

Gradients in Distribution of HLA – DRB1* Alleles in Castes and Tribes of South India

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ABSTRACT In the present study 520 individuals comprising eleven different populations (castes and tribes) from the states of Tamil Nadu and Kerala, South India were genotyped for HLA–DRB1* allele profile by PCR-SSP method. HLA DRB1*15 (subtype of DR2) was the allele consistently showing higher frequency in all populations studied. HLA DRB1*15 revealed a highest frequency in Kani tribe (45.19%) and the lowest frequency in Narikkuravars (Gypsies) (1.02%). The other predominant alleles based on their order of frequencies observed in each population were DRB1*10, 07 and 15 among Iyers; DRB1*07, 04, 15 and 08 among Kallars; DRB1*03 and 10 among Vanniyars and Vettuva Gounders; DRB1*07 and 10 among Sourashtrans; DRB1*07 and 04 among Pallars; DRB1*04, 03, 07 and 11 among Narikkuravars; DRB1*03 among Paliyar and Kani tribes; DRB1*13, 10, 04, 14 among Nairs; DRB1*10, 01, 13 and 11 among Namboothiris of Kerala. Alleles such as DRB1*01, 08, 09, 11, 12, 14 and 16 were either present in low frequencies or completely absent in many of the south Indian populations studied. Predominantly Caucasian allele DRB1*01 was present in higher frequencies in Namboothiris (12.85%) and Narikkuravars (8.53%) only. Allele DRB1*01 frequency in all other populations is significantly low. However, alleles DRB1*07 was present in many populations with higher frequencies (highest in Kallars with 23.58%). This could have been due to the higher prevalence of HIV/TB infectious and the presence of ancestral haplotype 57.1 in Indian populations. Implications of this differential distribution of these HLA-DRB1*alleles in different castes and tribes of South India are discussed in the context of high prevalence of infectious diseases such as AIDS and TB.

INTRODUCTION

The southernmost part of peninsular India, ‘Gondwanaland’ is thought to be one of the oldest geographical regions of the world (Majumdar 1961). The people of south India encompassing states of Tamil Nadu, Karnataka, Kerala, and Andhrapradesh speak the Dravidian languages. The origins are thought to be most likely Mediterranean (Sanghvi et al. 1981), Negroid (Harris et al. 1976) or Mongoloid (Festenstein et al. 1972). Further, it is inferred from historic documents that there have been many population and political invasions in to India and hence has been a melting pot of races (Dobzonsky 1973). There are about 3000 castes and tribes and more than

25,000 sub-castes existing in India today: predominantly a mixture of populations from middle East, Central Asia and Mongolia (Bhasin et al. 1994). The caste system is very rigid in Tamil Nadu and is characterized by endogamy, social restriction on inter-caste marriages and occupation based social classes (Sanghvi et al. 1981). It is well documented that the Dravidians of south India practiced a culture and unique social institution with a very ancient linguistic family further subdivided into many gene pools, differing in their origin, migration and population settlement (Menon 1996; Kivisild et al. 1999; Pitachappan 2002, 2003; Basu et al. 2003).

In the human species, the major histocompatibility complex (MHC) encompasses the HLA (Human Leukocyte Antigen) genes. On the short arm of chromosome 6, between 6p21.31 and 6p21.33, is characterized by a set of highly polymorphic genes with immunological and medical implications (Charron 1997). Last few decades has witnessed many development in HLA genetics and its impact in transplantation medi-

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cine, autoimmunity, infectious disease studies, allergy, cancer, vaccine designing and in anthropology and population genetics (Aidoo et al. 1995; Charron 2000). HLA allele and haplotype frequencies vary considerably across ethnic groups (Meyer et al. 2006; Meyer et al. 2007; Wolf et al. 1980; Mittal et al. 1982; Imanishi et al. 1992). Distribution of HLA class II alleles in various Indian population have been reported (Pitachappan et al. 1997; Mehra et al. 1994; 1998, Balakrishnan et al. 1996, Agrawal et al. 1999; Ganga et al. 2004, Shankarkumar et al. 2001; Chayya and Shankarkumar 2003; Shankarkumar et al. 2001; Kankonkar and Shankarkumar 2005; Agrawal et al. 2001; Bharadwaj et al. 2007; Jaini et al. 2002).

In the present study, the frequency distribution of HLA class II DRB1* alleles was analyzed by PCR-SSP method for 520 individuals representing eleven endogamous castes and tribes of south India. HLA-DRB1* allele frequencies for the eleven populations were presented and the phylogenetic relationships among the eleven populations and other Indian populations have been constructed. Allelic distribution was discussed in the context of the health, disease and molecular genetic epidemiological perspective.

