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Short population report

HLA-A, -B, -C, -DRB1 and -DQB1 alleles and haplotypes in 194 Southeast Asia Chinese from Peninsular Malaysia

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A B S T R A C T

A total of 194 Southeast Asia Chinese from Peninsular Malaysia were genotyped for HLA-A, -B, -C -DRB1, and -DQB1 loci using polymerase chain reaction sequence-specific oligonucleotide probe hybridization methods. In this report, the HLA-B, HLA-DRB1 and HLA-DQB1 were in Hardy-Weinberg proportions (HWEP) ($p > 0.05$). We observed significant deviation from HWEP in HLA-A ($p < 0.05$) and HLA-C ($p < 0.01$) loci. This genotype data was available in Allele Frequencies Network Database (AFND) Dos Santos et al. (2016).

Malaysia is a Southeast Asia country comprising the Peninsular Malaysia (also known as West Malaysia) and part of the Borneo island known as East Malaysia. The West and East Malaysia with a total land area of 329,750 km^2 is separated by the South China Sea (latitude 2°30′N, longitude 112°30′E). The total population of Malaysia is 32.4 million of which 89.8% are Malaysian citizens and 10.2% non-citizens [2]. Among the Malaysian citizens, the Malays and the *Bumiputra* (indigenous people with Malay origin) is the predominant ethnic group in Peninsular Malaysia, accounting for 69.1% (20.1 million), followed by the Chinese 23.0% (6.7 million), Indians 6.9% (2.0 million) and others 1.0% (0.3 million).

The Malaysian Chinese population are mainly descendants of the 19th and early 20th century Han Chinese immigrants from Southern China (particularly the provinces of Fujian, Guandong and Hainan) who came as traders, laborers and miners during the British colonization. The Chinese are distributed throughout Malaysia, mainly in the urban areas. They represent the second largest ethnic group in Malaysia. The Malaysian Chinese community is made up of three major dialect groups i.e., Hokkien (ethnologue three-letter language code, *nan*), Hakka (*hak*) and Cantonese (*yue*) [3]. Nevertheless, Mandarin (*cmn*) is the most commonly spoken and literate language in Chinese communities residing in Peninsular Malaysia.

The source of this report was obtained from the multicenter Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) case-control study, in which normal healthy subjects were enrolled between 2005 and 2009 from the urban and rural areas throughout Peninsular Malaysia [4–6]. In this report, we investigated a total of 194 Chinese healthy controls with complete data set for HLA-A, HLA-B, HLA-C, HLA-DRB1 and HLA-DQB1 alleles. Informed written consent was obtained from all participants and the anonymous genotyping data were used for research and public dissemination. The study was approved by the Medical Research and Ethics Committee, Ministry of Health, Malaysia.

All the DNA samples were genotyped for HLA-A, -B, -C, -DRB1, and –DQB1 loci using polymerase chain reaction and sequence-specific oligonucleotide probe hybridization (PCR-SSO) method (LABType®HD

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HLA Test kits, One Lambda Inc., CA, USA) with Luminex Multi-Analyte Profiling System (xMAP, Luminex Corporation, Texas, USA). HLA-A, -B and -C alleles were recognized as per release of IMGT/HLA Database (Release 2.28.0, January 2010) and the HLA-DRB1 and DQB1 alleles as per release of IMGT/HLA Database (Release 3.3.0, January 2011). The assignment of HLA typing was accomplished using the HLA Fusion software (version 1.3.0) provided by the manufacturer (One Lambda Inc., CA, USA). In addition, the HLA-A and HLA-B genotyping were supplemented with PCR sequence specific primer (PCR-SSP/HLA Allele-Specific) methods to distinguish between the following allelic groups e.g., HLA-A*01:01 and HLA-A*36:04 alleles; HLA-A*02:10 and HLA-A*92:01 alleles; HLA-B*55:02 and HLA-B*54:05 alleles; HLA-B*55:05 and HLA-B*56:16 alleles; and HLA-B*15:01 and HLA-B*46:16 alleles. Sequence-based typing were used to resolve the HLA allele's ambiguity where necessary [7]. In brief, the samples with HLA ambiguous data were prepared for sequencing using the commercial polymerase chain reaction-sequenced based typing (PCR-SBT) kits (SeCore® A/B/C/DRB1/DQB1 locus sequencing kit, Life Technologies, Brown Deer, WI, USA). Each template was sequenced bidirectionally for exon 2, 3, 4, where applicable, with BigDye™ Terminator v1.1 (Applied Biosystems, Foster City, CA) on an automated AB1 3130xl sequencer (Applied Biosystems, Hitachi, Japan) [8]. Alleles were assigned using uTYPE 6.0 CE-IVD Software and version 3.17.0 of the IPD-IMGT/HLA reference database released on July 2014 [9].

HLA allele frequencies were obtained by direct counting. The five-locus (A–B–C–DRB1–DQB1) haplotype frequencies were estimated using Expectation Maximization (EM) algorithm included in the ARLEQUIN software [10]. The Hardy-Weinberg equilibrium proportions (HWEP) were performed independently for HLA-A, -B, -C, -DRB1 and DQB1 (Arlequin version 3.5.2.2 software).

Our data showed that the commonest alleles were HLA-A*11:01 (allele frequency, AF = 0.30), HLA-B*40:01 (AF = 0.12), HLA-C*01:02 (AF = 0.18), HLA-DRB1*09:01 (AF = 0.14) and DQB1*03:01 (AF = 0.18) for the investigated loci (Supplementary Table S1). In this report, the HLA-B, HLA-DRB1 and HLA-DQB1 were in Hardy-Weinberg proportions (HWEP) ($p > 0.05$). We observed significant deviation from HWEP in HLA-A ($p < 0.05$) and HLA-C ($p < 0.01$) loci (Supplementary Table S2). The most common five-locus haplotype was A*33:01–B*58:01–C*03:02–DRB1*03:01–DQB1*02:01 (Supplementary Table S3). This work may provide future research with data relating to genetic architecture of the Chinese ethnic group particularly for population genetics, disease associations, and/or HLA-related drug hypersensitivity reaction studies in Southeast Asia, a region well-known to that harbor significant cultural, linguistic and genetic diversity. This genotype and frequency data are available in AFND ID 3652 under the name "Malaysia Peninsular Chinese" [1].

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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.2019.09.005.

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