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Short population report

Distribution of *HLA-DRB1*, *DPB1* and *DQB1* alleles and haplotypes in Mongolian Minority in China

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ABSTRACT

HLA-DRB1, -DQB1 and *-DPB1* allele frequencies and estimated haplotype frequencies from 496 unrelated healthy Mongol subjects who living in Inner Mongolia Autonomous Region of China has been reported. *HLA* genes were genotyped using high-resolution sequence-based typing method. Chinese-Mongolian belongs to northern group of East Asians, but with its specific *HLA-DRB1*, *DPB1* and *DQB1* alleles and haplotypes characteristic.

1. Introduction

As one of the major ethnic groups in China with 5,981,800 populations, Chinese-Mongolian distributed in 31 provinces and major living in the Inner Mongolia Autonomous Region of China [1]. They speak a language belongs to Mongolic languages which are a major group languages spoken in East central Asia, mostly in Mongolia and surrounding areas plus in Kalmykia. According to history record, by the mid-thirteenth century, the Mongols had subjugated north China, Korea, and the Muslim kingdoms of Central Asia and had twice penetrated Europe, covering some 33,000,000 square kilometers, founded the largest contiguous land empire in history. They established the first alien dynasty, the Yuan (1279–1368), to rule all China, hereafter, the trade communication major through Tea Road, population migration by War made Mongolians getting fusing with Han and Manchu [1,2]. Now, Mongolian Minority major live in the Inner Mongolia Autonomous Region, others distribute in Gansu, Qinhai, Xinjiang, Liaoning, Jilin and Heilongjiang province of China; shared historic relationship with Khalkh-Mongolian and Khoton-Mongolian in Mongolia. So, the genetic background of Mongolians is vital for studying origin, migration and disease association of populations in East central Asia.

In present study, 496 unrelated healthy Mongol subjects who living in Orqin Right Wing Middle Banner of Inner Mongolia Autonomous Region of China has been included with written informed consent, and *HLA-DRB1*, *HLA-DPB1* and *HLA-DQB1* were genotyped using high-resolution sequence-based typing method (Applied Biosystems, Foster City, CA, USA). The exon 2 and exon 3 of DRB1 and DQB1, all exons of DPB1, were amplified, followed by sequencing and identifying HLA alleles using SBTengine (Applied Biosystems, Foster City, CA, USA). The allele ambiguity was resolve by sequencing extra regions and the genotype ambiguity was resolved by Group Specific Sequencing Primer using the Dynamic Ambiguity Resolving Tool. The *HLA-DRB1, -DPB1* and *-DQB1* allele frequencies were calculated using the Pypop software based on the genotyping results [3–5]. The Hardy-Weinberg equilibrium was assessed using the Guo and Thompson method [6]. The *HLA-DRB1, -DPB1, -DQB1* haplotype was constructed based on the genotyping results using the expectation-maximization algorithm [3–5].

A total of 50 *HLA-DRB1*, 20 *HLA-DPB1* and 19 *HLA-DQB1* has been found (Supplementary Table 1) and the most three predominant alleles were listed in Table 1. A new *HLA-DPB1* allele, *DPB1*581:01* with *DPB1*05:01:01* has been identified. The predominant *DRB1* alleles, *DRB1*09:01:02* and *DRB1*15:01:01:01* common exist in East Asian populations, however the *DRB1*07:01:01:02* was prevalence in Mongolian, Chinese Han, Korean and Japanese, but rare in other ethnic groups in China [7,8]. The other two predominant alleles in Khoton-Mongolian and Khalkh-Mongolian, *DRB1*03:01:01:01* and *DRB1*04:01:01* existed in this Mongolian ethnic group with medium frequencies of 5.9% and 3.4%, respectively [9]. On *DQB1* locus, predominant allele *DQB1*03:01* was prevalent in all the East Asian populations, and *DQB1*06:01* also co-exist in East Asian populations but with a medium frequency of 7.4% in present Chinese-Mongolian. It is interesting to investigate that *DQB1*03:03* and *DQB1*02:01* existed commonly in Chinese-Mongolian (14.5% and 9.7%) and Khalkh-Mongolian (4.9% and 17.2%), but not identified in Khoton-Mongolian [9]. Moreover, *DQB1*02:02* with frequency of 6.8% in Chinese-Mongolian, were identified only in Japanese and South Korean among East Asian populations. For DPB1 locus be considered, common East Asian alleles *DPB1*05:01:01, DPB1*02:01:02, DPB1*04:01:01*, and *DPB1*04:02:01*

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Table 1
Allele frequencies and main summary statistics.

