Major Histocompatibility Complex, Class I, B

Alternative Names
HLA-B
HLA-B Histocompatibility Type
Abacavir Hypersensitivity, Susceptibility to

Record Category
Gene locus

WHO-ICD
N.B.: Classification not applicable to gene loci.

Incidence per 100,000 Live Births
N/A to gene loci

OMIM Number
142830

Mode of Inheritance
N/A

Gene Map Locus
6p21.3

Description
The genes of the Human Leukocyte Antigen (HLA) system reside on chromosome 6, and code for cell-surface proteins that play a crucial role in the presentation of endogenic peptides to effector cells of the immune system. The HLA Class I protein molecule is a heterodimer, made up of two chains; a heavy one and a light one (beta 2 microglobulin). The HLA-B gene is one of the three HLA Class I heavy chain paralogues. The HLA Class I protein presents peptides from the lumen of the endoplasmic reticulum to T-cells, thereby effecting a cascade of immunologic reactions.

Variations or polymorphisms in the HLA-B locus are associated with several disease conditions, including spondyloarthopathies, like ankylosing spondylitis (specifically, HLA-B27), psoriasis, Crohn’s Disease, and reactive arthritis. Certain HLA-B alleles also tend to react adversely to certain drugs. For instance, individuals with the HLA-B*1502 allele are highly susceptible to developing Steven Johnson syndrome, when administered carbamazepine. Similarly, individuals with HIV, who also carry the HLA-B*5701 allele, are known to be highly sensitive to the drug Abacavir, used to treat AIDS. Another point of interest with regards to the HLA-B locus is the resistance afforded by HLA-B53 allele to malaria. This is evidenced by the high frequency of this allele in the West African populations.

Molecular Genetics
The HLA-B gene spans a length of about 3 Kb. The encoded protein is made up of about 362 amino acids and weighs about 40 KDa. Like the HLA-A gene product, the HLA-B protein is also a single pass-membrane protein that is polyubiquinated as part of its post translational modifications. The protein forms an integral part of the MHC Class I complex, which is involved in the presentation of foreign antigens to the immune system.

Epidemiology in the Arab World
Oman
Agarwal et al. (1996) compared the frequencies of HLA-B antigens in 50 Omani patients diagnosed with Idiopathic Dilated Cardiomyopathy, with those of 247 healthy Omani control subjects. Data obtained was statistically analyzed by chi square test or the Fisher exact test (where appropriate) with the Bonferroni correction obtained by multiplying the P value by the numbers of antigens tested to correct the P value for any chance associations (PC). The antigens tested for included HLA-B 5, 7, 8, 12, 13, 14, 15, 16, 17, 18, 21, 22, 27, 35, 40, 41, 42, 47, 49, 53, 55, 57, w4, and w6. None of these antigens showed a significant difference in frequency between the patient and control group. Earlier studies performed in other populations had indicated HLA-B7 and B14 to be connected to dilated cardiomyopathy. However,
Williams et al. (1996) could not find any such correlation in this study.

White et al. (1999) determined the frequencies of histocompatibility antigens (HLA A and B) in 321 healthy Omani blood, kidney and bone marrow donors (who were not related to each other) by HLA serology. In locus B, 34 serological specificities were determined. The results which were expressed in percentages were statistically compared with those of other gulf countries. It was found that HLA-B17 (21%), B35 (30%), and B40 (15%) were significantly more frequent in Oman than in Saudi Arabia and Kuwait, while HLA-B21 (8%), B27 (0.3% - not significant) and B50 (2%) were significantly lower in Oman than in the other two countries.

Williams et al. (2000) reported a novel allele detected in two Omani individuals in a research undertaken to identify the allele frequencies in 118 healthy Omani subjects. DNA analysis of the subjects was undertaken by PCR amplification followed by analysis by sequence specific oligonucleotide probes (SSOP) in two steps which included typing by a medium-resolution HLA-B PCR-SSOP followed by allele typing by high-resolution SSOP systems according to the HLA-B result. A novel allele was detected under the family HLA-B*39 and was identified in two unrelated subjects who were from different tribes. It differed from HLA-B*39011 and HLA-B*3903 only at the start of exon 3 between positions 12 and 30. Further studies were performed by PCR amplification of exons 2 and 3 from the subjects, followed by purification and sequencing. The exon 2 and 3 alignments of HLA-B*39 variant (HLA-B*3921) were compared with HLA-B*3901, – B*3903, – B*39061 and – B*3910 and it showed similarity to HLA-B*3903 with one nucleotide change at 22 (T-to-C) in exon 3, resulting in methionine to threonine change at amino acid position 98. In both individuals, a positive hybridization signal was detected upon hybridization of a constructed oligonucleotide probe to HLA-B PCR products, confirming the existence of this cytosine mutation. The lack of this mutation in all other HLA-B alleles, and the absence of detection of HLA-B*3903 allele in the Omani population, suggested that the variant allele may have arisen from a conversion event and a point mutation from HLA-B*39061.

