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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 anthropolgy 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

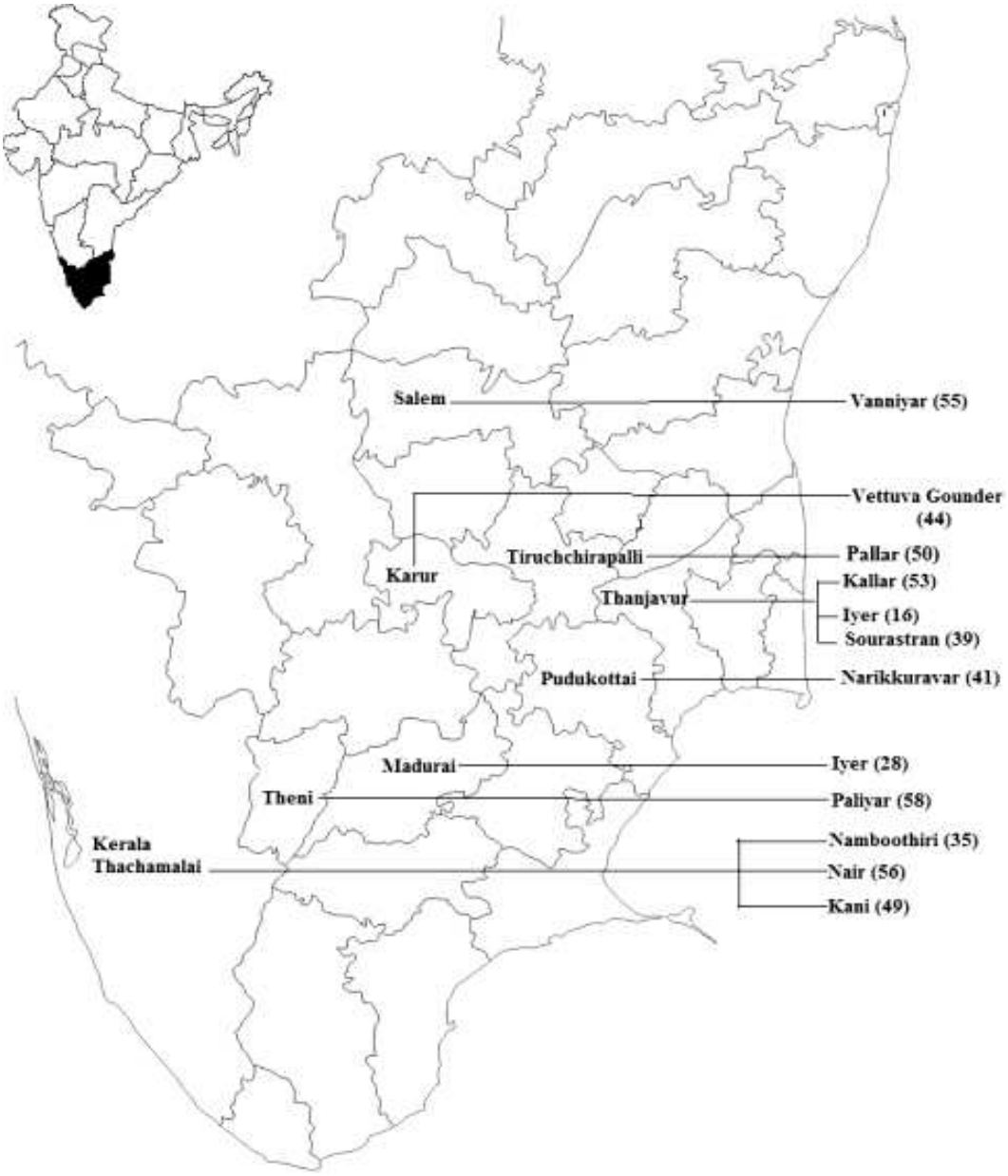

Fig. 1. Sampling sites of different population groups from Tamil Nadu and Kerala states of South India (number of samples in brackets).

