

# HLA-A\*0224 IN 'WELSH' BLOOD DONORS



**WELSH BLOOD SERVICE**  
*GWASANAETH GWAED CYMRU*

**WELSH TRANSPLANTATION AND  
IMMUNOGENETICS LABORATORY**



**J. THOMPSON, L. JAMES-SCAIFE,  
J. DOWNING AND C. DARKE**

**Table 1. HLA-A\*02 alleles in subjects with a possible A\*0224-bearing haplotype.**

Number of donors	HLA-A*02 alleles
39	A*0201/53N (5 apparent homozygotes)
1	A*0201/53N, A*0205/28
1	A*0205/28
3	A*0224

## Introduction

The first two examples of A\*0224 were identified by us when a comparison of 1,798 DNA and serological typing of blood donors on the Welsh Bone Marrow Donor Registry (WBMDR) revealed an HLA-A2 by serology that was not detected by PCR-SSP (Guttridge et al., 1999).

A\*0224 differs from A\*0201 by a single base (C/A) at position 453 in exon 3 and this substitution corresponded to the annealing site of a primer commonly used in A\*02-amplifying PCR-SSP mixtures. Accordingly, we modified our PCR-SSP mixtures to detect A\*0224 and to differentiate it during high resolution A\*02 typing.

Two further examples of A\*0224 have subsequently been identified, by chance, in our local blood donor population (largely north-western European Caucasoids). All four subjects, who are allegedly not closely related, possess:

A\*0224; B\*07; Cw\*0702; DRB1\*07; DQA1\*0201, DQB1\*0202 - suggesting that this is a major A\*0224-bearing haplotype.

## Population detection of A\*0224

### Strategy

To determine if A\*0224 is 'commonly' borne by this likely haplotype and to determine the frequency of A\*0224 in our local blood donor population we searched 11,290 HLA types of donors on the WBMDR for those possessing A\*02, B\*07, Cw\*07, DRB1\*07 and DQB1\*02 - 193 were identified.

In view of the strong linkage disequilibrium between B\*07 and DRB1\*15, and DRB1\*07 and B\*13, B\*14, B\*44 and B\*57, types possessing these combinations were removed. This resulted in 98 and 51 rejections, respectively.

The remaining 44 donors were considered as candidates for possessing the likely A\*0224-bearing haplotype. These were A\*02 'allele level' typed by PCR-SSP.

### Results of 'high resolution' HLA-A\*02 typing

Table 1 shows that 50 A\*02 alleles were encountered in this selected group of 44 donors. The A\*0201/53N : A\*0205/08 ratio (23 : 1) was similar to that found (29 : 1) in our local random blood donor population (Thompson et al., 1999).

## Minimum A\*0224 frequencies

The finding of the 3 A\*0224 subjects (3 out of 11,290 donors) indicates that the A\*0224 carriage frequency is at least 0.027% (about 1 in 4,000 random blood donors) and that the gene frequency is a minimum of 0.00013.

## Summary

A\*0224:

- Was first described in blood donors on the Welsh Bone Marrow Donor Registry.
- Differs from A\*0201 by a single base (C/A) at position 453 in exon 3.
- May not be detectable by all PCR-SSP A\*02 typing strategies.
- Appears to be on a haplotype with B\*07; Cw\*0702; DRB1\*07; DQA1\*0201, DQB1\*0202.
- Has a minimum carriage frequency of 0.027 (gene frequency- 0.00013 in our largely northwestern Caucasoid population of blood donors resident in Wales.

## Comment

A\*0224 was originally identified by its failure to be detected during PCR-SSP typing, employing commonly used PCR-SSP primer mixtures. Therefore, it is essential, particularly due to the frequency of this allele, that laboratories confirm their ability to detect A\*0224 by their DNA-based typing methods. If this is not done then it will be possible to miss an example of the ubiquitous and highly immunogenic HLA-A2 antigen.

## References

Guttridge, M.G., Street, J., Thomas, M. & Darke, C. (1999) Identification of HLA-A\*0224: Implications for PCR-SSP HLA typing. *Tissue Antigens* **53**, 190-193.

Thompson, J., James, D., Street, J., Bass, H., Thomas, M., Guttridge, M.G. & Darke, C. (1999) HLA-A2 alleles in Wales: detection, distribution and serology. *European Journal of Immunogenetics* **26**, 47.