Locus	N	K	H	HWE(p)	EW (Fnd)	EW(p)	Most Frequent Alleles
DRB1	496	50	0.740	0.583	−0.721	0.224	DRB1*09:01:02(12.7%), DRB1*07:01:01:02(12.4%), DRB1*15:01:01:01(9.8%)
DPB1	496	20	0.921	0.163	−0.658	0.273	DPB1*05:01:01(26.4%), DPB1*02:01:02(20.9%), DPB1*04:01:01(17.2%), DPB1*04:02:01(10.3%)
DQB1	496	19	0.859	0.436	−1.231	0.023	DQB1*03:01(24.6%), DQB1*03:03(14.5%), DQB1*02:01(9.7%)

N: sample size; k: number of alleles; H: heterozygosity; HWE: p-Value for Hardy-Weinberg equilibrium test; EW: Slatkin's implementation of EW homozygosity test of neutrality.

were predominant in Chinese-Mongolian. *DPB1*17:01:01* existed in Chinese-Mongolian (4.2%) and Khalkh-Mongolian (8.8%), but no identified in Khoton-Mongolian. *DPB1*13:01:01* exited only in Chinese-Mongolian (3.0%), but not identified in Khalkh-Mongolian and Khoton-Mongolian [9].

HLA haplotypes bearing 2–3 loci were estimated and the haplotypes with frequencies over 1% were listed in Supplementary Table 2. The common haplotypes bearing different loci showed that *DQB1*03:01* were linkage with other alleles. The common *DRB1-DPB1-DQB1* haplotypes included *DRB1*15:01:01:01-DPB1*04:01:01-DQB1*03:01*, *DRB1*09:01:02-DPB1*02:01:02-DQB1*03:01* and *DRB1*09:01:02-DPB1*05:01:01-DQB1*03:03*, which showed East Asian population's characteristic. On contrary, some haplotypes *DRB1*15:01:01:01-DQB1*03:01*, *DRB1*15:01:01:01-DPB1*04:01:01-DQB1*03:01*, *DRB1*15:01:01:01-DPB1*05:01:01-DQB1*03:01*, *DRB1*12:01:01-DPB1*02:01:02-DQB1*03:01*, *DRB1*12:02:01-DPB1*05:01:01-DQB1*03:01* were very rare in other populations worldwide, showed its specific Mongolian group characteristic (Supplementary Table 2).

Both in NJ tree and PCA constructed based on *HLA-DRB1*, *DPB1* and *DQB1* allele's frequencies (Fig. 1), Chinese-Mongolian cluster together with Khalkh-Mongolian, Khoton-Mongolian and Evenki ethnic group belonging to northern East Asian group. Moreover, Chinese-Mongolian showed closer relationship with Khalkh-Mongolian than Khoton-Mongolian, which indicate that the Chinese-Mongolian in China and the major Mongolians in Mongolia share the common ancient HLA genes along their immigration and fusing with other populations like Evenki.

In conclusion, Chinese-Mongolian belongs to northern group of East Asians, but with its specific *HLA-DRB1, DPB1* and *DQB1* alleles and haplotypes characteristic.

