

HLA Antigen Distribution in Gujarathi Speaking Hindu Population from Mumbai, Maharashtra, India

S.U.Chhaya¹, M.Panthaki² and U. Shankarkumar³

1. Department of Transfusion Medicine, Tata Memorial Hospital, Parel, Mumbai 400 012, Maharashtra, India
2. Sir Hurisondas Nurrotumdas Hospital and Medical Research Center, Raja Ram Mohan Roy Road, Mumbai 400 004, Maharashtra, India
3. HLA Department, Institute of Immunohaematology (ICMR), 13th Floor, NMS Bldg, K.E.M. Hospital, Parel, Mumbai 400 012

KEY WORDS HLA. Gujarathi Hindus. Population. Mumbai.

ABSTRACT Four hundred and fourteen unrelated Gujarathi speaking Hindu people residing in Mumbai, Maharashtra, (Western India) were studied for HLA A, B, C and DR locus antigen profiles. The phenotypic frequencies of HLA A1, A2, A9, A11, A24, B5, B35, B40, Cw4, DR2, DR3, DR4, DR5 and DR7 were increased while frequencies of HLA A10, A19, A26, A28, A29, B14, B16, B18, B21, B22, B27, B37, Cw1, DR1, DR6 and DR9 were decreased in the Gujarathi speaking Hindus. The genotype frequencies of HLA A3, A9, B18, B21, B22, B40, DR3 and DR5 were increased while that of A19, A28, B7, B13, B15, Cw1, Cw2, Cw8, DR1, DR6 and DR9 were decreased when compared with gene frequencies of other Indian Hindu populations reported. Two Locus haplotype analysis revealed that A1-B17, A10-B8 and A19-B12 were common Indian Hindu haplotypes where as A3-B18, A9-B5, A24-B5 and A11-B62 were unique for the Gujarathi Hindus. Haplotype A2-B40 observed in Gujarathi Hindus were also observed among South Indian Hindus, while A11-B35 have been observed among immigrant Indian Hindus. Another haplotype A3-B7 reported from both south Indian and north Indian Hindus was not observed in Gujarathi Hindus. Significant negative linkage disequilibrium was observed for haplotype A1-B35 in Gujarathi Hindus. Thus the observed antigen frequencies and linkage disequilibrium in Gujarathi Hindus suggest the influence of genetic drift caused by selection, geography and culture. Further the study reveals that the Hindu population of India cannot be considered as a single panmictic population with reference to genetic characteristics.

INTRODUCTION

India is thought to have been one the site of earliest human settlements. Subsequently the region has been subjected to successive waves of immigration and invasions from the Middle East, Central Asia and Mongolia, contributing to the present day gene pool (Bhasin et al., 1994). Risely (1969) was the first to study the "racial types" in Indian population. Malhotra (1978) described the Western and Southern Indian population as Australoid or Proto-Australoid ele-

ments. The present-day population is a panorama of social, cultural and ethnically distinct (Papiha, 1996). The population exhibits not only a wide variety of ethnic but also great cultural and linguistic diversity. With regard to the linguistic map, the Greater India (before 1947 partition) was divided into five major linguistic families viz.; Iranian, Indo-Aryan, Austro-Asiatic, Tibeto-Burmese and Dravidian languages. The Dravidian speaking population from South and Central India were believed to be the descendants of original inhabitants (Fuchs, 1973; Haimendorf, 1948). The social structure is governed by a large number of religious groups. Eighty two percent of Indian population is Hindu, while the other minor religions include Christians, Sikhs, Buddhists, Jains and Muslims. Numerous endogamous ethnic groups delineate within each linguistic or religious group based on biological and socio-cultural characteristics.

Maharashtra, the Western state of India, lying between 74° - 78° E longitude and 18° - 20° N latitude with Mumbai as its capital city consists of 32 districts. Hindus form 81.94% of the population while others are Muslims (8.4%), Christians (1.42%), Buddhists (6.48%), Shikhs (0.2%) and Jains (1.64%) (Dikshit, 1986). The greater part of Maharashtra is drained to the Bay of Bengal by two major rivers, the Godavari and the Krishna. The rest drained to the Arabian Sea by either Tapi River or Konkan stream emerging from Western Ghats. The Hindus distributed over Maharashtra speak Hindi, Marathi, Gujarathi, Kannada, Tamil, Malayalam, Telugu etc., the official language being Marathi and pray Hindu Gods. Gujarathi speaking Hindus studied here represent a single large intra-marrying ethnic group of the Indian subcontinent.

