# 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.

## 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Since the previous nomenclature report (Kennedy *et al.* 1999, 2000a), studies by J.L. Wagner (unpublished data) have identified locus specific primers for four transcribed class I genes.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).

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

| Official name | Previous equivalents | Molecular characteristics | References |
|---|---|---|---|
| **DLA-79** | DLA-79 | Non-classical class I gene associated with 7·9 kb *Hin*d III fragment, Not in DLA region | Burnett & Geraghty (1995), Burnett *et al.* (1997), Graumann *et al.* (1998) |
| **DLA-88** | DLA-88 | Class I gene associated with 8·8 kb *Hin*d III fragment | Burnett *et al.* (1997), Graumann *et al.* (1998) |
| **DLA-12** | DLA-12 | Non-classical class I gene associated with 12 kb *Hin*d III fragment | Burnett *et al.* (1997), Graumann *et al.* (1998) |
| **DLA-64** | DLA-64 | Non-classical class I gene associated with 6·4 kb *Hin*d III fragment | Burnett *et al.* (1997), Graumann *et al.* (1998) |
| DLA-DRA1 | DRA | DR $\alpha$ chain | Sarmiento & Storb (1988), Wagner *et al*. (1995) |
| DLA-DRB1 | DRB1, DRBB1 | DR $\beta$ chain | Sarmiento & Storb (1988, 1990a), Wagner *et al*. (1996b,c) |
| DLA-DRB2 | DRB2, DRBB2 | DRB pseudogene | Sarmiento & Storb (1988, 1990b), Wagner *et al*. (1996b,c) |
| DLA-DQA1 | DQA1 | DQ $\alpha$ chain | Sarmiento & Storb (1988), Wagner *et al*. (1996b) |
| DLA-DQB1 | DQB1 | DQ $\beta$ chain | Sarmiento & Storb (1988), Wagner *et al*. (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 *Hin*d III fragment | Burnett *et al*. (1997) |
| C1pg-26 | Class I processed gene associated with 2·6 kb *Hin*d III fragment Not in DLA region | Burnett *et al*. (1997) |
| DLA-53 | Class I pseudogene associated with 5·3 kb *Hin*d III fragment | Burnett *et al*. (1997) |
| DQB2 | ?Pseudogene | Sarmiento & Storb (1988), Wagner *et al*. (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.

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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 ($n > 800$) | Grey wolf ($n = 50$) | Red wolf ($n = 2$) | Mexican wolf ($n = 5$) | Coyote ($n = 4$) |
| 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 | + | | | | |
| **DRB1*03101** | ucd001, nw1 | AF336108 | l | | + | | | |
| **DRB1*03201** | | AY009941 | m | + | | | | |
| **DRB1*03301** | | AF343737 | m | + | | | | |
| **DRB1*03501** | | AF336109 | l | | + | | | |
| **DRB1*03601** | | AF336110 | l | | + | | | |
| **DRB1*03701** | | AF343738 | k | | + | | | |
| **DRB1*03801** | | 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 | + | | | | |
| **DQB1*00502** | | AF336111 | h | + | | | | |
| DQB1*00701 | 0701, dqb4, dqb1001 | Y07949, AF043149, AF016907 | b, c, d | + | + | | + | |
| DQB1*008011 | 0801, dqb1 | AF043492, AF043167 | e, c | + | + | | + | |
| **DQB1*008012** | | AF336112 | h | | | | | |
| **DQB1*00802** | | AF343731 | g | + | | | | |
| DQB1*01101 | dqb1101 | AF016904 | d | + | | | | |
| **DQB1*01201** | | AY009942 | h | + | | | | |
| DQB1*01301 | dqb13 | AF043158 | c | + | | | | |
| DQB1*01302 | dqb14 | AF043159 | c | + | | | | |
| DQB1*01303 | dqb7, dqb0901 | AF043152, AF016906 | c, d | + | | | + | |
| **DQB1*01401** | | 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 | + | | | | |
| **DQB1*02401** | | AY009940 | h | | + | | | |
| **DQB1*02601** | | AF113704 | i | + | | | | |
| **DQB1*02701** | | AF113706 | i | + | | | | |
| **DQB1*02801** | | AF343730 | g | + | | | | |
| **DQB1*03001** | dqb26 | AF241781 | i | + | | | | |
| **DQB1*03101** | dqb27 | AF241529 | i | + | | | | |
| **DQB1*03201** | | AJ311104 | f | | + | | | |
| **DQB1*03301** | | AJ311105 | f | | + | | | |
| **DQB1*03401** | | AJ311106 | f | | + | | | |
| **DQB1*03501** | | 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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