MATERIALS AND METHODS

Study Populations

Five hundred and twenty healthy unrelated individuals belonging to eleven different population groups from South India were included in this study. The populations selected for the present study includes Scheduled castes: Pallan; Schedule tribes: Paliyar and Kani; middle castes: Kallar, Vanniyar and Vetuva Gounder, Sourastran, Nairs of Kerala; Narikuravars of Tamilnadu (most backward community) and upper castes: Iyer of Tamilnadu and Namboothries from Kerala (Fig. 1). They belong to different geographical locations in the states of Tamilnadu and Kerala. All these populations belong to Dravidian linguistic group and Proto-Austroloid ancestry. Due care was taken to avoid sampling from related individuals and siblings. EDTA blood samples (2 ml) were drawn and the genomic DNA was extracted from mononuclear cells using the standard salting out procedure (Welsh and Bunce 1999) and quantified by spectrophotometer and gel analysis (Miller

et al. 1988). Institutional ethical clearance and the informed consent was obtained from all the individuals who participated in the study which includes demographical details such as age, gender and family history for major illness or disease if any. Molecular HLA typing was carried out using the polymerase chain reaction–sequence-specific primers (PCR-SSP) method for the class II antigen as described previously (Olerup and Zeterquist 1992).

Ethnographic Notes

1) Kani Tribes: Kani tribes also known as Kanikkaran, Kanikkar, Velanmars, Malaiarasan, Malavedan. They inhabit the hills of Trivandrum district and adjoining district of Quilon in Kerala and also in the Papanasam hills of Tirunelveli district and Pechiparai hills of Kanyakumari district of Tamilnadu. In Tamilnadu part they are conversant with the Tamil language in addition to their mother tongue (Malayalam) and use the Tamil script for writing. Kani tribes are following a maternal lineage of inheritance. These maternal clans are called as 'Illam'. Buchi (1953) postulated on the basis of a serogenetic study, a relationship with the Australian aborigines (Australoids). He further emphasized that the blood group gene distribution of the Kani puts them closer to the Caucasoids.

2) Paliyar Tribes: The Paliyars are scheduled tribes living in the south Western Ghats mountain rain forests in south India, especially in Tamilnadu and Kerala. They are traditional nomadic hunter-gatherers, honey hunters and foragers.

3) Pallars: The Pallars are an ancient community, engaged extensively in wet land farming and distributed mainly in Thanjavur, Madurai and Ramanathapuram districts (Ramaiah 2004). The Pallars are a rural community and placed lower in the social hierarchy and grouped as Adi Dravidar along with other socially backward communities (Singh 1998).

4) Narikuravars: Although all Kuravars come under one roof, based on their common clan name Kura-vars, there are twenty seven sub-sects in itself, including Narikuravars. Among these group of people, the most disadvantaged section is Narikuravar who still live as gypsies now placed under Most Backward Community list of Tamil Nadu and exist today as semi-urban-settlers. The main occupation is hunting. But as they were prohibited entry into the forests to pursue their livelihood, they were

