

# Nomenclature for factors of the dog major histocompatibility system (DLA), 2000: second report of the ISAG DLA Nomenclature Committee

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## Summary

The International Society for Animal Genetics (ISAG) Dog Leukocyte Antigen (DLA) Nomenclature Committee met during the 'Comparative Evolution of the Mammalian major Histocompatibility Complex (MHC)' meeting in Manchester, UK on 10 September 2000. The main points discussed were the naming of class I genes and alleles, and the inclusion of alleles from other canidae.

**Keywords** DLA, dog, genetics, MHC, nomenclature.

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## Introduction

The Major Histocompatibility Complex (MHC) of the dog and other canidae appears to be highly polymorphic, and alleles of these genes are likely to be functionally relevant in regulating the immune response and the susceptibility/resistance to immune-mediated diseases. Considerable effort has recently been made in characterizing the extent of the polymorphisms in DLA class II genes. The ISAG DLA nomenclature committee met during the recent 'Comparative Evolution of the Mammalian MHC' conference in Manchester in September 2000, and the report of this meeting is given below.

## Naming of genes within the DLA region

### Class I

Since the previous nomenclature report (Kennedy *et al.* 1999, 2000a), studies by J.L. Wagner (unpublished data)

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have identified locus specific primers for four transcribed class I genes. Thus the previously described alleles (Graumann *et al.* 1998) can be assigned unequivocally to particular loci. In order to avoid the suggestion that any DLA class I genes were homologues of particular HLA class I genes, it was decided that numbers rather than letters would be used at present to name DLA class I genes. The updated list of DLA genes is shown in Table 1a (with newly named genes in bold type), while Table 1b lists other genes which have yet to be confirmed and do not have official names. Since the first DLA nomenclature report, the DLA region has been mapped to dog chromosome 12 (Mellersh *et al.* 2000), and it has been confirmed that DLA-79 maps to a separate region on chromosome 18. Although DLA-79 and C1pg-26 are orphan genes not located in the DLA region, the DLA Nomenclature Committee considers that naming such genes falls within their remit.

### Class II

No new class II gene names were assigned.

## Naming of new alleles

The committee reaffirms the published conditions for naming new alleles (Kennedy *et al.* 1999, 2000a).

**Table 1a** Genes in the DLA complex.

Official name	Previous equivalents	Molecular characteristics	References
<b>DLA-79</b>	DLA-79	Non-classical class I gene associated with 7.9 kb <i>Hind</i> III fragment, Not in DLA region	Burnett & Geraghty (1995), Burnett <i>et al.</i> (1997), Graumann <i>et al.</i> (1998)
<b>DLA-88</b>	DLA-88	Class I gene associated with 8.8 kb <i>Hind</i> III fragment	Burnett <i>et al.</i> (1997), Graumann <i>et al.</i> (1998)
<b>DLA-12</b>	DLA-12	Non-classical class I gene associated with 12 kb <i>Hind</i> III fragment	Burnett <i>et al.</i> (1997), Graumann <i>et al.</i> (1998)
<b>DLA-64</b>	DLA-64	Non-classical class I gene associated with 6.4 kb <i>Hind</i> III fragment	Burnett <i>et al.</i> (1997), Graumann <i>et al.</i> (1998)
DLA-DRA1	DRA	DR $\alpha$ chain	Sarmiento & Storb (1988), Wagner <i>et al.</i> (1995)
DLA-DRB1	DRB1, DRBB1	DR $\beta$ chain	Sarmiento & Storb (1988, 1990a), Wagner <i>et al.</i> (1996b,c)
DLA-DRB2	DRB2, DRBB2	DRB pseudogene	Sarmiento & Storb (1988, 1990b), Wagner <i>et al.</i> (1996b,c)
DLA-DQA1	DQA1	DQ $\alpha$ chain	Sarmiento & Storb (1988), Wagner <i>et al.</i> (1996b)
DLA-DQB1	DQB1	DQ $\beta$ chain	Sarmiento & Storb (1988), Wagner <i>et al.</i> (1998a)
LMP2	LMP2		Gerlach, personal communication