Several workers have conducted numerous studies on the genetics of various populations in India. Literature have been reported on blood groups, red cell enzymes and serum protein polymorphism's (Bhatia and Rao, 1986; Bhasin et al., 1992). The HLA system, most polymorphic and complex set of genetic markers known in man, is of valuable significance in anthropological studies (Dausset, 1981). Distribution of HLA antigens in various ethnic groups of the world have been reported (Baur and Daniloves, 1980; Imanishi et al., 1992). Few reports are available on immigrant Indian population (Singal, 1972; Mittal et al., 1982) and regional Hindu populations (Raha, 1975; Pitchappan et al., 1984; Mehra et al., 1986; Selvakumar et al., 1988). However data is rather scanty from western part of India (Papiha, 1996). Therefore we felt that it is worthwhile to investigate the distribution of HLA antigens in this Gujarathi speaking Hindu population.

MATERIAL AND METHODS

Blood samples from random 414 healthy unrelated Gujarathi speaking Hindus from Mumbai were studied for HLA -A, -B, -C and -DR Locus antigen profiles. Ten to fifteen milliliters of venous blood (in heparin 50 IU/ml) was collected in a sterile tube from each individual. The lymphocytes were isolated by density gradient centrifugation on Histopaque (Boyum, 1968). HLA A, B, C and DR locus antigens were identified by NIH two - stage Microlymphocytotoxicity assay (Terasaki and McClelland, 1964) using T cells for class I typing and B cells isolated by a miniature nylon wool column for class II with a longer incubation period. A total of 190 antisera were used for defining 17 specificities for HLA A locus, 29 for HLA B locus, 8 for HLA C locus and 10 for HLA DR locus antigens. The antisera were commercial (Biotest, Germany; Behring, Germany Pelfreez, USA) in origin. The typing tray included a minimum of three antisera for each supertypic specificity. The phenotype frequency (PF), gene frequency (GF), standard error of gene frequency (SEGF), haplotype frequency (HF), Co-efficient of linkage disequilibrium (Delta) and t values were calculated following

the methods described by Baur and Daniloves (1980).

Table 1: HLA A, B, C and DR antigens in Gujarathi speaking Hindu population Mumbai, India

HLA antigens	N+	%PF	%GF	SEGF
N = 414				
A1	130	31.4	17.2	1.4
A2	103	24.9	13.3	1.3
A3	81	19.6	10.3	1.1
A9	137	33.1	18.2	1.5
A10	56	13.5	7.0	0.9
A11	100	24.2	12.9	1.2
A19	62	15.0	7.8	1.0
A23	0	0.0	0.0	0.0
A24	134	32.4	17.8	1.5
A25	0	0.0	0.0	0.0
A26	55	13.3	6.9	0.9
A28	54	13.0	6.7	0.9
A29	3	0.7	0.4	0.2
A30	19	4.6	2.3	0.5
A31	0	0.0	0.0	0.0
A32	14	3.4	1.7	0.5
A33	25	6.0	3.1	0.6
A-	105		13.6	
B5	149	36.0	20.0	1.6
B7	44	10.6	5.5	0.8
B8	37	8.9	4.6	0.7
B12	66	15.9	8.3	1.0
B13	21	5.1	2.6	0.6
B14	4	1.0	0.5	0.2
B15	42	10.1	5.2	0.8
B16	5	1.2	0.6	0.3
B17	76	18.4	9.6	1.1
B18	27	6.5	3.3	0.6
B21	26	6.3	3.2	0.6
B22	26	6.3	3.2	0.6
B27	13	3.1	1.6	0.4
B35	93	22.5	11.9	1.2
B37	8	1.9	1.0	0.3
B38	3	0.7	0.4	0.2
B39	2	0.5	0.2	0.2
B40	104	25.1	13.5	1.3
B44	62	15.0	7.8	1.0
B49	15	3.6	1.8	0.5
B50	6	1.4	0.7	0.3
B51	36	8.7	4.4	0.7
B52	3	0.7	0.4	0.2
B54	0	0.0	0.0	0.0
B55	2	0.5	0.2	0.2
B56	16	3.9	2.0	0.5
B62	34	8.2	4.2	0.7
B63	0	0.0	0.0	0.0
B-	87		11.1	0.0
Cw1	5	1.2	0.6	0.3
Cw2	11	2.7	1.3	0.4
Cw3	57	13.8	7.1	0.9
Cw4	126	30.4	16.6	1.4
Cw5	20	4.8	2.4	0.5
Cw6	18	4.3	2.2	0.5
Cw7	16	3.9	2.0	0.5

Table 1: Contd.....

