

BRIEF COMMUNICATION

Ten novel HLA-DRB1 alleles and one novel DRB3 alleleA. M. Lazaro¹, N. K. Steiner¹, M. E. Moraes², J. R. Moraes², J. Ng¹, R. J. Hartzman³ & C. K. Hurley¹¹ Departments of Oncology and Pediatrics, Georgetown University Medical Center, Washington, DC, USA² Laboratorio de Imunogenetica Instituto Nacional Do Cancer, Rio de Janeiro, Brazil³ C.W. Bill Young Marrow Donor Program, Naval Medical Research Center, Kensington, MD, USA**Key words**

DNA sequencing; HLA-DR

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Abstract

Ten novel HLA-DRB1 and one DRB3 alleles are described. Eight of the variants are single-nucleotide substitutions, four resulting in an amino acid change (DRB1*1145, *1148, *0828 and *1514) and four with silent substitutions (DRB1*040504, *130103, *160502 and DRB3*020204). Two alleles differ by two nucleotide changes altering one (DRB1*1447 and *1361) amino acid and one allele alters three nucleotides and two amino acids.

This article describes 10 novel HLA-DRB1 and one DRB3 alleles identified during low-resolution DNA-based sequence-specific probe typing. Exon 2 was amplified by the polymerase chain reaction using intron primers (I1-RB6, I2-RB7, I1-RB14, I2-RB28, I1-RB40, I2RB39, I1-RB9, I1-RB3, I1-RB32 and I2-RB36) described by Blasczyk and colleagues (1). Sequencing of the second exon was performed using sense primers (I1-RBSeq1 and -3) (1) and an antisense primer I1-RBSeq4 (5'-cagtcacagggactcag-3') in order to sequence both DNA strands.

The cells evaluated in this study are listed in Table 1. Table 2 compares the novel sequences to the sequences of the most homologous alleles.

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Table 1 Cells and their HLA alleles

Cell	HLA-A ^a	HLA-B ^a	HLA-DR ^b	GenBank Accession No. ^c
GN00419	A*02, A*23	B*35, B*4501	DRB1*040504 , DRB1*1104, DRB3*02	AY094139
MMMBR	A*0201, A*06802	B*4403, B*27	DRB1*0101, DRB1*0828^d	AY504815
NT00504	A*02, A*03	B*07, B*3905	DRB1*04, DRB1*1145	AY429723
NT00507	A*02, A*68	B*49, B*51	DRB1*1148 , DRB1*040501, DRB3*02	AY429728
GN00424	A*03, A*3402	B*35, B*4402	DRB1*130103 , DRB1*0101	AY178184
BY00049	Not tested	Not tested	DRB1*1361 , DRB1*1302	AY339247
BY00050	A*02, A*31	B*35, B*51	DRB1*1447 , DRB1*0407	AY267905
BY00051	A*02	B*1530, B*4901	DRB1*0101, DRB1*1448	AY267906
BY00052	A*11, A*24	B*15, B*35	DRB1*1501, DRB1*1514	AY429729
NT00502	A*11, A*24	B*35, B*51	DRB1*04031, DRB1*160502 , DRB5*0202,	AY428805
GN00418	A2, A31	B51, B60	DRB1*1405, DRB1*09012, DRB3*020404 , DRB4*01 ^d	AY094138

^aHLA-A and -B were assigned primarily by probe-based typing.

^bNovel allele is in bold type. The names have been officially assigned by the WHO Nomenclature Committee.

^cAccession number of novel allele.

^dDQ assignments – MMMBR: DQB1*0501, *0301; GN00418: DQB1*05031, DQB1*0303.

Table 2 Description of novel sequences

Novel allele ^a	Allele most homologous ^b	Difference (nucleotides)	Codon changes ^{c,d}	Amino acid changes	Polymorphisms found at the codon position changed	
					Within the group ^d	Within all DRB ^d
DRB1*040504	DRB1*040501	One	90-ACA to ACG	Silent	ACA (T) 49 ACG (T) 2	ACA (T) 379 ACG (T) 28 CAG (Q) 2 TCC (S) 1 CAC (H) 1 GTG (V) 1
DRB1*0828	DRB1*0804	One	47-TAC to TTC	Y to F	TAC (Y) 33 TTC (F) 2	TAC (Y) 285 TTC (F) 181 GCG (A) 2 TCC (S) 1 TCA (S) 1 TAT (Y) 1 CTC (L) 1
DRB1*1145	DRB1*1123	One	67-TTC to ATC	F to I	TTC (F) 43 ATC (I) 11 CTC (L) 10	CTC (L) 218 ATC (I) 132 TTC (F) 118 GAG (E) 2 CCA (P) 1 CTG (L) 1
DRB1*1148	DRB1*1102	One	47-TTC to TAC	F to Y	TTC (F) 58 TAC (Y) 6	TAC (Y) 214 TTC (F) 174 TAT (Y) 1 CTC (L) 1
DRB1*130103	DRB1*130101	One	78-TAC to TAT	Silent	TAC (Y) 71 TAT (Y) 1	TAC (Y) 330 TAT (Y) 46 GTG (V) 12 CAC (H) 1 TGC (I) 1

Table 2 Continued

DRB1*1361	DRB1*130101	Two	77-ACC to AAT	T to N	ACC (T) 70 AAC (N) 1 AAT (N) 1	ACC (T) 382 AAT (N) 52 AAC (N) 31 TGC (C) 2 GAC (D) 2 GCC (A) 1 TAC (Y) 1 TCG (S) 1
DRB1*1447	DRB1*1402	Two	77-ACC to AAT	T to N	ACC (T) 50 AAT (N) 2 GCC (A) 1	Same as above
DRB1*1448	DRB1*1402	Three	57-GAT to GTC 60-TAC to TCC	D to V Y to S	57 GAT (D) 35 GCT (A) 16 AGC (S) 1 GTC (V) 1 60 TAC (Y) 34 CAC (H) 18 TCC (S) 1	57 V and 60S Observed at some DRB1*07, 09, 12 and *1354
DRB1*1514	DRB1*150201	One	20-GGG to GCG	G to A	GGG (G) 21 GCG (A) 1	GGG (G) 469 GCG (A) 1 CCT (P) 1
DRB1*160502	DRB1*160501	One	69-GAA to GAG	Silent	GAA (E) 9 GAG (E) 1	GAG (E) 248 GAA (E) 218 AAG (K) 2 GGC (G) 1 CAG (Q) 1 CCT (P) 1 GGA (G) 1
DRB3*020204	DRB3*02020	One	58-GCC to GCG	Silent	GCC (A) 20 GCG (A) 2 GAG (E) 1	GCC (A) 298 GAG (E) 72 GCT (A) 66 GCG (A) 27 GCA (A) 3 TAC (Y) 2 TCC (S) 1 GGC (G) 1 ACC (T) 1 CCT (P) 1

^aThe names have been officially assigned by the WHO Nomenclature Committee (2–4).

^bMost homologous sequence obtained from IMGT/HLA Sequence Database (5).

^cFrom first codon of the mature protein. Most homologous allele to novel allele.

^dNew codon is bolded.

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