyghur. There were 49 males and 32 females in Han subjects (aged from 24 to 78 years) and 50 males and 27 females in Uyghur subjects (aged from 26 to 72 years). All participants provided written informed consent before enrollment in this study, and this study was approved by the Institutional Ethics Committee of the Affiliated Tumor Hospital of Xingjiang Medical University.

**Genomic DNA extraction**

Genomic DNA was extracted from whole blood samples using a Genomic DNA Extraction kit (Bioteke Corp., China) according to manufacturer’s instructions. DNA concentration and purity were determined using an ultraviolet spectrophotometer (Thermo Fisher Scientific Inc., Waltham, MA, USA), the A260/280 ratios were between 1.8 and 1.9, and DNA concentration was adjusted to 0.3–0.5 μg/μl. The DNA samples were stored at −20°C. HLA-DRB1 genotyping was performed using the polymerase chain reaction-sequence specific primers method.~[17]~

**Epstein-Barr virus-viral capsid antigen-immunoglobulin A detection**

Peripheral blood samples were obtained from NPC patients and stored at −20°C. Enzyme-linked immunosorbent assay (ELISA) was used to detect serum EBV-viral capsid antigen (VCA)-immunoglobulin A (IgA). ELISA kits were purchased from the Demeditec Company (Germany).

**Follow-up**

All patients were required to be followed up after treatment every 3 months. Each follow-up mainly included chest X-ray and magnetic resonance imaging of the nasopharynx, head, and neck areas. Patients who were considered at high risk for distant metastasis received additional computed tomography scans of chest and abdomen, as well as bone scans. Follow-ups were carried out by re-examinations, mailings, and/or telephone calls.

**Statistical analysis**

All statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). The allele frequencies between the case and control groups and between different clinical and pathological subgroups were analyzed by the Chi-square test, and two-tailed Fisher’s exact test was performed while Chi-square test was not applicable. Odds ratios (ORs) were calculated from allelic and genotype frequencies with 95% confidence intervals (CIs). Kaplan-Meier method was used to calculate 3-year overall survival (OS), 3-year disease-free survival (DFS), 3-year distant metastasis-free survival (DMFS), and 3-year local relapse-free survival (LRFS). The differences between subgroups were examined by the log-rank test. Univariate Cox regression model was used to evaluate the hazard ratios (HRs)
of HLA-DRB1 and different clinicopathologic factors. A value of $P < 0.05$ was considered statistically significant.

**RESULTS**

**Associations between human leukocyte antigen-DRB1 and nasopharyngeal carcinoma**

Among Uyghur subjects, the HLA-DRB1*0701 allele frequency in the NPC group was 25.0%, which was significantly higher than that (9.7%) in the healthy controls [Figure 1]; this result suggested that HLA-DRB1*0701 allele was associated with susceptibility to NPC (OR = 3.089, 95% CI = 1.300–7.341, $P = 0.008$). Among Han subjects, the HLA-DRB1*0701 allele frequencies were 11.0% in the NPC group and 10.5% in the healthy controls, without statistically significant difference ($P = 0.869$; Figure 2).

**Associations between human leukocyte antigen-DRB1 and clinicopathologic factors**

Among Han NPC patients, the HLA-DRB1*1501 allele frequency in the age group of <45 years was 15.8%, which was significantly higher than that (4.1%) in the age group of ≥45 years (OR = 0.228, 95% CI = 0.082–0.636, $P = 0.002$; Figure 3); the HLA-DRB1*0101 allele frequencies were 15.0% in the clinical Stage I + II group and 1.9% in the clinical Stage III + IV group [Figure 4], and the difference between two groups was statistically significant (OR = 0.107, 95% CI = 0.022–0.517, $P = 0.015$).

Among Han NPC patients, there was no statistical difference for the HLA-DRB1 allele frequencies detected in the subgroups grouped by histological classification, T stage, N stage, and short effects. Among Uyghur NPC patients, although the HLA-DRB1*1501 allele frequency in the age group of <45 years (6.7%) was lower than that (7.1%) in the age group of ≥45 years, and the HLA-DRB1*0701 allele frequency in the clinical Stage I + II group (0%) was lower than that (6.3%) in the clinical Stage III + IV group, these differences were not statistically significant (all $P > 0.05$). Similar to the Han NPC patients, there was no statistical difference in HLA-DRB1 allele frequency detected in the subgroups grouped by histological classification, T stage, N stage, and short effects in Uyghur NPC patients.

