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Assessment of the amino acid substitution in HLA-B*5719 for allorecognition

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We here describe the identification of the novel human leukocyte antigen (HLA) allele HLA-B*5719, which has been detected in a Ugandan individual in the course of sequencing-based HLA class I typing. Sequencing was performed for exons 2 and 3 after haplotype-specific amplification as previously described [1] using an Applied Biosystems 3730 sequencer and revealed the HLA type A*30CWTA, *34WM; B*4201, *5719.

The name B*5719 was officially assigned by the WHO Nomenclature Committee in August 2008. This follows the agreed policy that, subject to the conditions stated in the most recent Nomenclature Report [2], names will be assigned to new sequences as they are identified. Lists of such new names will be published in the next WHO Nomenclature Report bone marrow donor. The nucleotide sequence is available in the EMBL, GenBank and DDBJ Nucleotide sequence databases under the accession number FM207448.

The new allele differs from HLA-B*5701 by a non-synonymous G to T nucleotide exchange at position 539 in exon 3 (Figure 1A), replacing Leucin by Arginin at amino acid at position 156 in the $\alpha 2$ domain (Figure 1B).

The amino acid variation at position 156 distinguishing HLA-B*4402 (Asparagine 156) from HLA-B*4403 (Leucin 156) was found to be associated with a severe alloreactivity after allogeneic hematopoietic stem cell transplantation [3]. Although the peptide binding motif of these two B*44 alleles has been shown to be identical, B*4403 presents more unique peptides than B*4402. By X-ray crystallography it could be demonstrated that Leucin 156 is widening the peptide binding cleft causing a less stringent peptide binding allowing the accommodation of more peptides [4].

Based on the Risler score [5] describing the functional similarities of amino acids on a scale from 1 (highest similarity) to 100 (lowest similarity) the functional difference between Leucin and Arginin (24), distinguishing B*5701 from B*5719, is lower than between Asparagine and Leucin (60). While this might indicate that the variation between B*5701 and B*5719 has less influence on the peptide repertoire than it has been observed between the B*44 alleles, the central relevance of position 156 on the shape of the peptide binding cleft suggests that B*5719 should be considered a relevant mismatch to B*5701.

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[illegible]

Prot. Pos.	150	160	170
B*570101	A RVAEQ QL RAYL	EGLC VE WLRR	YLEN
B*570101	- - - - -	- - - - -	- - - - -
B*570102	- - - - -	- - - - -	- - - - -
B*570103	- - - - -	- - - - -	- - - - -
B*5702	- - - - -R - - - -	- - - - -	- - - - -
B*570301	- - - - -	- - - - -	- - - - -
B*570302	- - - - -	- - - - -	- - - - -
B*5704	- - - - -R - - - -	- - - - -	- - - - -
B*5705	- - - - -R - - - -	- - - - -	- - - - -
B*5706	- - - - -	- - - - -	- - - - -
B*5707	- - - - -	- - - - -S - - - -	- - - - -
B*5708	- - - - -	- - - - -	- - - - -
B*5709	- -E - - -D - - - -	- - - - -	- - - - -
B*5710	- - - - -	- - - - -	- - - - -
B*5711	- - - - -	- - - - -	- - - - -
B*5712	- - - - -R - - - -	- - - - -	- - - - -
B*5713	- -E - - -R - - - -	- -E - - - - - - -	- - - - -
B*5714	- - - - -	- - - - -	H - - -
B*5715	- - - - -	- - - - -	- - - - -
B*5716	- - - - -	- - - - -	- - - - -
B*5717	- - - - -	- - - - -	- - - - -
B*5719	- - - - - R - - - -	- - - - -	- - - - -

Figure 1.

(A) Nucleotide sequence alignment of codons 150 - 174 of the HLA-B*57 group. (B) Amino acid sequence alignment of positions 150 - 174 of the HLA-B*57 group.