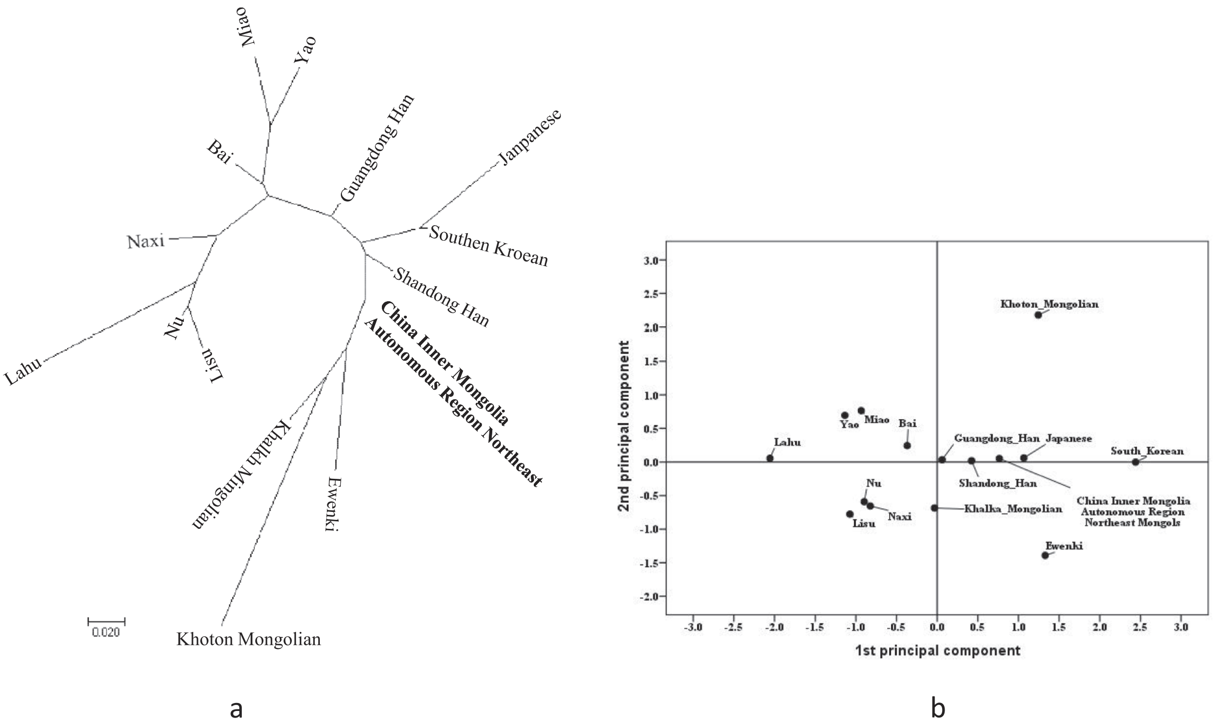

Fig. 1. Phylogenetic analyses showing relationships among Chinese-Mongolian and other East Asian populations. 1a. Neighbor-Joining tree of 15 populations in East Asia constructed by Nei's standard distance based on *HLA-DRB1*, *-DPB1*, and *-DQB1* frequencies. 1b. Principal component analysis using *HLA-DRB1*, *-DPB1*, and *-DQB1* frequencies of 15 East Asian populations.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humimm.2019.01.006.

References

[1] G. Yang, Analysis of migration situation of Mongolian nationality in China. China Statistics, 2013, 9.

[2] group W: A brief history of Mongolians. Huhehaote, China: Inner Mongolia people's publishing house, 1977.

[3] Y. Fan, Y.Q. Song, PyHLA: tests for the association between HLA alleles and diseases, BMC Bioinform. 18 (2017) 90.

[4] A.K. Lancaster, R.M. Single, O.D. Solberg, M.P. Nelson, G. Thomson, PyPop update–a software pipeline for large-scale multilocus population genomics, Tissue Antigens 69 (Suppl. 1) (2007) 192.

[5] A. Lancaster, M.P. Nelson, D. Meyer, G. Thomson, R.M. Single, PyPop: a software framework for population genomics: analyzing large-scale multi-locus genotype data, Pacific Symp. Biocomput. 8 (2003) 514.

[6] S.W. Guo, E.A. Thompson, Performing the exact test of Hardy-Weinberg proportion for multiple alleles, Biometrics 48 (1992) 361.

[7] S. Saito, S. Ota, E. Yamada, H. Inoko, M. Ota, Allele frequencies and haplotypic associations defined by allelic DNA typing at HLA class I and class II loci in the Japanese population, Tissue Antigens 56 (2000) 522.

[8] E. Trachtenberg, M. Vinson, E. Hayes, Y.M. Hsu, K. Houtchens, H. Erlich, et al., HLA class I (A, B, C) and class II (DRB1, DQA1, DQB1, DPB1) alleles and haplotypes in the Han from southern China, Tissue Antigens 70 (2007) 455.

[9] B. Munkhbat, T. Sato, M. Hagihara, K. Sato, A. Kimura, N. Munkhtuvshin, et al., Molecular analysis of HLA polymorphism in Khoton-Mongolians, Tissue Antigens 50 (1997) 124.