

HLA-DQA1 frequencies and DRB1/DQA1/DQB1 haplotype prevalence in blood donors resident in Wales



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Introduction

Accurate HLA-DQA1 allele typing is essential, e.g. to successfully assess renal patients with HLA-DQ antibodies and to evaluate risk haplotypes in some Class II-related diseases, e.g. coeliac disease.

As part of the on-going validation of our group-specific SBT DQA1 typing method (Lemin *et al. Int J Immunogenet* 2013, **40**, 415) and to improve our understanding of Class II haplotypes in our local population we have determined the frequency of DQA1 alleles and DRB1/DQA1/DQB1 haplotypes in local blood donors registered with the Welsh Bone Marrow Donor Registry (WBMDR).

Materials and methods

The 202 subjects were a random contiguous group previously 2nd field HLA-A, B, C, DRB1, DQB1 typed at enrolment on the WBMDR. All were young (aged <25) subjects resident in Wales and from a largely north western European (NWE) general population.

DQA1 typing employed 12 separate template reactions, using 21 template primers, simultaneously for each sample. Amplicons were linearly amplified using 9 generic DQA1 sequencing primers and separated by capillary gel electrophoresis.

Population genetics analysis included Hardy-Weinberg equilibrium (H-WE) and homozygosity analysis, carriage, allele and haplotype frequencies (HF) and linkage disequilibrium (D) and its significance.

Results

For all 6 loci the fit to H-WE (all $p > 0.94$) and the number of likely homozygotes identified (all $p > 0.12$) was good (DQA1 $p=0.95$ and 0.96 , respectively).

15 DQA1 alleles were found (Table 1).

Overall, the 2 and 3 loci haplotypes identified, i.e. HLA-A/B, A/B/C etc. were typical of a NWE population.

15 DQA1/DQB1 and 27 DRB1/DQA1/DQB1 haplotypes with significant corrected ($p < 0.01$) D values were identified.

Table 1. DQA1 frequencies (n=202 subjects)

DQA1 allele	Carriage freq.	Allele freq.
DQA1*0101	0.22772	0.12624
DQA1*0102	0.37129	0.20545
DQA1*0103	0.09406	0.04703
DQA1*0104	0.04455	0.02228
DQA1*0105	0.03465	0.01733
DQA1*0201	0.25743	0.13366
DQA1*0301	0.12871	0.06683
DQA1*0302	0.03960	0.01980
DQA1*0303	0.15842	0.08663
DQA1*0401	0.02970	0.01485
DQA1*0402	0.00495	0.00248
DQA1*0501	0.27723	0.14851
DQA1*0502	0.00495	0.00248
DQA1*0505	0.19307	0.10149
DQA1*0509	0.00990	0.00495

The 5 most frequent DQA1/DQB1 haplotypes were:

DQA1*05:01/DQB1*02:01 HF = 0.14818
DQA1*01:02/DQB1*06:02 HF = 0.13338
DQA1*01:01/DQA1*05:01 HF = 0.12326
DQA1*05:05/DQA1*03:01 HF = 0.10128
DQA1*02:01/DQA1*02:02 HF = 0.08415

27 DRB1/DQA1/DQB1 haplotypes with significant D values and HF >0.05% were found.

The 5 most frequent were:

DRB1*03:01/DQA1*05:01/DQB1*02:01 HF = 0.14709
DRB1*15:01/DQA1*01:02/DQB1*06:02 HF = 0.13009
DRB1*01:01/DQA1*01:01/DQB1*05:01 HF = 0.08666
DRB1*07:01/DQA1*02:01/DQB1*02:02 HF = 0.08416
DRB1*11:01/DQA1*05:05/DQB1*03:01 HF = 0.05296

Comment

These findings usefully add to the HLA information of local donors and provide valuable insights into DRB1, DQA1, DQB1 associations.