HLA antigens	N+	%PF	%GF	SEGF
Cw7	16	3.9	2.0	0.5
Cw8	0	0.0	0.0	0.0
N=191				
DR1	10	5.2	2.7	0.8
DR2	73	38.2	21.4	2.4
DR3	59	30.9	16.9	2.1
DR4	60	31.4	17.2	2.1
DR5	60	31.4	17.2	2.1
DR6	4	2.1	1.1	0.5
DR7	60	31.4	17.2	2.1
DR8	0	0.0	0.0	0.0
DR9	1	0.5	0.3	0.3
DR10	0	0.0	0.0	0.0
DR-	70		20.4	

20.4N+ = Number positive for the allele, % PF = Percentage Phenotype Frequency,

% GF = Percentage Genotype Frequency, SEGF = Standard Error of Genotype Frequency.

RESULTS AND DISCUSSION

The results on HLA A, B, C and DR antigen frequencies and standard error of gene frequencies in 414 unrelated healthy Gujarathi Hindus are presented in Table:1 The antigen frequencies of HLA A1, A2, A9, A11, A24, B5, B35, B40, Cw4, DR2, DR3, DR4, DR5 and DR7 were increased while HLA A10, A19, A26, A28, A29, B14, B16, B18, B21, B22, B27, B37, Cw1, DR1, DR6 and DR9 were decreased. HLA A23 (9), A25 (10), A31 (19), B45 (12), B63 (15), B54 (22), splits, as well as Cw8, DR8 and DR10 antigens were not identified in the Gujarathi Hindus as in the case of those earlier studies of mixed Indian population and caste groups (Baur and Daniloves, 1980; Imanishi et al., 1992). The comparison of HLA A, B, C and DR gene frequencies in Gujarathi Hindus with different Indian Hindus are presented in table 2. The gene frequencies of HLA A3, A9, B18, B21, B22, B40, DR3 and DR5 were found to be increased in Gujarathi Hindus. The frequencies of HLA A19, A28, B7, B13, B15, Cw1, Cw2, Cw8, DR1, DR6 and DR9 were found to be decreased in them when compared to other Hindus reported (Raha, 1975; Pitchappan et al., 1984; Mehra et al., 1986; Selvakumar et al., 1988). Table 3 presents a comparison of two locus haplotype frequencies and linkage disequilibrium of Gujarathi Hindus along with the identified haplotypes and linkage disequilibrium in other

Indian Hindu populations reported. It is interesting to note that haplotypes A3-B18, A9-B5, A24-B5 and A11-B62 had high delta and significant t values were unique to the Gujarathi Hindus and is virtually absent in other Indian Hindus reported. Haplotype A3-B7, absent in Gujarathi Hindus was observed in North and South Indian Hindus, while A2-B40 observed in Gujarathi Hindus was also observed in only South Indian Hindus. Haplotypes A1-B22, A19-B35, A3-B5 and A28-B5 were unique for South Indian Hindus, while A1-B37, A1-B63, A10-B16, A29-B12 and A30-B13 were unique for North Indian Hindus. The hplotypes A1-B17, A10-B8 and A19-B12 had significant t values and is observed in all the Hindu populations of India reported. Most of the newly identified and defined WHO Nomenclature for HLA antigens 1998 (Bodmer et al., 1999) have not been tested in these populations.

Theoretically high polymorphism of a gene can occur due to mutation rate, selection, genetic hitchhiking or a combination of all the three (Kaufmann, 1996). Studies of various human population using PCR based typing have revealed the extent of allelic diversity in HLA class II loci (Apple and Erlich, 1996). In addition these data have been used to generate hypothesis about the nature of selective forces operating on the HLA loci to elucidate the pattern of human evolution and migration. Worldwide most populations contain only 20 to 30 alleles in a HLA loci although over 100 alleles have been identified. Earlier population studies have indicated that there are many alleles and haplotypes that appear to be specific for a given population group. Indigenous populations or caste groups show a very restricted diversity of alleles at a particular HLA loci consistent within a population (Trachtenberg et al., 1995). Moreover specific alleles found uniquely in a particular indigenous group may have been generated by point mutation or gene conversion from the ancestral allele after the group separated from the other groups (Titus-Trachtenberg et al., 1994). Multiple polymorphic alleles in a population are maintained at appreciable frequencies due to either overdominance (heterozygous advantage), frequency dependent selection or other selective force (Elrich et al., 1991). Both selective forces