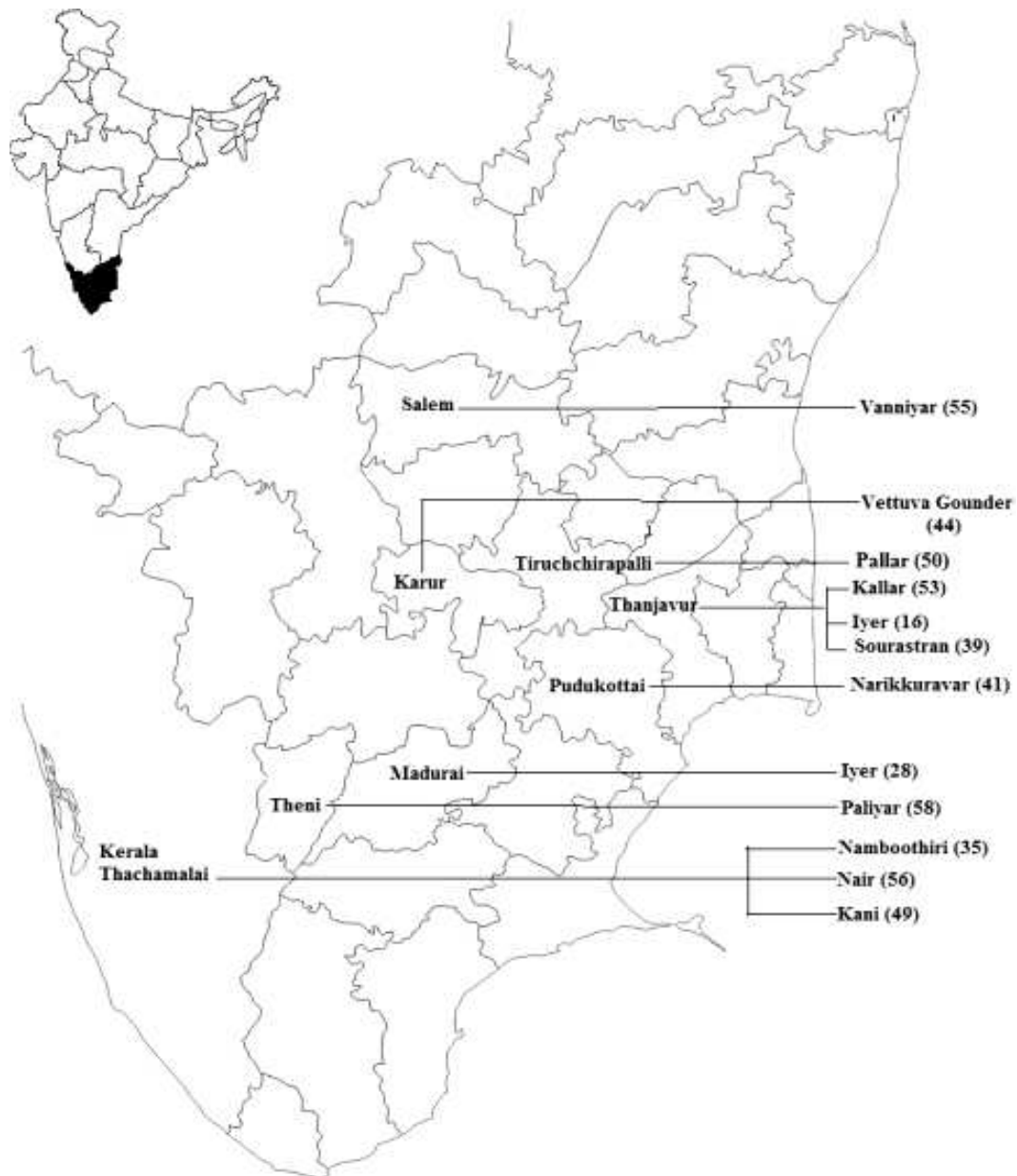


Fig. 1. Sampling sites of different population groups from Tamil Nadu and Kerala states of South India (number of samples in brackets).

forced to take up other alternatives such as selling beaded ornaments to survive. Hence they migrate from place to place to find a market for their beads.

5) *Kallars of Tanjore*: Kallars are a widespread, ancient population living in southern

parts of Tamil Nadu. Traditionally, they were described as semi agriculturists and semi warriors. Kallars are known to be the oldest immigrants of Neolithic period with Mediterranean racial elements (Malhotra et al. 1981). Kallars (Kallars of Thanjavur district of Tamil Nadu)

form one of the geographically differentiated endogamous groups of the dominant Kallar community of Tamil Nadu, who were described as a martial community in the early Chola and Pandya periods (Singh 1997). The Tanjore Kallars comprise an endogamous subgroup of the Kallar community exhibiting exogamy at the clan level while maintaining strict endogamy at the subgroup level.

6) Vanniyars: The Vanniyar community is predominant in Tamil Nadu (population size: around 20 million) (Singh 1998). The Vanniyars, known as Pallis, became soldiers and commanders during the medieval Pallava rule and came to be known as Padayatchis.

7) Vettuva Gounders: The Vettuva Gounders claim the lineage of Siva Bhakta Kannapa Nayanar. Today most Vettuva Gounders live in the districts of Salem, Namakkal, Erode, Karur, Trichy and Coimbatore.

8) Sourashtrians: Sourashtrians are mostly silk weavers and silk thread merchants, originated from the Sourashtra region (present day Gujarat, and parts of Maharashtra states) in northern India and later settled in Madurai and surrounding regions of Tamil Nadu, few centuries ago.

9) Iyers: Brahmins everywhere in India enjoy the highest social status in Hindu society and claim that they are the descendants of one of the seven rishis (saints) (Nilakanta Sastry 1955; Sanghvi and Balakrishnan 1981). Brahmins from different parts of India have adopted the local languages and customs of their place of settlement (for example, first-cousin and uncle-niece marriage in south India but not in north India), although their ideologies, profession and major language (Sanskrit) remained the same.

10) Namboothiris: The Namboothiris are the Brahmins of Kerala. Claiming priestly origin, the Namboothiris established superiority over the "Patters," the Tamil Brahmins.

11) Nairs: The Nairs are believed to be the first Dravidian invaders of Kerala, who belonged to the warrior class and later assumed the position of the governing and landowning class, while the Brahmins (Namboothiris) are the most recent immigrants to Kerala.