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

8) Sourashtrans: Sourashtrans 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) Iyer: 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 packages. Dendrogram analysis was performed by using the Arlequin v. 2.0 (http: //anth ropologie. 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 Vetuva 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 to 1.13 to 2.27%). In Sourashtrans, 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]Guajarati (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 clusted includes all other population of Tamilnadu and Kerala. However, Kerala populations such as Nair and Namboothriris 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 Narikkuravars 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-

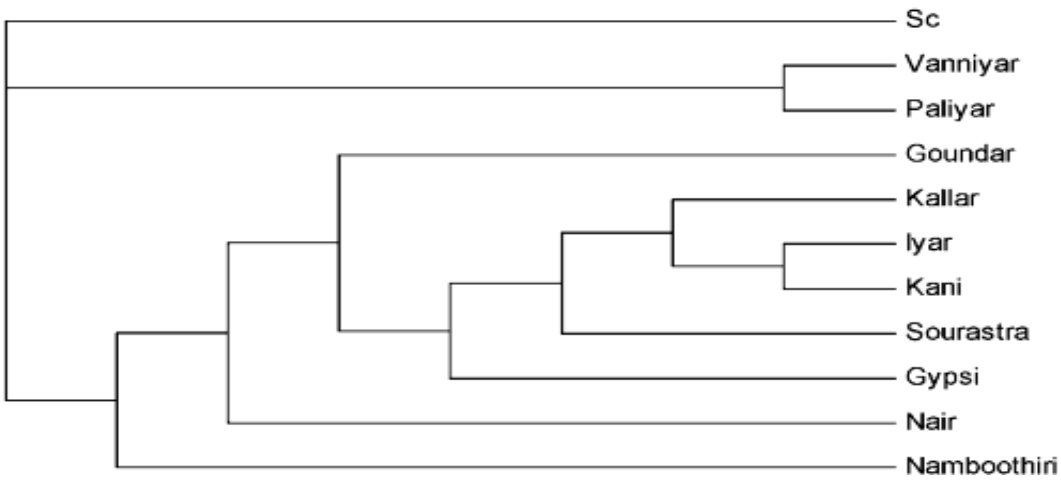

Fig. 2. Dendrogram analysis based on Neighbourhood – joining method of HLA – DRB1 gene frequencies for different South Indian populations.

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)*	*Sourastra (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 an 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 Oceaina (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 opportunitistic 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 ankloysing spontilytis 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 distsrict) (Shanmugalakshmi et al. 2003). Whereas in Vanniyars and Vetuva Gounders, an increased DRB1*03 was observed. This elevated frequency could be of some selective advantage in these populations. Differntial alleleic 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 quiet 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 hike 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.

REFERENCES

Agrawal S, Arundhati K, Bhardwaj U et al. 1999. HLA antigens and haplotype frequencies in Bhargavas and Chaturvedies of UP (India). *Ind J Hum Genet,* 5(1): 25-30.

Agrawal S, Batnagar S, Bhardwaj U, Khan Faisal, Sharma Arundhati, Talwar Sudha, Naik Sita 2001. Distribution of HLA class II antigens in three north Indian populations. *Int J Hum Genet,* 1(4): 283-291.

Ahuja MMS 1983. Diabetes in tropics-perspectives of research. *Tohoku J Exp. Med,* 141: 65-72.

Aidoo M, Lalvani A, Allsopp CEM et al. 1995. Identification of conserved antigenic components for a cytotoxic T lymphocytes- inducing vaccine against malaria. *Lancet,* 345: 1003-1007.

Balakrishnan K, Pitchappan RM, Suzuki K et al. 1996. HLA affinities of Iyers: A Brahmin population of Tamil Nadu, South India. *Human Biology,* 68(4): 523- 537.

Basu A, Mukherjee N, Roy S et al. 2003. Ethnic India: A genomic view, with special reference to peopling and structure. *Genome Res,* 13(10): 2277-2290.