Table 2: Gene Frequencies (in percentage) of Gujarathi Hindus compared with other Indian Hindus

HLA	Gujarathi Hindus (N = 414)	N.Indian Hindus ⁶ (N = 400)	S.Indian Hindus [*] (N = 385)	Indian Hindus [*] (N = 138)
A1	17.20	14.50	13.10	20.60
A2	13.30	11.90	16.41	10.30
A3	10.30	8.90	6.30	7.00
A9	18.20	14.50	16.72	14.00
A23	0.00	NT	NT	0.40
A24	17.80	NT	NT	13.60
A25	0.00	NT	NT	0.00
A26	6.90	NT	NT	0.40
A34	NT	NT	NT	NT
A66	NT	NT	NT	NT
A11	12.90	13.80	16.57	14.50
A19	7.80	18.40	11.58	NR
A29	0.40	2.10	NT	1.50
A30	2.30	3.50	NT	1.80
A31	0.00	2.10	NT	1.10
A32	1.70	5.00	NT	2.90
A33	3.10	2.00	NT	12.00
A74	NT	NT	NT	NT
A28	6.70	7.90	6.58	6.00
A68	NT	NT	NT	NT
A69	NT	NT	NT	NT
A36	NT	NT	NT	0.00
A43	NT	NT	NT	NT
A80/A-	13.60	NR	8.89	4.90
B5	20.00	16.00	18.14	14.90
B51	4.40	NT	NT	7.50
B52	0.40	NT	NT	6.40
B7	5.50	6.50	10.12	3.70
B8	4.60	4.40	1.84	3.70
B12	8.30	9.00	5.34	10.70
B44	7.80	7.50	NT	10.30
B45	0.00	1.30	NT	0.70
B13	2.60	4.00	3.03	3.30
B14	0.50	0.00	0.13	0.40
B64	NT	NT	NT	NT
B65	NT	NT	NT	NT
B15	5.20	6.90	5.89	8.30
B62	4.20	5.40	NT	3.30
B63	0.00	1.50	NT	3.30
B75	NT	NT	NT	NT
B76	NT	NT	NT	NT
B77	NT	NT	NT	NT
B16	0.60	1.10	0.39	2.20
B38	0.40	0.60	NT	1.80
B39	0.20	0.50	NT	0.40
B17	9.60	7.80	10.12	14.00
B57	NT	NT	NT	12.40
B58	NT	NT	NT	1.50
B18	3.30	2.20	0.52	2.60
B21	3.20	3.30	2.77	0.70
B49	1.80	0.70	NT	0.00
B50	0.70	2.50	NT	0.70
B22	3.20	2.90	2.50	1.10
B54	0.00	NT	NT	0.40
R55	0.20	NT	NT	0.70
B56	2.00	NT	NT	NT
B27	1.60	3.00	0.91	0.70
B35	11.90	14.50	10.27	17.00

Table 2: Contd.....

HLA	Gujarathi Hindus (N = 414)	N.Indian Hindus ⁶ (N = 400)	S.Indian Hindus [*] (N = 385)	Indian Hindus [*] (N = 138)
B37	1.00	2.40	NT	3.30
B40	13.50	12.20	8.12	9.10
B60	NT	NT	NT	2.60
B61	NT	NT	NT	1.80
B41	NT	0.13	NT	1.10
B42	NT	0.13	NT	0.00
B46	NT	NT	NT	NT
B47	NT	NT	NT	NT
B48	NT	NT	NT	NT
B53	NT	NT	NT	0.70
B59	NT	NT	NT	NT
B67	NT	NT	NT	NT
B70	NT	NT	NT	NT
B71	NT	NT	NT	NT
B72	NT	NT	NT	NT
B73	NT	NT	NT	NT
B78	NT	NT	NT	NT
B81	N	TN	TN	NT
B-	11.10	NR	17.57	1.40
Cw1	0.60	2.00	1.78	1.10
Cw2	1.30	2.00	2.99	0.70
Cw3	7.10	8.40	12.55	7.90
Cw4	16.60	8.90	22.54	14.90
Cw5	2.40	0.20	0.59	3.30
Cw6	2.20	1.80	13.23	2.20
Cw7	2.00	NR	13.91	0.00
Cw8	0.00	NR	1.18	0.00
Cw-	68.90	NR	31.23	69.90
N=191		N=134		N=138
DR1	2.7	7.3	NT	4.5
DR2	21.4	27.2	NT	19.4
DR3	16.9	14.0	NT	6.8
DR4	12.9	14.0	NT	8.7
DR5	17.2	12.3	NT	7.5
DR6	1.1	9.4	NT	2.9
DR7	17.2	11.9	NT	20.6
DR8	0.0	0.4	NT	4.8
DR9	0.3	1.5	NT	1.8
DR10	0.0	1.1	NT	1.8
DR-	20.0	NR	NT	13.1

