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HLA Antigen Distribution in Marathi Speaking Hindu Population from Mumbai, Maharastra, India

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ABSTRACT Three hundred and ninety two unrelated Marathi speaking Hindu people residing in Mumbai, Maharastra, (Western India) were studied for HLA A, B and C locus antigen profiles. The phenotypic frequencies of HLA A1, A2, A9, A11, A24, A33, B5, B7, B35, B40 and Cw4 were increased while frequencies of HLA A10, A23, A28, A31, B14, B16, B18, B21, B37, B39, B50, Cw1, Cw5 and Cw8 were decreased in the Marathi speaking Hindus. The genotype frequencies of HLA A9, A24, A33 and B40 were increased while that of A11, A28, A31, B15, B21, B37, B50, Cw1 and Cw8 were decreased when compared with gene frequencies of other Indian Hindu populations reported. Two loci haplotype analysis revealed that A1-B17, A10-B8 and A19-B12 were common Indian Hindu haplotypes where as A3-B35, A19-B15 and A11-B40 were unique for the Marathi Hindus. Haplotype A2-B40 observed in Marathi 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 Marathi Hindus. Significant negative linkage disequilibrium was observed for haplotypes A19-B40 and A2-B7 in Marathi Hindus. Thus the observed antigen frequencies and linkage disequilibrium in Marathi 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 elements. 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 per cent of Indian population is Hindus, 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.

Maharastra, 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 Maharastra 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 Maharastra speak Hindi, Marathi, Gujarathi, Kannada, Tamil, Malayalam, Telugu etc., the official language being Marathi and pray Hindu gods. Marathi 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; Imanshi et al., 1992). Few reports are available on immigrant Indian population (Singal, 1972, Mittal, 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 Marathi speaking Hindu population.

MATERIALS AND METHODS

Blood samples from random 392 healthy unrelated Marathi speaking Hindus from Mumbai were studied for HLA -A, -B and -C Locus antigen profiles. Five to ten 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 and C locus antigens were identified by NIH two – stage Microlymphocytotoxicity assay (Terasaki and McClelland, 1964). A total of 150 antisera were used for defining 17 specificities for HLA A locus, 29 for HLA B locus and 8 for HLA C locus antigens. The antisera were commercial (Biotest, Germany; Behring, Germany; Pelfreez, USA) as well as indigenous (Shankarkumar et al., 1998) 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).

RESULTS

The results on HLA A, B and C antigen

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

HLA antigens	*N+ N = 392*	*%PF*	*%GF*	*SEGF*
A1	100	25.5	13.7	1.3
A2	113	28.8	15.6	1.4
A3	51	13.0	6.7	0.9
A9	132	33.7	18.6	1.5
A10	31	7.9	4.0	0.7
A11	97	24.7	13.3	1.3
A19	91	23.2	12.4	1.3
A23	7	1.8	0.9	0.3
A24	125	31.9	17.5	1.5
A25	0	0	0	0
A26	31	7.9	4.0	0.7
A28	36	9.2	4.7	0.8
A29	19	4.8	2.5	0.6
A30	26	6.6	3.4	0.7
A31	2	0.5	0.3	0.2
A32	17	4.3	2.2	0.5
A33	27	6.9	3.5	0.7
A-	133		18.7	
B5	121	30.9	16.9	1.5
B7	108	27.6	14.9	1.4
B8	21	5.4	2.7	0.6
B12	61	15.6	8.1	1.0
B13	31	7.9	4.0	0.7
B14	4	1.0	0.5	0.3
B15	38	9.7	5.0	0.8
B16	6	1.5	0.8	0.3
B17	68	17.3	9.1	1.1
B18	9	2.3	1.2	0.4
B21	10	2.6	1.3	0.4
B22	22	5.6	2.8	0.6
B27	16	4.1	2.1	0.5
B35	86	21.6	11.6	1.2
B37	5	1.3	0.6	0.3
B38	4	1.0	0.5	0.3
B39	2	0.5	0.3	0.2
B40	99	25.3	13.5	1.3
B44	61	15.6	8.1	1.0
B49	9	2.3	1.2	0.4
B50	1	0.3	0.1	0.1
B51	61	15.6	8.1	1.0
B52	14	3.6	1.8	0.5
B55	8	2.0	1.0	0.4
B56	14	3.6	1.8	0.5
B62	31	7.9	4.0	0.7
B63	7	1.8	0.9	0.3
B-	79		10.6	
Cw1	3	0.8	0.4	0.2
Cw2	12	3.1	1.6	0.4
Cw3	36	9.3	4.8	0.8
Cw4	101	26.1	14.0	1.3
Cw5	6	1.6	0.8	0.3
Cw6	13	3.4	1.7	0.5
Cw7	14	3.6	1.8	0.5
Cw8	3	0.8	0.4	0.2
Cw-			76.7	

