

Five new HLA-A, B, C, DQB1 alleles with nonsynonymous mutations – A*11:241, B*49:43, C*03:321, C*08:132 and DQB1*02:72



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Introduction

During routine HLA typing of blood donors, for the Welsh Bone Marrow Donor Registry, five new HLA sequences exhibiting nonsynonymous mutations were identified in UK Europeans.

HLA typing was initially performed by Histogenetics and subsequently confirmed by sequencing of exons 2, 3 and 4 for HLA-A, B, C and exons 2 and 3 for DQB1.

All were WHO named in May 2016 and all differed from their closest sequence by a single nucleotide substitution:

Allele	Cell ID	Closest allele	Nucleotide difference	Exon	Amino acid difference
A*11:241	73936	A*11:01:01:01	215G>A	2	R48Q
B*49:43	16070844	B*49:01:01	362G>T	3	R97M
C*03:321	15200434	C*03:01:01	234G>C	2	Q54H
C*08:132	74324	C*08:02:01:01	587T>A	3	L172Q
DQB1*02:72	13381598	DQB1*02:01:01	185G>A	2	S30N

Serology

Serological HLA-A, B, C, DR, DQ typing, using 300 well-documented local antisera, and 144 monoclonal antibodies (One Lambda Inc.) showed that A*11:241 and C*08:132 each encode a normal serological specificity (others not tested).

Haplotypes

The new allele bearing haplotypes were predicted, where possible, from allele frequency and linkage disequilibrium estimates from local population genetics information, and elsewhere, as:

A*11:241, B*35:01, C*04:01, DRB1*04:07, DQB1*03:01

A*02:05, B*49:43, C*07:01, DRB1*04:01, DQB1*03:01/DRB1*01:02, DQB1*05:01

A*01:01, B*55:01, C*03:321, DRB1*04:07, DQB1*03:01

A*03:01, B*14:01, C*08:132, DRB1*07:01, DQB1*02:02 (confirmed by family studies)

A*02:01, B*58:01, C*07:18, DRB1*03:01, DQB1*02:72

Frequency

These five new alleles were identified in a sequence-based typed population of 32,530 subjects resident in Wales and largely UK Europeans. This suggests that each has a maximum allele frequency of 0.00002, and a carriage frequency of 0.0031%, in our local normal blood donor population.