@ Mehra et al 1986, # Pitchappan et al 1984, * Mittal et al., 1982.

NT = Not Tested, NR = Not Reported.

and a high rate of germline diversification are involved in the evolution of HLA allelic diversity. Among HLA class II alleles of recent origin, observed in human populations some may be thousands of years old, while most of them may be millions of years old (Ayala et al., 1994). Thus a newly arisen favorable variant allele might co-exist with the parental allele rather than replacing it when selective forces favoring diversity is operating. Recently in the South Indian population newer HLA alleles like B78,

Table 3: Haplotype frequencies and significant linkage disequilibrium identified in Gujarathi Hindus compared with other Indian Hindu population

Haplotype	HF	Delta (Δ)	t value ^a	χ^2
Gujarathi Hindus (N = 414)				
A1 - B17	46.7	30.3	4.57	26.16
A2 - B40	32.3	14.2	2.19	4.86
A11 - B35	36.4	21.0	3.31	12.98
A19 - B12	22.4	16.1	3.25	17.49
A33 - B44	12.1	9.7	2.65	15.33
A10 - B8	12.5	9.2	2.38	9.64
A3 - B18	11.3	7.9	2.17	6.90
A9 - B5	59.3	23.1	2.75	7.18
A11 - B62	15.2	9.8	2.32	6.97
A24 - B5	56.7	21.4	2.57	6.21
A26 - B8	12.6	9.3	2.41	10.08
A1 - B35 ^S	5.2	-15.2	-2.44	5.98
South Indian Hindus* (N=385)				
A1 - B17	42.2	28.5	4-5	NR
A3 - B7	21.6	15.2	3-4	NR
A10 - B8	9.6	10.3	2-3	NR
A19 - B35	23.3	12.0	2-3	NR
A2 - B40	30.0	16.8	2-3	NR
A1 - B22	6.8	3.4	-	NR
A19 - B12	14.5	8.6	-	NR
A28 - B5	21.8	9.9	-	NR
A3 - B5 ^S	8.9	-2.6	-	NR
A1 - B5 ^S	-	26.2	-	NR
A3 - B17 ^S	-	-9.4	3-4	NR
A28 - B15 ^S	-	-5.3	-	NR
A19 - B7 ^S	5.5	-5.8	-	NR
North Indian Hindus ^a (N= 400)				
A10 - B8	20.66	18.24	NR	54.8
A26 - B8	15.63	13.84	NR	40.03
A3 - B7	18.01	12.14	NR	9.76
A30 - B13	7.86	6.41	NR	9.47
A19 - B12	33.68	17.52	NR	8.14
A1 - B37	12.25	8.75	NR	8.08
A1 - B63	9.24	7.04	NR	7.91
A10 - B16	4.68	4.07	NR	7.90
A19 - B44	29.60	15.70	NR	7.45
A1 - B17	25.20	13.84	NR	6.85
A29 - B12	7.67	5.79	NR	5.88
Immigrant Indian Hindus ^a (N= 138)				
A1 - B17	88.00	59.00	4.3	NR
A1 - B57	81.00	56.00	4.2	NR
A1 - B37	29.00	22.00	2.7	NR
A10 - B8	22.00	21.00	2.5	NR
A26 - B8	22.00	21.00	2.5	NR
A33 - B44	39.00	27.00	2.5	NR
A33 - B12	39.00	26.00	2.4	NR
A11 - B5	50.00	28.00	2.3	NR
A9 - B63	20.00	16.00	2.1	NR
A24 - B63	20.00	16.00	2.1	NR
A11 - B35	52.00	27.00	2.1	NR

* Pitchappan et al 1984; ^a Mehra et al 1986; ^a Mittal et al 1982;

HF = Haplotype frequency per 1000.