Statistical Analysis

HLA allele frequencies were estimated by direct counting and POPGENE statistical pack-

ages. Dendrogram analysis was performed by using the Arlequin v. 2.0 (<http://anthropologie.unige.ch/arlequin>) (Excoffier and Slatkin, 1995). Phylogenetic trees were constructed by the neighbor joining method using the data for the Indian populations and the population studied in the present work (Tables 1 and 2). For these constructions alleles were grouped based on serological specificities.

RESULTS

Caste Populations of Tamil Nadu: Percentage allele frequencies at HLA DRB1* locus in eleven populations were presented in Table 1. Among Iyers, the most frequent alleles were DRB1*10 (19.32%), DRB1*07 and DRB1*15 (18.18% each). Moderate frequencies were observed for the alleles such as DRB1*03 (7.95%), DRB1*04 (6.82%) and DRB1*16 (5.68%). Alleles HLA-DRB1*08 (3.41%), DRB1*11 (4.55%), DRB1*14 (2.27%) and DRB1*01 (1.14%) were observed less frequently. Alleles DRB1*09 and DRB1*12 were completely absent. In Kallars, the most common alleles observed were DRB1*07 (23.58%), DRB1*15 (18.86%), DRB1*04 (12.26%), DRB1*14 (10.37%), DRB1*08 (6.60%) and DRB1*12 (5.66%). DRB1*13 (0.94%), DRB1*16 (2.83%) and DRB1*01 (1.88%) were less frequently distributed. Alleles DRB1*03 and DRB1*11 were not at all present.

Among Vanniyars the most frequent allele was DRB1*03 (36.27%) followed by alleles DRB1*15 and DRB1*10 (each 21.56%). Other alleles identified were DRB1*04, DRB1*07, DRB1*08 (each 3.92%), DRB1*11 (2.94%), DRB1*13 and DRB1*14 (each 1.96%). In Vettuva Gounders, the most common allele was DRB1*03 (35.22%) followed by alleles DRB1*10 (25.0%) and DRB1*15 (20.45%). Moderate frequencies were observed for DRB1*04 (5.68%), DRB1*01 (3.40%) and DRB1*13 (3.40%). DRB1*07, DRB1*11, DRB1*14 and DRB1*08 were found with low frequencies (ranging from 1.13 to 2.27%). In Sourashtrians, the commonest alleles were DRB1*15 (30.76%), DRB1*07 (19.23%), DRB1*10 (11.53%) and DRB1*03 (6.41%). Lower frequencies were observed for alleles DRB1*11, DRB1*12, DRB1*14 and DRB1*01 (each 5.12%). The frequencies of DRB1*09 and DRB1*04 were very low (1.28% and 2.56% re-

Table 2: Percentage frequencies of HLA-DRB1* alleles in selected Indian populations

HLA alleles DRB1*	¹ Yadavas (n = 233)	¹ P.Kallars (n = 202)	¹ Vanniyar (n = 132)	¹ Random (n = 84)	⁵ Nadars (n = 84)	² Iyer (n = 74)	³ Irula (n = 191)	³ Malayali (n = 42)	⁶ Lucknow random (n = 123)	⁶ Delhi random (n = 308)	⁷ Delhi random (n = 47)	⁶ Kashmir Brahmin	⁵ Mumbai Maratha (n = 113)	⁴ Marathi (n = 96)	⁴ Gujarati (n = 59)	⁴ Random (NI) (n = 210)
*01	3.3	4.9	2.9	1.7	1.19	9.2	9.3	7.4	1.7	3.08	-	1.3	7.96	5.2	0.8	4.27
*02	12.9	26	13.6	22.5	10.71	14.6	15.3	21.3	19.8	21.42	13.8	12.0	24.4	26.04	12.7	21.65
*03	14.34	11.6	13.8	6.9	11.9	6.3	2.2	4.9	9.1	6.98	7.45	3.9	3.09	11.45	11.8	10.71
*04	18.5	10.78	7.9	11.3	11.9	18.6	6.6	12.7	7.4	7.79	12.75	12.0	5.75	8.33	5.0	14.4
*05	6.1	3.96	3.2	9.2	3.57	10.7	4.9	16.4	13.1	11.84	11.6	13.6	12.81	7.28	18.5	5.93
*06	4.93	8.3	7.6	5.2	20.23	4.01	7.2	10.0	17.8	13.95	28.8	15.8	7.07	17.73	21.1	16.16
*07	13.7	8.2	12.4	20.1	28.57	17.0	9.8	12.7	19.8	13.96	14.9	27.5	13.27	8.33	13.5	14.04
*08	5.73	4.6	5.1	5.7	-	8.5	22.6	4.9	0.4	0.64	1.1	-	2.65	1.56	-	0.94
*09	1.63	0.5	1.9	0.6	-	4.8	6.1	6.1	1.2	0.64	1.1	-	3.09	-	-	1.42
*10	8.22	10.0	7.2	9.44	11.9	5.6	14.4	3.6	9.1	5.51	3.2	3.9	7.96	8.85	5.9	1.9
Blank	9.20	10.49	22.4	6.84	-	1.2	1.6	-	0.6	0.24	5.30	10.0	11.94	-	-	-