**Prognostic value of human leukocyte antigen-DRB1 and clinicopathologic factors in nasopharyngeal carcinoma**

The median follow-up time of Han patients was 38.5 months (ranging from 3 to 69 months). The median follow-up time of Uyghur patients was 37.0 months (ranging from 5 to 67 months). In the Uyghur patients, both 3-year OS and 3-year LRFS of HLA-DRB1*0701 group were 66.7%, the 3-year OS and 3-year LRFS of non-HLA-DRB1*0701 group were 71.1% and 88.9%, respectively. The 3-year OS and 3-year LRFS of HLA-DRB1*0701 group were lower than those of non-HLA-DRB1*0701 group, but the differences were not statistically significant [Table 2].

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**Figure 1:** The HLA-DRB1 allele frequencies between Uyghur NPC patients and Uyghur healthy controls, *$P = 0.008$. HLA: Human leukocyte antigen; NPC: Nasopharyngeal carcinoma.

**Figure 2:** The HLA-DRB1 allele frequencies between Han NPC patients and Han healthy controls. HLA: Human leukocyte antigen; NPC: Nasopharyngeal carcinoma.
Figure 3: HLA-DRB1 allele frequencies between age groups of <45 years and ≥45 years in Han patients with nasopharyngeal carcinoma, *P = 0.002. HLA: Human leukocyte antigen.

Figure 4: HLA-DRB1 allele frequencies between clinical Stage I + II group and clinical Stage III + IV group in Han patients with nasopharyngeal carcinoma, *P = 0.015. HLA: Human leukocyte antigen.

Table 2: Log-rank analysis of prognostic factors in Uyghur NPC patients (n = 22)

| Items                              | Number, n | 3-year OS (%) | 3-year DFS (%) | 3-year DMFS (%) | 3-year LRFS (%) |
|------------------------------------|-----------|---------------|----------------|-----------------|-----------------|
| HLA-DRB1*0701 status              |           |               |                |                 |                 |
| HLA-DRB1*0701                     | 11        | 66.7          | 78.8           | 60.6            | 66.7            |
| Non-HLA-DRB1*0701                 | 11        | 71.1          | 51.9           | 50.8            | 88.9            |
| Gender                            |           |               |                |                 |                 |
| Male                              | 15        | 60.6          | 67.7           | 50.3            | 70.3            |
| Female                            | 7         | 80.0          | 66.7           | 66.7            | 80.0            |
| Age                               |           |               |                |                 |                 |
| <45 years                         | 15        | 82.5          | 76.0           | 68.1            | 88.9            |
| ≥45 years                         | 7         | 50.0          | 44.4           | 33.3            | 50.0            |
| Histological classification       |           |               |                |                 |                 |
| Differentiated type               | 7         | 100           | 83.3           | 83.3            | 100             |
| Nondifferentiated type            | 15        | 52.2          | 58.8           | 42.6            | 59.0            |
| Clinical stage                    |           |               |                |                 |                 |
| I + II                            | 1         | 100           | 100            | 100             | 100             |
| III + IV                          | 21        | 65.2          | 64.6           | 53.5            | 71.5            |
| T-stage                           |           |               |                |                 |                 |
| T1 + T2                           | 4         | 100           | 66.7           | 66.7            | 100             |
| T3 + T4                           | 18        | 62.2          | 66.6           | 53.8            | 69.0            |
| N-stage                           |           |               |                |                 |                 |
| N0 + N1                           | 6         | 100           | 66.7           | 66.7            | 100             |
| N2 + N3                           | 16        | 61.7          | 66.0           | 53.3            | 68.4            |

NPC: Nasopharyngeal carcinoma; HLA: Human leukocyte antigen; OS: Overall survival; DFS: Disease-free survival; DMFS: Distant metastasis-free survival; LRFS: Local relapse-free survival.
Among the Han patients, the 3-year OS of HLA-DRB1*1501 and non-HLA-DRB1*1501 groups were 78.5% and 83.6%, respectively, without statistically significant difference [Table 3]. The 3-year OS, DFS, DMFS, and LRFS of HLA-DRB1*0101 and non-HLA-DRB1*0101 groups were 83.3%, 100%, 100% and 82.6%, 73.4%, 82.5%, 82.3%, respectively, and there were no statistically significant differences [Table 3]. Univariate Cox regression indicated that HLA-DRB1 allele and clinicopathological parameters were not predictors for prognosis of Uyghur NPC patients [Table 4]. In the Han population, the clinical stage was a predictor for 3-year OS [HR = 2.651, 95% CI = 1.182–5.947, P = 0.018; Table 5], while other clinicopathological parameters and HLA-DRB1 allele could not be considered as potential predictors for the prognosis.