**Table 1b** Other unconfirmed genes associated with the DLA complex.

Name	Molecular characteristics	References
DLA-A	Unknown	Sarmiento & Storb (1990a)
DLA-12a	Class I pseudogene associated with 12 kb <i>Hind</i> III fragment	Burnett <i>et al.</i> (1997)
C1pg-26	Class I processed gene associated with 2.6 kb <i>Hind</i> III fragment Not in DLA region	Burnett <i>et al.</i> (1997)
DLA-53	Class I pseudogene associated with 5.3 kb <i>Hind</i> III fragment	Burnett <i>et al.</i> (1997)
DQB2	?Pseudogene	Sarmiento & Storb (1988), Wagner <i>et al.</i> (1998a)
DPA	DP $\alpha$ chain	Sarmiento & Storb (1988)
DPB1	DP $\beta$ chain	Sarmiento & Storb (1988)
DPB2	DP $\beta$ chain	Sarmiento & Storb (1988)
DOB	DO $\beta$ chain	Sarmiento & Storb (1988)

Since the last nomenclature report, 48 DLA-88, 16 DLA-DRB1, 6 DLA-DQA1 and 15 DLA-DQB1 alleles have been named. Although there is some evidence for 2, 3 and 4 alleles, respectively, for DLA-12, DLA-64 and DLA-79 (Graumann *et al.* 1998), no sequence alignments have been published, and no alleles have been lodged in GenBank to date. Therefore no allele names have been assigned for these class I loci. Tables 2–5 list all the named alleles at the following loci: DLA-88, DLA-DRB1, DLA-DQA1 and DLA-DQB1. The tables show new alleles in bold type, and include previous names, accession numbers, and for class II, the canidae in which each allele has been found to date.

The class I alleles for the DLA-88 locus have been named according to the rules defined in the previous nomenclature report. Some of these alleles have an additional amino acid at codon 156, and these alleles have

received names starting at DLA-88\*50101. The sequential numbering for the nucleotides and the codons therefore includes codon 156, although many alleles are missing that codon.

### Naming of MHC alleles from other canidae

The principles for naming the MHC genes and alleles in different canidae (dog, grey wolf, red wolf and coyote lineages), and how to apply them to sub-species and hybrids have been considered. The principles established here for the canidae group may have applications in other animals which have been domesticated.

At this point of time it is not considered possible to distinguish class II alleles from domestic dogs, grey wolves, red wolves and coyotes. As can be seen from Tables 3–5, there is some overlap (especially for DLA-DQA1) in the occurrence