Cf: 1-Shanmugalakshmi et al. (2003); 2-Balakrishnan et al. (1996); 3-Pitchappan et al. (1997); 4-Kanakonkar and Shankarkumar (2005); 5-Shankarkumar et al. (2004); 6-Mehra (1998); 7-Rajalingam et al. (2002).

spectively). DRB1*08 was completely absent in this linguistic group. In Pallars, the most predominant allele observed was DRB1*15 (43%) followed by alleles DRB1*07 (11%), DRB1*04 (10%), DRB1*10 (7%), DRB1*11 (7%), DRB1*16 (6%), DRB1*14 (5%) and DRB1*03 (4%). Alleles DRB1*01, DRB1*09 and DRB1*13 were observed in very low frequencies (each 1%). Among Narikuravars, the most common allele was DRB1*04 (41.46%) followed by alleles DRB1*03 (14.63%), DRB1*07 (12.19%), DRB1*11 (9.75%), DRB1*01 (8.53%) and DRB1*13 (7.31%). Alleles DRB1*08, DRB1*10 and DRB1*15 revealed very low frequencies. DRB1*09, 12 and DRB1*14 were completely absent.

Tribes of Tamil Nadu: In Paliyars, the most common alleles were DRB1*03 (69.49%) and DRB1*15 (12.06%). Moderate frequencies were observed for alleles DRB1*10 (4.23%) and DRB1*14 (3.38%). Alleles DRB1*01, 07, 08, 11, DRB1*13, DRB1*04, DRB1*12 and DRB1*16 were observed in lower frequencies. In Kani tribes, the frequency of DRB1*15 (45.91%) was the highest followed by DRB1*03 (46.93%). DRB1*01 was observed in only one individual (1.02%). All other alleles were absent in Kani tribes.

Populations from Kerala: Among Nairs, the most common allele was DRB1*15 (28.57%) followed by DRB1*13 (16.07%), DRB1*10 (13.39%), DRB1*04 (10.71%), DRB1*14 (10.71%), DRB1*07 (7.14%), DRB1*03

(5.35%) and DRB1*01 (3.57%). Alleles DRB1*11 and DRB1*12 (both sub-types of DR5) were observed in lower frequencies. DRB1*08, DRB1*09 and DRB1*16 were completely absent. Among Namboothiris the commonest allele was DRB1*10 (18.57%) followed by alleles DRB1*15 (17.14%), DRB1*01 (12.85%), DRB1*13 (11.42%), DRB1*11 (10%), DRB1*07 (8.57%), DRB1*03 (7.14%). Moderate frequencies were observed for DRB1*04 and DRB1*14 (each 5.71%). DRB1*08 and DRB1*09 were observed in lower frequencies (each 1.42%). DRB1*16 and DRB1*12 were completely absent.

Phylogenetic Analysis: A proto-Austroloid population, Pallar stands unique. Vanniyar and Paliyar tribe formed a separate cluster. Third clustered includes all other population of Tamilnadu and Kerala. However, Kerala populations such as Nair and Namboothiris branch out as separate groups from Tamil Nadu caste populations. Tamil Nadu populations Kallars, Iyers and Kani tribes forms a unique cluster and Sourastrans and Narikuravars stands apart and these clustering reflects their ethnic affinities and racial admixture (Fig. 2; Table 1).

DISCUSSION

The present study revealed the HLA DRB1* allele profile of 520 individuals belongs to different population groups of Tamil Nadu and Kerala states of southern India. Each popula-