**DISCUSSION**

HLA is the most polymorphic gene complex of all human genetic systems, which consists of more than two hundred genes located close together on chromosome 6 and can be categorized into Class I, Class II, and Class III. The Class I and II molecules display endogenous and exogenous antigens to the immune system, while Class III molecules involve in other immune functions. Different alleles of HLA can be a susceptible or protective allele of NPC. Individuals carrying specifically susceptible allele have increasing risk of developing NPC. The variations in susceptibility to NPC might reflect the differences in the anti-EBV capability of HLA haplotypes. Individuals with susceptible HLA alleles might not be able to mount enough cytotoxic immune response to eliminate EBV-infected cells.[4] Rubicz et al.[18] found the level of anti-EBV EBNA1 IgG is related with HLA-DRB1 loci, suggesting that specific HLA loci might also influence anti-EBV humoral immune response. Most studies of HLA alleles and NPC susceptibility investigated the patients in Southern China.[19,20] Recently, Wang et al.[21] reported that HLA-B*46 was significantly associated with NPC in Xinjiang region.

Few studies have been done to investigate the relationship between HLA-II alleles and NPC. It has been reported that HLA-DRB1*0405 is a susceptible allele, and HLA-DRB1*1501 is a protective allele[22] among Caucasians in America where the incidence rate was low. Different from these low incidence areas, HLA-DRB1*03 and HLA-DRB1*13 alleles were demonstrated to be associated with susceptibility to NPC, while HLA-DRB1*05 was a protective allele in Tunisia (an intermediate incidence area).[23] No associations between the HLA-DRB1 alleles and NPC were reported in high incidence areas, such as Southern China.[12,24] The correlation between HLA-II allele and NPC seemed to be inconsistent in different races from different studies. Here, we reported that in Uyghur population, the HLA-DRB1*0701 allele frequency in the NPC patients was higher than that in healthy controls (P = 0.008), indicating that the allele and clinicopathological parameters were not predictors for prognosis of Uyghur NPC patients [Table 4]. In the Han population, the clinical stage was a predictor for 3-year OS [HR = 2.651, 95% CI = 1.182–5.947, P = 0.018; Table 5], while other clinicopathological parameters and HLA-DRB1 allele could not be considered as potential predictors for the prognosis.

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**Table 3: Log-rank analysis of prognostic factors in Han NPC patients (n = 118)**