**Table 2** Accession numbers and references for DLA88 alleles.

Allele	Previous equivalent	Accession numbers Exon 2, Exon 3	Reference
DLA-88*00101	dla88-01	AF100567, AF101486	a
DLA-88*00201	dla88-02	AF100568, AF101487	a
DLA-88*00301	dla88-03	AF100569, AF101488	a
DLA-88*00401	dla88-04	AF100570, AF101489	a
DLA-88*00402	dla88-12	AF100578, AF101497	a
DLA-88*00501	dla88-05	AF100571, AF101490	a
DLA-88*00601	dla88-06	AF100572, AF101491	a
DLA-88*00701	dla88-07	AF100573, AF101492	a
DLA-88*00801	dla88-08	AF100574, AF101493	a
DLA-88*00901	dla88-09	AF100575, AF101494	a
DLA-88*01001	dla88-10	AF100576, AF101495	a
DLA-88*01301	dla88-13	AF100579, AF101498	a
DLA-88*01401	dla88-14	AF100580, AF101499	a
DLA-88*01501	dla88-15	AF100581, AF101500	a
DLA-88*01601	dla88-16	AF100582, AF101501	a
DLA-88*01602	dla88-40	AF100606, AF101525	a
DLA-88*01701	dla88-17	AF100583, AF101502	a
DLA-88*01801	dla88-18	AF100584, AF101503	a
DLA-88*01901	dla88-19	AF100585, AF101504	a
DLA-88*02001	dla88-20	AF100586, AF101505	a
DLA-88*02201	dla88-22	AF100588, AF101507	a
DLA-88*02301	dla88-23	AF100589, AF101508	a
DLA-88*02401	dla88-24	AF100590, AF101509	a
DLA-88*02501	dla88-25	AF100591, AF101510	a
DLA-88*02601	dla88-26	AF100592, AF101511	a
DLA-88*02701	dla88-27	AF100593, AF101512	a
DLA-88*02801	dla88-28	AF100594, AF101513	a
DLA-88*02802	dla88-29	AF100595, AF101514	a
DLA-88*03001	dla88-30	AF100596, AF101515	a
DLA-88*03101	dla88-31	AF100597, AF101516	a
DLA-88*03401	dla88-34	AF100600, AF101519	a
DLA-88*03501	dla88-35	AF100601, AF101520	a
DLA-88*03701	dla88-37	AF100603, AF101522	a
DLA-88*03801	dla88-38	AF100604, AF101523	a
DLA-88*03901	dla88-39	AF100605, AF101524	a
DLA-88*04101	dla88-41	AF100607, AF101526	a
DLA-88*04201	dla88-42	AF100608, AF101527	a
DLA-88*04301	dla88-43	AF100609, AF101528	a
DLA-88*04401	dla88-44	AF100610, AF101529	a
DLA-88*04801	dla88-48	AF218299, AF218300	b
DLA-88*50101	dla88-11	AF100577, AF101496	a
DLA-88*50201	dla88-33	AF100599, AF101518	a
DLA-88*50301	dla88-36	AF100602, AF101521	a
DLA-88*50401	dla88-46	AF218297, AF218298	b
DLA-88*50501	dla88-32	AF100598, AF101517	a
DLA-88*50601	dla88-47	AF218303, AF218304	b
DLA-88*50701	dla88-49	AF218301, AF218302	b
DLA-88*50801	dla88-21	AF100587, AF101506	a

a = Graumann *et al.* (1998), b = Wagner *et al.* (2000a).

of alleles in these different canidae, at all three of the class II loci studied to date. Given that the sample sizes are small for some of the canidae presently examined, it would seem likely that the degree of overlap will increase. As full-length genomic sequences are not as yet available, there are no data as to whether the other exons and the intron sequences are also identical. Compelling evidence of MHC identity exists between these canidae, as several three locus haplotypes have been shown to be shared between dogs, wolves and coyotes.

The DLA class II alleles found in any of these canidae will be named in a common series, until such time as they can be shown to be different.

### Updated sequence alignments

The updated sequence alignments have been published elsewhere (Kennedy *et al.* 2001).

### Sequence database

The DLA allele sequences will be integrated into a non-human section of the Immunogenetics/HLA database (<http://www.ebi.ac.uk/imgt/hla>). The alignments should also become available on a web site in the near future. In the meanwhile, the alignment files are available by e-mail from [lorna.kennedy@man.ac.uk](mailto:lorna.kennedy@man.ac.uk).

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**Table 3** Accession numbers and references for DLA-DRB1 alleles and their distribution in different canidae.

