

A FURTHER EXAMPLE OF HLA-B*2712



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Introduction

The HLA-B*2712 allele possesses the Bw6 rather than the Bw4 motif. Although the B*2712 product readily reacts with Bw6 antibodies, it is not easily detected with B27 antibodies. However, it does react with some antibodies directed towards HLA-B40/B60.

Here we report our experience of finding an example of this rare B*27 allele and the serological reactivity of its product by both cytotoxicity testing and flow cytometry.

Detection

After routine 'split-specificity' level typing by PCR-SSP a stem cell volunteer (SS) appeared to be homozygous for HLA-B*18 but possessed both Cw*02 and Cw*12.

As B*18; Cw*02 is an unexpected haplotype SS was investigated further. The donor was found to possess B*2712.

This finding identified a flaw in our routine 'split-specificity' level PCR-SSP typing strategy.

Since B*2712 has the Bw6 motif this allele would only have been suspected in the presence of an HLA-B allele with Bw4.

This defect has now been rectified!

HLA-B2712-bearing haplotype

A family study showed that B*2712 was on the haplotype:

A*02; B*2712; Cw*0202; DRB1*15; DQB1*06.

This is in accord with a previously published example of B*2712.

Cytotoxicity testing of the B*2712 specificity

Standard cytotoxicity testing of SS showed that the B*2712 product reacted variably with 3 out of 7 well validated B27 alloantisera and gave weak reactions with 3 out of 14 sera containing an anti-B40 component. Since SS was HLA-B18 (Bw6) it was not possible to evaluate the serological reactivity of the B*2712 product's Bw6 epitope.

Flow cytometry testing of the B*2712 specificity

Flow cytometry testing of SS, by our standard HLA-B27 typing protocol (Eur J Immunogenet 1998, 25, 29), showed that the B*2712 product was readily detected by the ABCm3 monoclonal antibody (anti-B27, B2708, B7+) but was negative against the FD705 antibody (anti-'B2705', 'B2702') – Table 1.

Table 1. Detection of HLA-'B2712' by flow cytometry

HLA phenotype	Median channel fluorescence intensity with:	
	ABCm3 monoclonal antibody	FD705 monoclonal antibody
'B2712'	2.91	Less than 1
'B2702'	>4	>1 < 2
'B2705'	>4	>4
'B2708'	>4	Less than 1
B22, B37, B44	>1 <2	Less than 1
B42, B73	>2 <4	Less than 1
B7	<5 >4	Less than 1
Negative for all specificities above	Less than 1	Less than 1

This pattern and the level of median channel fluorescence intensity of HLA-'B2712' with monoclonal antibodies ABCm3 and FD705 would trigger PCR-SSP-based testing of the subject, including B*27 'allele level' typing with our current HLA-B27 typing protocol.

Summary

This study has:

- Shown the value of identifying and investigating unusual HLA-B;C associations.
- Confirmed the reactivity of the B*2712 product with some B27 and some B40 alloantisera.
- Confirmed the presence of B*2712 on a specific haplotype.
- Established that the B*2712 product is detectable by flow cytometry using the ABCm3 monoclonal antibody.