HLA-B27 allele diversity in Indians: impact of ethnic origin and the caste system

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ABSTRACT

HLA-B27 is a serological specificity which encompasses an increasing number of subtypes that show varied racial/ethnic prevalence in the world. Here, data from 5129 Indians (4500 population and caste; 629 tribal) is compiled from the literature. In addition, HLA-B27 subtyping of 58 positive individuals from Maharastra is presented. Analysis revealed an increased B27 antigen frequency among the north Indian groups (>5%) compared to the south Indian groups (<5%). HLA-B27 subtyping identified B*2704 (34.48%), B*2705 (36.2%), B*2707 (15.51%), B*2708 (10.34%) and B*2714 (3.44%) alleles in the population groups from Maharastra, but these differed in their distribution among the caste and tribal groups studied. The study showed that more extensive subtyping in other Indian caste groups will be necessary to resolve the evolutionary implications of HLA-B27 subtypes and their relationship to disease association in the Indian context.

KEY WORDS: Alleles. Ethnic groups. HLA-B27 antigen. Social class.

Introduction

HLA-B27 shows a remarkable association with ankylosing spondylitis (AS) and related seronegative spond-arthropathies (SSA), and plays a direct role in disease pathogenesis.[1] It is a serological specificity that encompasses an increasing number of alleles (subtypes) which show varied racial/ethnic prevalence in the world.[2]

HLA-B27 represents a family of 25 closely related alleles (B*2701–B*2725).[3] These subtypes differ by one or more amino acid substitutions in the antigenic peptide-binding groove.[4] The Indian population is well known for its genetic diversity, and distributions of HLA antigens among regional Indian populations are available;[5-22] however, data from indigenous caste and tribal groups are limited.[23-26]

The present study aims to identify the HLA-B27 antigen frequencies among different Indian caste/tribal population groups reported in the literature, and to identify the subtypes among 58 B27-positive individuals belonging to different caste and tribal groups from western India.

Materials and methods

Data from 5129 Indians (population/caste 4500; tribes 629) were compiled for their HLA-B27 antigen frequency distribution based on the regional, caste and tribal distribution. Molecular subtypes in the 58 B27-positive individuals identified from a cohort of 1129 normal healthy individuals belonging to different caste and tribal groups from Maharastra were initially carried out by serological methods.[27]

Details of the caste and tribal groups are described elsewhere.[28] DNA extracted from the 58 B27-seropositive individuals was then confirmed by polymerase chain reaction (PCR)-based sequence-specific primer (PCR-SSP) analysis using a commercial kit (BAG histotype DNA-B27, Germany). The subtypes were genotyped using a reverse line strip sequence-specific oligo nucleotides probe (RLS-SSOP) hybridisation kit (Roche Molecular, Oakland, CA). Phenotype and genotype frequencies were estimated using standard methods.

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Results

B27 antigen frequency distribution among the Indian population, caste groups and tribal groups are presented in Table 1. Comparative results showed an increased prevalence of the HLA-B27 allele among north Indian caste/population groups (2.7–29%) over the south Indian caste/population groups (0.9–2.1%).

Christian (an amalgamation of different caste groups) and Lucknow populations showed increased B27 frequency; whereas, the B27 allele was not identified among the tribal groups in the Malayali and Irula tribes from south India. Tribal groups are more isolated than caste groups because their population distribution is restricted to the hill regions; thus, their HLA-B27 allele frequencies were increased (2.6–8.6%) when compared to the caste and population groups. Furthermore, western Indian caste/population groups from the Maharashtra and Gujarat states showed a different B27 frequency (1.4–15%).

Subtypes among the selected caste and tribal groups from western India (Table 2) included B*2704, B*2705, B*2707, B*2708 and B*2714. HLA B*2704 and B*2705 subtypes were found in most of the caste and tribal groups, while B*2708, B*2707 and B*2714 showed a restricted distribution among the selected caste or tribal groups studied.

Table 1. HLA-B27 distribution among different Indian populations.