Delta = Linkage disequilibrium per 1000.

S = Significant negative linkage disequilibrium.

^a = t value > 2 indicates positive for Delta.

NR = Not Reported.

B5102, and B3506 have been identified to co-exist with other alleles (Tait et al., 1998).

One of the characteristic properties of HLA diversity in human population is the phenomenon of linkage disequilibrium, the non-random association of particular alleles at HLA loci. Certain haplotypes are very much more frequent than any other combination of alleles. Strong linkage disequilibrium between closely linked loci may be due to lack of cross-over between the loci and more likely selection for a particular combination of allele (Apple and Erlich, 1996). In principle population admixture may also create linkage disequilibrium patterns but that is unlikely to account for extensive disequilibrium observed in human populations. Thus elucidation of the extended haplotypes in the Gujarathi Hindu population by molecular typing for newly identified antigens will reveal the HLA allelic diversity and enable to identify newly arisen favorable variant alleles co-existing in the population.

ACKNOWLEDGEMENTS

We thank Dr.J.V.Undevia for his critical evaluation, Dr.K.Ghosh and Dr.Rajadhyakshya for providing suggestion and discussions, our Directors for their constant encouragement in preparing this Manuscript.

REFERENCE

- Apple, R.J. and Erlich, H. A.: HLA class II Genes: Structure and diversity. In: *HLA and MHC: Genes, Molecules and Function*. Browning, M.J and Mcmichael, A.J (Eds.). BIOS Scientific Publishers. Oxford. 97-112 (1996).
- Ayala, F.J. Escalante, A., O'Huigin, C., and Klein, J.: Molecular genetics of speciation and human origin. *Proc. Natl. Acad. Sci. USA*, 91: 6787-6794 (1994).
- Baur, M.P. and Danilovs, J.A.: Population analysis of HLA A, B, C, DR and other genetic markers. In: *Histocompatibility Testing 1980*. Terasaki P.I. (Ed.). UCLA Press, Los Angeles. 955-1210 (1980).
- Bhasin, M.K., Walter, H. and Danker-Hopfe, H.: *Distribution of Genetical, Morphological and Behavioural Traits Among the Peoples of Indian Region*. Kamla-Raj Enterprises, Delhi (1992).
- Bhasin, M.K., Walter, H. and Danker-Hopfe, H.: *People of India: An Investigation of Biological Variability in Ecological, Ethno-Economic and Linguistic Groups*. Kamla-Raj Enterprises, Delhi, India (1994).
- Bhatia, H.M. and Rao, V.R.: *Genetic Atlas of Indian Tribes*. Institute of Immunohaematology, Indian Council of