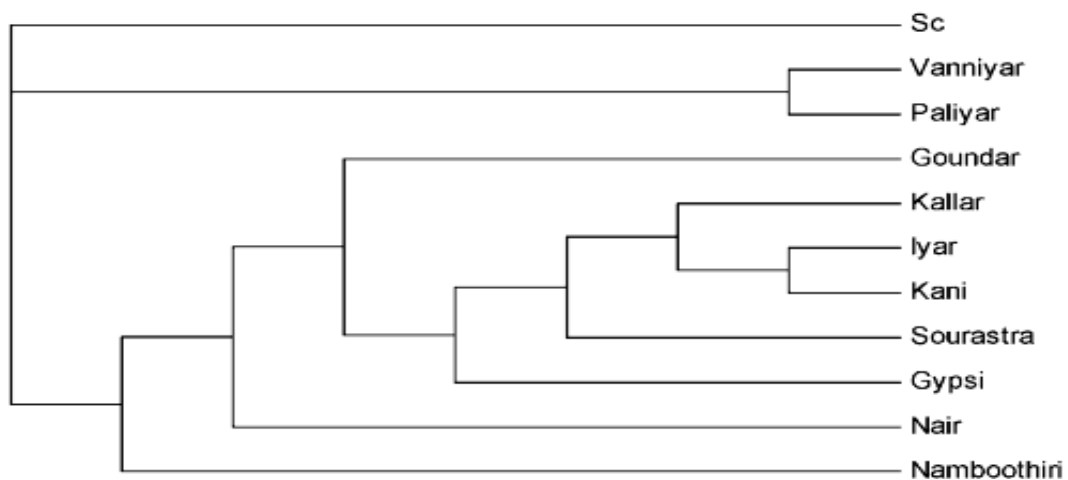


Fig. 2. Dendrogram analysis based on Neighbourhood – joining method of HLA – DRB1 gene frequencies for different South Indian populations.

Table 1: Percentage frequencies of HLA-DRB1* alleles in different populations

HLA-DR allele specificity	Kani(n = 49)	Paliyar (n = 58)	Pallar (n = 50)	Narikkuravar (n = 41)	Kallar (n = 53)	Vanniyar (n = 51)	V.Goundar (n = 44)	Sourashtra (n = 39)	Iyer (n = 44)	Namboothiri (n = 35)	Nair (n = 56)
DRB1*01	1.02 (1)	0.84 (1)	1 (1)	8.53 (7)	1.88 (2)	-	3.40 (3)	5.12 (4)	1.14 (1)	12.85 (9)	3.57 (4)
DR2	52.03 (51)	13.79 (16)	49 (49)	1.21 (1)	21.69 (23)	21.56(22)	20.45 (18)	34.60 (27)	23.86 (21)	17.14 (12)	28.57 (32)
DRB1*15	45.91 (45)	12.06 (14)	43 (43)	1.21 (1)	18.86 (20)	21.56 (22)	20.45 (18)	30.76 (15)	18.18 (16)	17.14 (12)	28.57 (32)
DRB1*16	6.12 (6)	1.69 (2)	6 (6)	-	2.83 (3)	-	-	3.84 (3)	5.68 (5)	-	-
DRB1*03	46.93 (46)	69.49 (82)	4 (4)	14.63 (12)	-	36.27 (37)	35.22 (31)	6.41 (5)	7.95 (7)	7.14 (5)	5.35 (6)
DRB1*04	-	1.69 (2)	10 (10)	41.46 (34)	12.26 (13)	3.92 (4)	5.68 (5)	2.56 (2)	6.82 (6)	5.71 (4)	10.71 (12)
DR5	-	2.53 (3)	7 (7)	9.75 (8)	5.66 (6)	2.94 (3)	2.27 (2)	10.24 (8)	4.55 (4)	10.00 (7)	4.45 (5)
DRB1*11	-	0.84 (1)	7 (7)	9.75 (8)	-	2.94 (3)	2.27 (2)	5.12 (4)	4.55 (4)	10.00 (7)	2.67 (3)
DRB1*12	-	1.69 (2)	0 (0)	-	5.66 (6)	-	-	5.12 (4)	-	-	1.78 (2)
DR6	-	4.22 (5)	7 (7)	7.31 (6)	11.31 (12)	3.92 (4)	4.53 (4)	8.96 (7)	14.77 (13)	17.14 (12)	26.78 (30)
DRB1*13	-	0.84 (1)	2 (2)	7.31 (6)	0.94 (1)	1.96 (2)	3.40 (3)	3.84 (3)	12.50 (11)	11.42 (8)	16.07 (18)
DRB1*14	-	3.38 (4)	5 (5)	-	10.37 (11)	1.96 (2)	1.13 (1)	5.12 (4)	2.27 (2)	5.71 (4)	10.71 (12)
DRB1*07	-	0.84 (1)	11 (11)	12.19 (10)	23.58 (25)	3.92 (4)	2.27 (2)	19.23 (15)	18.18 (16)	8.57 (6)	7.14 (8)
DRB1*08	-	0.84 (1)	3 (3)	2.43 (2)	6.60 (7)	3.92 (4)	1.13 (1)	-	3.41 (3)	1.42 (1)	-
DRB1*09	-	1.69 (2)	1 (1)	-	0.94 (1)	1.96 (2)	-	1.28 (1)	-	1.42 (1)	-
DRB1*10	-	4.23 (5)	7 (7)	2.43 (2)	16.03 (17)	21.56 (22)	25.0 (22)	11.53 (9)	19.32 (17)	18.57 (13)	13.39 (15)

tion/caste group showed an unique HLA DRB1* allele profile. It is well documented that the distribution of HLA antigen frequencies among populations showed marked differences.