| Items                                  | Number, n | 3-year OS (%) | χ² | P     | 3-year DFS (%) | χ² | P     | 3-year DMFS (%) | χ² | P      | 3-year LRFS (%) | χ² | P      |
|----------------------------------------|-----------|---------------|-----|-------|----------------|-----|-------|----------------|-----|--------|----------------|-----|-------|
| HLA-DRB1*1501 status                   |           |               |     |       |                |     |       |                |     |        |                |     |        |
| HLA-DRB1*1501                          | 23        | 78.5          | 0.034| 0.853 | 2.350          | 0.125| 0.947 | 1.970          | 0.160| 95.2   | 2.371          | 0.124|        |
| Non-HLA-DRB1*1501                      | 95        | 83.6          |     |       |                |     |       |                |     |        |                |     |        |
| HLA-DRB1*0101 status                   |           |               |     |       |                |     |       |                |     |        |                |     |        |
| HLA-DRB1*0101                          | 7         | 83.3          | 0.236| 0.627 | 1.877          | 0.171| 1.187 | 0.277          | 1.403| 0.236 |                |     |        |
| Non-HLA-DRB1*0101                      | 112       | 82.6         |     |       |                |     |       |                |     |        |                |     |        |
| Gender                                 |           |               |     |       |                |     |       |                |     |        |                |     |        |
| Male                                   | 82        | 81.4         | 0.455| 0.500 | 0.023          | 0.880| 0.214 | 0.644          | 0.008| 0.928 |                |     |        |
| Female                                 | 36        | 85.5         |     |       |                |     |       |                |     |        |                |     |        |
| Age                                    |           |               |     |       |                |     |       |                |     |        |                |     |        |
| <45 years                              | 57        | 87.6         | 0.842| 0.359 | 1.168          | 0.280| 0.103 | 0.749          | 1.526| 0.217 |                |     |        |
| ≥45 years                              | 61        | 77.9         |     |       |                |     |       |                |     |        |                |     |        |
| Histological classification            |           |               |     |       |                |     |       |                |     |        |                |     |        |
| Differentiated type                    | 45        | 75.1         | 0.773| 0.379 | 0.292          | 0.589| 0.023 | 0.879          | 0.531| 0.466 |                |     |        |
| Nondifferentiated type                 | 73        | 87.0         |     |       |                |     |       |                |     |        |                |     |        |
| Clinical stage                         |           |               |     |       |                |     |       |                |     |        |                |     |        |
| I + II                                 | 10        | 88.9         | 1.003| 0.317 | 0.242          | 0.623| 0.476 | 0.490          | 0.003| 0.953 |                |     |        |
| III + IV                               | 108       | 81.9         |     |       |                |     |       |                |     |        |                |     |        |
| T-stage                                |           |               |     |       |                |     |       |                |     |        |                |     |        |
| T1 + T2                                | 28        | 84.3         | 0.019| 0.889 | 0.025          | 0.874| 0.057 | 0.811          | 0.087| 0.768 |                |     |        |
| T3 + T4                                | 90        | 82.0         |     |       |                |     |       |                |     |        |                |     |        |
| N-stage                                |           |               |     |       |                |     |       |                |     |        |                |     |        |
| N0 + N1                                | 45        | 88.3         | 0.838| 0.360 | 0.026          | 0.872| 0.732 | 0.392          | 0.052| 0.820 |                |     |        |
| N2 + N3                                | 73        | 78.0         |     |       |                |     |       |                |     |        |                |     |        |

NPC: Nasopharyngeal carcinoma; HLA: Human leukocyte antigen; OS: Overall survival; DFS: Disease-free survival; DMFS: Distant metastasis-free survival; LRFS: Local relapse-free survival.
and the patients carrying HLA-DRB1*0701 allele had a 3-fold risk of developing NPC (OR = 3.089, 95% CI = 1.300–7.341). This HLA-DRB1*0701 allele might serve as a susceptible allele in Uyghur population. Similar to the researches from high incidence areas, we also found no associations between HLA-DRB1 allele with NPC in Han population. The previous study’s ethnic origin was from Southern China, our research focused on Xinjiang region including Han and Uyghur populations. The HLA-DRB1 allele distribution in Uyghur population was different from Han population, which might be due to the difference between the two ethnicities. Moreover, we also detected the EBV VCA-IgA level in Han and Uyghur NPC patients and found no statistically significant difference between these two groups, which indicated the different frequency distribution of HLA-DRB1 between two ethnicities might have no relation with EBV infection.

There are several reports on the relationships between HLA-Class II alleles and the clinicopathological characteristics of some malignant tumors. The frequency of HLA-DQB1*07 allele was reported to be significantly higher in early nonsmall cell lung cancer (NSCLC) than that in advanced cancer. The above studies indicated that HLA alleles can influence in the disease development and severity, and further affect treatment outcome. Our study found that among Han NPC patients, HLA-DRB1*1501 and HLA-DRB1*0101 alleles were associated with age and clinical stage, respectively, but not with gender, histology, T stage, N stage, and short effects. In our study, the frequency of HLA-DRB1*1501 allele in the age group of <45 years was higher than that in the age group of ≥45 years (OR = 9.158, 95% CI = 0.082–0.636, P = 0.002), suggesting this allele might contribute to the age of onset in Han NPC patients. In addition, our study found that HLA-DRB1*0101 was associated with clinical stage in the Hans, which indicated that this allele might play a role in the pathogenesis of Han NPC patients. Among Uyghur NPC patients, no associations were found between HLA-DRB1 with clinicopathologic factors including histological classification, T stage, N stage, clinical stage, and short effects. Moreover, further investigation on these aspects is needed.

