

OBSERVATIONS ON THE HLA-A2403 SPECIFICITY



WELSH BLOOD SERVICE
GWASANAETH GWAED CYMRU

WELSH TRANSPLANTATION AND
IMMUNOGENETICS LABORATORY



HLA-A2403 specificity is not unique to A*2403

A local cadaveric organ donor (i.d. 26586) was typed as HLA-A2403 by serology (varied by one serum reaction with our established pattern for A2403 [Tissue Antigens (1996), 47, 307]) but typed as an A*24 variant by PCR-SSP.

Nucleotide sequencing of exons 2 and 3 showed it to be the second example of A*2423 (cell identification 26586; accession number AJ278667).

The HLA phenotype of 26586 by serology was:

A2, A2403; B51 (Bw4), B62 (Bw6); Cw3; DR4, DR13; DQ1, DQ3. By PCR-SSP and nucleotide sequencing the type was: A*02, A*2423; B*51, B*15; Cw*0303, Cw*0304; DRB1*0407, DRB1*1301; DRB3*0202; DRB4*01; DQA1*0103, DQA1*03; DQB1*0603, DQB1*0302.

Possible HLA-A*2423-bearing haplotype

Interestingly, the original A*2423 (EA31) was also B*51 and Cw*0304 so a 'common' A*2423-bearing haplotype is likely to be: A*2423; B*51; Cw*0304.

High resolution typing of 37 "A2403" subjects

Since the A*2423 product had an apparent HLA-A2403 specificity we did 'high resolution' A*24 typing, by PCR-SSP, on 37 subjects who we had previously assigned as 'A2403'.

Of these 37, six were HLA-A2403 by serology alone; 31 possessed the PCR-SSP allele group A*2403/10/18/22/23/33, of which 17 typed as HLA-A2403 by serology.

High resolution typing showed that 35 of the 37 'A2403' subjects were A*2403. However, the remaining two were A*2410.

Studies on A*2410

Neither of the A*2410 subjects had been originally typed by serology and only one was available for further study.

A family analysis showed the A*2410-bearing haplotype to be:

A*2410; B*08; Cw*0701; DRB1*0301; DRB3*01; DQB1*0201.

This A*2410 typed serologically as HLA-A2403.

There was no possible haplotype sharing with the other A*2410 donor whose phenotype was: A*2410, A*11; B*18, B*51; DRB1*15, DRB1*1202; DQB1*0501, DQB1*0601.

J STREET, L HAMMOND, J DOWNING,
J THOMPSON AND C DARKE

A*2403, A*2410 and A*2423 all have the A2403 specificity

These studies indicate that not only the A*2403 product but also the products of A*2410 and A*2423 have the HLA-A2403 specificity.

Possible epitopes of HLA-A9, A23, A24 and A2403

Some anti-HLA-A9 (A23+A24) and anti-A24 sera do not react with A2403. This 'short' reaction pattern identifies the HLA-A2403 specificity.

HLA-A9 antibodies that react with A23, A24 and A2403 are likely to be directed towards an HLA-A9/A2403 'public' epitope that includes 63E and 65G in the alpha 1 domain helix.

However, epitopes unique to, or shared by A23 and A24 (but not A2403) are probably dependent on combinations of amino acids including 166D and 167G in the alpha 2 domain helix.

The amino acid sequences of the A*2403/10/18/22/23/33 group of alleles all possess 166E (except A*2423 (166D)) and all have 167W.

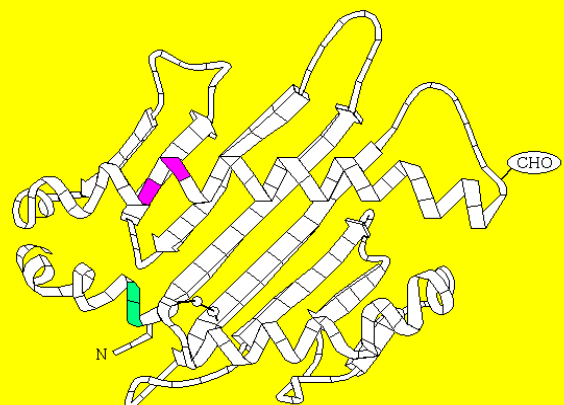
Thus, antibodies directed towards the epitope involving 166D, 167G should fail to react with all the products of the A*2403/10/18/22/23/33 group.

This view is supported by our serological findings for A*2403, A*2410 and A*2423.

This clearly suggests that the products of A*2403, A*2410, A*2418, A*2422, A*2423 and A*2433 will **all** be seen to possess the A2403 specificity when tested with a variety of well documented HLA-A9 and A24 antisera.

A schematic view of these epitopes is shown in Figure 1.

Figure 1. Epitopes involved in the identification of the HLA-A2403 specificity. D – Asp, E – Glu, G – Gly, W – Trp. Products of A*2408 and A*2424 both lack the 63E 65G epitope.



Yellow: Antibodies directed towards 63E 65G will react with most HLA-A*23 and A*24 products including A*2403/10/18/22/23/33
Green: Antibodies directed towards 166D 167G will react with all HLA-A*23 and A*24 products except A*2403/10/18/22/23/33 which have 166E/D 167W