The most frequent HLA DR alleles observed in the Indian caste populations are DRB1*03, DRB1*05, DRB1*06, DRB1*07, DRB1*10, DRB1*14 and DRB1*15 (Agrawal et al. 2001; Kankonkar et al. 2005; Bharadwaj et al. 2007; Chayya and Shankar Kumar 2003; Shanmugalakshmi et al. 2003; Balakrishnan et al. 1996; Pitchappan et al. 1997). DRB1*15 was the most frequent allele found in all south Indian caste and tribal groups enrolled in the present study. HLA –DRB1*15 was reportedly present in all the eleven population studied with a highest frequency of 45.19% in Kani tribes and a lowest frequency of 1% in Narikuravars. The disease predisposition studies of HLA-DR2 and its subtype DRB1*1501 revealed an association with pulmonary tuberculosis in South India (Brahmajothi et al. 1991; Ravikumar et al. 1999). The predominance of HLA-DR2 and its subtype DRB1*1501 in south Indian populations and prevalence of pulmonary tuberculosis (TB) needs further exploration. Discussion on HLA –DR2 is of special interest for that DR2 occurs with relatively high frequencies in many population and is known to be positively or negatively associated with several diseases such as narcolepsy, multiple sclerosis, Good pasture's syndrome, systemic lupus erythematoses and insulin- dependent diabetes mellitus (Juji et al. 1984; Olerup et al. 1991; Hartung et al. 1992; Ilonen et al. 1978). Distribution of DR2 subtype is significantly different among different ethnic groups. The predominance of DRB1*1501 and the absence and/or rarity of DRB1*1601 in Korean and other Asian population (Imanishi et al. 1992; Tanaka et al. 1997) have reported. DRB1*1501 is predominant (>50% of DR2 sub type) in most Caucasians and Asian population (Lee et al. 1999; Imanishi et al. 1992; Tanaka et al. 1997). DRB1*1601 is predominant in Romaninan, Sardinian and Spanish Gypsy (Imanishi et al. 1992), but is rare in populations of Asia Oceania (Gao et al. 1991; Trejaut et al. 1996; Imanishi et al. 1992; Tanaka et al. 1997).

Among eleven population studied, the frequencies of HLA –DRB1* alleles revealed that the tribal communities such as Kani and Paliyar tribes showed markedly different HLA-DR an-

tigen profile when compared to other population groups. In Kani tribe, only three DR alleles such as DRB1*15 (45.91%), DRB1*03 (46.93%) and DRB1*16 (6.12%) were reported. Complete absence of many of the HLA alleles in this tribe could be attributed to the geographical isolation, endogamy and consanguineous marriages that are very common among these tribes. In the present study, a rare allele in Asian populations, DRB1*16 was observed less frequently only in four populations viz., Kani tribes, Pallars, Iyers and Kallars. Complete absence (Shankarkumar et al. 2003) or very low frequency of DRB1*1601 among few Indian groups has been reported (Agarwal et al. 2001; Shanmugalakshmi et al. 2003; Bharadwaj et al. 2007). Thus it is interesting to explore further the presence of this otherwise rare allele only in few south Indian populations. In Paliyar tribe, a majority of the individuals possesses DRB1*03 and DRB1*15. All other remaining alleles were observed only in very low frequencies. India has the world's highest number of (HIV) infections for any country outside Africa with estimated 2.47 million infections. A recent study from South India has indicated that HIV-1 clad C accounts for over 90% of all HIV infections in the country (Siddappa et al. 2004). The predominant opportunistic infection noted among AIDS patients in India is tuberculosis and it is the most potent risk factor associated with disease progression. High incidence of HIV-TB and predominance of HLA-DR2 (DRB1*1501) in many of the south Indian population needs further clarification.

Among Narikuravars, DRB1*04 (41.46%) was the predominant allele. HLA DRB1*04 was well studied for its predisposition for ankylosing spondylitis and rheumatoid arthritis (Yelamos et al. 1993; Taneja et al. 1992; Ollier et al. 1991). In the present study of Narikuravars, 13/43 (30.23%; unpublished data) were reportedly showing the symptoms of joint pain or suffering from rheumatoid arthritis. The observation of presence of alkaptanuria among these Narikuravars and the association (if any) of these alleles is worth exploring. A comparison of previous reports on Spanish Gypsies (SG) revealed some striking similarities and differences between these two populations. In SG, DR14 (subtype of DR6) was the highest followed by DR16 (subtype of DR2 (de Pablo et al., 1992; Ramal et al. 2000). In Narikuravars, these two alleles