N+ = Number positive for the allele
% PF = Percentage Phenotype Frequency
% GF = Percentage Genotype Frequency
SGEF = Standard Error of Genotype Frequency

frequencies and standard error of gene frequencies in 392 unrelated healthy Marathi Hindus are presented in table 1. The antigen frequencies of HLA A1, A2, A9, A11, A24, A33, B5, B7, B35, B40 and Cw4 were increased while HLA A10, A23, A28, A31, B14, B16, B18, B21, B37, B39, B50, Cw1, Cw5 and Cw8 were decreased. HLA A25 (10), B54 (22), split antigens were not identified in the Marathi 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 and C gene frequencies in Marathi Hindus with different Indian Hindus are presented in table 2. The gene frequencies of HLA A9, A24, A33 and B40 were found to be increased in Marathi Hindus. The frequencies of HLA A11, A28, A31, B15, B21, B37, B50, Cw1 and Cw8 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

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

HLA	*Marathi Hindus (N = 392)*	*N.Indian Hindus@ (N = 400)*	*S.Indian Hindus# (N = 385)*	*E.Indian Hindus* (N = 92)*
A1	13.70	14.50	13.10	36.41
A2	15.60	11.90	16.41	16.30
A3	6.70	8.90	6.30	4.35
A9	18.60	14.50	16.72	11.96
A23	0.90	NT	NT	NT
A24	17.50	NT	NT	NT
A10	4.00	5.40	3.44	16.85
A25	0.00	NT	NT	NT
A26	4.00	NT	NT	NT
A34	NT	NT	NT	NT
A66	NT	NT	NT	NT
A11	13.30	13.80	16.57	14.13
A19	12.40	18.40	11.58	NT
A29	2.50	2.10	NT	NT
A30	3.40	3.50	NT	NT
A31	0.30	2.10	NT	NT
A32	2.20	5.00	NT	NT
A33	3.50	2.00	NT	NT
A74	NT	NT	NT	NT
A28	4.70	7.90	6.58	NT
A68	NT	NT	NT	NT
A69	NT	NT	NT	NT
A36	NT	NT	NT	NT
A43	NT	NT	NT	NT
A80/A-	18.70	NR	8.89	NR
B5	16.90	16.00	18.14	23.91
B51	8.10	NT	NT	NT
B52	1.80	NT	NT	NT
B7	14.90	6.50	10.12	18.48
B8	2.70	4.40	1.84	20.11
B12	8.10	9.00	5.34	22.83
B44	8.10	7.50	NT	NT
B45	0.00	1.30	NT	NT
B13	4.00	4.00	3.03	14.67
B14	0.50	0.00	0.13	NT
B64	NT	NT	NT	NT
B65	NT	NT	NT	NT
B15	5.00	6.90	5.89	NT
B62	4.00	5.40	NT	NT
B63	0.90	1.50	NT	NT
B75	NT	NT	NT	NT
B76	NT	NT	NT	NT
B77	NT	NT	NT	NT
B16	0.80	1.10	0.39	NT
B38	0.50	0.60	NT	NT
B39	0.30	0.50	NT	NT
B17	9.10	7.80	10.12	NT
B57	NT	NT	NT	NT
B58	NT	NT	NT	NT
B18	1.20	2.20	0.52	NT
B21	1.30	3.30	2.77	NT
B49	1.20	0.70	NT	NT
B50	0.10	2.50	NT	NT
B22	2.80	2.90	2.50	NT
B54	0.00	NT	NT	NT
B55	1.00	NT	NT	NT
B56	1.80	NT	NT	NT
B27	2.10	3.00	0.91	NT
B35	11.60	14.50	10.27	NT
B37	0.60	2.40	NT	NT
B40	13.50	12.20	8.12	NT
B60	NT	NT	NT	NT
B61	NT	NT	NT	NT
B41	NT	0.13	NT	NT
B42	NT	0.13	NT	NT
B46	NT	NT	NT	NT
B47	NT	NT	NT	NT
B48	NT	NT	NT	NT
B53	NT	NT	NT	NT
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	NT	NT	NT	NT
B-	10.60	NR	17.57	NR
Cw1	0.40	2.00	1.78	NT
Cw2	1.60	2.00	2.99	NT
Cw3	4.80	8.40	12.55	NT
Cw4	14.00	8.90	22.54	NT
Cw5	0.80	0.20	0.59	NT
Cw6	1.70	1.80	13.23	NT
Cw7	1.80	NR	13.91	NT
Cw8	0.40	NR	1.18	NT
Cw-	76.70	NR	31.23	NT

@ Mehra et al. (1986). # Pitchappan et al. (1984). * Raha (1975).

