

GENETICS, SEROLOGY AND SEQUENCES OF SIX LOW FREQUENCY HLA-CLASS I ALLELES

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Introduction

We have an ongoing programme to improve our serological and DNA-based HLA typing. Accordingly, we take every opportunity to identify and investigate apparent new and rare HLA alleles.

Here we present our findings on the genetics, serology and distribution of 6 low frequency HLA class I alleles: A*0220, A*2502, A*2608, B*3802, B*3910 and B*5802.

Genetics

A*0220 - found, during a study of A*02 alleles, in two blood donors on the Welsh Bone Marrow Donor Registry (WBMDR). This allele was present on the haplotype: A*0220, B*44, Cw*0501, DRB1*1301, DRB3*01, DQB1*0603.

A*2502 - 3 cases identified during bone marrow recipient and donor typing. A*2502 bearing haplotypes include: A*2502, B*0801, Cw*07, DRB1*0301, DRB301, DQB1*0201, BfS, C4A0, C4B1.

A*2608 - several examples found in WBMDR donors; likely haplotypes include: A*2608, B*15, Cw*03, DRB1*various and A*2608, B*51, DRB1*01.

B*38021 - identified in the family of an Asian renal patient on the haplotype: A*0203, B*3802, Cw*0702, DRB1*1404, DRB3*02, DQB1*05031.

B*3910 – identified in a Somali renal patient who was homozygous for B*3910. Likely haplotypes were: B*3910, Cw*1203/6, DRB1*07, DRB4*0101/3, DQB1*0202, BfS, C4A4, C4B2 and B*3910, Cw*1203/6, DRB1*0804, DQB1*0301, BfS, C4A4, C4B2.

B*5802 - identified in 4 Black patients, haplotypes include: A*30, B*5802, Cw*0602 and A*68, B*5802, Cw*0602.

Serology

The serological reactivity of the 6 specificities was investigated using our standard HLA-A,B typing tray sera, which included 6 anti-A2; 16 anti-B17/B57 and 10 anti-B16/38/39, and two additional groups of up to 31 sera for the study of A*2502/A*2608 and B*5802 products.

The 6 different allele products reacted as expected of their specificities denoted by the first two characters of the allele.

Distribution

A search was made for these alleles in 20,666, largely Northern European Caucasoid blood donors, on the WBMDR's panel.

A total of 9 donors with A*2608, 2 with B*3802 and 1 with A*2502 were identified. No donors were found possessing either B*3910 or B*5802.

This suggests that: A*2502, B*3802, B*3910 and B*5802 have a phenotype frequency of < 0.01% and a gene frequency of < 0.00005 in our local blood donor population, while A*2608 has a phenotype frequency of < 0.05% and a gene frequency of < 0.00025.

Note: A*0220 is detected, but not differentiated, by our routine PCR-SSP typing method.

Confirmatory sequencing

Nucleotide sequencing, using the Li-Cor 4200 DNA sequencer, of exons 2 and 3 of: HLA-A*2502, B*3802, B*3910 and B*5802 confirmed the previously reported sequences.

HLA-A*0220 and A*2608 were confirmed by our sequence-based typing protocol.

EBV-transformed B-cell lines

Using our standard procedures (Bass et al. Eur J Immunogenet (1999) 26, 72 and Eur J Immunogenet (2000) 27, 294) B-cell lines were produced from examples of all six rare alleles. These are available on request.

Comment

New HLA allele sequence information alone, unsupported by serological, distribution and haplotype information is of limited value to clinical histocompatibility and immunogenetics (H&I) laboratories; particularly those supporting an unrelated bone marrow donor transplant programme and providing services for an unrelated bone marrow donor registry.

New HLA alleles, particularly HLA-A, B and DRB1, should be investigated for the serological reactivity of their products, their distribution in populations of known ethnic background and for details of their related haplotype(s). In addition, suitable material should always be made readily available to the H&I community for HLA typing quality assurance purposes.