Population	Place	State	Region	Size	%PF	%GF	Reference
S.Indian Hindus	USA		USA	138	1.4	0.7	5
Dravidian Hindus	South Africa		South Africa	424	2.0	1.0	6
South India (populations)							
S.Indian Hindus	Chennai	Tamil Nadu	South India	240	2.1	1.0	7
S.Indian Hindus	Madurai	Tamil Nadu	South India	385	1.8	0.9	8
Dravidian Hindus	Chennai	Tamil Nadu	South India	113	0.9	0.4	9
Caste							
Nadars	Madurai	Tamil Nadu	South India	101	2.0	1.0	17
Kallars	Madurai	Tamil Nadu	South India	36	0.0	0.0	17
Naidus	Madurai	Tamil Nadu	South India	57	1.8	0.9	17
Iyers	Madurai	Tamil Nadu	South India	74	1.4	0.6	18
Tribal group							
Malayali	Yercaud	Tamil Nadu	South India	42	0.0	0.0	23
Irulas	Kothagiri	Tamil Nadu	South India	191	0.0	0.0	23
Koya		Andrapradesh	South India	94	3.2	1.6	24
Kota		Andrapradesh	South India	103	3.8	1.9	25
Badagas		Andrapradesh	South India	58	8.6	4.3	25
North India (populations)							
N.Indian Hindus	Delhi	Delhi	North India	400	6.0	3.0	10
N.Indian Hindus	Delhi	Delhi	North India	289	5.2	3.0	11
N.Indian Hindus	Lucknow	U.Pradesh	North India	59	19.6	9.8	12
Marathi Hindus	Mumbai	Maharastra	Western India	392	4.1	2.1	13
Gujarathi Hindus	Mumbai	Maharastra	Western India	414	6.3	3.2	14
Jains	Mumbai	Gujarat	Western India	161	3.7	1.9	15
Parsi	Mumbai	Maharastra	Western India	67	0.0	0.0	16
Christians	Mumbai	Maharastra	Western India	31	29.0	15.8	*
Muslims	Mumbai	Maharastra	Western India	105	9.5	4.9	*
Caste							
Gurkhas	Siliguri	Bengal	Eastern India	50	8.0	4.0	19
Bhargavas	Lucknow	U.Pradesh	North India	100	0.0	0.0	20
Chaturvedis	Lucknow	U.Pradesh	North India	100	0.0	0.0	20
Brahmins	Mumbai	Maharastra	Western India	55	5.5	2.8	21
CKP	Mumbai	Maharastra	Western India	50	10.0	5.2	21
Kunbi	Mumbai	Maharastra	Western India	26	11.5	6.0	21
Mahars	Mumbai	Maharastra	Western India	32	0.0	0.0	21
Maratha	Mumbai	Maharastra	Western India	289	11.7	6.1	22
Patels	Nadiad	Gujarat	Western India	112	2.7	1.4	16
V Prajapathi	Surat	Gujarat	Western India	50	10.0	5.2	16
Tribal group							
Pawra	Dhule	Maharastra	Western India	38	2.6	1.4	26
Bhils	Dhule	Maharastra	Western India	53	7.5	3.8	26
Orans	Mumbai	Orissa	Eastern India	50	4.0	2.1	*
			Total	5129			

* Present study

Discussion

It is well established that HLA-B27 subtypes differ in their ethnic distribution, perhaps as a result of genetic and geographical origin; however, the B*2705 subtype is present in almost all the populations studied worldwide, and is over-represented in the circumpolar and subartic regions of Eurasia and North America.

In contrast, B*2704 is virtually restricted to Oriental and Polynesian populations. B*2707 has been detected in Asian populations.[30,31] B*2708, which is a rare subtype, has been identified in those from the Azores, Britain and in western

Table 2. HLA-B27 allele subtype distribution among different western Indian population groups.

Population	Total	N + (%)	B*2704	B*2705	B*2707	B*2708	B*2714
Tribal group							
Bhils	50	4(7.5%)	2(50%)	1(25%)	1(25%)		
Pawra	50	1(2.63%)	1(100%)				
Oran	50	2 (4%)		2(100%)			
Caste							
Maratha	289	21(7.26%)	6(28.57%)	11(52.38%)	1(4.76%)	3(14.28%)	
Kunbi	26	2(7.69%)					2(100%)
Religious group							
Gujarathi	152	6(3.94%)	2(33.3%)	2(33.3%)		2(33.3%)	
Jain	161	2(1.2%)	1(50%)			1(50%)	
Christians	31	1(3.2%)			1(100%)		
Muslims	105	4(3.8%)	1(25%)	2(50%)	1(25%)		
Scheduled caste	215	15(6.97%)	7(46.66%)	3(20%)	5(33.33%)		
Total	1129	58(5.17%)	20(34.48%)	21(36.2%)	9(15.51%)	6(10.34%)	2(3.44%)

Indians[32,33] of the Jains, Maratha and Gujarathi caste groups. B*2714, a recently identified subtype, has been reported in North American Indians, Siberians, western Indians[33] and among those of the Kunbi caste in India.

Amino acid variation among subtypes and their distribution in world populations strongly suggest that B*2705 could be the ancestral B27 subtype from which all others have evolved, possibly by genetic mechanisms of reciprocal recombination, point mutation or antigen-driven gene conversion.[34] Furthermore, the HLA-B27 allele has also been associated with patients with haemophilia and chronic synovitis.[35]

Population-specific distribution of HLA alleles is necessary both in population genetics and in HLA disease association studies.[36] Anthropological studies show that the distribution of HLA alleles differs from one ethnic group to another, and new alleles may yet be discovered in the Indian population.[37] The various Indian caste groups differ in their origin, migration and settlement, although they have embraced Hinduism since ancient times.

Analysis of genetic data suggests that the inhabitants of the western part of the Eurasian Steppes, originally settled by Caucasoid people speaking Indo-European languages, migrated in various directions, including towards Iran and India. It is believed that these pastoral nomads often formed hierarchical societies and introduced the caste system to the Indian subcontinent.[38]

Migration has a linear effect on HLA-B27 antigen frequency and Neolithic demic diffusion, and could be the cause of nationwide genetic gradients. Thus, more extensive typing of the Indian population will be necessary to resolve the evolutionary implications of HLA-B27 subtypes and their population demography and relative disease association in the Indian context. □

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