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Original Article

HLA haplotype diversity in the South Indian population and its relevance

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ABSTRACT

Background: South India (SI) is the area encompassing India's states of Andhra Pradesh, Karnataka, Kerala, Telangana, and Tamil Nadu as well as the union territories of Lakshadweep and Pondicherry. South Indians are heterogeneous population with different ways of life, language, and physical appearance. A majority of Indians from the southern region speak one of the languages: Tamil, Telugu, Kannada, Malayalam, or Tulu. A large number of south-Indians have now migrated to different parts of the world and often need human leukocyte antigen (HLA) matched donors for treatment of different disorders. Knowledge of allele and haplotype frequencies of the HLA system is important in the search for unrelated bone marrow donors. The South Indian population is very heterogeneous and the HLA system is highly informative of populations because of the high level of polymorphisms. We investigated distribution of HLA A, B and DRB1 loci in five linguistic groups from SI.

Materials & methods: All the data were collected from the Marrow Donor Registry India (MDRI) which has pool of volunteer stem cell donors from these linguistic groups. DNA extracted from EDTA-blood sample of recruited donors, and HLA typing done using Luminex XMAP technology and sequence specific primer (SSP) technique at low–intermediate resolution. Graph pad InStat 3 and the software from National Marrow Donor Program (NMDP) were used for determining *p* values and haplotype frequency respectively.

Results: MDRI donors belonging to these five linguistic groups namely Tamil, Telugu, Tulu, Kannada, and Malayalam speaking donors were analyzed. The most common haplotypes were A*01-B*57-DRB1*07, A*33-B*44-DRB1*07, A*02-B*40-DRB1*15, A*24-B*07-DRB1*15, A*24-B*40-DRB1*15. A few unique haplotypes were seen as most common haplotype in each linguistic group.

Conclusion: Each linguistic group has unique haplotypes along with a few common haplotypes. In order to adequately represent the Indian population on the registry, each linguistic group should be targeted for donor recruitment. This would enable a better chance for any patient to find a matched unrelated donor.

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1. Introduction

South India (SI) is one of the oldest geophysical regions occupied mainly by Dravidian language-speaking people. The major Dravidian languages are Tamil, Telugu, Malayalam, Kannada, and Tulu.[1] We analyzed MDRI donor samples from these five linguistic groups from SI to study the human leukocyte antigen (HLA) characteristics of each group. South Indians from the above mentioned linguistic groups represent 20% of Indian population and about 11 million South Indians have immigrated to various parts of the world[2–6] (Table 1).

The HLA system is synonymous with the human major histocompatibility complex (MHC). These HLA genes express their gene products on the surface of white blood cells and were originally recognized to contain the genes encoding ''tissue antigens'' or ''tissue types''. These HLA have to be matched for increasing the chances of graft acceptance and reduce the risk for graft versus host disease.

Marrow Donor Registry India (MDRI) is a nongovernment organization working toward the cause of searching unrelated matched donors for patients from India and abroad requiring stem cell transplantation.

Aim:

1. To determine the HLA ABDRB1 allele and haplotype pattern in southern Indians
2. To assign ranks for each haplotype found in all groups. As well as to compare the haplotypes within different groups to identify the most common and unique haplotypes.

Materials and Methods:

1. Subjects – 1893 voluntary bone marrow donors from southern India were included in this study.
2. DNA extraction was done by salting out technique (Invitrogen, WI, USA) followed by sequence specific oligonucleotide probes (SSOP) technique using Luminex xMap technology (Gen-probe, CT, USA).
3. Ambiguities were resolved using the sequence specific primer (SSP) technique (Bag Healthcare, Lich, Germany).
4. Graph pad Instat 3 software was used for statistical analysis and software developed at the National Marrow Donor Program (NMDP), USA along with Arlequin 3.1 software was used for determining the haplotype frequency.

2. Results

MDRI donors from 5 linguistic groups ($n > 100$) namely Kannada ($n = 281$), Malayalam ($n = 443$), Tamil ($n = 463$), Telugu ($n = 450$), and Tulu ($n = 256$) respectively were tested for the HLA ABDRB1 alleles.

2.1. *Distribution of HLA A, B and DRB1 alleles in each linguistic group*

Percentage of HLA A, B and DRB1 alleles in each linguistic group is tabulated below (Tables 2–4). All linguistic groups had higher prevalence of A*01(13.3 ± 3.82), A*02(15.06 ± 2.2), A*11 (14.3 ± 2.2), A*24(16 ± 2.2), and A*33(12.9 ± 5.77) over other HLA A alleles. Similarly B*35(13.9 ± 1.47), B*44(8.17 ± 2.59), B*51(9 ± 2.97), and B*52(8.17 ± 2.7) were prevalent HLA B alleles in all linguistic groups. DRB1*07(16.5 ± 3.06) and DRB1*15 (23.12 ± 5.49) are extremely common in all groups.

2.2. *Common haplotypes in 5 linguistic groups*

1893 donors from 5 South Indian linguistic groups were analyzed to see their haplotypes using the software developed at the NMDP, USA.

The average haplotype frequency percentage (AHF%) of common haplotypes were A*01-B*57-DRB1*07 (AHF% = 3.19%), A*33-B*44-DRB1*07 (AHF% = 3.36%), A*02-B*40-DRB1*15 (AHF% = 2.10%), A*24-B*07-DRB1*15 (AHF% = 1.61%), and A*24-B*40-DRB1*15 (AHF% = 1.61%) (See Table 5).

2.3. *Unique haplotypes in 5 linguistic groups*

Besides the common haplotypes that were seen across all 5 linguistic groups, we found a few unique haplotypes in each group (see Table 6). A*33-B*51-DRB1*15 is a haplotype seen very commonly in Kannada speaking population and is statistically significant. A*01-B*57-DRB1*04, A*02-B*35-DRB1*15, A*02-B*52-DRB1*15, A*03-B*35-DRB1*15, and A*11-B*52-DRB1*15 are the haplotypes that are significantly increased in Telugu speaking population ($p < 0.001$). A*24-B*15-DRB1*13 and A*24-B*40-DRB1*04 were statistically significant in Tamil speaking population. Similarly 4 haplotypes namely A*24-B*40-DRB1*08, A*24-B*44-DRB1*07, A*24-B*52-DRB1*04, and A*11-B*40-DRB1*14 were significantly increased in Malayalam speaking population. The Tulu speaking population demonstrated 6 unique haplotypes that were statistically significant,

Table 1 – Distribution of Dravidian speaking population in South India.

State	Language	Population (% of population of India)	Population worldwide	References
Andra Pradesh (AP)	Telugu	84,655,533 (7%)	2,360,000	2
Tamil Nadu (TN)	Tamil	72,138,958 (5.6%)	6,375,927	3
Karnataka (KA)	Kannada	61,130,704 (5.05%)	175,000	4
Kerela (KE)	Malayalam	33,387,677 (2.76%)	2,190,133	5
Karnataka and northern Kerela	Tulu	2,000,000 (0.16%)	Unknown	6
		228,550,914 (20.6%)	11,101,060	