Bharadwaj U, Faisal Khan, Sanjeev S et al. 2007. Phylogenetic applications of HLA Class II Loci. *Int J Hum Genet,* 7(2): 123-131.

Bhasin MK, Walter H, Danker-Hopfe H 1994. *People of India. An Investigation of Biological Variability in Ecological, Ethno-Economic and Linguistic Groups.* Delhi: Kamla-Raj Enterprises.

Bhatia E, Mehra NK, Taneja V et al. 1985. HLA-DR antigen frequencies in a north Indian type I diabetic population. *Diabetes,* 34: 565-567.

Brahmajothi V, Pitchappan RM, Kakkanaiah VN et al. 1991. Association of pulmonary tuberculosis and HLA in South India. *Tubercle,* 72: 123-132

Buechi EC 1953. ABO, MN, Rh blood groups and secretor factor in Kanikkar: A genetic survey in South Travancore and a contribution to the race problem in India. *Bull Anth Surv India,* 2: 83–98.

Charron D 1997. *Genetic Diversity of HLA Functional and Medical Implications*. Paris: EDK Medical and Scientific International Publishers, Vol. I: 314–320.

Charron D 2000. HLA 2000. Proceedings of 26th Congress of International Society for Blood Transfusion. *Vox Sang,* 78(Supple 2): 27-28.

Chaudhuri S, Cariappa A, Tang M et al. 2000. Genetic susceptibility to breast cancer: HLA DQB*03032 and HLA DRB1*11 may represent protective alleles. *Proc Natl Acad Sci,* 97: 11451–11454.

Chayya SU, Shankarkumar U 2003. HLA antigen distribution in Jain community from Mumbai, Maharashtra, India. *Ind J Med Res,* 114: 25-29.

de Pablo R, Vilches C, Moreno ME, Rementeria MC, Solis R, Kreisler M 1992. Distribution of HLA antigens in Spanish Gypsies: A comparative study. *Tissue Antigens,* 40: 187-196.

Dobazhansky T 1973. *Genetic Diversity and Human Equality*. New York: Basic Books.

Excoffier L, Slatkin M 1995. Maximum-likelihood estimation of molecular haplotype frequency in a diploid population. *Mol Biol Evol,* 12: 921–927.

Festenstein H, Adams E, Burke JM, Oliver RT, Sachs JA, Wolf E 1972. *Histocompatibility Testing*. Copenhagen: Munksgaard.

Ganga U , Vaidyanathan B, Jaini R, Puthezath SN, Mehra K 2004. HLA haplotypes associated with type 1 diabetes mellitus in north Indian children. *Human Immunology,* 65**:** 47–53.

Gao X, Serjeantson SW 1991. Heterogeneity in HLA-DR2 related DR, DQ haplotypes in eight populations of Asia Oceania. *Immunogenetics,* 34: 401.

Harris H, Hopkinson DA 1976. *Hand book of Enzyme Electrophoresis in Human Genetics*. Amsterdam: North Holland.

Hartung K, Baur MP, Coldewey R, Fricker M, Kalden JR, Lakomek HJ, Peter HH, Schendel D et al. 1992. Major histocompatibility complex haplotypes and complement C4 alleles in systematic lupus erythematosus. Results of multicenter study. *J Clin Invest,* 90: 1346.

Ilonen J, Herva E, Tiilikaninen A, Akerblom HK, Koivukangas T, Kouvalainen K 1978. HLA –Dw2 as a marker of resistance against juvenile diabetes mellitus. *Tissue Antigens*, 11: 44.

Imanishi T, Akaza T, Kimura A, Tokunaga K, Gojobori T 1992. Allele and haplotype frequencies for HLA and complement loci in various ethnic groups. In: K Tsuji, M Aizawa, T Saszuki (Eds.): *HLA 1991. Vol. 1.* New York: Oxford University Press.

Jagannathan L, Chaturvedi M, Satish B et al. 2011. HLA-B57 and gender influence the occurrence of tuberculosis in HIV infected people of south India. *Clin Dev Immunol*, 549-023. Epub 2011 Aug 25.