- Medical Research, New Delhi (1986).
- Bodmer, J.G., Marsh, S.G.E., Albert, E.D., Bodmer, W.F., Bontrop, R.E., Dupont, B., Erlich, H.A., Hansen, J.A., Mach, B., Mayr, W.R., Parham, P., Petersdorf, E.W., Sasazuki, T., Shreuder, G.M., Strominger, J.L., Svejgaard, A. and Terasaki, P.I.: Nomenclature for factors of the HLA system 1998. *Tissue Antigens*, **53**(II): 47–55 (1999).
- Boyum, A.: Separation of leucocytes from blood and bone-marrow. *Scand. J. Clin. Lab. Invest.*, **21**(Supp): 97 (1968).
- Dausset, J.: Major histocompatibility complex in man: Past, present and future (Nobel Lecture). *Science*, **213**: 1469–1474 (1981).
- Dikshit, K.R.: *Maharashtra in Maps*. Govt. of Maharashtra (Eds.). India (1986).
- Erlich, H.A. and Gyllenstein, U.G.: Shared epitopes among HLA class II alleles: Gene conversion, common ancestry and balancing selection. *Immunology Today*, **11**: 411–414 (1991).
- Fuchs, S.: *Aboriginal Tribes of Eastern India*. Cosmo Publications. New Delhi (1973).
- Haimendorf, C. von Furer: Culture strata in Deccan. *Man*, **48**: 87–90 (1948).
- Imanishi, T., Akaza, T., Kimura, A., Tokunaga, K. and Gojobori, T.: Allele and haplotype frequencies for HLA and Complement loci in various ethnic groups. In: Tsuji, K., Aizawa, M., Sasazuki, T., (Eds.): *HLA 1991*. Proceedings of the Eleventh International Histocompatibility Workshop and Conference Vol. 1. Oxford University Press, Oxford 1066–1220 (1992).
- Kaufmann, J.: Evolution of Major Histocompatibility Complex and MHC like molecules. In: *HLA and MHC: Genes, Molecules and Function*. Browning, M.J and mcMichael, A.J (Eds.). BIOS Scientific Publishers. Oxford. 1–17 (1996).
- Malhotra, K.C.: Morphological composition of the people of India. *J. Hum. Ecol.*, **7**: 45–53 (1978).
- Mehra, N.K., Taneja, V., Kailash, S., Raizada, N. and Vaidya, M.C.: Distribution of HLA antigens in a sample of North Indian Hindu population. *Tissue Antigens*, **27**: 64–74 (1986).
- Mittal, K.K., Naik, S., Sansonetti, N., Cowherd, R., Kumar, R. and Wong, D.M.: The HLA antigens in Indian Hindus. *Tissue Antigens*, **20**: 223–226 (1982).
- Papiha, S.S.: Genetic variation in India. *Human Biology*, **68**: 607–628 (1996).
- Pitchappan, R.M., Kakkaniyah, V.N., Rajasekar, R., Arulraj, N. And Muthukaruppan, V.R.: HLA antigens in South India: I Major groups of Tamil Nadu. *Tissue Antigens*, **24**: 190–196 (1984).
- Raha, P.K.: HLA distribution amongst Bengalee population. *Ind. J. Med. Res.*, **63**: 242–252 (1975).
- Risley, H. 1969 [1915]. *The People of India*. Orient Book Reprint Corporation. Delhi, India (1969).
- Selvakumar, A., Damodharan, C. and Chandrasekaran P.: Distribution of HLA antigens in the native South Indian Hindus. *Tissue Antigens*, **31**: 136–140 (1988).
- Singal, D.P.: The Distribution of HLA Leukocyte antigen in Indians. In: *Histocompatibility Testing 1972*. Dausset, J. And Colombani, J. (Eds.). Munksgaard, Copenhagen 179–186 (1972).
- Tait, B.D., Hammond, M., Stavropoulos-Giokas, Varney, M., Gorodey, C., G.de la Rosa, Moreno, M., Gomey, D., Magafia, A., Boyle, A., Gavrilidis, A., Ashdown, L., Simons, M., Andrien, M., Bignon, J.D., Bouillenne, C., Bias, W., Bohinjee, M., Dupont, E., Fainbacin, L., Gonzales-Escribano, M.F., Hasheni, S., Kastelass, A., Kawasaki, M., Kfir, B., McAuley, J., Park, M.S., Peroli, L., Pitchappan, R., Schroeder, M.L., Scorza, R., Tiercy, J.M. and William, R.C. AHS# 4: B5, B35, B53, B18, B5102, B5103, B78. In: *Genetic Diversity of HLA* Charron D (Eds.) EDK Publishers. Paris Vol. 1: 47–55 (1998). volution in cayapa Indians of Ecuador. *Am. J. Hum. Genet.*, **57**: 415–424 (1995).
- Terasaki, P.I. and McClelland, J.D.: Microdroplet assay of human serum cytotoxins. *Nature*, **204**: 998–1000 (1964).
- Titus-Trachtenberg, E.A., Rickards, O., Destefano, G.F. and Erlich, H.A.: Analysis of HLA class II haplotypes in the cayapa Indians of Ecuador: A novel DRB1 allele reveals evidence for convergent evolution and balancing selection at position 86. *Am. J. Hum. Genet.*, **55**: 160–167. (1994).
- Trachtenberg, E.A., Erlich, H.A., Rickards, O., Destefano, G.F., Klitz, W.: HLA class II Linkage disequilibrium and haplotype ehuman serum cytotoxins. *Nature*, **204**: 998–1000 (1964).
- Trachtenberg, E.A., Erlich, H.A., Rickards, O., Destefano, G.F., Klitz, W.: HLA class II Linkage disequilibrium and haplotype evolution in cayapa Indians of Ecuador. *Am. J. Hum. Genet.*, **57**: 415–424 (1995).