Allele	Previous equivalents	Accession numbers	Ref	Allele found in				
				Dog ( <i>n</i> > 800)	Grey wolf ( <i>n</i> = 50)	Red wolf ( <i>n</i> = 2)	Mexican wolf ( <i>n</i> = 5)	Coyote ( <i>n</i> = 4)
DRB1*00101	Dw4, D1	M57529	a	+				
DRB1*00102	Dw3, D3	M57528, S76138	a, h	+				
DRB1*00201	Dw1, D2	M57537	a	+				
DRB1*00202	D2a	U44777	b	+				
DRB1*00301	0902	AJ003012	d	+				
DRB1*00401	D4, D4m	M57532	a, b	+				
DRB1*00501	D24, 2302	AJ003017, AF098496	d, e	+				
DRB1*00601	D6, D6m	M57534	a, b	+	+		+	
DRB1*00701	D7	M57533	a	+				
DRB1*00801	D8, D8m	M57535	a, b	+				
DRB1*00802		AJ012456	f	+				
DRB1*00901	D9	M57531	a	+	+			
DRB1*010011	D25	AF016910	g	+				
DRB1*010012	Cafa-10, 1102	X93572	c	+				
DRB1*01101	2102, Cafa-11, 1112	X93573	c	+				
DRB1*01201	1902	AJ003015	d	+	+			
DRB1*01301	D13	U44778	b	+				
DRB1*01401	D14	U44779	b	+				
DRB1*01501	D15/Dw8, D15m, D24 (partial seq)	M57536 AF016912	a, b, g	+				
DRB1*01502	1502	AJ003013	d	+				
DRB1*01503	1503	AJ003014	d	+				
DRB1*01601		AJ012454	f	+				
DRB1*01701	D17	U44780	b	+				
DRB1*01801	D18	U44781	b	+				
DRB1*01901	D19	U44782	b	+				
DRB1*02001	D20	U58684	b	+				
DRB1*02101	D21	U44783	b	+				
DRB1*02201	D22	U58685	b	+				
DRB1*02301	2301	AJ003016	d	+				
DRB1*02401	2401	AJ003018	d	+				
DRB1*02501	2501	AJ003019	d	+				
DRB1*02601	2601	AJ003020	d	+				
DRB1*02701	drb 26	AF061039	i	+				
DRB1*02801	drb 25	AF061038	i	+				
DRB1*02901		AJ012455	f	+	+			
DRB1*03001	D23	AF016911	g	+				
Partial sequence	1-Dob-A	M30129	j	+				
Partial sequence	1-Dob-B	M30130	j	+				
Partial sequence	2-Dob	M30131	j	+				
Partial sequence	3-Lab	M30132	j	+				
Partial sequence	4-Pood	M30133	j	+				
<b>DRB1*03101</b>	ucd001, nw1	AF336108	l		+			
<b>DRB1*03201</b>		AY009941	m	+				
<b>DRB1*03301</b>		AF343737	m	+				
<b>DRB1*03501</b>		AF336109	l		+			
<b>DRB1*03601</b>		AF336110	l		+			
<b>DRB1*03701</b>		AF343738	k		+			
<b>DRB1*03801</b>		AF343739	k		+		+	

Table 3 (Contd.)

Allele	Previous equivalents	Accession numbers	Ref	Allele found in				
				Dog (n > 800)	Grey wolf (n = 50)	Red wolf (n = 2)	Mexican wolf (n = 5)	Coyote (n = 4)
DRB1*03901		AF343740	k, n		+	+		
DRB1*04001		AF343741	k	+				
DRB1*04101		AF343742	k, n		+			
DRB1*04201		AF343743	k, n					+
DRB1*04301		AF343744	k, n				+	
DRB1*04401		AF343745	k, n		+			
DRB1*04501		AF343746	k, n		+			+
DRB1*04601		AF343747	k	+				
DRB1*04701		AF343748	k	+				

a = (Sarmiento *et al.* 1990), b = (Wagner *et al.* 1996c), c = (Francino *et al.* 1997), d = (Kennedy *et al.* 1998), e = Wagner, GenBank 1998, unpublished, f = (Kennedy *et al.* 2000b), g = Francino, GenBank 1997, unpublished, h = (He *et al.* 1994), i = (Wagner *et al.* 1998b), j = Motoyama, GenBank 1996, unpublished. k = LJ Kennedy unpublished. l = LJ Kennedy and JM Angles unpublished. m = JM Angles unpublished. n = LJ Kennedy and P Hedrick unpublished.

Table 4 Accession numbers and references for DLA-DQA1 alleles and their distribution in different canidae.

Allele	Previous equivalents	Accession numbers	Ref	Allele found in				
				Dog (n > 800)	Grey wolf (n = 57)	Red wolf (n = 1)	Mexican wolf (n = 6)	Coyote (n = 2)
DQA1*00101	0101, Dqa2	M74907, U44786	a, c	+	+		+	+
DQA1*00201	0201, Dqa9	M74909, U75455	a, d	+	+		+	
DQA1*00301	0301	Y07944	b	+			+	
DQA1*00401	0203, Dqa4	Y07943, U44788	b, c	+	+			
DQA1*005011	0202, Dqa3	M74910, U44787	a, c	+	+		+	
DQA1*005012	Dqa5	U44789	c	+				
DQA1*00601	0103, Dqa6	Y07942, U44790	b, c	+	+			
DQA1*00701	Dqa7	U44842	c	+	+	+		
DQA1*00801	Dqa8	U61400	d	+				
DQA1*00901	0102, Dqa1	M74908, U44785	a, c	+			+	+
DQA1*01001		AJ130870	e	+	+			
DQA1*01101		AF343733	f		+			
DQA1*01201		AF343734	g	+	+			+
DQA1*01301		AF343735	f		+			
DQA1*01401		AF336107	f	+	+			
DQA1*01501		AF343736	g	+				