were absent. However, DRB1*04 was over represented in Narikuravars when compared to SGs. As a striking contrast, the frequency of DRB1*15 was very low (1.21%) in Narikuravars when compared to all other South Indian populations (present and many previous studies). The frequency was almost similar in Narikuravars and SGs (Ramal et al. 2000). It is DRB1*1501, that was predominantly present (among DR2 subtypes) in almost all Asian and Indian populations studied (Shanmugalakshmi et al. 2003; Ravikumar et al. 1999; Kankonkar and Shankar Kumar 2005). Thus, the SGs and Narikuravars could have descended from two different founding populations. Hence, the popular notion of Indian origin of Spanish Gypsies is at stake. This needs to be clarified at community genomics level.

The DRB1*03 was completely absent in Kallars of Tanjore as that of previous report on Piramalai Kallars (southern parts of Tamil Nadu, Madurai district) (Shanmugalakshmi et al. 2003). Whereas in Vanniyars and Vettuva Gounders, an increased DRB1*03 was observed. This elevated frequency could be of some selective advantage in these populations. Differential allelic frequencies among population living in geographically close areas throws light on the role of these alleles in health and disease in different environmental setting. Further, the DRB1*03 allele was implicated in type 1 diabetes in south India (Ahuja 1983; Bhatia et al. 1985; Uma Ganga 2004).

It has been reported that the HLA-Class II alleles DRB1*07 and DRB1*09 (both predominantly of Caucasoid) were occurring with the least frequency in Indian populations (Mehra 1998). In contradiction to the previous report, DRB1*07 distribution was quite high among Kallars (23.58%), Sourastrans (19.23%), Iyers (18.18%), Narikuravars (12.19%) and Namboothiris (8.57%) and less frequent among Vanniyars (3.92%), Vettuva Gounders (2.27%) and Paliyar tribes (0.84%). Allele DRB1*07 was found higher in Brahmin groups India (Balakrishnan 1992; Balakrishnan et al. 1996; Shankarkumar et al. 2000). This allele along with DQ3 (Ancestral haplotype 57.1) has been implicated in the hypersensitivity to RT inhibitor Abacavir, in Western Australian population (Mallal et al. 2002). The role of DRB1*07 and other class I alleles especially B17 (B*57) was worth exploring further. HLA-A*1-B*17 (B*57),

the commonest HLA haplotype (that evolved in India) is associated with the aetiology of *Psoriasis vulgaris* and attributed to hitch hiker phenomenon (Pitchappan 1988). The role of HLA-B*57 on the evolution of HIV escape mutants (Kiepiela et al. 2004) and gender influence on the occurrence of TB in HIV infected people of South India have been reported (Jagannathan et al. 2011). Studies on genetic susceptibility to abacavir hypersensitivity are carried on the 57.1 ancestral haplotype (Mallal et al. 2002). Thus, Indian subcontinent is an ideal setting to carryout studies related to immunogenomics of infectious diseases.

Except Namboothries from Kerala, DRB1*01 in all study population revealed low frequencies. The DRB1*01 was reportedly low in other Indian groups studied (Kankonkar and Shankarkumar 2005). DRB1*01, is characteristic of European populations. DRB1*10 was the most frequent allele among Vetuva Gounders (25%), Vanniyars (21.56%), Iyers (19.32%), Namboothries (18.57%), Kallars (16.03%) and Nairs (13.39%) and less frequent among Pallars (7%) and Narikuravars (2.43%). The frequency of DRB1*11 was 10% in Namboothries, 9.5% in Narikuravars, 7% in Pallars and 5.12% in Sourastrans. This allele has been implicated in predisposing breast cancer. HLA-DRB1*11 alleles were overrepresented ($P < 0.0001$) in controls (16.3%) as compared with patients with early – onset breast cancer (3.5%) affording a protective role in Caucasians (Chaudhuri et al. 2000). The role of these alleles needs further analysis in Indian scenario.

The heterogeneous nature of the Indian population suggested that the population as such or even a linguistic or regional population within it could not be considered as a panmictic pool; only a caste group might be considered as a homogenous gene pool with its diverse haplotype combinations and high rates of consanguinity. In addition, these data have been used to generate hypothesis about the natural selection forces operating on the HLA loci to elucidate the pattern of human evolution, migration, dispersal and aetio-pathogenesis of infection diseases. These differences can be attributed to migration and expansion of human communities but the evidences of heterozygote advantage and balancing selection still operating in these loci have been evident from HLA frequency differences and stratifications. The study

of human genomic allelic variation among individuals can help us to understand the nature and intensity of actions of various forces that have modulated our evolutionary course. It can also provide valuable data for understanding of various diseases that afflict us.

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