Jaini R, Naruse T, Kanga U, Kikkawa E, Kaur G, Inoko H et al. 2002. Molecular diversity of the HLA-A*19 groups of alleles in North Indians: Possible oriental influence. *Tissue Antigens,* 59: 487–91.

Juji T, Satake M, Honda Y, Doi Y 1984. HLA antigens in Japanese patients with narcolepsy. All the patients were DR2 positive. *Tissue Antigens,* 24: 31.

Kankonkar SR, Shankarkumar U 2005. HLA DRBI Gene study in different population groups from Mumbai, Maharashtra, India. *Int J Hum Genet,* 5: 267.

Kiepiela P, Leslie AJ, Honeyborne I et al. 2004. Dominant influence of HLA-B in mediating the potential co-evolution of HIV and HLA. *Nature,* 432(7018): 769–775

Kivisild T, Bamshad MJ, Kaldma K et al. 1999. Deep common ancestry of Indian and western-Eurasian mitochondrial DNA lineages. *Curr Biol,* 9(22): 1331-1334.

Lee A, Huang R, Yan L, Shaw CK, Zeng S, Lin PY, Lee TD 1999. Heterogeneity of HLA-DR2 haplotypes in Caucasoid Americans, Africans, Chinese Americans, Native Americans and Xiamen Chinese. *Eur J Immunogenet,* 26: 275.

Majumdar DN 1961. *Races and Culture of India.* London: British Museum

Malhotra KC, Balakrishnan V, Karve I 1981. Anthropometric Variation in Tamil Nadu. In: LD Sanghvi, V Balakrishnan, I Karve (Eds.): *Biology of the People of Tamil Nadu.* Pune: The Indian Society of Human Genetics and Calcutta, The Indian Anthropological Society, pp. 50–74.

Mallal S, Nolan D, Witt C et al. 2002. Association between presence of HLA-B*5701, HLA-DR7, and HLA-DQ3 and hypersensitivity to HIV-1 reverse-transcriptase inhibitor abacavir. *Lancet,* 359: 727-732.

Mehra NK, Bouwens AGM, Naipal A et al. 1994. Asian Indian HLA DR2, DR4 and DR52 related genotypes analysed by PCR based non-radioactive oligo nucleotide typing: Unique haplotypes and a novel DR4 subtype. *Hum Immunol*, 39: 202-206.

Menon TM 1996. *Encyclopedia of Dravidian Tribes*. Thiruvanathapuram: International School of Dravidian Linguistics.

Meyer D, Single R, Mack S et al. 2006. Single locus polymorphism of classical HLA genes. In: JA Hansen (Ed.): *Immunobiology of the Human MHC: Proceedings of the 13th International Histocompatibility Workshop and Conference.* Vol. 1. Seattle: IHWG Press, pp. 653–704.

Meyer D, Single R, Mack SJ, Erlich HA, Thomson G 2007. Signatures of demographic history and natural selection in the human MHC loci. *Genetics*, 173: 2121–2142.

Miller SA, Dykes DD, Polesky HF 1988. A simple salting out procedure for extracting DNA from human nucleate cells. *Nucleic Acids Res,* 16: 1215.

Mittal KK, Naik S, Sansonetti N et al. 1982. The HLA antigens in Indian Hindus. *Tissue Antigens,* 20: 223-226.

Nilakanta Sastry KA 1955. *A History of South India: From Prehistoric Times to the Fall of Vijayanagar.* Madras: Oxford University Press.

Olerup O, Zetterquist H 1992. HLA-DR typing by PCR amplification with sequence-specific primers (PCR-SSP) in 2 hours: An alternative to serological DR typing in clinical practice including donor-recipient matching in cadaveric transplantation. *Tissue Antigens*, 39: 225.

Ollier WER, Stephens C, Award J et al. 1991. Is rheumatoid arthritis in Indians associated with HLA antigen sharing a DRBl epitope? *Ann Rheum Dis*, 50: 25.