a = Sarmiento *et al.* (1992), b = Polvi *et al.* (1997), c = Wagner *et al.* (1996a), d = Wagner, GenBank 1996, unpublished data, e = Kennedy *et al.* (2000b), f = Kennedy & Angles, unpublished data, g = Kennedy, unpublished data.

**Table 5** Accession numbers and references for DLA-DQB1 alleles and their distribution in different canidae.

Allele	Previous equivalents	Accession numbers	Ref	Allele found in				
				Dog (n = 200)	Grey wolf (n = 40)	Red wolf (n = 2)	Mexican wolf (n = 7)	Coyote (n = 0)
DQB1*00101	0101, dqb2, dqb0102	M90802, AF043147, AF016905	a, c, d	+				
DQB1*00201	0201, dqb3, dqb0203	M90803, AF043148, AF016908	a, c, d	+				
DQB1*00301	0301, dqb6	M90804, AF043151	a, c	+				
DQB1*00401	0401, dqb5	M90805, AF043150	a, c	+				
DQB1*00501	0501, dqb12	Y07947, AF043157	b, c	+				
<b>DQB1*00502</b>		AF336111	h	+				
DQB1*00701	0701, dqb4, dqb1001	Y07949, AF043149, AF016907	b, c, d	+	+		+	
DQB1*008011	0801, dqb1	AF043492, AF043167	e, c	+	+		+	
<b>DQB1*008012</b>		AF336112	h					
<b>DQB1*00802</b>		AF343731	g	+				
DQB1*01101	dqb1101	AF016904	d	+				
<b>DQB1*01201</b>		AY009942	h	+				
DQB1*01301	dqb13	AF043158	c	+				
DQB1*01302	dqb14	AF043159	c	+				
DQB1*01303	dqb7, dqb0901	AF043152, AF016906	c, d	+			+	
<b>DQB1*01401</b>		AF343732	f		+			
DQB1*01501	dqb15	AF043160	c	+		+		
DQB1*01601	dqb16	AF043161	c	+				
DQB1*01701	dqb17	AF043162	c	+	+			
DQB1*01801	dqb18	AF043163	c	+				
DQB1*01901	dqb9	AF043154	c	+				
DQB1*02001	dqb20, dqb23	AF043165, AF113705	c, i	+				
DQB1*02002	dqb19	AF043164	c	+	+			
DQB1*02101	dqb11	AF043156	c	+				
DQB1*02201	dqb10	AF043155	c	+				
DQB1*02301	dqb8, dqb0303	AF043153, AF016909	c, d	+	+			
Partial sequence	0302	Y07946	b	+				
Partial sequence	0601	Y07948	b	+				
Partial sequence	0202	Y07945	b	+				
<b>DQB1*02401</b>		AY009940	h		+			
<b>DQB1*02601</b>		AF113704	i	+				
<b>DQB1*02701</b>		AF113706	i	+				
<b>DQB1*02801</b>		AF343730	g	+				
<b>DQB1*03001</b>	dqb26	AF241781	i	+				
<b>DQB1*03101</b>	dqb27	AF241529	i	+				
<b>DQB1*03201</b>		AJ311104	f		+			
<b>DQB1*03301</b>		AJ311105	f		+			
<b>DQB1*03401</b>		AJ311106	f		+			
<b>DQB1*03501</b>		AJ311107	f	+	+			

a = Sarmiento *et al.* (1993), b = Polvi *et al.* (1997), c = Wagner *et al.* (1998a), d = Francino, GenBank 1997, unpublished data, e = Polvi, GenBank 1998, unpublished data, f = Kennedy & Angles, unpublished data, g = Kennedy, unpublished data, h = Angles, unpublished data, i = Wagner *et al.* (2000b).

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