Five new HLA-A, B, DRB1, DQB1 alleles with synonymous mutations - A*01:01:65, A*01:01:66, B*44:03:35, DRB1*15:01:30 and DQB1*02:01:24

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Introduction

During routine HLA typing of blood donors, for the Welsh Bone Marrow Donor Registry, five new HLA sequences exhibiting synonymous 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 and B, exon 2 for DRB1 and exons 2 and 3 for DQB1.

Differences from reference allele

The following differ by single nucleotide substitutions in exon 3:

A*01:01:65 (cell identification 71554) differs from A*01:01:01:01 at position 576C>T, codon 168 (CTC>CTT, leucine);

A*01:01:66 (cell identification 16328744) differs from A*01:01:01:01 at position 573G>T, codon 167 (GGG>GGT, glycine).

Similarly, the following differ by single nucleotide substitutions in exon 2:

B*44:03:35 (cell identification 74027) differs from B*44:03:01:01 at position 256C>A, codon 62 (CGG>AGG, arginine);

DRB1*15:01:30 (cell identification 10RZB4) differs from DRB1*15:01:01:01 at position 198C>T, codon 37 (TCC>TCT, serine);

DQB1*02:01:24 (cell identification 48834) differs from DQB1*02:01:01 at position 351G>A, codon 85 (TTG>TTA, leucine).
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Serology

Serological typing, using 300 well-documented local antisera, and 144 monoclonal antibodies (One Lambda Inc.) showed that A*01:01:65, B*44:03:35 and DQB1*02:01:24 each encode a normal specificity (others not tested).

Haplotypes

Family studies indicated that the likely A*01:01:65-bearing haplotype is:

A*01:01:65, B*07:02, C*07:02, DRB1*14:01, DQB1*05:03.

The other new allele bearing haplotypes were predicted from allele frequency and linkage disequilibrium estimates from local population genetics information as:

A*01:01:66, B*35:03, C*12:03, DRB1*15:01, DQB1*06:02;

A*02:01, B*44:03:35, C*16:01, DRB1*07:01, DQB1*02:01/02;

A*25:01, B*18:01/17N, C*12:03, DRB1*15:01:30, DQB1*06:02 and

A*01:01, B*08:01, C*07:01/06, DRB1*03:01, DQB1*02:01:24.

Frequency

These five novel 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 0.00002, and a carriage frequency of 0.0031%, in our local normal blood donor population.