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

Population	*Haplotype*	*HF*	*Delta (Δ)*	*t value*[a]	*Ki*[2]
Marathi Hindus					
(N = 392)	A1 - B17	31.2	18.5	3.94	19.41
	A2 - B40	39.3	18.6	3.40	12.45
	A11- B35	29.3	13.8	2.82	8.68
	A19- B15	17.3	11.4	3.19	14.63
	A3 - B35	17.1	9.2	2.44	7.04
	A19 - B12	18.4	8.9	2.24	5.62
	A33-B44	8.8	6.1	2.29	8.07
	A10-B8	5.3	4.2	2.03	8.46
	A11-B40	27.5	10.1	2.02	4.08
	A19-B40[5]	0.9	- 14.4	- 3.47	10.68
	A2- B7[5]	8.9	- 14.5	- 2.71	7.31
South Indian Hindus*					
(N = 385)					
	A1-B17	2.2	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	8.9	- 2.6	-	NR
	A1-B5[5]	-	26.2	3 - 4	NR
	A3-B17[5]	-	- 9.4	3 - 4	NR
	A28-B15[5]	-	- 5.3	-	NR
	A19-B7[5]	5.5	- 5.8	-	NR
North Indian Hindus@					
(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*					
(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). @ Mehra et al, (1986). # Mittal et al. (1982).
HF = Haplotype frequency per 1000.
Delta = Linkage disequilibrium per 1000.
[5] = singificant Negative Linkage diseqiulibrium.
[a] = t value > 2 indicates positive for Delta.

linkage disequilibrium of Marathi Hindus along with the identified haplotypes and linkage disequilibrium in other Indian Hindu populations reported. It is interesting to note that haplotypes A3-B35, A19-B15 and A11-B40 had high delta and significant t values were unique to the Marathi Hindus and is virtually absent in other Indian Hindus reported. Haplotype A3-B7, absent in Marathi Hindus was observed in North and South Indian Hindus, while A2-B40 observed in Marathi 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 haplotypes 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.

DISCUSSION

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 forces (Elrich, 1991). Both selective forces 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, B5102, and B3506 have been identified to coexist 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 or more likely selection for a particular combination of alleles (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 Marathi 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.

REFERENCES

Apple, R.J. and Erlich, H. A.: HLA class II genes: Structure and diversity. In: *HLA and MHC: Genes, Molecules and Function.* M.J. Browning, and A.J. McMichael (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 Daniloves, J.A.: Population analysis of HLA A, B, C, DR and other genetic markers. pp.955 – 1210 In: *Histocompatibility Testing 1980.* Terasaki P.I. (Eds). UCLA Press, Los Angels (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. (Eds.): *Genetic Atlas of Indian Tribes.* Institute of Immunohaematology, Indian Council of Medical Research, New Delhi, India (1986).

Bodmer, J.G., Marsh, S.G.E., Albert, E.D., Bodmer, W.F., Bontrop, R.E. and Dupont, B.: 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. *Scan. J. Clini. 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.: *Maharastra in Maps.* Govt of Maharastra (Eds). India (1986).

Erlich, H.A. and Gyllensten, 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, NewDelhi, India (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: K. Tsuji, M. Aizawa and T. Sasazuki (Eds). HLA 1991. *Proceedings of the Eleventh International Histocompatibility Workshop and Conference Vol I.* 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.* M.J. Browning and A.J. McMichael (Eds). BIOS Scientific Publishers, Oxford, 1-17(1996).

Malhotra, K.C.: Morphological composition of the people of India. *J. Hum. Evol.,* **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., Kakkaniah, 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).

Shankarkumar, U., Gupte, S.C., Gupte, S.S., Pednakar, S.V.,

Ghosh, K. and Mohanty, D.: Frequency and potential application of HLA antibodies from pregnant women in Mumbai. *J. Bio. Sci.*, **23**: 601- 604 (1998).

Singal, D.P.: The distribution of HLA leucocyte antigen in Indians. In: *Histocompatibility Testing 1972*. L. Dausset and J. Colombani (Eds.). Munksgaard, Copenhagen; 179-186 (1972).

Tait, B.D., Hammond, M., Stavropoulos-Giokas, Varney, M., Gorodeyty, C., G.de.la.Rosa., et al., AHS# 4 : B5, B35, B53, B18, B5102, B5103, B78. In: *Genetic Diversity of HLA*. Charron D (Eds) EDK Publishers. Paris Vol: 1. 47-559 (1998).

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., and Klitz, W.: HLA class II Linkage disequilibrium and haplotype evolution in cayapa Indians of Ecuador. *Am. J. Hum. Genet.*, **57**: 415-424 (1995).