Pitachappan RM 1988. Founder effect explains the distribution of the HLA-A1-B17 but not the absence of the A1-B8 haplotype in India. *J Aenet*, 67: 101-111.

Pitchappan RM 2002. Castes, migration, immunogenetics, infectious diseases and South India. *Community Genet,* 5: 157–161.

Pitchappan RM, Balakrishnan K, Sundarsen V et al. 1997. Sociobiology and HLA genetic polymorphism in hill tribes, Irulas of Nilgiris and Malayalis of Shevroy, South India. *Human Biology*, 69: 59-74.

Ramaiah 2004. Untouchability and inter- caste relations in rural India: The case of southern Tamil villages. *Journal of Religious Culture,* 70: 1-13.

Ramal LM, de Pablo R, Gaudix MJ et al. 2001. HLA class II distribution in the gypsy community of Andalusia, southern spain. *Tissue Antigens*, 57: 138–143

Ravikumar M, Dheenadhayalan V, Rajaram K et al. 1999. Association of HLA DRB1, DQB1 and DPB1 alleles with pulmonary tuberculosis in South India. *Tubercle and Lung Disease,* 79(5): 309-17.

Sanghvi LD, Balakrishnan V, Karve I 1981. *Biology of the People of Tamil Nadu*. Indian Society of Human Genetics, Pune, and The Indian Anthropological Society, Kolkata.

Shankarkumar U, Ghosh K, Mohanty D 2000. HLA Class I

antigen profile among Brahmins and related caste groups from Mumbai, Maharashtra, India. *J Human Genet*, 6: 21-28.

Shankarkumar U, Ghosh K, Mohanty D 2001. HLA distribution in Maratha community from Mumbai, Maharashtra, India. *Int J Hum Genet*, 1(3): 173- 177.

Shanmugalakshmi S, Balakrishnan K, Manoharan K, Pitchappan RM 2003. HLA DRB1*, DQB1* in Piramalai Kallars and Yadhavas, two Dravidian speaking castes of Tamil Nadu, South India. *Tissue Antigens*, 61: 451- 464.

Siddappa NB, Dash PK, Mahadevan A et al. 2004. Identification of subtype C human immunodeficiency virus type 1 by subtype-specific PCR and its use in the characterization of viruses circulating in southern parts of India. *Journal of Clinical Microbiology*, 42 (6): 2742-2751.

Singh KS 1998. *India's Communities. People of India*. National Series. Volume IV. Delhi: Oxford University Press.

Tanaka H, Tokunaga K, Inoko H et al. 1997. Distribution of HLA- A, B, and DRB1 alleles and haplotypes in Northeast Asia. In: Charron D (Ed.): *Genetic Diversity of HLA: Functional and Medical Implication.* Vol I. Paris: EDK Publisher.

Taneja V, Mehra NK, Kailash S, Anand C, Malaviya AN 1992. Protective and risk DR phenotypes in Asian Indian patients with rheumatoid arthritis. *Ind J Med Res*, 96: 16.

Trejaut J, Bhatia K, Grevelli WD et al. 1996. HLA-DR2 haplotypic diversity in populations of South – East Asian, Northern China, Melanesia and Australian aborigines using PCR-RFLP for DRB1, DRB5, DQA1 and DQB1. A novel DRB1 allele: DRB1*16022. *Eur J Immunogenet*, 23: 437.

Welsh KI, Bunce M 1999. Molecular typing for the MHC with PCR-SSP. *Rev Immunogenet*, 1: 157-176.

Wolf E, Fine PEM, Pritchard J et al. 1980. HLA-A, B and C antigens in south Indian families with leprosy. *Tissue Antigens*, 15: 436–46.

Yelamos J, Garcia-Lozano JR, Moreno I et al. 1993. Association of HLA-DR4-DWI 5 (DRBI "0405) and DRlO with rheumatoid arthritis in a Spanish population. *Arthritis Rheum*, 36: 811.