Both HLA-Class I and Class II alleles were reported to be associated with survival in some tumors. HLA-DRB1*01 and HLA-DRB1*02-null were reported to be associated with shorter OS in chronic lymphocytic leukemia. In a study of malignant lymphoma, HLA-Cw*0701 was found to be associated with poorer OS in patients with diffuse large B-cell lymphoma, and HLA-A*0101 was associated with poorer OS, while HLA-DRB1*13 and HLA-B*84 were associated with better OS in patients with follicular lymphoma. From a research on 695 NSCLC patients in Japan, HLA-A*02 was indicated as an unfavorable prognostic factor in the Stage I NSCLC and HLA-A*24 as an unfavorable prognostic factor in Stage II + III NSCLC.

| Factors                     | 3-year OS HR (95% CI) | P   | 3-year DFS HR (95% CI) | P   | 3-year DMFS HR (95% CI) | P   | 3-year LRFS HR (95% CI) | P   |
|-----------------------------|-----------------------|-----|------------------------|-----|------------------------|-----|------------------------|-----|
| HLA-DRB1*0701 status       | 0.891                 | 0.208 | 0.651                 | 0.857 |
| HLA-DRB1*0701 HLA-DRB1      | 1                     | 1     | 1                     | 1     |
| Non-HLA-DRB1*0701 HLA-DRB1 | 0.882 (0.146–5.311)   | 2.977 (0.544–16.289) | 1.377 (0.344–5.510) | 1.180 (0.196–7.117) |
| Gender                      | 0.428                 | 0.729 | 0.455                 | 0.584 |
| Male                        | 1                     | 1     | 1                     | 1     |
| Female                      | 0.412 (0.046–3.697)   | 0.740 (0.135–4.065) | 0.543 (0.109–2.699) | 0.531 (0.055–5.123) |
| Age                         | 0.361                 | 0.242 | 0.233                 | 0.290 |
| <45 years                   | 1                     | 1     | 1                     | 1     |
| ≥45 years                   | 2.316 (0.383–14.018)  | 2.614 (0.524–13.056) | 2.332 (0.580–9.386) | 2.637 (0.437–15.919) |
| Histological classification | 0.332                 | 0.292 | 0.162                 | 0.333 |
| Differentiated type         | 1                     | 1     | 1                     | 1     |
| Nondifferentiated type      | 42.742 (0.022–84,224.802) | 3.188 (0.369–27.580) | 4.466 (0.547–36.430) | 42.585 (0.021–85,148,450) |
| Clinical stage              | 0.676                 | 0.674 | 0.617                 | 0.579 |
| I + II                      | 1                     | 1     | 1                     | 1     |
| III + IV                    | 22.770 (0.000–834,943.116) | 22.280 (0.000–4,337,407.866) | 22.422 (0.000–4,810,491.419) | 29.711 |
| T-stage                     | 0.535                 | 0.943 | 0.492                 | 1     |
| T1 + T2                     | 1                     | 1     | 1                     | 1     |
| T3 + T4                     | 26.478 (0.001–538,949.647) | 0.925 (0.108–7.931) | 1.229 (0.151–10.001) | 29.732 (0.002–478,273.514) |
| N-stage                     | 0.509                 | 0.725 | 0.589                 | 0.470 |
| N0 + N1                     | 1                     | 1     | 1                     | 1     |
| N2 + N3                     | 27.888 (0.001–538,949.647) | 1.471 (0.171–12.629) | 1.783 (0.219–14.541) | 30.767 (0.003–332,472.900) |

NPC: Nasopharyngeal carcinoma; HLA: Human leukocyte antigen; OS: Overall survival; DFS: Disease-free survival; DMFS: Distant metastasis-free survival; LRFS: Local relapse-free survival; HR: Hazard ratio; CI: Confidence interval.
Our study found that HLA-DRB1*0101 status had no prognostic value in either Han or Uyghur population which suggested that its role in prognosis should be further elucidated.

In conclusion, our findings indicated that HLA-DRB1*0701 was a genetic predisposing factor for NPC in Uyghur population. HLA-DRB1*0101 influenced NPC disease progression and HLA-DRB1*1501 might contribute to the low morbidity of NPC in Han population. HLA-DRB1 could be identified as a prognostic indicator for NPC neither in Han patients nor in Uyghur patients. HLA-DRB1 alleles could potentially be valuable for the evaluation of risk for NPC and its disease progression.

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Conflicts of interest
There are no conflicts of interest.

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