

Should HLA-A43 be an official split of HLA-A10?

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Introduction

During studies on new HLA-A*26 alleles/specificities we used 18 local antisera and 13 monoclonal antibodies (One Lambda) reacting, by CDC, with various combinations of HLA-A10 split specificities, some with additional HLA-A specificities. All had been well-documented in our laboratory over many years.

Fortuitously, the opportunity recently arose to assess these antibodies against HLA-A43.

Reactivity of HLA-A43

The anti-HLA-A10 (anti-A25,A26,A34,A66), anti-A26,A34,A66 and 1/3 of the anti-A26 polyclonal and/or monoclonal antibodies were positive with HLA-A43 while anti-A25,A26,A66, anti-A34,A66, anti-A25, 2/3 anti-A26, anti-A34, anti-A66 were HLA-A43 negative. 1/5 of the anti-HLA-A10 monoclonal antibodies was also HLA-A43 negative.

These findings were much as expected since it has long been recognised that the HLA-A10 CREG contains HLA-A43 and that the 'HLA-A10 alleles' probably arose from HLA-A*26.

Nucleotide/amino acid sequences

A review of relevant nucleotide sequences reinforced the close relationship of HLA-A*43 with all the 'HLA-A10 alleles' especially HLA-A*26 and posed the question why HLA-A43 is not considered a split of HLA-A10.

Thus, A*43:01 differs from A*26:01:01 at 3 nucleotides at positions 257, 259 and 261. This gives rise to two amino acid changes at positions 62 and 63.

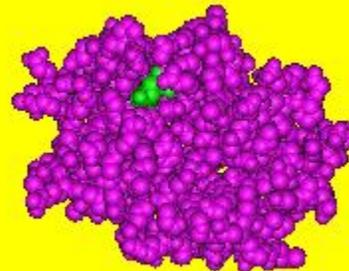
Nucleotide differences

cDNA	250	260	270
A*26:01:01	CCGGAGTATT	GGGACCGGAA	CACACGGAAT
A*43:01	-----	-----T-C-	G-----

Amino acid differences

AA Position	60	70	80
A*26:01:01	WIEQEGPEYW	DRNTRNVKAH	SQTDRLNGT
A*43:01	-----	-LQ-----	-----

Figure showing positions 62 and 63 (highlighted in green) from the top of the HLA molecule.



Inspection of HLA Class I amino acid sequences

We inspected HLA Class I amino acid sequences for motifs providing information on the possible epitopes responsible for the reaction patterns of our antisera/monoclonal antibodies.

38 motifs, unique to various single/combinations of HLA-A10 specificities, some involving other HLA-A specificities, were identified.

16 out of the 38 motifs involved all HLA-A10 specificities.

12 of the 16 motifs included HLA-A43 thus possibly explaining the reactivity of most anti-A10 sera/monoclonal antibodies with HLA-A43.

4 of the 16 motifs covered all HLA-A10 specificities but not HLA-A43, possibly accounting for the HLA-A43 non-reactive anti-HLA-A10 monoclonal antibody.

Importantly, one motif was possessed by HLA-A26, -A34, -A66 and A43, which could account for the reactivity of the anti-A26, A34, A66 monoclonal antibody with HLA-A43.