Williams et al. (2001) used a two-stage sequence specific oligonucleotide probe (SSOP) typing method to determine the HLA-B allele frequencies in six populations of different ethnic and geographical locations, which included 118 unrelated, healthy Omani subjects, representing the normal population of Oman. DNA of the subjects was amplified by PCR and medium resolution HLA-B SSOP analysis was done, which was followed by typing the samples to allele level using a secondary SSOP systems depending on the initial results obtained from the first stage system. The PCR products were dot blotted, hybridized with digoxigenin probes and detected with chemiluminescence procedures. Population genetic analysis were performed, which included the validity of Hardy-Weinberg equilibrium and analysis of homozygosity (both assessed by Pearson’s chi square test which showed a good fit to that expected for all populations), gene frequency estimates and HLA-A/B haplotype frequencies (derived from maximum likelihood analysis) as well as linkage disequilibrium parameters. In all populations a total of 87 (38%) alleles were detected in this study. Some allele families had one or more variants within a population, and when one allele was predominant in frequency in most of the populations (HLA-B*3501 and – B*4403), it would represent the ancestral allele. In none of the studied populations was the allele family HLA-B*59 expressed. Among the Omani population, a total of 38 alleles were identified with HLA-B*5101 being the predominant one with a frequency of 17.5%. The least represented alleles had frequencies of 0.4% and were HLA-B*705/06, -B*1401, - B*1513, -B*1516, - B*1517, -B*2702, -B*3503, - B*3701, -B*3801, -B*3910, -B*4415, -B*4701, and HLA-B*5703. In this study, two novel HLA-B alleles were detected. The first of these, HLA-B*3924, was found within the Omani population and was expressed in two individuals. In another Omani subject, an allele, HLA-B*4415, which was previously identified in one occasion, was identified. Identical typing patterns of HLA-B*0705 and – B*0706 were observed within the designed typing system which led to unresolved heterogeneous assignments in three types. These indistinguishable types were HLA-B*1402 and – B*1404 in one subject, -B*5301 and – B*7802 in six, and HLA-B*3521 and –B*5105 in one subject. In this population, unique alleles, HLA-B*4006 (8.4%) and –B*7301 (0.8%) were identified, with the HLA-B*4006 being the only allele from the HLA-B*40 family identified among the Omani population. Analysis of HLA-A/B haplotypes revealed four significant ones among the Omani population, HLA-A*1101 and -B*4006, HLA-A*3002 and –B*1402, HLA-A*3101 and –B*3906, and HLA-A*3301 and – B*8101. Williams et al. (2001) explained the
importance of haplotype frequency data in distinguishing populations with similar allele frequencies but different haplotype.

Saudi Arabia
In a study comparing the HLA-B phenotypes among 109 Saudi Arabian males with Caucasian subjects, Ollier et al. (1985) found that the HLA-Bw50 was seen in a very high frequency among the Saudi subjects.

In a study of the HLA gene and antigen frequency among Saudi Arabian subjects, Sheth et al. (1985) discovered that the B21 antigen showed the highest gene frequency (14.6%) among all Middle Eastern populations. The various different HLA-B antigens showed the following gene frequencies: B5 (18.5%), B21 (14.6%), and B35 (10.2%). These frequencies were similar to those observed in the Yemenite population, prompting Sheth et al. (1985) to suggest an influence of such other populations on the Saudi Arabian population.

References

Related CTGA Records
Major Histocompatibility Complex, Class I, A
Major Histocompatibility Complex, Class I, C
Major Histocompatibility Complex, Class II, DR

External Links
http://www.emedicine.com/oph/topic721.htm
http://www.genecards.org/cgi-bin/carddisp.pl?gene=HLA-B

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